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Edited by

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Paediatric Intensive Care

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Preface

In writing this book, we have aimed to provide a comprehensive, practical guide to the care of the critically ill child, both on an intensive care unit and in other clinical areas—wherever children need to be stabilized and failing organ systems need to be supported. Throughout, we have tried to stick to the underlying principles that guide us in everyday practice—the application of applied physiology; an understanding of disease processes; a reckoning of what is likely and what is possible; and the provision of care driven by compassion for our patients and their families.

The book is not just for intensivists and intensive care trainees. We hope that it will help clinicians who provide care to sick children outside the intensive care unit as well, in emergency departments, on paediatric wards and adult units that are occasionally asked to support a critically ill child. Of course, we hope that it will also prove to be a useful resource for doctors and nurses who do work in intensive care, either as specialists or on rotation. It is a book to be picked up to find the answers to specific problems and for guidance on how to manage specific issues. Where appropriate, we have tried to provide more in-depth information, highlighting areas of controversy and stimulating further reading.

The preparation of the book has been made easy by the work of the various contributors, who delivered chapters on time and to length. They are listed on page xv. We hope that in editing their work we have not taken too many liberties.

Whilst writing the handbook, we were saddened by the deaths of Heinrich Werner and David Todres, colleagues who we hoped would contribute and comment on our work. Children's intensive care, and this handbook, are less without them.

We thank Julie Edge, James Greening, and David Luyt for their comments and help with specific chapters. We would also like to thank Susan Crowhurst, Anna Winstanley, and Helen Liepman at the Oxford University Press for keeping us on track and seeing the project through from conception to publication.

Finally, we thank our families for their support and forbearance.

PWB, KM, TA.
Oxford, Leicester, and Birmingham, 2009

Additional disclaimer

We have checked all drugs and dosages suggested in this handbook, but the ultimate responsibility for their use in a particular patient rests with the prescriber.

Foreword

The specialty of paediatric critical care medicine has come of age. When it began to emerge as a specialty in its own right in the 1970s, much of what was done was learnt from adult intensive care medicine. Paediatric intensive care units (PICUs) were largely run by anaesthetists because they were the experts in airway and ventilation management and understood cardiac and respiratory physiology. In those days, diseases like Reye syndrome and *Haemophilus influenzae* acute epiglottitis were diseases that presented unique challenges to those involved in paediatric critical care, where the use of recently introduced invasive monitoring and skilful airway management could dramatically influence survival. It also saw the dawn of a new era in surgery for congenital heart disease which saw major improvements in survival and the eventual evolution of paediatric cardiac critical care as a specialty. Thirty years ago, little of the evidence for the therapies we used was ever subjected to the rigor of clinical trials, there was little formalized training, and paediatric critical care was a part-time specialty. Much has changed. Many countries have established formalized training schemes with specialty examinations, full-time career intensivists with academic positions are being appointed, and the specialty has its own journal. There are also a number of published textbooks in paediatric critical care medicine. Do we need another and, if so, how is *Paediatric Intensive Care* different? The answer is yes, we do, if it presents knowledge in a different and more accessible format. I particularly appreciate the way it deals with the important issues in an abbreviated arrangement which presents knowledge in an easily accessible layout. It has a comprehensive coverage of the important physiological principles and, as someone from the previous era where anaesthesia was the entry into PICU, I am pleased to see that prominence is given to airway management and the use of anaesthetic drugs.

We are entering a new era in the specialty where what we do will be judged by our results. The public and profession are rightly less tolerant of errors and less than optimal care. At the same time the intensive care specialist is dealing with increasing amounts of new knowledge which he or she has to absorb in a very demanding clinical specialty. Having access to a reference source such as *Paediatric Intensive Care* which gives them vital information presented in such an easy to navigate format will make that task less burdensome.

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Symbols and abbreviations

🕮	cross reference
⚠	warning
💣	controversial
↑	increased
↓	decreased
>	greater than
<	less than
~	approximately
♂	male
♀	female
🖱	website
A–a	alveolar–arterial
ABC	airway, breathing, and circulation
ABG	arterial blood gas
ACS	abdominal compartment syndrome
ACT	activated clotting time
ADH	antidiuretic hormone
ADR	adverse drug reaction
AET	atrial ectopic tachycardia
ALI	acute lung injury
ALTE	apparent life-threatening event
ANP	atrial natriuretic peptide
ANZICS	Australian and New Zealand Intensive Care Society
AP	aortopulmonary
APRV	airway pressure release ventilation
aPTT	activated partial thromboplastin time
AR	aortic regurgitation
ARB	angiotensin receptor blocker
ARDS	acquired respiratory distress syndrome
ARF	acute renal failure
ASD	atrial septal defect
ATN	acute tubular necrosis
AV	atrioventricular
AVP	arginine vasopressin
AVSD	atrioventricular septal defect
AXR	abdominal X-ray

BAL	bronchoalveolar lavage
BE	base excess
BIPAP	bilevel positive airway pressure
BIS	bispectral index
BMR	basal metabolic rate
BOOP	bronchiolitis obliterans organizing pneumonia
BP	blood pressure
BPA	British Paediatric Association
BSD	brainstem death
BT	Blalock–Taussig
Ca	calcium
CAP	community acquired pneumonia
CARS	counterinflammatory acute response syndrome
CCAM	congenital cystic adenomatoid malformation
CIPNM	critical illness polyneuropathy and myopathy
CN	cranial nerve
CNEP	continuous negative extrathoracic pressure
CNS	central nervous system
CO	carbon monoxide
CO_2	carbon dioxide
CoA	coarctation of the aorta
COHb	carboxyhaemoglobin
CPAP	continuous positive airway pressure
CPB	cardiopulmonary bypass
CPP	cerebral perfusion pressure
CRBSI	catheter-related blood stream infection
CRP	C-reactive protein
CSF	cerebral spinal fluid
c-spine	cervical spine
CSW	cerebral salt wasting
CVP	central venous pressure
CVVH	continuous veno-venous haemofiltration
CVVHDF	continuous veno-venous haemodiafiltration
CXR	chest X-ray
DF	dengue fever
DHCA	deep hypothermic circulatory arrest
DHF	dengue haemorrhagic fever
DI	diabetes insipidus
DIC	disseminated intravascular coagulation
DNAR	Do Not Attempt Resuscitation [order]

DO_2	oxygen delivery
DSS	dengue shock syndrome
ECF	extracellular fluid
ECG	electrocardiogram
Echo	echocardiogram
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
ECPR	extracorporeal cardiopulmonary resuscitation
EEG	electroencephalogram
EFW	electrolyte free water
EHS	exertional heat stroke
ET	endotracheal
$EtCO_2$	end-tidal carbon dioxide
ETS	endotracheal secretions
ETT	endotracheal tube
FAO	fatty acid oxidation
FFP	fresh frozen plasma
FFS	flexible fibrescope
FHF	fulminant hepatic failure
FiO_2	fraction of inspired oxygen
FISH	fluorescent in situ hybridization
FOB	fibreoptic bronchoscopy
FRC	functional residual capacity
GABA	gamma-amino butyric acid
GALT	gut-associated lymphoid tissue
GBS	Guillain–Barré syndrome
GFR	glomerular filtration rate
GI	gastrointestinal
GVHD	graft-versus-host disease
h	hour/s
HAART	highly active antiretroviral therapy
Hb	haemoglobin
HbCO	carboxyhaemoglobin
HBOT	hyperbaric oxygen therapy
HCAI	healthcare associated infection
HDU	high dependency unit
HE	hepatic encephalopathy
HELLP	haemolytic anaemia, elevated liver enzymes, low platelets
HFJV	high frequency jet ventilation
HFOV	high frequency oscillatory ventilation

HFV	high frequency ventilation
HIT	heparin-induced thrombocytopenia
HIV	human immunodeficiency virus
HR	heart rate
HRG	Healthcare Resource Group
HUS	haemolytic uraemic syndrome
I:E	inspiration:expiration [ratio]
IBD	inflammatory bowel disease
ICPM	intracranial pressure monitoring
ICTPICM	Intercollegiate Committee for Training in Paediatric Intensive Care Medicine
ICU	intensive care unit
IF	intestinal failure
IM	intramuscular
IMD	inherited metabolic disorders
IO	intraosseous
IOA	intraosseous access
IPPV	intermittent positive pressure ventilation
IRDS	infant respiratory distress syndrome
iTBI	inflicted traumatic brain injury
ITP	idiopathic thrombocytopenic purpura
IV	intravenous
IVC	inferior vena cava
IVIG	intravenous immunoglobulin
J	joule/s
JET	junctional ectopic tachycardia
K	potassium
kg	kilogram/s
L	litre/s
LA	left atrial
LCOS	low cardiac output state
LIP	lymphoid interstitial pneumonitis
LVEDP	left ventricular end diastolic pressure
LVOTO	left ventricular outflow tract obstruction
m	metre/s
MAC	minimum alveolar concentration
MAP	mean arterial pressure or mean airway pressure
MAPCA	major aortopulmonary collateral artery
MARS	molecular adsorbent recirculating system
mcg	microgram/s
Mg	magnesium

MH	malignant hyperthermia
min	minute/s
mL	millilitre/s
mm	millimetre/s
MR	mitral regurgitation
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MRS	magnetic resonance spectroscopy
MUF	modified ultrafiltration
MVB	manual ventilation bag
N	newton/s
NAHI	non-accidental head injury
NAI	non-accidental injury
NCSE	non-convulsive status epilepticus
NEC	necrotizing enterocolitis
NEPV	negative extrathoracic pressure ventilation
NHS	National Health Service [UK]
NI	nosocomial infection
NIBP	non-invasive blood pressure
NICE	National Institute for Health and Clinical Excellence
NIRS	near infrared spectroscopy
NIV	non-invasive ventilation
NMBA	neuromuscular blocking agent
NNRTI	non-nucleoside reverse transcriptase inhibitor
NO	nitric oxide
NRTI	nucleoside reverse transcriptase inhibitor
NSAID	non-steroidal anti-inflammatory drug
OER	oxygen extraction ratio
O_2	oxygen
OI	oxygenation index
OSA	obstructive sleep apnoea
P	pressure
Pa	pascal
PA	pulmonary artery
PAC	pulmonary artery catheter
PAOP	pulmonary artery occlusion pressure
PBF	pulmonary blood flow
PCA	patient-controlled analgesia
PCCMDS	paediatric critical care minimum dataset
PCT	primary care trust
PD	peritoneal dialysis

PDA	patent ductus arteriosus
PDEI	phosphodiesterase inhibitors
PEA	pulseless electrical activity
PEEP	positive end-expiratory pressure
PEF	peak expiratory flow
PEP	post exposure prophylaxis
PH	pulmonary hypertension
PI	protease inhibitor
PIC	paediatric intensive care
PICANet	Paediatric Intensive Care Audit Network
PICM	paediatric intensive care medicine
PICS	Paediatric Intensive Care Society
PICU	paediatric intensive care unit
PIE	pulmonary interstitial emphysema
PIP	peak inspiratory pressure or positive inspiratory pressure
PN	parenteral nutrition
PP	pulsatile perfusion
PPHN	persistent pulmonary hypertension of the newborn
PPV	positive-pressure ventilation
PR	pulmonary regurgitation
PTH	parathyroid hormone
PV	pressure–volume
PVR	pulmonary vascular resistance
PVRi	pulmonary vascular resistance index
RAD	reactive airway disease
RBC	red blood cell
RCPCH	Royal College of Paediatrics and Child Health
RCT	randomized control trial
RH	relative humidity
RMSF	Rocky Mountain spotted fever
rpm	revolutions per minute
RSE	refractory status epilepticus
RSI	rapid sequence induction
RSV	respiratory syncytial virus
RTA	road traffic accident
RVEDP	right ventricular end diastolic pressure
RVOTO	right ventricular outflow tract obstruction
s	second/s
SBE	standard base excess

SC	subcutaneous
SCI	spinal cord injury
SIADH	syndrome of inappropriate secretion of antidiuretic hormone
SID	strong ion difference
SIMV	synchronized intermittent mandatory ventilation
SIRS	systemic inflammatory response syndrome
$SjvO_2$	jugular venous oxygen saturation
SNP	sodium nitroprusside
SUDI	sudden unexpected death in infancy
SV	stroke volume
SVC	superior vena cava
SVP	saturated vapour pressure
SVR	systemic vascular resistance
SVRi	systemic vascular resistance index
SVT	supraventricular tachycardia
TAPVD	total anomalous pulmonary venous drainage
TBI	traumatic brain injury
TBM	tracheobronchomalacia or tuberculous meningitis
TCD	transcranial Doppler
TCPC	total cavopulmonary connection
TDM	therapeutic drug monitoring
TED	thromboembolus deterrent
TEE	total energy expenditure
TGA	transposition of the great arteries
THAN	transient hyperammonaemia of the newborn
TM	tracheomalacia
TNF	tumour necrosis factor
TOE	transoesophageal electrocardiogram
TPG	transpulmonary gradient
TPN	total parenteral nutrition
TR	tricuspid regurgitation
TSH	thyroid stimulating hormone
TSS	toxic shock syndrome
TTE	transthoracic echocardiogram
TTP	thrombotic thrombocytopenic purpura
URTI	upper respiratory tract infection
U&E	urea and electrolytes
US	ultrasound
V	volume

VAD	ventricular assist device
VAP	ventilator-associated pneumonia
Vd	volume of distribution
VF	ventricular fibrillation
VHF	viral haemorrhagic fever
VILI	ventilator-induced lung injury
VPS	ventriculoperitoneal shunt
VSD	ventricular septal defect
VT	ventricular tachycardia
W	watt/s
WHO	World Health Organization
WPW	Wolff–Parkinson–White

Section 1

General introduction to paediatric intensive care

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Chapter 1

An introduction to paediatric intensive care

Definitions

Paediatric intensive care (PIC) may be defined as:

- A service to support children and young people with threatened or established organ failure arising as a result of an acute illness, trauma, or a predictable phase in a planned treatment programme (i.e. post surgery), which is potentially recoverable.

A ***paediatric intensive care unit (PICU)*** is a specially built or adapted ward, appropriately equipped, where critically ill children and young people receive medical, nursing, and other clinical care from a multidisciplinary team of specifically experienced and trained staff.

The evolution of paediatric intensive care

- The speciality of PIC has evolved from the specialities of anaesthesia, adult intensive care, and neonatal intensive care, but has its origins in the poliomyelitis epidemic of 1952 in Denmark, when children (and adults) were ventilated by hand. Further development was rapid and PICUs became established around the world. Research lead to major advances in the understanding and treatment of critical illness in children and paediatric intensive care medicine (PICM) became a recognised discipline both in the medical fraternity and with the public.
- The first intensive care unit (ICU) primarily for children was established by Dr Goran Haglund, an anaesthetist, in Göteborg (Gothenburg), Sweden in 1955. Developments in PICM occurred very much in parallel in Australasia, Europe, and North America. In the early 1960s, reports of prolonged tracheal intubation in children came from Australia and in 1967 the first PICU in the United States was established in Philadelphia. Much of the experience and knowledge of managing children requiring organ support came from paediatric anaesthetists who extended their activities beyond the realm of operating theatres.
- Surgery for congenital heart disease provided a predictable group of patients. Advances in technology have stimulated major advances in PICM. The advent of gas analysis on small samples of blood (Severinghaus and Clark electrodes) revolutionized the care of the ventilated patient as did the introduction of sophisticated positive pressure ventilators. Currently PICM is established all over the world. In the developing world, where resources are few, PICM may be less technology dependent but the same principles of intensive care are increasingly applied in the management of seriously ill children.

Developments in the UK

The first designated PICU was opened at Alder Hey hospital, Liverpool in 1964 by G. Jackson Rees, an anaesthetist. This PICU developed the first PIC Retrieval Service in the UK in 1976.

The Paediatric Intensive Care Society (PICS) was set up in the UK in 1987. It aims to provide a forum for discussion, the provision of specialist advice, and the promotion of training, education, and research.

Organization of PIC services

In the UK prior to the 1990s, critically ill children could be found in a variety of locations within a hospital. The two main areas being:

- Adult ICUs; occasionally with a dedicated paediatric area
- Specialist postoperative cardiac ICUs; dealing with both neonates and infants.

PICUs evolved in an ad hoc manner often branching out from paediatric cardiac ICUs. It was clear, however, that this fragmented provision of care was unsatisfactory. In 1993, the British Paediatric Association (BPA) published a report of a multidisciplinary working party on the state of paediatric intensive. It demonstrated that:

- Care was fragmented
- Paediatric units were understaffed
- The staff were undertrained.

Standards for PIC were developed and by 1997 a Department of Health (UK) working party published 'A Framework for the Future'; describing a coordinated plan for the future of PIC services in the UK. This described a hub and spoke provision of care for critically ill children—each region should have a lead centre to provide most, if not all, the PIC for the region and support smaller hospitals within the region. The lead centre has responsibility for providing the regional retrieval service for critically ill children (Box 1.1).

Evidence for centralization of PIC services

There has been considerable effort in the UK over recent years to centralize high cost low volume services.

For PIC the advantages include:

- A greater experience and expertise of the medical and nursing staff
- Access to a range of paediatric subspecialists
- Higher standard of nursing care
- Access to paediatric support services, e.g. physiotherapy, radiology
- Parental wish to be in an experienced centre.

Disadvantages are

- The service is not necessarily local to the patient's home
- De-skilling of staff in district hospitals.

Providing evidence of a mortality benefit with centralisation of PIC is difficult as mortality rates are low at ~5%.

Box 1.1 Standards of a lead centre in the UK

- Medical staff:
  - Consultants to have approved training in PIC
  - Cover all the working week by consultant who has no other clinical responsibilities
  - Resident specialist registrar 24h/day with no other responsibilities and with advanced paediatric resuscitation skills
  - Access to tertiary paediatric subspecialty consultants
- Nursing staff:
  - Lead nurse providing focus for development of standards, staff, and education
  - Intensive and continuous supervision of each child by a registered children's nurse qualified in intensive care
- Size and activity:
  - Minimum of 8 beds
  - Minimum of 500 ventilated admissions per year
- Competencies and equipment:
  - Appropriate equipment
  - Ability to undertake advanced therapies such as positive pressure ventilation and renal replacement therapy
- Access to laboratory and radiological services 24h/day
- 24-h retrieval service
- Appropriate family services and support
- Ongoing education for staff
- Commitment to clinical governance issues and research.

Developments across the world

In Australia there are a small number of large PICUs based within the major cities which support a network of retrieval services covering large geographical areas of low population density. In the USA some centres have a number of different subspecialty PICUs within the same hospital. PICM training is undertaken as a Fellowship following a residency programme.

Despite the variety in healthcare systems in different countries, PICM has established itself as a worldwide discipline. Major units now exist in South America, India, Japan, and South Africa. Staffing and training may differ between countries, but there is a truly international ethos to PICM around the world. In 1997 the World Federation of Pediatric Intensive Critical Care Societies was established with a vision of disseminating information across international boundaries. A World Congress of Pediatric Intensive Care is held every 4 years to allow sharing of research findings and networking of PIC staff from around the world.

Staffing

Medical staff

Paediatric intensivist

A paediatric intensivist is a medical consultant from a paediatric, paediatric anaesthetic, or paediatric surgical background who has undertaken subspecialty training in PICM. They lead and integrate the multidisciplinary care of children within a PICU. PIC is an interactive and hands-on speciality which combines practical and diagnostic skills with education, teaching, and research.

Training in PICM

In 1998, the Intercollegiate Committee for Training in Paediatric Intensive Care Medicine, (ICTPICM) approved units in the UK to provide recognized training in PICM, built upon a 2-year competency-based training programme. In addition, paediatric trainees undertake a minimum of 6 months in anaesthesia and anaesthetic trainees work for 6 months in neonatology or paediatrics. Paediatric Surgeons undertake both anaesthesia and neonatology. The Royal College of Paediatrics and Child Health has recognized PICM as a subspecialty of paediatrics.

Nursing staff

The organization of the nursing workforce varies between different PICUs and will depend on the size of the PICU, the complexity or dependency of the patients, and the nursing structure within the hospital. A senior nurse has responsibility for the appointment and management of the nursing workforce and the delivery of nursing for all grades of staff.

As well as nurses to provide bedside care, other roles include:

- Team leaders/coordinators
- Retrieval nurses
- Education/training
- Research
- Nurse consultant / advanced nurse practitioner.

Professions allied to medicine

PICM is very much a multidisciplinary speciality. Dietitians, pharmacists, physiotherapists, and radiographers have key roles in PIC delivery on a daily basis. Clinical psychologists have input to selected patients and their families. Physical measurement technicians provide support with clinical monitoring and equipment maintenance. Play specialists work with patients, siblings, and families. In some countries respiratory therapists provide clinical input for ventilated patients.

Chaplains/bereavement care staff

The nature of critical illness in children and the relatively high mortality rate, in comparison to a ward, place an enormous stress on families and staff. Ministers of religion, bereavement specialists, and others (psychologists, social workers) can provide support to patients, their families and the PIC team.

Clerical and other support staff

The PICU has a range of clerical staff who are telephone receptionists, prepare the admission and discharge documentation, meet families and their visitors, undertake audit and data collection roles, order disposable equipment, and manage staff rostering.

Levels of patient dependency

The PICS (UK) has defined 4 levels:

Level 1

- High dependency, i.e. close monitoring and observation required but not mechanical ventilation
- Recommended nurse to patient ratio 1:2
- May require single organ support (excluding intubated children)
- Step down from ICU, following major surgery and/or receiving advanced analgesic techniques (epidural, intrathecal morphine).

Level 2

- Requiring continuous nursing supervision
- Recommended nurse to patient ratio 1:1
- Often intubated and ventilated or unstable non-intubated.

Level 3

- Children who need intense supervision at all times requiring complex nursing and therapeutic procedures.
- Recommended nurse to patient ratio 1.5:1
- Intubated, ventilated, requiring inotropes or multiple organ failure.

Level 4

- Unstable children requiring intense interventions or managed in a single occupancy cubicle.
- Recommended nurse to patient ratio 2:1
- ECLS (ECMO), haemofiltration.

More recently a classification of 7 Healthcare Resource Group (HRG) levels has been developed for use in the UK, informed by daily collection of a Paediatric Critical Care Minimum Dataset (PCCMDS).

Currently most units in the UK receive funding based on a block contract that pays little or no attention to the dependency levels. In the near future, HRGs are likely to inform Payment by Results, with a bed day tariff based on patient complexity.

The multidisciplinary approach

The paediatric intensivist leads and integrates the complex multidisciplinary care of the critically ill child. Good communication and teamwork is of the essence and underpins this multidisciplinary approach (Box 1.2).

Box 1.2 Open versus closed units

- Traditionally intensive care grew out of anaesthesia. Consultant anaesthetists would undertake practical procedures and make decisions relating to airway, breathing, and circulation (ABC) but relied heavily on paediatric specialists to advise on differential diagnosis, investigation, and other non-ABC management. This describes an *open* unit, where a number of teams are actively involved in making decisions relating to patient care.
- More recently, with the development of appropriately trained paediatric intensivists (whatever their background) a *closed* approach has become the norm. Day-to-day decision making is done by the PIC team and complex diagnostic or therapeutic interventions, such as haemofiltration, extra-corporeal life support, and bronchoscopy, are undertaken by the PIC team. Consultation with relevant specialties is still essential but ultimately the coordination of decision-making is done by the PIC consultant.

Admission and discharge criteria

Admission criteria

- New admissions to intensive care should always be discussed with the consultant in charge of the PICU
- Ideally there should be consultant to consultant referral
- Development of hospital outreach training may prevent some admissions and readmissions to PICU (📖 p.35)
- High dependency units (HDU) may allow some categories of patients to be looked after in HDU rather than PICU.

Also see Box 1.3.

Discharge criteria

See Box 1.4.

Box 1.3 Criteria for admission to PICU

Mandatory

- All intubated children receiving mechanical ventilation
- Acute rescue non-invasive ventilation
- Multiorgan failure
- Ongoing cardiopulmonary resuscitation or post resuscitation.

Relative

- Potential airway compromise
- Evidence of shock (impaired tissue oxygenation)
- Acute organ failure, e.g. cardiovascular, respiratory
- Significant injury
- Deteriorating level of consciousness
- Severe metabolic derangement
- Following surgery: high-risk patient (e.g. cardiac, respiratory, neuromuscular disease)
- High-risk surgery.

Box 1.4 Criteria for discharge from PICU

- Extubated with an uncompromised airway for >4h
- No mechanical ventilation
- Receiving <40% oxygen
- Minimal respiratory distress
- Cardiovascular stability (no or low-dose inotropes)
- Adequate level of consciousness to protect airway
- Organ function improving or stable.

Exceptions

- Long-term ventilated patients
- Long-term chronic dialysis.

Further reading

British Paediatric Association (1993). *The Care of Critically Ill Children*. Report of The Multidisciplinary Working Party on Paediatric Intensive Care Convened By The British Paediatric Association. British Paediatric Association, London.

Department of Health (1997). *Paediatric Intensive Care 'A Framework for the Future'*. Report from the National Coordinating group on Paediatric Intensive Care to the Chief Executive of the NHS Executive. DH, London.

Paediatric Intensive Care Society (1996). *Standards for Paediatric Intensive Care Including Standards of Practice for Transportation of the Critically Ill Child*. Saldatore, Bishop Stortford.

Appendix

Box 1.5 Formula for calculation of required numbers of PICU beds

The number of beds (n) required to satisfy demand 95% of time

$$n = x + 1.64\sqrt{x}$$

where x = [(population) x (rate of demand per annum) x (length of stay)] ÷ [365 x occupancy]

Example:

- Population 1 million
- Rate of demand is 1.2 per 1000 children per annum
- Mean length of stay is 4 days
- 80% occupancy.

$$x = \frac{1{,}000{,}000 \times 0.0012 \times 4}{365 \times 0.8} = 16.44$$

Number of beds required $= x + 1.64\sqrt{x} = 16.44 + 1.64\sqrt{16.44}$

= 23 beds to satisfy demand 95% of the time

Chapter 2

Epidemiology and outcome of paediatric intensive care

Epidemiology of PIC

Audit of PIC activity

Since 2002 PICANet (Paediatric Intensive Care Audit Network) has been the national audit database for PIC in the UK. It consists of demographic and clinical details of all PICU admissions and activity in order to:

- Identify best clinical practice
- Monitor supply and demand
- Monitor and review outcome of treatment
- Study the epidemiology of critical illness in children
- Facilitate future planning and resource allocation.
- Support collaborative research.

PICANet data allows for comparison of local PICU activity to national benchmarks. It also provides an important evidence base on outcomes, processes, and structures that permits planning for future practices, research, and interventions. Australia and New Zealand have a similar system (Australian and New Zealand Intensive Care Society—ANZPICS).

The patients in PICU

- PICU patients in the UK are generally aged 0–16 years of age
- Standard UK practice is for pre-term and term newborns requiring intensive care to be managed on neonatal ICUs except for those that have been discharged (to wards or home) or have had surgery that requires PIC expertise (complex cardiac surgery in particular)
- Occasionally older patients are also admitted to PICU with conditions that require PIC expertise (such a congenital heart defects, severe neurological disability and developmental delay)
- Each PICU has a unique profile of patients which relates to the different subspecialties that exist in its hospital, e.g. cardiac surgery, neurosurgery, neonatal surgery, oncology
- The Department of Health has recently produced guidance on which paediatric subspecialties should be co-located with each other and with PIC
- From current UK PICANet data:
  - There are >45,000 admissions per year to PICU in UK
  - The mortality rate is approximately 5%
  - Most admissions are <1 year old (47%)
  - Boys (58%) outnumber girls (42%)
  - 54% of admissions are unplanned
  - 67% of patients are invasively ventilated
  - Overall, cardiac patients are the biggest admission category followed by respiratory patients and then neurological patients
  - There is an increase in admission rates in the winter months due to respiratory illness, specifically respiratory syncytial virus (RSV) bronchiolitis.

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Measuring performance in PIC

Outcome

Although the goal of all therapy is to prevent avoidable death, mortality rate is but one measure of outcome in PIC. Comparison between units is hampered by differences in diagnosis and severity of critical illness. To account for these differences (and others), clinical scoring systems (prediction models) have been developed to help make comparisons and aid in assessment of performance.

A PICU is not delivering adequate care if it is not measuring its performance.

Measures of outcome include:

- *Effectiveness*—does the treatment work?
  - Usually expressed as standardized mortality rate or long-term mortality
  - Often hampered by case mix
- *Efficiency*—is treatment cost effective?
  Maximal efficiency is manifest by:
  - Only very sick patients in PICU
  - High bed occupancy
  - Short lengths of stay
- *Quality*—are performance objectives being attained? This may include:
  - Measurement of quality indicators, such as rates of unplanned extubation, early readmission ('rebound') to PIC, ventilator-associated pneumonia (VAP), and catheter-related blood stream infection (CRBSI)
  - Quality of life issues—physical and psychological morbidity
  - The patient's/family perspective.

Standardized mortality rate (SMR)

The effectiveness of PIC is frequently expressed as a ratio of actual and expected mortality in a population of patients adjusted for the severity of illness

SMR = actual death rate ÷ expected death rate

- SMR compares the effectiveness of care with that of a large reference population of PICU patients
- If the observed mortality is lower than expected, this suggests a superior performance in the study group compared with reference PICU population (SMR <1)
- SMR >1 implies poorer performance than expected in the group being studied
- Trends in SMR allow a unit to track their performance over time (Cusum technique).

Severity of illness and risk adjustment

Risk adjustment is used to account for case mix diversity. Adjustments can be made for:

- Diagnosis and illness severity
- Age, racial, and social background
- Pre-PICU treatment
- Background health (chronic health status).

Predictions models (scoring systems)

- Paediatric Risk of Mortality Score (PRISM) (see 📖 p.18):
  - Based on physiological variables in first 24h after admission
  - Does not include chronic health evaluation (i.e. calculation is not affected by background health)
  - Developed in USA
  - Used extensively in risk, cost, and quality assessments
  - Computer program sold as a commercial venture
- Paediatric Index of Mortality (PIM) (see 📖 p.18):
  - Less data required, hence 'user' friendly
  - Data items relate to point of first contact with patient
  - Developed in Australia and UK
  - Requires acute parameters and chronic health data
  - Non-commercial and used in national database PICANet.

Mortality prediction

- Mathematical models are developed from logistic regression analysis
- Predictive variables (e.g. systolic blood pressure (BP), heart rate, PaO_2, base excess etc.) are weighted to give a mortality risk
- Probability of death is calculated from mortality risk
- The mortality prediction model is validated prospectively ('how well it fits') by:
  - Comparing predicted mortality risk in groups (strata) of ICU patients to the actual mortality rate
  - Testing for its discriminatory power (sensitivity and specificity are compared to give receiver operating characteristic)
- Allows for calculation of expected mortality in a comparable population (PICU patients) and thus calculation of SMR
- Mortality prediction must ***never*** be applied prospectively to individual patients to inform clinical decision making
- All models require 'recalibration' on a regular basis as performance tends to improve over time such that the number of actual deaths falls consistently below the number of predicted deaths, SMR <1.

Further reading

ANZPICS: 🖱 http://www.anzics.com.au/section.asp?Section=paediatric

PICANet (2008). National report of the paediatric intensive care network Jan 2005–Dec 2008. Available at: 🖱 http://www.picanet.org.uk

Pollack MM, Patel KM, Ruttimann UE (1996). PRISM III: an updated Pediatric Risk of Mortality score. *Crit Care Med* **24:**743–52.

Slater A, Shann F, Pearson G (2003). PIM2: a revised version of the paediatric index of mortality. *Intensive Care Med.* **29:**278–85.

Appendix

PIM 2

Chronic health variables

- Cardiac arrest before ICU admission
- Cardiomyopathy or myocarditis
- Severe combined immune deficiency
- Hypoplastic left heart syndrome
- Leukaemia/lymphoma
- Liver failure
- Admitted following cardiac bypass
- Spontaneous cerebral haemorrhage
- Neurodegenerative disorder
- Severe developmental delay
- Human immunodeficiency virus (HIV).

Acute variables recorded

- Systolic BP
- PaO_2
- FiO_2
- Base excess
- Pupil reaction
- Intubation.

Score depends on whether admission was elective or emergency.

PRISM III

Acute variables recorded

- Systolic BP
- Temperature
- Mental status
- Heart rate
- Pupil reflexes
- pH
- Total CO_2
- PaO_2, $PaCO_2$
- Glucose
- Potassium
- Creatinine
- Urea nitrogen
- White cell count
- Platelet count
- Prothrombin or partial thromboplastin time.

There are 4 categories of age included:

- Neonate (<1 month)
- Infants (1 month to 1 year)
- Children (12 months to 12 years)
- Adolescent (>12 years).

Paediatric resuscitation and critical care outreach

Introduction

Paediatric cardiac arrest:
- Is rarely a primary event
- Usually occurs after gradual deterioration in the child's condition
- Is usually associated with a poor outcome.

Early recognition and treatment of the critically ill child will reduce the incidence of respiratory and cardiac arrest.

The critically ill child may be identified by parents, nursing or medical staff, or early warning systems (📖 p.36)

Current resuscitation treatment algorithms are:
- Based on the 2005 consensus guidelines
- Adopted by the European and UK Resuscitation Councils
- Based on the best evidence available
- Taught on several courses run on behalf of the Resuscitation Council (UK) and the Advanced Life Support Group
- Are fully revised every few years as new information becomes available.

Resuscitation skills
- Should be taught to all healthcare professionals commensurate with their role and experience
- Are best learned in workshops or scenarios
- Should be regularly updated
- Should be practised by the team on a regular basis
- Should include a team debrief to improve performance.

Scope of resuscitation
Paediatric resuscitation is a discipline that includes a number of elements:
- Training of lay rescuers
- Provision of a skilled ambulance service
- Communication systems between the ambulance service and hospitals
- Training of healthcare professionals and the resuscitation team
- Resuscitation team deployment
- Provision of equipment
- Early recognition of the critically ill child
- Management of a child in respiratory or cardiac arrest
- Post-resuscitation care including transport to an area for definitive care
- Audit of processes and outcomes
- Identification of patients in whom resuscitation would not be beneficial.

Most hospitals have a Resuscitation Services Department which co-ordinates these activities.

Basic life support

The aim of providing basic life support is to maintain the patient's oxygenation and circulation until the circulation can be restored (Fig. 3.1).

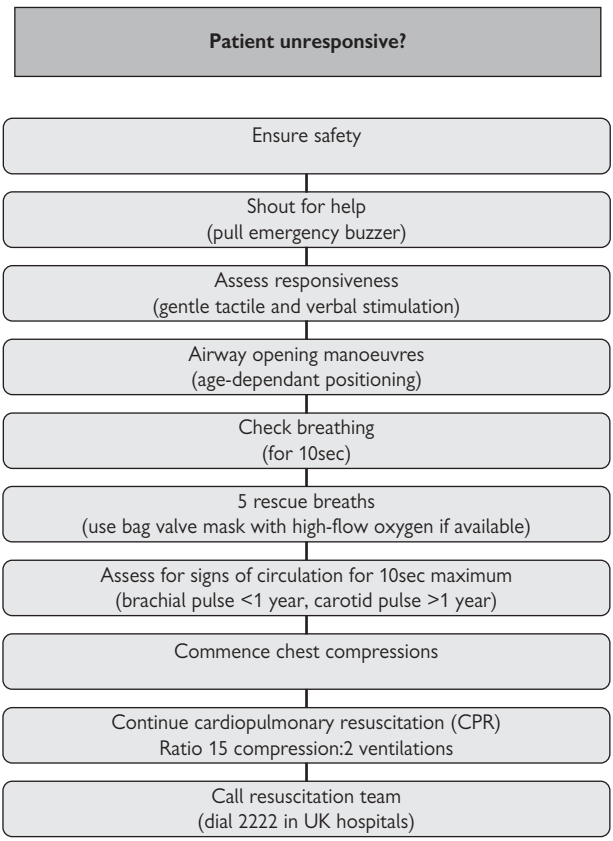


Fig. 3.1 Basic life support algorithm.

Airway opening manoeuvres

- Under 1 year—head in neutral position with chin lift or jaw thrust
- Over 1 year—head in slight extension with chin lift or jaw thrust (sniffing position).

Breathing

- Bag-valve-mask ventilation with high-flow oxygen—'mouth to mouth' may be used if no equipment is available
- Rescue breaths are given with an inspiratory time of ~1s
- Lowest pressure which will inflate the lungs so the chest rises
- 5 breaths are given over about 10s.

Circulation

- Checked by taking a central pulse and observing for signs of circulation such as spontaneous movement
- If no pulse is present—start chest compressions
- If the pulse rate is <60/min and the child is unresponsive—start chest compressions
- Lay rescuers are no longer taught to take a pulse but to look for signs of life such as coughing, breathing, or movement.

Chest compressions

Hand position

- Middle of the chest on the sternum
- 1 finger breadth above the xiphisternum for baby or small child
- 2 finger breadths above for large child.

Chest compressions

- Rate of compressions is 100 compressions per minute
- Depth should be 1/3 of the original anteroposterior diameter of the chest
- Inadequate compressions will fail to generate sufficient cardiac output
- Optimal cardiac compressions generate ~30% of normal cardiac output
- Relaxation phase between compressions should allow the chest to return to normal diameter
- Time of compression and relaxation should be equal to allow both ejection and filling of the heart
- The rescuer providing compressions should be swapped every 2min.

Quality cardiopulmonary resuscitation (Q-CPR)

- Cardiopulmonary resuscitation must be done well if patient outcomes are to be optimized
- Devices are available which monitor and give auditory feedback on the rate and effectiveness of both ventilation and cardiac compressions
- These devices are only designed for adults.

Some patients may have return of spontaneous circulation after a short period of basic life support. These patients should be transferred to an area with appropriate monitoring and facilities for post-resuscitation care.

Patients who do not have a rapid return of spontaneous circulation move seamlessly to advanced life support with the arrival of the resuscitation team.

Advanced life support

- Advanced life support is built on the foundation of ongoing effective basic life support
- Advanced life support targets the cause of the collapse and provides specific therapy to aid the return of spontaneous circulation (Fig. 3.2).

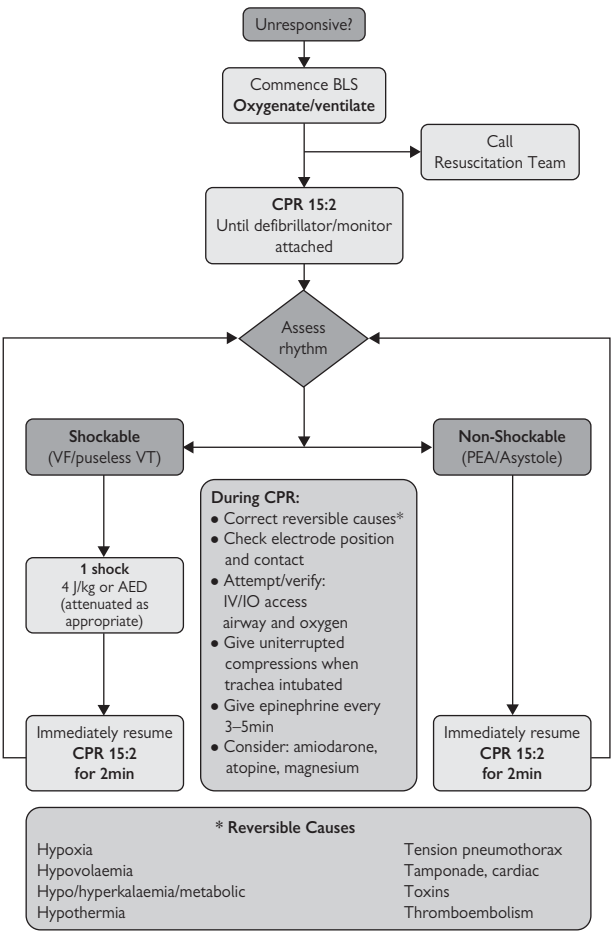


Fig. 3.2 Advanced life support algorithm. Reproduced with permission from the Resuscitation Council (UK) 2005.

Rhythm recognition

- Rhythm recognition is a vital task in advanced life support
- The rhythm may be shockable or non-shockable
- Identification requires monitoring of the electrocardiogram (ECG)
- This is achieved using hands-free patches or 3-lead ECG.
  ⚠ Defibrillator paddles and gel pads can be used as a quick look but there is an associated risk of spurious asystole especially after repeated defibrillation attempts
- Cardiac arrest in children is rarely due to a rhythm disturbance
- Pulseless electrical activity and asystole are more common.

Non-shockable rhythms

- Non-shockable rhythms are asystole and pulseless electrical activity.
  - ***Asystole*** (Fig. 3.3a) is recognized on ECG as a rhythm without any ventricular activity, although P waves may be present

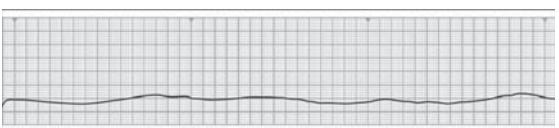


Fig. 3.3a Asystole

  - ***Pulseless electrical activity (PEA)*** (Fig. 3.3b) exists when the ECG shows electrical activity which should produce a pulse but no pulse is present

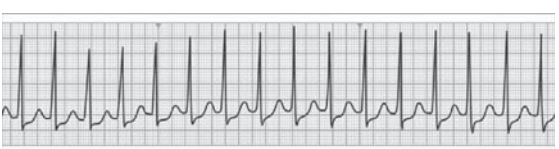


Fig. 3.3b Pulseless electrical activity.

- Epinephrine is administered via the intravenous (IV) or intraosseous (IO) route (epinephrine 10mcg/kg = 0.1mL/kg of 1 in 10,000 every 3–5min)
  - There is no human data to show epinephrine improves the long-term outcome of cardiac arrest
- When the patient is intubated, compressions and ventilation can be carried out asynchronously without interrupting compressions
- The rate of ventilation for a child should be 12–20/min
- Care should be taken to avoid hyperventilation of the intubated child which may easily occur during CPR. This could have detrimental effects, specifically vasoconstriction in the cerebral circulation.

In the setting of cardiac arrest, venous CO_2 values will be much higher than arterial values—do not titrate ventilation based on a central venous or peripheral venous pCO_2. Obtain an arterial value.

Common reversible causes of cardiac arrest are contained within the mnemonic: 4Hs and 4Ts:

Hypoxia
- Reversed by ventilation with high-flow oxygen.

Hypovolaemia
- Rapid infusion of IV fluid to restore intravascular volume.

Hypothermia (📖 p.527)
- Can be missed by a standard thermometer—diagnose using a low-reading thermometer.

Hyperkalaemia and other metabolic disorders
- Suspect in known renal patients
- Diagnosed by biochemical investigation
- Point of care testing for blood gas and electrolytes allows detection of metabolic disorders which if found should be corrected.

Tension pneumothorax
- Detected by clinical examination
- Reduction or absence of breath sounds and hyper-resonance on affected side
- Tracheal deviation away from the pneumothorax is a late sign
- Decompress with large cannula—2nd intercostal space, mid clavicular line
- Followed by insertion of an intercostal chest drain (📖 p.422).

Tamponade (cardiac)
- Usually occurs in the setting of thoracic trauma or post cardiac surgery
- Treatment is pericardiocentis or thoracotomy and evacuation of clot.

Toxins
- May be suggested from the history
- Arrhythmias caused by tricyclic antidepressant overdose may respond to alkalinization of the blood
- Check drug charts of inpatients—which drugs were administered prior to collapse?

Thromboembolic disease
- Rare in children
- A suggestive history in adults is treated with thrombolytic drugs
- CPR must be continued for 1h post thrombolysis as it often takes this long for clot lysis to occur.

⚠ Do not assume only one reversible cause—these can coexist.

Shockable rhythms

Ventricular fibrillation (VF) (Fig. 3.4a) and ***pulseless ventricular tachycardia (VT)*** (Fig. 3.4b).

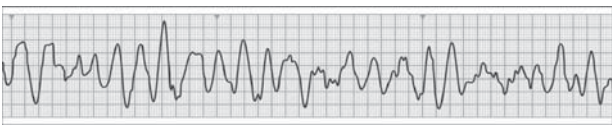


Fig. 3.4a Ventricular fibrillation.

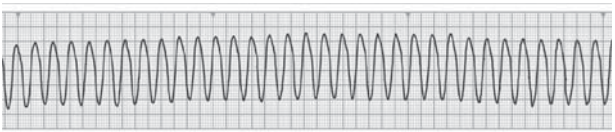


Fig. 3.4b Pulseless ventricular tachycardia.

Both of these pulseless shockable rhythms are treated by external defibrillation at 4J/kg.

- Energy chosen is rounded up to the next energy level available on the defibrillator if the exact value is not available
- A single shock is administered followed by 2min of CPR
- Sometimes asystole and fine VF can be difficult to differentiate
- Fine VF is not likely to convert to sinus rhythm with cardioversion
- Cardiac compressions may turn fine VF into coarse VF which is more likely to convert on subsequent defibrillation.

Defibrillation

Biphasic versus monophasic defibrillators

Monophasic defibrillators produce a waveform resembling a heavily damped sinusoidal impulse with a mainly uniphasic characteristic. Biphasic defibrillation alternates the phases of the impulse.

- In adults modern biphasic defibrillators have the advantage of a lower energy required for successful defibrillation—this also results in less burn and myocardial injury
- In children there is no current evidence to support reducing defibrillation energies with biphasic defibrillators. Standard energy (4J/kg) used for defibrillation.

Safe defibrillation

- Safety is the responsibility of the person who is defibrillating
- Must be balanced with minimizing interruptions in chest compressions
- High-flow oxygen should be removed to at least 1m away from the patient (unless it is attached to an endotracheal tube, ETT)
- Defibrillation pads/paddles should be at least 12–15cm away from pacemakers

- Jewellery should be avoided (it may not be possible to remove it)
- The chest should be dry and free from adhesive patches
- A clear audible warning should be given when charging the defibrillator
- A visual check should be done to ensure that no one is in direct or indirect contact with the patient before defibrillation occurs.

Automated external defibrillators

- Over the age of 8 years an automated external defibrillator may be used with standard adult hands-free pads
- Between the ages of 1–8 years, attenuated shock energy should be used by using a paediatric programme or attenuated paediatric pads
- There is no evidence for or against the use of automated external defibrillators under the age of 1 year.

Drugs used during cardiac arrest

Epinephrine

- Standard dose 10mcg/kg (0.1mL/kg 1 in 10,000 or 0.01 mL/kg 1 in 1000)
- Give via the IV or IO route, followed by an IV saline flush
- High-dose epinephrine (100mcg/kg) has been associated with poor neurological outcome and is no longer recommended except in circumstances such as beta-blocker overdose or severe anaphylaxis
- In the absence of vascular access, rarely epinephrine has to be administered via the intratracheal route—the dose is 10 times larger if the intratracheal route has to be used
- Epinephrine acts as an alpha-1-agonist causing vasoconstriction and therefore increasing the coronary and cerebral perfusion pressure
- Epinephrine is administered every 3–5min during resuscitation in both shockable and non-shockable rhythms:
  - In shockable rhythms, epinephrine is administered just before the 3rd shock
  - In non-shockable rhythms, epinephrine is administered as soon as IO or IV access is established.

Amiodarone

- Antiarrhythmic which acts as a membrane stabilizer
- Increases the duration of the action potential and the absolute and relative refractory periods
- Reduces the likelihood of circus currents which cause arrhythmias
- Dose during VF/VT arrest is 5mg/kg body weight
- Is flushed with 5% dextrose
- Given immediately before the 4th shock in the VF algorithm
- Can cause profound hypotension if given quickly
- In the arrest situation the priority is to terminate VF
- In the arrest situation may be given via a peripheral line
- In the non-arrest situation is given by infusion via a central line, as can cause significant extravasation injury.

Membership of the resuscitation team

- Varies from hospital to hospital
- The following roles should be considered an absolute minimum:
  - Team leader
  - Airway management clinician
  - Dedicated trained assistant for airway management clinician
  - Chest compressions
  - Vascular access and drug administration
  - Scribe to document events, actions, and times
  - Runner
- The team works best with a leader who directs the team but does not get involved in the completion of tasks
- In most hospitals the team leader will be a middle grade or senior paediatrician or senior nurse
- There must be an experienced clinician to manage the airway; this role is usually filled by the on-call anaesthetist or intensivist.

Team training

- Resuscitation courses are very useful in acquiring and practicing the skills required for resuscitation of a child
- The resuscitation team should train as a team in practice scenarios.
  - Many hospitals now carry out this type of training and there is evidence to show it enhances team performance.

Resuscitation equipment

- The Resuscitation Council (UK) list of suggested equipment for paediatric resuscitation is a minimum standard and items may be added according to local need
- A full range of sizes of resuscitation equipment should be immediately available in all paediatric clinical areas
- The Broselow system gives a good way of storing equipment by size
- It tends to be used in clinical areas where paediatric resuscitation is an infrequent event
- Equipment should be checked on a daily basis and omissions corrected—a clear audit trail should exist for resuscitation equipment.

Oxygen

- High-flow oxygen (15L/min) is used during resuscitation
- Care must be taken to avoid depletion of oxygen when cylinders are used.

Research is investigating whether resuscitation using room air (21% oxygen) produces better survival and neurological outcomes than conventional resuscitation using 100% oxygen.

Bag valve mask

- A self-inflating bag is the first choice for resuscitation
- The advantage over an anaesthetic breathing circuit is that it may still be used without a supply of oxygen allowing ventilation with room air
- The bag is used for positive pressure ventilation by squeezing an appropriate tidal volume through a mask or endotracheal tube into the lungs
- High-flow oxygen and a reservoir bag allow high oxygen concentrations to be delivered.
  ⚠ The bag should not be used for spontaneous respiration as the inspiratory valve and rigid nature of the bag provides a high inspiratory resistance
- If spontaneous respiration or continuous positive airway pressure is required, an anaesthetic breathing circuit should be used.

Endotracheal tubes

- Oral intubation is used in an arrest situation
- Induction of anaesthesia with drugs is not necessary in the cardiac arrest situation as the patient is already unconscious
- Children in respiratory arrest may occasionally require drugs for induction of anaesthesia to abolish the cough reflex
  - This should only be done by an individual trained in their use
- There are a number of formulae for the size of the endotracheal tube:
  - Internal diameter of tube (mm) = [age (in years)/4) +4
  - Use at least one size smaller if using a cuffed tube.

Intraosseous needles (📖 p.65)

- In an emergency IV access is often difficult to obtain in a small child.
- Rapid vascular access may be gained by the insertion of an IO needle
- These come in a variety of sizes. Many hospitals only stock the 18G size
- IO needles may be either smooth ended or have a screw thread and may have end- or side-holes
- Insertion of an IO needle is taught on resuscitation courses
- Care should be taken to identify the surface of bone and a careful steady pressure with screwing action should be used until a loss of resistance is felt
- The most common insertion area is in the upper tibia below the growth plate—in older patients other sites include humerus, iliac crest
- There are now devices available which use a type of rivet gun for automatic insertion to the appropriate depth
- Drugs, fluids and blood products can be administered via an IO needle.
- The most common complication is extravasation, which should be looked for
- Rarer complications include damage to the growth plate and infection.

Post-resuscitation care

- Aims to optimize oxygen delivery and to prevent secondary damage
- Respiratory and cardiovascular support are given as necessary
- Consider the possibility of post-hypoxic seizures:
  - EEG (electroencephalography) may be helpful if unable to assess clinically
  - SSEPS (somatosensory evoked potentials) may provide prognostic information
- Hypothermia is frequently used in the adult population to optimize neurological outcome after cardiac arrest
- No definitive study on the effect of hypothermia in children after cardiac arrest
- Some clinicians extrapolate from the adult data and use hypothermia selectively in children
  ⚠ The causes of cardiac arrest are very different in children compared to adults—it is unwise to extrapolate from adult studies
- Maintain normothermia to prevent secondary injury associated with hyperthermia.

Audit

- Unexpected cardiac arrest should be viewed as a serious untoward incident in the paediatric population
- Each arrest should be investigated for the cause and a thorough evaluation of avoidable factors carried out
- The aim should be to avoid all cardiac arrests through earlier recognition of the sick child, whether in the community or in hospital
- The process and outcome of resuscitation from cardiovascular collapse should be audited and reviewed by the Resuscitation Committee
- The standard format for data collection has been agreed internationally and is termed the Utstein style reporting template.

Stopping resuscitation

- Resuscitation attempts are stopped when there is a return of spontaneous circulation or on discovery of a valid Do Not Attempt Resuscitation (DNAR) order
- When resuscitation attempts are unsuccessful, the decision to stop resuscitation attempts should be taken by the team leader in collaboration with the resuscitation team
- The decision to stop should be made on the basis of history, response to treatment, and length of time resuscitation efforts have continued
- When resuscitation attempts are stopped careful evaluation of the patient must take place looking for signs of life
- A weak pulse or respiratory effort may have been overlooked during the resuscitation attempt
- If there are signs of life, ongoing resuscitation care may be re-instituted.

Based on large outcome studies of children admitted to hospital after out-of hospital cardiac arrest it is advisable to stop resuscitation efforts if there has been no return of spontaneous circulation 20min after arrival in hospital. The situations in which longer resuscitation may be justified include cardiac arrest associated with severe hypothermia and a child with arrhythmias associated with a tricyclic overdose.

Do Not Attempt Resuscitation order

- It may be inappropriate to attempt resuscitation for some patients
- Each set of circumstances is unique and should be fully discussed with the family. Where it is decided that resuscitation in the event of cardiac or respiratory arrest is not appropriate a DNAR order is documented
- This order should be subject to regular review.

Limitation of Treatment Agreement

- For some patients with a life-limiting illness a DNAR order does not cover all the possible options
- The palliative care plan may include treatment such as suction, oxygen, and bag-valve-mask ventilation while excluding intubation and cardiac compressions
- In the UK the PICS has developed the Limitation of Treatment Agreement. This formalizes the plans made with families including a clear written agreement of the palliative care package and limitations.

Witnessed resuscitation

- Many parents want to be with their child during resuscitation attempts
- They may wish to support the child and ensure that 'everything is being done'
- Parents need to be supported by a dedicated team member during and after the resuscitation attempt
- If the resuscitation attempt is not successful the decision to stop lies with the team leader rather than the parents
- A parent should not be made feel guilty if their decision is not to be present but should be similarly supported by a dedicated member of staff.

Extracorporeal resuscitation (ECPR)

- Resuscitation using extracorporeal membrane oxygenation (ECMO, see 📖 p.211) for cardiorespiratory support
- A small number of patients worldwide have been placed on ECMO during resuscitation for cardiac arrest.
- The first use of ECMO was during cardiac arrest in hypothermic patients where ECMO was used for rewarming
- The use of ECMO has been extended to other cardiac arrest patients where reversible pathology has caused the arrest and there is a chance of neurological recovery. This strategy, termed ECPR, requires rapid deployment for success and is not offered in many PICUs
- Mortality and neurological deficit remain high despite ECPR.

Anaphylaxis

Pathophysiology

- Anaphylaxis is an acute systemic Type I hypersensitivity allergic reaction to ingested, injected, or inhaled allergen
- This triggers a release from mast cells of large quantities of immunological mediators (histamines, prostaglandins, leukotrienes) resulting in:
  - Systemic vasodilation
  - Oedema of bronchial mucosa (resulting in bronchoconstriction and difficulty breathing).

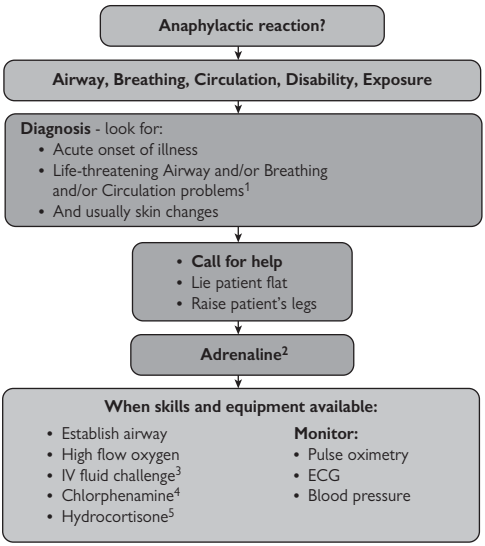
Anaphylactic shock can lead to death in a matter of minutes if untreated.

Immediate management of anaphylaxis (Fig. 3.5)

- Epinephrine is the most important agent:
  - Alpha-receptor effects counteract vasodilation whilst beta-receptor effects increase cardiac output and reverse bronchoconstriction
- It is recommended to be given via the intramuscular (IM) route
- It may be given IV rather than IM in the setting of cardiac arrest related to anaphylaxis, or in the rapidly deteriorating patient:
  - Titrate the dose to effect
- Give volume to counteract vasodilatation
- Steroids, salbutamol, and antihistamines are also used as secondary agents in severe cases (Fig. 3.5).

Indications for intubation

- Airway obstruction
- Cardiorespiratory collapse.



[1] Life-threatening problems:

Airway:	swelling, hoarseness, stridor
Breathing:	rapid breathing, wheeze, fatigue, cyanosis, SpO_2 < 92%, confusion
Circulation:	pale, clammy, low blood pressure, faintness, drowsy/coma

[2] Adrenaline *(give IM unless experienced with IV adrenaline)*

IM doses of 1:1000 adrenaline (repeat after 5 min if no better)

• Adult	500 micrograms IM (0.5mL)
• Child more than 12 years:	500 micrograms IM (0.5mL)
• Child 6 - 12 years:	300 micrograms IM (0.3mL)
• Child less than 6 years:	150 micrograms IM (0.15mL)

Adrenaline IV to be given **only by experienced specialists**

Titrate: Adults 50 micrograms; Children 1 microgram/kg

[3] IV fluid challenge:

Adult - 500 – 1000mL

Child - crystalloid 20 mL/kg

Stop IV colloid if this might be the cause of anaphylaxis

	[4] Chlorphenamine (IM or slow IV)	[5] Hydrocortisone (IM or slow IV)
Adult or child more than 12 years	10 mg	200 mg
Child 6 - 12 years	5 mg	100 mg
Child 6 months to 6 years	2.5 mg	50 mg
Child less than 6 months	250 micrograms/kg	25 mg

Fig. 3.5 Immediate management of anaphylaxis. Reproduced from Soar J *et al.* (2008). Emergency treatment of anaphylactic reactions—guidelines for healthcare providers, *Resuscitation* **77**: 157–69, with permission of Elsevier.

Managing the intubation

- If the child has airway obstruction with stridor, call for urgent anaesthetic and ENT support
- Give epinephrine 10 mcg/kg IM and epinephrine 5mL 1:1000 nebulized
- If intubation is required the child will require gas induction by an experienced anaesthetist.

Ventilation

With bronchospasm (📖 p.153):

- Use pressure control ventilation(keep PIP <40mmHg) or pressure-limited volume control ventilation
- Use a slow rate, long expiratory time, and tolerate hypercapnia
- Watch for air trapping (intrinsic or auto-PEEP) and progressive hyperinflation leading to loss of venous return and collapse in cardiac output
- Disconnection and manual decompression of the chest may be necessary (preoxygenate with 100% oxygen beforehand).

Other

- Consider sodium bicarbonate for refractory acidosis after 20min (0.5–1mmol/kg/dose IV)
- Epinephrine infusion for bronchospasm and shock
- Consider norepinephrine for resistant vasodilatation.

Investigation

- Blood samples (1mL serum) should be taken for mast cell tryptase
  - As soon as possible after the reaction (within 1h)
  - 3h post reaction
  - 24h post reaction
- Ensure labelling with the time of the reaction and time of sample
- A clinician must be identified for follow-up investigations and patient/parent information
- Refer to the local paediatric allergy service for follow-up.

Critical care outreach

Paediatric critical care outreach is a system of care that aims to identify clinically deteriorating hospitalized children, in a timely manner, so that experienced clinicians can respond to stabilize the child and if needed transfer them to an area of closer observation or intensive care.

- 5–15% of all children admitted to hospital require an enhanced level of care and up to 3% need immediate medical assistance for treatment of actual or impending cardiac arrest
- Failure to identify developing critical illness leads to cardiac arrest with associated morbidity and mortality
- Warning signs precede unexpected death, unplanned intensive care admission, and cardiac arrest in 50–90% of episodes
- Children suffer cardiac arrest usually due to poor oxygenation or infection and seldom (10%) have a cardiac rhythm that would respond to defibrillation
- On paediatric wards more than half of the patients suffering cardiac arrest are younger than 1 year of age.
- The reported survival after in-hospital cardiac arrest is ~25% in children, 65% of who show good short-term neurological outcome. There are, however, concerns of significant neuropsychological deficits that can only be measured in the longer term
- The implementation of critical care outreach has been shown to lead to improved survival, a decrease in unexpected cardiac arrest, and an increase in unplanned intensive care admissions
- In 2005 21% of UK hospitals caring for children had some form of paediatric early warning score in place and 9% had an emergency response team
- There is no evidence to recommend one system above another and no scores have, as yet, been fully validated.

Identification of sick children is only a small part of the bigger system. Improved outcomes need a comprehensive, multilevel systems approach (Box 3.1).

Box 3.1 Outreach system requirements

- Standards for appropriate documentation of observations and monitoring of hospitalized children
- Improved documentation of the respiratory rate, one of the most important predictors
- Early warning scores embedded into observation charts
- Integration with electronic monitoring systems to improve use and accuracy
- Education on recognition of developing critical illness
- Communication of the locally agreed response to early identification
- An experienced emergency response or stabilization team that can respond to stabilize, treat, or transfer a child developing critical illness
- Sufficient capacity in high dependency and intensive care areas to monitor and treat patients when required
- A governance and review system that will monitor the effectiveness of the system and identify all in-hospital cardiac arrest calls as potentially avoidable life-threatening events.

Paediatric early warning scores

- Paediatric early warning scores consist of a combination of:
  - Physiological parameters
  - Diagnostic categories
  - Therapeutic interventions
- They should identify clinical deterioration early to encourage timely intervention
- A limited number of published scores have been adapted and designed for children
- Developmental physiology requires that normal ranges for respiratory rate, heart rate, and BP are defined for each age range
- There is poor agreement on cut-off ranges for normal and abnormal
- No score has been fully validated and there is no information about reproducibility or comparability between the scores
- There are two main forms of early identification—trigger scores and early warning scores:
  - *Trigger scores* contain a list of physiological, therapeutic or diagnostic thresholds. When one (single parameter) or more (multiple parameter) items are transgressed a call for assistance is initiated
  - *Early warning scores* are a composite collection of physiological and therapeutic parameters where increasing deviation from normal accrues an increasing aggregate score. A call for assistance is made once a particular threshold score has been reached and in some circumstances the response can be calibrated to the magnitude of the aggregate score
- Trigger scores are simple and easy to use but aggregate scores allow the patient's condition to be tracked graphically over time.

Emergency response teams

- The response to early identification differs considerably between systems and is usually adapted to local needs
- This response involves a call for clinical review of the patient and varies from calling:
  - The patient's own team (junior doctor or consultant)
  - Specialized nurses (nurse led outreach)
  - A specialized multidisciplinary team (medical emergency team or critical care outreach team)
  - Intensive care doctors
- The optimal model for paediatrics is unknown.

Monitoring the effectiveness of early identification and stabilization systems

The UK National Health Service (NHS) Clinical Negligence Scheme for Trusts (CNST) has set the standard that all NHS hospitals must have an early warning system in place. This is the first implicit requirement for the development of paediatric early identification and stabilization systems.

The National Institute for Health and Clinical Excellence (NICE) has issued 'Clinical Guideline 50: Acutely ill patients in hospital; recognition of and response to acute illness in adults in hospital'. This guidance for the implementation, audit, and monitoring of critical care outreach in adults follows a systems-based approach.

The recommendation is to collect primary data to ascertain whether the core quality improvements are being achieved (unexpected cardiac arrests, non-do-not-resuscitate deaths and unplanned intensive care admissions per 1000 discharges) and secondary data (survival, length of stay, cost, staff satisfaction, and turnover) to enable more detailed evaluation of the system and to assess impact between institutions.

Key points

- Systems for early recognition of the critically ill child should exist in all hospitals to avoid respiratory and cardiac arrests
- All frontline healthcare personnel should be regularly trained in resuscitation and resuscitation teams should have team training to optimize team performance.

Further reading

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Chapter 4

Clinical assessment

Introduction

Assessment of the new admission to a PICU is an important moment. Firstly, such patients are, almost by definition, suffering from complex and multisystem diseases. The history and examination therefore need to be both broad and thorough, and this can be difficult in sick patients where there are urgent clinical considerations. However, information from this early assessment may be crucial to the child's care, and much more difficult to obtain later. Also, patients will often require input from more than one 'specialist team' whilst in PICU. Those teams may not maintain the holistic overview of the whole problem (including social and ethical dimensions) that is needed, and the intensive care team must be careful to ensure this is maintained.

The new patient

Immediate responsibilities

ABCs

The first priority when faced with any new patient is to evaluate their vital functions. Doctors and nurses working in paediatric intensive care often take responsibility for patients who have been previously looked after by staff inexperienced in intensive care. These patients need to be reviewed critically, and staff should remain aware that acute deterioration around the time of handover can also occur. This basic assessment should not take more than 2–3min and *should precede history taking or note review.*

- This approach is comfortable for trainees from an anaesthesia background but more difficult for paediatric trainees as it is very different to the approach practised in non-intensive care settings.
- Key aspects of this initial evaluation are shown in Table 4.1.

History and initial assessment

Once it has been ascertained that the patient is, at least in the short term, adequately stable, then time should be available to take a more detailed history. An initial history is often from a referring team, but a detailed history from the primary carers is needed at some point.

Key aspects of the history

- Chronology of current illness
- Previous history:
  - Previous admissions
  - Previous investigations and results (including those from other hospitals)
- Social/family history:
  - Family tree
  - Family history of significant illnesses
  - Social history (including social service involvement with family)
- Current drug history
- Allergies.

When taking a history, there are some important considerations that should be applied:

- Question the diagnosis. Be sure that you are comfortable that other possible diagnoses have been considered and evaluated properly
- Is there any possibility of non-accidental injury (NAI)?:
  - Unexplained coma in an infant
  - Unusual pattern or number of injuries
  - Incompatibility between history and examination
  - Delayed presentation of significant illness
  - Evidence of neglect.

Table 4.1 Initial evaluation

System	Issue	Check for
Airway	Patency	Noise (stridor/stertor), effort (sternal tug), ET tube position
	Protection	Cough, gag, drooling, conscious level
Breathing	Effort	Respiratory rate, recession, use of accessory muscles
	Effectiveness	Air entry, pulse oximetry O_2 saturation, chest expansion, tidal volumes (if ventilated)
	Local signs	Crackles, dullness, reduced air entry, bronchial breathing
Circulation	Perfusion	Temperature, colour, capillary refill, heart rate, central and peripheral pulse volume, BP, urine output, major bleeding
	Heart	Rate, rhythm, size, murmurs
Disability	Brain	Conscious level, pupillary reaction
	Peripherally	Flaccidity (?cord injury), focal signs/ asymmetry

Clinical examination should follow. A full examination should be carefully documented, directed towards the problems causing admission, but recognizing that all aspects of the child should be reviewed. Most units follow a problem-based approach, and so the examination should be focused around the identified problems, and broadly address each of the major body systems. A systems list is shown in Box 4.1. This is in no way exhaustive, but will ensure that all areas are considered.

Box 4.1 A systems list for clinical examination

- Respiratory
- Cardiovascular
- Sepsis
- Fluids and renal
- Gastrointestinal (GI) and nutrition
- Neurology
- Numbers
- Drugs
- Social.

This systems approach then forms the basis of subsequent management planning and ensures a comprehensive plan is in place.

Examination should follow the conventional approach, but there are additional considerations:

- Specific diseases. Depending on the reason for admission, patients may warrant specific examination techniques in different circumstances. These are generally addressed in the relevant chapter of this book
- Trauma. Patients admitted following severe trauma will not always have completed their secondary survey and may be admitted before they have been log rolled and fully examined. Secondary survey will need to be completed in PICU
- Neurosurgical admissions. Documentation of focal neurological abnormalities present on admission, such as weakness or asymmetric reflexes, is important. Without this, subsequent abnormal neurology can be difficult to put into context and this may become difficult to later unravel
- Suspected NAI. In this situation a full examination needs to be carefully charted including the site of any drips or drains. If such an examination is not recorded, then the discovery of subsequent injuries can be difficult to explain and it may make their interpretation more complicated.

Initial management

By this stage, the major clinical issues should be clear, and an initial management plan should be put in place. This needs to address the cardio-respiratory plan, as well as any unstable organ function (e.g. renal or neurological problems) that needs immediate attention.

Key issues include a plan for ventilation (ventilator settings, FiO_2 etc.) and for maintenance of circulation (inotrope requirement, fluid bolus, etc.). Baseline fluids should be decided at this time. The detail of this early plan depends on a number of factors. In relatively stable patients it may be possible to set out a plan that addresses several hours of care, but often plans at this stage are designed for the next hour or so while further investigations or opinions are obtained.

Investigations and interventions

A discussion of the appropriate tests for patients is beyond the scope of this section. It is fair to comment, however, on two principles that

should underlie such tests. Firstly, there should be a clear logic behind the ordering of any investigation, so that the purpose of the test—and indeed the response to the result—are understood. Secondly, it is crucial that all tests are recorded in the notes. Many of the more obscure investigations we initiate may not be reported until long after the child leaves PICU. Any summary therefore needs to record all outstanding tests and clarify who is responsible for locating and acting on the results.

Good intensive care is about attention to detail.

Planning

Lastly, a clear plan needs to be put in place for the ongoing care of the child. For each problem that has been identified, there should be clarity about the plan and the 'alarm limits', that is to say acceptable physiological parameters and the setting of monitor alarm limits. Each component of the plan needs to be time limited ('we will continue with these antibiotics until Tuesday') or have clearly defined parameters ('call me if the mean arterial pressure falls below 60mmHg').

Regular assessment

Clinical findings and physical signs change quickly in the critically ill child. As a minimum a daily examination of every patient is essential.

- It is very easy for this to be missed but it takes <5min to carry out a head-to-toe examination and will detect important new physical signs.

Documentation and communication

This is one of the most important, yet often poorly undertaken, tasks in PICU. The success of any unit depends to a great extent on the wide variety of experts from other teams who pass through and jointly manage complex patients. One key role for any intensivist is to be able to facilitate these different teams and pull together a coordinated plan. This requires careful documentation and communication to ensure that all parties involved understand and agree to a common plan.

Changes in patient management should be coordinated through the PICU team. If multiple teams can make changes directly, for example in drug therapy, it can result in confusion and a high risk of error.

Important considerations

- Clear and precise notes from medical and nursing staff:
  - All entries dated and signed (with name and designation)
  - Legible
  - Any interventions justified and timed
  - Treatment cessation (e.g. extubation or central line removed) similarly recorded
  - Notes from specialist teams clearly set out
  - Drug charts fully completed and signed

- Any discussions and consequent decisions made with the family should be recorded
- Critical events (e.g. a cardiac arrest) should be detailed as soon after they occur as possible.

Communication is similarly essential. In a shift-dependent unit, staff changes will occur 2 or 3 times a day, and the continuity of care is easily lost. Clear handover arrangements between staff are essential. This includes a thorough handover from ***both*** surgical and anaesthesia staff when a post-surgical case is admitted to the ICU.

Communication with families needs to be managed carefully to avoid confusion, especially in patients who are in PICU for prolonged periods.

PICU discharge

Good communication with the ward team is essential:

- A written discharge letter should accompany each patient
- A verbal handover is essential if there are urgent unresolved issues
- If a trigger or early warning system is in use in the ward area initial observation type and frequency should be prescribed, along with thresholds for seeking review.

Summary

Clinical examination and history taking in PICU is an essential aspect of care. It is made more difficult by the breadth of problems, and by the complexity of the problems seen. At times the central role of coordinating care with all the teams involved can make it seem like a juggling act but this is a key role for the PIC team. Careful documentation and communication underpins a unit's ability to perform well.

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Chapter 5

Physics and clinical measurement

Key components

It is what we think we know that prevents us from learning
(Claude Bernard)

Whilst it may appear to an outsider that ICM is entirely reliant on complex monitoring systems, this would, in fact, be a gross misunderstanding. Monitoring is a merely an aid for observing our patients and ***must never be used as a substitute for thorough history and clinical examination.***

Monitoring systems should be accurate, reproducible, and easily understood. They should be reliable in tracking changes in the patient (i.e. with minimal delay), but above all they should be relatively painless and free from major risks.

Advances in microcircuit computer technology and data retrieval have produced a bewildering choice of systems for monitoring in PIC. As a paediatric intensivist you will need to be able to look beyond the shiny new machines and concentrate on the key components of monitoring:

- Basic physics
- Principles of measurement
- Advantages and disadvantages of each system.

These key components, combined with a firm grasp of physiological principles, will allow the intensivist to interpret data obtained in a critical and, above all, useful manner.

Basic physics

Knowledge of simple physics is required in order to understand the function of much of the equipment used by the paediatric intensivist

Units

It is standard to use the International System of Units (SI units).

- Pressure: pressure is measured in pascals (newtons per metre^2) and in mmHg.

  Atmospheric pressure (at sea level) = 760mmHg = 101kPa = 1.01 bar

  1mmHg = 133Pa = 1.36cmH_2O

- *Time* is in seconds (s)
- *Mass* is in kilograms (kg)
- *Length* is in metres (m)
- *Force* is in newtons (N)
- *Work* and energy are in newton metres (m) or joules (J)
- *Power* is joules per second (Js^{-1}) or watts (W).

Basic definitions

- *Velocity* is distance travelled per unit time (ms^{-1} or m/s)
- *Acceleration* is the rate of change of velocity (ms^{-2} or m/s^2)
- *Force* (N) = mass × acceleration.
- *Pressure* (Pa) is force per unit area = force (N)/area (m^2).
- *Work* (joules) = force × distance (Nm)

- *Energy* is the capacity for work. Same units as work
- *Power* (Js^{-1}) is the rate of work = work × time (W).

Matter

Matter can exist in solid, liquid, or gaseous phases:
- In solids, molecules oscillate around a fixed point
- In liquids, molecules are faster and move more freely
- In gases, molecules move most freely.

Fluids

- Both gases and liquids are termed fluids:
  - Liquids are incompressible and occupy a fixed volume at constant temperature
  - Gases have no fixed volume but occupy the space of any container
  - Heating a liquid increases the kinetic energy of its molecules, allowing molecules to leave the surface in a process of vapourization
  - Loss of these more energetic molecules leads to reduction in the energy state of the liquid and cooling. Thus evaporation causes cooling. This why wet babies get cold quickly
  - If a gas is compressed it can condense into a liquid
  - At or above a particular temperature (the 'critical temperature') a gas cannot be compressed into a liquid however much pressure is applied
  - Gases below their critical temperature are called vapours
- Collision of molecules in the gaseous phase with the walls of a container causes the pressure exerted by a gas:
  - The pressure of the vapour above a liquid is called the saturated vapour pressure (SVP)
  - SVP increases with temperature of the liquid (as molecules have more energy and therefore leave the liquid for the gaseous phase)
  - When SVP equals atmospheric pressure, the liquid boils
  - Thus at altitude when the atmospheric pressure is lower, liquids boil at lower temperature.

Pressure

Boyle's law

(Robert Boyle, 1627–1691, English scientist.)
- At a constant temperature, the volume (V) of a given mass of gas varies inversely with the pressure (P):

$$P = 1/V$$

- Thus, a full oxygen cylinder (size E) at a pressure of 137 bar (13,700kPa) will contain 680L of oxygen. If, during use the pressure on the gauge falls to 68.5 bar, the cylinder will be half full.

Box 5.1 Dalton's law and the alveolar gas equation

(John Dalton, 1766–1844, English chemist)

Dalton's law of partial pressures states that in a mixture of gases in a container, the pressure exerted by each gas is the same as that which it would exert if it occupied the container alone.

- Thus, in a cylinder of compressed air at 100bar, the pressure exerted by oxygen is 21 bar (i.e. 21%)
- The partial pressure of oxygen in atmospheric air (PiO_2) can be calculated:

  $PiO_2 = FiO_2 \times P_B = 0.21 \times 100 = 21kPa$

  (P_B, barometric pressure is approximately 100kPa at sea level)
- To calculate the partial pressure of alveolar oxygen P_AO_2, the *alveolar gas equation* is used. This takes water vapour pressure into account. Thus:

  $P_AO_2 = [F_iO_2 \times (P_B - P_{H2O})] - (P_aCO_2 \div R) + F$

  (P_{H2O} refers to SVP of alveolar air saturated with water vapour; P_aCO_2 refers to the partial pressure of arterial carbon dioxide which is assumed to be the same as alveolar carbon dioxide (because carbon dioxide is so soluble in blood); R is the respiratory quotient (0.8); and F is a correction factor that is usually ignored)
- Thus breathing air at sea level:

  $P_AO_2 = [0.21 \times (101.3 - 6.3)] - (5.3/ 0.8) = 13.3kPa$ at sea level
- If one is at altitude, e.g. Mexico City at 2240m above sea level, which has a barometric pressure of 77kPa, then breathing air:

  $P_AO_2 = [0.21 \times (77 - 6.3)] - (4/0.8) = 14.8 - 5 = 9.8kPa$

  (mild hyperventilation gives a P_aCO_2 of 4kPa in Mexico City).

Laplace's law

(Pierre-Simon Laplace, 1749–1827, French scientist.)

- For a hollow distensible structure, e.g. artery, alveolus or ventricle then:

  $P = 2T/R$ or rearranging $T = PR/2$

  Where P is pressure, T is wall tension, and R is radius.
- This has clinical importance when:
  - Ventricular cardiac muscle must generate greater tension when the heart is dilated than when normal size, in order to produce the same intraventricular pressure. Thus a failing heart must contract more forcibly to sustain BP. Hence the benefit of reducing preload
  - Collapse of alveoli is prevented by surfactant which reduces surface tension.

Flow

Flow is the movement of a volume of substance passed a given point per unit time.

- Flow will only occur if there is a gradient, e.g. pressure or voltage
- Gases and liquids flow down pressure gradients
- Flow varies with *viscosity*
- Flow may be laminar or turbulent
- Laminar flow is more efficient than turbulent flow, i.e. greater flow per unit pressure.

Viscosity

- Viscosity is the property of a liquid that resists flow. Viscosity of liquids decreases with increasing temperature whereas viscosity of gases increases with increasing temperature
- When viscosity is constant, fluids are referred to as *Newtonian*.
- Blood is non-Newtonian because erythrocytes distribute themselves such that viscosity varies with flow.

Laminar flow

- Laminar flow is smooth orderly flow
- Molecules have varying velocities: the faster ones in the axial stream and the slowest in contact with the wall of the tube (see Fig. 5.1)
- In a tube, flow is determined by the Hagen–Poiseuille formula (see Box 5.2).

Box 5.2 The Hagen–Poiseuille formula

(Jean Poiseuille 1797–1869, French physiologist; Gotthilf HL Hagen 1797–1884, German engineer)

Pressure difference (ΔP) = flow x resistance (R)

Therefore: $\text{flow} = \Delta P / R$

The formula for resistance is: $R = 8\eta l / \pi r^4$

Hence: $\text{flow} = \pi \Delta P r^4 / 8\eta l$

- Thus we can see that laminar flow is proportional to:
  - Pressure difference (ΔP)
  - The fourth power of the internal radius of a tube (r)
- And inversely proportional to:
  - Length of the tube (l)
  - Viscosity of the fluid (η)
- This only applies to Newtonian fluids
- Blood is non-Newtonian but we apply the Hagen–Poiseuille formula for simplicity's sake (see Box 5.3).

Box 5.3 Applications of flow theory in clinical practice

The most important determinant of laminar flow is tube radius (r^4). Therefore, applying the Hagen–Poiseuille equation: if radius is doubled then, flow increases 16× for the same pressure gradient (ΔP). Additionally halving the length of a tube effectively doubles the flow rate.

- Airway narrowing in infants has a proportionately greater effect on flow. That is why croup is a disease of children and airway narrowing is more concerning for the smaller child:
  - If an airway of diameter 4mm develops mucosal oedema of 0.5mm then the resulting airway diameter will be 3mm (i.e. the radius will be 1.5mm): assuming constant pressure, airflow will fall from 2^4 to 1.5^4, i.e. 16 to 5. Thus airflow will have fallen by >2/3
  - Stridor is caused by turbulent flow (normal quiet breathing is laminar)
  - Reducing the density of inhaled air with helium addition converts turbulent flow to laminar flow and has been used in airway narrowing such as croup and asthma
- Transfusion of fluids through IV cannulae (Fig. 5.4):
  - Flow exponentially improves with wider cannulae
  - Flow is better with shorter cannulae
  - For rapid infusion, short, wide cannulae are more effective than long narrow cannulae (e.g. multilumen central lines)
- Endotracheal tubes (ETTs) (Fig. 5.5):
  - Flow improves with bigger ETTs, allowing less pressure from the ventilator to achieve the same lung volumes
  - Use the widest and shortest ETTs possible to reduce work of breathing for patients on spontaneous breathing modes, e.g. CPAP (continuous positive airway pressure) or pressure support).

Turbulent flow

- Turbulent flow is haphazard with eddies and swirls (see Fig. 5.2)
- Varies with density rather than viscosity
- Occurs with sudden changes in velocity, e.g. around bends, narrowings, or orifices
- Tends to make a noise, e.g. heart sounds, breath sounds
- Requires more pressure to get the same flow rate as laminar flow
- In general, flow is neither purely laminar nor turbulent. Flow may be laminar until velocity increases to a critical point (critical velocity) at which flow becomes mixed laminar and turbulent (see Fig. 5.3).

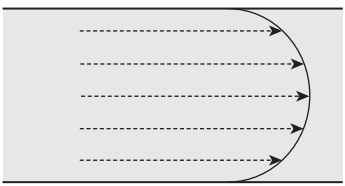

Fig. 5.1 Laminar flow. Reproduced from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, Elsevier.

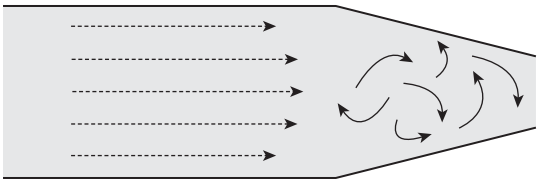

Fig. 5.2 Turbulent flow. Reproduced from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, Elsevier.

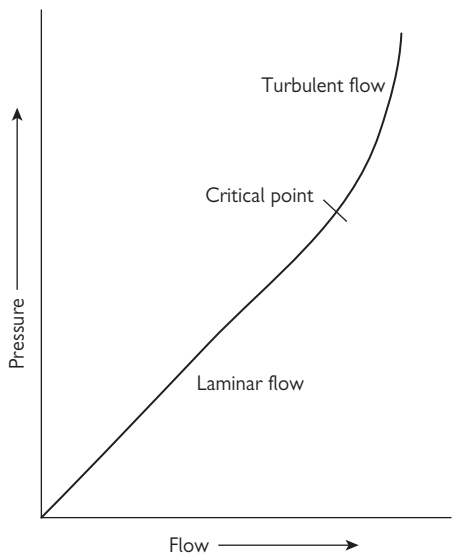

Fig. 5.3 The relationship between pressure and flow in a fluid. Reproduced from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, Elsevier.

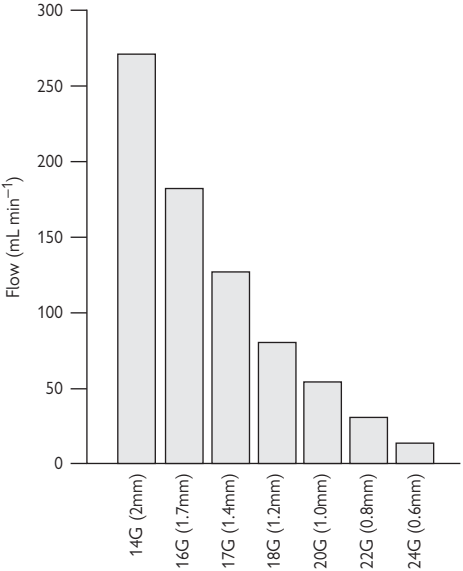

Fig. 5.4 Flow rates with peripheral cannulae.

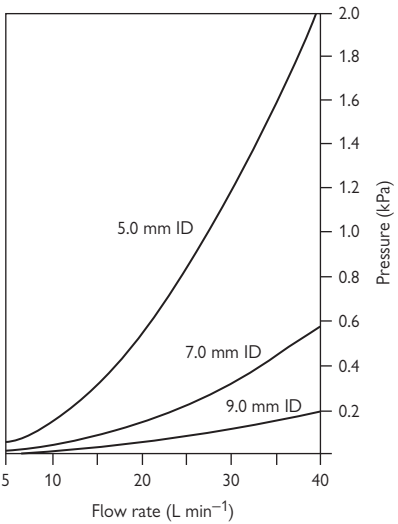

Fig. 5.5 ETTs and flow rates. Reproduced from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, with permission of Elsevier.

The Bernoulli principle

(Daniel Bernoulli 1700–1782, Swiss mathematician.)

- This states that as a fluid passes through a narrowing there is an increase in velocity of the fluid and consequently an increase in kinetic energy. Because energy must be constant (law of conservation of energy) then there is a reduction in potential energy reflected in a reduction in pressure. Beyond the narrowing, velocity decreases to the initial value (see Fig. 5.6).
- Venturi (Giovanni Venturi 1746–1822, Italian physicist) placed a tube just distal to the narrowing which has been called *Venturi's injector* (see Fig. 5.7 and Box 5.4).

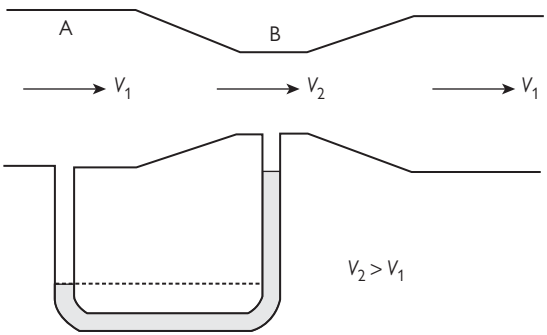

Fig. 5.6 Bernoulli principle. Modified from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, with permission of Elsevier.

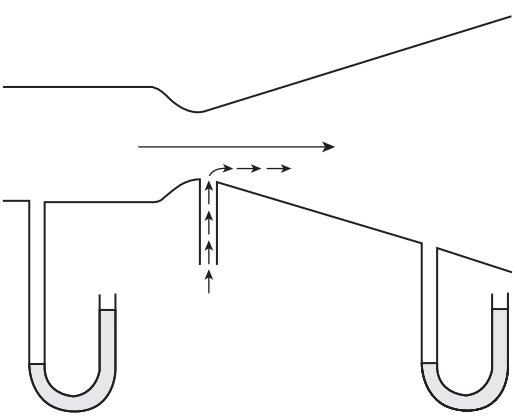

Fig. 5.7 Diagram of Venturi injector. Reproduced from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, with permission of Elsevier.

Box 5.4 Clinical use of the Venturi injector

- *Oxygen therapy:* several types of venturi masks are available which provide oxygen-enriched air. With the correct flow (usually >4L min^{-1}), air is entrained. This results in a total gas flow that exceeds the patient's peak inspiratory flow, thus ensuring that the inspired oxygen concentration is constant
- *Nebulizers:* these are used to entrain liquid from a reservoir which may be broken up into a fine mist
- Portable suction apparatus
- Humidification in ventilator—again as superfine mist
- As a driving gas in some ventilators.

Humidification

- Absolute humidity is the mass of water vapour present in a volume of gas (mg L^{-1})
- Absolute humidity increases with increasing temperature, i.e. the warmer the gas the more water it carries until saturated
- Relative humidity (RH) is the ratio of the amount of water in a gas to the maximum water capacity (saturated vapour pressure)
- Humidity is measured by hygrometers (hair, wet and dry bulb)
- When air is drawn into the respiratory tract its temperature is raised from room to body temperature. Thus, inspired air is fully saturated (i.e. relative humidity of 100%) by the time it reaches the respiratory tree. This is mainly done by the nose:
  - The SVP in the lungs (at 37°C) is 6.3kPa. The concentration of water is 44mg L^{-1}
  - The SVP in room air (21°C) is considerably less and carries 18mg L^{-1}
  - Thus if a patient is ventilated with dry gases, not only will the respiratory mucosa be damaged but both water and heat will be lost from the patient. Humidification prevents this.
- Mechanical ventilators in PICU usually use heated water baths to produce about 25mg L^{-1} water vapour. Inspired gas must be 100% relative humidity at 37°C before inspiration. Inspired gas is heated above 37°C to produce 90% humidity and then cooled to 37°C in the tubing just proximal to the ETT to achieve 100% relative humidity
- If inspiratory gases cool down then 'rain out' will occur with water accumulating in the ventilator tubing
- Similarly, cooling of expiratory gases require water traps
- Hot water baths can provide a reservoir for infection (if too cold; the heat prevents bacterial growth) and can burn the respiratory tract (if too hot).

Principles of clinical measurement

There are a wide variety of measurement systems available to assess patient clinical status or response to therapy. These systems are so common in PICU that the complexity involved in converting high frequency data (e.g. an arterial trace) into a continuous waveform is often not appreciated. The list of potential problems due to human, electronic, and mechanical errors is long and errors in measurement can be easily introduced. Since major decisions are often based on readouts from monitors it is essential that the intensivist has some understanding of the basic principles involved. Before embarking on aggressive treatments for low BP or high intracranial pressure it is important to ask the question 'is this number correct?'.

Measuring pressure

Pressure can be measured via:

- *Manometers:* height of the column is proportional to the pressure. Mercury or saline (for intracranial pressure) can be used
- *Aneroid gauge*, e.g. bourdon gauges on gas cylinders ('a-neros' means without liquid)
- *Transducers*, e.g. arterial and central venous pressure lines (see 'Transducers').

Components necessary for pressure measurements using transducers include:

- Catheter in place (e.g. arterial, central vein)
- A column of uncompressible fluid to transmit pressure (usually in non-compliant tubing)
- A mechanical transducer that converts a change in pressure in the tubing to an electrical signal that can be processed and displayed
- A suitable monitor.

Transducers

- Usually incorporate a diaphragm.
- Movement of the fluid column back and forth causes changes in flattening of diaphragm which are converted to voltage changes.
- Need to be *zeroed* at standard reference point on body-generally the midaxillary line (right atrium).
- ***Must*** be repositioned if the patient is moved
- Modern transducers should be zeroed every 12-h shift.

Distortion in measurement

- Damping of a system can distort the true amplitude of a signal
- Overdamping underestimates BP and is caused by:
  - Bubbles in the fluid tubing
  - Tubing is too compliant
  - Tubing is too long (should be kept as short as possible)
- Underdamping leads to overestimation of BP and may be due to resonance in the system
- Impedance in blood vessels increases towards the periphery (i.e. more distal) giving higher BP readings.

Measuring flow

- Flow can be described as movement of a volume per unit time
- Flow and volume are dependent on one another and thus devices in intensive care that measure flow often also measure volume.

In PICU, measurements of flow are usually for

- Blood flow, namely cardiac output
- Gas supply: generally oxygen/air mixes from:
  - Wall or cylinder supply (rotameters)
  - Ventilators
- Patient: expired flow is measured for respiratory function tests.

Cardiac output measurement

Measurement of cardiac output in both adult and paediatric intensive care has a rather chequered history:

- Measured cardiac output is usually indexed to body surface area and is known as *cardiac index*. The normal values for cardiac index are 3.5–5.5L/min/m^2 regardless of patient age and size.
- Pulmonary artery catheterization and thermodilution was considered the best 'standard' of measurement but the risks associated with its use outweigh the benefits
- Errors of measurement in all techniques are considerable but trends may be useful (assuming measurement artefacts are constant)
- There is no evidence that measurement of cardiac output specifically improves outcome in children (and evidence is debatable in adults)
- Consequently it is not common to see cardiac output monitors in PICU

There are 3 different approaches to measuring cardiac output based on different principles.

- Indicator dilution and other techniques based on the Fick principle (Box 5.5)
- Doppler ultrasonography
- Thoracic electrical bioimpedance.

Box 5.5 The Fick principle

- The Fick principle defines flow by the ratio of uptake or clearance of a tracer within an organ to measurements of the arteriovenous difference in concentration. In practice, the tracer is oxygen: thus oxygen consumption is measured and related to arteriovenous oxygen content difference. The technique has been used for cardiac output as well as cerebral and renal blood flow. With no major cardiac shunt, cardiac output = pulmonary blood flow, and:

$$\text{Pulmonary blood flow} = \frac{\text{oxygen consumption}}{\text{arterio} - \text{venous oxygen content difference}}$$

- Traditional techniques for measurement of oxygen consumption and content required the use of spirometry and a co-oximeter respectively. Portable metabolic monitors have been used but are hampered by errors. Mixed venous oxygen content is calculated from the pulmonary artery samples.

Indicator dilution

- This technique requires a pulmonary artery catheter (PAC)
- An indicator is injected as a bolus into the right heart (via a central venous port in the PAC) and the concentration measured downstream is plotted against time
- The cardiac output during the period of measurement is the ratio of the dose of indicator to the average concentration and is calculated from the area under the concentration–time curve

$$\text{Cardiac output} = \frac{\text{indicator dose}}{\text{average concentration} \times \text{time}}$$

- The smaller the curve the higher the flow, i.e. the higher the cardiac output (Fig. 5.8)
- Indicators used include dye (indocyanine green) but more commonly cold saline or water (thermodilution) was used with a PAC (the temperature detected by a thermister in the pulmonary artery and was plotted against time)
- More recently lithium chloride has been used as an indicator in adults and children
- This technique cannot be used with an anatomical shunt or with significant valve regurgitation and thus has limitations in congenital heart disease.

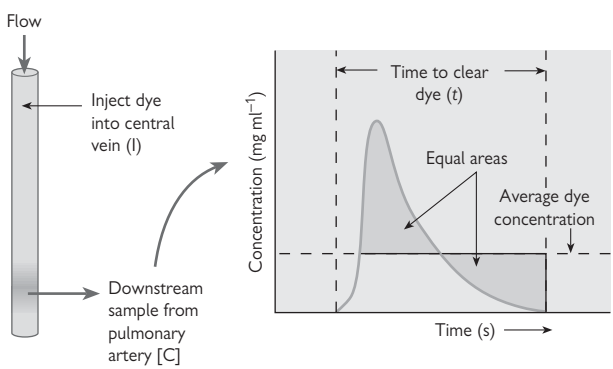

Fig. 5.8 Concentration–time curve for injection of dye and calculation of flow. Modified from Pocock G, Richards CD (eds) (2006). *Human Physiology: The Basis of Medicine*, 3rd edn. Oxford University Press, Oxford.

Arterial pulse contour analysis (PiCCO®, LiDCO®)

- The arterial pressure waveform (from a peripheral arterial line) varies with left ventricular stroke volume and inversely with resistance
- Cardiac output is measured (usually by thermodilution) and arterial waveform is 'calibrated'
- The arterial (pulse) contour is then analysed by microprocessors to give continuous cardiac output and stroke volume measurement
- This technique requires regular recalibration of the cardiac output with the thermodilution.

Doppler ultrasound

- Cardiac output is measured using Doppler ultrasound
- Blood velocity is calculated from the frequency shift of reflected ultrasound waves using the Doppler principle
- Measurements are taken from the aorta via transthoracic (sternal) or transoesophageal probes
- Aortic diameter is necessary and is calculated from a normogram (available for children)
- The assumptions inherent in the normogram produce an error in cardiac output unique to each patient
- This technique is relatively non invasive and trends of measurement can be followed with some confidence.

Echocardiography

Echocardiography in the hands of a skilled operator provides a vast amount of functional information as well as morphological diagnosis

- Valve regurgitation
- Shortening and ejection fraction
- Diastolic function, chamber dilatation, regional wall dysfunction, and chamber interdependence.

Bioimpedance

- The thorax is regarded as an electrical conductor whose impedance is altered by blood volume and velocity with each heartbeat
- Electrodes are placed on the chest (or neck or abdomen)
- Stroke volume and hence cardiac output are calculated
- Not commonly used in intensive care.

Measuring gas flow and volume

Measurements of gas volumes depend on collecting the gases in a calibrated spirometer or passing the gas through some type of gas meter.

Spirometers

- Dry spirometers, e.g. 'the Vitalograph', are used for lung function testing
- Gas displaces a rolling diaphragm or bellows and the volume is recorded by a stylus on a volume–time chart
- Vital capacity, forced vital capacity, and forced expiratory volume in 1s are measured (see Fig. 5.9).

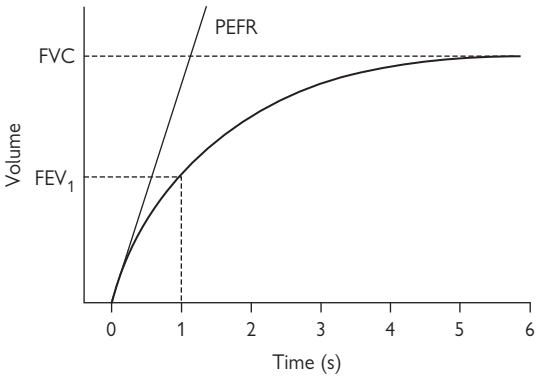

Fig. 5.9 Diagram of spirometer readings. FEV_1, forced expiratory volume in 1s; FVC, forced vital capacity; PEFR, peak expiratory flow rate. Reproduced from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, with permission of Elsevier.

- Spirometry is particularly useful in assessing respiratory muscle strength in Guillain–Barré disease and myasthenia gravis
- Spirometry is only feasible in older children as it requires active cooperation of the patient.

Measurement of gas flow rate

The rotameter

- Variable orifice constant pressure flow meter, i.e. works on the principle that the orifice through which gas flow enlarges with increasing flow rate so the pressure difference across the orifice stays constant
- Consists of a graduated vertical glass tube containing a bobbin which is conical shaped—increasing flow pushes the bobbin up the tube (Fig. 5.10)
- Rotameters are calibrated for the density and viscosity of a particular gas and can be only used accurately for that gas
- Rotameters are commonly used for oxygen, air, and nitrous oxide, and used in wall outlets, gas cylinders, and anaesthetic machines.

Peak flow meters

- Used for measuring air flow rates up to 1000L min^{-1}
- Airflow causes a vane to rotate or a piston to move against the constant force of a light spring
- The maximum reading corresponds to the peak expiratory flow
- Accuracy demands good technique, i.e. held horizontally (minimizes effect of gravity) and rapid exhalation
- Used to assess asthma.

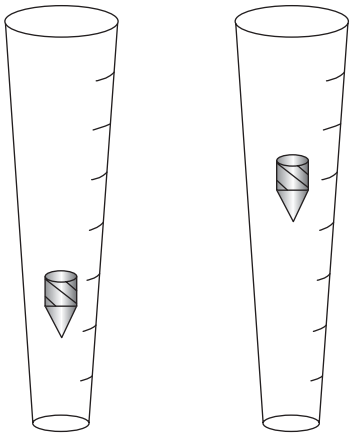

Fig. 5.10 Diagram of rotameter. Reproduced from Aitkenhead AR, Smith G, Rowbotham, DJ (2007). *Textbook of Anaesthesia.* 5th edn. Churchill Livingstone, with permission of Elsevier.

Pneumotachograph

- Variable pressure constant orifice flow meter
- Measures flow rate by sensing pressure drop across a small but laminar resistance
- Very sensitive and used mainly in respiratory and anaesthetic research.

Chapter 6

Vascular access and clinical monitoring

Vascular access

Peripheral venous access

Almost all paediatric patients admitted to ICUs will require some form of IV access. Cannulation of small paediatric veins can be a challenging exercise, particularly if the children have had previous NICU/PICU admission. See Box 6.1 and Table 6.1.

Peripheral cannulae should be secured firmly with clear dressings. Cannulation of 'tissue' regularly and inadvertent extravasation of drugs into subcutaneous tissue can cause significant skin necrosis (see Box 6.2). Limbs must never be wrapped in bandages or secured in such a way as to hide the cannula site or its surrounds.

Box 6.1 Choice of cannula for rapid infusion

- Flow of fluid through a tube is subject to Hagen–Poiseuille's law, i.e. it is inversely proportional to viscosity and length and directly proportional to the pressure difference and the radius to the power of 4 (see 📖 p.49)
- If rapid infusion is required, the best cannulae to use are the shortest with the widest diameter, e.g. peripheral cannulae
- Multilumen central lines guarantee access but are not optimal for rapid transfusion
- Syringing the fluid from a 3-way tap will allow for rapid infusion but pressure applied should be minimized with rapid blood transfusion in order to avoid haemolysis and hyperkalaemia.

Table 6.1 IV cannulae, typical dimensions, and flow rates (UK)

Gauge	Diameter (mm)	Length (mm)	Flow rate (mL/min)
24G	0.7	19	24
22G	0.9	25	36
20G	1	32	55
18G	1.2	40	90
16G	1.7	42	170
14G	2	45	250

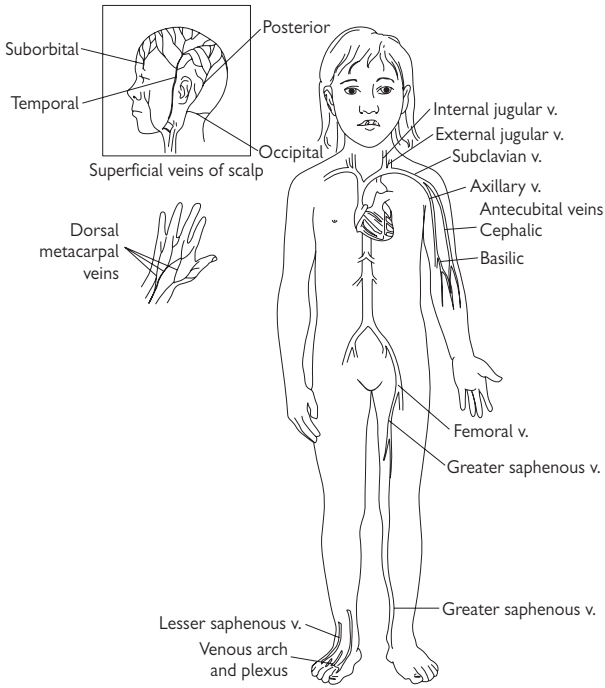

Fig. 6.1 Venous sites. Reproduced from Levin DL, Morriss FC (1997). *Essentials of Paediatric Intensive Care*, 2nd edn. Churchill Livingstone, Elsevier.

Box 6.2 Treatment of extravasation injury

Extravasation of drugs, particularly inotropes, into skin and subcutaneous tissues from IV cannulae can cause extensive damage and result in significant disabling and disfiguring injury. Early recognition and prompt management can reduce the impact of such injuries. If possible avoid obscuring the site of IV cannulae (use clear dressings) and regularly check all insertion sites.

Extravasation injury treatment involves the infiltration of hyaluronidase to break down and hydrolyse the hyaluronic acid of connective tissue. This allows saline to be flushed through subcutaneous tissues to achieve dilution and removal of the extravasating agent. It is imperative that the procedure is begun as soon as the injury is discovered.

- What you need:
  - Sterile gloves and sterile pack
  - A skin cleaning agent such as chlorhexidine
  - 1500 units hyaluronidase
  - 0.9% normal saline
  - 21G needle, 22G cannula, 20mL syringe, and 1% lidocaine
- Hyaluronidase infiltration:
  - Infiltrate the area with 1% (10mg/mL) lignocaine (<max. dose 3mg/kg)
  - Infiltrate the subcutaneous tissues extensively with hyaluronidase. Neonate: 500–1000 units; infant or older: 1000–1500 units
- Saline washout:
  - Insert 20G cannula across extravasation so cannula exits skin on the other side
  - Remove needle from cannula and attach 20-mL syringe of saline
  - Slowly withdraw cannula across area whilst flushing with saline
  - Repeat 2 more times with a new entry/exit site each time. There should now be 6 puncture sites
  - Insert cannula into any of the puncture sites and flush with 20-mL aliquots of saline. Saline should emerge from the other puncture sites. Repeat this process—neonates: 60mL; infants/small children: 60–240mL; adolescent: 500mL
- Dress site with sterile material and elevate for 24h. Review the site every 6h and consult plastic surgeons if possible
- Remember that this procedure can be very painful. Please use sedation and local anaesthetic
- Photographic records (before and after infiltration for several days) are recommended if possible
- If infection supervenes then start IV antibiotics.

Adapted from protocol by Dr R. Matsas, Dr A Shefler, and Mr H Giele.

Intraosseous access (IOA)

- IOA is widely recommended in emergency situations where peripheral access is difficult
- IOA is safe, reliable, and a rapid way of administering fluids, medications and blood products into the circulation
- IOA is appropriate in children aged 0–7 years (including neonates); however it can be attempted in patients of any age
- Contraindications include bony fractures and obvious overlying infection due to possibility of disseminating infection
- Usually a needle containing a trochar is used but if these are not available lumbar puncture (spinal needles) can be used (the largest available).

Sites

- Anteromedial surface of proximal tibia: 1–3cm below tibial tuberosity
- Flat portion of distal tibial surface: proximal to medial malleolus angled 10–15° cephalad to avoid epiphyseal plate
- Anterolateral surface of distal femur: 3cm above the lateral condyle.

Technique

- Apply gloves for patient and personal protection
- Clean site with alcohol or appropriate cleaning solution wipes
- Position and stabilize patient
- Insert the needle at 90° to the skin
- Continue to advance the needle using a rotational motion until a loss of resistance is felt. Avoid rocking the needle side-to-side as this may enlarge the opening into the bone and promote extravasation
- Once loss of resistance is felt, remove the trochar and attempt to aspirate marrow. Often it is difficult to aspirate
- Flush with appropriate fluid looking for signs of extravasation
- Secure needle
- Complications include local infection, rarely, cellulitis or osteomyelitis (↑ in prolonged IO use), fluid extravasation, local haematoma and pain
- Once correct placement is confirmed, drugs and fluids (crystalloids, colloids, blood products) can be infused via the IO route. Drugs will require a flush and rapid infusion can be given with gentle pressure from a syringe. As soon as feasibly possible alternative IV access should be sought. The longer the IO needle is in use the greater the risk of complications.

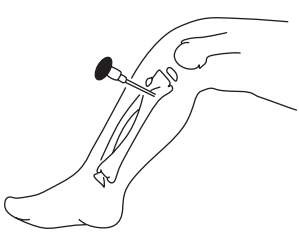

Fig. 6.2 Intraosseous access.

Cardiovascular monitoring

Electrocardiography

- All patients should have continuous ECG monitoring
- Standard ECG monitoring is with 3 leads—2 on the chest and 1 abdominal
- Readings are commonly taken from lead II
- Rate is determined by detecting QRS complexes and averaging time for 3 beats or more
- Often incorporates respiratory plethysmography to determine respiratory rate
- Visual display of waveform allows for detection of arrhythmias and occasionally ischaemia (ST depression) but can only be confirmed on formal 12-lead ECG
- Alarms generally detect tachycardia, bradycardia, and arrhythmias. ST segment analysis can be unreliable
- In PICU tachycardia may be an indication of:
  - Fever
  - Pain
  - Anxiety
  - Circulatory insufficiency
  - Hypoxaemia
  - Hypercapnia
- Bradycardia may indicate:
  - Hypoxaemia
  - Drug side effects.

Blood pressure measurement (see Box 6.3)

Blood pressure (BP) is an indirect measurement of perfusion:

$$BP = Q \times R$$

where Q is blood flow (i.e. cardiac output) and R is vascular resistance.

4 parameters are measured:

- Systolic pressure
- Diastolic pressure
- Pulse pressure (systolic–diastolic)
- Mean arterial pressure (MAP), i.e. diastolic pressure plus 1/3 pulse pressure.

Box 6.3 Non-invasive blood pressure

The manual method was first described by Nikolai Korotkoff in 1905. The more recent automated method (e.g. Dinamap®) which is microprocessor controlled is standard on PICU:

- Cuff inflates to above systolic pressure and then deflates incrementally whilst pulsations are detected by a transducer
- Dinamap® readings have been validated in children
- Errors commonly arise from incorrect cuff size—narrow cuffs overestimate and wide cuffs underestimate pressure
- Cuff width should be 40% of the mid-point circumference of the limb and length should be twice the cuff width
- Measurements are inaccurate with arrhythmias and hypotension
- Thigh readings are generally higher than arm readings.

Invasive arterial pressure monitoring

Arterial catheter placement is used commonly in ICU for:
- Continuous systemic BP monitoring. Particularly during IV fluid resuscitation or inotropic support
- Serial arterial blood gas (ABG) analysis
- Calculating cerebral perfusion pressure when intracranial pressure monitoring is used.

Insertion of arterial cannulae

Arterial access requires a certain amount of skill and experience. Techniques vary and the skill necessary for success must be clinically taught and cannot be learnt through a book. It is essential that the child stays still and attention to sedation and paralysis is imperative for success. Arterial lines can be placed in a manner similar to a peripheral venous cannula or a transfixation technique can be used. Either way a Seldinger wire may assist in difficult patients.

Sites

- In newborns the most commonly used site for arterial cannulation is the umbilical artery or radial artery.
- In older children the radial, posterior tibial and dorsalis pedis arteries are the preferred sites due to the presence of collateral supply in the hand and foot.
- The femoral arteries can be used.
- The brachial arteries should be avoided as there is limited collateral circulation
- One should regularly examine limbs with arterial catheters, looking for signs of ↓arterial supply.

Cannulae

Arterial catheters are inserted using aseptic technique and either by percutaneous catheterization or rarely by direct arterial cutdown. The smallest bore catheters which provide reliable monitoring as well as sampling should be used to avoid decreasing the arterial flow.

A recommendation is:
- 24G—extremities of preterm infants
- 22G—term to 30kg children
- 20G—larger children.

Equipment and mechanism of action

- An arterial catheter is inserted into the selected artery. Commonly a specifically designed arterial set is used which comprises a column of saline, a flushing device, and transducer. The transducer is connected to an amplifier and oscilloscope which in turn relays the information to the monitoring equipment. As the column of saline moves back and forth with each arterial pulsation a pressure wave is generated, resulting in an arterial pressure waveform (see 🕮 p.70)

- It is vital that the transducer is kept at heart level (mid axillary line is right atrial level, if supine). Changes in patient position (e.g. sitting up or head-up tilt) or bed elevation will produce changes in the pressure readout if the transducer is not repositioned
- A continuous slow (1mL/h) arterial infusion (of heparinized or non-heparinized saline) is required to maintain patency of the artery and to prevent the migration of blood into the tubing and transducer.

Interpreting the arterial waveform (Fig. 6.3)

- The information gained from an arterial trace includes:
  - Heart rate
  - Pulse pressure
  - Left ventricular contractility
  - Stroke volume
  - Vascular tone or systemic vascular resistance
- The MAP is the average throughout the cardiac cycle. Stroke volume is proportional to the area under the arterial curve up to the dicrotic notch (closure of aortic valve)
- The slope of the upstroke of the wave represents myocardial contractility (dP/dt). A slow rise upstroke can indicate poor myocardial contractility and the need for inotropic support
- Short systolic time (beginning of systole to dicrotic notch) is seen with high peripheral resistance and hypovolaemia
- A steep downstroke and low dicrotic notch is seen with vasodilatation and low peripheral resistance e.g. sepsis.
- 'Swinging trace' (Fig. 6.4) with respiration (pulsus paradoxus) is seen in:
  - Hypovolaemia
  - Pericardial effusion
  - Asthma (in non-ventilated patients—'pulsus paradoxus')
  - High PEEP or high peak pressures (with IPPV).

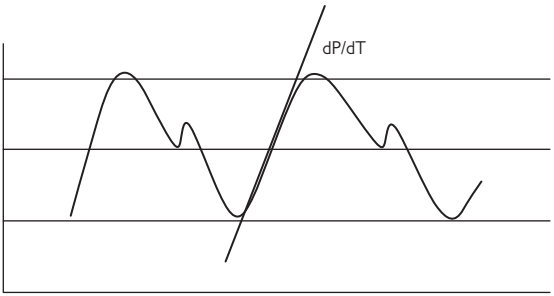

Fig. 6.3 Normal arterial waveform. Myocardial contractility can be estimated from the gradient of the upstroke dP/dt. Reproduced from Hughes J, Ali T (2004). Understanding simple monitoring in paediatric intensive care. *Current Paediatrics* **14**: 459–64, with permission of Elsevier.

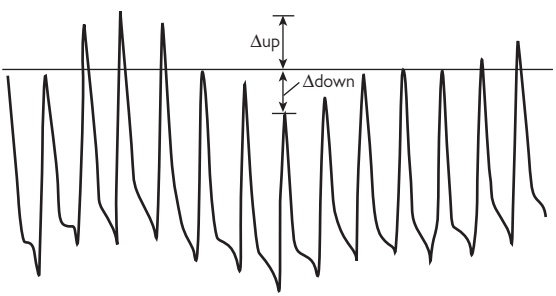

Fig. 6.4 Diagram of swinging trace. Reproduced from Hughes J, Ali T (2004). Understanding simple monitoring in paediatric intensive care. *Current Paediatrics* **14**: 459–64, with permission of Elsevier.

Damping

- It is important that the system is correctly damped. An underdamped system will give a 'spiky' waveform and will overestimate systolic pressure
- A common problem in PICU is the overdamped system with 'rounded' waveforms is seen. This is underestimates systolic pressure and is often misdiagnosed as hypotension
- To check for damping, briefly flush the system and see if the waveform and pressure reading changes. A correctly damped system should return to the waveform immediately. If the system is overdamped the return is slow. A brisk flush may correct an overdamped trace
- Overdamping may be due to air bubbles in the line or pressure tubing that is too long or too compliant.

Tips and warnings

- The arterial waveform should be displayed continuously to alert one to damping or changes in the waveform
- Arterial lines should be labelled carefully—inadvertent drug injection may cause distal arterial vasospasm and significant damage
- Watch for tissue ischaemia distal to the cannula
- Arterial thrombus does occur but rarely causes significant ischaemia or necrosis
- Inadvertent disconnection will cause bleeding
- Local infection is rare (± 20%) and systemic infection even rarer
- Rarely arterial venous fistulae have been reported.

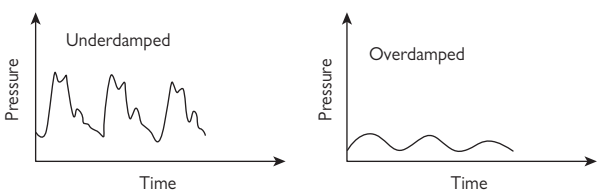

Fig. 6.5 Diagram of underdamped and overdamped traces.

Central venous pressure monitoring

Central venous lines are common in the PICU. They allow for:

- Measurement of central venous pressure (CVP)
- Secure and reliable IV access
- Administration of hypertonic solutions or drugs which require central administration such as inotropes or total parenteral nutrition (TPN)
- Measurement of central venous oxygen saturation (SvO_2) and acid–base balance
- Transvenous cardiac pacing.

Central venous pressure

- CVP uses the same electromechanical pressure transducers as arterial pressure monitors
- The recommended position of the tip is at the junction of right atrium and heart (on chest X-ray—CXR) or in the inferior vena cava (IVC) below the renal veins (L3) if femoral
- CVP monitoring is used to provide an estimate of right atrial pressure and therefore right ventricular end-diastolic pressure provided the patient has a normal tricuspid valve.
- CVP varies with:
  - Intravascular volume
  - Right heart function
  - Intrathoracic pressure
  - Venous tone
- Primarily CVP is used as a marker for intravascular volume status
- The normal CVP trace has 3 waves: a, c, and v:
  - The a wave represents atrial contraction, the c wave is caused by ventricular contraction against the closed tricuspid valve, and the v wave represents atrial filling.

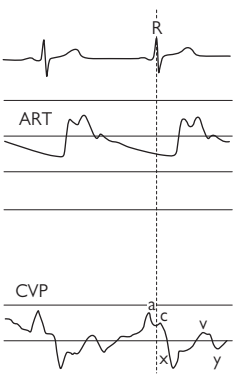

Fig. 6.6 Simultaneous ECG, arterial, and CVP waveforms. Reproduced from Hughes J, Ali T (2004). Understanding simple monitoring in paediatric intensive care. *Current Paediatrics* **14**: 459–64, with permission of Elsevier.

Interpretation of central venous pressure

Generally hypovolaemia is associated with a falling CVP and right heart failure with a rising CVP. Absolute figures are rarely of use with CVP interpretation. Far more useful is the trend, either up or down.

- CVP varies with intrathoracic pressure and thus ventilation:
  - Normal spontaneous inspiration produces a fall in CVP whereas mechanical positive pressure ventilation causes a rise in mean CVP
  - Positive end-expiratory pressure (PEEP) may also increase the CVP
  - CVP is best measured at the end of expiration
- Elevated pulmonary artery pressure can cause elevated CVP and mask hypovolaemia (e.g. in severe acute lung injury)
- The early signs of hypovolaemia (Box 6.4) may be masked by an increase in venous tone which may initially maintain CVP
- Cardiac tamponade and pericardial constriction can cause elevated CVP in association with falling BP
- Cannon waves on CVP are large 'a waves' associated with atrioventricular asynchrony or junctional rhythm when the atrium contracts against a closed tricuspid valve.

Box 6.4 The fluid challenge

Hypovolaemia will result in organ failure if not treated rapidly. Circulatory volume must be restored before any other forms of cardiovascular support are used. Clinical signs of hypovolaemia such as tachycardia and slow capillary refill are useful but low CVP and hypotension are 'late' signs. Clinical suspicion should be confirmed by raising the legs of a supine patient (in a larger child) or gentle liver compression which can give an 'endogenous' fluid challenge—if this results in a better BP and a higher CVP, then the patient may benefit from further volume resuscitation. Otherwise an 'exogenous' IV fluid challenge should be used.

Rate and choice of fluid

The aim is to achieve a rapid intravascular expansion (there is no point in giving fluid slowly if the patient is losing fluid at a faster rate). Crystalloids (10–20mL/kg) or colloids, blood, or blood products (5–10mL/kg) can be given over 10–20min. Crystalloids will leak from the circulation into the extracellular fluid and larger volumes may be needed more often.

Assessing the response

The response of heart rate, BP, and CVP should be monitored during the challenge:

- If there is no or little improvement (i.e. CVP rises <2mmHg) then further fluid is required, and the challenge should be repeated

(*Continued*)

Box 6.4 The fluid challenge (*Continued*)

- An improvement in these parameters indicates that the child needed the volume. Often the improvement in CVP is short lived (i.e. CVP rises and then falls) indicating that further fluid challenges are required. This occurs when the patient has compensated for hypovolaemia with veno- and vasoconstriction. This tends to occur in the older child (>1 year). It may also indicate that circulating volume is continuing to be lost from, for example, bleeding or capillary leak.
- A large rise in CVP (>5mmHg) that is sustained indicates that the patient is adequately filled and fluid resuscitation should be stopped for the time being.

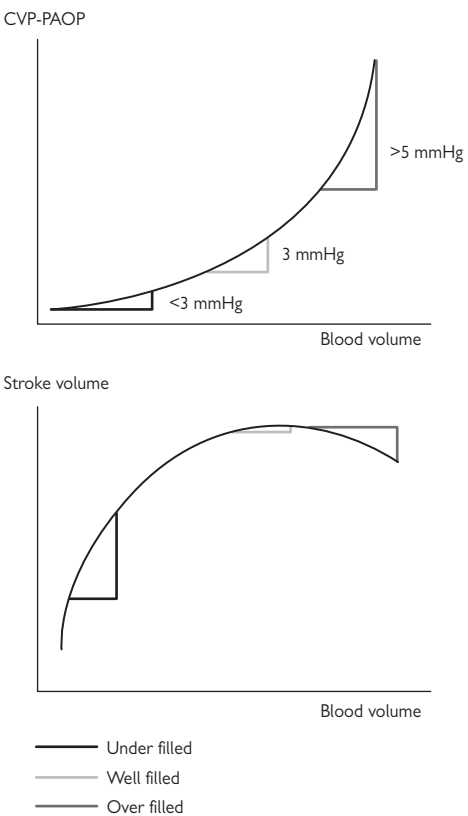

Fig. 6.7 CVP and stroke volume response to fluid challenge. Modified from Singer M, Webb AR (2009). *Oxford Handbook of Critical Care*, 3rd edn. Oxford University Press.

Central venous catheter insertion

Types of catheter

- Multilumen catheters
- Large-bore double lumen catheters for haemofiltration
- Single-lumen cannulae
- Tunnelled lines for long-term use (e.g. Hickmann line).

Insertion of central venous lines

- In neonates, percutaneous peripheral central lines are commonly used and veins routinely used include the median basilic and long saphenous veins. Numerous other veins have been used with success
- In infants and older children the commonly used sites are the femoral and internal jugular veins. The subclavian veins can be used but have the disadvantage that if excess bleeding occurs (from inadvertent arterial puncture or coagulopathy) then one cannot press directly on the vessel to stem the flow. Pneumothorax is also more common via the subclavian approach (Fig. 6.8)
- The percutaneous approach using the modified Seldinger technique is generally the most widely used and most successful method for central venous cannulation (see Fig. 6.9 and Box 6.5)
- Extreme caution should be used in patients who are coagulopathic. The subclavian route is to be avoided and clotting factors and platelets should be given if possible
- If available, it is recommended to place internal jugular lines and subclavian lines under ultrasound control
- Central lines have been associated with vessel and heart perforation. It is recommended that the tip does not lie within the heart.

Management of central venous pressure lines

- Central lines can last up to 2 weeks but should not normally be used for longer
- Central line lumens block easily and require continuous infusion of (heparinized) saline
- There is some evidence that heparin-bonded central lines have less thrombotic complications and lower infection rates
- If infection is suspected, remove the line and send the tip for bacterial culture. Avoid central access if possible. Appropriate antibiotics, e.g. vancomycin for coagulase-negative staphylococci, should be given for 1 week or 1 week from the last negative blood culture
- Culturing from the lumens, e.g. blood cultures taken through the lumens, can be misleading and may represent colonization of the catheter. Positive peripheral blood cultures are preferred for diagnosis.

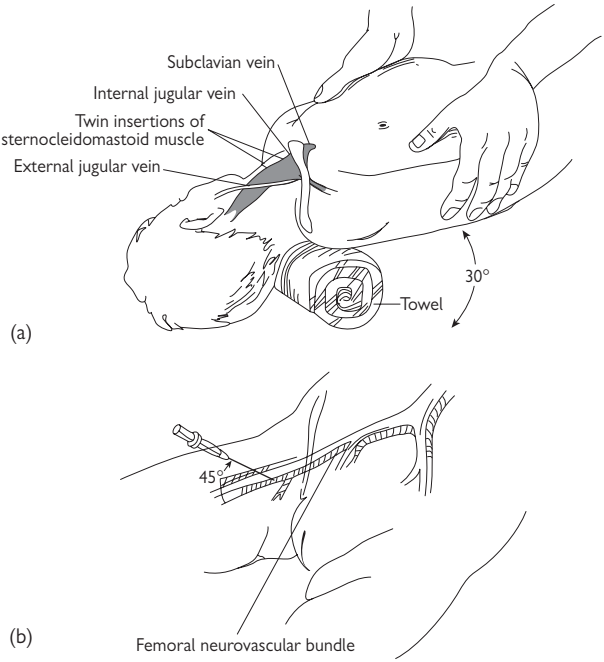

Fig. 6.8 (a) Central venous catheterization—Trendelenburg position. (b) Technique for femoral vein catheterization. Reproduced from Levin DL, Morriss FC (1997). *Essentials of Paediatric Intensive Care*, 2nd edn. Churchill Livingstone.

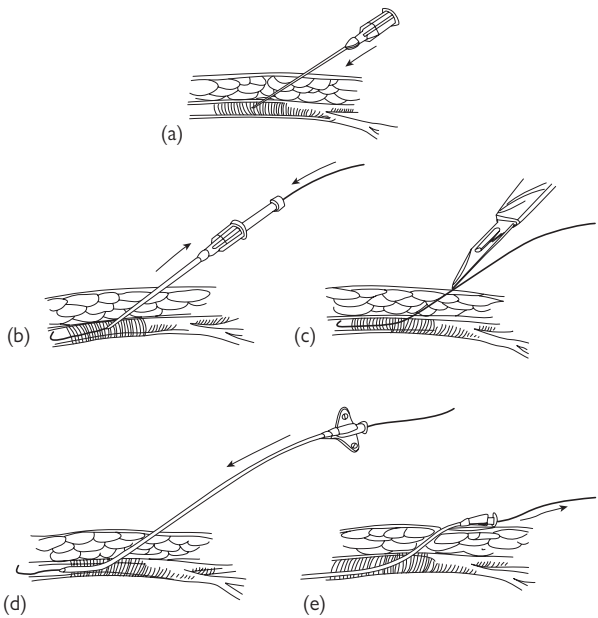

Fig. 6.9 Percutaneous venous access—Seldinger technique. Reproduced from Levin DL, Morriss FC (1997). *Essentials of Paediatric Intensive Care*, 2nd edn. Churchill Livingstone.

Box 6.5 Seldinger technique

Femoral venous access

This should be an aseptic procedure with appropriate analgesia, sedation, and paralysis.

- Position patient with leg externally rotated and everted at the hip
- Palpate femoral artery just below the midpoint of the inguinal ligament (runs between anterior superior iliac spine and symphysis pubis)
- Using a needle attached to a syringe the vein is entered just medial to the femoral artery about 1–2cm below the inguinal ligament. Enter the vessel at an angle of 45° aiming for the umbilicus
- Once the vein is punctured the syringe can be carefully removed and using the Seldinger technique a flexible guidewire can carefully be inserted in the vein. The wire should advance with no resistance
- Once the wire has been passed easily the needle can be removed. The catheter is then placed over the guidewire and advanced into the vessel. A dilator may be needed to enable passage of the catheter through the fascial planes

(*Continued*)

Box 6.5 Seldinger technique (*Continued*)

- Once the catheter is in the appropriate position, the guidewire is removed, the catheter secured and covered with an appropriate occlusive dressing
- The catheter can then be connected to the appropriate infusion and monitoring devices
- Catheter position should be confirmed radiologically. Ideally the catheter tip should lie below the level of the renal veins, i.e. L3
- Complications include vascular damage, arterial puncture, infection, air embolism, haematoma, damage to femoral head, peritonitis, thrombosis.

Internal jugular venous access

This is a fully ***aseptic*** procedure (gown and gloves) and requires appropriate analgesia, sedation, and paralysis.

- Position the child head down with a pad beneath the shoulders and the head turned away from the proposed cannulation site
- There are numerous approaches but the most widely used puncture site is at the junction of the sternal and clavicular heads of the sternocleidomastoid muscle. The vessel lies just anterior and lateral to the carotid artery
- Identify vein with ultrasound probe (if available)
- Insert the needle at an angle of 30° aiming for the ipsilateral nipple (i.e. away from the carotid artery), gently aspirating while advancing. If the vein has not been pierced in 2cm withdraw the needle with continuous gentle aspiration and try again. The angle may need to be adjusted slightly laterally or medially
- Once the vessel is penetrated, disconnect the syringe, occluding the needle end to prevent air entry and blood loss, and insert the guide wire into the needle
- Remove the needle, making sure the wire remains in the vein. Advance the catheter over the wire which then can be removed
- Secure appropriately
- Obtain CXR to confirm position. The catheter tip should lie in the superior vena cava (SVC) just outside the pericardial reflection
- Complications include pneumothorax, haematoma, arterial puncture, infection, and thrombus.

The pulmonary artery catheter

Although pulmonary artery catheters (PACs) have been in clinical use for >30 years in adult ICU, in recent years there has been a trend away from their usage as large randomized trials have shown that they are of limited benefit and carry appreciable morbidity. Additionally, new and less invasive cardiac output monitors have been introduced such as Doppler ultrasound and pulse contour analysis.

PACs are rarely used in the paediatric population:

- Despite the advent of small-gauge PACs they remain relatively large and difficult to insert. The incidence of associated iatrogenic problems is significant

- There is no reliable index in children of the many variables measured by a PAC, thus limiting its use.

Indications/uses

- PACs are usually inserted in cardiac patients in order to measure PA pressures in patients with pulmonary hypertension
- Cardiac output is rarely measured (thermodilution) and is inaccurate in patients with intracardiac shunts
- The balloons on paediatric PACs are usually not inflated and pulmonary artery occlusion pressure (PAOP) is rarely measured in smaller children. PAOP (with balloon inflation) approximates to left atrial (LA) pressure. Direct LA pressure is generally preferred if LA pressure is desired (see 📖 p.80)
- Derived variables such as vascular resistance, ventricular stroke work index, and oxygen delivery and consumption are rarely used in PICU.

Practicalities

- The PAC is inserted through a large-bore cannula in a central vein (femoral is easiest in children)
- Paediatric sizes are available:
  - 7F (adult): for adolescents
  - 6F: >18kg
  - 4–5F: 10–18kg
  - 3F: <10kg
- Complications include infection, thrombus, bleeding, tamponade, PA rupture, and systemic air embolus with R-to-L shunts.

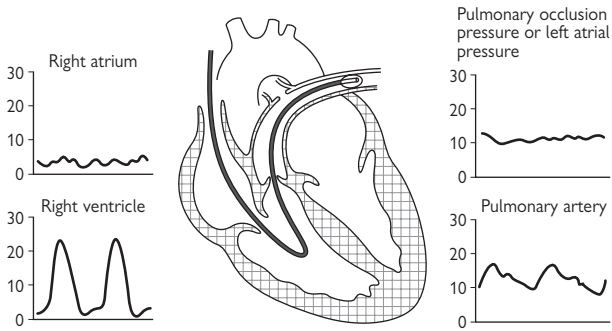

Fig. 6.10 The pressure waveforms encountered during insertion of a pulmonary artery catheter.

Direct pulmonary artery and left atrial pressure lines

Whilst it is almost mandatory that a postop cardiac patient has 1 or more CVP lines in place, occasionally patients with complex cardiac disease or at risk of pulmonary hypertension may have direct PA or LA catheters inserted through the PA or LA wall by the surgeon in the operating theatre. Pressure readouts and waveform give a rational basis for manipulating heart rate, intravascular volume, pulmonary and systemic vascular resistances, and myocardial contractility.

PA lines

- Monitor pulmonary hypertension, e.g:
  - Long term L to R shunts, e.g. atrioventricular septal defect (AVSD), truncus, unrepaired transposition with VSD
  - Newborn neonates—high pulmonary vascular resistance (PVR)
  - Pulmonary venous obstruction—total anomalous pulmonary venous drainage (TAPVD) or pulmonary vein stenosis
- Normal PA pressure in children is 10–20mmHg (mean 13mmHg)
- Mean PA pressure in ventilated postop cardiac patients is often >15mmHg but should be <25mmHg
- PA lines allow for saturation data that can identify residual L-to-R shunts.

LA lines

- LA pressure is unaffected by PA pressure and reflects left ventricular end-diastolic pressure. It is raised in:
  - Left ventricular failure secondary to myocardial dysfunction (e.g. from ischaemia or post bypass) or from outflow tract obstruction (pressure load) or aortic regurgitation (volume load)
  - Mitral regurgitation
  - Volume overload or massive L-to-R shunt.
- LA pressure is usually 1–3 mmHg higher than CVP (RA pressure)
- Normal LA pressure in ventilated postop cardiac patients is >6 mmHg and <14mmHg.
- Low LA pressure is caused by hypovolaemia (see Box 6.6 CVP vs LAP)
- LAP and CVP are elevated in cardiac tamponade.
- Raised LA pressure leads to pulmonary venous hypertension and pulmonary oedema by increasing hydrostatic pressure across the pulmonary capillary wall (see 🕮 p.240).

Box 6.6 CVP vs. LA pressure

In children with significant pulmonary hypertension CVP can be misleading. It may be raised secondary to raised PA pressure despite the patient being hypovolaemic. Consequently when the patient is hypotensive it can be difficult to know whether to give volume, increase inotropic support, or use pulmonary vasodilators. In this situation a low LA pressure is an indication for intravascular volume replacement despite a high CVP. Volume can be titrated in fluid challenges in exactly the same way as recommended for CVP (see 🕮 p.73) and pulmonary dilators or inodilators should be considered.

Precautions

- Complication rates from intracardiac catheters are 1–2 %, namely bleeding
- Try to remove LA and PA lines early, i.e. on day 1 or 2 post surgery
- Correct all coagulopathy (including platelets) before removal
- Keep at least 1 patent postop drain *in situ* in order to monitor bleeding when catheters are removed.

Skilled echocardiography and improved patient selection over recent years (i.e. before pulmonary hypertension becomes too severe) have reduced the need for PA and LA catheters.

Pulse oximetry

- The advent of pulse oximetry in the 1980s was a major medical advance. It now has widespread use in modern hospitals (but see Box 6.7 for limitations).
- Pulse oximetry gives a continuous measure of haemoglobin saturation with oxygen (SaO_2) and thus provides a useful monitor of patient oxygenation (see Box 6.8).

Principles

- Pulse oximeters combine the principles of plethysmography and oximetry to non-invasively measure oxygen saturations. A pulse oximeter transmits 2 different wavelengths of light (660 and 940nm), both of which have different absorption spectra for oxygenated and deoxygenated haemoglobin
- A light-emitting diode transmits light through an arterial bed such as the finger, earlobe, or toe. A microprocessor subsequently compares the absorption of the 2 waveforms to determine the ratios of oxygenated and deoxygenated haemoglobin, thus giving a percentage saturation of haemoglobin with oxygen.
- Most modern pulse oximeters will display a waveform, pulse rate, and oxygen saturations.

Box 6.7 Limitations of pulse oximetry

- Pulse oximeters have been calibrated using normal patients and as a result have a high potential for error at low saturations
- This is particularly important in patients with cyanotic congenital heart disease. If in doubt, accurate saturations can be obtained from co-oximeter-containing blood gas machines (some gas machines calculate SaO_2 from PO_2, which cannot be relied upon)
- Carboxyhaemoglobin (smoke or fume inhalation) and methaemaglobin (from nitric oxide use) can provide falsely high oximetery saturations. Again, many modern blood gas machines can exclude these haemaglobinopathies
- Poor perfusion, nail varnish, ↑ambient light, motion artefact, as well as venous pulsation in, for example, severe right AV-valve regurgitation can all be sources of errors in pulse oximetry
- Heat from the light source can cause burns if the probe is not moved from time to time
- Further uses of pulse oximetry technology are continuous mixed venous oxygen saturations ($ScvO_2$) and non-invasive cerebral oximetry.

Box 6.8 SaO_2 versus PaO_2

In several ways continuous SaO_2 monitoring is a more useful measurement in PICU than PaO_2:

- SaO_2 is measured continuously and gives an overall picture of patient oxygenation rather than the 'snapshot' PaO_2 which can be misleading and is dependent upon on the condition of the child when the sample is taken (i.e. crying following physiotherapy, arterial pressure, or handling etc.)
- Pulse oximetry (and capnography) avoids the need for repetitive blood sampling
- SaO_2 is a major determinant of oxygen delivery (see 🕮 Box 6.9, p.86):

$$\text{Oxygen delivery} = (SaO_2/100 \times Hb \times 1.34) \times (\text{cardiac output})$$

- Thus, if cardiac output and Hb are adequate (i.e. the child has a normal BP and Hb >7g/dL) then one can be confident in letting the SaO_2 fall to 90% without compromising oxygen delivery too much. This allows one to confidently reduce potentially damaging levels of FiO_2 and ventilator pressures whilst maintaining oxygen delivery to the patient's vital organs.
- PaO_2, on the other hand, tells us about how well the lungs are working at uptaking O_2 but not about oxygen delivery. PaO_2 is particularly useful in the context of the alveolar gas equation, allowing the calculation of the alveolar-arterial difference (see 🕮 p.118). This is a useful index of lung function.

Transcutaneous oxygen and carbon dioxide measurement

- Transcutaneous oximetry ($TcPO_2$) is a useful non-invasive way of measuring oxygen levels without the need for repeated blood gas analysis.
- Transcutaneous carbon dioxide ($TcPCO_2$) monitoring is also a useful way of measuring CO_2. It is more widely used in neonatal intensive care, and has been shown to be particularly useful in neonatal transport where repeated blood gas analysis is not freely available
- A sensor is placed on a cleaned area of skin and requires an airtight collar to ensure no ambient oxygen leaks into the sensor membrane.
- The sensor detects oxygen emanating from the skin, as it flows through the membrane an electrochemical current results which is then converted into a number on the monitor
- Transcutaneous monitors can be unreliable and vary with skin perfusion, BP, and quantity of subcutaneous fat or oedema.

Capnography

- Capnography provides continuous non-invasive measurement and graphical representation of expired carbon dioxide tension
- End-tidal carbon dioxide ($EtCO_2$) is defined as the peak CO_2 value during the expiratory phase of ventilation and approximates arterial pCO_2 in patients with normal hearts and lungs, thereby providing a useful non-invasive assessment of ventilation
- Capnography is the simplest and most reliable way to confirm correct tracheal tube placement following intubation and is mandatory on all PICUs
- Examination of the phasic changes in capnography can aid diagnosis (Fig. 6.11).

Principles

- Capnography relies on the principle of infrared spectroscopy
- When infrared light is shone through a chamber of CO_2, the amount of light absorbed by the CO_2 is proportional to the partial pressure of CO_2 in the chamber
- A capnograph consists of a sample chamber, a light source, and a photodetector opposite the light source, although disposable CO_2 detectors are available
- The capnograph is usually placed between the ETT and the expiratory limb of the ventilator tubing, ideally as close to the end of the ETT as possible.

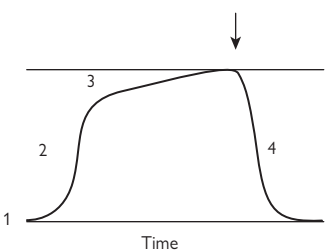

Fig. 6.11 A normal capnography trace. Phase 1: early expiration. Mainly dead space. Phase 2: rapid rise in CO_2 from alveolar gas. Phase 3: plateau phase. Slope of phase varies with airway obstruction. Phase 4: inspiration and rapid fall on CO_2. Arrow indicates the end-tidal value.

Table 6.2 Conditions that alter $EtCO_2$

Increases in $EtCO_2$	• Hypoventilation or ↑CO_2 production, i.e. fever, malignant hyperpyrexia, and catabolism
Decreases in $EtCO_2$	• ↓CO_2 production, i.e. hypothermia • ↓cardiac output • Pulmonary embolism • Air embolism • ↓pulmonary perfusion
Absent $EtCO_2$	• Oesophageal intubation • Disconnection from ventilator

Because end-tidal CO_2 approximates $PaCO_2$, ($EtCO_2$ generally reads as slightly less than $PaCO_2$), capnography allows alveolar ventilation to be monitored continuously in patients. This can be both during IPPV or when breathing in weaning modes on a ventilator. This is particularly useful as it gives an overall picture of ventilation rather than the 'snap-shot' that one gets from intermittent blood gas measurement.

- Recognition of changes in the capnogram is a useful tool in the management of ventilated patients (see Fig. 6.12).

Point to remember:

Right-to-left intracardiac shunts produce a discrepancy between $EtCO_2$ and $paCO_2$. The $paCO_2$ tends to rise above the $EtCO_2$. This is sometimes referred to as an 'apparent dead space'.

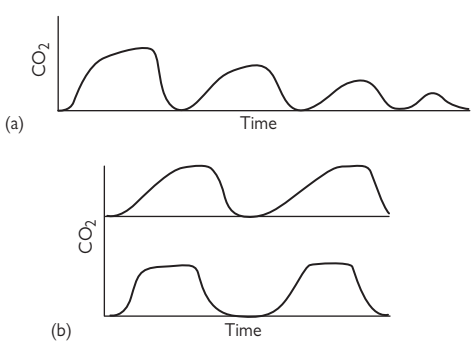

Fig. 6.12 (a) A decrease in the size of successive capnograms is seen with a rapid decrease in pulmonary perfusion secondary to sudden hyptotension or cardiac arrest. (b) The slow rise of the capnogram in the upper panel is seen with bronchospasm. The improved capnogram in the lower panel is after bronchodilator therapy. Reproduced from Hughes J, Ali T (2004). Understanding simple monitoring in paediatric intensive care. *Current Paediatrics* **14**: 459–64, with permission of Elsevier.

Measurement of oxygen delivery and consumption (oxygen flux)

All cells require a constant supply of oxygen to maintain metabolic demands and cellular function. Situations such as shock, as defined by oxygen demand exceeding supply, can result in organ dysfunction and failure (see 📖 p.576). Early detection and correction of tissue hypoxia is fundamental in the management of critically ill patients.

Oxygen delivery (DO_2) from atmosphere to body cells requires the following:

- Inspired O_2 diffuses across the alveolar membrane into the blood
- O_2 combines reversibly with haemoglobin in red blood cells
- Bound O_2 is delivered by cardiac output to the tissues.
- At the target tissue O_2 dissociates from the haemoglobin, diffuses into the cells and ultimately reaches the mitochondria where it is utilized to supply energy.

Box 6.9 Determinants of oxygen flux

- The amount of oxygen delivered to the tissue can be calculated from:

  Oxygen delivery (DO_2) = CO x CaO_2

  where CO is the cardiac output and CaO_2 is the oxygen content of arterial blood.

  Cardiac output = stroke volume x heart rate

  $$CaO_2 = [\frac{SaO_2(\%)}{100} \times Hb \times 1.34] + dissolved\ O_2$$

  (1.34 is the volume of oxygen in mL that combines with 1g of Hb. Dissolved O_2 is calculated from $0.0031 \times PO_2$ and is negligible at normal atmospheric pressure).

- Global oxygen consumption (VO_2) is the amount of oxygen consumed by tissues per minute and can be defined by:

  Oxygen consumption (VO_2) = CO x [CaO_2 – CvO_2]

  where CvO_2 is the oxygen content of mixed venous blood.

  $$CvO_2 = [\frac{SvO_2(\%)}{100} \times Hb\ concentration\ x\ 1.34]$$

One can see that the important determinants of DO_2 are cardiac output, SaO_2 and haemoglobin concentration**.**

Example

Thus, theoretically (and rather simplistically) for a child of 10kg with a cardiac output of 1.2L/min, Hb 15g/dL, SaO_2 of 100%; and SvO_2 75% then:

$CaO_2 = 100/100 \times 15 \times 1.34 = 20.1mL/dL$

$CvO_2 = 75/100 \times 15 \times 1.34 = 15mL/dL$

Box 6.9 Determinants of oxygen flux (*Continued*)

Thus the arteriovenous oxygen difference is ($AVDO_2$) is 5mL/dL.

Correcting units to mL then:

$DO_2 = 1200 \times [1 \times 15/100 \times 1.34] = 240$mL/min

$VO_2 = 1200 \times [20.1/100 - 15/100] = 60$mL/min

Thus oxygen consumption is 6 mL/kg/min (this is usually 7–9mL/kg/min in neonates and 3–4mL/kg/min in adults)

Global measurements of DO_2 and VO_2

- PAC (also see Box 6.10):
  - Arterial CaO_2 and mixed venous CvO_2 (from the PA) are measured from samples and multiplied by the measured cardiac output (indirect Fick principle) to give DO_2 and VO_2
  - Therapy (e.g. inotropes and transfusion) can be titrated in order to maximize VO_2
  - DO_2 and VO_2 can be plotted and oxygen extraction ratio calculated (OER).

Box 6.10 Game over for the PAC?

Several large, recent multicentre trials of the use of PACs in adult ICU have failed to show an improvement in mortality in sepsis, ARDS, and heart failure. This information coupled with the difficulty in insertion and the potential side effects mean that there are few indications for PAC insertion in children.

- Indirect calorimetry:
  - O_2 content of inspired and expired gases are compared and O_2 consumption (and CO_2 production) calculated
  - Readings are often inaccurate due to leaks in circuit and around ETTs
  - More useful for guiding nutritional therapy (from resting energy expenditure) than for guiding DO_2.

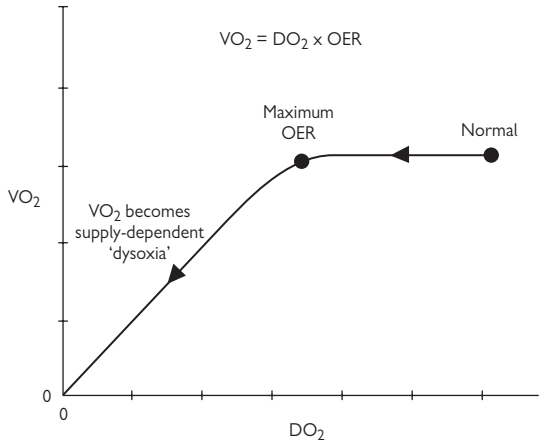

Fig. 6.13 Graph of DO_2 versus VO_2 with explanation of OER (oxygen extraction ratio). As DO_2 decreases, the OER increases proportionately and the VO_2 remains constant. When the OER reaches its maximum level (0.5–0.6), further reduction in DO_2 leads to a proportional decrease in VO_2. VO_2 becomes supply dependant and production of adenine triphosphate (ATP) is limited by the supply of oxygen. This condition of oxygen-limited energy reduction is called dysoxia.

Indirect global estimates of DO_2 and VO_2

In PICU the easiest and least invasive ways of estimating the balance between delivery and consumption are to measure:

- Mixed venous saturation ($ScvO_2$)
- Lactate production.

Mixed venous saturation ($ScvO_2$)

- Central mixed venous saturations are a simple and useful indirect measure of oxygen delivery and consumption
- $ScvO_2$ <70% is generally indicative of reduced oxygen delivery and hence ↑oxygen extraction leading to ↓venous oxygen content (see Table 6.3). This is seen in shock states such as cardiogenic, hypovolaemic, and septic shock
- Aiming for $ScvO_2$ >70% is accepted as a goal for therapy
- 'True' $ScvO_2$ measurements should come from the PA after complete mixing of superior and IVC blood and coronary sinus blood has occurred. Unfortunately without a PAC or a direct PA line 'true' $ScvO_2$ sampling is not possible
- $ScvO_2$ taken from a central line is an valuable alternative:
  - IVC $ScvO_2$ is usually slightly higher than SVC $ScvO_2$ (the kidneys do not extract as much oxygen but receive a higher proportion of cardiac output than the brain and upper body) but in shock it may read lower as blood is diverted from the splanchnic and renal circulations to the brain and heart.
  - These regional differences mean that trends are often more useful to follow than absolute values.

Table 6.3 $ScvO_2$ changes and their causes

$ScvO_2$	Cause	Diagnosis
↓$ScvO_2$	• ↓DO_2 (↑OER) • ↑VO_2	• Shock: cardiogenic, hypovolaemic, septic • Hypoxia • Severe anaemia • Fever • Thyrotoxicosis
↑$ScvO_2$	• ↓VO_2	• Cytotoxic hypoxia-cyanide poisoning

Lactate measurement

- Analysers are available to measure lactate. Often this measurement is incorporated into blood gas analysis
- Normal whole blood lactate is <2mmol/L
- Lactate levels are raised in tissue hypoxia and shock states (hypovolaemic, cardiogenic, septic) (see Box 6.11)
- Raised lactate predicts risk of mortality and adverse events in children with sepsis and following cardiac surgery
- Trends in lactate are useful:
  - A gradual and continuous decrease in blood lactate level during resuscitation is usually associated with a better outcome.
  - Persistent increase in blood lactate is associated with progressive multiorgan dysfunction and poor outcome
  - High-dose epinephrine, through combined vasoconstriction and hypermetabolism can cause significantly raised lactate
- Raised lactate is not a sensitive measure—many children deteriorate with normal lactate
- Lactate itself is a buffer—situations of hyperlactataemia may develop (e.g. during haemofiltration) without concurrent acidosis.

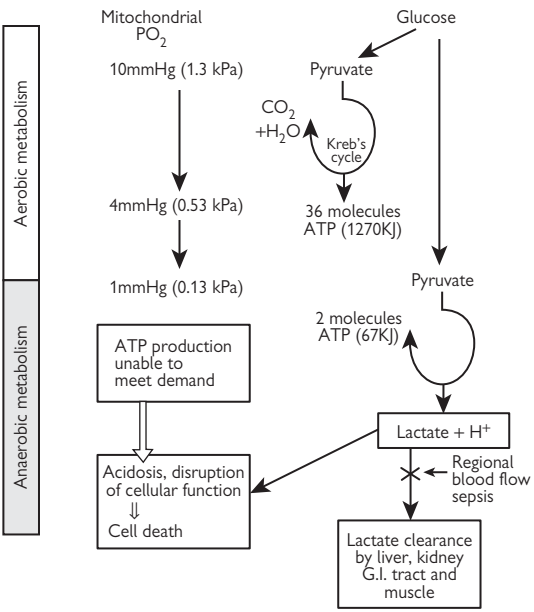

Fig. 6.14 Diagram of glycolysis and Kreb's cycle. Adapted from Duke T (1999). Dysoxia and lactate. *Arch Dis Child* **81**: 343–50 with permission from BMJ Publishing Group Ltd.

Box 6.11 Biochemistry of lactate production

- Cells require oxygen for continuous production of ATP—the body's principal energy source
- Glucose is metabolized to pyruvate (*glycolysis*). Most of this is metabolized (by *pyruvate dehydrogenase*) to acetyl CoA, the major substrate of *Kreb's* cycle which results in ATP production (Fig. 6.14).
- This process occurs in cell mitochondria and is called *oxidative phosphorylation*. It consumes oxygen and generates CO_2 (*aerobic* cell respiration)
- 1 molecule of glucose produces 36 molecules of ATP.
- In situations of mitochondrial dysfunction (*hypoxia* and *sepsis*), anaerobic metabolism increases and pyruvate is converted to ***lactate.*** This generates significantly less ATP (2 molecules per molecule of glucose) and H^+ ions are produced leading to acidosis
- *Dysoxia* refers to when ATP production is limited by hypoxia. Often with accompanying lactic acidosis
- If hypoxia is reversed before cell death occurs then oxygen radicals are generated which cause lipid peroxidation and cell damage. This is known as *reperfusion injury* and can cause *systemic inflammatory response*
- Lactate can be cleared efficiently by the liver (and kidney, gut, and muscle). Lactate can be converted into glucose (Cori cycle)
- Lactate levels therefore depend on:
  - Lactate production: raised in states of ↑anaerobic metabolism or aerobic hypermetabolism
  - Lactate clearance: reduced in shock states
- Lactic acidosis occurs when lactic acid production is in excess of removal
- Certain drugs that interfere in gluconeogenesis cause lactic acidosis, e.g. metformin, salicylates, ethanol, methanol, ethylene glycol (antifreeze)
- Raised lactate can be secondary to congenital mitochondrial disease (see 🕮 p.701).

Management of raised lactate

- Optimize oxygen delivery:
  - Maintain SaO_2. IPPV, Paralyse.
  - Maintain circulating volume and cardiac output. Use fluid boluses. Start inotropes if indicated. Monitor invasive BP, CVP, urine output and arterial gases
  - Keep Hb >7g/dL
- Treat underlying cause, e.g. antibiotics, surgery if indicated
- If lactate is rising or persistently elevated, e.g. >5 mmol/L:
  - Consider reducing epinephrine and substituting dopamine
  - Start inodilator milrinone
  - ***Has ischaemic/necrotic/perforated bowel been excluded?***
  - Consider ECMO.

Organ-specific measurements of oxygen delivery and consumption

- Brain oxygen consumption can be measured and optimized with use of the jugular venous bulb saturation ($SjvO_2$), (see 📖 p.101)
- Cerebral oxygen extraction ratio = $SaO_2 - SjvO_2/SaO_2$.
- Positron emission tomography, near infrared spectroscopy, and tissue microcatheters and sensors are all very much in the developmental stage.

Electroencephalography and cerebral function monitoring

EEG

The EEG records cortical electrical function via scalp electrodes and thus gives useful information about cerebral function, particularly when a patient is sedated and/or paralysed with muscle relaxants.

- EEG readings are dependent on cerebral perfusion and oxygenation
- Seizure activity is evident on EEG
- EEG may aid with diagnosis:
  - Encephalopathy—EEG activity alters.
  - Movement disorders can be distinguished from seizure activity
  - Electrocerebral silence in the absence of sedation confirms brain death (cortical).
- Drugs, e.g. barbiturates, can be titrated against EEG to reduce cerebral metabolic activity (burst suppression) in head injury or hypoxic states

Children's EEGs require interpretation by expert neurophysiologists. Generally the paediatric EEG is characterized by bursts of slower rhythm (which become more infrequent with adulthood). Brain injury and encephalopathy are associated with slower rhythm (frequency) and smaller amplitude.

Whilst continuous EEG recording are possible on PICU, simplified systems have been developed (usually involving less scalp electrodes) to give continuous recordings. These are known as cerebral function (analysing) monitors (CFM/CFAM).

CFM

- Usually recorded from a pair of scalp electrodes (occasionally a midline reference electrode is used
- Cumulative voltage is displayed in a single trace
- Voltage (μV) is displayed against time (6–30cm/h).

CFM allows for 'coarse interpretation' by the intensivist. Normal variable traces can be recognized as can seizure activity, burst suppression, and poor prognostic patterns. CFM gives no information regarding frequency distribution of the EEG activity. Subsequent innovations have given crude estimates of the percentage contribution of various frequencies known as CFAM.

Use of CFM

- Sedation causes a fall in baseline voltage (see Box 6.12)
- A fall to <5μV with sedation (thiopentone) corresponds with minimal brain metabolic activity (equivalent to burst suppression)
- Seizure activity causes paroxysmal increases in baseline voltage
- Diagnosis:
  - Prolonged periods of electrical inactivity are associated with ischaemia (burst suppression)
  - Several different patterns are associated with poor prognosis (see 📖 Fig. 6.15 p.94).

Box 6.12 Bispectral index (BIS)

BIS is a recently developed form of processed EEG that assesses sedative/hypnotic effects of sedative and anaesthetic agents on a scale of 0–100.

- BIS can be used clinically to measure sedation and has been validated in adults (mainly undergoing surgery)
- BIS has been used in PICU but as yet cannot be relied upon as a sedation monitor.

Evoked potentials

EEG responses to external stimuli can be detected to infer integrity of relevant pathways e.g.:

- Somatosensory—peripheral, spinal, and cortical nerve conduction may be assessed following trauma
- Auditory and visual evoked potentials assess hearing and visual pathways and are rarely used in PICU.

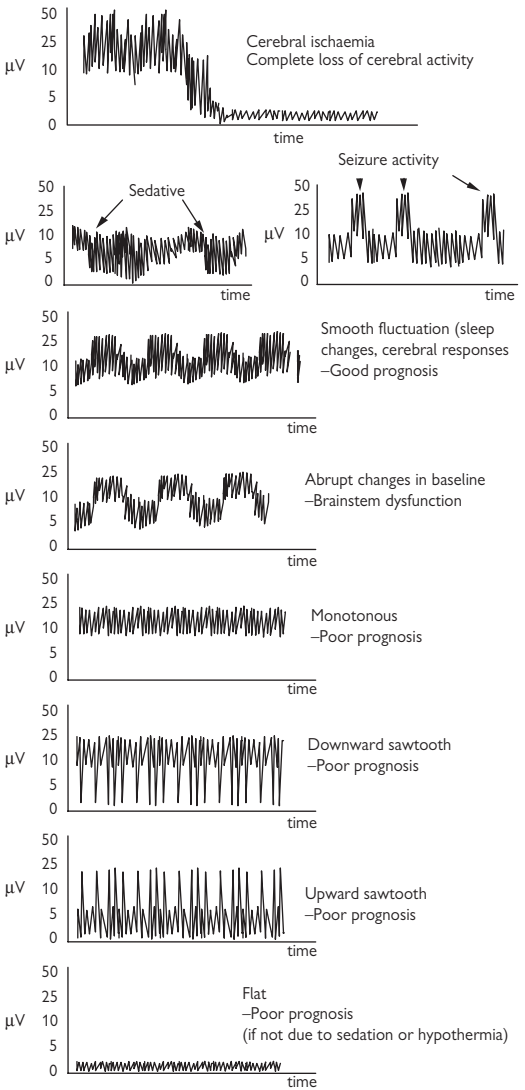

Fig. 6.15 Waveforms of CFM. Reproduced from Singer M, Webb AR (2009). *Oxford Handbook of Critical Care*, 3rd edn. Oxford University Press.

Intracranial pressure monitoring

The measurement of ICP has become routine in many PICUs, particularly in those dealing with head trauma and neurosurgery. ICP monitoring (ICPM) requires a certain level of expertise in both insertion and management and can only be recommended when there is neurosurgical expertise in close vicinity. Despite the absence of class 1 evidence demonstrating the benefit of ICP measurement on outcome, there is a large body of clinical evidence supporting its use in guiding treatment, detecting mass lesions, and assessing prognosis.

ICP is monitored in order to:
- Confirm the diagnosis of raised ICP
- Monitor ICP response to therapeutic manoeuvres
- To maintain cerebral perfusion pressure.

Indications
- Head injury
- Post neurosurgery
- Intracranial haemorrhage
- Encephalopathy (occasionally).

Intracranial pressure monitoring is contraindicated by coagulopathy (INR >2 or thrombocytopenia).

Methods
- There are 2 methods commonly used for ICPM (compared in Table 6.4):
  - Intraventricular catheter: inserted into the lateral ventricle via a burr hole
  - Intraparenchymal microtransducer tipped catheter (can also be used subdurally): incorporating fibreoptic technology (Camino®) or semiconducting strain gauges (Codman®)
- If the ventricles are accessed during neurosurgery then an intraventricular catheter may be inserted and left in for postoperative care. This allows for easy direct measurement via a transducer or by connection to a reservoir of CSF. The reservoir can be adjusted in height (e.g. 10–15cmH_2O) to allow for drainage of CSF and control of ICP (see Fig. 6.16)
- Generally intraparenchymal catheters are easier to insert in closed head injury when the ventricles are often very compressed. This is easily done under local anaesthetic on PICU in a ventilated patient. A small burr hole is required and the transducer should be tunnelled to a distant insertion site (5cm) in order to reduce risk of intracranial infection

Complications
- Infection
- Haematoma.

Table 6.4 Comparison of ICPM devices

Method	Advantages	Disadvantages
Intraventricular	• Gold standard • Allows CSF drainage • Measures global pressure • Can be recalibrated *in vivo*	• Difficult to insert. • Higher incidence of infection and haematoma.
Intraparenchymal	• Robust • Simple insertion • Low infection rate • Low complication rate	• No *in vivo* re-calibration and tendency for the measurement to drift • Measures local pressure: pressure may appear normal whilst ICP is globally high

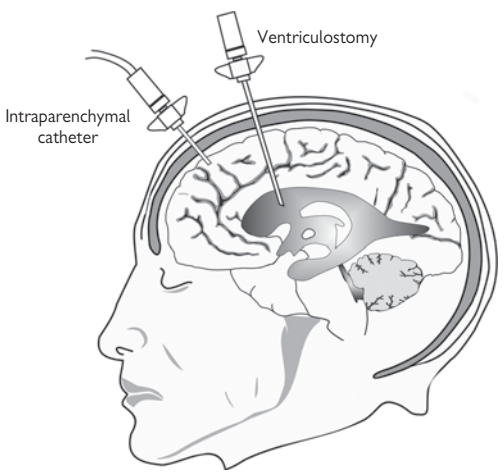

Fig. 6.16 Placement of ICPM. Reproduced from Waldmann C, Soni N, Rhodes A (2008). *Oxford Desk Reference: Critical Care.* Oxford University Press.

Box 6.13 ICP

The principles of ICP changes outlined by professors Munro and Kellie in the 1820s, were in essence, that (after the first few months of life when skull structures have fused) the skull is a rigid case of bone enclosing the brain. Therefore the contents of the skull must stay in constant volume to maintain constant pressure. The intracranial cavity contains 3 compressible components—the brain, the blood, and the CSF—an increase in the volume of one component will lead to the reduction in the volume of the other or a rise in ICP will result.

Component	% of volume	Cause of expansion in volume
Brain	83%	Tumour, tissue oedema, abscess
Blood	6%	Vasodilatation, haemorrhage, venous obstruction, aneurysm, AV malformation
CSF	11%	Hydrocephalus

As brain tissue is relatively incompressible, any increase in ICP due to brain swelling leads to an extrusion of CSF and venous blood from the intracranial cavity as compensation.

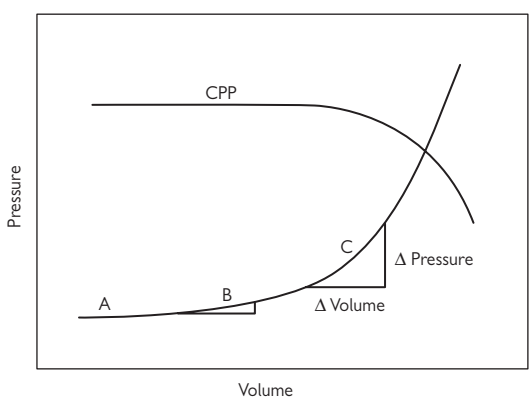

Fig. 6.17 The relationship between intracranial volume and intracranial pressure. As brain swelling occurs, a fixed increase in volume leads to a progressively greater increase in pressure, and cerebral perfusion pressure (CPP) falls. Reproduced from Webb A *et al.* (1999). *Oxford Textbook of Critical Care*, Oxford University Press.

ICP-guided therapy

ICP varies with age, position, and brain condition (see Box 6.13 and Fig. 6.17). Normal ICP is 7–15mmHg in a supine adult, <10mmHg in children, and <6mmHg in infants. In adults the threshold for initiating treatment is >20mmHg.

Whilst increasing ICP correlates with a higher risk of mortality and morbidity this does not mean that all patients with high ICP have a poor outcome.

Cerebral perfusion pressure (CCP)

CPP is the difference between the mean arterial pressure (MAP) and the mean ICP. Thus:

$$CPP = MAP - ICP$$

Reductions in CPP below threshold levels are associated with poor outcome in traumatic brain injury (see Box 6.14).

CPP thresholds vary with age:
- 40–50mmHg in infants and toddlers
- 50–60mmHg in children
- 60–70mmHg in adolescents

CPP can be sustained above threshold values by:
- Maintaining MAP—with attention to fluid balance and use of pressor agents, e.g. norepinephrine
- Reducing ICP:
  - *First tier*: sedation, analgesia, paralysis, head-up tilt (30°), CSF drainage (if ventriculostomy drain present), mannitol, hypertonic saline
  - *Second tier*: barbiturate coma (thiopentone), decompressive craniectomy.

Box 6.14 CPP vs ICP-directed therapy

Whilst traditional management of traumatic brain injury was aimed at reducing ICP, there has been a move in the past decade towards maintaining CPP above threshold levels. Both endpoints have their advocates but currently there is no evidence to suggest one over the other. High CPP (>upper threshold limit for age) should be avoided. There is some evidence that overelevated CPP may result in worsening vasogenic cerebral oedema and pulmonary oedema.

Cerebral blood flow (CBF) (Fig. 6.18)

CBF is tightly regulated to meet the brain's metabolic demands. Too much CBF results in raised ICP and too little results in ischaemia. The brain, like other organs, displays autoregulation. This maintains CBF over a range of BPs. When autoregulation is lost, CBF becomes pressure dependent and varies linearly with BP.

Autoregulation is lost under following circumstances:
- Severe hypotension: low CBF and CPP leads to ischaemia

- Acute, severe hypertension: high CBF and CPP disrupts the blood–brain barrier leading to cerebral oedema and ischaemia
- Trauma
- Cerebral hypoxia
- Seizures

Hypercapnia and hypoxia

- CBF (and consequently ICP) varies directly with $PaCO_2$:
  - CO_2 diffuses across the blood–brain barrier causing a fall in brain pH and subsequent vasodilation
  - The relationship between $PaCO_2$ and CBF is almost linear. A $PaCO_2$ of 10.6kPa almost doubles CBF
  - The effect is rapid and sudden acute rises in $PaCO_2$ can cause sudden rises in ICP. This should be avoided in situations of raised ICP
  - Conversely, reductions in $PaCO_2$ following hyperventilation can lead to falls in ICP but this effect does not last for more than a few hours
- CBF stays constant over a range of PaO_2 (including hyperoxia and moderate hypoxia) but below 6kPa vasodilatation and ↑CBF (and consequently ↑ICP) occurs.

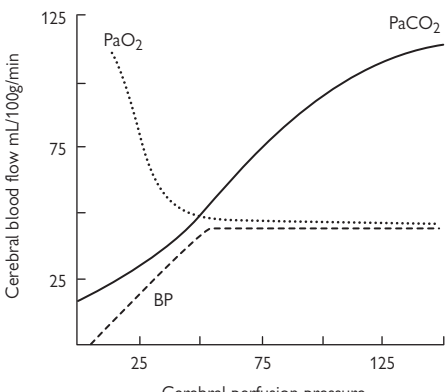

Fig. 6.18a Cerebral blood flow (CBF) alterations as a result of changes in $PaCO_2$, PaO_2, and cerebral perfusion pressure. Notice that CBF is relatively constant with perfusion pressure between 50–150mmHg, is increased as PaO_2 drops below ~50mmHg and is related linearly to $PaCO_2$ in the normal range of $PaCO_2$. Reproduced from Rogers MC, Traystman RJ (1985). An overview of the intracranial vault: physiology and philosophy. *Crit Care Clin* **1**: 199, with permission from Elsevier.

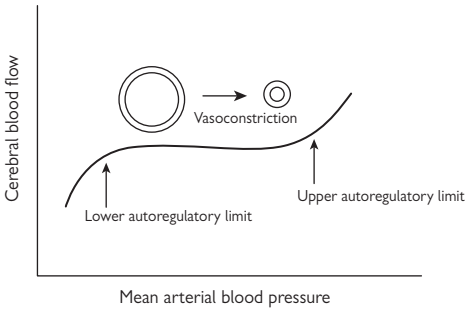

Fig. 6.18b Autoregulation of cerebral blood flow with arterial blood pressure.

ICP waves

- ICP varies with intrathoracic pressure—the baseline of the ICP trace will increase with positive pressure ventilation but fall with spontaneous inspiration
- ICP waves are complex but can be grouped into 5 distinct patterns:
  - *Low and stable ICP* (<20mmHg): uncomplicated head injury before brain swelling occurs
  - *High and stable* ICP (>20mmHg): seen commonly in head injury
  - *Slow plateau* rises in ICP lasting 5–20min: these are known as 'A' waves and are a sign of reduced intracranial compliance
  - ICP waves that vary with arterial pressure
  - Refractory high pressure trace that usually heralds death.

Jugular bulb oximetry

Retrograde passage of a fibreoptic oximetry probe from the internal jugular vein to the jugular bulb enables continuous monitoring of jugular venous bulb saturation ($SjvO_2$).

Insertion of $SjvO_2$ probes requires a degree of skill and is not recommended in smaller children.

- Normal $SjvO_2$ is 65–70%
- With normal oxygen delivery (absence of anaemia and normal SaO_2):
  - $SjvO_2$ >75% reflects luxury perfusion (hyperemia) or global infarction with reduced oxygen utilization
  - Falling $SjvO_2$ reflects ↑oxygen extraction
  - $SjvO_2$ 40–55% reflects hypoperfusion
  - $SjvO_2$ reflects global brain ischaemia
- Despite 85% of brain venous drainage passing down one internal jugular vein (usually the right), $SjvO_2$ is usually equal on both sides unless there is a specific focal injury
- Samples can be taken to measure venous lactate
- Cerebral oxygen extraction ratio = $(SaO_2 - SjvO_2)/SaO_2$.

Management

Falling $SjvO_2$ may be an indication to:

- Increase CPP by increasing MAP or reducing ICP
- Increase DO_2 by transfusing blood.

Box 6.15 New technologies

Despite enthusiastic attempts to introduce new technologies into monitoring the brain, the measurement of ICP has become established as a robust and minimally invasive form of monitoring that can be realistically used on many PICUs.

New technologies include:

- Positron emission tomography: used for quantification of cerebral blood volume, CBF, brain oxygen consumption, and oxygen extraction. Calculations may be subject to mathematical coupling
- Transcranial Doppler ultrasound: looks at blood flow velocities in cerebral arteries. Used to assess vasospasm or hyperaemia and to assess whether autoregulation is still intact. Not useful as a gauge of cerebral oxygenation
- Near infrared spectroscopy: utilizes the absorption and reflection spectra of haemoglobin (oxy- and deoxy-) and cytochrome oxidase to determine cerebral oxygenation, oxygen consumption, and CBF. Near infrared wavelengths can penetrate thin bone and thus its use has been mostly in premature neonates with thin skulls
- Implantable tissue oxygen and pH sensors
- None of the these technologies have been fully validated in the PICU setting and as such are generally used as research tools.

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Chapter 7

Applied physiology and bedside assessment

Introduction

Assessment of cardiovascular and respiratory functions in paediatric intensive care patients requires a thorough understanding of the physiology and pathophysiology of both systems. Cardiovascular and respiratory systems are not only closely related but interdependant. Assessment of function should be interpreted in terms of their fundamental purpose, namely oxygen delivery and consumption.

Principles of cardiovascular physiology

The cardiac cycle

- Phase of contraction (*systole*): consists of phase of *isovolumic contraction* and *rapid ejection* when the arterial valve opens
- Phase of relaxation (*diastole*): consists of *isovolumic relaxation* and opening of the atrioventricular valve followed by filling. Atrial systole contributes to end-diastolic filling.

Blood pressure

BP = cardiac output × systemic vascular resistance (SVR)

- Low BP may be due to low cardiac output, low SVR or both
- BP is often normal (or slightly low) in situations of low cardiac output because the SVR rises. This is a compensatory response mediated via the sympathetic nervous system (the cold, clammy patient). Beyond maximal compensation BP will fall. This is seen in both hypovolaemic and cardiogenic shock
- In septic shock (warm shock), the SVR is low due to vasodilation.

Ventricular function

Ventricular performance is determined by both systolic and diastolic function—abnormalities of either can cause cardiac failure.

Cardiac output

Cardiac output = stroke volume (SV) × heart rate (HR)

SV falls in situations of both hypovolaemia and myocardial dysfunction and leads to fall in cardiac output.

Stroke volume

Systolic function determines SV which is in turn dependent on 4 factors. Low cardiac output may be caused by any combination of these factors:

- HR
- Preload
- Inotropy or contractility
- Afterload.

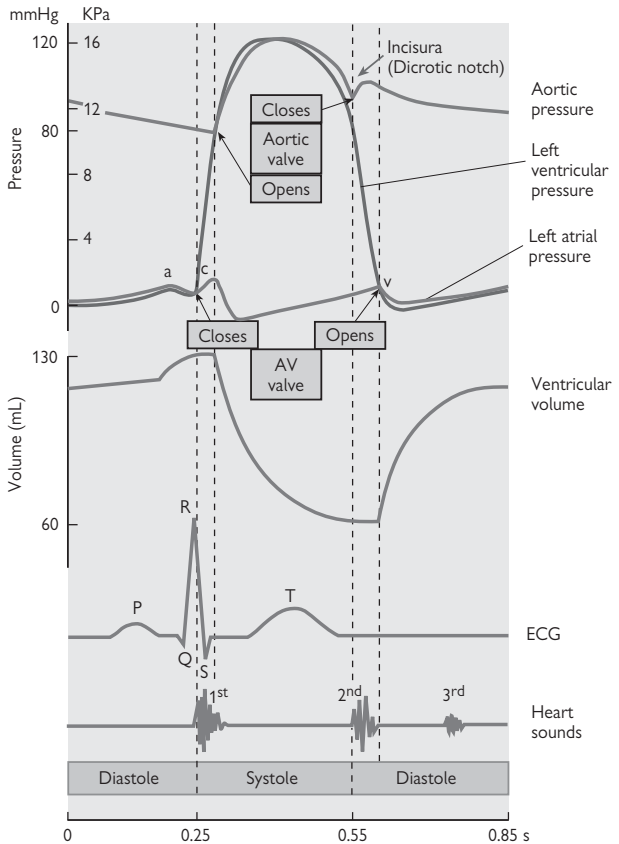

Fig. 7.1 The cardiac cycle. Reproduced from Pocock G, Richards, CD (eds) (2006). *Human Physiology: The Basis of Medicine*, 3rd edn. Oxford University Press.

Heart rate

- Tachycardia may compensate for a falling SV (again a sympathetic response) to a degree but, if excessive, may reduce ventricular filling time to a degree that worsens SV and hence cardiac output
- Severe bradycardia and tachyarrhythmias generally cause falls in cardiac output.

The Otto Frank and Ernest Starling Law of the Heart states 'the energy of contraction is a function of the length of the muscle fibre', therefore as ventricular filling (preload) increases, SV (and therefore cardiac output) increases. Due to its dependency on preload and afterload it follows that cardiac output is a crude index of ventricular performance.

Preload

- Preload is the passive force that stretches resting muscle fibres
- It represents end diastolic volume and is inferred from end diastolic pressure
- Preload depends upon:
  - Circulating blood volume (filling)
  - Venous tone
- For clinical purposes CVP and LAP provide an estimate of right ventricular and left ventricular preload, by acting as surrogates of RVEDP and LVEDP respectively
- Although CVP may be raised secondary to elevated right ventricular pressures, generally a low CVP equates to low preload and underfilling. In this instance volume loading will raise preload, hence cardiac output and thus blood pressure (see 📖 p.73).

Afterload

- Afterload is the force opposing ventricular ejection, i.e. the force opposing muscle fibre shortening
- An increase in afterload will increase myocardial work and reduce cardiac output
- Minimizing afterload can reduce ventricular stroke work (stroke work = SV × BP) and myocardial oxygen consumption. This can be an effective treatment for the failing myocardium. Reductions in SVR must be balanced against maintaining perfusion pressure (to other vital organs) and diastolic pressure (coronary perfusion) (see Box 7.1).

The systemic vascular resistance index (SVRi) and the pulmonary vascular resistance index (PVRi) are measures of the afterload of the systemic and pulmonary circulations respectively (indexed for weight).

SVRi = [MAP – CVP] / cardiac index

PVRi = [Mean PAP – LAP] / cardiac index

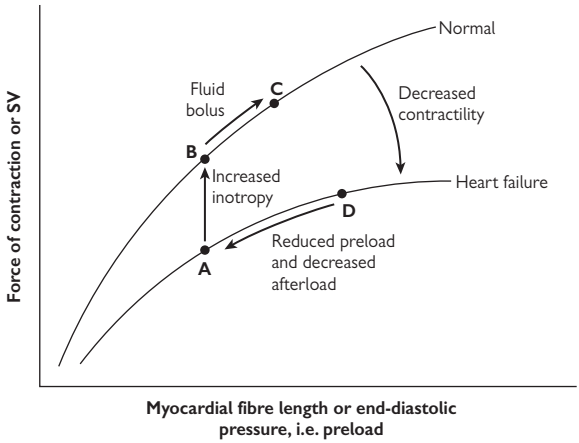

Fig. 7.2 Starling curves effect of filling and increased inotropy. Y-axis: force of contraction can be represented by cardiac output, SV, or stroke work. X-axis: myocardial fibre length can be represented by end-diastolic volume or end-diastolic pressure. A→B represents increased contractility from inotropic therapy. B→C represents a fluid bolus. D→A represents preload or afterload reduction by vasodilators and/or diuretics.

Box 7.1 Paediatric versus adult heart failure

In adults, myocardial dysfunction secondary to ischaemic heart disease is the usual cause of heart failure and pulmonary oedema. In children the usual cause of pulmonary oedema is high pulmonary blood flow (PBF) and ventricular volume overload due to left-to-right shunt. It seems rather illogical to describe a child's heart in this state as failing as it is often working very hard. In some cases of cardiac failure the heart is consuming so much energy there is little left for growth, leading to failure to thrive.

When myocardial dysfunction is severe, reductions in both preload and afterload can be achieved by positive pressure ventilation as well as by veno- and vasodilation.

Inotropy/contractility

- ↑inotropy provides ↑SV and hence cardiac output for the same preload and afterload conditions
- The net effect is an upward and leftward shift of the Frank–Starling curve
- Inotropes increase myocardial oxygen consumption and are often best combined with vasodilators to reduce preload and afterload to minimize this effect
- There is no adequate bedside measure for contractility. At best echocardiography gives a qualitative estimate of ventricular function (see 🕮 Echocardiography, p.341).

Ventricular performance and dysfunction

Pressure–volume (PV) relationship

- By plotting ventricular pressure against ventricular volume throughout the cardiac cycle, a pressure–volume loop can be constructed which can be used to provide objective information about the *compliance* of the ventricle and ventricular *contractility* and *arterial elastance*
- Fig. 7.3 shows the normal LV and RV pressure–volume relationships during a single cardiac cycle. The area within the PV loop is the *stroke work* whilst the width of the loop is the *SV*
- By constructing a series of PV loops under different conditions of preload and afterload, a series of loops can be obtained, from which a number of parameters can be derived (Fig. 7.4):
  - The slope of the end-diastolic PV curve gives information about the compliance of the ventricle
  - The slope of the end-sytolic PV curve is a measure of ventricular contractility
- Ventricular PV loops are not suitable as bedside tools but demonstrate the importance of systolic and diastolic contractility and compliance in myocardial performance.
- See also Box 7.2.

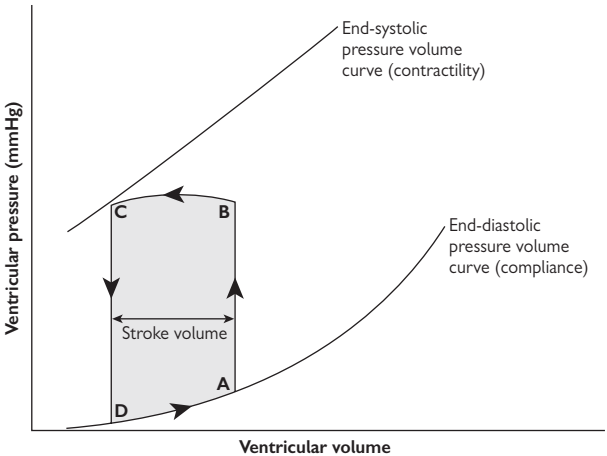

Fig. 7.3 Normal pressure volume relationship. During diastole the ventricle fills and pressure increases from D → A. Pressure then rises sharply from A → B during isovolumic contraction and from B → C during ventricular ejection. From C → D the aortic valve closes and pressure falls (isovolumic relaxation).

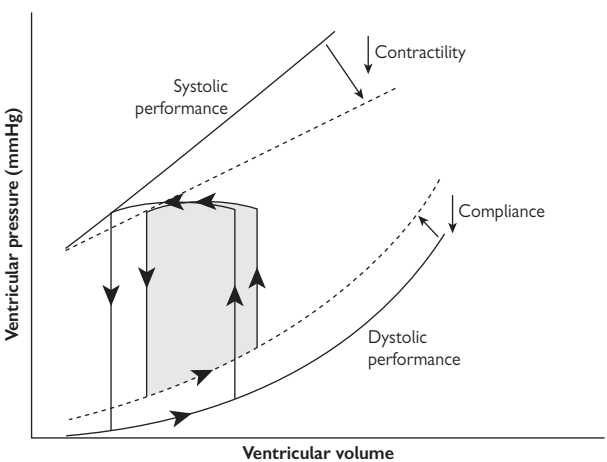

Fig. 7.4 Pressure valve curve with reduced contractility (systolic performance) and reduced compliance (diastolic performance).

Box 7.2 Diastolic dysfunction

Diastolic dysfunction is an increasingly recognized phenomenon both in children and adults. In cases of poor ventricular compliance, higher filling pressures will be required for a given end-diastolic volume. In classic cases of diastolic dysfunction, such as tetralogy of Fallot, higher filling pressures (CVP) may be required to ensure adequate ventricular filling. Additionally, positive pressure ventilation and tachycardia are less well tolerated as they reduce venous return and ventricular filling.

Cardiovascular function and age

Newborn hearts show functional immaturity. As infancy and childhood occur the myocardium develops.

- Neonates have limited inotropic reserve and stiff uncompliant ventricles. Their cardiac output and BP are dependent on circulating volume and they do not tolerate hypovolaemia well
- Sympathetic innervation of the neonatal heart is relatively undeveloped and relatively resistant to β-adrenergic catecholamines, e.g. adrenaline
- Both bradycardia and increases in afterload cause ↓cardiac output in neonates
- The neonatal left ventricle is non-concentric and is dependent on right ventricular and septal function.

Echocardiography

Echo can be used to provide an estimate of myocardial fibre shortening.

- M-mode echo can be used to estimate the fractional shortening of the left ventricular diameter, a one dimensional assessment (see 📖 p.341).

$$FS = \left[\frac{\text{LV end-diastolic diameter} - \text{LV end-systolic diameter}}{\text{LV end-diastolic diameter}}\right] \times 100$$

  - Normal fractional shortening is 28–44%
- 2D Echo can be used to estimate the ejection fraction of the ventricle, by estimating the fractional area change from 2 echo views

EF = [End-diastolic volume – end-systolic volume]/end-diastolic volume

$$EF = \left[\frac{\text{LV end-diastolic diameter}^3 - \text{LV end-systolic diameter}^3}{\text{LV end-diastolic diameter}^3}\right] \times 100$$

  - Normal ejection fraction is >65%.

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Cardiopulmonary interactions

The heart and lungs should be thought of as a single functional unit – the aim of this system is to optimize oxygen supply/demand relationship. Those who manipulate respiratory support in children with cardiac abnormalities or vice versa must understand the basis of this relationship.

Alterations in respiratory physiology due to congenital heart disease

Box 7.3 Physiology of interstitial and pulmonary oedema

(see 🕮 p.240)

The rate of filtration of fluid across a capillary bed depends on a balance of forces, sometimes called Starling forces. A hydrostatic pressure gradient (pressure within the capillary minus the pressure within the interstitial fluid) encourages fluid filtration into the interstitium whilst an osmotic pressure gradient across the capillary wall discourages it.

Any lesion that results in ↑intracapillary pressure may lead to interstitial oedema or even alveolar oedema if severe. Lesions associated with elevated pulmonary artery pressure but low/normal capillary pressure will not result in pulmonary oedema, e.g. hypoplastic pulmonary arteries.

Pulmonary congestion (Box 7.3)

May result from:

- ↑PBF due to a left-to-right (L→R) shunt
- Pulmonary venous obstruction as in TAPVD
- Pulmonary venous hypertension secondary to elevated LAP:
  - Mitral stenosis
  - Left ventricular failure

Effects can be:

- Ventilation–perfusion (V/Q) mismatch
- ↑shunt and hypoxia
- Increase in lung weight
- Airway obstruction with gas trapping
- ↑airway pressures (if ventilated).

These alterations can cause hypoxia, reduced lung compliance. Supporting these patients acutely should include oxygen therapy, diuresis, inotropic and vasodilator therapy. Some children may need positive pressure ventilation.

Decreased PBF

Due to right-to-left (R→L) shunts (e.g. tetralogy of Fallot), and/or ↓PBF (pulmonary atresia). Alterations in respiratory mechanics may be due to:

- V/Q mismatch (↑physiological dead space)
- Decrease in lung weight
- May develop airway hypoplasia →± ↑ airway resistance.

For reasons that are not clear, a sudden fall in PBF, e.g. during balloon dilation of pulmonary valve, results in a fall in lung compliance.

Alterations in cardiovascular physiology during mechanical ventilation

- The ***right ventricle*** is more sensitive to respiratory changes than the left. This is more apparent in children
- Increases in positive pressure leads to a reduction in venous return, and thus reduction in RV preload
- RV afterload can be manipulated by judicious use of ventilation; under or over expansion of the lung → ↑PVR → ↑RV afterload (Fig. 7.5)
- Ventilatory effects on both RV contractility and myocardial perfusion are more pronounced in cardiac disease and postoperative states
- In the setting of severe restrictive right ventricular physiology following tetralogy of Fallot repair, positive pressure ventilation is poorly tolerated:
  - Aim to wean ventilation relatively quickly if possible
  - Negative pressure ventilation has been used successfully
- CPAP and positive pressure ventilation both reduce ***left ventricular*** afterload. In children with LV dysfunction one should aim to optimize oxygenation, reduce mean airway pressure (to augment preload), and maintain positive pressure ventilation to reduce LV afterload.

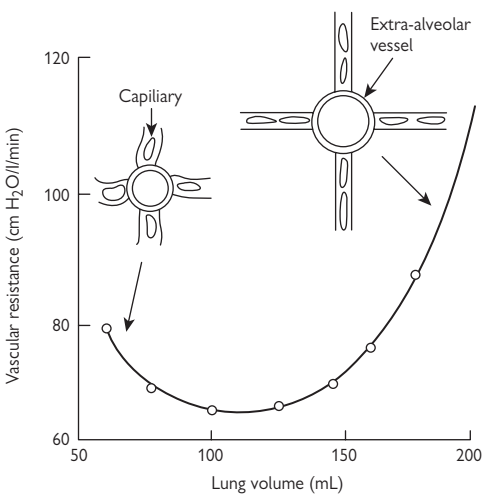


Fig. 7.5 The relationship between lung volume and pulmonary vascular resistance. Reproduced from West JB (2008). *Respiratory Physiology: The Essentials*, 8th edn. Lippincott Williams & Wilkins with permission.

Assessment of pulmonary function

The various causes of hypoxaemia and hypercapnia can be distinguished by a thorough understanding of the underlying pathophysiology. For sake of simplicity and interpretation pulmonary function can be divided into 2 major components:

- Pulmonary gas exchange
- Respiratory mechanics.

Pulmonary gas exchange

Arterial gases are the most commonly performed of all ICU tests. Adequacy of gas exchange depends on the balance between pulmonary ventilation and capillary blood flow. Derangements in gas exchange lead to both hypoxia and hypercapnia.

The primary derangements are:

- ***Hypoventilation*** i.e. not breathing adequately (Box 7.4)
- ***Diffusion impairment***
- ***Shunt*** i.e. blood supply without ventilation
- ***Ventilation perfusion inequalities (V/Q mismatch)***
- ***DO_2/VO_2 inbalance.***

In reality most disease processes cause hypoxaemia and hypercapnia through a combination of these processes. The intensivist make therapeutic interventions with this in mind.

Box 7.4 Hypoventilation and the alveolar gas equation

Hypoventilation or reduced alveolar ventilation causes a rise in $PaCO_2$. One can see from the alveolar gas equation that a rise in $PaCO_2$ will result in a fall in P_AO_2 and consequently a fall in PaO_2.

The alveolar gas equation:

$$P_{Alv}O_2 = PiO_2 - (PaCO_2/R) + F$$

(PiO_2 is the partial pressure of inspired O_2; R is the respiratory quotient (usually 0.8 on mixed diet); and F is a correction factor that is usually ignored.)

One can also see that by increasing inspired O_2 (PiO_2) the PaO_2 can be maintained despite an increasing $PaCO_2$. This is a technique used for apnoeic oxygenation in brainstem death tests. It is also the reason for preoxygenating in a rapid sequence induction or why one should increase inspired oxygen to 100% for several minutes before elective intubation or reintubation—buying precious time for the procedure before hypoxaemia ensues.

Diffusion

Diffusion abnormalities reduce the time available for equilibration of alveolar gas and pulmonary capillary blood. Causes include fibrotic lung conditions.

Shunt (Figs. 7.6 and 7.7 and Box 7.5)

- Most hypoxaemia is caused by low V/Q match, of which 'true' shunt is an extreme form: V/Q = 0
- In contrast to hypoxaemia from hypoventilation, true shunt is unaffected by increases in inspired oxygen
- Shunt fraction (low V/Q) increases when:
  - The small airways are occluded (bronchiolitis, asthma)
  - Alveoli are fluid filled (pneumonia, pulmonary oedema)
  - Alveoli are collapsed (pneumonia, atelectasis)
- Hypoxaemia from the above (low V/Q) should be corrected via alveolar recruitment manoeuvres (CPAP, PEEP, HFOV; see 📖 p.157) rather than just increasing inspired O_2 (which can be toxic)
- $PaCO_2$ is unaffected by shunt but may fall as the patient hyperventilates (initially) or rise as the patient tires and hypoventilation ensues (further aggravating hypoxaemia.

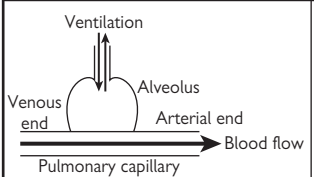
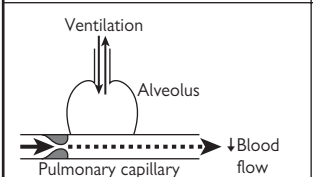
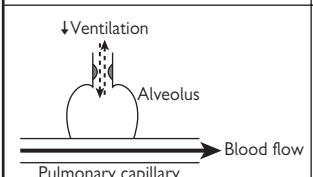
	V/Q ratio	Affect on blood gases
	V/Q: 1	Normal PaO_2 Normal $PaCO_2$
	V/Q >1 i.e. ↑Dead space	↓PaO_2 ↑$PaCO_2$
	V/Q <1 i.e. shunt or venous admixture	↓PaO_2 Normal or ↓$PaCO_2$

Fig. 7.6 Ventilation–perfusion (V/Q) abnormalities and the effect on blood gases—shunt occurs when blood flows across non-ventilated alveoli. It is also known as venous admixture.

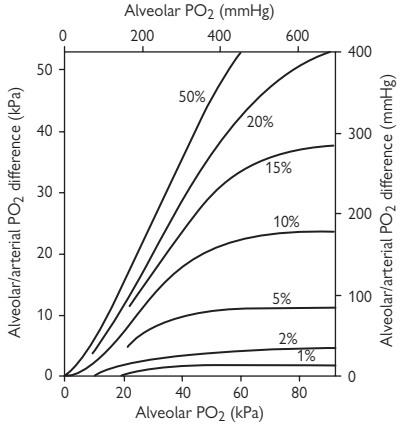


Fig. 7.7a Influence of shunt on alveolar/arterial PO_2 difference at different levels of alveolar PO_2. Figures in the graph indicate shunt percentage of total pulmonary blood flow. For small shunts, the difference (at constant alveolar PO_2) is roughly proportional to the magnitude of the shunt. For a given shunt, the alveolar/arterial PO_2 difference increases with alveolar PO_2 in a non-linear manner governed by the oxygen dissociation curve. Reproduced from Lumb AB (2006). *Nunn's Applied Respiratory Physiology*, 6th edn, with permission from Elsevier.

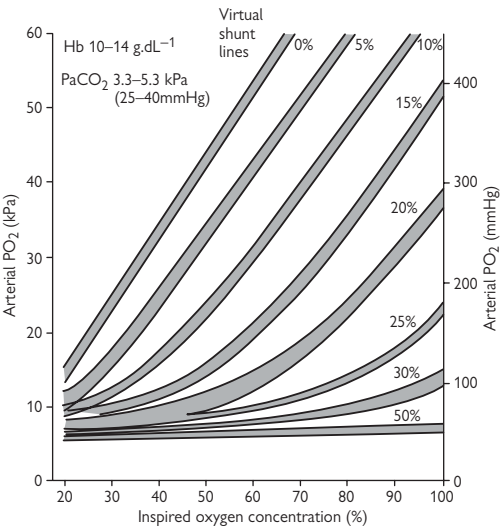


Fig. 7.7b Effect of V/Q mismatch and shunt on arterial PO_2 with varying inspired oxygen concentration. Reproduced from Benator SR, Hewlett AM, Nunn JF (1973) The use of iso-shunt lines for control of oxygen therapy. *Br J Anaesth* **45**: 711–18 with permission of Oxford University Press/*British Journal of Anaesthesia*.

Box 7.5 The shunt equation

Shunt can be calculated from the shunt equation to give an estimate of the proportion of blood flowing past poorly ventilated alveoli (Q_S) as compared with total lung blood flow (Q_T)

$$Q_S/Q_T = [C_c - C_a] \div [C_c - C_v]$$

Q_S= shunt flow; Q_T=total flow (cardiac output); C_c= oxygen content of end capillary pulmonary venous blood (assumed for simplicity to be the same as P_AO_2); C_a= oxygen content of arterial blood (calculated from co-oximeter in blood gas machine); C_v =oxygen content of mixed venous blood (taken from PA or central line).

In practice this is rarely calculated in PICU (it is usually calculated during cardiac catheterization, on 100% oxygen).

'V/Q mismatch'

- Low V/Q match is the commonest cause of hypoxaemia (Fig. 7.8)
- V/Q mismatch covers a range of V:Q ratios in the lung that tend from areas of shunt (low V/Q) through to areas that equate with physiological dead space (high V/Q, i.e. ventilated but not perfused areas)
- V/Q varies with posture and causes a small physiological alveolar–arterial difference (A–a difference):
  - Upper areas of the lung often have high V/Q ratios (good ventilation, less perfusion)
  - Dependent areas have ↑shunt fraction, i.e. low V/Q (poor ventilation better perfusion)
- Pulmonary venous blood from areas of low V/Q (V/Q <<1) have similar composition to mixed venous blood. Blood draining high V/Q areas (V/Q >>1) have similar composition to inspired gas. This blood then mixes in the pulmonary vein to give normal ABG composition
- Ventilating the lung with large breaths can compress pulmonary vessels leading to rises in pulmonary vascular resistance and, thus, abnormal V/Q
- It is worth noting that non-selective pulmonary vasodilators such as milrinone and prostacyclin can aggravate V/Q mismatch in areas of low V/Q but may improve V/Q match in areas of high V/Q.

DO_2/VO_2 imbalance (📖 see p. 88)

This usually occurs in situations of low cardiac output. Thus:

- DO_2 is reduced.
- In response oxygen extraction increases (↑OER)
- Mixed venous SvO_2 falls to less than 70%.

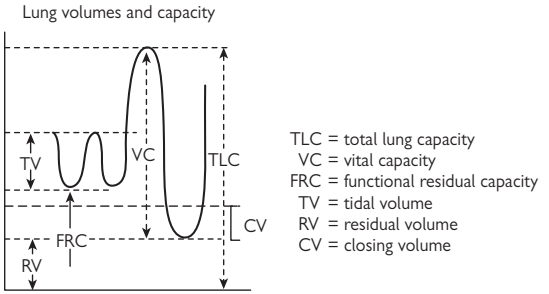


Fig. 7.8 Diagram of lung volumes. Closing volume is the volume at which small airways and hence alveoli collapse. FRC falls in children with lung parenchymal disease on ventilators. Thus alveoli are de-recruited (following small airways collapse at closing volume) and V/Q of these areas will fall causing hypoxaemia. Application of PEEP or CPAP increases FRC and improves V/Q matching and thus oxygenation. Modified from Singer M, Webb AR (2009). *Oxford Handbook of Critical Care*, 3rd edn. Oxford University Press.

Evaluating hypoxaemia and hypercapnia

Hypoxaemia

When a patient has a blood gas with significant reduction in PO_2, there are 3 principal disorders to consider:

- Hypoventilation: normal A–a DO_2
- Pulmonary disorder: ↑A–a DO_2
- Reduced DO_2 and ↑OER.

Evaluation of hypoxaemia

- The first step is to calculate A–a DO_2 (see Box 7.6).
  - *Normal A–a DO_2* indicates hypoventilation as the primary cause, e.g. neuromuscular conditions, central hypoventilation
  - ↑ *A–a DO_2* indicates V/Q abnormality, e.g. ↑shunt fraction (low V/Q)
- Check SvO_2 in situations of low cardiac output. If $SvO_2 < 70\%$, then low cardiac output is contributing to hypoxaemia.

Box 7.6 The alveolar–arterial difference

The most useful tool in interpreting hypoxaemia and how it relates to the severity of lung disease is to calculate the A–a DO_2. An A-a DO_2 >4kPa represents significant lung dysfunction.

$$\text{i.e. A–a } DO_2 = P_AO_2 - P_aO_2$$
$$= (P_iO_2 - P_aCO_2/R + F) - P_aO_2$$

P_i is the pressure of inspired O_2. R is respiratory quotient. Ignoring F then:

$$\text{A–a } DO_2 = [(P_{atm} - P_{water}) \times F_iO_2 - P_aCO_2/0.8] - P_aO_2$$

P_{atm} is atmospheric pressure, P_{water} is the SVP of water.

Then at sea level:

$$\text{A–a } DO_2 = [(101 - 6.2) \times F_iO_2 - P_aCO_2 \times 1.25] - P_aO_2$$

$$\text{A–a } DO_2 = (94.8 \times F_iO_2 - P_aCO_2 \times 1.25) - P_aO_2$$

Thus if with normal lungs, breathing air (F_iO_2 0.21), having a P_aO_2 13kPa and P_aCO_2 4kPa then:

$$\text{A–a } DO_2 = (19 - 5) - 13 = 1\text{kPa, which is normal.}$$

- Physiological A–a DO_2 is higher in babies and the elderly (up to 3.3kPa in both) but is normally 0.2–1.5kPa
- Serial measurements of A–a DO_2 is useful to track improvement worsening of lung function in ventilated patients on PICU
- Note that altitude will alter atmospheric pressure and thus the values for P_AO_2 and P_aO_2 but not the A–a difference
- Also, A–a DO_2 will vary with F_iO_2 (it increases with ↑F_iO_2). See Fig. 7.7a.

Hypercapnia

- Hypercapnia is commonly due to ↓alveolar ventilation, e.g. when a patient gets tired from ↑work of breathing (asthma, bronchiolitis, pneumonia)
- Lung disease can also cause ↑physiological dead space from V/Q mismatch (V/Q >1) which contributes to hypercapnia
- Hypercapnia with *normal A-a DO_2* is due to neuromuscular weakness or central hypoventilation (e.g. drugs, rare brain disorders)
- Dead space can be calculated from the Bohr equation (rarely done in PICU):

$$V_D/V_T = (P_aCO_2 - \text{expired } PCO_2) / P_aCO_2$$

Expired PCO_2 can be estimated from $EtCO_2$

Respiratory mechanics in ventilated patients

Modern ventilators incorporate monitoring systems that allow for measurement and graphical representation of pressure, volume, and flow during mechanical ventilation (see Box 7.7).

Many ventilators have in-built sensors. Unfortunately measurements taken will always include anomalies from the resistance and compliance of the ventilator and its tube connections. For an accurate picture of patient mechanics the sensors should be at the patient end, i.e. at the end of the ETT.

Some measurements in children are due to the leak that is often present between ETT and airway. Absolute values should not be completely relied upon but trends and graphs can be interpreted with some confidence.

Box 7.7 Esoteric pulmonary function tests

'Static' compliance is rarely measured in ICU. It requires the use of a large calibrated 'super' syringe—incremental volumes are injected sequentially into the lungs and pressure is measured at the airway when there is 'zero flow'. A compliance curve is thus constructed.

Other examples of research pulmonary function tests that have been used in ICU include:

- Transdiaphragmatic pressure measurement. This requires oesophageal and gastric manometry. It is a measure of respiratory muscle strength
- Intrapleural pressure. Requires oesophageal manometry and measures work of breathing
- Functional residual capacity. Uses a closed circuit and helium dilution, or open circuit nitrogen washout. Measures lung volumes
- Ventilation—perfusion. Inert gas-isotope technique used.

Pressure–volume measurement

- Easily obtained in relaxed fully ventilated patients
- Allows for interpretation of 'dynamic' compliance (lungs and chest wall)
- Lung compliance (L/cm H_2O) = Δ volume/Δ pressure
- Total compliance can be estimated in sedated, ventilated patients from

Compliance = tidal volume / (end inspiratory pause pressure – PEEP)

- Incorporates errors from leaks, airway resistance and changes in gas flow.
- See Boxes 7.8 and 7.9

The pressure–volume (compliance) curve (Fig. 7.9)

- There are 3 phases separated by 2 inflexion zones:
- Phase 1: below the *lower inflexion point*. An initial increase in pressure with no significant volume change. The small airways are closed and alveoli are not yet recruited
- Phase 2: above the *lower inflexion point*. A linear increase in volume and pressure. This slope represents 'dynamic' compliance and is the phase of alveolar recruitment
- Phase 3: above the *upper inflexion point*. A further period of pressure increase with no volume change. Alveolar overdistension.

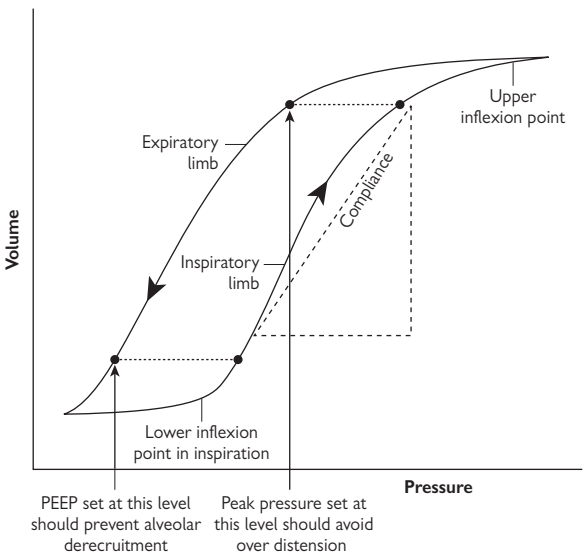


Fig. 7.9 The compliance curve.

Box 7.8 The PV curve and strategies in ARDS

The PV curve can be used to guide ventilator management in ARDS. There is good evidence that ventilator-induced over-distension causes lung injury and ↑ morbidity and mortality in ARDS:

- Setting PEEP at the lower inflexion point enables recruitment of alveoli and allows them to stay open
- Do not set peak pressure above the upper inflexion point so as to avoid alveolar over-distension (volume/barotraumas).

Box 7.9 Deflation limb of the PV curve

The 'real life' PV curve will be dependent on the ventilator history of the lung. Once alveoli are recruited the lung behaviour is actually best described by the deflation limb of the PV curve. From Fig. 7.9 it can be seen that the optimal PEEP can in fact be lower than that suggested by the inflation PV curve, and that use of the peak inspiratory pressure suggested by the deflation limb of the PV curve will avoid over distension.

Flow–volume loops

This is a plot of inspiratory flow (vertical axis) against volume (horizontal axis). Convention dictates that inspiration is negative and expiration positive. Whilst flow volume loops are used primarily in non-intubated patients using a spirometer, they can be of some diagnostic value in intubated and mechanically ventilated patients.

- Monitor changes in resistance
- Detect intrathoracic and fixed obstruction in intubated/ventilated patients
- Monitors efficacy of bronchodilator treatment.

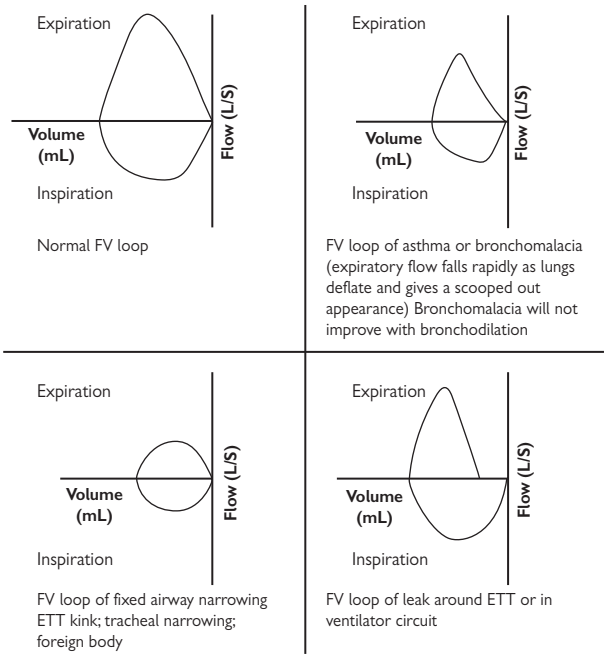


Fig. 7.10 Typical flow–volume loops.

Auto-PEEP (intrinsic PEEP)

- Refers to the component of PEEP contributed by the patient's own lungs
- Auto-PEEP is caused by air trapping in the child's alveoli at the end of expiration. It is seen in conditions of:
  - Airway narrowing, e.g. asthma
  - Dynamic compression of airways, e.g. intrathoracic tracheobronchomalacia
  - Vigorous expiratory muscle contraction at end expiration
  - Insufficient time between expiration and inspiration phases on ventilator, i.e. respiratory rate too high
- Auto-PEEP is to be suspected when flow does not return to baseline at end expiration on flow–time trace
- Auto-PEEP can be measured by an end-expiratory occlusion by many modern ventilators
  - Auto-PEEP = PEEP displayed after expiratory hold minus set PEEP

- Auto-PEEP can be estimated (e.g. in severe asthma) by disconnecting the paralysed patient from the ventilator at end expiration and counting the time for expiration to cease (by listening at the end of the ETT)
- Trends in auto PEEP values can be used clinically to gauge improvement/deterioration in asthma and airway malacia and the response to bronchodilation or ventilator manoeuvres
- Application of extrinsic PEEP to the same value or more of auto-PEEP may splint open airways, e.g. in tracheobronchomalacia.

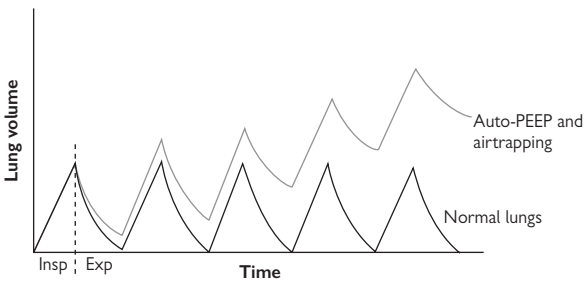


Fig. 7.11 Auto-PEEP can lead to dynamic hyperinflation.

Assessment of oxygen delivery

- It is imperative that both pulmonary and cardiac function are assessed in the context of global oxygen delivery and consumption
- Oxygen delivery is determined from the product of cardiac output and the oxygen content (see 📖 Box 6.9, p.86) (by SaO_2 rather than PaO_2) and the means by which oxygen is transported to the cell (haemoglobin level and cardiac output) the intensivist can assess the patient in terms of global oxygen delivery
- Oxygen delivery is influenced by the behaviour of the oxyhaemoglobin dissociation curve (Box 7.10):

Box 7.10 Oxygen transport and the haemoglobin dissociation curve

The affinity for oxygen by haemoglobin increases with increased arterial saturation (SaO_2). As a result the oxygen haemoglobin curve has a sigmoid shape.

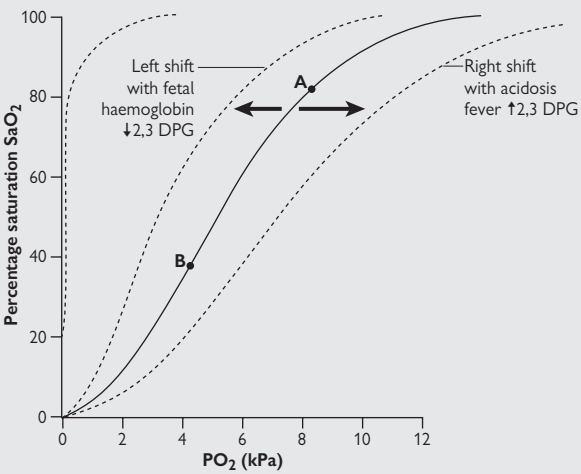


Fig. 7.12 Diagram of the oxyhaemoglobin dissociation curve. In a normal adult, point A represents a serious hypoxia and B the level at which consciousness is lost. The point of note is that A is dangerous because it is on the inflection point of the curve so that a small drop in oxygen tension causes a profound drop in oxygen saturation of haemoglobin and hence oxygen content.

(*Continued*)

Box 7.10 Oxygen transport and the haemoglobin dissociation curve (*Continued*)

Certain conditions can displace the oxygen dissociation curve. These will affect SaO_2 and therefore delivery (DO_2).

- Factors which shift curve to right and help offload O_2 to tissues include:
  - ↑2,3-diglycerophosphate
  - Acidosis
  - Hyperthermia, e.g. fever
- Factors which shift curve to left and therefore reduce DO_2 (i.e. increase haemoglobin saturation) include:
  - ↓2,3-diglycerophosphate
  - Alkalosis
  - Hypothermia
- Abnormal haemoglobins such as carboxyhaemoglobin not only shift the curve to the left but also have ↑oxygen binding capacity. As a result severe tissue hypoxia can result.

- Cardiac output and hence oxygen delivery varies inversely with blood viscosity. Normally haematocrit dictates blood viscosity—a high haematocrit is associated with falling DO_2. The optimal haematocrit for maximum DO_2 is unknown but there is good evidence that a lower limit of Hb of 7g/dL is adequate for most children
- Global estimates of total body oxygen delivery allow for bedside interpretation:
  - Metabolic acidosis
  - Lactate production
  - $S_{CV}O_2$ (from a central line).

Conclusion

An appreciation of basic physiology of both pulmonary and cardiac systems allows the intensivist to make in-depth bedside evaluations of their patients based on underlying pathophysiology.

Further reading

Lumb AB (2006). *Nunn's Applied Respiratory Physiology*, 6th edn. Elsevier.
West JB (2008). *Respiratory Physiology: The Essentials*, 8th edn. Lippincott Williams & Wilkins.

Section 2

Organ system support and related practical procedures

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Airway management and ventilation

Intubation

Indications

- Apnoea or inadequate respiratory drive
- Ineffective respiratory effort, e.g. Guillain–Barré syndrome
- 'Lung' failure, e.g. pneumonia
- Airway protection, e.g. in coma
- Upper airway obstruction, e.g. epiglottitis
- To facilitate mechanical ventilation to reduce work of breathing and oxygen consumption, e.g. septic shock, post-cardiac surgery
- To protect/maintain airway during anaesthesia, e.g. for invasive procedures.

Endotracheal tube selection

Cuffed vs. uncuffed tubes

In infants and younger children, the cricoid ring is the narrowest part of the upper airway and an uncuffed ETT is commonly used. In older children and adults a cuffed ETT is required. The appropriate internal diameter (ID) and length of ETT can be estimated using formulae:

Table 8.1 Formulae for ETT selection

Age	ETT size (ID mm)	ETT length (cm): oral	ETT length (cm): nasal
Prem neonate	2.5–3.0	6–8	Not recommended
Term–6 months	3.5–4.0	9–11	11–13
6–12 months	4.0–4.5	10–12	12–15
12–24 months	4.5–5.0	11–13	14–16
>24 months	Age (years)/4 + 4	Age (years)/2 + 12	Age (years)/2 + 15

Some centres now use cuffed ETTs in all age groups, including neonates, with successful outcomes. In certain situations in which it could be difficult to reintubate a patient, a cuffed tube should be considered from the outset. A smaller diameter tube to that suggested by the formulae in Table 8.1 will be needed.

Special situations

- In children where there is marked narrowing of the upper airway (e.g. severe laryngotracheobronchitis) a standard tube of the appropriately small ID may be too short. In such cases a 'croup tube' should be used—these are extra long, small diameter ETTs
- In patients with facial burns the ETT length must take account of the very marked facial swelling that will occur after the injury. If an ETT does not have sufficient length to allow for this, there is a risk that the tube will be pulled up out of trachea as the face swells and it may

be very difficult to reintubate the patient. Similarly, a cuffed ETT is recommended in a patient with facial burns regardless of age.

Route of intubation

- The nasal route is often chosen over an oral ETT in children as it is easier to secure a nasal tube to the face, particularly once the patient becomes mobile. Nasal ETTs may be used for several weeks in children if required and as a result tracheostomy is rarely required, in contrast to adult ICU practice
- Contraindications to nasal intubation include coagulaopathy and facial or base of skull fractures. In the emergency situation, oral intubation will secure the airway more rapidly. A nasal ETT can be substituted in a controlled manner once the patient's condition is stabilized.

ETT fixation

It is vital that the ETT is securely fixed to the patient's face. Accidental extubation can rapidly lead to life-threatening hypoxia. There are many methods used to secure ETTs, reflecting the fact that no one technique is ideal. A simple method is to use cloth tape secured around the tube and across the face between the top lip and nose (Fig. 8.1).

Fig. 8.1 ETT fixation.

Complications of intubation

Immediate complications of intubation include trauma to mouth, teeth and larynx, malpositiion of the ETT (oesophageal or endobronchial intubation) and haemodynamic instability as a result of sedative drugs and initiation of positive pressure ventilation. Late complications include ventilator associated pneumonia, trauma to the subglottic region leading to subglottic oedema or stenosis and pressure effects causing trauma to the nose or mouth. Some of these can be minimized by the use of appropriate monitoring, correct choice of ETT size and reliable tube fixation.

Rapid sequence induction (RSI)

The goal of RSI is to secure the airway with an ETT quickly while minimizing the risk of aspiration of gastric contents. Any critically ill child should be considered at risk for aspiration. RSI involves the use of an IV anaesthetic induction agent and a muscle relaxant. Before deciding to use RSI in a given situation, it is essential to appreciate that 2 gambles are being taken. The first is that the patient will prove possible to intubate with the available personnel and equipment, or at the very least that maintenance of oxygenation and ventilation of the lungs will be possible by other means (e.g. bag and mask) for the duration of action of the muscle relaxant. The second is that the dose of induction agent chosen will be sufficient to ensure lack of awareness while the airway is secured without precipitating cardiovascular collapse in a critically ill patient.

It is therefore necessary to make an assessment of the patient's airway (see difficult intubation section) and to have knowledge of the effects of various anaesthetic drugs. If the odds are not favourable, particularly on the first gamble, then you should not embark on a rapid sequence induction (see 🕮 Difficult intubation, p.135).

Preparation

The equipment and monitors that are required are shown in Boxes 8.1 and 8.2. All equipment should be checked—do not rely on others having done this for you. In addition there should be equipment available to deal with the 'can't intubate, can't ventilate' situation, i.e. kit for cricothyroid puncture and ventilation via that route. IV fluids and vasopressors should be prepared to deal with the adverse cardiovascular effects of sedation and ventilation.

The person performing the intubation needs competent assistance to pass equipment and apply cricoid pressure. If the intubator is inexperienced, there should be direct supervision by someone competent in the technique. Additional personnel are needed to administer drugs and IV fluids. There must be a backup plan if intubation proves difficult and your assistants should be briefed.

Unless contraindicated (possible unstable c-spine) the patient's head needs to be in the 'sniffing the morning air' position—cervical flexion and atlantoaxial extension. Infants have a relatively large occiput, which produces natural cervical flexion. Older children may need a towel, pillow or head ring behind the head to achieve this.

Box 8.1 RSI equipment

- Laryngoscopes (2 working)
- ETTs of appropriate size (including smaller and larger sizes than predicted)
- Gum elastic bougie, stylet
- Suction capable of aspirating gastric contents and airway secretions
- Breathing system (e.g. Ayre's T-piece) capable of positive pressure ventilation of lungs with 100% oxygen.
- Oxygen supply
- Face mask
- Guedel airways of appropriate size
- Magill's forceps for nasal intubation
- Syringe (for cuffed ETT)
- Tape to secure ETT
- A pillow (for older children/adults).

Box 8.2 RSI monitoring

- Capnography
- Pulse oximeter
- ECG
- BP
- Stethoscope.

Choice of drugs—induction agents

(Properties of these agents and scenarios for use are covered in detail in 📖 Chapter 9.)

Ketamine and *thiopentone* are the induction agents most commonly used for intubation in PIC. Of the other induction agents, *Propofol* is likely to cause marked cardiovascular depression, Benzodiazepines such as midazolam have too slow an onset of action. Opioids such as fentanyl may be used as adjuncts to the induction agents, but do not produce loss of consciousness when used alone.

Choice of drugs—muscle relaxants

(Details of muscle relaxants are in 📖 Chapter 10.)

The role of the muscle relaxant is to facilitate intubation and subsequent ventilation by the complete paralysis of skeletal muscles through blockade of neuromuscular transmission. The patient is then entirely reliant on external means to maintain ventilation and oxygenation. In RSI desirable properties of a muscle relaxant drug include rapid onset of action, minimal side effects, and a short duration of action (to allow the return of spontaneous breathing if intubation fails). *Suxamethonium* is the only drug that fulfils this requirement—it has an onset of action of 20–40s and produces excellent intubating conditions (after total body fasciculations). It wears off in 5min However, it is associated with a number of undesirable effects including bradycardia, acute, severe hyperkalaemia in burns or spinal cord injury, rhabdomyolysis in muscular dystrophies, and a relatively high incidence of allergic reactions. *Vecuronium, atracurium, rocuronium* (see Box 8.3), and

pancuronium are suitable for more elective intubation when you can be sure to intubate.

Box 8.3 Rocuronium

Rocuronium may soon be a suitable alternative to suxamethonium in RSI. A novel agent (sugammadex) may prove useful in reversing the effects of rocuronium rapidly in the failed intubation situation. Currently there is little data regarding the use of sugammadex use in children. Rocuronium has few of the side effects of suxamethonium

Technique of RSI

- Preoxygenation (to fill FRC of lungs with oxygen)
- Rapid injection of induction agent followed by muscle relaxant
- Application of cricoid pressure to occlude the oesophagus (and thus prevent regurgitation of gastric contents into the oropharynx)
- Intubation of the trachea after 45–60s
- Cricoid pressure is released once the ETT is confirmed to be in the trachea by capnography and the cuff has been inflated.

Standard adult teaching has been not to ventilate the lungs with bag and mask before intubation. However, in young children, particularly with lung pathology, this is likely to lead to significant hypoxia. Therefore the technique should be modified by the use of bag-mask ventilation once cricoid pressure has been applied.

Difficult intubation

Some syndromes associated with difficult intubation

(See 🕮 Chapter 38.)

- Pierre–Robin
- Treacher–Collins
- Goldenhar
- Mucopolysaccharidoses (Hurler's, Hunter's etc.)
- Crouzon's, Apert's.

Other situations where intubation may be difficult

- Facial trauma
- Infection (epiglottitis, Ludwig's angina)
- Burns
- Cervical spine trauma or instability.

Airway assessment

- Always assess the airway of any patient you plan to intubate
- Examine the patient, particularly looking for small mandible, limited mouth opening, restricted neck movement, cleft palate, 'syndromes'
- Assess for signs of upper airway obstruction (e.g. stridor)
- Assess for risk of aspiration (e.g. full stomach, trauma, acute abdomen)
- Past history of airway management—make sure you look at previous anaesthetic records but beware of progressive conditions such as mucopolysaccharidoses.

Techniques

A simple decision tree is shown (Fig. 8.2). The overriding principle is that if difficult airway management is predicted then spontaneous breathing should be maintained until the airway is secured. In adult practice awake intubation may be performed under local anaesthesia. Awake intubation is also possible in neonates. However, this requires skill on the part of the intubator and assistant and may result in hypertension and hypoxia.

In paediatric patients the following approach is recommended:

- Get senior help (experienced anaesthetist, ENT surgeon)
- Consider passing NG tube to empty stomach (not in epiglottitis)
- Prepare equipment (see Box 8.4) and apply monitors—SpO_2, ECG, NIBP
- Give atropine or glycopyrronium 30min preintubation to reduce secretions (preferably IM)
- Induce anaesthesia with volatile anaesthetic agent (sevoflurane or halothane)
- Maintain spontaneous ventilation
- The depth of anaesthesia required for laryngoscopy may cause marked cardiovascular depression—frequent measurement of NIBP and palpate central pulse volume
- Perform laryngoscopy once deep plane of anaesthesia is reached
- The view at laryngoscopy may be improved by:
  - Repositioning patient (e.g. pillow, extend head on neck)
  - External manipulation of larynx (back, up, and to the right—BURP manoeuvre)
  - Use of different laryngoscope blade

- If unable to intubate either wake patient up or proceed to special techniques (e.g. fibreoptic intubation) (Box 8.4)
- Do not persist with attempts to intubate using a failed technique
- The laryngeal mask airway may provide a means to maintain ventilation and oxygenation and act as a conduit for fibreoptic intubation.

Box 8.4 Difficult airway equipment

- Laryngeal mask airway—have range of sizes available.
- Bougies
- Stylet
- Range of ETT sizes
- Paediatric fibreoptic bronchoscope
- Cricothyroidotomy set plus means to ventilate
- McCoy laryngoscope—tip of blade can be flexed
- Airway exchange catheter—can provide oxygenation.

ETT position confirmation

- The gold standard for ETT position confirmation is detection of $ETCO_2$ with trace or disposable detector—$ETCO_2$ detection is mandatory in PICU.
- ETT seen to go through cords
- Fogging inside ETT
- Chest rises and falls with ventilation
- Equal breath sounds on auscultation (listen in axillae).

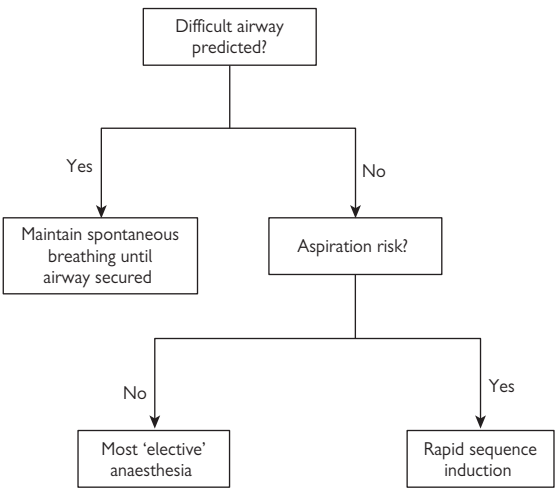

Fig. 8.2 Decision tree for difficult intubation.

Failed intubation drill

- Recognize failure early—patients do not die from failure to intubate but from failure to oxygenate
- Maintain oxygenation and ventilation using bag and mask and Guedel airway. Send for help (experienced anaesthetist, ENT surgeon)
- Do not persist with attempts using a failed technique—this can rapidly result in glottic oedema and make mask ventilation impossible or preclude techniques such as fibreoptic intubation
- If bag-mask ventilation fails:
  - Try 2-person technique (1 to hold mask and perform jaw thrust and other to squeeze bag)
  - Try laryngeal mask airway (Table 8.2)
- If ***can't intubate, can't ventilate*** scenario occurs and severe hypoxaemia ensues then perform *cricothyroidotomy* and oxygenate by this route (see 🕮 Cricothyroidotomy, p.137)
- If mask ventilation is successful, oxygenate patient and use techniques for difficult intubation outlined earlier if skilled or await senior help.

Table 8.2 LMA sizes

Weight kg	LMA size
<5	1
5–10	1½
10–20	2
20–30	2½
30+	3

Cricothyroidotomy

Cricothyroidotomy is a technique of failure. It is very rarely undertaken in children, but has the potential to be life-saving in the '***can't intubate, can't ventilate situation***'. Equipment should be available wherever a patient will be intubated. Suitable kits are available—you should familiarize yourself with the available equipment in your hospital

Indications

Any condition associated with upper airway obstruction and difficult intubation, resulting in a can't intubate, can't ventilate scenario:

- Foreign body
- Epiglotittis
- Burns
- Angio-oedema
- Facial trauma
- Retropharyngeal abscess.

Methods

Needle cricothyroidotomy (Boxes 8.5 and 8.6)

- Suitable for any age child
- A cannula may be placed through the cricothyroid membrane and connected to a high-pressure oxygen supply allowing for intermittent ventilation—this technique requires an unobstructed upper airway for expiration or severe barotrauma will result.

Box 8.5 Needle cricothyroidotomy equipment

- Largest size cannula available* and 5-mL syringe
- Ventilation circuit. This consists of bubble oxygen tubing, a Luer lock connection at one end and an opening to the atmosphere that can be occluded. It must be long enough to reach from the wall oxygen supply to the patient
- Local anaesthetic
- Roll/pad for under the shoulders.

*Purpose-made cannulae are available in various sizes; 12g for adults, 14g for children and 18g for babies.

Box 8.6 Needle cricothyroidotomy technique

- Prepare and check equipment
- Place patient in supine position
- Extend neck with the roll/pad (consider risk/benefit if c-spine injury suspected)
- Identify the cricothyroid membrane
- If time, clean the neck with an alcohol swab and infiltrate with local anaesthetic
- Attach the syringe to the metal stylet of the cannula
- Place finger on cricoid cartilage as a guide and to stabilize neck
- Insert the cannula through the cricothyroid membrane at a 45° angle caudally, aspirating as you go
- When air is aspirated stop advancing the cannula
- Slide the cannula off the needle into the trachea
- Remove the needle and reattach the syringe to the cannula. Make sure that air can still be aspirated
- Fix the cannula in place and attach the circuit to it (the circuit ***must*** be open to atmosphere when connected)
- Attempt insufflation of oxygenation, starting at 2L/min minimum (initial oxygen flow (L/min) = patient's age in years)
- Occlude opening in tubing for 1s and release for 4s
- Increase by 1L/min until chest is seen to rise and oxygenation improves or 15L/min is reached.

⚠ Expiration is passive via the upper airway and will occur in most cases. If this is completely obstructed then insufflation must stop once the chest has risen sufficiently.

Sugical cricothyroidotomy (Boxes 8.7 and 8.8)

- Alternatively a small tracheal tube may be placed through the cricothyroid membrane and connected to a bag-valve system for ventilation
- Suitable for children over 12 years of age.

Box 8.7 Sugical cricothyroidotomy equipment

- Surgical cricothyroidotomy set, or cutdown set and size 4.0 ETT or tracheostomy tube (cutdown set should include scalpel and artery forceps)
- Bougie/introducer (if not included)
- LA
- Roll/pad
- Self-inflating bag.

Box 8.8 Sugical cricothyroidotomy technique

- Prepare and check equipment
- Place patient in supine position
- Extend neck with the roll/pad (consider risk/benefit if c-spine injury suspected)
- Identify the cricothyroid membrane
- If time, clean the neck with an alcohol swab and infiltrate with local anaesthetic
- Make vertical skin incision from cartilage to cartilage
- Open skin and control bleeding with a finger either side of the wound
- Make a horizontal stab through cricothyroid membrane (do not incise laterally)
- Open up membrane horizontally with artery forceps
- Insert bougie/introducer
- Railroad airway device over bougie/introducer and remove
- If possible, check position by aspirating air
- Attach 15mm Portex connector
- Attach self-inflating bag and commence ventilation
- Check for chest movement, air entry and $ETCO_2$.

Complications

- Asphyxia
- Aspiration
- Haemorrhage
- Haematoma
- False passage
- Subcutaneous emphysema
- Oesophageal perforation
- Barotrauma.

Reasons for failure of technique

- Equipment not available
- Inability to identify landmarks
- Inability to access trachea
- Excessive escape of gas through upper airway
- Complications.

Caveats

- The most difficult part of the procedure is making the decision to do it. The alternative may be that the patient dies. You have nothing to lose
- Always call for an ENT surgeon to undertake a formal tracheostomy; needle cricothyroidotomy will only buy you minutes and may fail
- Consider sedating/paralysing the patient in extremis
- Identification of the cricothyroid membrane is difficult in babies and infants, as the thyroid cartilage is less prominent—it is easy to mistake the hyoid bone for the thyroid cartilage
- The cricothyroid membrane is only 2.5mm long and 3mm wide in neonates—too small to take an ETT
- Filling the syringe with some saline often makes identification that air has been aspirated easier (you see bubbles in the syringe)
- Needle cricothyroidotomy will help oxygenate, but will not ventilate the patient
- Surgical cricothyroidotomy will allow ventilation as well as oxygenation, providing the upper airway leak is not too great.

Box 8.9 The dreaded mediastinal mass

Rarely mediastinal masses may present in children with signs of respiratory distress (stridor, cough, orthopnoea) and SVC compression (facial swelling). These patients are at substantial risk of death with poorly planned attempts at anaesthesia or intubation. The use of IV anaesthetic agents and particularly muscle relaxants may lead to rapid airway compression and SVC occlusion. The level of compression may be such that endotracheal intubation fails to relieve this obstruction and in addition cardiovascular collapse may result from SVC or pulmonary artery compression. ***Never*** attempt intubation in a child with suspected significant mediastinal mass without very experienced anaesthetic assistance unless you absolutely have to.

Tracheostomy

- Tracheostomy is performed much less frequently in PIC than in adult intensive care practice
- Children may be ventilated safely using an ETT for many weeks
- Percutaneous dilational tracheostomy is very rarely used in children
- The majority of tracheostomies in children will be performed as planned procedures under general anaesthesia in the operating room
- There is a significant mortality associated with tracheostomy tube blockage or displacement in children, particularly below 1 year of age (approximately 2% in reported case series)
- Approximately half of tracheostomies are performed in children <1 year of age
- There are considerable implications for the family, who will need to learn to care for a tracheostomy before they can take their child home, and for the child, particularly with swallowing and speech
- Decannulation is eventually achieved in approximately 40–60% of children, depending on the indication for tracheostomy and their underlying condition (e.g. severe neurological impairment).

Indications

- Subglottic stenosis (e.g. following prolonged intubation in premature neonates)
- Congenital defects causing upper airway obstruction
  - Craniofacial disorders (e.g. Pierre–Robin, Crouzon's)
  - Laryngeal cleft
  - Vascular malformations
  - Cystic hygroma
- Bilateral vocal cord palsy
- Severe tracheomalacia
- Need for prolonged mechanical ventilation
- Airway protection in patients with long-term neurological impairment (e.g. following severe intracranial injury)
- Tracheostomy is now rarely used in acute inflammatory conditions causing upper airway obstruction (e.g. epiglottitis).

Care of the new tracheostomy

- The patient is at greatest risk of complications from blockage or displacement of the tracheostomy in the first 7–10 days before there is a well-defined tract between skin and trachea
- Nurses must be skilled in tracheostomy care and the patient initially managed in a HDU or PICU environment
- Staff caring for the patient should be aware of whether the patient is likely to be difficult to intubate orally and if there were difficulties performing the tracheostomy. Check for the presence of stay sutures placed through the trachea
- A spare tracheostomy tube of the appropriate size must always be kept with the patient
- As the upper airway is bypassed, inspired gases must be humidified
- A CXR must be obtained to assess tube position and exclude pneumothorax

- The tracheostomy tube must be properly secured with tapes—it is best to leave this to experienced nursing staff (or a skilled parent).

Blocked tracheostomy

- Send for help—senior anaesthetist or intensivist, ENT surgeon
- Give oxygen via face mask and tracheostomy. Assess whether there is movement of bag of breathing system
- Try to pass suction catheter
- Remove inner tube if present—with double cannula tracheostomy tube
- Apply monitors—SpO_2, capnography
- Deflate cuff if patient making respiratory effort
- Consider oral intubation or replacing tracheostomy tube.

Displaced tracheostomy

- From about 10 days following formation there should be a well-defined tract and a tracheostomy tube can usually be reinserted without difficulty. Before this time there is a risk of failure to recannulate or creation of a false passage
- If the tracheostomy tube is dislodged early after formation, then it is usually best to secure the airway with a standard oral ETT
- In situations where this is not possible (e.g. very difficult intubation), the tracheostomy tube will need to be reinserted through the stoma. The use of a bougie or the presence of stay stitches to the trachea may aid reinsertion
- If the patient is breathing and can maintain an adequate airway without the tracheostomy in place, it is advisable to await senior help.

Changing the tracheostomy tube

- It is standard practice to electively change a tracheostomy tube after 10–14 days, by which time the tract should be well formed
- Position the patient so as to expose the neck, preoxygenate
- A well-lubricated tracheostomy tube of the appropriate size is placed through the stoma and the inner obturator removed
- If the tube requires changing early after formation, a bougie or airway exchange catheter may be used to guide reinsertion. Facilities for oral intubation should be immediately available if needed.

Types of tracheostomy tube

The most commonly used tracheostomy tubes in children are single cannula tubes. Table A.8 in the Appendix (📖 p.869) shows details of Shiley® tubes (Tyco Healthcare), similar tubes are available from other manufacturers. Cuffed tubes are useful to reduce aspiration of oral contents and to facilitate mechanical ventilation.

- Double cannula tubes have an inner cannula that may be removed for cleaning or if it becomes blocked
- The Bivona® FlexTend™ (Smiths Medical) tube has a flexible tube extension on the proximal side of the neck flange to keep connections away from the neck
- Fenestrated tubes allow air to escape upwards into the oropharynx to aid speech

- Speaking valves may be used to assist speech. Some are suitable for mechanically ventilated patients
- Most tracheostomy tubes have an anterior curve that in some patients may cause the tip to abut against the tracheal wall causing partial obstruction. Custom-made tracheostomy tubes may be obtained for patients with a particularly challenging trachea.

Ventilation via tracheostomy

Most tracheostomy tubes have a 15-mm connector that will connect to standard ventilator tubing. Uncuffed tubes often have a substantial leak around the outside. If mechanical ventilation is required, then a cuffed tube may be substituted initially. In the emergency situation an alternative is to place a cuffed ETT through the stoma or via the oral route to secure the airway, taking care to avoid endobronchial intubation.

Long-term issues

Infection may occur at the insertion site. Colonization of the stoma with bacteria is very common. Granulation tissue frequently forms around the stoma and within the tracheal lumen. This should be assessed for periodically by an ENT surgeon and may require debridement.

For details of neonatal and paediatric tracheostomy sizes see 🕮 p.869.

Oxygen therapy

Oxygen therapy should be instigated at first contact in all critically ill patients. In spontaneously breathing patients, a non-rebreathing face mask should be used, with an initial flow of 15L/min. If the patient is apnoeic a bag-valve-mask with a reservoir bag and similar oxygen flows should be used instead. The oxygen can be titrated once monitoring of oxygen saturations (SpO_2) and ABGs has been established. The SpO_2 should be maintained above 90%, unless the child has a congenital heart defect that allows right-to-left shunting or there is pre-existing compromise of pulmonary blood flow. Below 90% there is a rapid drop off of PaO_2 as this equates to the steep portion of the oxygen dissociation curve. Care should also be taken in premature neonates because of the risk of cerebral vasoconstriction and retinopathy of prematurity with high oxygen concentrations. Low SpO_2 values may occur spuriously when there is poor peripheral perfusion, motion artefact, a poorly fitting probe, and severe tricuspid regurgitation.

Principles

The purpose of oxygen therapy is to help maximize oxygen delivery to the tissues, by optimizing the oxygen concentration in the blood. Oxygen delivery to tissues is determined by the *oxygen flux equation* (see 🕮 Box 6.9, p.86) and is dependant on SaO_2, haemoglobin concentration and cardiac output.

Normal PaO_2 in arterial blood for a patient breathing air at sea level is 13kpa.

Factors determining PaO_2

(See 📖 p.86 and 📖 p.118.)

- Alveolar PO_2 is largely determined by the *alveolar gas equation* (see 📖 Box 7.4, p.114), i.e. it is dependent mainly on the inspired oxygen concentration and the alveolar PCO_2.
- PaO_2 (the arterial oxygen tension) is determined by the *alveolar–arterial oxygen difference* which varies in disease and depends on:
  - *Shunt*: pulmonary or cardiac right to left.
  - *Ventilation–perfusion matching*
  - *Alveolar diffusion.*

Inspired oxygen concentration

- Depends on type of oxygen delivery system used, most will not deliver an FiO_2 >0.6
- Oxygen concentration reaching the patient will not necessarily reflect FiO_2, recorded on the delivery device as there may be leaks in the system and dilution with entrained air
- High inspired oxygen can keep a hypoventilating patient well oxygenated (i.e. normal SaO_2) whilst they are developing significant hypercapnia.

Indications for oxygen therapy

- Main indication is hypoxaemia, as monitored by pulse oximetry or ABGs. Depends on patient's normal SpO_2. Chronic hypoxaemia, as in cyanotic congenital heart disease, is well tolerated by most patients
- Other indication is clinical signs that may be indicative of hypoxaemia, e.g. cyanosis, high or low respiratory rate, grunting, chest retractions, and inability to talk or drink.
- Where oxygen delivery may be compromised—hypovolaemia, cardiomyopathy, anaphylaxis, sepsis
- Specific clinical situations, such as CO poisoning, chronic lung disease, and pulmonary hypertension.

Contraindications

No specific contraindications.

Cautions

- Paraquat poisoning
- Bleomycin therapy
- Hypoxic respiratory drive (see Box 8.10)
- Single-ventricle pathology congenital heart disease
- Duct-dependent circulation
- High risk of retinopathy of prematurity
- High FiO_2 may be associated with absorption atelectasis and direct toxic effect on lungs.

Box 8.10 Hypoxic respiratory drive

In adults with COPD there is a tendency to titrate the oxygen concentration to the PaO_2 and $PaCO_2$ values, due to concerns about abolishing the patient's hypoxic respiratory drive. There are very few paediatric patients in whom such a situation exists. As always the priority in the critically ill patient is to maintain oxygenation, and oxygen therapy should not be withheld because of this theoretical concern. Providing oxygen and carbon dioxide levels are monitored and normalized for that patient, they will not come to any harm.

Methods

This requires a wall oxygen outlet or oxygen cylinder and a delivery system to supply the oxygen to the patient. Devices can be fixed or variable performance.

Fixed performance device

An accurate concentration of oxygen is supplied to the patient at a flow rate exceeding the patient's peak inspiratory flow rate, thus avoiding air entrainment and dilution of the FiO_2.

Variable performance device

Oxygen is supplied at a fixed flow rate and relies on the mask or nasopharynx to provide a reservoir of oxygen for the patient to inspire. If the reservoir and fresh gas flow are not large enough to cover the patient's peak inspiratory effort and tidal volume, air entrainment occurs to supplement the gas flow, thus reducing the FiO_2. The FiO_2 will therefore vary depending on the patient's size and minute ventilation, and the fresh gas flow.

Monitoring a patient receiving oxygen therapy

Patient

- Clinical—colour, heart rate, respiratory rate, conscious level
- Pulse oximetry
- ABG
- Transcutaneous oximetry.

Circuit

- Flow meter
- Oxygen analyser.

Weaning

Oxygen therapy should be titrated against SpO_2 and PaO_2 values appropriate for the patient. Weaning can occur with resolution of the underlying clinical problem and improvement in respiratory function. Oxygen concentrations <50% are unlikely to do the patient any harm, so if in doubt, maintain therapy until fully recovered.

Mechanical ventilation and oxygen support systems

Critically ill children often require endotracheal intubation and mechanical ventilatory support as part of their intensive care management. Although the techniques of mechanical ventilation have not changed greatly in recent years, our application of these techniques has, due to an increasing awareness of the pathophysiology of ventilator-induced lung injury (VILI) and use of high-frequency oscillatory ventilation (HFOV).

Physiology

There are a number of adverse physiological factors in infants and young children that increase their susceptibility to ventilatory failure in the presence of respiratory disease:

- Narrower airways
- ↑airway resistance
- More compliant chest wall
- More horizontal ribs
- Lower FRC
- Lower position on lung compliance curve
- Closing volume impinging on tidal ventilation
- Less functional alveoli
- Less type 2 (slow-twitch) respiratory muscle fibres.

Mechanical ventilation is rarely indicated on non-clinical grounds (i.e. on numbers) alone but by evaluating the clinical situation with clinical examination and physiological variables.

Criteria for considering mechanical ventilation

- Clinical condition—tachypnoea, grunting, accessory muscle use, tachycardia, bradycardia, impaired consciousness, cyanosis, exhaustion
- FiO_2 >0.6
- Abnormal PaO_2, $PaCO_2$, and pH (H^+) values
- A–aDO_2 >450mmHg
- PaO_2/FiO_2 <20
- Oxygenation index (OI) >13.

Clinical situations associated with mechanical ventilation

Respiratory

- Hypoxaemia
- Hypercapnia
- Apnoea/inadequate respiratory effort
- Inhalational injury
- Flail chest
- Pulmonary oedema
- Airway obstruction.

Cardiovascular

- Circulatory instability
- Vascular access
- Heart failure.

Neurological
- Neurological failure/encephalopathy
- Apnoea
- ↓conscious level/airway protection
- Cerebral oedema
- Control of ICP.

Therapeutic
- Tracheobronchial toilet
- CO_2 control
- Surfactant administration
- Administration of resuscitation drugs.

Other
- Postoperative—awakening/stability/surgical
- Transportation
- Imaging.

In general, if you think a patient needs mechanical ventilation, they probably do!

Ventilator modes

There are two main modes of ventilatory support in paediatric practice; IPPV and HFOV. The former is by far the most common method employed and is suitable for the majority of patients. HFOV is generally limited to those with severe impairment of respiratory function, which is difficult to manage with conventional ventilatory techniques.

Intermittent positive-pressure ventilation (IPPV)

IPPV is a form of artificial ventilation where inspirations are provided by application of positive pressure to the airways, achieving alveolar ventilation close to physiological tidal volumes and rates. It can be adjusted to achieve the desired oxygen and carbon dioxide levels in arterial blood. Only the inspiratory phase is active, with exhalation occurring through the ventilator, by passive recoil of the chest. It can be delivered in either control or support modes, depending on the patient's intrinsic respiratory effort.

Positive-end expiratory pressure (PEEP)

PEEP is used to prevent alveolar collapse at the end of expiration, maintain FRC and reduce pulmonary oedema. All ventilated patients should receive some PEEP (3–5cmH_2O) to prevent the ventilation cycle from drifting below the lower inflection point of the pressure–volume curve as a result of airway and alveolar closure. In severe lung pathology, higher levels of PEEP (10–15cmH_2O) may be needed to maintain lung volume. Only very high levels of PEEP for sustained periods of time will recruit collapsed alveoli, so it is often preferable to undertake an alveolar recruitment manoeuvre when lung volume has been lost and use PEEP to prevent reoccurrence. High PEEP can cause barotrauma, cardiovascular

compromise, impaired pulmonary blood flow, CO_2 retention, and ↑work of breathing, particularly when applied inappropriately.

Control modes

Volume control (VC) ventilation

Each breath is fully supported by the ventilator with a preset volume control breath. If the patient stops breathing, a minimum number of breaths are still supplied. If additional breaths are taken, each is supported by a volume control breath, provided the triggering mechanism is set correctly. Flow is delivered in a constant flow pattern across inspiration (Fig. 8.3). A pause time is typically applied at the end of inspiration during which the ventilated breath is held in the lungs.

Pressure control (PC) ventilation

Each patient breath is delivered at a fixed inspiratory pressure with a decelerating flow waveform (Fig. 8.3). May have advantages in terms of more even distribution of gas flow within the lungs, but tidal volume will vary depending on changes in the compliance and resistance.

Pressure-regulated volume control

Pressure-supported breath that aims to supply a fixed tidal volume to the patient, irrespective of changes in lung compliance and resistance. The waveform is like a pressure-control breath, with a square waveform and decelerating flow pattern, but the peak pressure will be varied by the ventilator, depending on the tidal volume delivered with the previous breath. In theory brings together the advantages of both VC and PC control with a prescribed tidal volume delivered via a decelerating flow.

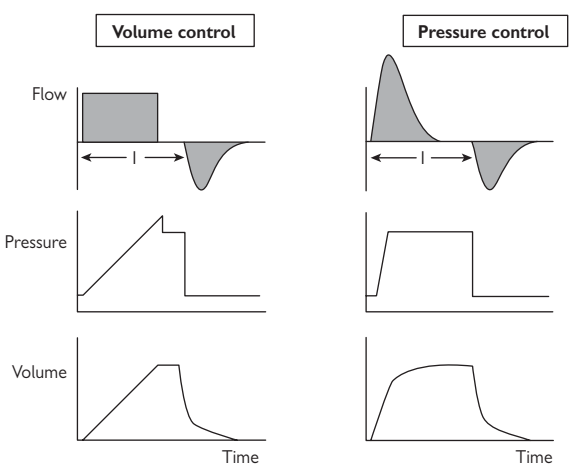

Fig. 8.3 Volume control and pressure control ventilation.

Support modes

For weaning patients who are making spontaneous respiratory effort. A number of modes are available which can be used in isolation or in combination, for example synchronized intermittent mandatory ventilation (SIMV) + pressure support. There is no evidence that one mode is better than another in terms of speed and success of weaning or extubation.

Triggering (Box 8.11)

In order for the ventilator support to be synchronized with patient effort there needs to be a way for the patient's respiratory effort to be sensed back at the ventilator. This is done by setting the 'trigger sensitivity' on the ventilator to detect a reduction in pressure or flow within the expiratory limb of the circuit and ventilator as a result of the patient drawing gas flow from the circuit during early inspiration. Modern ventilators are able to produce effective synchronization with only minimal lag time.

Box 8.11 Triggering the ventilator

It is common to observe problems with triggering of the ventilator in PICU. On many occasions these go unnoticed for some time. Two extreme situations demonstrate the importance of setting the trigger sensitivity at the appropriate threshold:

1. Trigger threshold set too high

Example: patient on SIMV, PEEP 5cmH_2O, trigger set at –16cmH_2O. Patient noted to have laboured breathing, ventilator not synchronizing with the patient, not 'triggering'. In this situation the patient must make sufficient inspiratory effort to lower the circuit pressure 16cmH_2O below the PEEP level, to –11cmH_2O, before the ventilator detects a patient effort and releases additional gas flow into the inspiratory limb of the circuit. Most patients will not be capable of generating sufficient effort to do this and so will not be able to trigger the ventilator to provide gas flow for respiratory efforts over and above the SIMV rate. They breathe like a fish out of water!

2 Trigger sensitivity set low resulting in 'auto-triggering' of the ventilator

In this situation the trigger threshold is set appropriately but something other than the patient results in a change in pressure or flow within the ventilator circuit which is interpreted by the ventilator as patient effort—the result being additional ventilator support each time the triggering rule is met. By far the commonest cause of this is a build up of water within the ventilator circuit as a result of rain-out—the 'to and fro' motion of the water is enough to cause a fluctuation in pressure or flow in the circuit. In adults an active cardiac impulse may be sufficient to cause this. The patient in this situation will be observed to be triggering a very high ventilator rate, often >100/min. Such a high rate should make you suspicious that the problem is auto-triggering—ensure that all water is evacuated from the circuit.

In either of these situations the immediate management is to take the patient off the ventilator and place them on a T-piece bagging circuit. In situation 1 the patient will immediately be more comfortable as a result of having a continuous supply of fresh gas flow. In situation 2 the patient will no longer breathe at such a high rate—in fact as a result of hypocapnia they will typically not breathe much at all!

SIMV

A fixed number of volume control (SIMV-VC) or pressure control (SIMV-PC) breaths are synchronized with the patient's respiratory effort. Breaths can be triggered by the patient during the SIMV period of the respiratory cycle. If the patient fails to initiate a breath, the ventilator will deliver a mandatory breath at the end of the SIMV period.

Pressure support ventilation

A fixed-pressure, decreasing flow breath is delivered to the patient during spontaneous respiration. At a given pressure, tidal volume will vary depending on lung compliance, airway resistance and the duration of inspiration. In contrast to other modes pressure supported (and volume supported) breaths are flow cycled rather than time cycled—that is to say Ti is not fixed, inspiration terminates when flow falls to ~25% of peak inspiratory flow.

Volume support ventilation

Each patient breath is supported by a variable amount of pressure support in order to deliver a fixed tidal volume. As lung compliance improves, so the level of pressure support delivered with each breath reduces. The tidal volume necessary to produce satisfactory gas exchange can also be reduced.

Proportional assist ventilation

A unique method of ventilation, whereby the ventilator guarantees to undertake a fixed proportion of the patient's work of breathing by varying the pressure support delivered. The ventilator constantly monitors patient respiratory effort and adjusts the level of support accordingly.

Airway pressure release ventilation (APRV)

CPAP-based method, where a high inspiratory pressure is maintained for most of the respiratory cycle and intermittently released to allow tidal ventilation and CO_2 clearance. The high MAP means it is good for conditions where oxygenation is compromised by alveolar derecruitment. Spontaneous breathing can occur at either the higher or the lower pressure level.

Bilevel positive airway pressure (BIPAP)

Similar concept to APRV but with a more conventional inspiratory and expiratory time and I:E ratio. Spontaneous breathing is possible throughout the ventilator cycle at either the high or low pressure levels. Note this is BIPAP; *BiPAP*® is the patented term used by Respironics for a mode on their non-invasive ventilators and is analogous to patient-triggered pressure control ventilation.

CPAP

High-flow gas at a constant pressure is delivered to the patient, maintaining FRC and alveolar recruitment. Oxygenation is optimized, but there is no support for alveolar ventilation and thus CO_2 clearance.

Principles of ventilation

- Deliver tidal volumes of 7–10mL/kg
- Titrate PEEP to maintain the FiO_2 ≤0.4
- Maintain plateau pressure of ≤ 30cmH_2O and peak pressure at ≤ 35cmH_2O

- Initial RR should be appropriate for the age and subsequently guided by $PaCO_2$ on ABG analysis
- I:E ratio of ~1:2 unless expiration delayed, e.g. asthma
- Good humidification.

Initial settings (Table 8.3)

Initial FiO_2 will be dependent on the presence or absence of pulmonary pathology. Some patients can be comfortably managed in air, while those with severe lung disease will often require an initial FiO_2 of >0.7. Caution must be exercised in infants with congenital heart disease where the pulmonary circulation is dependent on a shunt, as a high FiO_2 may cause pulmonary vasodilatation and 'steal' from the systemic circulation.

Table 8.3 Sample initial ventilator settings

	Age				
	Prem	**Neonate–1 year**	**1–5 years**	**5–12 years**	**>12 years**
PIP (cmH_2O)	20	15	n/a	n/a	n/a
PEEP (cmH_2O)	5	4–10	4–10	4–15	4–15
V_T (mL/kg)	n/a	5–10	5–10	5–10	5–10
RR	40–60	25–40	20–25	15–20	12–15
I:E ratio	1:1	1:2	1:2	1:2	1:2
T_i (secs)	0.4–0.5	0.65–0.8	0.8–1.0	1.0–1.2	1.5

I:E ratio: inspiratory time:expiratory time ratio, RR: respiratory rate; PEEP: positive end-expiratory pressure; PIP: peak inspiratory pressure; Ti: inspiratory time; VT: tidal volume.

Monitoring of a ventilated patient

- Standard: ECG, pulse oximetry, BP, $ETCO_2$
- ABGs: pH, PaO_2, $PaCO_2$, BE, HCO_3^-
- Ventilatory: volumes, airway pressure, flows, loops, compliance
- CXR: pathology, chest expansion, position of hardware
- Measurement of auto-PEEP (PEEPi): asthma, bronchiolitis, tracheobronchomalacia

Troubleshooting

Low PaO_2

- Increase FiO_2
- Increase mean airway pressure, by
  - Increasing PEEP
  - Increasing inspiratory time/I:E ratio (greater proportion of ventilator cycle spent at PIP) (see also Box 8.12)
  - Increasing tidal volume/PIP —not recommended as may result in volu- and barotrauma
- Improve V/Q matching (recruitment manoeuvre, proning, bad lung dependent).

High $PaCO_2$

- Increase V_T
- Increase respiratory rate
- Increase tidal volume/PIP (but only if safe to do so)
- Consider reducing PEEP if evidence of overdistension
- Control CO_2 production (reduce dextrose, cool, paralyse)
- Improve V/Q matching.

Box 8.12 Inverse ratio ventilation (I:E ratio >1)

Close analysis of the trials of inverse ratio ventilation in adults with ARDS found that the beneficial effect on oxygenation was from PEEP generated from preventing adequate expiration as a result of shorter expiratory time. Interestingly inverse ratio ventilation also resulted in improved CO_2 clearance.

High airway pressures

- Suction secretions
- Treat bronchospasm
- Treat ventilator asynchrony
- Worsening lung compliance
- Exclude pneumothorax or atelectasis
- Exclude kinking of ETT or circuit
- Exclude endobronchial intubation
- Consider ↑intra-abdominal pressure
- Consider high levels of auto-PEEP
- Check for fluid in the circuit
- Reduce V_T
- Reduce inspiratory rise time
- Increase T_i.

High peak/plateau pressure gap

- Only applicable in VC mode in which a pause time is added at end-inspiration
- Implies high resistance to inspiratory flow, since the pressure falls significantly under conditions of no flow, i.e. during the inspiratory pause period

- Common causes include:
  - Asthma/bronchospasm
  - Secretions
  - Short inspiratory time for age and Tv
  - Small diameter ETT for age and Tv (croup).

Difficulty triggering ventilator

- Reduced patient effort (exhaustion, residual paralysis, hypokalaemia)
- High auto-PEEP
- Leak around uncuffed ETT or tracheostomy
- Trigger sensitivity set too high.

Special situations

Acute lung injury/ARDS

- 'High lung volume'/'open lung' approach to improve oxygenation
- Strategies which will increase mean airway pressure:
  - High PEEP, lengthen Ti (but avoid auto-PEEP)
  - 'Best-PEEP' can be determined by serial changes in PEEP and documentation of effect on dynamic lung compliance (Tv/(PIP-PEEP)) and effect on oxygen delivery, assessed using SvO_2, lactate, CO if available
- Limit tidal volume to 3–6mL/kg, limit PIP to 30–35cmH_2O
- Low Tv strategy will result in hypercapnia—tolerate respiratory acidosis
- Consider HFOV.

Diaphragmatic hernia

Offer 'gentilation', with short T_i, low tidal volumes, high rate, low inspiratory pressures and permissive hypercapnia. Low threshold for instigating HFOV.

Asthma

- Increase the expiratory time to avoid breath stacking and air trapping.
  - Monitor level of auto-PEEP using an expiratory hold and observe expiratory flow waveform to minimize degree of gas-trapping
  - Note: the level of auto-PEEP is the difference between total PEEP displayed at the end of an expiratory hold and the level of ventilator (extrinsic) PEEP
  - Allow permissive hypercapnia if prolonged expiratory time and I:E ratio of 1:4 or 1:5 necessary
- Use low/minimal levels of PEEP in the ventilated asthmatic
- CPAP, higher levels of PEEP will reduce work of breathing in the spontaneously breathing asthmatic with significant levels of auto-PEEP
  - The level of auto-PEEP cannot be measured in spontaneously breathing patient
  - Titrate level of CPAP / PEEP cautiously and observe effect on WOB.

PPHN

Try and avoid factors that will increase or exacerbate pulmonary hypertension such as hypoxia, hypercapnia and acidosis. Maintain a high FiO_2 and low normal $PaCO_2$. Consider iNO with or without HFOV.

Cavopulmonary shunt/Fontan

High PEEP, plateau and mean airway pressures will compromise pulmonary blood flow, oxygenation and cardiac output. Minimize the degree and duration of positive-pressure ventilation. Keep Ti short, use physiological levels of PEEP to prevent atelectasis.

Permissive hypercapnia

The concept of VILI is now well recognized. By limiting tidal volumes and ventilatory pressures, the incidence can be minimized. This often means ventilating a patient at V_T of 3–6mL/kg, and allowing the $PaCO_2$ to rise (7–9kPa) and the blood pH to fall (7.15–7.25).

Complications

- Barotrauma: pneumothorax, pneumomediastinum, subcutaneous emphysema, pulmonary interstitial emphysema (PIE)
- Breath stacking and gas trapping
- Ventilator associated pneumonia
- Airway oedema, subglottic stenosis
- Unplanned extubation
- Chronic lung disease
- Obstruction
- Reduced cardiac output
- Extubation failure.

A useful acronym to remember for the commoner acute complications of mechanical ventilation is DOPE—this stands for **D**isplacement of breathing tube, **O**bstruction, **P**neumothorax and **E**quipment failure.

Weaning and predictors of extubation

Mechanical ventilation has inherent risks to the patient, so it is important to determine at what point an attempt can be made to commence the process of weaning. Once the weaning process is complete, it is also important to determine at what point the patient should undergo a trial of extubation.

Weaning

Weaning protocols have not been shown to be superior in children. The initial indication for ventilation must be resolved before weaning is commenced. The most commonly used weaning modes are SIMV-PS and PS-CPAP.

Principles

- Reduce FiO_2 to maintain PaO_2 >8kpa
- Reduce ventilator RR unless spontaneous RR increases by >20%
- Maintain PS/CPAP level to deliver V_T 5–7mL/kg
- Minimum PS levels to overcome resistance of ETT have been suggested: 3.0–3.5mm ETT—10cmH_2O; 4.0–4.5mm ETT—8cmH_2O; ≥5.0mm ETT—6cmH_2O

- Other work suggests similar levels of PS are required across this range as peak inspiratory flows will also vary with age and size—a lower limit of 5cmH_2O is used by many.

Predictors

- Adult predictors of success or failure do not generally apply to children
- Spontaneous breathing trial: connect to flow-inflating bag with 5cmH_2O CPAP for 15min. Completion of trial is sensitive predictor of successful extubation
- Pressure-rate product (PRP): assessment on T-piece most accurate in predicting PRP post-extubation. Reduced by both PS and CPAP
- No difference in successful extubation if given breathing trial with PS or T-piece
- Various: V_T, RR, P_i(max) and f/V_T. Rapid shallow breathing index (RSBI)—all poor indicators of success.

Failure to wean

Failure to wean from ventilation—consider the six 'F's:

- *Failure of organ systems*: respiratory, cardiovascular, musculoskeletal, neurological, renal, critical illness myoneuropathy
- *Feeding*: inadequate nutrition, negative nitrogen balance, catabolism, loss of muscle mass and strength, high glucose load, abdominal distension
- *Fear, pain, and anxiety*: inadequate analgesia or anxiolysis, and inability to synchronize with the ventilator, poor cooperation
- *Fluid and electrolytes*: positive fluid balance with pulmonary oedema, reduced compliance and ↑WOB, hypokalaemia, hypocalcaemia, hypophospataemia
- *Fever*: active sepsis causing ↑ metabolic rate, oxygen requirements, and CO_2 production
- *Farmacological* (sic): drug overdose, side effects, or residual effects, symptoms of drug withdrawal.

Extubation

Criteria

- Resolution of underlying disease process
- Awake and coughing
- Minimal ventilatory support: PS <10cmH_2O
- Oxygen requirement less than 0.5 and PEEP <8cmH_2O with normal PaO_2
- Adequate alveolar ventilation: $PaCO_2$ normal or compensated, if raised
- Haemodynamically stable
- Age appropriate respiratory rate
- Electrolytes within normal limits.

Failure

Uncommon: 5–10% patients. Associated with:

- Younger age (<2 years)
- Ventilation for longer >48h
- Higher FiO_2, MAP, and oxygenation index
- Low V_T indexed to body weight for spontaneous breaths

- Higher peak inspiratory ventilator pressures and decreasing mean inspiratory flow
- Presence of chronic respiratory and neurological disease
- Dysgenetic and syndromic conditions
- Use of epinephrine, steroids and heliox
- Acute or chronic use of NIPPV.

Management post-extubation

- Observe and monitor in PICU until the patient has stable respiratory function and is unlikely to need reintubation
- Prepare to reintubate if necessary—consider special equipment or personnel if likely to prove difficult
- CPAP or non-invasive ventilation (NIV) is often useful in patients with limited respiratory or cardiovascular reserve following extubation. This may be delivered by nasal prongs, a nasopharyngeal airway, or close-fitting mask
- Some patients, particularly with a reduced level of consciousness, may benefit from a nasopharyngeal airway to assist in removal of secretions
- Indications to reventilate include deteriorating blood gases (hypoxia, hypercapnia), respiratory distress, inability to cough effectively and clear secretions, or cardiovascular instability
- Feeds may be restarted once the patient has stable respiratory function and is unlikely to need reintubation.

Post-extubation complications

Stridor is a common problem following extubation of children (Box 8.13). The most common cause is glottic and subglottic oedema, however other factors should be considered such as recurrent laryngeal nerve palsy following intrathoracic surgery, or subglottic stenosis.

Risk factors for post-extubation stridor include:

- Upper airway infection
- History of difficult intubation or multiple attempts
- Trisomy 21
- Children with neurological abnormalities—may have bulbar dysfunction and poor pharyngeal tone causing stridor and upper airway obstruction.

Box 8.13 'Dextubating' the patient

Patients at high risk for post-extubation stridor may be given steroids. Give dexamethasone IV 0.2mg/kg qds for 4–6 doses. Start 1h before extubation. Stridor that develops after extubation is again treated with steroids and nebulized epinephrine (0.4mg/kg, max. 5mg).

Some patients will have problems with *sputum retention* and require reintubation. This is most likely if there is reduced level of consciousness or muscular weakness.

High-frequency ventilation

- Defined as ventilation at rate >150 breaths/min
- Delivers a small tidal volume, usually less than or equal to anatomical dead space volume
- Expiration may be passive or active, depending on the design of the ventilator
- Precise mechanism of gas exchange uncertain, but likely to be combined effects of convection and molecular diffusion
- Technologies include HFOV and high-frequency jet ventilation (HFJV)
- The majority of high-frequency ventilators work on the principle of maintaining consistent lung volume with a continuous distending pressure and having a mechanism for rapid exchange of small volumes of gas to allow CO_2 clearance.

Indications for HFV

- Rescue following failure of conventional ventilation
- Air leak syndromes (pneumothorax, PIE)
- To reduce barotrauma when conventional ventilator settings are high
- Clinical trials have not shown definite survival benefit from HFV, although short-term improvement in oxygenation is frequently reported.

HFOV

The Sensormedics 3100 A/B are the most used ventilators for HFOV and this discussion will focus on these devices. Some neonatal ventilators (e.g. Draeger Babylog) offer HFOV modes, although these may only be usable in small babies. The Sensormedics 3100 A is suitable for premature neonates through to children with no set upper weight limit. The 3100 B was designed for patients >35kg, including adults, but may be used for smaller children.

Principle of operation

The Sensormedics oscillator essentially comprises a circuit providing continuous distending pressure and a diaphragm resembling a large loud speaker cone that vibrates to move gas in and out of the lungs. Both inspiration and expiration are therefore active, in contrast to conventional mechanical ventilators and some other forms of HFV.

Settings

- Oxygenation is determined by FiO_2 and mean airway pressure (MAP). Increasing these parameters will usually improve oxygenation, unless there is overdistension of the lungs (see Table 8.4)
- CO_2 clearance is a function of the amplitude of oscillation (ΔP) and the frequency (Hz). CO_2 clearance is usually increased by increasing amplitude and *reducing* frequency
- Initial setting for frequency will depend on patient's age and weight:
  - Premature neonate <1kg: 15Hz
  - Neonate: 10–12 Hz
  - Infant and small child: 7–10Hz
  - Large child and adult: 5–6Hz

- Bias flow is usually set at 20L/min, but may be reduced in neonates and increased in larger children – this will alter MAP
- Inspiratory time should generally be left at 33%. Increases may cause gas trapping.

Table 8.4 HFOV settings

Setting	Initial value	Subsequent change
Bias flow	20–30L/min	
Inspiratory time	33%	
FiO_2	Similar to CMV setting	Depends on SpO_2 and PaO_2
Frequency	Age dependent (4–15Hz)	Reduce to increase CO_2 clearance
MAP	5cmH_2O above CMV value	Change by 2cmH_2O increments
ΔP	15–20cmH_2O above CMV PIP	Change by 5cmH_2O increments

Disease groups and ventilation strategies (Box 8.14)

In ARDS and IRDS there is a diffuseprocess with loss of lung volume bilaterally as the alveoli are collapsed and filled with debris. The goal is to recruit these parts of the lung. On changing to HFOV a recruitment manoeuvre is undertaken and the MAP is set 10–15% above the *mean* airway pressure achieved on conventional ventilation (CMV). FiO_2 is set to 100% and reduced as necessary. After 1–4h a CXR must be obtained to assess the extent of lung recruitment, the goal being 8–9 posterior ribs visible. Once lung volume has been recruited it is generally possible to reduce both FiO_2 and MAP.

Where there is air leak the goal is to minimize MAP as far as possible. The MAP on HFOV should be set at the level of MAP achieved on CMV initially. Lower lung volumes should be aimed for as assessed on CXR. FiO_2 may need to be high to compensate.

In all patients CO_2 clearance depends on an adequate chest wiggle, which should be visible bilaterally from chest to lower abdomen. ΔP is adjusted until this is achieved and blood gases monitored. If CO_2 remains high, then the frequency should be reduced, having assessed that lung recruitment is adequate by obtaining a CXR.

Problems and troubleshooting on HFOV

- The ventilator circuit is quite rigid and generally requires the patient to be heavily sedated and immobile
- Changes in the lungs (e.g. reduced compliance, secretions) may not be easily detected, but can lead to marked changes in $PaCO_2$
- Assessment of lung volume requires CXR
- Over-inflation of the lungs may cause barotrauma
- Over-inflation of the lungs can impair venous return and compromise cardiac output

- Abrupt rises in pCO_2 may be caused by:
  - Blocked or kinked ETT
  - Secretions
  - Under or over-distension of the lungs (check CXR)
- A leak around the ETT will *increase* CO_2 clearance
- Disconnection of the circuit for suction or physiotherapy will lead to de-recruitment. Often a short-term increase in MAP is required after these interventions
- A useful rule of thumb is that ΔP should be <3× MAP. If settings are outside this range to achieve CO_2 clearance factors such as need for suction, frequency (Hz) and adequacy of lung volumes should be assessed
- Transition to CMV is usually performed once MAP is below 20–24cm H_2O, FiO_2 below 60% and with adequate CO_2 clearance.

Box 8.14 Open lung strategy during HFOV

HFOV is based on a constant distending pressure and unlike conventional ventilation does not incorporate phasic increases in airway pressure during which lung volume is recruited. As a result attention is needed during HFOV to recruit the lung after each disconnection and at other times when derecruitment may occur. A number of approaches have been described including: 1) increasing MAP to 30–40cm H_2O with the aim of recruiting the lung close to total lung volume; 2) empiric increase in MAP by 5cmH_2O for 5min after reconnection.

After recruiting the lung MAP is slowly reduced until the point is reached at which lung volume begins to fall steeply (Fig. 8.4)—this point has to be inferred from a fall in PaO_2 or SpO_2 in the absence of a bedside measure of lung volume. Body impedance technology (Respitrace) is used in some units to assess change in lung volume during HFOV.

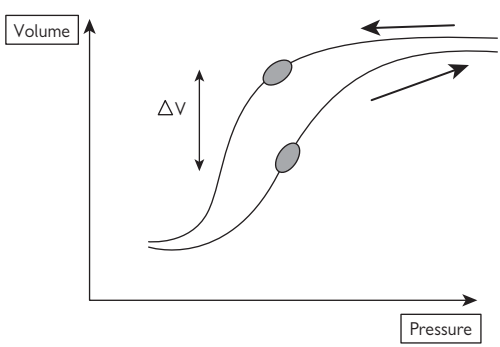

Fig. 8.4 Effect of a recruitment manoeuvre in a patient with significant lung hysteresis on HFOV. An increase in MAP drives the lung up the inspiratory limb of the PV curve, recruiting the lung. On decreasing MAP the lung volume falls along the deflation limb. Note for the same pressure there is a significant gain in lung volume which will result in improved oxygenation.

Non-invasive ventilation (NIV)

CPAP

- CPAP can be used
  - To provide respiratory support and avoid the need for intubation
  - To provide 'step-down' supplementary ventilatory support postextubation
- It reduces the work of breathing, increases FRC and oxygenation, and prevents apnoeas.

BIPAP

BIPAP provides the same effects as CPAP, as well as supplementing alveolar ventilation and improving CO_2 clearance. It can be used as an alternative to IPPV in patients where ventilation is compromised, but intubation is not yet indicated.

Indications for NIV

Acute

- ↑WOB
- Poor oxygenation
- Apnoeas
- Cardiac failure
- Pulmonary oedema
- Atelectasis
- Acute neuromuscular failure—critical illness polyneuropathy/myopathy, Guillan–Barré syndrome
- Chest trauma—lung contusion, flail chest
- Augmentation of cardiac output (Fontan, tetralogy of Fallot).

Long term

- Central hypoventilation syndrome
- Obstructive sleep apnoea
- Chronic lung disease
- Chest wall deformities—Jeune syndrome, scoliosis
- Neuromuscular disease—muscular dystrophy, spinal muscular atrophy, myasthenia gravis, phrenic nerve palsy.

Rationale

- ↑functional residual capacity
- ↓work of breathing
- ↓oxygen consumption
- Beneficial effect on cardiac afterload and cardiac output
- ↑alveolar ventilation and CO_2 clearance.

Types

Positive pressure approaches

- CPAP
- BIPAP

Negative pressure approaches

- Continuous negative extrathoracic pressure (CNEP)
- Negative extrathoracic pressure ventilation (NEPV).

Methods

- Mask—nasal or full-face (CPAP, BiPAP)
- 'Short tube'/nasopharyngeal prong (CPAP)
- Nasal pillows or prongs (CPAP)
- Negative pressure cuirass (NEPV).

Settings

CPAP

- Flow: 0.2–0.3L/kg/min (may be determined by ventilator)
- Pressure: +5–12 cmH_2O.

BiPAP

- Inspiratory pressure: +10–20 cmH_2O
- Expiratory pressure: +5–12 cmH_2O
- Respiratory rate: 15–25.

CNEP

- Inspiratory pressure: −20–30 cmH_2O.

NEPV

- Inspiratory pressure: −20–30 cmH_2O
- Expiratory pressure: +5 cmH_2O
- Respiratory rate: 30–50.

Reasons for failure

- Patient acceptance/cooperation
- Problems triggering ventilation
- Excessive leaks
- Equipment inadequacies
- Pressure areas
- Excessive secretions.

Complications

- Failure of technique
- Drying of mucosa and secretions
- Pressure sores
- Gastric distension—insert NG tube
- Pneumothorax
- Reflux and aspiration
- Upper airway obstruction (CNEP, NEPV)
- Maxillary deformity (long term).

Monitoring

- Clinical
- Oxygen saturations
- ABG/CBG
- Ventilatory pressures
- Spirometry
- Plethysmography.

Predictors

Success

- Drop in respiratory rate and PCO_2 in first 2h
- FiO_2 <0.8 after 1h.

Failure

- Diagnosis of ARDS
- Uncooperative patient.

Surfactant

Pulmonary surfactant is a surface active lipoprotein complex formed by type II alveolar cells. Its function is to increase lung compliance and prevent alveolar collapse at end expiration.

In preterm babies (esp. <30 weeks' gestation) lack of surfactant causes IRDS. In the ARDS there is ↓surfactant production, abnormal surfactant composition, and inhibition of its function.

Types of surfactant

Natural surfactant is derived from bovine or porcine lungs. Synthetic surfactant is available in some countries. The licensed indication is the treatment of IRDS in premature infants. There is no evidence that any one preparation is superior. Surfactant is expensive, particularly at doses that would be required in larger children or adults.

Therapeutic uses of surfactant

- IRDS:
  - Surfactant has revolutionized treatment of IRDS
  - Early prophylactic surfactant administration appears beneficial in babies at high risk of IRDS
- Meconium aspiration—trials have shown benefit with surfactant administration
- Congenital diaphragmatic hernia—no benefit of surfactant in term infants with diaphragmatic hernia
- ARDS:
  - Short-term improvement in oxygenation
  - No benefit in terms of survival in ARDS.

Complications of surfactant administration

- Need for intubation for administration
- ETT blockage
- Airleak (pneumothorax), hyperoxia, or respiratory alkalosis as lung compliance rapidly increases if pressure control mode of ventilation used.

Genetic disorders of surfactant

- Surfactant protein B deficiency causes severe respiratory failure shortly after birth that is only transiently improved with surfactant administration. The condition is usually lethal
- Disorders of surfactant protein C may present from shortly after birth to adulthood. The condition may cause interstitial pneumonitis in infancy with progressive respiratory failure. Some studies have reported improvement with steroids or immunosuppressants. If severe respiratory failure develops lung transplantation will be required.

Inhaled medications

Methods of administration

Aerosol

Airborne drug in the form of liquid droplets or solid particles, e.g. β2 agonists, steroids, anticholinergics.

Nebulization

Principle of converting a liquid into an aerosol, which can then be inhaled into the lower respiratory tract, e.g. β2 agonists, steroids, anticholinergics, mucolytics, antibiotics, antivirals, surfactant, epoprostenol:

- Particle size: 1–6μm
- Minimum driving gas flow rate: 8L/min
- Use oxygen in asthma, otherwise air
- Minimum volume: 3–4mL
- Deliver over 10min
- Types: jet, ultrasonic, vibrating mesh, small particle aerosol generator (SPAG).

Vapour

Gas phase in equilibrium with identical matter in a liquid state below its boiling point, e.g. halogenated anaesthetics.

Gas

Matter in a compressible fluid phase, e.g. nitric oxide, heliox, nitrous oxide.

Drugs

Bronchodilators

- Steroids: beclomethasone, budesonide, fluticasone
- β2 agonists: salbutamol, terbutaline
- Anticholinergics: ipratropium
- Halogenated vapours: halothane, isoflurane, sevoflurane.

Mucolytics

- Dornase alfa
- Acetylcysteine
- Hypertonic saline (3% or 7.5%).

Antibiotics/antivirals

- Tobramycin
- Pentamidine
- Colistin
- Ribavirin.

Miscellaneous

- NO
- Epoprostenol
- Surfactant
- Heliox
- Nitrous oxide.

Indications

- Bronchospasm: β2 agonists, steroids, ipratropium, halogenated vapours
- Atelectasis: 3% saline, dornase alfa, acetylcysteine
- Pulmonary hypertension: NO, iloprost
- RSV and adenovirus infection: ribavirin
- Respiratory distress syndrome: NO
- Upper airway obstruction: epinephrine, budesonide, heliox
- Analgesia: nitrous oxide
- Anaesthesia: halogenated vapours
- Cystic fibrosis: tobramycin, pentamidine, colistin
- Fungal pneumonia: amphotericin B.

Inhaled drug doses/concentrations

- Acetylcysteine: 0.1mL/kg of 10% solution 6–12-hourly (max. 5mL)
- Adrenaline: 0.4mL/kg of 1/1000 solution (max. 5mL)
- Amphotericin B: 5–10mg 12-hourly
- Beclometasone: 50–400mcg 12-hourly
- Budesonide: 2mg (nebulizer) 6-hourly
- Colistin: 500,000–2 million U 12-hourly nebulized
- Dornase alfa: 2.5mg 12-hourly nebulized
- Fluticasone: 1–2mg 12-hourly (nebulized); 50–200mcg (inhaled)
- Halothane: 0.75–2% (maximum 5%)
- Heliox: 79% helium 21% oxygen mixture
- Hypertonic saline: 4–10mL nebulized PRN
- Iloprost: 0.5mcg/kg 3–4-hourly
- Ipratropium: 0.25–1mL of respiratory solution (250mcg/mL) diluted to 4mL every 4–8h (nebulizer). 2–4 puffs (20mcg/puff) 6–8-hourly (aerosol)
- Isoflurane: 1.5–3% (maximum 5%)
- Nitric oxide: 1–40ppm as premixed gas. Monitor concentration and NO_2 levels
- Nitrous oxide: 50% in oxygen as Entonox
- Pentamidine:* 6mL (600mg) daily (treatment); 3mL (300mg) daily (prophylaxis) nebulized
- Ribavirin:*: 20mg/mL solution 18h/day for 3–5 days (SPAG)
- Salbutamol: 2.5–5mg PRN
- Sevoflurane: 2–4% (maximum 8%)
- Terbutaline: 2.5–10mg PRN (nebulized); 250–500mcg 4–6-hourly (inhaler)
- Tobramycin: 40–80mg in 4mL 12-hourly (up to 300mg >6 years).

⚠*Potentially toxic drug requiring precautions when administered

Nitric oxide delivery

- NO relaxes vascular smooth muscle by binding to the haem moiety of cytosolic guanylate cyclase, activating guanylate cyclase and increasing intracellular levels of cyclic guanosine 3',5'- monophophate (cGMP), which then leads to vasodilatation
- When inhaled, NO produces pulmonary vasodilatation. Its beneficial effects include lowering of pulmonary artery pressure (by lowering PVR) and improving VQ mismatch by causing selective pulmonary vasodilatation of capillary beds adjacent to ventilated iNo containing alveoli and away from areas of very low VQ and shunt
- NO readily reacts with oxygen to form nitrogen dioxide (NO_2) which is toxic. NO combines with haemoglobin to form methaemaglobin, the concentration of which is measured by standard blood gas analysers with co-oximetry. Inhaled concentrations of NO above 20ppm are unlikely to have additional clinical benefit, but will increase the concentration of these potentially harmful substances. Abrupt withdrawal of NO may cause an acute rise in pulmonary artery pressures and worsen oxygenation, even in patients where there was no apparent benefit on starting the drug. For this reason it should be weaned gradually
- In North America and Europe, NO is available as a licensed product (INOmax) for the management of persistent pulmonary hypertension in term and near term neonates. Efficacy has not been demonstrated in other patient groups (e.g. adults with ARDS, congenital diaphragmatic hernia). Although NO may improve hypoxia in other patient groups, this may not result in improved outcome (e.g. survival, duration of ventilation)
- Any NO delivery system should allow maintenance of constant concentrations of NO in the inspired gas throughout the respiratory cycle. Precise monitoring of inspired NO and NO_2 should be provided. Sample gas for analysis should be drawn before the Y-piece, proximal to the patient
- The INOvent system is an example of a commercially available NO delivery system that allows for precise control of inhaled concentration and monitoring. The system includes a metered valve that measures the duration of administration of NO for the purpose of charging for its use. It is important to shut off these valves upon discontinuing the drug to avoid excessive costs. Portable systems are also available for use during patient transport.

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy (HBOT) involves delivery of 100% oxygen inside a treatment chamber at a pressure greater than sea level. This increases dissolved oxygen content of blood (and hence PaO_2). At 3 atmospheres pressure the resting oxygen requirements of tissues can be supplied without the oxygen carrying capacity of haemoglobin.

A multiplace chamber can accommodate a patient with attendants and would be required for any critical care situation. Within the UK there are about 9 facilities capable of receiving patients who may require advanced life support either immediately or during HBOT. These are not evenly distributed on a geographical basis.

Indications for HBOT

- Emergency treatment:
  - Decompression illness
  - Air and gas embolism
  - CO poisoning
- Urgent treatment required within 24h:
  - Necrotizing fasciitis
  - Gas gangrene.

Risks of HBOT

- Risks of transporting patient to distant facility
- Facilities for managing critically ill patient may be suboptimal
- Oxygen toxicity (exposure should be limited to <2h, including attendants)
- Hyperoxic seizures
- Reversible myopia
- Fire (commonest cause of fatalities).

Carbon monoxide poisoning

- Cognitive sequelae lasting 1 month or more occur in 25–50% of patients with loss of consciousness or with carboxyhaemoglobin (COHb) levels >25%. The recommended treatment for acute CO poisoning is 100% normobaric oxygen. This reduces the half-life of COHb from 300min breathing air to 80min. HBOT is often recommended for patients with acute CO poisoning, especially if they have lost consciousness or have severe poisoning
- Advantages of HBOT include accelerated elimination of CO, although COHb levels are likely to be low by the time the patient reaches a HBOT facility. Potential benefits include prevention of lipid peroxidation in the brain and preservation of ATP levels in tissue exposed to CO. Some adult studies show benefit in long-term cognitive outcome after 3 HBOT treatments within 24h of symptomatic CO poisoning. However no clinical variables, including COHb levels, identify a subgroup of CO-poisoned patients for whom HBOT is most likely to provide benefit or cause harm and no child was enrolled in any of the clinical trials.

Chest physiotherapy

Principles

Chest physiotherapy involves a number of techniques to clear the airway of sputum, treat atelectasis, improve ventilation-perfusion matching, encourage coughing and improve breathing. It usually involves optimizing patient position, before manual percussion and vibration of the chest wall. In the presence of an ETT, it may be combined with manual expansion of the chest through PPV and suctioning of sputum via a catheter. In extubated patients PPV or CPAP may be applied through a face mask or mouthpiece attached to a suitable ventilator.

Indications

- ↑sputum production: infection, inhalational injury, intubation
- ↓sputum clearance: reduced consciousness, poor cough due to sedation, muscle weakness, inadequate humidification
- Atelectasis
- Ventilator-associated pneumonia
- Underlying disease, e.g. cystic fibrosis

Techniques

- Postural drainage
- Breathing exercises
- PPV
- CPAP
- Manual hyperinflations: 3–4 slow PP breaths approximately 1.5× patient's tidal volume, followed by an inspiratory hold and quick release of the bag
- Percussions: manual clapping of the chest wall over the affected area with a cupped hand
- Vibrations: manual vibration, shaking and compression of the chest wall during expiration
- Saline lavage.

Contraindications/cautions

- Unstable neck injury
- Spinal injury
- Raised ICP
- Coagulopathy or thrombocytopenia
- Cardiovascular instability
- Low cardiac output state
- Acute asthma
- Pneumothorax
- Rib fractures
- Uncooperative patient.

Side effects/complications

May worsen hypoxaemia or precipitate hypo/hypertension, bradycardia, bronchspasm, pneumothorax, reflux, raised ICP or lead to accidental extubation.

Suctioning

For catheter sizes and ETTs see 🕮 Appendix, p.868.

Ideally, OD of catheter should be 30–50% <ID of ETT:
Catheter size (Fg) = ID ETT (mm) × 1.5 (50% less)
Or catheter size (Fg) = ID ETT (mm) × 2 (30% less).

Procedure (see Box 8.15)

- Prepare (equipment)
- If appropriate, explain procedure to patient
- Administer sedation/analgesia as required
- Wash hands with antiseptic solution
- Preoxygenate patient: FiO_2 1.0 for 1min
- Turn on wall suction unit to appropriate pressure depending on the age of the patient: infants: 60–90mmHg; older children: 90–110mmHg
- Attach suction catheter to tubing whilst still covered with sterile wrapping
- Apply sterile glove to dominant hand and withdraw suction catheter from wrapping, avoiding contamination
- With non-dominant hand disconnect ventilator tubing and instil saline solution 0.5–2mL (if required)
- Attach manual ventilation bag (MVB) and manually ventilate patient
- Disconnect MVB and insert suction catheter to predetermined depth with gloved hand, avoiding suctioning
- Apply intermittent suction whilst slowly rotating and withdrawing the suction catheter over no more than 5–10s
- Either reattach the ventilator tubing or the MVB and recommence ventilation
- Repeat the process as necessary
- Reduce FiO_2 as tolerated
- Flush suction tubing with saline and discard used equipment
- Wash hands
- Clinically reassess patient.

Complications

As for chest physiotherapy (🕮 p.167).

Box 8.15 Controversies

- Open vs. closed systems: closed systems expensive, but may preserve lung volume
- Graduated vs. non-graduated catheters: graduated catheters more expensive, but easier to control depth of suctioning
- Deep vs. shallow: deep more traumatic and can cause lobar collapse; shallow won't aspirate secretions from the bronchus
- Use of the same catheter for 24h: cost-effective and no difference in incidence of pneumonia
- Saline: often used if thick secretions are difficult to mobilize
- Blunting pressor response: indicated in patients at risk of raised ICP or at risk of pulmonary hypertensive crises. Use IV alfentanil (15–30mcg/kg), fentanyl (5–10mcg/kg), remifentanil (1–4mcg/kg), esmolol (2mg/kg) and lignocaine (1.5–2mg/kg), or intratracheal lignocaine (2–5mg/kg).

Fibreoptic bronchoscopy

Advances in technology mean that fibreoptic bronchoscopy (FOB) with a flexible fibrescope (FFS) can now be undertaken in most patients on the PICU, irrespective of size or pathology. It is indicated for mainly diagnostic reasons, but it may also be important for therapy. Generally, the yield has been shown to be good, with positive findings in >80% patients. In some patients the FFS may also be used for intubation purposes and should be part of the difficult airway equipment.

Indications

Diagnosis

- Bronchoalveolar lavage (BAL)
- Persistent parenchymal abnormality
- Persistent wheeze
- Dynamic airway pathology
- Upper airway obstruction
- Foreign body
- Vascular ring
- Pulmonary haemorrhage/haemoptysis
- Tracheal trauma.

Treatment

- Segmental collapse
- Mucus plug
- BAL
- Drug administration, e.g. DNase.

Other

- Intubation
- ETT position and obstruction
- Failed extubation
- Endobronchial biopsy
- Lung biopsy

Contraindications/cautions

- Diagnosis of acute epiglottitis
- Massive haemoptysis
- Coagulopathy
- Removal of foreign body
- Lack of training in FOB
- Need to secure airway immediately
- Hypoxaemia

Equipment

FFS sizes

The ideal size of FFS to use depends on whether it is being used for intubation or bronchoscopy. Intubation requires an ETT size that is only slightly larger than the diameter of the FFS, so that it is a snug fit. It will also be an appropriate length for the size of patient. Bronchoscopy may require the FFS to be passed through the ETT, whilst ventilation is maintained. In this

circumstance the diameter of the FFS needs to be sufficiently smaller than the ETT to allow adequate ventilation. Table 8.5 indicates the size of FFS which can be used, both through an ETT and through an LMA. The former is based on it occupying approximately 70% of the internal diameter of the ETT.

Table 8.5 Flexible fibroscope sizes

Age	ETT size (ID mm)	Bronchoscope size (OD mm): ETT	Bronchoscope size (OD mm): LMA
Prem	2.5–3.0	2.2	2.4
Term	3.0–3.5	2.2	3.0
6 months	3.5–4.0	2.4	3.0
1 year	4.0–4.5	3.0	3.4
2 years	4.5–5.0	3.0	3.4
3 years	5.0–5.5	3.6	4.0
5 years	5.5–6.0	4.0	5.0
10 years	6.5–7.0 cuffed	4.4	6.0
14 years	7.0–7.5 cuffed	5.0	6.0

The size of FFS available depends on the manufacturer and the scope designation (intubation vs. broncoscopy); although the length will normally be the same. The smallest FFS with a suction channel is 2.7mm. Note that the widest portion of some FFS is the body and not the tip.

Methods

There are 2 main methods of undertaking FOB in PICU patients. If the patient is intubated it may be possible to pass the scope through the ETT. The main risk is that the scope may be too large to allow adequate ventilation, risking hypoxia, hypercapnia, and ↑PEEP. Alternatively, FOB can be undertaken through an LMA, which will allow a bigger scope to be passed relative to the size of the patient and improved ventilation. It also allows the laryngeal inlet, vocal cords, and subglottic area to be visualized. However, an LMA does not provide a secure airway and spontaneous ventilation may be ineffective in PICU patients with significant respiratory compromise.

ETT

- Spontaneous breathing rarely possible
- Best if patient has significant respiratory compromise and already intubated
- Can be undertaken with sedation and topical anaesthesia alone
- Select FFS with smaller diameter than the ID of the ETT (ideally <70% diameter ETT to allow ventilation)
- Ventilate patient in 100% oxygen

- Lubricate FFS and introduce through an angle connector with a hole in the top, e.g. Portex®
- Inject 2% lignocaine in 0.5–1-mL aliquots PRN (maximum 5mg/kg) unless patient paralysed
- Remove FFS if hypoxaemia (SpO_2 <90%) or difficulty ventilating patient
- Undertake procedure as quickly as possible and return patient to ventilator.

LMA

- Difficult in the presence of significant lung disease or oxygen requirement
- Make sure LMA doesn't have aperture bars or these are removed prior to insertion
- Anaesthesia necessary for insertion and tolerance of LMA: sevoflurane or halothane in 100% oxygen ± 0.5–1mg/kg propofol boluses
- Try and maintain spontaneous respirations
- Apply topical lignocaine (2–4%) to cords and airway under direct vision, then insert LMA
- Connect angle connector to LMA and insert FFS
- Larynx should be visible at the end of the LMA (epiglottis may be folded over)
- Advance FFS and undertake procedure
- Apply further topical lignocaine PRN
- Remove LMA and replace with ETT if required.

Complications

- Hypoxia
- Laryngospasm/bronchospasm
- Trauma
- Pressor response (tachycardia and hypertension)
- Haemorrhage
- ↑PEEP during procedure
- Air leak (lung biopsy).

Bronchoalveolar lavage

BAL is a diagnostic or therapeutic procedure to wash out epithelial lining fluid from the lungs, by instilling saline deep into the lower airways and aspirating the sample back. It can be done under direct vision (bronchoscopic) or undertaken blind (non-bronchoscopic see Appendix p.870). Bronchoscopic BAL has advantages in terms of accuracy, for both therapeutic and diagnostic procedures.

Most BAL samples will be obtained without bronchoscopic assistance. Up to 60% of patients undergoing BAL will have their antimicrobial treatment changed. The alternative method of sampling endotracheal secretions (ETS) can be unreliable at diagnosing true infection as opposed to colonization of the respiratory tract. Unless they are present in significant amounts and obtained early in the respiratory illness, there is a high incidence of false positive results with ETS, which may lead to unnecessary antibiotic treatment.

Principles

- A bronchoscope or suction catheter is wedged into a bronchus of similar diameter
- 0.9% saline is instilled into the airway below
- Fluid is immediately withdrawn into sterile containers for processing
- The procedure is repeated as necessary up to a total of 1mL/kg saline.

Indications

Diagnostic

- Undiagnosed respiratory failure
- Suspected VAP
- Change in colour/character/quantity of ETS
- Diffuse lung infiltrates or cavitary lesion on CXR
- Radiological evidence of new or ↑lung infiltrates
- Pulmonary pathology in an immunocompromised host
- Diagnosis of non-infectious lung disease, e.g. alveolar proteinosis, alveolar haemorrhage.

Therapeutic

- Mucus plugging and lobar collapse
- Removal of airway material, e.g. lipoid pneumonia
- Smoke inhalation injury
- Whole-lung lavage in alveolar proteinosis.

Samples

If these are not being processed immediately, they need to be kept at 4°C to optimize cell viability. The appearance and cell content of the fluid will aid diagnosis of non-infectious lung disease.

Microbiology

- MC&S
- Fungi
- Legionella
- AFBs.

Virology
- Immunofluorescence
- Culture
- Chlamydia.

Histology
- Cytology
- Silver stain for fungi
- PCP
- Fat-laden macrophages.

Complications
- Coughing (unparalysed patients)
- Hypoxia
- Bradycardia
- Worsening of gas exchange
- Trauma
- Haemorrhage
- Fever
- Transient pulmonary infiltrates
- Bronchospasm
- Surfactant washout
- Airway contamination.

Further reading
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Matthay MA (ed) (2003). *Acute Respiratory Distress Syndrome*. Informa Health Care. ISBN 0824740769.
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Chapter 9

Anaesthesia

Principles of anaesthesia

Acquisition of anaesthetic knowledge and skills are vital for any practising paediatric intensivist. One hardly needs to exaggerate the importance of airway maintenance and adequate ventilation in a critically ill child.

Whilst the principles and detail covered in both this chapter and 🕮 Chapter 8 ('Airway management and ventilation') should provide enough information for the trainee intensivist, there can be no substitute for the experience gained from hands-on anaesthetic practice. We would recommend that any trainee dealing with critically ill children spends a period of time working in the operating theatre environment and receiving practical tuition from experienced anaesthetists.

Whilst the trained paediatric intensivist may have the knowledge and skills to manage a child's airway and ventilation on the PICU or the emergency room, we would recommend (unless they are also a trained anaesthetist) that they leave the practice of paediatric anaesthesia to a safer pair of hands, i.e. an anaesthetist.

Key concepts

- Anaesthesia (from Greek an- 'without' + aisthesis 'sensation') has traditionally meant the condition of having the feeling of pain and other sensations blocked
- Inhalational anaesthesia was first demonstrated in 1846 and by 1848 the first death had been recorded attributed to anaesthesia
- General anaesthesia refers to a complete loss of consciousness during which patients are not rousable, even by painful stimulation
- Regional anaesthesia is loss of pain sensation in certain regions of the body due to nerve blockade by local anaesthetics:
  - Spinal (subarachnoid) anaesthesia results from a small volume of local anesthetics being injected into the spinal canal
  - Epidural (extradural) anaesthesia results from an injection of a local anesthetic into the extradural space.

Anaesthetic rules (UK)

- The safety of modern anaesthesia in the UK is founded on tight control by regulating bodies and the strict adherence to guidelines and protocols produced by the Royal College of Anaesthetists, the Association of Anaesthetists of Great Britain and Ireland, and other related anaesthesia societies
- Comprehensive perioperative care can only be provided by an anaesthesia team led by consultant anaesthetists. All members of the team must be trained to nationally agreed standards
- The safe administration of anaesthesia cannot be carried out single-handedly. Anaesthetists must have dedicated qualified assistance wherever anaesthesia is administered, whether in the operating department, the PICU or any other area
- The anaesthetist must be present and care for the patient throughout the conduct of an anaesthetic
- ***Minimal monitoring includes:***
  - Pulse oximeter
  - Non-invasive BP

  - ECG
  - Airway gases: O_2, CO_2, and volatile agent
  - Airway pressure measurement
- Monitoring devices must be attached before induction of anaesthesia and their use continued until the patient has recovered from the effects of anaesthesia
- The anaesthetist must ensure that all equipment has been checked before use. Alarm limits for all equipment must be set appropriately before use. Audible alarms must be working during anaesthesia.

Preoperative assessment

- All patients should undergo comprehensive preoperative assessment by an anaesthetist before undergoing anaesthesia. Ideally, this should be the doctor who is to give the anaesthetic
- PICU staff should ensure that the appropriate information and investigations are available to allow a thorough preoperative assessment.

Preoperative fasting

- The aim of preoperative fasting (Box 9.1) is to reduce the volume of gastric contents and minimize the risk of passive regurgitation and pulmonary aspiration during anaesthesia
- In most cases on PICU IV maintenance fluid therapy should be started in the fasting period.

Box 9.1 Fasting times

Formula milk has slower gastric emptying than breast milk:

• Clear fluids	2h before anaesthesia
• Breast milk	4h before anaesthesia
• Formula milk	6h before anaesthesia
• Food, cows' milk	6h before anaesthesia

NG feeds (whatever type) should be stopped 4h before anaesthesia in patients on PICU and the NG tube aspirated before induction.

Box 9.2 The safe anaesthetist

The safe anaesthetist not only knows how to avoid trouble but also accepts the unexpected happens and knows what to do when it does. Careful planning underpins the safe practice of anaesthesia in critically ill children:

- Safe environment: never anaesthetize a child in an unfamiliar setting if it can be avoided. Most critically ill children can be transferred safely to a more familiar environment (resuscitation room in emergency department, PICU, operating theatres)
- Check and arrange equipment: see 🕮 p.132
- Call for help: make sure that you have skilled assistance that you are familiar with (operating department personnel, anaesthetic nurses, PICU nurses and colleagues)

(*Continued*)

Box 9.2 The safe anaesthetist (*Continued*)

- Use familiar techniques: Keep it simple
- Preoxygenate the patient: Always preoxygenate the critically ill patient for as long as possible. Sometimes this is not easy with a critically ill child but high flow facemask oxygen (with a reservoir)is better than air. Preoxygenation buys the anaesthetist time and can be life saving.

Anaesthetic technique

Induction of anaesthesia

Induction may be IV or gaseous:

- *IV induction* is the standard way to induce anaesthesia in a patient who has a reliable form of venous access. It is an essential part of a RSI and is recommended for raised ICP
- *Gaseous induction* is often used in children for elective surgery who have difficult venous access or are needle phobic. ***Gaseous induction is mandatory (and IV induction contraindicated)*** in situations of airway compromise when airway maintenance or intubation cannot be guaranteed. For example epiglottitis, facial/jaw abnormalities.

Maintenance of anaesthesia

- The patient may be spontaneously breathing or paralysed and ventilated as part of the anaesthetic technique
- Anaesthesia is maintained by continuous administration of volatile agent via an anaesthetic machine or IV agent (usually via a syringe driving pump)
- Administered oxygen is usually at a minimum of 30%
- Concurrent analgesics can be given as an adjunct to volatile agent as they reduce the response to painful stimulus:
  - Opioid analgesics, e.g. morphine, fentanyl
  - Local anaesthetic can be given as regional anaesthesia
  - Nitrous oxide is often given as a gaseous anaesthetic/analgesic
- If the patient is paralysed and ventilated then neuromuscular blockers, e.g. atracurium, vecuronium, rocuronium can be used.

Emergence of anaesthesia and recovery

- When it is time to awaken the patient the anaesthetic maintenance (volatile or IV) is turned off and neuromuscular blockade reversed with anticholinesterase and anticholinergic (e.g. neostigmine and atropine or glcopyrronium)
- The responsibility of anaesthetists for the care of their patients extends into the postoperative period and includes the management of postoperative pain
- Emergence from anaesthesia is potentially hazardous and patients require close observation until recovery is complete

- Continuous individual observation of each patient is required on a one-to-one basis until the patient is able to maintain his/her own airway, has cardiovascular stability, and is able to communicate, if appropriate
- Supplementary oxygen is required in recovery to prevent hypoxaemia secondary to respiratory depression from pain, residual anaesthetic agents, and opioids
- Be aware that hypercapnia may occur from respiratory depression whilst the patient's SaO_2 is high because they are on supplemental oxygen.

Box 9.3 Brief scenarios

Certain situations in critically children require careful tailoring of technique. More detail are in the relevant chapters:

- ***Asthma***: intervene before exhaustion sets in. Preoxygenate with high-flow oxygen via face mask sitting up. Fluid bolus 10mL/kg 0.9% saline (or equivalent). RSI with ketamine and suxamethonium. Lie down after induction—apply cricoid. Avoid atracurium. Initially stabilize with fentanyl and midazolam/ketamine infusion. Avoid natural tendency to over zealous bag ventilation.
- ***Croup, epiglottitis, tracheitis***: senior assistance. Ear, nose, and throat surgeon present. Equipment for tracheostomy present. Gas induction by experienced anaesthetist. Halothane if available is best. Sevoflurane is best converted to isoflurane before laryngoscopy attempted. Always wait another 60s after 'ready' to laryngoscopy. Aim for 'bubble of air' with 'strawberry larynx in epiglottitis'. Tracheitis greets the intubator with lots of pus.
- ***Head injury, status epilepticus, meningitis/encephalitis***: RSI thiopentone and suxamethonium. Head injury will need c-spine stabilization—manually or with collar. Trauma case may need fluid loading before hand. Maintain mean arterial pressure to preserve cerebral perfusion pressure. Monitor $EtCO_2$ and aim for normocapnia. Give muscle relaxant and if CT scan required then consider short-term propofol infusion until PICU: 1–4mg/kg/h. Keep head up 20–30°.
- ***Shock (hypovolaemic, septic):*** fluid load 10–30mL 0.9% saline or equivalent. RSI with ketamine or reduced dose thiopentone. In septic shock try to site central, arterial lines with urgency before severe capillary leak tissue swelling becomes severe. Start inotropes/pressors if indicated.
- ***Aortic stenosis (outflow tract obstruction), right-to-left shunt (e.g. Fallots):*** try to avoid dropping SVR. Use ketamine or careful dose of thiopentone with fentanyl. Avoid propofol. If hypotension occurs, give fluid 10mL/kg IV, start pressor (noradrenaline, phenylephrine) and ventilate with 100% O_2.

Intravenous anaesthetic agents

Thiopentone

- Short-acting agent used for induction of anaesthesia
- Potent anticonvulsant by bolus or infusion (prolonged elimination)
- Induction dose: 2–4mg/kg in neonates and infants, 5–6mg/kg in children
- ***Induction dose must be reduced in critically ill patients*** Hypotension and respiratory depression are dose dependant and more pronounced in hypovolaemic or cardiovascularly unstable patients
- Recovery from single bolus dose is due to redistribution. Reduced clearance and prolonged elimination half-life of 19h in neonates compared with 6–12h in older children

Used as an infusion to reduce cerebral metabolic requirements in cases of severe head injury (see 🕮 p.505).

Ketamine

- A phencyclidine derivative—an antagonist at NMDA receptors
- Produces 'dissociative anaesthesia' characterized by catalepsy, catatonia, and amnesia. The eyes may remain open following administration
- Is a potent analgesic
- Can be given IV, IM, or orally
- Induction dose: 2–3mg/kg IV; 5–10mg/kg IM
- Very suitable for shock (reduce dose to 1–2mg/kg), asthma, right-to-left shunt cardiac patients (i.e. cyanotic): has an indirect sympathomimetic effect, mediated by the release of endogenous catecholamines, which usually prevent hypotension unless the host sympathetic response is maximal, e.g. in severe shock
- Anaesthesia after a single IV dose lasts 5–10min. The analgesic effect lasts longer
- Recovery from single bolus dose is due to redistribution. It undergoes hepatic metabolism to norketamine. Elimination half-life is approximately 3h. Neonates have a larger apparent Volume of distribution and a lower clearance than older children
- Airway is better maintained compared to propofol and thiopentone. There is some preservation of protective airway reflexes but is not guaranteed to protect against aspiration
- Less respiratory depression compared with thiopentone and propofol.
- Has bronchodilator properties and is used in severe asthma
- ↑salivation and airway secretions. Atropine 20mcg/kg or glycopyrronium 10mcg/kg can be given concurrently
- Can cause nightmares or hallucinations on emergence from anaesthesia, which can be reduced by administration of concurrent benzodiazepines.

Propofol

- Short-acting agent used for induction and maintenance of anaesthesia
- Induction dose: 3–5mg/kg in infants, 4–5mg/kg in children
- ***Induction dose must be reduced in critically ill patients*** Hypotension and respiratory depression are dose dependant and more pronounced in hypovolaemic or cardiovascularly unstable patients

- Recovery from single bolus dose is due to redistribution resulting in rapid, clear-headed emergence after brief procedures. Elimination following repeated doses or infusion is more rapid compared to thiopentone
- It causes pain on injection
- Currently contraindicated in UK for use as an infusion for sedation of children <16 years of age in PICU due to the risk of 'propofol infusion syndrome' comprising metabolic acidosis, rhabdomyolysis, life-threatening cardiac failure, cardiac arrest.

Neuromuscular blocking agents

See 🕮 p.196.

Inhalational anaesthetic agents

- Commonly used 'volatile' anaesthetic agents are; sevoflurane, isoflurane, desflurane and halothane
- Sevoflurane is the commonest agent used for inhalational induction. Halothane is still used especially for the potentially difficult airway
- Isoflurane and desflurane are unsuitable for inhalational induction due to airway irritation
- All can cause dose-dependant cardiovascular depression
- All are bronchodilators by direct relaxation of bronchial smooth muscle and can be used in the treatment of severe asthma
- Potency of anaesthetic agents are measured by minimum alveolar concentration (MAC) values of volatile agents, i.e. the amount to keep 50% of patients still in surgical operations. MAC values vary with age (Table 9.1):
  - Infants and small children need higher concentrations of volatiles, and neonates need less compared to adults.
  - MAC values are for comparison between agents and are not applicable to individual patients.

Table 9.1 MAC value and age (in healthy patients)

	Sevoflurane	Isoflurane	Desflurane	Halothane
Neonate	3.3	1.6	9.1	0.9
Infant	3.2	1.9	9.4	1.2
Child	2.5	1.6	8.6	0.9
Adult	2.0	1.16	6.0	0.76

Sevoflurane

- Commonest agent for inhalational induction. Minimal airway irritation means that a concentration of 8% can be readily used from the start which speeds induction

- Significant respiratory depression or apnoea at high concentrations. Its low potency can result in apnoea occurring before intubating depth of anaesthesia is reached
- Delirium and distress on emergence can occur in children.

Halothane

- Rarely used nowadays in UK but its potency and lack of airway irritation are ideal for inhalational induction—particularly suitable for difficult airway, e.g. epiglottitis, congenital abnormalities
- Takes a long time to wear off
- Halothane hepatitis is rare in children.

Isoflurane and desflurane

- The commonly used agents for maintenance of anaesthesia
- Airway irritant makes them unsuitable for inhalational induction.

Nitrous oxide (N_2O)

- Do not confuse with nitric oxide (NO)
- Used as a carrier gas for volatile anaesthetic agents. Addition of N_2O will reduce the MAC of a volatile anaesthetic agent
- Negligible cardiovascular or respiratory depressant effects
- Also used for analgesia as a 50/50 mixture with oxygen—Entonox or Equanox
- Absorbed into air-filled spaces causing ↑pressure in non-compliant spaces, e.g. middle ear and expansion of compliant spaces, e.g. pneumothorax, ETT cuff. Often avoided in laparoscopic surgery, bowel surgery, middle ear surgery, some ophthalmic procedures, and procedures with a risk of intraoperative pneumothorax
- Potential toxicity due to effects on methionine synthetase and vitamin B12 during prolonged administration.

Local anaesthetic agents

- Local anaesthetics are used for local infiltration of wounds, peripheral nerve blockade and regional anaesthesia
- Toxicity (Table 9.2)—cerebral signs usually appear before cardiovascular collapse in awake patients, e.g. postoperative epidural infusion.

Table 9.2 Maximal safe doses of local anaesthetic agents in children

Drug	Bolus mg/kg	Bolus <6 months mg/kg	Epidural infusion mg/kg/h	Epidural infusion <6 months mg/kg/h
Levobupivacaine	2.5	1.25	0.4	0.25
Bupivacaine	2.5	1.25	0.4	0.25
Lignocaine	3.0–7.0	1.5	N/A	N/A

Extradural anaesthesia and analgesia

- Also known as *epidural*
- Usually involves placement of catheter in extradural space through which local anaesthetic ± opioid can be injected as bolus or infused
- Provides profound sensory blockade and (less) motor blockade
- Commonly sites are thoracic, lumbar (can be used caudally through sacral hiatus)
- Useful for intra- and postoperative analgesia following major thoracic, abdominal, spinal, pelvic, and lower limb surgery
- Contraindications include coagulopathy sepsis, cardiovascular instability
- Potentially serious side effects include:
  - Hypotension following sympathetic chain blockade—can be reversed with vasoconstrictor, e.g. metaraminol, noradrenaline. Rare <8 years old
  - Accidental spinal/extensive block—total spinal occurs over minutes following bolus into epidural catheter: ascending sensory and motor block; apnoea, bradycardia and cranial nerve block (fixed, dilated pupils), and loss of consciousness. Manage with attention to ***ABCs,*** intubation, ventilation, vasoconstrictors and IV fluid. Full recovery is expected
  - Rarely extradural haematoma or abscess—requires prompt surgical intervention.

Epidural infusion for postoperative analgesia

- Used to provide analgesia after thoracic, abdominal or major lower body surgery
- 0.1% or 0.125% bupivacaine or levobupivacaine is widely used. Maximum infusion rates are given in Table 9.2. 0.1% concentration of bupivicaine is 1mg/mL. Therefore mg/kg/h rates are equivalent to mL/kg/h rates
- Opioids are commonly added to solutions for epidural infusion, e.g. fentanyl 1–2 mcg/mL of epidural infusion solution
- Hypotension related to sympathetic block is unusual in children below about 8 years of age. If it does occur, in the absence of surgical bleeding, treat with fluid bolus—10mL/kg 0.9% saline and consider pressor agent. Contact the responsible anaesthetist
- Observations:
  - Document in specific recording documentation forming part of a management protocol overseen by the Acute Pain Team
  - Include: HR, BP, respiratory rate, and oxygen saturation (continuous pulse oximetry and ECG), pain assessment, sedation score, nausea and vomiting score, condition of epidural catheter insertion site, dermatomal level of block (check for temperature sensation with ethyl chloride spray or ice cube)
- Patient position should be changed 2-hourly for pressure area care
- If top-up boluses are required for inadequate or low block then give 0.1–0.2mg/kg (0.1–0.2mL/kg of 0.1%) as a bolus and record vital signs every 5min for 20min, then at 30min, then hourly
- Side effects of epidural infusions include; itching, nausea and vomiting (associated with opioids), urinary retention (a urethral catheter should be inserted as part of the surgical procedure), and respiratory depression.

Malignant hyperthermia (MH)

- MH is an autosomal dominant condition of skeletal muscle, induced by exposure to triggering agents e.g. suxamethonium and volatile agents causing loss of normal calcium homeostasis within the muscle excitation-contraction coupling process
- Incidence is 1:10,000–1:15,000
- Mortality is 2–3% compared with 70–80% when first described due to ↑awareness and changing anaesthetic practice
- Presentation is a spectrum from a life-threatening classic fulminant episode with severe hyperthermia and metabolic derangement to elevation of $EtCO_2$, tachycardia or hyperthermia of unknown cause. It may develop several days following anaesthesia with myoglobinuria and/or renal failure due to rhabdomyolysis.

Pathophysiology/diagnosis

- ↑metabolism—tachycardia, hypercapnia, tachypnoea, metabolic acidosis, pyrexia (rise in core temperature of >2°C/h)
- Generalized muscle rigidity (masseter spasm after suxamethonium)
- Dysrhythmias
- Metabolic acidosis
- Disseminated intravascular coagulation
- Hypercalcaemia
- Elevated creatine kinase
- Myoglobinuria
- Renal failure.

Management

- A treatment protocol should be readily available in every anaesthetic area
- Get help from local anaesthesia department
- Remove trigger agent (including anaesthetic machine). Convert to propofol/remifentanil I/V anaesthesia for duration of surgery
- Initially attend to ***ABCs***
- Hyperventilate (intubate) with 100% oxygen using high flows
- Dantrolene 1mg/kg IV repeated every 10min (total of 10mg/kg)
- Active cooling. Cooling blanket, ice in groins and axillae, peritoneal lavage, cold (potassium free) IV fluids
- Blood samples:
  - ABGs
  - Clotting screen
  - Potassium/calcium
  - Creatine kinase
- Institute invasive monitoring
- Urinary catheter—send urine for myoglobin measurement
- Treat hyperkalaemia if necessary
- Postoperative management in PICU.

Further reading

Doyle E (2007). *Oxford Specialist Handbook of Paediatric Anaesthesia.* Oxford University Press.

Chapter 10

Analgesia and sedation

Introduction

Effective analgesia and sedation for critically ill children involves caring for both their physical and psychological comfort. Correctable environmental and physical factors causing discomfort should be addressed prior to the introduction of pharmacological agents. Examples include lying on lines or catheters, infrequent turns, full bladder or bowels, noise or distressing scenes elsewhere on the unit.

Distraction therapy with play, toys, or music and television may be appropriate, and cuddling by parents or care givers where possible should not be underestimated as an anxiolytic.

► *Always assume your patient is aware*—even if paralysed and sedated
- Talk appropriately and calmly to the child
- Tell them who you are, what you are doing, warn them of painful procedures, and tell them who is at the bedside
- Limit conversation around the child to what is appropriate for them to hear—both about their condition and your social life!

Analgesia

Box 10.1 Recommendations for analgesia in critically ill children

- All critically ill children should have adequate relief of their pain
- Address any correctable environmental and physical factors causing discomfort
- Encourage a normal pattern of sleep—pay attention to lighting, environmental noise, and day/night patterns
- Perform pain assessment regularly using a scale appropriate to the age of the patient and document routinely
- Assess patients who cannot communicate for the presence of pain-related behaviours and physiological indicators of pain
- Establish a therapeutic plan for analgesia for each patient and review this regularly
- Continuous IV infusions of morphine or fentanyl are recommended for relief of severe pain
- Infusions take time to reach therapeutic levels and steady state—typically 4–5 half-lives. Consider loading dose, either as a small bolus ⚠ or more rapid infusion over an hour.
- If in pain, or before painful procedures, boluses of analgesics are more effective than increasing the infusion rate
- Giving sets and lines have a dead space. If this is, e.g. 2mL, and you give an infusion at 0.5mL/h, the patient won't get any analgesia for 4h—consider an initial bolus when starting therapy ⚠
- Non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol may be used as adjuncts to opioids
- Local and regional anaesthetic techniques should be considered.
- A PCA device may be useful in older children.

Analgesia assessment

- Pain is a subjective experience, and provided there is no clear reason to doubt them, a patient's reporting of their own pain is the single most reliable indicator of pain
- In neonates and children <3 years of age, behavioural observational scales are the primary tools available for the assessment of pain
- From 3–8 years of age children are generally able to use self-reporting techniques such as 'faces scales'
- Above 8 years of age, competent children can usually use validated unidimensional tools, such as the visual analogue scale.

Analgesic agents (Table 10.1)

Opioids

- Produce analgesia via a variety of central and peripheral opioid receptors, particularly μ- and κ-receptors
- Interaction at other receptors may be responsible for adverse effects
- Withdrawal effects may occur on discontinuation (see 🕮 p.195).

Morphine

- Valuable opioid for severe pain
- Relatively slow onset (5min) and long duration of action (around 2h when administered as a single dose)
- Peak analgesic effect 20min following IV administration
- Not suitable as an adjunct to intubation unless adequate time is given for it to take effect (at least 5min)
- Reduces behavioural and hormonal responses to painful stimuli
- Improves ventilator synchrony
- Does not reliably reduce awareness or give amnesia: may however be used as a combined analgesic/sedative in the short term where excessive sedation is to be avoided, i.e. postop patients expected to extubate rapidly
- Side effects:
  - Respiratory depression
  - Nausea and vomiting
- May stimulate histamine release resulting in vasodilatation and hypotension:
  - Particularly following bolus administration
  - Some centres avoid morphine in asthmatics, although there is no evidence that morphine worsens bronchospasm
- Active metabolites, particularly morphine-6-glucuronide, which are renally excreted. These can accumulate in renal impairment
- May precipitate coma in hepatic impairment—avoid or use with care
- Morphine may be given orally as Oramorph® oral solution:
  - Child aged 1–5 years: max. dose 5mg (2.5mL)
  - Child aged 6–12 years: max dose 5–10mg (2.5–5mL)
- May be given SC or IM if no venous access, but absorption variable.

Fentanyl

- Potent synthetic opioid with a rapid onset of action
- Suitable as an adjunct to intubation if rapid onset is desired
- Relatively short half-life of 30–60min owing to rapid redistribution to peripheral compartments
- Reduces pain-related increases in PVR and ICP
- Less haemodynamic instability than other opioids
- Causes less histamine release than morphine, and therefore less risk of hypotension—may be preferred in asthmatics
- Side effects:
  - Vagal bradycardia (particularly if given in high doses >5mcg/kg or in combination with vecuronium)
  - Chest wall rigidity
  - Tolerance may rapidly develop
- Accumulates with prolonged administration
- Hepatic metabolism, avoid or reduce dose in liver failure
- Renal excretion of metabolites, avoid or reduce dose in renal failure.

Remifentanil

- Synthetic opioid
- Short half-life of 3min in all age groups
- Prolonged use is associated with the rapid development of tolerance
- Respiratory and cardiovascular depressant effects
- High cost
- May have more potential for procedural analgesia in critical care given its rapid onset and offset times rather than as an infusion.

NSAIDs

- Provide analgesia through the non-selective, competitive inhibition of cyclo-oxygenase, a critical enzyme in the inflammatory cascade
- Reduce opioid requirements in post-surgical pain, and used as 'opioid sparing' in critically ill children, despite lack of systematic studies
- Side effects:
  - Gastric irritation (less common than in adults)
  - Hypersensitivity—rashes, bronchospasm, anaphylaxis
  - Reduced urine output/renal impairment
- Avoid in asthma and renal failure.

Paracetamol

- Used to treat mild to moderate pain
- Opioid-sparing effect when used in combination with opioid agents
- May be given orally, rectally, or IV
- Rectal administration is associated with variable absorption
- Side effects rare:
  - Rashes and idiosyncratic reactions
  - Hypotension reported rarely with IV use
  - Liver damage with overdose
- IV preparation useful if oral and rectal routes not available
- Compound preparations containing paracetamol and opioids (co-codamol) are available but offer little benefit over paracetamol alone and cause more side effects. They should be avoided.

Sucrose solutions

A number of studies have shown an analgesic effect of oral sucrose solutions in infants experiencing minor procedural pain.

Complex pain management

- Complex pain may occur as part of neuropathic pain or functional pain syndromes. Associations may include:
  - Guillain–Barré syndrome
  - Post-herpetic neuralgia
  - Peripheral neuropathy
  - Trauma
- Therapy may include:
  - Antidepressants or antiepileptics
  - Nerve blocks
  - Transcutaneous electrical nerve stimulation
- Management is complex and should be led by a specialized pain team, including physiotherapy and psychology support.

PCA

- Used if the patient can understand the concept, and is awake enough to press the button
- Typically children aged 6–8 years and above
- Consists of infusion of morphine, with bolus function and optional background infusion
- Typical regimen:
  - Morphine 0.5mg/mL in 50mL
  - Bolus (demand) dose 1mL (which gives 20mcg/kg/mL concentration)
  - Lockout time 5min (when no additional boluses can be given)
  - ↑lockout time of bolus to 20min if using background infusion
  - Optional background infusion 0–1mL/h (0–20mcg/kg/h)
- PCA normally managed by anaesthetist or pain control team
- Observe patient for signs of overdosage or inadequate analgesia
- Ensure only the patient is pushing the demand button.

Topical anaesthesia

EMLA

- Used for topical anaesthesia of the skin
- Can usefully ↓pain of needle insertion, injection, or cannulation
- Contains lidocaine 2.5% and prilocaine 2.5%
- Must only be applied to intact skin, and not to open wounds
- 30–60min to take effect
- Contraindicated aged <1 year, in anaemia, or methaemoglobinaemia.

Amethocaine gel (Ametop®)

- Quicker acting than EMLA
- Causes vasodilatation, which aids venous cannulation
- Risk of rapid absorption and toxicity if used in wounds—avoid.

Local anaesthesia

- Local anaesthesia is often forgotten in PICU, but is useful to provide local analgesia for painful procedures in patients who are not on systemic analgesics. Conventional doses of opiates do not abolish the acute pain of cannulation.

- Contraindications:
  - Allergy to LA drug
  - Local infection
- Lidocaine is the LA used most frequently for local infiltration:
  - Available in 0.5%, 1%; and 2% solutions
  - Normally use, 1% 'plain' lidocaine (without epinephrine)
- Lidocaine acts rapidly and the effects last about 30–60min (for plain lidocaine) to 90min (for lidocaine with epinephrine/adrenaline)
  - Duration of action varies with the dosage and the local circulation.
- Max. dose for infiltration is 3mg/kg ~1mL/year of age of 1% plain lidocaine
- Toxic effects from overdosage or inadvertent intravascular injection
- Symptoms include lightheadedness, confusion, and drowsiness. Hypertension, tachycardia, convulsions, and coma can occur.

Sedation

Box 10.2 Recommendations for sedation in critically ill children

- Provide adequate analgesia to all critically ill children regardless of the need for sedation
- Assess the level of sedation regularly and document using a sedation assessment scale, such as the COMFORT scale[1]
- There is insufficient evidence to support the routine use of neurophysiological techniques such as the bispectral index (BIS) in PICU
- Identify the desired level of sedation for each patient and regularly reassess
- Doses of sedative agents should be titrated to produce the desired level of sedation
- Midazolam is the recommended agent for the majority of critically ill children requiring IV sedation. ☞ It should be given by continuous infusion
- ☞ Clonidine given by continuous IV infusion may be used as an alternative sedative agent to midazolam
- ☞ Some centres use intermittent boluses of sedation rather than continuous infusions—less risk of over sedation, less side effects, and cheaper; but more risk of under sedation
- Propofol should not be used to provide continuous sedation in children
- Heavy sedation inhibits movement and coughing, encouraging dependent oedema and secretion accumulation
- Use enteral sedative agents where possible
- Consider the potential for withdrawal syndrome (see 📖 p.195).

Reference

1. Ambuel B (1992) *J Pediatr Psychol* **17:** 95–109.

Sedative agents (Table 10.1)

Benzodiazepines

- Act at gamma-aminobutyric acid (GABA) receptors, which form part of the major inhibitory system of the central nervous system
- Midazolam, diazepam, and lorazepam are commonly used for sedation in PICU.

Midazolam

- Produces reliable sedation and antegrade amnesia
- Following an IV bolus the time to peak sedation is 5–10min, and the duration of action of 30–120min.
- The duration of action is significantly longer with a continuous infusion, and may persist for 48h following discontinuation after prolonged administration
- Accumulation of active metabolites may produce prolonged sedative effects in patients with renal insufficiency
- Can be administered by nasal, rectal, IM, or IV routes
- Adverse effects:
  - Development of tolerance, dependence and withdrawal following discontinuation (withdrawal can occur after <24h infusion)
  - Hypotension may occur, particularly following bolus administration in the setting of hypovolaemia
  - Reduced sedative efficacy when administered to younger children
  - Care in renal or hepatic failure
- Diazepam has a rapid onset, and a long duration of action from active metabolites. May be given orally. Inexpensive.
- Lorazepam has a slower onset and longer duration of action after a single bolus, but less accumulation with an IV infusion.

Clonidine

- α_2-adrenoreceptor agonist, analgesic properties are probably mediated through the prevention of substance P release
- Produces sedation without respiratory depression
- Anxiolytic effect comparable to that produced by benzodiazepines
- May be given by intermittent IV slow bolus, IV infusion, or orally
- Adverse effects include bradycardia and hypotension
- Withdrawal after prolonged administration has been associated with hypertension and seizures
- Abrupt discontinuation of clonidine should be avoided.

Propofol

- Short-acting sedative used in general anaesthesia and for ICU sedation in adults
- Activates GABA receptors, and inhibits the NMDA receptor
- Crosses the blood–brain barrier rapidly and has a rapid onset of action
- Quickly metabolized to inactive metabolites, so short duration of action—effects wear off in minutes, even after prolonged infusion
- No dose adjustment is necessary for hepatic or renal insufficiency
- Not associated with tolerance or withdrawal symptoms

- Decreases cerebral O_2 consumption and ICP
- No analgesic properties
- Side effects:
  - Hypotension and CVS depression
  - Apnoea may occur
  - Pain on injection.

❗ Long-term (>24h) propofol infusion may be associated with 'propofol infusion syndrome'—metabolic acidosis, lipidaemia, rhabdomyolisis and acute circulatory collapse. Propofol should not be used to provide continuous sedation in children.

Ketamine

- Ketamine is a dissociative anaesthetic drug and may be given IM or IV
- NMDA receptor antagonist
- Provides strong analgesia and sedation in subanaesthetic dosage
- Airway-protective reflexes are maintained, but airway obstruction is a potential hazard. Ketamine should not be used by those who do not have appropriate airway skills
- Respiratory depression is uncommon at normal dosage, unless the drug is given too rapidly
- Ketamine is a bronchodilator and may be used in asthmatics
- It stimulates the cardiovascular system and causes tachycardia and hypertension, so is good in shock and cardiovascular instability
- May be given IV or IM
- Side effects:
  - May cause severe hallucinations in adults and older children, but these are seen (or recognized) less in young children
  - Hallucinations are less likely if a small dose of midazolam is given as well
  - Cerebral vasodilatation—may increase ICP
  - Sympathetic stimulation may increase pulmonary arterial pressures.

Enteral sedative agents

The most commonly used enteral agents include the hypnotic agents chloral hydrate or triclofos sodium, and the sedating antihistamines such as promethazine or alimemazine (trimeprazine). Chloral hydrate and promethazine, when used in combination, have been shown to be more effective than IV midazolam in providing maintenance sedation in critically ill children. Chloral hydrate is rapidly absorbed from the GI tract and starts to act within 15–60min.

Table 10.1 Recommended analgesic and sedative agents[1]

Drug	Intravenous bolus	Intravenous infusion
Morphine	<60kg; 100–200mcg/kg/dose >60kg; 5–10mg/dose	<60kg; 10–60mcg/kg/h >60kg; 0.8–3mg/h
Fentanyl	<60kg; 1–2mcg/kg/dose >60kg; 50–200mcg/dose	<60kg; 4–10mcg/kg/h >60kg; 25–100mcg/h
Remifentanil	0.5–1mcg/kg/dose	0.05–1mcg/kg/min

Table 10.1 Recommended analgesic and sedative agents[1] *(Continued)*

Drug	Enteral dose	Max. daily dose
Ibuprofen	<60kg; 6–10mg/kg/dose, 6-hrly >60kg; 200–600mg/dose, 6-hrly	<60kg; 30mg/kg/day >60kg; 2.4g/day
Paracetamol	<60kg; 10–15mg/kg/dose, 4-hrly >60kg; 650–1000mg/dose, 4-hrly	<3 months; 60mg/kg/day 3 months–12 yrs; 90mg/kg/day >12 years; 4g/day
Drug	**Intravenous bolus**	**Intravenous infusion**
Midazolam	<60kg; 0.1–0.2mg/kg/dose >60kg; 5mg/dose	<60kg; 2–10mcg/kg/min >60kg; 5–15mg/h
Clonidine	<60kg; 3–5mcg/kg slow IV >60kg; 50–300microgm/kg **NG**; 1–5mcg/kg/dose 8-hrly	0.1–2mcg/kg/h
Ketamine	IV: 1–2mg/kg slow IV IM: 2–4mg/kg	<60kg; 4mcg/kg/min
	Enteral dose	**Max dose**
Chloral hydrate	NG; 20–50mg/kg/dose 4–6-hrly	Maximum 2g per dose Max daily dose; 200mg/kg/day
Promethazine	NG; 1–2mg/kg/dose 6-hrly	Maximum 50mg per dose
Alimemazine (Trimeprazine)	NG; 2–4mg/kg/dose 6-hrly	Maximum 90mg per dose

Reference

1. United Kingdom Paediatric Intensive Care Society Sedation, Analgesia and Neuromuscular Blockade Working Group (2006). *Intensive Care Med* **32:** 1125–36 with permission from Springer Science + Business Media.

Intravenous and inhalational anaesthetic agents

📖 See Chapter 9.

Non-pharmacological approaches

- Play (📖 p.822) and distraction techniques are useful to reduce anxiety around practical procedures
- Physical restraints are used in many units to facilitate the tolerance of invasive monitoring and therapy and to reduce the risk of patients inadvertently interfering with treatment—such as self extubation or pulling out indwelling cannulae—where this may lead to the development of life-threatening complications

- Restraint in this context includes physically holding down, and the use of splints across joints to limit movement
- Restraint use may increase agitation and lead to significant injury
- Restraining therapy should not be used to allow reductions in nurse staffing levels
- The need for restraining therapies should be explained to children and their parents, and consent obtained.

Sedation for practical procedures

Intensive care staff are often asked to sedate a child for a test (such as a CT scan) or procedure (such as endoscopy). In general you should avoid such ad hoc arrangements. Sedation provided by an appropriately trained and resourced sedation service is to be preferred.

- The person providing the sedation should:
  - Have proper training and skills to ensure patient safety
  - Not be performing the procedure
  - Not have any other responsibilities during the procedure
  - Continuously and closely monitor the child
- Risk assessment:
  - Document pre-existing medical conditions, drug therapy, allergies and the time of the last food and drink
  - Patients should be fasted before IV sedation
  - Risks include respiratory depression, ↓cardiac output, and aspiration of gastric contents
  - If there is any uncertainty, cancel the procedure or get expert help
- Equipment:
  - A trolley which can be tilted head-down
  - Suction, resuscitation equipment and drugs, including reversal agents must be immediately available
  - Adequate and appropriately staffed area for post-sedation recovery
- Drugs:
  - All sedative drugs will produce anaesthesia if you give too much
  - Single-agent sedation is safer than using 2 or more sedatives
  - Use the minimum amount that will give adequate sedation and allow the procedure to be completed satisfactorily
  - Midazolam is the most commonly used drug. Combinations of midazolam and opioids may lead to apnoea and prolonged sedation
  - May be given oral, IV, or intranasal (bitter taste)
  - Propofol or ketamine should only be used by staff with specific training
- Monitoring
  - Level of sedation
  - Pulse oximetry
  - Respiratory rate
  - HR
- After the procedure you are responsible for the patient until they have fully recovered from sedation.
  - Give appropriate post-sedation advice
  - Make sure someone appropriate is looking after them
  - Review the patient and document this before they go home or back to the ward.

Withdrawal syndrome

- May occur following the discontinuation of any sedative or analgesic agent
- Thought to be related to the total drug dose received (and so is more common following prolonged admission and continuous infusion)
- Incidence has been estimated at up to 35% of PICU admissions
- Rarely occurs with <2 weeks intermittent administration
- Withdrawal is very distressing for the child, their family, and PICU staff
- Features include:
  - CNS manifestations such as agitation, seizures, arterial desaturation, hallucinations, and psychosis;
  - Autonomic features such as vomiting, tachycardia, hypertension, and fever
  - Features are similar regardless of the drug involved
- Features can occur within a few hours of stopping the drug responsible
- The time of onset will vary depending on the half-life of the drug and any active metabolites
- There are no validated PICU scoring systems to assess withdrawal
- Commonly used practices to avoid withdrawal include:
  - Regularly reviewing the need for sedatives and analgesics, and using the minimum effective dose
  - Planned substitution of one class of agent for another ('drug holidays')
  - Routine tapering of sedative and analgesic agents
- There is however no evidence (as yet) that these practices reduce the incidence of withdrawal.[1]
- Withdrawal syndromes should be actively considered after discharge from PICU—In some units this is done by the pain service or the outreach team
- Management involves:
  - Prescribing appropriate sedatives to alleviate withdrawal symptoms
  - Planned and phased withdrawal of sedative and analgesic agents
  - Use of oral agents where possible (see Box 10.3)
  - This may take as long or longer than the original admission
  - Use of a written management plan that is regularly reviewed

Box 10.3 Withdrawal regimen—conversion of IV to oral[2]

- Suggested dose conversion:
  - Midazolam 45mcg/kg/h = diazepam 1mg oral (6-hourly)
  - Midazolam infusion reduced by 1/3 with 2nd and 4th dose of oral diazepam, discontinued with 6th dose of diazepam.
- IV clonidine:oral clonidine conversion:
  - 1.4mcg/kg/h = 40mcg oral (6-hourly).

References

1. United Kingdom Paediatric Intensive Care Society Sedation, Analgesia and Neuromuscular Blockade Working Group (2007). *Paediatr Anaesth* **17:** 675–83.
2. Cunliffe M, Mcarthur L, Dooley F (2004). Managing sedation withdrawal in children who undergo prolonged PICU admission after discharge to the ward. *Pediatr Anesth* **14:** 293–8.

Neuromuscular blocking agents (NMBA)

► NMBAs do not prevent pain or anxiety

- Indications for the use of NMBAs in PICU include:
  - Prevention of patient-ventilator dyssynchrony
  - Management of specific medical conditions such as raised ICP or pulmonary hypertension
  - Induced hypothermia, in order to prevent shivering
  - Specific surgical operations to protect the repair in the postoperative period.
- The most commonly used agents for prolonged neuromuscular blockade on PICU are vecuronium, pancuronium, or atracurium
- Immobility from prolonged NMB may result in muscle atrophy, joint contractures, pressure sores, pulmonary atelectasis and pneumonia, corneal drying, and permanent corneal damage
- Continuous administration of NMBAs may lead to critical illness polyneuropathy and myopathy (CIPNM) although this is exceedingly rare in children.
- Some NMBAs produce histamine release, leading to hypotension, tachycardia, or bradycardia, particularly after bolus dosing
- Tolerance following prolonged infusions of NMBAs may occur, and there may be cross-resistance between different agents. Monitoring the level of neuromuscular blockade is essential
- Individual variation makes it difficult to predict the onset, degree, and duration of NMB in a specific patient
- Peripheral nerve stimulation is widely used in adults to monitor NMB, but has limitations in small children particularly if oedematous
- Monitoring uses train-of-four (TOF) nerve stimulation pattern
- 4 electrical impulses are delivered to the nerve
- The degree of NMB can be determined from the number of muscle contraction seen in response to 4 impulses (Table 10.2). 2 or fewer contractions following TOF stimulation suggests adequate blockade in most PICU situations
- The ulnar nerve is the usual first site stimulated for TOF testing as it is superficial and accessible:
  - The distal electrode is placed over the ulnar nerve (just medial to the ulnar artery by palpation or Doppler) at the proximal flexor crease of the wrist. The 2nd electrode is placed proximal to the 1st along the line of the nerve
  - Stimulation of this nerve causes movement of the thumb and little finger
- The facial nerve is also easily accessible:
  - The 1st electrode is placed slightly above the eyebrow, the 2nd electrode is placed over the facial nerve in front of the ear
  - Stimulation of this nerve causes twitching of the eyebrow or eyelid
- Even if no contractions are observed during TOF testing, the diaphragm may not be completely paralysed.

Table 10.2 Assessment of neuromuscular blockade by train of four stimulation

Visible contractions seen	% receptor blockade (approx.)
0	100
1	90
2	80
3	70
4	0

Commonly used NMBAs

- Dosing schedules of commonly used NMBAs are shown in Table 10.3
- Suxamethonium (1mg/kg) is the drug of choice for RSI and is discussed in 📖 Chapter 9
- Choice of NMBA is based on individual preference and familiarity, the reason for NMBA use, and patient characteristics.

Atracurium

- Broken down primarily by enzyme based Hoffman degradation and non-specific ester hydrolysis via plasma cholinesterase
- Minimal renal excretion so safe in renal and liver failure
- Effects prolonged in hypothermia
- May cause cardiovascular effects due to histamine release.

Cis-atracurium

- Little histamine release. Fewer cardiovascular effects than atracurium
- Similar degradation and excretion to atracurium—safe in renal and hepatic failure
- Higher cost than atracurium.

Rocuronium

- Rapid onset
- Few cardiovascular effects (in high doses it may cause some vagolysis)
- Higher cost than atracurium
- In emergencies, rocuronium can be given IM, but onset of action takes ~4min.

Pancuronium

- Non-depolarizing NMBA
- Long duration of action
- May cause tachycardia and hypertension
- Reduce dose in neonates
- Caution in renal and hepatic failure
- Lower cost than atracurium.

Vecuronium

- Derivative of pancuronium
- Relative lack of unwanted effects.
- Increase bolus dose in neonates due to relative large Vd but infusion dose should be reduced due to reduced liver and renal function
- Caution in renal and hepatic failure.

Box 10.4 Recommendations for neuromuscular blockade[1]

- Ensure adequate analgesia and sedation before commencing NMBAs.
- Review the need for NMBAs regularly; discontinue as soon as possible
- If safe to do so, discontinue NMBA infusions at least once every 24h until spontaneous movement returns so that levels of analgesia and sedation can be assessed
- Atracurium or vecuronium given by continuous infusion are the recommended agents for the majority of critically ill children requiring NMB. Intermittent doses of pancuronium may be considered
- Where continuous infusions are employed, the degree of NMB should be assessed at least every 24h
- Administered doses of NMBAs should be titrated to provide the optimum level of neuromuscular blockade.

Table 10.3 Dosing schedules for NMBAs[1]

Drug	Bolus	Infusion
Vecuronium	IV bolus; 80–100mcg/kg/dose	IV infusion; 50–100mcg/kg/h
Rocuronium	IV bolus; 600mcg/kg/dose	IV infusion; 300–600mcg/kg/h
Atracurium	IV bolus; 300–600mcg/kg/dose	IV infusion; 0.3–1.7mg/kg/h
Cisatracurium	IV bolus; 150mcg/kg/dose	IV infusion; 60–180mcg/kg/h

Reference

1. United Kingdom Paediatric Intensive Care Society Sedation, Analgesia and Neuromuscular Blockade Working Group (2007). *Paediatr Anaesth* **17:** 881–8.

Chapter 11

Circulatory support

Pharmacological support of the cardiovascular system

- The cardiovascular system pumps and carries de-oxygenated blood to the lungs for oxygenation, and oxygenated blood to the tissues
- Oxygen delivery is dependent on cardiac output, haemoglobin concentration and oxygen saturation (📖 Chapter 7).

Cardiac dysfunction is relatively common in the critically ill child. After restoring intravascular volume, attention must be paid to supporting the heart.

Inotropes and other drugs are used to optimize cardiac output and flow, and their correct use is based on an understanding of cardiovascular physiology (📖 Chapter 7), the pharmacology of the drugs, and the pathophysiology of the disease process.

Receptors and the cellular basis of inotrope use

The most commonly used vasoactive drugs are sympathomimetic agents that stimulate adrenergic receptors. Receptor activation is different with each drug and for a particular drug may be dose dependent. There are 4 broad categories of receptors (Box 11.1).

Box 11.1 Categories of receptors

Alpha receptors

- Peripheral α_1 and α_2 receptor stimulation produces vasoconstriction leading to an increase in peripheral vascular resistance (primarily an α_1 effect)
- Stimulation of myocardial α_1 receptors leads to ↑cardiac contractility, especially at low heart rates
- Central α_2 receptor stimulation produces metabolic changes and is not relevant to this discussion.

Beta receptors

- β_1 receptor stimulation produces an inotropic effect on the heart:
  - This occurs by an increase in cAMP, resulting in an influx of calcium into the cell from the sarcoplasmic reticulum
  - The neonatal myocardium has reduced responsiveness to β_1 stimulation
- β_2 receptor stimulation produces mild vasodilatation: this vasodilatation is much less than that produced by drugs such as milrinone which are discussed later.

Dopaminergic receptors

- Stimulation produces renal and splanchnic vasodilatation
- Also results in a natriuresis and a diuresis.

Vasopressin receptors

- Vasopressin is a relatively new addition to the vasoactive drugs list
- Stimulation of V_1 receptors results in powerful vasoconstriction.

Receptor downregulation

- A phenomenon where by the receptors become less sensitive to catecholamine stimulation with time, thereby rendering the catecholamine less effective
- Normally happens within 72h of starting a continuous infusion, as well as in acute disease states when acidosis and hypoxia render the receptors less responsive, and in chronic states such as cardiomyopathies where the body's adrenergic system is in overdrive in order to maintain adequate cardiac output
- In these cases, the receptors become downregulated or suffer from 'stimulation fatigue'.

The neonate also has limited responsiveness to inotropes due to:

- A relatively large non-contractile portion of the heart
- A ↓pool of endogenous catecholamines
- A less mature sympathetic nervous system
- Less efficient use of intracellular calcium.

Vasoactive drugs

4 categories of vasoactive drugs will be considered (also see Table 11.1 and Box 11.2):

Inotropes

- Drugs that increase the contractility of the heart thereby increasing the cardiac output and providing support to the failing myocardium.
  - Examples are dopamine and epinephrine.

Inodilators

- Drugs that produce a combination of inotropy and vasodilatation.
  - Examples are dobutamine and milrinone.

Vasodilators and vasocontrictors

- Drugs that act on the peripheral circulation and modulate systemic (or pulmonary) vascular resistance
  - Examples of vasodilators are nitroglycerine and nitroprusside
  - Examples of vasoconstrictors are norepinephrine. and phenylephrine.

Chronotropes

- Drugs that work primarily by increasing the heart rate.
  - An example would be isoprenaline.

In practice, most vasoactive drugs are a mixture of these types and also have variable dose dependent effects. Additionally, some agents provide more or less specific effects to the pulmonary or systemic circulations.

Box 11.2 Choice of agents

The choice of agents varies a lot from centre to centre and yet the end result is not dissimilar. Some are 'dopamine units', whilst others preferentially use dobutamine. Similarly there are 'epinephrine units' and 'norepinephrine units'.

The statements in the rest of this section on dose-receptor effect are largely based on *in vitro* studies and may not be a true representation of the situation *in vivo*. In addition large inter-individual variability is likely.

Inotropes

Note: dobutamine is discussed under inodilators, and norepinephrine under vasoconstrictors

Dopamine

- Is a naturally occurring catecholamine. It is perhaps the most commonly used catecholamine on PICU and has multiple dose-dependent receptor effects:
  - 3–5mcg/kg/min: stimulates dopamine receptors in the splanchnic and renal vessels, increasing renal blood flow and causing an increase in urine output
  - 5–10mcg/kg/min: causes stimulation of β-receptors (β_1 receptors) and an increase in myocardial contractility
  - 10–20mcg/kg/min: β-receptor stimulation persists but α-receptor activation starts to appear and increases with increasing dose. The alpha effects will lead to constriction of blood vessels leading to hepatic and mesenteric ischaemia, an increase in the work of the heart, and an increase in oxygen consumption
- *Side effects*: tachycardia, tachydysrhythmias, and pulmonary vasoconstriction
- Critical issues:
  - Tissue necrosis following extravasation—administer via central line
  - If no central line, in cases of emergency or profound hypotension, dopamine may be given peripherally using normal infusion diluted 10× while preparation for central line is underway
  - Extravasation: may result in sloughing and tissue necrosis. Treatment: stop infusion; infiltrate area of extravasation with phentolamine (0.1–0.2 mg/kg up to 10mg diluted in 10mL normal saline); use a fine needle; to be effective within 12h
  - Short half-life—administer by a continuous infusion
  - No convincing evidence that low dose 'renal dopamine' improves renal function or outcome in ICU, but it is often used in doses up to 10mcg/kg/min, and is associated with an increase in cardiac output, stroke volume, and BP.

Epinephrine (adrenaline)

- Powerful inotrope with both α and β effects:
  - 0.05–0.2mcg/kg/min β_1 effects predominate
  - >0.5mcg/kg/min α effects predominate
- Side effects:
  - α effects can lead to an increase in myocardial work and oxygen consumption
  - Constriction of renal and splanchnic vesssels
  - Tachyarrhythmias
  - Hyperglycaemia
  - Type B lactic acidosis.
- Critical issues:
  - As it is a powerful inotrope it should be considered relatively early in patients with refractory hypotension. Should be infused through a central line due to extravasation tissue necrosis
  - Short half-life—administer by a continuous infusion

  - Well absorbed in the lung if given via the endotracheal route
  - Thought to work during cardiac resuscitation by increasing left ventricular perfusion as a result of its α effects
- *Other situations* in which it is used are anaphylactic shock, asystolic arrest, nebulized as a mucosal vasoconstrictor in croup, and as a bronchodilator in asthma (although more specific and safer β_2 agonists are available).
- Some centres start epinephrine after first-line inotropes such as dopamine and/or dobutamine If so, it is worth starting at a reasonable dose (such as 0.1mcg/kg/min and escalating the dose quickly to 0.5–1mcg/kg/min) in order to be able to determine whether non-catecholamines, such as vasopressin, should be added or consideration given to other forms of cardiovascular support
- Other centres advocate the first-line use of epinephrine, as there is little evidence supporting the use of other drugs before it.
- Titrate dose to response. Patients on epinephrine infusions need continuous BP monitoring through an arterial line (Box 11.3).

Box 11.3 Titration of catecholamines

Catecholamines should be administered in doses to produce a BP that is appropriate for the child's age and that is associated with a urine output of 1–2ml/kg/h.

Whilst a 'good or luxurious BP' looks impressive on the monitor if it is achieved by administering higher than necessary doses of catecholamines, there will be an associated cost to the heart due to an increase in SVR (and hence afterload; 📖 p.106), i.e. an increase in the work of the heart at a time when the heart is already under considerable stress.

Inodilators (see also Box 11.4)

Dobutamine

- A synthetic catecholamine that does not have any dopaminergic effect but when commenced at a dose of 5mcg/kg and above has inotropic (β_1) effects as well as mild vasodilatory (β_2) effects
- It is used commonly in the management of septic shock in combination with norepinephrine
- At doses of 7–10mcg/kg/min, dobutamine has been shown to increase cardiac output and BP
- 5–20mcg/kg/min—selective β effects with an increase in cardiac contractility and an increase in heart rate. β_2 effects produce mild peripheral vasodilatation. No dopaminergic or α effects seen.
- Side effects:
  - Tachyarrhythmia—can be significant particularly in older children
  - Peripheral vasodilatation (can lead to hypotension if hypovolaemic).

Critical issues

- Does not cause vasoconstriction and so can be given peripherally—useful in cases where central access not obtained/obtainable
- Due to afterload reduction is useful in a child with myocardial failure

- In some neonatal and infant studies, dobutamine gives a more reliable increase in cardiac output and BP than equivalent amounts of dopamine.

Box 11.4 Phosphodiesterase inhibitors (PDEI)

PDEIs have become essential pharmacological agents in the management of adults and children who have congestive cardiac failure and low cardiac output syndrome. There is evidence that a combined therapy of catecholamine and PDEI is superior to single drug therapy in the management of heart failure because of synergy between these 2 types of drugs.

These drugs produce:
- Inotropy with an increase in the speed and force of cardiac contraction
- Vasodilatation resulting in a decrease in systemic and pulmonary vascular resistances and in filling pressures
- 'Lusitropy' which is the property of diastolic relaxation of cardiac muscle, particularly useful in hypertrophic hearts.

The PDEIs work by reducing the breakdown of cyclic AMP. ↑cyclic AMP leads to calcium mobilization which in turn promotes myocardial contraction.

Theoretical advantages over catecholamines
- PDEIs act via a different mechanism and therefore do not interact with adrenergic receptors. This potentially helps with the problem of receptor downregulation
- In addition, there is less of an increase in myocardial oxygen consumption and there are less tachyarrhythmias associated with PDEIs
- However, as PDEIs are powerful vasodilators these drugs should be used with caution in patients with a marginal BP.

Milrinone
- Particularly useful in the management of low cardiac output following cardiopulmonary bypass (see 📖 p.373)
- Milrinone with its short half-life and few side effects is the PDEI of choice in the management of heart failure in PICU.
- Dose:
  - 0.25–1mcg/kg/min
  - In order to get an effective plasma level quickly, the drug is often initiated by a loading dose of 75mcg/kg over the 1st hour.
- Side effects:
  - Arrhythmias have been reported but occur rarely in the neonatal and paediatric population
  - Hypotension occurs and is more severe in a hypovolaemic child
  - Haematological abnormalities may occur infrequently, although compared with amrinone thrombocytopenia is much less frequent.

Note:

- For an equivalent increase in cardiac output, milrinone is more effective than dobutamine in reducing systemic vascular resistance which is of obvious benefit in a child with cardiomoypathy or myocarditis
- A large study in the paediatric population called 'Prophyactic use of Milrinone After Cardiac Operations in Paediatrics (PRIMACORP)' concluded that milrinone administration significantly reduced the incidence of low cardiac output state.
- Another study in children with non hyperdynamic septic shock showed a significant increase in cardiac index, stroke volume right and left ventricular stroke volume index and oxygen delivery

Enoximone

Is less potent than milrinone but has similar clinical effects.

- Dose:
  - 5–20mcg/kg/min IV
  - Has to be administered on its own, but can be administered through 1 lumen of a central line
  - Can be given orally
- Side effects: as per milrinone.

Amrinone

- Was the 1st PEDI introduced
- Has similar clinical characteristics and side effects as milrinone and enoximone
- High incidence of associated thrombocytopenia
- Rarely used in paediatric practice now.
- Dose: loading dose of 1–3mg/kg IV over 1h followed by a continuous infusion of 5–15mcg/kg/min.

Other agents

Levosemendan

- Binds to troponin C leading to an increase in sensitivity to available calcium without increasing calcium levels
- Functions as an inodilator
- Associated with inotropic and chronotropic effects
- Pulmonary vasodilatation by paradoxically decreasing sensitivity to calcium in the pulmonary circulation.
- Dose: loading dose of 6–24mcg/kg/min over 10min followed by an infusion rate of 0.1–0.4 mcg/kg/min for a maximum of 24h.
- Side effects: vasodilatation and hypotension in hypovolaemia.
- Critical issues:
  - Levosemendan has been shown to be beneficial in adults with acute severe heart failure but its efficacy and side-effect profile in children have not been fully established.
  - It is currently expensive—cost/risk/benefit needs further evaluation.

Vasodilators

↑SVR occurs in heart failure due to activation of the sympathetic nervous system and the renin–angiotensin system. This increases the work of the heart and myocardial oxygen demand. Reduction of SVR in this clinical setting is therefore of benefit.

Nitroprusside

- Is a potent short-acting venous and arterial vasodilator
- It acts by the liberation of NO which is responsible for the vasodilatory effect
- Cyanide is a by-product and prolonged use can give rise to methaemoglobinaemia and cyanide toxicity
- This is rarely a problem at doses below 4mcg/kg/min.
- Dose:
  - Initial dose 0.5–5mcg/kg/min
  - As a powerful vasodilator, dosage increments should be small.
- Side effects:
  - Vasodilatation and hypotension.
  - Cyanide toxicity—watch for lactic acidosis as a possible indication of cyanide toxicity.
  - Use with caution in patients with left-sided obstructive lesions, e.g. aortic stenosis or obstructive cardiomyopathy—there is the potential for coronary ischaemia due to a steal syndrome from vasodilatation
  - Should be protected from light.

Nitroglycerin (GTN)

- Less potent short-acting vasodilator which has a greater effect on the venous circulation than the arterial
- Approximate equivalent dose for arterial vasodilatation 1mcg/kg/min SNP = 5mcg/kg/min GTN
- Is also a coronary vasodilator
- Acts by the liberation of NO
- Tachyphylaxis occurs to its effects.
- Dose: 1–8mcg/kg/min.
- Side effects:
  - Hypotension and tachycardia
  - Hypoxia due to worsening of V/Q mismatch since GTN is not a selective pulmonary vasodilator.

Other vasodilators

Hydralazine

- A directly acting arterial vasodilator used predominantly in the management of systemic hypertension
- Dose: 0.1–0.2 mg/kg/dose every 6h (maximum of 3.5 mg/kg/day)
- Onset of action: 5–20min
- Side effects: hypotension, tachycardia

Nifedipine

- A calcium channel blocker that prevents the influx of Ca^{2+} through the cell membrane and therefore blocks contraction of smooth muscle
- The ensuing vasodilatation causes a fall in BP

- Dose: 0.2–0.5 mg/kg/dose for hypertensive emergencies (maximum 1–2 mg/kg/day)
- Onset: 2–5min given sublingually, 20min when given orally (though some dispute whether sublingual absorption occurs)
- Side effects:
  - Hypotension, syncope, and dizziness
  - Hyperglycaemia and hyperuricaemia.

⚠ Avoid vasodilator use in raised ICP. The resulting vasodilatation of cerebral vessels may lead to ↑cerebral blood volume with a resultant worsening of raised ICP. Hypertension in that setting should be treated by managing the ICP.

Vasoconstrictors

- Norepinephrine is a powerful vasoconstrictor and is often used in combination with dobutamine in the management of septic shock
- Epinephrine and dopamine also cause vasoconstriction in higher doses.

Norepinephrine (noradrenaline)

- Particularly useful in 'warm shock' when the peripheral vascular resistance has dropped significantly leading to a low perfusion pressure
- It has more potent α than β effects
- Dose: 0.1–1mcg/kg/min.
- Side effects:
  - Bradycardia
  - Main problem is its potent alpha effects reducing tissue perfusion
- Critical issues:
  - Useful in shock due to profound vasodilatation
  - Often used along with epinephrine in cases of resistant shock requiring high dose epinephrine

Phenylephrine

- Pure α agonist. Used occasionally in tetralogy of Fallot hypercyanotic spell and situations where rapid increase in SVR is needed
- Dose: 2–10mcg/kg stat, then 1–5mcg/kg/min.
- Side effects: severe vasoconstriction and reduced urine output

Metaraminol

- A potent sympathomimetic amine used in the prevention and treatment of hypotension, particularly as a complication of anaesthesia.
- Dose: 10mcg/kg stat, then 0.1–1mcg/kg/min
- Side effects: severe vasoconstriction and reduced urine output.

Vasopressin

- Used in the management of infants and children with refractory hypotension after surgery or with sepsis particularly when the diastolic BP is low.
- Useful in treating hypotension associated with brainstem death
- One of the most powerful vasoconstrictors available and in contrast to the catecholamines acts on different receptors, the V1 receptors
- Acts on the phospholipase C system which leads to an increase in intracellular Ca^{2+} and pulmonary and systemic vasoconstriction

- The antidiuretic and water retention properties that are traditionally associated with arginine vasopressin are a result of stimulation of the V2 receptors present in the kidneys.
- Dose: 0.003–0.0015U/kg/min or 0.02–0.09U/kg/h
- Side effects: severe vasoconstriction
- Critical issues: theoretical concerns regarding splanchnic and peripheral ischaemia due to vasoconstriction.

Chronotropes

Isoprenaline

- Used in very selected situations for its chronotropic effect
- May buy time until a pacemaker is inserted in complete heart block
- Dose: 0.05–1.5mcg/kg/min
- Side effects: will increase myocardial oxygen consumption and may cause tachyarrhythmias
- Critical issues: can be administered peripherally.

Other agents

⚠ There is little trial data to support the use of the following agents.

- *Dopexamine:*
  - Has effects on the β_2 and dopaminergic receptors, and reduces re-uptake of norepinephrine
  - Main effects are chronotropy and vasodilatation, especially of the splanchnic and renal beds
  - Limited date for its use in children
  - Dose: 0.5–6mcg/kg/min
- *Digoxin:*
  - Positive inotropic effect from improving calcium availability, but offset by augmented vagal tone and ↓sympathetic effects
  - HR limitation can reduce cardiac output
  - Rarely used as an inotrope
  - Used in some arrhythmias and to promote diastolic relaxation
  - Dose: 15mcg/kg loading dose then 3–5mcg/kg 12-hourly
- *Calcium:*
  - Dose: 0.4mL/kg/h of 10% calcium gluconate
- *Steroids:*
  - Functional or actual adrenal insufficiency can result in hypotension. If inotropes aren't working, consider giving 'physiological dose' of 1mg/kg 6-hourly of hydrocortisone (see 🕮 p.561)
  - High-dose steroids should be avoided in septic shock
  - Further paediatric studies are needed before corticosteroid use in paediatric sepsis becomes standard practice.
- *Triiodothyronine (T3):*
  - In acute septic shock circulating T3-concentrations are ↓.
  - In some studies this is a marker of poor outcome
  - Supplementation may or may not be helpful
  - Dose: 0.1–0.2mcg/kg/h liothyronine

Table 11.1 Effects of inotropic drugs

	Heart rate	Contractility	SVR	Route	Dose
Dopamine	++	++	+	C	2–20
Dobutamine	+++	++	↓	C/P	2–20
Epinephrine	+++	+++	++↑	C	0·01–2·0
Norepinephrine	↓ to +	+↑	+++↑	C	0·01–2·0
Enoximone	++↑	++↑	↓	C/P	5–20

SVR, systemic vascular resistance; C, central; P = peripheral. Doses are in micrograms/kg/min.

Selected clinical scenarios (see Boxes 11.5 and 11.6)

Box 11.5

There is very little trial data to guide us in the selection and use of vasoactive drugs. The rational for one approach rather than another is largely drawn from adult or animal studies, from an interpretation of physiological principles, and from local practice (or prejudice!). Attention to detail and a willingness to review your approach in the light of a changing situation are important in obtaining a good outcome.

We use two broad approaches which may be more or less appropriate depending on the severity of shock and clinical progress over time:

- Escalating approach—adding in agents and going up on doses if inadequate response
- Early aggressive approach—use the big guns early (epinephrine) and escalate or de-escalate as appropriate.

Early management of the infant with a low cardiac output state of unknown aetiology

- Ensure adequate ventilation and oxygenation
- Optimize intravascular volume (aim for a CVP of 10–15mmHg)
- Start dobutamine or dopamine peripherally at 10mcg/kg/min while obtaining central access:
  - In infants dobutamine will give a greater increase in oxygen delivery than dopamine, but make sure there is not excessive tachycardia
  - Diastolic BP must be maintained so caution with inodilators/vasodilators
- Dilute strength epinephrine can be given via a peripheral cannula in the short term if the situation is serious, until central access is available.
  - Alternatively insert IO needle and start epinephrine infusion
- Obtain central venous access—whatever you do best!
- Failure to respond to dobutamine or dopamine 10–15mcg/kg/min.
  - Start epinephrine at a dose of at least 0.1mcg/kg/min escalating fairly quickly to between 0.5–1.0mcg/kg/min if the systolic blood pressure and urine output are still suboptimal

- If the response is still inadequate review your diagnosis, the child's fluid status, ventilation and oxygenation, and consider adding a vasoconstrictor such as norepinephrine (or vasopressin)
  - If the diastolic <half systolic and signs of organ under-perfusion a vasoconstrictor should be tried
- Echocardiography is a good way of assessing volume status and contractility:
  - If contractility is good, consider vasoconstrictors
  - If contractility poor, use epinephrine and consider calcium
- Some authorities would advocate using steroids (1mg/kg 6-hourly of hydrocortisone), or T_3 but the evidence for both is poor
- If the response is still inadequate, review your management so far and consider ECMO.

Low cardiac output following cardiac surgery (📖 p.373)

Septic shock (📖 Chapter 26).

Box 11.6 Choice of inotropes

- Many units use a combination of vasoactive drugs as first-line management of septic shock. Dobutamine and norepinephrine or milrinone and epinephrine are examples
- The clinical picture can be divided into patients with warm peripheries and low SVRi ('warm shock'), and those with vasoconstriction and high SVRi ('cold shock')
- Adult septic shock is commonly associated with low SVR and a hyperdynamic, high cardiac output state, making vasopressor therapy the main treatment
- In children with sepsis, vasoconstriction and a low cardiac output state predominate, making drugs such as milrinone and adrenaline useful inotropes to increase cardiac output.

Mechanical support of the circulation

Types of mechanical support
- Extracorporeal membrane oxygenation (ECMO)
- Ventricular assist devices (VADs)
- Intra-aortic balloon pump (IABP).

ECMO

ECMO uses modified cardiopulmonary bypass technology to provide respiratory or cardiorespiratory support in ICU for prolonged periods, sometimes up to several weeks.
- It is indicated when the patient has a potentially reversible condition and conventional management is failing.

There are 2 main types of ECMO:
- Veno-venous, VV, for respiratory support
- Veno-arterial, VA, for cardiorespiratory support.

⚠ ECMO should only be performed in centres with appropriate facilities, staff and experience.

The ECMO circuit must be managed by a trained ECMO specialist (usually a specially trained nurse) or certified Perfusionist 24/7.

The ECMO circuit

- Different from cardiopulmonary bypass circuit (📖 p.223)
- Areas of blood stasis are eliminated to allow minimal heparinization of the ECMO patient.

Constituents (see Fig. 11.1)
- Pump
  - servo-regulated roller (bladder box or venous pressure) or
  - centrifugal with inlet (venous line) pressure measurement
- Oxygenator
- Heat exchanger
  - integral in oxygenator or in line after the oxygenator.
- Bridge to connect arterial return and venous drainage lines
  - Allows circuit maintenance, usually kept clamped.
  - Some circuits have a bridge that is only inserted when needed.
- Pre and post oxygenator pressure monitors
- Venous line saturation useful
  - Provides continuous assessment of oxygen extraction
- Ultrasonic flow meter for centrifugal pumps
- Emergency cart containing circuit spares and hand crank, back-up pump if no hand crank.

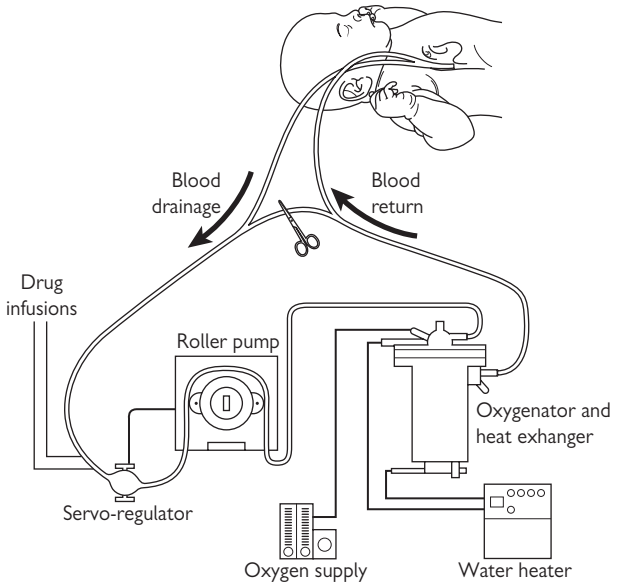

Fig. 11.1 Figure of ECMO circuit.

Cardiac ECMO

Indications

- Failure to wean from CPB
- Low cardiac output syndrome (myocarditis, pulmonary embolus, poor function postoperatively, dilated cardiomyopathy only as a bridge to transplant)
- Cardiac arrest (ECPR, extracorporeal cardiopulmonary resuscitation)
- Failure to oxygenate a patient with cyanotic heart disease (blocked BT shunt, poor mixing in TGA, obstructed TAPVD), usually better on VV
- Intervene before irreversible end-organ damage has occurred, judged on an individual patient basis
- In postoperative patients ECMO will only be successful if the cardiac repair has been successful.

Contraindications

- Inadequate repair: either technical failure (revise repair), or because the substrate will not allow a successful repair
- Moribund patient: established organ failure esp. brain injury
- Inability to tolerate limited heparinization (relative contraindication):
  - IVH >grade 2 absolute contraindication.

Expected survival

- Quote around 50% to parents
- 30% if ECPR.

Cannulation

- Contact:
  - Intensivist if not already present
  - ECMO Coordinator
  - Cardiac Surgeon
  - Perfusionist
  - Theatre Team
  - Blood Bank
  - Cardiologist

The trick is to make each of them believe you are calling them first!

- Order blood to prime the circuit (1–2 units of packed RBC)
  - Also order more blood and products for after cannulation
- Cannulation is an emergency surgical procedure. Full asepsis must be adhered to, which requires additional awareness if cannulation undertaken on PICU rather than in theatres
- Prepare medications
  - Anaesthetic agents, e.g. ketamine 1–2mg/kg
  - Prophylactic antibiotics according to local protocol, e.g. flucloxacillin, vancomycin, or teicoplanin
  - Heparin 50–100U/kg to be given immediately prior to cannulation, once haemostasis achieved and vessels identified—the surgeon will tell you when
  - 'Arrest drugs' and 'volume' (colloid or blood as appropriate)
- Venous access:
  - Ensure reliable access, ideally via central line, not at the cannulation site
  - Venous access must be accessible when the patient is draped—use an extension line, remember dead space of this when giving drugs
- Anaesthesia:
  - Give anaesthetic drugs when everyone ready
  - Ensure access to airway (particularly if hand ventilating) as access to the patient is restricted during cannulation
- Cannulation will be VA usually, via the previous sternotomy:
  - Sometimes via the right side of the neck, in which case the carotid and jugular vessels will usually be ligated
  - Patients with Fontan and Glenn circulations may also need femoral cannulae
  - Cyanotic patients with a good cardiac output better on VV ECMO
- Go on slowly; rapid initiation of ECMO with 'old' blood prime can cause hypocalcaemic, hyperkalaemic cardiac arrest,—give $CaCl_2$

ECMO management

- Increase blood flow to ~100mL/kg/min for VA (120 for VV)
- Give volume to ensure adequate venous drainage: limit venous line pressure –20 to 30mmHg for baby (–50 to 60 adolescent).
- Set initial sweep gas flow to the same as the blood flow
- Measure central venous blood gas.
  - Aim for PvO_2 of 4–6 KPa, SvO_2 >65% (extraction ratio <35%)
  - If SvO2 is lower than this ↑ ECMO flow
  - Aim for $PvCO_2$ 6–8 KPa
  - To remove more CO_2 ↑ sweep flow, to remove less ↓ sweep flow

- ↓ ventilation to allow lung rest but maintain coronary oxygenation
  - Rate 10, PIP 20, PEEP 5–10, FiO_2 40–50%.
  - Adjust blood gases by manipulating ECMO circuit flow and sweep
- Once SvO_2 >65% adjust BP by manipulating SVR with vasoconstrictors/dilators.
  - Keep an inotrope on to stop the left heart dilating, e.g. dopamine 5–mcg/kg/min
- Once activated clotting time (ACT) starts to fall after cannulation and if the patient is not bleeding, start heparin infusion 20–50U/kg/h (keep ACT 160–200)
- Check Echo for LV dilatation
- Transfuse to maintain Hb 12–14g/dL, INR <1.5, platelets >150, and fibrinogen >2
- Prevent bleeding i.e. avoid heel prick, central line etc.
- Continue doing intensive care as normal i.e. nutrition, renal replacement therapy if needed (connect to ECMO circuit), antibiotics etc
- Set temperature on ECMO circuit water bath
  - Usually 37.5°C gives a patient core temperature of 36–37°C
  - Consider cooling to 34–35°C for 48h if post cardiac arrest or if tachy-dysrhythmia present.

Selected problems

- *Bleeding*. Step wise approach:
  - Initially reduce ACT to 160–180, transfuse to INR <1.5, fibrinogen >2 ,and platelets >150
  - Aprotinin 1mL/kg loading over 30min then 1mL/kg/h infusion.
  - Reduce heparin to 10U/kg/h and ignore ACT.
  - Factor VII concentrate (Novoseven®) 90mcg/kg (repeat in 2h, contraindicated with mechanical valve and non-functioning ventricle) ~1% serious thrombosis.
  - Stop heparin and maintain high circuit flows
  - Surgical exploration of the cannulation site may be appropriate
  - Moving the ECMO cannulae to the neck and closing chest often stops the bleeding
  - Application of this protocol will cause the circuit to clot—usually slowly but sometimes suddenly, the whole team must be informed and a new circuit should be on stand-by
- Circuit failure:
  - ECMO specialist-clamp the patient off ECMO and try to fix/replace the circuit
  - Call ECMO team including perfusion
  - Intensivist: try and keep the patient alive (hand ventilation, drugs, volume and CPR) until ECMO flow can be re-established
- Inadvertent decannulation:
  - As for 'circuit failure' also with massive haemorrhage/entrainment of air from the cannulation site.
  - Controlled by pressure (re-open chest if transthoracic)

- LV distension:
  - VA ECMO off-loads RV but can lead to LV distension (high afterload to the failing LV)
  - May be seen on Echo, high LA pressure, flat arterial trace
  - LV must be urgently decompressed (surgical venting or atrial septostomy) to prevent pulmonary haemorrhage and consolidation
- Sepsis:
  - May be masked by lack of fever (temperature controlled by heat exchanger)
  - ↑CRP, ↑WCC, ↑CO_2 production—ask if sweep flow has had to be ↑.
- Tamponade: even a small pericardial effusion can cause enough atrial collapse to impede venous drainage to the ECMO circuit.

Signs of improvement

- Settling capillary leak
- Heart ejecting
- Improvement on daily Echo (must be done when clamped off ECMO)
- Reduction in ECMO flow needed to maintain target venous gases
- Improvement will usually occur in the first few days. If not:
  - Ensure adequate cardiac repair (cardiac catheter, TOE or exploration of the chest)
  - Survival unlikely (although rarely possible) if still on ECMO at 1 week and extremely unlikely if heart is not ejecting at 1 week
  - Each case judged individually but futile treatment is not in anybody's best interests.

Trial off VA ECMO

- Once heart has recovered and flow weaned to minimum (30mL/kg/min)
- Start inotropes and heparin on patient, ventilate normally and clamp off flow through ECMO cannulae
- Circuit recirculated via bridge, heparin continued on circuit, sweep off
- Patient and circuit ACTs 180–200s
- Flush cannulae q10min by unclamping
- If stable for 2h decannulate:
  - Echo, lactate and venous blood gas best guides to assess adequacy of cardiac output
  - If high dose inotropes needed (> 0.4mcg/kg/min epinephrine) restart ECMO.

Decannulation

- Similar to cannulation, same team, same anaesthetic:
  - The surgeon removes cannulae
  - Send tips for MC&S.
- Beware temperature spike as patient 're-learns' thermoregulation
- Treat aggressively as temperature can rise rapidly to >40C

Respiratory ECMO

- VV mode of choice, even if a patient is on large doses of inotropes as long as they are responding
- For cardiorespiratory failure use VA.

Neonatal ECMO

Indications

- Meconium aspiration sydrome, iRDS, sepsis (usually Group B Strep), PPHN and CDH all cause persistent fetal circulation with right-to-left shunting and hypoxia
- If OI is >40, ECMO improves outcome[1]
  - OI = FIO_2/MAP × PaO_2 in mmHg, multiply kPa by 7.5
  - Lower OI may be appropriate if patient is on adjunctive therapy (i.e. iNO), with no improvement.

Contraindications

- Weight <2kg
- Gestation <32/40
- IVH >grade 2
- High pressure or high FiO_2 ventilation >9 days
- Moribund patient
- Congenital abnormality inconsistent with reasonable quality of life.

Expected survival

- Quote parents >85%
- >90% for meconium aspiration syndrome
- ~50% for CDH.

Cannulation

- Largely as for cardiac (see earlier).
- VV double lumen (VVDL) cannula 12 or 15F via right jugular vein, not usually ligated
- VA via right neck for patients too small for VVDL or for cardio-respiratory support, vessels usually ligated.

Management

Largely as for cardiac, except:

- Ventilator rest settings 20/10, rate 10, FiO_2 30%
- Set ECMO flow on VV against PaO_2 (target 6–8KPa) if low turn up the flow, SpO_2 >85% is adequate if Hb>12g/dL.
  - Maximum flow 120mL/kg/min (recirculation occurs above this).
- Set sweep gas on VV against $PaCO_2$ (target 4–6KPa)
- Transfuse to Hb 12–14g/dL, INR<1.5, fibrinogen>1.5, platelets > 75–100 if not bleeding
- Daily head ultrasound scan
- Daily ECHO to estimate PA pressures
- Surfactant and/or steroids may be given if not improving after 4 or 5 days—but little direct evidence for efficacy.

Signs of improvement

- Improved lung compliance
- Clearing CXR
- Lower ECMO flow needed to maintain PaO_2
- Return of PA pressure to normal (1/3 to 1/2 systemic).

Signs of irreversibility

- Failure to wean from ECMO after>1000h.
- Surfactant B deficiency
- Capilliary alveolar dysplasia.

Trial off VV ECMO

Once on minimum flow (~50mL/kg):

- Turn up ventilator, disconnect sweep gas, measure arterial gas
- Circuit continues as normal but becomes gas exchange neutral
- If in doubt VV trial off can be continued for 12–24h.
- If FiO_2 >60% or PIP>25cmH_2O, the patient is not ready to come off.

Paediatric ECMO

As for cardiac and neonatal respiratory, except:

Indications

- ARDS or pneumonia of various causes, RSV bronchiolitis and asthma:
  - VV mode of choice for most patients
  - VA for cardiorespiratory support.

Contraindications

ECMO does not improve survival in these conditions:

- Meningococcal sepsis in first 24h or with massive sepsis and haemodynamic collapse
- Pertussus with high lymphocyte count
- Oncology patient with failed BMT and neutropenia
- First presentation of AIDS
- High pressure ventilation or high FiO_2 for >9 days (1 month old) or >7 days (18 years old)
- Active intracranial bleeding
- Moribund patient
- Underlying chronic condition with very poor prognosis.

Expected survival

- Quote parents ~70%.

Cannulation

- Largely as for cardiac (see earlier)
- VV 18F double lumen via right jugular (non-ligation) up to 10kg
- Larger children may require 2 or 3 cannulae, i.e. via right neck and femoral vessels, sizes from 14F to 28F
- VA via carotid or femoral artery (beware distal ischaemia) for cardio-respiratory support.

Management

All as for neonate except:

- Rest settings: rate 10, PIP 20–25cm H_2O, PEEP 10–15cm H_2O, FiO_2 30%
- Daily head ultrasound and Echo to measure PA pressure not required
- Surfactant rarely used, steroids may be given if not improving after 7 days
- HFOV may be useful for lung recruitment
- DNAse and acetyl-cysteine may be used, particularly if there are persistent focal areas of consolidation
- Fibreoptic bronchoscopy for airway suction
- Prone position
- CPAP or low pressure HFOV for barotrauma, air leak syndrome.

Signs of improvement
- Improved lung compliance
- Clearing CXR
- Lower ECMO flow needed to maintain PaO_2

Signs of irreversibility
- Failure to wean from ECMO after>1000h
- Pulmonary Hypertension (>2/3 systemic) after 3 weeks

Trial off VV ECMO
- Once on minimum flow (~50mL/kg):
  - As per neonatal VV ECMO
  - If FiO_2 >60% or PIP>30cmH_2O, the patient is not ready to come off.

VADs

These comprise extracorporeal centrifugal pumps or pulsatile pneumatic systems that drain blood from right atrium and return it to the pulmonary artery for right ventricular support, and from the left ventricle (or the left atrium) and return it to the ascending aorta for left ventricular support.

Centrifugal pumps
- These include the BioMedicus Biopump, CentriMag®, and RotaFlow®, amongst others. This type of pump has been used since the early 1990s for short-term support in children with postoperative cardiac failure but competent lung function
- Based on vortex technology, these systems use a magnet to drive a spinning turbine, creating a flow of 5–6L/min without significant mechanical damage to the blood cells
- Each VAD system is designed for single ventricular support (left or right). 2 pumps connected in series may provide biventricular support, although this is technically challenging.

Pneumatic pulsatile ventricular assist devices
- Several types of VADs have been used in older children. 2 pneumatically driven VADs designed specifically for smaller children and infants currently in routine use
- These include the Berlin Heart Excor® and the Medos HIA pulsatile systems. Both consist of a pneumatic compressor-operated diaphragm pump with valves. The pump is extracorporeal and connected to the body by special silicone cannula
- The systems are transparent to allow early thrombus detection, and being external can be changed rapidly if required in the event of a problem such as malfunction, blockage or thrombus formation.

Advantages
- Relative ease of use (compared to ECMO)
- Ease of implantation
- Fast setup time
- Low priming volume
- Less anticoagulation than ECMO (since it usually does not have an oxygenator or a heat exchanger)
- Lower cost.

Disadvantages
- Shorter duration of usage
- Thrombus formation in the circuit
- Nonpulsatile flow nature.
- Functioning right ventricle needed since it supplies preload to the left ventricle supported by the VAD.
- Size limitation if biventricular support is needed.

Intra-aortic balloon pump (IABP)

The IABP is an expandable balloon that is inserted into the descending aorta. The balloon is periodically filled and emptied of helium gas, and this pulsation augments cardiac function.
- In diastole the IABP inflates, sending blood both proximally and distally. This augments the aortic diastolic pressure and hence coronary perfusion. (See Fig. 11.2).

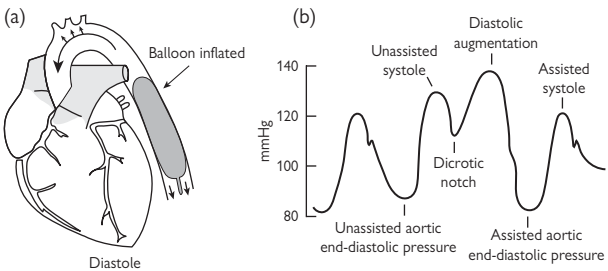

Fig. 11.2 a) Ideal location of the balloon. b) Effect of augmentation on the aortic arterial trace. Reproduced from Collison SP, Dagar KS (2007) The role of the intra-aortic balloon pump in supporting children with acute cardiac failure. *Postgrad Med J* **83:** 308–11, with permission from BMJ Publishing Group Ltd.

- Balloon deflation is timed to the onset of ventricular contraction and the opening of the aortic valve. The space occupied by the balloon in the aorta is suddenly released as the ventricle empties. This reduces pressure in the aorta, thereby reducing ventricular afterload and ventricular wall stress, and improving cardiac performance
- This device is less effective in smaller children than in adults due to increased compliance of the aorta, small aortic size, and higher heart rates leading to difficulty in synchronization
- Advantages of IABP for providing left ventricular support:
  - Less invasive than ECMO and VAD
  - Less anticoagulation needed (compared to ECMO)
  - No extracorporeal circuit is required
  - May be less expensive than the other modalities
- Disadvantages:
  - Shorter duration of use
  - Questionable utility in smaller children due to technical limitations
  - Only a left ventricular support modality
  - Limitation with certain anatomy/physiology (such as patent ductus arteriosus or aortic insufficiency)

- Complications including mesenteric ischemia and arterial injury
- The right ventricle is not supported by IAB.

Table 11.2 Comparison of mechanical support options

	ECMO	Centrifugal VAD	Pulsatile VAD	IABP
Paeds experience	Large	Limited	Limited	Minimal
ICU cannulation	Yes	No	No	Yes
Univentricular support	Yes	Yes	Yes	Left
Biventricular support	Both	Possible, but difficult	Possible, but difficult	No
Oxygenator?	Yes	Difficult	Difficult	No
Complexity	High	Moderate	Moderate	Low
Anti-coagulation needed	High	High (but less than ECMO)	High (but less than ECMO)	Low
Complication rate	Moderate to high	Low	Low	Low to moderate
Duration	Days to weeks	Days to weeks	Weeks to months	Days
Need for LA decompression	Occasional	No	No	No
Cost	High	Moderate	High	Moderate/ low

Reference

1. UK Collaborative ECMO (Extracorporeal Membrane Oxygenation) Trial Group. UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation. *Lancet* **348**: 75–82.

Further information and reading

Chang AC, McKenzie ED (2005). Mechanical cardiopulmonary support in children and young adults: extracorporeal membrane oxygenation, ventricular assist devices, and long-term support devices. *Pediatr Cardiol* **26:** 2–28.

Collison SP, Dagar KS (2007). Meyer S, Gortner L, McGuire W, *et al.* (2008). Vasopressin in catecholamine-refractory shock in children. *Anaesthesia* **63:** 228–34

- UK ECMO Centres:
  - Glenfield Hospital, Leicester, 0116 2541414
  - Great Ormond Street Hospital, London, 0207 829 8652
  - Freeman Hospital, Newcastle upon Tyne, 0191 223 1016
  - Yorkhill Hospital, Glasgow, 0141 201 0255
- Rest of the World: http://www.elso.med.umich.edu/

Chapter 12

Cardiopulmonary bypass

Introduction

Cardiopulmonary bypass (CPB) takes over the function of the heart and lungs to allow surgery on the heart, great vessels, or airway. It is the only way to achieve a still, bloodless heart while maintaining circulation to the rest of the body.

Alternatives to bypass include deep hypothermic cardiac arrest (DHCA), during which the circulation is completely stopped under hypothermic protection. Despite recent advances in technology, CPB and DHCA can cause many problems to the post-cardiac surgery child.

The essential functions of CPB are:
- Oxygenation
- Ventilation (CO_2 removal)
- Circulation
- Temperature control.

Preoperative assessment

Usually the cardiac surgery/cardiology team will have discussed the indications for surgery using CPB and consent will have been taken. It is important to also assess the following:
- Teeth: carious teeth increase the risk of endocarditis and should be dealt with prior to cardiac surgery (if time allows)
- Weight: the risk of CPB is much higher in patients <2kg
- DiGeorge syndrome: 22q11 microdeletion, detected by FISH test, is common in cono-truncal defects. Patients need irradiated and CMV-negative blood and products (these can take up to 24h to obtain)
- Brain: ventilated neonates who have suffered a significant hypoxic-hypotensive insult should have a full neurological assessment including imaging with US/CT/MRI as appropriate prior to surgery
- Blood and products: 4 units packed cells and 10mL/kg of FFP, platelets, and cryo-precipitate will be required:
  - The adult dose of products is 4–6 units of each, so once the calculated dose in mL/kg exceeds this, the adult dose is used (25–30kg).
  - Some of the blood will be used to prime the pump and the rest will be available postoperatively.

The cardiopulmonary circuit

Standard components

- Atrial cannula (right atrial, caval, or femoral)
- Venous line
- Venous reservoir
- Venous outlet
- Pump (peristaltic roller pump or centrifugal)
- Oxygenator (usually hollow fibre with an integral heat exchanger)
- Arterial filters and bubble detector
- Arterial line
- Arterial cannula (aortic, femoral, or axillary)
- Monitoring (minimum is venous saturation, pre- and post-oxygenator pressure)
- Pumps.

Pumps

- Peristaltic:
  - Most widely used
  - Tubing compressed by rotating rollers, pushing blood along the tubing
  - Flow dependent on size of tubing, length being compressed, and the speed of the rollers (revolutions per minute, rpm)
  - If the arterial line is obstructed the high pressures generated can cause tubing rupture
- Centrifugal:
  - Rapidly rotating (2000–3000rpm) plastic cones generate a pressure difference, leading to flow
  - Non-occlusive
  - Flow reduced by increases in afterload.

Oxygenators

- Microporous hollow fibre oxygenators made from polypropylene are the most widely used:
  - Gas exchange occurs across a microporous membrane which separates blood and gas phases
  - Large surface area (for gas diffusion) achieved by hollow fibre design with blood flow either inside or outside the fibres, or a folded envelope design
  - Ventilation and oxygenation are relatively independent. Simplistically, ventilation is dependent upon gas flow (sweep gas flow) through the oxygenator, and oxygenation is dependent upon the FiO_2 of the sweep gas, and the CPB circuit blood flow
- Bubble oxygenators are less commonly used.

Heat exchangers

- Cool or warm blood, controlling the temperature of the patient and of cardioplegia if required
- Integral part of most oxygenators
- Operate between 2–42°C. Protein denaturing occurs outside of this range. Although cardioplegia may be given at around 8°C, the patient temperature is never dropped below 14°C as there is a high incidence of choreo-athetosis and poor neurological outcome when such extreme hypothermia is used.

In the operating room

- *Access:*
  - Is usually via a median sternotomy, but in re-do surgery extra-thoracic cannulation via the neck or groin may be used
  - Blood is drained from the venous system and returned to the arterial tree
  - Additional vents may be inserted into the left atrium to keep the heart empty
- *Typical target flows on CPB:*
  - Patients <10kg – flow = 150mL/kg/min
  - Patients >10kg – flow = 2400mL/m^2/min
- *Cannula sizes:*
  - Once the flow rate is calculated the choice of arterial and venous cannula size can be made (see 🕮 Table 6.1, p.62)
  - In the case of venous cannulation, the choice as to single (right atrial) or double (SVC and IVC) cannulation is made
  - Bi-caval cannulation is used primarily in operations where the right side of the heart needs to be entered
- *Priming the circuit:*
  - The CPB prime composition is calculated such that the combined patient and bypass pump blood haemoglobin is at least 8–9g/dL
  - Prime volume is minimized to use as little donor blood as possible
  - Patients >10kg may have a bloodless prime if their Hb is >12g/dL
- *Typical CPB prime 'recipe':*
  - Total diluent volume calculated on the basis of the patient's Hb and blood volume
  - Constituents depend on the blood used (fresh heparinized; citrated whole blood; or packed cells)
  - CPB prime constituents may include:
    - blood
    - heparin
    - calcium chloride
    - magnesium
    - sodium bicarbonate
    - dextrose
    - 20% albumin
    - steroids (typically 30mg/kg methyl-prednisolone to a maximum of 1g, to limit inflammatory activation)
    - crystalloid, plasma, or plasma substitute to make up to volume
  - The biochemical and acid–base balance of the prime is tested prior to the initiation of bypass and modified to normal values
- *Heparin:*
  - 300U/kg is administered to the patient prior to initiation of CPB
  - This causes complete anticoagulation of the blood as measured by an activated clotting time (ACT) of around 500–1000s
- *Hypothermia:*
  - Most surgery requires cooling which can vary from 14–32°C depending on the condition
  - Complex surgery in cyanotic patients is done colder in order to reduce the metabolic rate (10% per degree) and allow lower bypass flows (less blood in the surgical field)

- *Aortic cross clamp and cardioplegia:*
  - Cardioplegia is used to stop the heart to allow intracardiac surgery
  - The heart is isolated from the circulation, the aorta is cross-clamped, and cardioplegic solution is infused into the coronary arteries below the clamp
  - There are many different recipes but the most commonly used is 30mL/kg cooled blood (8°C) with added potassium (concentration 85mmol/L). This stops the heart in diastole
  - Cardioplegia infusion must be repeated every 20–40min
- *DHCA:*
  - Needed to allow surgery in small patients with limited surgical access; surgery around the aortic arch; and other complex repairs
  - The patient is cooled to around 14°C
  - DHCA is kept as short as possible—the risk of neurologic injury from cerebral hypoxia during DHCA rises with time
  - DHCA times of 30–40min are not unusual: Times >45min are associated with adverse neurological outcome
  - Sometimes steroids (methyl-prednisolone 30mg/kg) are given as an aid to neuroprotection. The evidence for this is weak.

Cerebral protection

Haemodilution

- Too much haemodilution reduces cerebral oxygen delivery and is associated with an adverse outcome
- Aim for a haematocrit ~30% on CPB.

Acid–base management on CPB

- With hypothermia, the oxyhaemoglobin dissociation curve shifts to the left, reducing oxygen availability and CBF
- Two distinct strategies of pH management may be used:
  - *Alpha-stat,* which maintains the pH at 7.4 without compensation for temperature, and
  - *pH-stat,* which adds carbon dioxide to the circuit to enhance haemoglobin dissociation and increase cerebral blood flow, increasing cerebral tissue oxygenation. Intracellular pH falls
- For DHCA the best evidence is to use pH-stat during cooling, switching to alpha-stat just before arrest and for rewarming, this ensures more even brain cooling and prevents cerebral vasoconstriction
- There is a strong correlation between rapid cooling/warming and poor neurological outcome.

Glucose management

- Hyperglycaemia during CPB is associated with adverse outcome in some, but not all studies
- Too tight control of blood glucose could lead to hypoglycaemia, so tight glycaemic control is not without risks.

Drug therapy

- Prophylactic steroid therapy reduces inflammation and brain injury in animal and some human studies
- No consensus on steroid dose, timing, or treatment regimen

- Other drugs, such as barbiturates, propofol and others have neuroprotective effects in experimental studies, but these have not been verified in clinical practice.

Intermittent cerebral perfusion

- Animal studies of intermittent systemic recirculation during DHCA improves neurological outcome. Little or no paediatric clinical data
- May be considered if DHCA becomes unduly prolonged.

Low-flow CPB

- Allows some perfusion to the brain which may improve neurologic outcome
- Minimum safe flow not established. May compromise the surgical field and make repair more difficult.

Regional low-flow cerebral perfusion

The brain is perfused through the right innominate and right vertebral arteries maintaining some flow to the brain during cardiac arrest and potentially improving neurologic outcome. No definitive clinical studies.

Monitoring during CPB

- Normal recommendations for patient monitoring during anaesthesia should be followed
- Monitor CPB circuit parameters continuously:
  - Gas tensions and flow, blood flow and temperature, blood and (where relevant) cardioplegia pressure in the circuit
- Patient monitoring should include:
  - ACT to confirm adequate levels of anticoagulation
  - ABG and electrolytes; blood sugar
  - SvO_2 and lactate to estimate oxygen uptake and utilization
  - Cerebral monitoring (see Box 12.1).

Pulsatile versus non-pulsatile flow

- The perfusion provided by CPB pumps is relatively non-pulsatile
- Pulsatile perfusion (PP) may improve microcirculatory flow, myocardial perfusion, oxygenation, indices of contractility, and decrease lung water retention
- PP also reduces the rise in SVR seen during CPB, thought to be secondary to changes in the renin–angiotensin system
- However, clinical studies have been unable to detect a benefit of PP
- Pulsatile flow is difficult to achieve in infant CPB, because of damping that occurs in small arterial cannulae.

Box 12.1 Cerebral monitoring

Estimates of post-CPB neurological injury range from 2–30% in neonates. Monitoring cerebral function during CPB may allow interventions to reduce this. Possible approaches include monitoring of SVC or jugular venous bulb oxyhaemoglobin saturation (SvO_2), regional cerebral oxygen saturation by NIRS, cerebral blood flow velocity by transcranial Doppler, EEG, or processed EEG.

Transcranial Doppler (TCD)

- Measures blood flow velocity typically in the middle cerebral artery, estimating cerebral blood flow
- Useful in detecting cerebral under perfusion (especially in low-flow CPB), and cerebral over perfusion
- Minor changes in probe position may result in significant signal alteration (can be a problem in the operating theatre)
- Complications rare. Avoid directing the probe at the eyes
- May detect signals representing cerebral emboli. Clinical significance of these signals uncertain.

Near infrared spectroscopy (NIRS)

- Non-invasive estimate of oxyhaemoglobin saturation in a volume of brain tissue (regional cerebral saturation index rSO_2i), reflecting brain tissue oxygen content
- Best used as a trend monitor over time
- Low rSO_2i associated with cell dysfunction and risk of death.
- Adverse neurological outcome related to low baseline rSO_2i and time spent at nadir of rSO_2i
- Complications uncommon, but include skin sensitivity and burns or pressure injury from the light source.

Combined monitoring

- May improve prediction of adverse outcomes, but difficult to apply multiple monitors to the small foreheads of infants
- In one study, 90% of abnormal events detected by NIRS and 10% by TCD.

Modified ultrafiltration (MUF)

- The inflammatory response initiated by CPB causes ↑capillary permeability and ↑extravascular fluid
- Perioperative MUF decreases total body water and improves the haemodynamic and pulmonary status
- Aim to remove 100mL/kg of filtrate in infants (dependent on stable haemodynamics)
- Amount of filtrate removed will vary in larger children.

De airing

- After the intracardiac repair has been completed air is removed from the cardiac chambers and the cross clamp is released
- Small amounts of air are retained in the heart and can enter the right coronary artery and cause transient ischaemia and RV dysfunction.

Box 12.2 Criteria for discontinuing bypass

- Satisfactory rhythm and ventricular rate (paced if necessary)
- Nasopharyngeal temperature 36.5–37.5°C
- K^+ 4.0–5.5
- pH 7.30–7.50
- pO_2 appropriate for anatomy
- Anaesthetist ventilating.

Rewarming and coming off CPB (see Box 12.2)

- The patient is fully rewarmed and then weaned from CPB usually with the aid of inotropes
- Heparin is reversed with protamine
- Most patients have temporary epicardial pacing wires placed. The ventricular wires are brought out to the left of the sternum and the atrial wires to the right (in situs solitus)
- Pressure monitoring lines may be placed in the RA, LA, or PA and brought out through the chest wall
- Myocardial swelling may prevent sternal ± skin closure. A silastic membrane may be sewn into the skin edges
- All patients have mediastinal and/or pleural chest drains.

Times

- Long CPB time: systemic inflammatory response, fluid shifts
- Long DHCA time: ~risk of neurological injury, especially >60min
- Long aortic cross clamp time: ~myocardial dysfunction.

Selected postoperative complications

Postoperative management and general complications following CPB are covered in 📖 Chapter 20.

Further reading

Association of Anaesthetists of Great Britain and Ireland (2000). *Recommendations for standards of monitoring during anaesthesia and recovery.* Association of Anaesthetists of Great Britain and Ireland, London. Available at: 🖱 www.aagbi.org

Chikwe J, Bedow E, Glenville B (2006). *Oxford Handbook of Cardiothoracic Surgery. Oxford* University Press.

Jones TJ, Elliott MJ (2006). Paediatric cardiopulmonary bypass: bypass in a high risk group. *Perfusion* **21**: 229.

Williams G, Ramamoorthy C (2007). Brain monitoring and protection during pediatric cardiac surgery. *Semin Cardiothorac Vasc Anesth* **11:** 23.

Chapter 13

Managing fluids, electrolytes, and acid–base

Intravenous fluid and electrolytes

❗ This section assumes infants and children are unable to take oral or enteral fluids. Guidance on enteral feeding and fluids is given in 📖 Chapter 15.

► First establish the weight of the infant or child which can be estimated by Broselow tape or, for children between 1–10 years, by formula:

weight (kg) = 2 × (age in years +4).

General points

Water

- 80% of the body weight at birth is water
- This is reduced to 60% by 1 year of age
- Approximately 2/3 is intracellular and 1/3 extracellular. ECF is proportionately greater in neonates (initially 2/3) and falls as the child grows and cells increase in number
- Adipose tissue stores less water, so post-pubertal girls have a lower total body water content than boys and pre-pubertal girls.

Electrolytes

- Within the intracellular compartment:
  - Potassium (K^+) is the principal cation
  - Phosphate (PO_4^-) and proteins are the main anions
- Within the extracellular compartment:
  - Sodium (Na^+) is the principal cation
  - Bicarbonate (HCO_3^-) and chloride (Cl^-)are the main anions.

Daily requirements

Fluid requirements: fluid needs can be calculated with the weight of the child using the calculations in Table 13.1.

Table 13.1 Algorithm for daily fluid requirement calculation

Child's weight (kg)	'Maintenance' mL/24h
2–10kg	100mL/kg
10–20kg	1000mL plus 50mL/kg for each kg >10kg
>20kg	1500mL plus 20mL/kg for each kg >20kg
Maximum amounts: males 2500mL/24h; females: 2000mL/24h	

- This guide amount is reduced:
  - In neonates: 50mL/kg/day on day 1 of life, 75mL/kg/day on day 2
  - After major surgery (i.e. see 📖 p.371)
  - If child is intubated on humidified ventilation (25–50% reduction).
  - Where fluid is being retained (cardiac failure or renal impairment)
- It is ↑ in children:
  - With abnormal skin (e.g. burns 📖 p.517)
  - Who are pyrexial or on phototherapy (25% increase)
  - With tachypnoea or on non-humidified mask ventilation
  - Who are losing fluid (diarrhoea or vomiting, polyuria)

- ***Electrolyte requirements:*** summarized in Table 13.2.

Table 13.2 Daily electrolyte requirements (mmol/kg/day)

Na^+	2–4
K^+	2–3
Ca^{2+}	1
Mg^{2+}	1
Cl^-	3–5
PO_4^-	2–3

⚠ Potassium concentrations should not normally exceed 40mmol/L for peripherally administered solutions (risk of extravasation injury).

⚠ Avoid giving calcium via peripheral lines unless absolutely essential. Monitor peripheral cannulation sites carefully where calcium is added to fluid as skin burns can result from extravasation.

Fluid replacement (Table 13.3)

- Ideally all fluid, electrolyte, and calorie replacement would be given by the enteral route, and IV fluids should only be prescribed when this is not possible or appropriate.

Table 13.3 Composition of commonly used IV fluids

	Serum	0.9% Saline	0.9% Saline/ g5w	0.45% Saline	0.45% Saline/ g5w	0.18% Saline/ g4w	HS
Na^+	135–145	154	154	77	77	31	131
K^+	3.5–5						5
Ca^{2+}	2.2–2.6						2
Cl^-	95–105	154	154	77	77	31	111
HCO^{3-}	24–32						29*
Na^+/Cl^-	1.28–1.45:1	1:1	1:1	1:1	1:1	1:1	1.18:1
Glucose	4–6		50g/L		50g/L	40g/L	
Osmolality	275–295						276
EFW		0	0	50	50	80	16
Tonicity		Iso	Iso	hypo	hypo	v.hypo	Iso

All values in mmol/L, except Na^+/Cl^- (ratio); osmolality (mOsm/kg); electrolyte free water (EFW; %). g5w, 5% glucose; g4w, 4% glucose; HS, Hartmann's solution. *As lactate.
Iso, isotonic; hypo, hypotoniv; v.hypo, very hypotonic. (Data from McLellan NJ (2009). BCH clinical guidelines, Birmingham Children's Hospital, UK.)

- 0.9% saline or 0.9% saline with 5% glucose has become the fluid of choice for maintenance and deficit replacement in most cases
- Previous use of 0.45% saline with 5% glucose ('half normal with glucose') or 0.18% saline with 4% glucose ('four and a fifth') has declined with concerns about hyponatraemia (📖 p.238)
- Glucose content of fluid can be adjusted to the needs of the child

⚠ Hypotonic solutions (5% or 10% glucose, or 4% glucose + 0.18% saline) are not normally used because of the risks of hyponatraemia

- Pre-term and newborn infants may be an exception to this rule as they have limited ability to excrete Na^+. They may be managed with 10% Glucose, added electrolytes and regular monitoring.

Osmolality and tonicity

- Osmolality is a measure of the solute concentration, or the number of solute particles present in solution and is independent of the size or mass of the particles
- Tonicity is the *effective osmolality* and is equal to the sum of the concentrations of all the solutes that have the capacity to exert an osmotic force *across a membrane*
- Solutes that penetrate freely across a membrane do not exert an osmotic force across it
- When infusing 5% glucose, for instance, the glucose is taken up and metabolized by cells, leaving only electrolyte-free water.

How to calculate osmolality

$$\text{Calculated osmolality} = 2 \times [Na^+] + 2 \times [K^+] + [\text{glucose}] + [\text{urea}]$$

If the calculated osmolality is less than the laboratory measured osmolality, then there is another osmotically active substance present, i.e. sugar, mannitol etc.

Fractional excretion of water and sodium (FEH_2O and $FENa^+$)

- The FEH_2O is the fraction of the glomerular filtrate volume that appears as urine, expressed as a percentage
- The $FENa^+$ is the fraction of the sodium filtered by the glomeruli which appears in the urine, expressed as a percentage (Box 13.1)
- Values depend upon water intake, ADH levels, the renin/angiotensin system, renal health and maturation, medications and other factors
- Children with healthy kidneys can lower both FE values to <1%
- In renal hypoperfusion, the $FENa^+$ is <1%
- In intrinsic ARF, it is >2.5%
- Recent use of diuretics makes interpretation of FE values difficult
- Together, urinary sodium concentration, urinary osmolality, $FENa^+$ and FEH_2O can be interpreted to understand a patient's fluid and electrolyte status (see Fig. 13.1)
- Urinary sodium concentration cannot be interpreted alone, as sodium and water excretion may vary together or independently.

Box 13.1 Calculation of FEH_2O and $FENa^+$

$$FEH_2O = (PCr/UCr) \times 100$$

$$FENa = [(UNa/PNa) \times (PCr/UCr)] \times 100$$

- PNa = plasma sodium, mmol/L
- UNa = urine sodium, mmol/L
- PCr = plasma creatinine, μmol/L
- UCr = urine creatinine, μmol/L
  (UCr often reported in mmol/L, may need multiplication, × 1000)

FE values are expressed as %

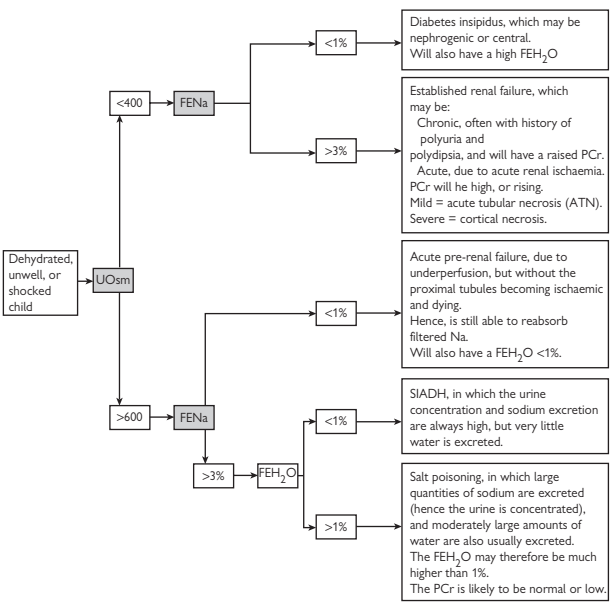

Fig. 13.1 Simplified algorithm to diagnose the pathophysiology of the water and salt balance of unwell children. Reproduced from Coulthard MG (2008). Will changing maintenance intravenous fluid from 0.18% to 0.45% saline do more harm than good? *Arch Dis Child* **93:** 335–40.

Box 13.2 IV fluids—a few points, some myths and some fancies

Sick infants and small children are particularly susceptible to ↑ ADH secretion as part of the 'stress response'

- This is not 'inappropriate' ADH syndrome but an evolutionary physiological response to real or potential hypovolaemia (e.g. following surgery or trauma), when the body thinks it will need to retain fluid
- Obviously evolution did not anticipate the advent of IV fluid therapy. Combine ↑ADH secretion and prescribed hypotonic IV maintenance fluids and iatrogenic hyponatraemia becomes a major problem with a significant associated mortality.

IV maintenance fluids may be very hypotonic; hypotonic; isotonic; or hypertonic (see Table 13.3)

- Very hypotonic fluids are associated with hyponatraemia whereas the moderately hypotonic and the isotonic fluids appear to be safer
- Isotonic solutions should be prescribed for 'maintenance fluids' in most cases
- If hypotonic fluids are prescribed, the child should be reviewed regularly, particularly if they are, or have recently been, sick.

The accepted formulae for IV fluid prescription (see Table 13.3) may in fact be excessive

- This calculation is based on calorie consumption (1mL of fluid for every kcal consumed) which itself is based on the child's weight
- 80% of energy expenditure occurs in the major organs which account for <10% of body weight. The assumption that ↑weight results in a direct proportional increase in energy expenditure is incorrect. Energy expenditure and hence fluid requirements may be overestimated, particularly in obese children
- Sick children consume significantly less energy than well children due to inactivity

All these factors have implications for hospitalized children:

- All very hypotonic IV fluids are restricted to specialized use only.
- IV maintenance should be isotonic (e.g. 0.9% saline or Hartmann's solution/Ringer's lactate) or moderately hypotonic (0.45% saline with glucose 2.5% or 5%)
- All additional losses, e.g. NG losses or excessive diarrhoea/stoma losses should be replaced with 0.9% saline
- The volume of 'maintenance fluid prescribed should be restricted in all cases where ADH secretion is raised (e.g. postoperatively, CNS and lung pathology). Prescribe 66–75% of full maintenance (based on body weight).

Box 13.2 IV fluids—a few points, some myths and some fancies (*Continued*)

PICU patients have even more reasons to restrict IV fluid prescriptions:

- Children are extremely inactive (sedated and paralysed)
- Mechanical ventilation reduces work of breathing and therefore calorie consumption
- Insensible loss is reduced through humidification of inspired gases
- ADH secretion is induced by positive pressure ventilation, lung pathology, CNS insults, and other common situations on PICU
- This means that children on ventilators should be restricted to 50–75% of normal IV maintenance fluids (calculations based on their weight).

Note: this does not apply to children with large fluid requirements, e.g. burns, sepsis etc, or to NG feeding prescriptions (📖 p.278).

Fluid deficits and rehydration

- Shock states or ongoing losses of body fluids should be treated initially with normal saline, plasma expanding colloids or 4.5% human albumin solution (see Box 13.3). Further losses may necessitate the use of blood products
- A fluid deficit is estimated by weight or clinical examination, and the deficit added into maintenance fluids for replacement at a rate which is governed by the extent of the deficit and its cause
- Fluid deficit is most accurately gauged by a change in weight
- Where weighing is impossible or no recent weight is available for comparison, a clinical estimate of dehydration may be made
- This is expressed as the number of mL of water lost per 100g of body weight or the percentage of dehydration
- Rates of rehydration need careful recalculation and adjustment in each child.

Clinical estimation of dehydration

- *5% dehydration*: reduced skin turgor, sunken eyes and or fontanelle, dry mucus membranes, ↓peripheral perfusion, irritability, oliguria, pyrexia
- *10% dehydration*: lax skin, poor perfusion, drowsiness, anuria
- Using this estimate the child's fluid deficit can then be calculated:
  Deficit in litres = (weight (kg) × % dehydration)/100

Rate of deficit replacement

- Shock needs to be addressed swiftly (see 📖 p.579)
- Deficit replacement over 24–36h is appropriate in most cases
- In hypernatraemia and hyponatraemia (see later sections), 48–72h may be needed for deficit replacement. This is necessary to avoid neurological complications caused by rapid changes in serum Na^+.

Severe dehydration

- Children who are ≥10% dehydrated are prone to complications such as renal vein and cerebral venous sinus thrombosis

- These complications should be remembered when the expected responses in urine output or conscious level are not obtained with fluid therapy
- Appropriate further examination and investigation should be undertaken.
- Significant 'contraction alkalosis' can also occur in dehydrated children (see Acidosis 📖 p.255) masking the severity of their acidosis. Such children may need bicarbonate therapy during rehydration.

Box 13.3 A word on colloids

Colloids are aqueous electrolyte solutions containing large molecules-proteins in the case of human albumin solution (molecular weight 68,000 daltons) and gelatins in gelofusine and haemaccel (molecular weight 30,000). The large molecules slow 'leakage' from the circulation through the capillary endothelium and therefore these solutions exert a colloid osmotic (oncotic) pressure. The advantage of colloids is that they stay in the circulation longer and thus less is needed to resuscitate the intravascular space when compared to crystalloids. In theory they should also cause less oedema. In practice, when capillary leak occurs it appears as if colloids do leak and potentially may cause more resistant oedema.

Human albumin solution 4.5% is a heat-sterilized human blood by-product that has a half-life of 16h in the circulation. Gelofusine and haemaccel persist for less time in the circulation but for longer than crystalloids. All 3 solutions contain plasma like concentrations of sodium and chloride. Larger molecular solutions such as hespan and pentaspan as well as dextran should be avoided.

Crystalloids versus colloids

Whilst it is standard practice to prescribe maintenance IV therapy with crystalloid solutions there is controversy regarding the suitability of colloids in resuscitating patients with hypovolaemia and sepsis. Proponents of colloid point to their efficiency (less required for the same effect) and physiological effect. Opponents point to their cost (colloids are considerably more expensive) and lack of evidence base. Indeed the evidence (from adults) is pretty clear so far: colloid therapy offers no clear advantage over crystalloid therapy (large paediatric trials are limited). However, most intensivists in our experience use a combination of both depending on the situation—often starting resuscitation with IV crystalloids, e.g. at 20mL/kg, and introducing colloids if more aggressive resuscitation is required (5–10mL/kg). Postoperative cardiac patients are often treated with colloid IV and many intensivists use human albumin for meningococcal sepsis.

Please note that over zealous use of colloids can overfill the circulation and tip the patient into pulmonary oedema (by increasing pulmonary venous pressure, see 📖 Box 13.5). Human albumin solution 20% is not recommended for resuscitation.

Monitoring fluid therapy (Box 13.4)

The key to effective and safe practice in fluid and electrolyte therapy is careful documentation and regular monitoring of the following:

Clinical parameters
- Weight: remember individual weighing-scales differ in accuracy
- Fluid balance: intakes – outputs all need to be charted
- Perfusion state: pulses and central capillary refill time
- Conscious level: GCS should not drop
- Hydration state
- Cannulation sites

Laboratory parameters
- Serum electrolytes: especially where supplements are given
- Serum urea and creatinine: rising values alert to renal impairment
- Haematocrit: a marker of intravascular status if no bleeding
- Blood glucose
- Urine electrolytes: urine Na^+ and Cl^- <20mmol/L in hypovolaemia.

Fluid losses
- Losses incurred such as haemorrhage and capillary leak can be assumed to have a similar composition to ECF
- Losses from the GI tract will depend on their origin and may require specific replacement intravenously (Table 13.4).

Table 13.4 Composition of GI fluids (mmol/L)

Fluid	Sodium	Potassium	Chloride
Gastric	20–80	5–20	100–150
Pancreatic	120–140	5–15	40–80
Biliary/upper small intestine	100–140	5–15	80–130
Ileostomy	40–140	5–15	20–120
Diarrhoeal	10–90	10–80	10–110

Box 13.4
- Fluid balance fluctuates rapidly and widely in seriously ill patients
- Carefully measured input (IV and enteral) and output (urine, drain losses, GI losses) values must be recor;ded hourly
- Insensible losses are often overlooked
  - Important as children have a ↑surface area to body weight ratio
  - Come from skin and respiratory tract
  - Vary with the patient's temperature, dimensions, and ventilation (humidification of inspired gases ↓ respiratory losses by 80%).
- 10–30mL/kg/day (300mL/m^2/day) is a reasonable estimate of insensible losses.

Hyponatraemia: Na^+ <130mmol/L

- Initial checks:
  - Check where sample drawn from to identify contamination
  - Correct serum sodium result for hyperglycaemia

$$\text{Corrected } Na^+ = \text{measured } Na^+ + 0.3\{\text{Gluc} - 5\}$$

  - Check osmolar gap between measured and calculated plasma osmolality.

Causes: see Table 13.5.

Treatment of hyponatraemia (Fig. 13.2)

- Best dealt with by taking preventive measures—restrict intake to 50–75% of normal maintenance for patients on positive pressure ventilation and receiving humidified gases
- If hyponatraemia due to water retention (i.e. SIADH), restrict fluid to 25%–50% of normal maintenance rather than ↑ sodium supply
- With severe (or symptomatic) hyponatraemia <125mmol/L, fluid restriction alone would take too long to rescue the patient from dangerously low sodium concentrations. Use 3% saline (i.e. 513mmol/L or 0.5mmol/mL):
  - The exact sodium deficit can be calculated (assuming a volume of distribution of Na^+ of 60% body weight) using the classic formula

$$Na^+ \text{ deficit (in mmol)} = \text{weight (kg)} \times 0.6 \times (125 - \text{plasma } Na^+)$$

  - I.e. in a 10kg child with plasma sodium of 120mmol/L the sodium deficit (to a serum sodium of 125mmol/L) is 30mmol. Therefore give 3% sodium (0.5mmol/mL) at 15mL/h for 4h. The figure 0.6 is used as an (over) estimate of body extracellular fluid volume
  - If symptoms are severe, e.g. child is fitting give 4mL /kg 3% saline over 30min. If symptoms persist give 2mL/kg over 15min and repeat if symptoms persist
  - ⚠ Stop at plasma sodium of 125mmol/L or if plasma sodium increases by >0.5mmol/h
  - If hyponatraemia is chronic (>48h) then take care not to correct the plasma sodium too quickly—aim for plasma sodium of 125mmol/L (risk of central and extrapontine pontine demyelination).

Further management

- Take a detailed history focusing on precipitating factors: water excess, D&V, chest infection, habitual juice drinking, head injury
- Examine the child with particular attention to hydration state, perfusion, and neurological system
- Order base-line tests: serum osmolality, urea and creatinine, urine osmolality and electrolytes (Na^+ and Cl^-), FBC, blood gas.

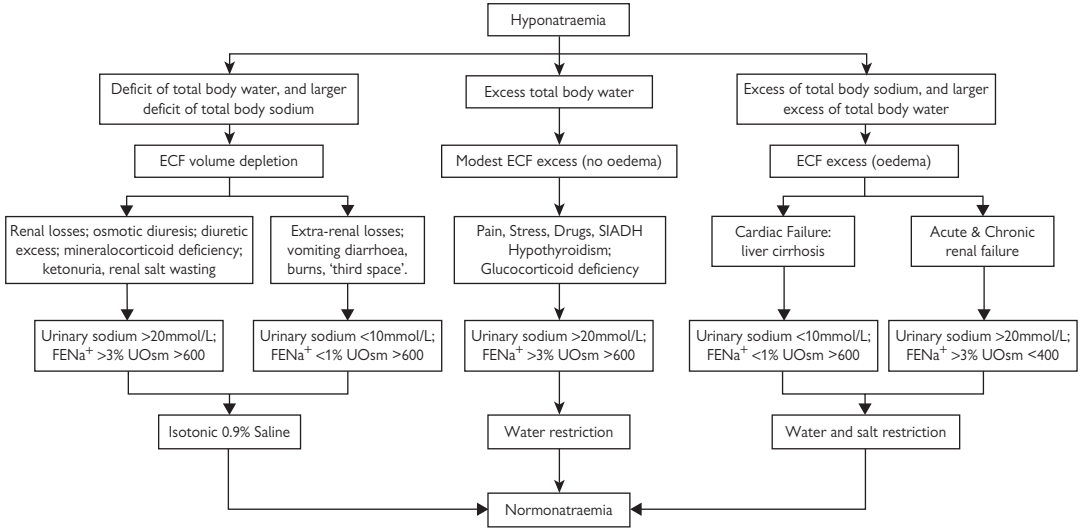

Fig. 13.2 Diagnostic and treatment algorithm for hyponatraemia. Reproduced from Rees L, Webb NJA, Brogan PA (eds) (2007). *Paediatric Nephrology*. Oxford University Press.

Table 13.5 Causes of hyponatraemia in ICU*

ECF volume status	Ur Na^+ <20mmol/L	Ur Na^+ >20mmol/L
Normal	–	H_2O excess, SIADH, NSAID use, hypo-adrenal/ thyroid
Increased (oedema)	Capillary leak syndrome, low cardiac output, hepatic failure	ARF
Decreased	3rd space loss, GI loss, burns	Polyuric phase of ARF, osmotic diuresis, CSW

ARF, acute renal failure; SIADH, syndrome of inappropriate ADH secretion; CSW, cerebral salt wasting, Ur, urine. *Webb N, Postlethwaite R (2003). *Clinical Paediatric Nephrology*, 3rd edn. Oxford University Press.

- Causes of hyponatraemia can be grouped by assessment of extracellular fluid volume status and urine Na^+
- Measurement of fractional excretion of sodium and water, and urinary osmolality help in the diagnosis
- More than one cause may coexist (e.g. SIADH and CSW in head injury)
- SIADH (📖 p.685).

Oedema (see Box 13.5)

Box 13.5 Mechanisms of oedema

Movement of fluid across the capillary wall endothelium depends on:
- The nature of the molecule i.e. its size, charge, water and fat solubility
- The balance of forces across the capillary wall
- The permeability of the capillary wall.

Water and water-soluble molecules (NaCl, glucose) pass across the capillary membrane with greater ease than large molecules such as proteins (albumin) or gelatins (gelofusine). This movement produces a low protein filtrate that we refer to as interstitial fluid. This is the extracellular fluid that sits in is outside the vascular compartment.

The balance of forces affecting fluid distribution across the capillary membrane was identified by the British physiologist Ernest Starling in 1896 and still stand true today. He described the balance between hydrostatic forces [capillary hydrostatic pressure (P_c) – interstitial fluid hydrostatic pressure (P_i)], forcing fluid out of the capillary and the osmotic forces [capillary colloid osmotic pressure (π_c) – interstitial fluid colloid osmotic pressure (π_i)], sucking fluid into the capillary. Thus:

$$\text{Flow of fluid} = k\,[(P_c - P_i) - \sigma\,(\pi_c - \pi_i)]$$

where k is a filtration coefficient and σ is the coefficient that represents the permeability of the endothelium.

Box 13.5 Mechanisms of oedema (*Continued*)

Capillary hydrostatic pressure falls from approximately 30mmHg at the arterial end (forcing fluid out of the capillary) to about 15mmHg at the venous end of the capillary. The pulmonary circulation has lower capillary pressures. These pressures are also slightly lower in infants and smaller children. Capillary colloid osmotic pressure (oncotic pressure) is generated by the 'pull' of intravascular protein and is normally 25mmHg. Interstitial colloid osmotic pressure is about 10mmHg.

In health the volume of fluid leaving the capillary exceeds that absorbed by a small amount. This excess is absorbed by the lymphatics, resulting in lymph.

When capillary filtration exceeds lymphatic drainage there is an excess of interstitial fluid and ***oedema*** results. In ICU this is commonly seen in the peripheral subcutaneous tissues, the lungs (pulmonary oedema), in the pleural space (effusion), and abdominal (ascites) and pericardial spaces. Oedema may reflect disease severity but also impairs oxygen and nutrient delivery from the capillary to the cell.

From Starling's equation we can see that oedema may result from 3 causes:
- ↑ capillary pressure (P_c), e.g. in right heart failure, fluid overload or in dependent oedema
- ↓ colloid osmotic pressure (π_c); when there is a fall in plasma protein, e.g. malnutrition (↓intake), nephrotic syndrome (protein loss), hepatic failure (reduced synthesis)
- ↑ capillary permeability (↓ σ); in diseases of inflammation circulating cytokines can cause massive and widespread capillary leak, e.g. SIRS, MODS, sepsis (see 📖 p.576). In these conditions the oedema is usually high in protein content (>30g/L)

Additionally oedema may result from reduced lymphatic flow, e.g. following surgery to lymph node groups or in tropical filariasis (nemotode disease).

Pulmonary oedema

Pulmonary oedema occurs when pulmonary lymphatics become exhausted—initially interstitial oedema occurs but this progresses to alveolar oedema with accompanying reduction in compliance and intrapulmonary shunting. Classic signs are dyspnoea and hypoxaemia.
Pulmonary oedema may be either:
- *Cardiogenic*: myocardial dysfunction or inadequate emptying of left ventricle or atrium leads to subsequent increases in left ventricular end-diastolic pressure, left atrial pressure, and pulmonary venous pressure resulting in ↑pulmonary capillary pressure and pulmonary oedema. Causes include left ventricular outflow tract obstruction, myocardial ischaemia and mitral valve stenosis and regurgitation. Apart from correcting defects the mainstay of treatment is afterload reduction and inotropy to reduce capillary pressures.
- *Non- cardiogenic*: this mainly due to ↑capillary permeability and is seen in ARDS and pneumonia.

(Neurogenic pulmonary oedema has a cardiogenic origin in that it is due to severe vasoconstriction secondary to massive catecholamine release following head injury.)

Hypernatraemia: Na^+ >150mmol/L

- Results from either:
  - Water deficiency (more than sodium loss)
  - Sodium excess (more than water gain).

Causes (Table 13.6)

- Loss of water (more than sodium):
  - GI water loss
  - Insensible water loss (fever, hyperventilation, burns)
  - Diuretic therapy
  - Hyperglycaemia (osmotic diuretic)
  - Renal disease
  - Diabetes insipidus
- Sodium excess (more than water):
  - Excess ingestion—including salt poisoning, MSBP, iatrogenic (IV fluids or salt containing drugs)
  - Near-drowning (seawater)
  - Cushing's syndrome
  - Conn's syndrome

Management

- Targeted history focusing on causes (diarrhoea and vomiting, head injury, thirst and polyuria, milk formula use) and any neurological symptoms
- Clinical signs of dehydration may be masked as ECF volume is protected by the high Na^+
- Order baseline tests: glucose, urea & creatinine, urine electrolytes and osmolality, FBC, blood gas
- Either cautious rehydration with 0.9% saline where dehydration is evident (48–72h for deficit replacement) or diuretics in salt excess (but replace water). Aim for a slow fall of Na^+ at 0.25mmol/L/h
- Specific replacement of ADH is indicated for central or neurogenic diabetes insipidus (📖 p.683)
- Resistance to replacement therapy suggests a nephrogenic cause.

Table 13.6 Causes of hypernatraemia in ICU (all figures in mmol/L)

Urine sodium	Urine osmolality		
	<800	**Variable**	**>800**
<20	_	_	GI water loss
Variable	Diabetes insipidus	_	↓water intake
>20	Hyperglycaemia	_	_
>75	_	↑Na^+ intake	_

Hypokalaemia: serum K^+ <3.5mmol/L

- Ensure sample not contaminated
- If K^+ <2.5mmol/L ECG changes normally evident (ST depression + U waves).

Causes

- Inadequate intake (typically in PICU patient in IV fluids)
- Potassium loss:
  - GI
  - Diuretic therapy
  - Hyperglycaemia (osmotic diuretic)
  - Renal disease
  - Cushing's syndrome
  - Conn's syndrome
- Movement of potassium into cells:
  - Acidosis correction
  - Insulin use
  - B_2 agonist use.

Management

- Assess for alkalosis by a blood gas. Where present this should also be treated—KCl therapy may be used as a source of both K^+ and Cl^- in the setting of diuretic-induced alkalosis
- Assess need for urgent correction of deficit:
  - Is the child symptomatic (cardiac arrhythmia, severe muscle weakness or ileus)?
  - Or at risk (congenital heart disease, myopathy, severe illness)?
- Urgent replacement—use high strength KCl via a central line in aliquots of 0.5mmol/kg over 1h then recheck K^+

⚠ Do not give boluses of potassium solutions

- Non-urgent enteral supplements (preferred) and/or parenteral replacement by peripheral IV with K^+ additives in maintenance fluid (max concentration 40mmol/L)
- Elucidate cause by considering depletion (diet, renal or gut loss) or redistribution (alkalosis, thyrotoxicosis, familial paralysis).

Hyperkalaemia: serum K^+ >5.5 mmol/L

Normal ranges for K^+ higher in infants who also tolerate hyperkalaemia better than older children.

- Ensure sample not haemolysed
- Stop exogenous administration of K^+
- Elucidate causes: consider sources of and evaluate renal function.

Causes

- Excess K^+ (TPN, blood transfusion, supplements)
- Acute renal failure
- Cell destruction:
  - Tumour-lysis syndrome
  - Rhabdomyolysis
  - Acute burns
  - Trauma—crush injuries
- Congenial adrenal hyperplasia

- Addison's disease
- Drugs
- Movement of potassium out of cells
  - Haemolysis during/after sampling – artefactually high K^+
  - Acidosis
  - Insulin deficiency (DKA) – but total body sodium often depleted.

Management

- Hyperkalaemia necessitates ECG monitoring—if K^+ >6.5mmol/L ECG changes normally evident (long PR + peaked T waves)
- If arrhythmia present give calcium gluconate 10%. 0.5–1mL/kg over 5–10min (↓toxic effect and stabilizes myocardium)
- If no arrhythmia, start with salbutamol. IV 4mcg/kg over 10min ***or*** nebulized (5mg >10kg; 2.5mg <10kg); (shifts K^+ into cells)
- Sodium bicarbonate 8.4% 1–2 mmol(mL)/kg over 30min
- Glucose and insulin:
  - Bolus 0.1units/kg insulin with 2mL/kg 50% glucose

  or
  - Infuse 1g/kg/h glucose (i.e. 5mL/kg/h 20% glucose or 10mL/kg/h 10% glucose) with
  - Insulin infusion 0.1unit/kg/h
  - Monitor blood glucose every 15min for first hour, then hourly thereafter
  - Watch for late hypoglycaemia
- Calcium resonium 1g/kg orally or rectally with oral lactulose
- Consider renal replacement therapy.

Calcium, magnesium, and phosphate

These ions affect cardiac function and need to be monitored closely in the perioperative period of cardiac surgical cases. They are also important for skeletal system repair and growth.

Calcium

- Total Ca^{2+} lab values, corrected for albumin, should be 2.0mmol/L.
- Ionized Ca^{2+} (normal 1.0–1.5mmol/L) is not age or albumin dependent. It is affected by acid–base status (↑ by acidosis and ↓ by alkalosis).

⚠ Use ionized Ca^{2+} as the guide to treatment rather than total or corrected total—threshold for IV calcium supplementation should be <0.7 unless symptomatic or using as a vasopressor

Hypocalcaemia

- Likely to be triggered as a result of a convulsion or the presence of tetany, the clinical hallmark of hypocalcaemia
- Difficult to give an exact figure at which emergency intervention is required but serum calcium concentrations below 1.7mmol/L (ionized calcium <0.7mmol/L) are likely to be associated with problems.

Management

- Get adequate venous access in a large vein. IV calcium is very corrosive and may cause serious extravasation injury
- Commence slow IV injection of 10% calcium gluconate (1–2 mL/kg (9–18 mg elemental calcium/kg or 0.225 –0.45mmol/kg)) over 3h with ECG monitoring

- Repeat every 6–8h whilst symptoms persist
- May need longer continuous infusion as total body calcium may be low
- Maintenance therapy with 0.5–1.0g elemental calcium per day and at the same time, start treatment with oral vitamin D (calciferol) 1500IU/day in neonates or 3000IU/day in older children
- Do not use 1α-hydroxyl-cholecalciferol at this stage, or until definitive diagnosis has been made
- Low Mg^{2+} can cause hypocalcaemia—treat Mg^{2+} to prevent recurrence of hypocalcaemia

⚠ Calcium chloride and gluconate formulations contain different amounts of Ca^{2+}. Both are irritant to veins (gluconate milder).

Hypercalcaemia causes tachyarrhythmias, hypotonia, coma and seizures.
- Seen in Williams syndrome (📖 p.777) and volume depletion
- Treated by volume expansion and loop diuretics or haemofiltration if severe.

Magnesium
- Normal plasma Mg^{2+} 0.7–1.0 mmol/L
- Mg^{2+} and Ca^{2+} absorption are linked
- Low Mg^{2+} levels are pro-arrhythmic
- Ionized fraction is the active fraction (like calcium) but not routinely measured in most centres.

Hypomagnesaemia

Causes
- ↓ Intake
- ↑ Renal losses:
  - Drug induced: diuretic-induced losses commonest cause on PICU
  - Aminoglycosides, amphotericin and others
  - Acute renal failure (polyuric phase)
- Poor GI absorbtion/ ↑GI losses (diarrhoea, laxatives)
- Endocrine causes: i.e. hypoparathyroidism; hyperthyroidism.

Management
- If urgent give 0.2mmol/kg IV over 10min (0.1mL/kg of 50% magnesium sulphate diluted 5× with 0.9% saline)
- Neonates may be given 0.4mmol/kg, appropriately diluted and given slowly
- Smaller doses of 0.1mmol/kg are used in treating torsade de pointes (polymorphic VT), pulmonary hypertension and acute severe asthma (nebulized or IV).

Hypermagnesaemia
- Rarely seen except in renal failure and when given therapeutically (see earlier).
- Leads to muscle weakness and coma but not until very high levels are reached—often ↑ to 2–3mmol/L in setting of Mg^{2+} treatment for pre-eclampsia, asthma etc.

Phosphate

- Serum PO_4^- varies with age and acid–base (↑ in infancy and acidosis)
- Keeping level >1.0mmol/L helps cardiac function and bone growth
- ↓ in:
  - Critical illness
  - Starvation/poor intake
  - Diuretic and renal replacement therapies
  - Parenteral nutrition
  - Hyperparathyroidism
- Accumulates in renal failure and haemolysis
- Hypophosphataemia → muscle weakness (rarely apparent clinically)
- Low levels are treated with 0.5mmol/kg over 10h (over 1h if urgent) as 1mL/kg of 13.6% potassium acid phosphate diluted ×10 with 0.9% saline (this also gives same dose of potassium).

Acid–base balance

Acid–base disorders are common in PICU patients. Acidosis, both metabolic and respiratory, are the hallmarks of multiple organ failure and seen in sepsis, trauma, and postoperative patients (particularly cardiac surgery) as well as in renal, metabolic, and endocrine conditions. Both respiratory and metabolic alkalosis also occur with regularity in PICU. Thus it is important that the intensivist not only understands the underlying processes involved in acid–base disorders but can apply this to managing the conditions properly. This is vital as there is good anecdotal and research based evidence that misinterpretation and consequent mismanagement of acid–base disorder is common in hospital medicine.

Key points

- Regulation of normal extracellular pH (7.4) and intracellular pH (7.0) is vital for organ function in the long term
- Apart from in primary metabolic disorders (see 📖 Chapter 33) most acid–base disorders in PICU should be viewed as a complex physiological response to a underlying pathological abnormality
- Despite some controversy in mechanisms it is best to approach acid–base disorders via the principles of pH/$PaCO_2$ relationship (Henderson–Hasselbach equation), calculation of the base excess (BE) and the anion gap (AG).

Box 13.6 Some history

'Acid' derives from the Latin acidus which means sour. Sorensen first suggested pH terminology in 1908 and Hasselbach used this to describe the Henderson–Hasselbach equation in 1916. By 1920, Bronstead and Lowry had independently described acids and bases as proton (H^+ion) donors and acceptors respectively. Acid–base examination really came to the forefront following the Copenhagen polio epidemic of 1952 when Astrup began measurement of $PaCO_2$ and pH on ventilated patients. Later, in Copenhagen, Siggard–Andersen introduced the concept of base excess and by 1962 had published the normogram that interpolated $PaCO_2$, bicarbonate and BE. Despite some disagreement between the 'Boston school' ('standard BE') and Copenhagen about whether BE should be calculated for whole blood or ECF ('the great transatlantic debate'), the use of BE has now been generally accepted in ICU medicine. To further complicate matters a Canadian physiologist Peter Stewart introduced a physicochemical approach known as 'strong ion difference' in the 1980s which challenges some previously held views.

Physiological principles

Acid production

As a fire makes smoke metabolism makes acids. Acids are primarily:

- *Respiratory acid:* CO_2 which is excreted via the lungs. This combines with H_2O to produce H_2CO_3 which dissociates into HCO_3^- and H^+ ions.

- *Metabolic acid:* fixed organic acids (not excreted by lungs) which dissociate into anions$^-$ (A^-) and H^+ ions and are excreted in the urine.
  - Lactate from carbohydrate metabolism
  - Ketoacids (acetoacetate and β hydroxybutyrate) from fat metabolism
  - Phosphates and sulphates from protein metabolism.

Acid–base regulation

For acid–base balance the amount of acid excreted must equal the acid produced. The body has 3 processes to regulate acid–base balance:

- *Immediate buffering:* the body has a huge capacity to buffer via the process: $A^- + H^+ \rightarrow HA$. Thus a 1mmol/L fall in A^- requires 10^6 nanomol/L (1mmol/L) of H^+ ions to be 'mopped' up by another buffer. The main buffers are bicarbonate (HCO_3^-), plasma proteins, haemoglobin and phosphates
- *Immediate respiratory response:* H^+ ions stimulate chemoreceptors to increase ventilation and more CO_2 is excreted (lowering $PaCO_2$) as follows:
  $H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$
- *Slow renal response:* the kidney reabsorbs filtered bicarbonate ions (raising plasma HCO_3^-) and excretes fixed acids in response to respiratory acidosis. Plasma bicarbonate is reduced in alkalosis. This response takes between 12h and several days.

Definitions

- ***Acidosis*** is an abnormal process or condition which would lower arterial pH if there were no compensatory response
- ***Alkalosis*** is an abnormal process or condition which would raise arterial pH if there were no compensatory response
- ***Acidaemia*** is arterial pH <7.35. Can cause hyperkalaemia as potassium exits cells to preserve transmembrane potential
- ***Alkalaemia*** is arterial pH >7.45. Associated with hypokalaemia due to potassium movement into cells
- In mixed acid–base disorders coexisting disorders may have opposite effects on pH. Generally the most severe disorder dictates the pH.

Box 13.7 pH and hydrogen ions

H^+ concentration ($[H^+]$ is expressed in nanomol/L, i.e. a millionth of a mmol. Thus the concentration of Na^+, Cl^+, K^+, and other strong ions are a factor of a million times more concentrated in ECF and ICF than H^+. Due to the scale of this, the $[H^+]$ is routinely expressed as the negative logarithm (base 10) of $[H^+]$.

- pH 7.4 corresponds to $[H^+]$ 40nmol/L
- The normal range for pH is 7.35–7.45 ($[H^+]$ 45–35nmol/L), i.e. the change in $[H^+]$ is only 10nmol/l-this is an indication of how tightly controlled $[H^+]$ is in normal daily processes, e.g. exercise
- Due to the logarithmic nature of pH; at the acidotic end of the scale, the change in $[H^+]$ is much higher than at the alkalotic end. i.e. pH7.1= 80nmol/L $[H^+]$; pH 7.7= 20nmol/L. A drop in pH from 7.4 to 6.8 involves a 6-fold increase in [H+].
- For conversion of pH to $[H^+]$ see 📖 p.867.

Acid–base disorders

- ***Respiratory acidosis:***
  - Ph <7.35
  - $PaCO_2$ ≥5.5KPa
  - Metabolic compensation through renal bicarbonate retention. Expect calculated BE and HCO_3 to be high.
- ***Respiratory alkalosis:***
  - pH >7.45
  - $PaCO_2$ <4.5kPa
  - Normal calculated BE and HCO_3.
- ***Metabolic acidosis:***
  - pH <7.35
  - $PaCO_2$ ≤ 4.5kPa in compensation (unless unable to do so because on ventilator)
  - High negative BE (base deficit) and low HCO_3.
- ***Metabolic alkalosis:***
  - pH >7.45
  - $PaCO_2$ >5.5kPa in compensation
  - Expect high BE and HCO_3. Watch for confusion with compensated respiratory acidosis when pH should be near normal.
- Mixed disorders: must be viewed in clinical context and occur when compensation is incomplete.

Box 13.8 How to classify acid–base disorders

Acidaemia

- Step 1: confirm *pH <7.35*
- Step 2: what is $PaCO_2$?
  - *$PaCO_2$ ≤4.5kPa i.e. low or normal* indicates *primary metabolic acidosis*
  - *$PaCO_2$ ≥5.5kPa i.e. high* indicates *primary respiratory acidosis*
- Step 3: the pH will determine whether this is an acute (low pH) or chronic (normal pH).

Alkalaemia

- Step 1: confirm *pH >7.45*
- Step 2: what is $PaCO_2$?
  - *$PaCO_2$ normal or high (≥5.5kPa)* indicates *primary metabolic alkalosis*
  - *$PaCO_2$ low (<4.5kPa)* indicates *primary respiratory alkalosis.*
- Step 3: again the pH dictates acute (raised pH) or chronic (normal pH).

Mixed disorder

- If pH normal:
  - $PaCO_2$ high indicates mixed respiratory acidosis/metabolic alkalosis
  - $PaCO_2$ low indicates mixed respiratory alkalosis/metabolic acidosis.

Further examination of acid–base status

There are 3 accepted models for quantifying acid–base status in common use:

- Bicarbonate/$PaCO_2$ relationship, i.e. Henderson–Hasselbach equation

- BE and AG calculation
- Stewart's quantitative approach, i.e. strong ion difference.

Bicarbonate/PaCO$_2$

- CO_2 is directly measured in blood gas analysers
- CO_2 combines with water to form carbonic acid which can dissociate:
  - $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
- Bicarbonate (HCO_3^-) is not directly measured but is calculated from the Henderson–Hasselbach equation:
  - $pH = pK + Log_{10}[HCO_3^-]/[CO_2]$
  - K is the equilibrium constant (6.1)
- The normal range for bicarbonate concentration [HCO_3^-] is 18–26mmol/L but can be lower (12–16mmol/L) in preterm babies.

Base excess

- The BE is a single calculated variable that is used to quantify the metabolic (non-respiratory) component of a patient's acid–base status
- BE is defined as the quantity of alkali (bicarbonate) required to titrate blood to a pH of 7.4 with a fixed $PaCO_2$ of 5.3kPa (i.e. normal) at 37°C. In practice this is calculated from the Siggard–Andersen normogram by most modern blood gas analysers
- A negative BE (base deficit)implies metabolic acidosis
- A positive BE implies metabolic alkalosis
- Standard BE refers to the BE of ECF (Boston school) as opposed to BE of blood (Copenhagen).

Anion gap

- This is a parameter used to establish the cause of a patient's metabolic acidosis, i.e. is the underlying problem:
  - Secondary to accumulation of unmeasured anions and thus H^+ ions? i.e. *raised AG*

  or
  - Secondary to accumulation of chloride ions (Cl^-)? i.e. *normal AG*
- In order to maintain electrical neutrality anions must balance cations:

  Thus $[Na^+] + [UC^+] = [Cl^-] + [HCO_3^-] + [UA^+]$

  (where UC are unmeasured cations and UA are unmeasured anions)

  $AG = UA - UC$

  Therefore $AG = ([Na]+[K]) - ([Cl+HCO_3])$
- Normal AG is 8–16mmol/L. If this is clearly raised, i.e. ≥20mmol/L, then this represents significant unmeasured anions in plasma/ECF
- *Raised AG metabolic acidoses* include unmeasured anions from:
  - Organic acidosis: most commonly lactic acidosis in shock states but also includes ketoacidoses in diabetes
  - Sulphates and phosphates accumulated in renal failure
  - Poisons, e.g. ethanol, methanol, salicylates, ethylene glycol
- *Normal AG metabolic acidoses* may be from either bicarbonate loss (e.g. from diarrhoea, upper GI losses or renal tubular acidosis) which leads to renal chloride retention or exogenous chloride administration (see 'Stewart's approach or strong ion difference (SID)').

Box 13.9 Urinary AG

To differentiate between bicarbonate loss from kidneys and GI tract (GIT) one needs to calculate the urinary AG (UAG) from urine electrolytes: Again to preserve electroneutrality

$$Cl^- + UA = Na^+ + K^+ + UC$$

where UA are unmeasured anions, e.g. phosphates and sulphates and UC are unmeasured cations eg Mg^{2+} and Ca^{2+}

$$UAG = UA - UC = ([Na]+[k] - [Cl])$$

- Positive UAG implies renal HCO_3 loss, e.g. renal tubular acidosis
- Negative UAG implies GIT HCO_3 loss.

- The AG needs to be corrected for hypoalbuminaemia:
  - Normal albumin is 40g/L
  - Albumin gap = 40– measured albumin
  - *Corrected AG = AG + albumin gap/4*
  - For example: in a child with an albumin of 18g/L and an apparently high/normal AG of 15, the corrected AG= 15+(40–18)/4 = 20.5 which is significantly raised.

Stewart's approach or strong ion difference (SID)

Like the AG this model applies the laws of electrical neutrality to the study of acid–base, i.e. anions must balance cations

- This approach acknowledges that the variables CO_2 and HCO_3 used in the Henderson–Hasselbach equation are in fact entirely dependent on each other via carbonic acid dissociation, and thus cannot be seen as independent variables. In short, in the SID model the role of HCO_3 in metabolic acidosis/alkalosis is questioned and thus ignored
- In this model acidosis is secondary to changes in 3 independent variables:
  - $PaCO_2$, i.e. respiratory acidosis
  - Total weak non volatile acids known as A^{TOT}
  - SID
- A^{TOT} is mainly represented by albumin, plasma proteins, inorganic phosphate and has a relatively minor effect on acid–base balance, but hypoalbuminaemia can lead to mild alkalosis.
- ***SID = ([Na$^+$] + [K$^+$] + [Ca^{2+}]) – ([Cl$^-$] + [unmeasured strong anions])*** With normal protein levels SID is usually 40–42
- From this equation it can be seen that an increase in unmeasured anions leads to a fall in SID (i.e. SID <40) and an increase in AG. As a result, water dissociates to produce H^+ ions to preserve electroneutrality. This results in a metabolic acidosis, i.e. the H^+ response is as a result of the strong ion change rather than the primary cause

- Stewart's theory is particularly useful in explaining the worsening metabolic acidosis that is often seen with seemingly adequate fluid resuscitation in PICU: i.e. when BE is significantly negative but the AG is normal/mildly elevated. The cause may be due to hyperchloraemia secondary to excess IV 0.9% normal saline administration. In this situation the kidney excretes the sodium load but chloride is retained and SID will fall. Switching fluids from normal saline (with a [Cl] of 154mmol/L) to Hartmann's or Ringer's lactate (with a [Cl] of 109–111mmol/L) may be beneficial

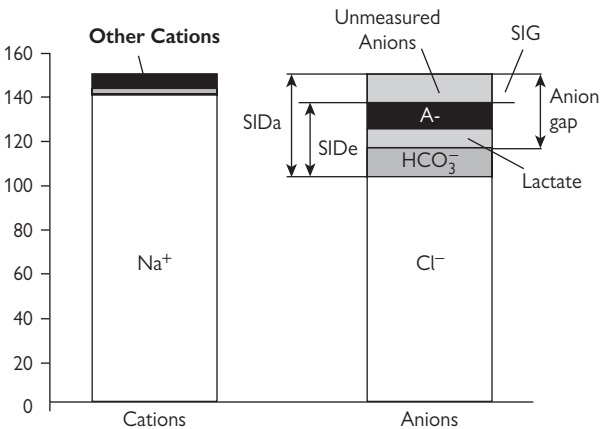

Fig. 13.3 Charge balance in human plasma according to Stewart's strong ion theory. SIDa, apparent strong ion difference; SIDe, effective strong ion difference; SIG, strong ion gap. Reproduced with permission from Gunnerson, KJ, Kellum, JA (2003). Acid-base and electrolyte analysis in critically ill patients: are we ready for the new millennium? *Curr Opin Crit Care* **9:** 468–73.

Box 13.10 Strong ions and weak smiles

Let's be honest, many clinicians find Stewart's theory of SID embarrassingly difficult to understand, never mind use clinically. We suggest that a simple understanding of the theory is all that is required and recommend that sticking with the tried and tested approach as described in this chapter involving measurement of pH and $PaCO_2$. Calculation of base excess and corrected AG is adequate for almost all clinical scenarios of acid–base disorder in PICU.

Management of acid–base disorders

'Treat the patient not the blood gas.' Blood gas results must be interpreted within the clinical context of the child. Generally treatment of the underlying condition improves the acid–base upset.

Respiratory acidosis

- Usually occurs secondary to respiratory failure, e.g. ventilation perfusion abnormalities, low compliance, ↑airway resistance, ↓respiratory drive, airway obstruction, ↑dead space
- In chronic setting metabolic compensation (provided renal function is adequate) usually normalizes pH.
- Pay attention to ***ABCs***, i.e. intubate and ventilate if necessary and treat underlying cause of respiratory failure
- Heparin contamination of a gas sample can lower $PaCO_2$ and HCO_3 measurements and can mask renally compensated respiratory acidosis.

Box 13.11 Approach to diagnosis and management of metabolic acidosis

Key points

- Attempt to identify the underlying cause by calculation of corrected AG (and strong ion difference if indicated)
- Most metabolic acidoses seen in PICU are lactic acidosis (with normal plasma lactate—this only rises in more severe cases, 📖 see p.90) secondary to shock (reduced oxygen delivery) or seizures (↑oxygen consumption) and improves with attention to fluid resuscitation and oxygen
- Aim for target pH ≥7.25 if possible. Consider ventilatory support if pH <7.2
- Maintain supportive measures and organ support even in absence of diagnosis until pH improves
- Consider bicarbonate therapy if indicated (see Box 13.12).

1. Confirm diagnosis

- Arterial pH <7.35
- Base excess < –3mmol/L
- Is $PaCO_2$ appropriate for acidosis? I.e. it is usually low when hyperventilatory compensation occurs but is often high if there is also a respiratory acidosis component or normal in ventilated paralysed patients.

2. Check blood and urine

- Measure serum Na, K, Cl, urea, creatinine, lactate, glucose and albumin
- Check urine for pH, ketones
- Calculate AG and correct for hypoalbuminaemia.

3. AG >16 Consider clinical context and treat cause

- Lactic acidosis—does this fit with clinical context? E.g. hypotension, fluid/blood loss, myocardial dysfunction, septic shock, seizures etc.
- Ketoacidosis

(*Continued*)

Box 13.11 Approach to diagnosis and management of metabolic acidosis (*Continued*)

- Renal failure
- If none of these consider underlying metabolic disease (see 📖 p.701) or poisoning.

4. AG <16 Consider clinical context and treat cause

- Check chloride, is it raised?
- Excess chloride from drugs, infusions
- ?Bicarbonate loss from GIT
- ?Bicarbonate loss from kidneys (renal tubular acidosis) see p. 657, Fig. 31.3.

Box 13.12 Buffer/alkali therapy

- The use of buffers is common but lacks consensus on indications and possible benefits.
- ***Sodium bicarbonate 8.4%*** (1mmol/mL) is commonly used and may be indicated by:
  - Metabolic acidosis due to bicarbonate loss, e.g. diarrhoea, upper GI losses, renal tubular acidosis
  - Specific treatment for drug overdose
  - In severe acidosis (pH <7.1) and hypotension when inotropes appear to be ineffective due to receptor dysfunction
- Sodium bicarbonate may worsen intracellular acidosis, hypokalaemia and hypocalcaemia. It may increase risk of cerebral oedema in diabetic ketoacidosis
- Sodium bicarbonate should not be given as rapid bolus but as slow infusion (i.e. 1–2mL/kg/h of 8.4% sodium bicarbonate = 1–2mmol/kg/h) and titrate to effect, i.e. target pH ≥7.2
- ***Tham*** (tromethamine) is a sodium-free buffer that doesn't generate CO_2. Despite its attractive qualities it has not yet been shown to have clinical advantages over sodium bicarbonate. It has also been linked with the adverse effects of hyperkalaemia, hypoglycaemia, and apnoea.

Alkalosis

Disorders of high pH are classified into those resulting from excess removal of CO_2 (respiratory alkalosis), and those resulting from loss of non-volatile acids or accumulation of buffer (metabolic alkalosis).

Respiratory alkalosis

- Hyperventilation from different causes leads to respiratory alkalosis
- This commonly occurs from excessive minute volume when a patient is initially intubated and ventilated. It can be minimized from monitoring early arterial gases or from use of $EtCO_2$ monitoring—severe hypocapnia and respiratory alkalosis from overventilation can significantly reduce brain perfusion and aggravate cerebral ischaemic injury
- Other causes include anxiety and central hyperventilation from brain injury, encephalopathy, encephalitis, salicylate toxicity, hypoxia

- Treatment consists of treating specific cause
- Further measures include reducing minute volume and/or introducing dead space into the ventilator circuit for patients on ventilators

Metabolic alkalosis

- Often results from chloride depletion (secondary vomiting or loop diuretic therapy)
- It is rarely due to alkali administration, laxative, or diuretic abuse
- Both severe vomiting and diuretics can cause hypokalaemia and an aggravating 'paradoxical aciduria' which worsens the alkalosis, as seen in pyloric stenosis
- Standard rehydration with 0.9% normal saline and potassium supplementation is usually adequate therapy
- Some causes of chloride depletion are resistant to replacement therapy such as renal tubular defects (Barrter's syndrome treated with indomethacin) and mineralocorticoid excess (treated by steroid sparing therapies)
- Administration of acid is only very occasionally needed for metabolic alkalosis:
  - 0.5mL/kg of 5.35% ammonium chloride into a central vein over 1h (do not give in liver impairment)
  - In liver impairment use 5mL/kg of 100mmol/L hydrochloric acid into a central vein over 1h.

Contraction alkalosis

This may occur when severe dehydration contracts the extracellular and intravascular fluid spaces concentrating HCO_3^- to give misleadingly normal HCO_3^- and pH values even when HCO_3 depletion is present. Additionally ECF contraction leads to proximal tubular Na retention and thus K^+ and H^+ loss in urine ('again paradoxical aciduria'). Look out for signs of severe dehydration, hypokalaemia or raised haematocrit to suggest diagnosis. Treat with normal saline IV and K supplementation.

Further reading

Kellum JA (2005) Clinical review: reunification of acid-base physiology. *Critical Care* **9**: 500–7. Biomedi Central.

Taylor D, Durward A (2004). Pouring salt on troubled waters. *Arch Dis Child* **89:** 411–14.

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Chapter 14

Renal replacement therapies

Introduction

Renal replacement therapies play a vital role in modern PICUs. There is an ↑mortality of up to 50% associated with the addition of acute renal failure to respiratory failure. In some studies, ICU mortality can be reduced by the early provision of renal replacement therapy.

There has been an increase in the use of continuous veno-venous haemofiltration (CVVH) and haemodiafiltration (CVVHD); however these are not the only choices. Which to use should be a weighted decision based on advantages and disadvantages as well as experience and availablilty of each method. Indications for acute dialysis are given in Box 14.1.

Box 14.1 Indications for acute dialysis

Fluid overload
- Pulmonary oedema
- Congestive cardiac failure
- Refractory hypertension
- Hindrance to adequate nutrition
- Oliguria following recent heart surgery
- Oliguria during ECMO.

Symptomatic electrolyte or acid–base imbalances unresponsive to other therapies
- Hyperkalaemia (K^+ >7.0)
- Hypo- or hypernatraemia
- Severe metabolic acidosis.

Toxins
- Uraemia (puritus, pleuritis, pericarditis, CNS symptoms)
- ↑Creatinine
- Hyperuricaemia
- Exogenous toxins: lithium, salicylate, ethanol, methanol, bromide
- Ethylene glycol, aminoglycosides
- Poisonings.

Inborn errors of metabolism (📖 Chapter 33):
- Encephalopathy
- Hyperammonaemia.

Peritoneal dialysis

Peritoneal dialysis (PD) is still widely used as a renal replacement therapy for children. Although its role in PIC has diminished with the increase in popularity and ease of use of CVVH and CVVHD, it still has a role to play, particularly in the postoperative cardiac patient, where the placement of a PD catheter can be done under direct visualization.

In PD, dialysate is introduced into the peritoneal cavity, where it dwells for a set time. Water flows across the peritoneal membrane into the hyperosmolar (sugar-rich) dialysate. The concentration of sugar in the dialysate, the volume instilled, and the dwell time determine the amount of fluid removed. Higher dialysate sugar concentrations, greater volumes, and shorter cycle times ↑ fluid removal. Solutes diffuse across the peritoneal membrane from a higher to a lower concentration. Manipulation of the concentration of solutes in the dialysate can be used to alter solute removal.

Box 14.2 Advantages

- PD is widely available and technically easy to perform
- Arterial or central venous access and anticoagulation are not needed.
- Large amounts of fluid can be removed in haemodynamically unstable patients; this allows other fluids (such as TPN) to be given
- Acid–base and electrolyte imbalance are corrected gradually with less metabolic disruption
- PD access placement is relatively easy in children.

Box 14.3 Disadvantages

- Slow clearance of water and electrolytes
- Peritonitis (60% staphylococci, 20% Gram –ve organisms, <5% fungi)
- Risk of exit-site infection
- Catheter malfunction
- Hyperglycaemia (glucose in dialysis fluid)
- Interferes with respiration by splinting diaphragm.

Box 14.4 Contraindications

- Diaphragmatic hernia
- Omphalocoele
- Gastroschisis
- Possibility of intra-abdominal catastrophe
- Recent abdominal surgery
- Multiple adhesions
- Peritonitis
- Presence of VP shunt.

What do you need?

- Peritoneal access
- Dialysis fluid
- A delivery system incorporating timer and measuring device
- Fluid warmer.

Peritoneal access

The best form of access is obtained by either surgical or percutaneous insertion of a tunnelled double cuffed Tenckhoff catheter, with antibiotic cover. In an ideal world these should not be used for 2 weeks (to reduce the risk of leakage); however in the PICU setting this is rarely practical.

Catheter insertion on CICU

- A Seldinger technique is normally used. Trocar and catheter systems have a risk of perforating abdominal contents and should be avoided
- Local/general anaesthesia or sedation will be needed depending on age and cooperation of the patient.
- Appropriate consent should be taken
- Check for coagulopathy and ensure blood has been grouped and saved in case urgent transfusion is needed
- Secure IV access should be in place before PD catheter insertion
- Site of insertion:
  - Most commonly in the midline 1cm below the umbilicus
  - Alternatively, an approach on the left side (usually), lateral to a line drawn from the umbilicus to the anterior superior iliac spine, just lateral to the rectus sheath
  - Take care to ensure that there is no abdominal organ (such as an enlarged spleen) beneath your chosen insertion site
  - US guidance can be used to increase safety of placement
- Equipment:
  - Sterile pack, skin prep, gloves (gown, mask, and hat), drapes
  - PD cannula.
  - 1% lignocaine, needles, and syringes
  - Dialysate, giving set, and collection system.

Seldinger technique

- Ensure the bladder is empty (the patients and yours)
- Aseptic technique—gown and gloves.
- Prepare the PD lines and fluids
- Clean the area and drape the patient
- Infiltrate the area with lignocaine for local anaesthesia. Additional sedation may be needed
- Make small skin incision, 0.5–1cm in length. Do not cut the muscle layer
- Insert a 22G cannula, perpendicular to the abdominal wall, and directing the catheter down towards the pelvis. A 'pop' may be felt as the peritoneum is entered. Advance the cannula over the needle.
- *Some centres connect the cannula needle to the dialysate prior to insertion, and observe the flow of fluid. Dialysate will not flow until the peritoneal cavity is entered. At this point advance the cannula over the needle.*
- *For small infants and patients with very scaphoid abdomen, infusing 10mL/kg PD fluids to prime the abdomen before catheter insertion, reduces the risk of traumatic puncture of underlying viscous*

- Insert the guidewire through the cannula. Direct it towards the pelvis. Undue force should not be necessary
- Remove the cannula
- Insert dilator over the guidewire and dilate the tract (not always necessary in smaller patients and with some systems)
- Insert the PD catheter over the guidewire
- Remove guidewire, suture PD catheter in place
- Secure the catheter
- Connect the catheter to the PD lines
- Allow fluid to run in and check catheter patency
- Observe PD drainage for presence of blood or faeces.

Box 14.5 Complications of insertion

Potential complications of catheter insertion include:
- Bowel perforation,
- Perforation of abdominal organ (spleen/liver)
- Bleeding
- Leakage of PD fluid
- Mechanical obstruction
- Infection.

As with all practical procedures experience reduces complications.

Dialysis fluid

In PD the peritoneum acts as the semi-permeable membrane, allowing 3 forces—diffusion, convection, and osmosis—to play a role in fluid and solute transfer. The dialysis fluids use glucose as the main osmotic agent (Table 14.1). The higher the glucose concentration the higher the fluid removal; however due to absorption of glucose into the body, this can lead to hyperglycaemia. The dialysate glucose concentration should be as low as possible to achieve the required fluid removal.

Table 14.1 Typical peritoneal dialysate fluid composition

Glucose	1.36%	2.27%	3.86%
Osmolality	340mOsm/L	385mOsm/L	465mOsm/L
Na^+		132–135mmol/L	
Ca^{++}		1.75mmol/L	
Mg^{++}		0.5–0.75mmol/L	
Cl^-		102–105mmol/L	
Lactate			
or			
HCO_3^-		35–40mmol/L	

The dialysate is either buffered with bicarbonate or lactate. In general there has been a trend to using bicarbonate solutions, as they can be used in liver failure, lactic acidosis, and reduce infusion pain.

The dialysate fluid can be used as an effective method of temperature control. The fluid is normally heated to 37°C; however a lower temperature provides an efficient method of central cooling.

Delivery system

This can be as simple as a connecting the dialysis fluid to a burette then to the catheter via a 3-way tap, with the 3rd connection to a waste bag with a measuring device inbuilt. It must all be sterile at all times. There are also automated systems to simplify the process for the user, although these are generally unable to go below 100-mL fill volumes.

Cycles and fluid volumes

Volumes

The starting volumes should be 10–15mL/kg, which can be slowly ↑ to a normal maximum of 30mL/kg. Higher volumes may sometimes be tolerated, up to 50mL/kg.

The larger the volume the more diffusion can occur and thus ↑efficiency of the dialysis; however, the larger the volume the more likely respiratory compromise, cardiovascular instability, and exit site leakage.

Cycles

The filling usually occurs over a 10-min period and then a dwell of 30–60min, followed by draining period over the next 10min. Cycle times should be adjusted to achieve the desired effect. If fluid is still draining after 10min, drainage should be continued until it is minimal. If fluid removal is the main aim dwell times can be reduced. In neonates the response to dwell time varies considerably.

Cross-flow

In situations where large volumes of dialysate in the abdomen cannot be tolerated it is possible to insert 2 PD catheters, normally on opposite sides of the abdomen, allowing 1 to be used to fill and the other to drain. The fill volumes are the same; however, it is infused over 1h and drained at the same time. Cross-flow is less efficient than cycled PD.

Additives

PD fluid can be added to if necessary, in particular it is common to add heparin to prevent fibrin deposits (be careful of systemic absorption which may rarely occur), antibiotics to prevent or treat peritonitis, and potassium to prevent hypokalaemia. Dose as shown in Table 14.2.

Table 14.2 PD fluid additives and dose

Cefuroxime	125mg/L
Vancomycin	30mg/L
Ceftazidime	125mg/L
Teicoplanin	20mg/L
Cefazolin	125mg/L
Tobramycin	8mg/L
Heparin	Max. 500U/L
Potassium	Max. 5mmol/L

Peritonitis

Peritonitis is a major concern in PD as it can be life threatening. It is very rare in the setting of acute PD although more common in patients requiring long-term PD for end-stage renal failure. The standard symptoms of pain, fever, and cloudy PD fluid do not have to be present. The antibiotics can be added to the PD fluid at the doses shown in Table 14.2. The choice should be based on local policy and ultimately on bacterial sensitivities, in discussion with a microbiologist. Our current regimen is:

- MRSA-negative:
  - Load with tobramycin (16mg/L) and cefuroxime (500mg/L)
  - Subsequent maintenance doses as Table 14.2
  - Dwell times 6h
- MRSA-positive:
  - Load vancomycin (500mg/L) and cefuroxime (500mg/L)
  - Subsequent maintenance doses as Table 14.2
  - Dwell times 6h
- Remember to take drug levels initially at 48h
- Total treatment duration is 2 weeks except for *S. aureus* and *Pseudomonas* which should be 3 weeks
- If infection persists or reoccurs catheter removal may be necessary
- Fungal peritonitis can occur with few signs and often necessitates catheter removal and fluconazole treatment.

Leakage

This is more common in the acute PD catheters and it greatly increases the likelihood of infection.

- Ensure catheter cannot move at entry site
- Apply pressure dressing to site. Remember to weigh prior to application, in neonates, to allow calculation of fluid balance
- Purse string suture around catheter
- Consider a new catheter if leakage continues.

Troubleshooting (see Table 14.3)

Table 14.3 PD: troubleshooting

Problem	Cause	Solution
No/reduced flow on drain.	Clamped or kinked lines or catheter	Unclamp or un-kink lines
	Fibrin blockage. Omentum	Flush catheter with heparin and NaCl and add heparin to bags.
	Position of catheter obstructing drain	Reposition patient
	Fluid may have fully drained out straight into drain bag	Clamp Ureofix clamp. Perform 1 cycle with no dwell time, observing closely for signs of over filling
More fluid removal required.	Increase strength of dialysis fluid	Use higher strength bag
		NB: try using a mix of 2 strengths as opposed to going straight to a higher strength
	Decrease dwell times	Shorten the length of time the dialysate stays in the patient
		This can increase the fluid removal but can also have an effect on solute removal.
	Increase fill volumes	Increasing the amount of fluid going into the patient can sometimes increase fluid removal but should be done cautiously.
		This will also increase the solute removal.
Too much fluid being removed	Decrease the glucose concentration	Use a weaker strength bag
		NB: try using a mix of 2 strengths
	Lengthen the dwell time	Leaving the dialysate in the patient for longer will remove less fluid.
More clearance of waste and electrolytes required	Urea	Longer dwell times are required to remove more urea.
	Potassium	Shorter dwell times are required to remove more potassium
		Continuous dialysis can cause hypokalaemia requiring the addition of potassium to the PD fluid

Table 14.3 PD: troubleshooting (*Continued*)

Problem	Cause	Solution
	Sodium	Sodium should be lowered slowly to avoid any adverse effects. 1mmol/h is a safe reference to use
		Very hypernatraemic patients should have sodium chloride added to the dialysate to avoid lowering levels too quickly
	Calcium	Calcium contents of the unit prepared solutions can be adjusted to remove more if required
		Pre-made solutions are available with different calcium concentrations ranging from 0–1.75mmol/L
	Creatinine	Creatinine is not removed very well during short dwell peritoneal dialysis. It is however, a useful indicator of kidney function and should be observed in the acute setting for any improvement
Pain on infusion	Internal position of catheter	Tidal dialysis can be tried in order to keep a pool of fluid in the peritoneum to float the catheter
		Change patient position
		Reposition catheter (acute only)
	Intra-abdominal pressure	Reduce fill volume
		Try cross flow dialysis
	Air under diaphragm	Normal corrects over 30min
		Analgesia
		Try cross flow dialysis
Pain on outflow	Internal position of catheter	As for pain on infusion
Breathlessness	Intra-abdominal pressure	Reduce fill volume
		Cross flow dialysis
	PD fluid passing into chest to cause a pleural effusion. Can be confirmed by documenting high glocose concentration on fluid drained from chest	Change to CVVH/CVVHDF or intermittent HD

Continous veno-venous filtration and haemodialysis (CVVH, CVVHD, and CVVHDF)

Principles

- In CVVH (Fig. 14.1):
  - Blood flows down one side of a highly permeable membrane
  - Water and small molecules (<20,000 daltons) pass across it (ultrafiltrate) from an area of high to low pressure
  - This occurs because of convection—the flow of fluid across the membrane drags solute particles along with it
  - Plasma proteins and cells are too big to pass across the membrane
  - The ultrafiltrate is removed and replaced by a physiologically appropriate replacement solution
  - The higher the volume of ultrafiltrate, the greater the solute clearance.

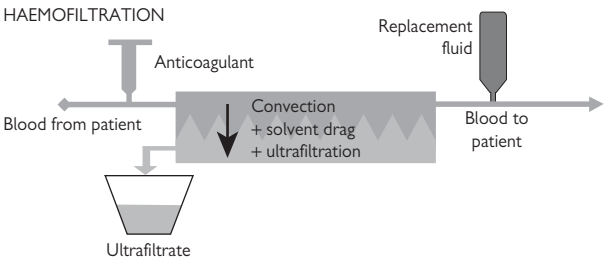

Fig. 14.1 Continous veno-venous haemofiltration. Reproduced from Singer M, Webb AR (2009). *Oxford Handbook of Critical Care*, 3rd edn. Oxford University Press.

- In CVVHD:
  - Blood flows down one side of a highly permeable membrane
  - Dialysate flows past the other side of the membrane in the opposite (counter current) direction to the blood
  - Small molecules pass across the membrane down the concentration gradient at a rate inversely proportional to their molecular weight
  - This occurs because of diffusion—the movement of solute is dependent upon a concentration gradient.
- In CVVHDF (Fig. 14.2):
  - Blood flows down one side of a highly permeable membrane
  - Water and small molecules (<20,000 daltons) pass across it (ultrafiltrate) from an area of high to low pressure
  - Dialysate flows past the other side of the membrane in the opposite (counter current) direction to the blood
  - Small molecules pass across the membrane down the concentration gradient because of diffusion— the movement of solute is dependent upon a concentration gradient.
  - Thus CVVHDF combines diffusion and convection.

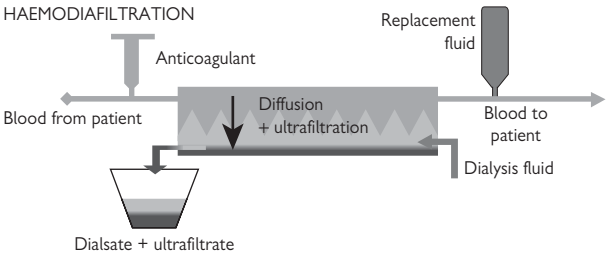

Fig. 14.2 Continuous veno-venous haemodiafiltration. Reproduced from Singer M, Webb AR (2009). *Oxford Handbook of Critical Care*, 3rd edn. Oxford University Press.

What do you need?

- Access
- Filter
- Pump
- Fluid
- Fluid warmer
- Anticoagulation.

Access

In most cases double lumen lines are used, but occasionally 2 single lines can be used in cases of low flow rate, or low weight. In general the bigger the better (see Table 14.4). Even with a large cannula, there can be flow problems and these can often be improved by rotation, slight retraction of the cannula, or swapping venous/arterial connections. Insertion can be made more successful with US guidance.

Table 14.4 Weight to cannula size

Weight (kg)	Size (FG)
<3	5
3 to 10	6.5
10 to 20	8
20 to 50	11
>50	12

Filter

Which filter to use is partly dependant on the machine to be used. In general the filter surface area should not exceed the patient's and the total circuit volume should be <10% of the patient's circulating blood volume. Exceptions can be made, in particular when using ECLS.

The filter materials vary with manufacturer, and these can have consequences; i.e. unsurface treated AN69 membranes are associated with the bradykinin release syndrome. This means anyone starting filtration should be aware of the possible side effects of their filter membranes

Priming of the filter and circuit, following local guidelines, can be started while the catheter is being inserted, as even with modern machines this is time consuming.

Most manufacturers recommend changing the circuit after 72h.

Pump

At its most basic this could be a volumatic pump; however this produces a high degree of inaccuracies, and thus has been generally replaced with fully automated weight controlled machines. These have the additional advantages of error control and data gathering. These machines have to be specified to allow slow pump speed for use in children.

Fluid

As with PD, fluid can be found buffered with lactate or bicarbonate (Table 14.5). In PICUs bicarbonate has become the first choice as lactate is often one of the waste products renal replacement therapy is commenced to remove. Electrolyte concentration may need to be changed to meet the clinical need; i.e. adding sodium if the patient is extremely hypernatraemic (Na >160) to reduce the speed of sodium reduction.

Table 14.5 Typical haemofiltration fluid composition

Contents (mmol/L)	Hemosol BO	Prismasol 4	Hemolactol	Lactosol
Glucose	0	22	1.1	0
Osmolality	287	301	301.6	287.5
Na^+	140	140	140	140
Ca^{++}	1.75	1.75	1.75	1.75
Mg^{++}	0.5	0.5	0.75	0.75
Cl^-	109.5	113.5	109	105
Lactate	3	3	40	40
HCO_3^-	32	32	0	0

Fluid warmer

CVVH/HD/HDF is an excellent way of controlling the central body temperature. Most modern machines have a blood warmer attached which ensures the blood returning to the body is at the correct temperature. If this is not available it is possible to wrap the lines and circuit in silver foil to reduce heat loss.

Anticoagulation

- Normally needed to stop the filter from clotting. Although CVVH/CVVHD/CVVHDF can be performed without anticoagulation, relatively low flows in paediatric practice make this less common
- May be reduced or omitted in children who have recently had surgery, who have DIC, hepatic failure, or thrombocytopenia
- Anticoagulants maximize the circuit life
- The choice of anticoagulant depends on the local preference and practice, and the patient's condition
- Anticoagulation should be monitored routinely (activated clotting time (ACT) or activated partial thromboplastin time (aPTT))
- In the UK, heparin is the most common form of anticoagulation.
  - Loading dose of 50U/kg followed by a continuous infusion to achieve ACT of 1.2–1.8× normal or aPTT ratio of 1.2–1.5× baseline
- Anticoagulation may be regional—affecting the circuit only, or systemic—affecting the patient and circuit
- Regional anticoagulation involves infusion of an anticoagulant into the circuit pre filter, with an antagonist being given to the patient or on the return blood line to deactivate the anticoagulant
- Monitoring for regional anticoagulation involves measuring the aPTT or ACT of the patient and the circuit (usually post filter)
- In regional anticoagulation aim for a normal aPTT for the patient and an aPTT ratio of 1.2–1.5× baseline for the circuit
  - Advantages of regional anticoagulation are a reduction in bleeding episodes
  - Disadvantages include ↑ monitoring requirements and frequent adjustment of dosage of both the anticoagulant and antagonist
- Sodium citrate is increasingly used to provide regional anticoagulation:
  - Works by chelating ionized calcium, prior to filtration
  - Calcium is then infused after filtration, typically systemically via a central line infusion
  - Some machines have an automated function to achieve this
- Prostacyclin *(2–10ng/kg/min)* can be used, although if used alone reduces circuit life, and has been used in combination with heparin with more success:
  - It can cause profound hypotension and is costly.

Starting parameters

Table 14.6 shows a guide for starting parameters, which should be tailored to the patient's needs. For example, in metabolic disease, sepsis, or drug removal a higher volume treatment is required. In all cases, regular review of electrolytes, fluid status, and pH are essential.

Starting

At initiation of treatment there is often a period of hypotension. This is due to reasons, such as the inflammatory response to the circuit and transient reduction in serum inotrope levels as well as the increase to the total circulating volume. Volume replacement and changes in inotropic support may be required.

Table 14.6 Initial parameters for pre-filter replacement fluid

Exchange/ replacement turnover / ultrafiltrate rate	30mL/kg/h	This will exchange about 50% body weight in 24h taking into account 25% lost to pre-dilution
		Needs to be much higher if using for ammonia clearance or to rapidly improve biochemistry (>100mL/kg/h)
Blood flow	6–9mL/kg/min	This should be at least 10× filtration rate and prevents excessive haemoconcentration in the filter
Dialysate flow rate	20ml/kg/h	Maximal efficacy is achieved at 2–3 × the blood flow rate
Fluid loss	Individualize	The net fluid loss through haemofiltration will depend on patient's needs. Practically difficult to achieve a negative balance of >5–10% of the patient's body weight in 24 h

Complications

- Haemodynamic instability (esp. at start)
- Disconnection and blood loss
- Clotting off of filter
- Electrolyte or fluid imbalance
- Inadvertent (excessive) fluid removal
- Heat loss
- Drug dose alterations needed
- Haemorrhage (due to anticoagulation)
- Infection risk.

Troubleshooting

- Circuit pressures are measured in mmHg and reflect the flow within the circuit
- Arterial pressure is always negative as the blood pump is sucking blood out of the patient. Arterial = access pressure; venous = return pressure
- At all times protect the patient from air embolism and blood loss. When troubleshooting (see Table 14.7) it may be safer to disconnect from the patient and recirculate. Always flush the access lines if this is being done to prevent them clotting off. Circuits should be spiked onto a small bag of 0.9% sodium chloride and a partly-open 3-way tap may be used to mimic arterial and venous pressure.

Table 14.7 CVVH/CVVHD/CVVHDF: troubleshooting

Problem	Cause	Solution
Excessively negative arterial pressure	Clamp/kinked line	Unclamp/kink line
	Catheter up against the vessel wall	Swap lines so arterial connects to venous side of catheter
	Arterial line/access clotting	Check coagulation and increase anticoagulation if necessary. Aspirate and flush access
Positive arterial pressure	Disconnection or patient coughing	Clamp lines and reconnect if no air in circuit or wait for coughing to stop.
	Clamp/kinked line	Unclamp/unkink line
Excessively positive venous pressure	Venous line/access clotting	Bed side clotting check and increase anticoagulation if necessary
	Disconnection	Clamp lines and reconnect if no air in circuit.
Low/negative venous pressure	Low flow in small patients	Partially occlude venous line to generate higher venous pressure
	Filter/circuit clotting	Check no clamps on ultrafiltrate line or bag
Rise in TMP/filter pressure rising	Ultrafiltrate too high for filter/blood flow rate	Check filtration fraction below 25% Increase pre-dilution % age Check maximum ultrafiltrate for filter size Stop circuit if filter clotted
Air detector	Air in venous line	Remove air, if large amounts are present take patient off and flush access with saline. Recirculate circuit and remove air while patient isolated. Find source of air.
		Stop treatment if real blood leak.
	May also be caused by circuit clotting.	Continue if possible but filter likely to clot off.
	Blood in ultrafiltrate	Seek liver opinion
	Fiscus ultrafiltrate, associated with liver failure	
Blood leak	Air in blood leak detector	Remove air from blood leak detector
	Air detector out chamber	Put blood leak detector back into position
	Dirty mirror on detector	Clean mirror
High NH_3	↑ production	Increase UF rate or add HD, so convert to CVVHDF

Haemoperfusion

- Uses activated charcoal cartridges with a large surface area placed in a veno-venous extracorporeal circuit as an absorbent to remove toxins.
- It has been used historically for toxic drug removal.
- Other more reliable methods of drug removal include plasmafiltration and the molecular adsorbent recirculating system (MARS).
- MARS is a haemodiafiltration method using an albumin-enriched dialysate to remove albumin bound toxins.
- The cartridges contain a synthetic, asymmetric membrane, impermeable to albumin, but which allow the passage and reversible binding of albumin-bound substances (Fig. 14.3)
- It requires a CVVHD circuit as well as the MARs circuit (see Fig. 14.4).
- MARS used primarily for liver support—i.e. in fulminant hepatic failure—on ICU
- Limited paediatric data at present.

Intermittent haemodialysis

- IHD is high efficiently dialysis and is useful for drug, toxin, and metabolite removal
- It should only be performed in renal centres where dedicated staff are available
- Requires high blood flows—good vascular access essential
- Haemodynamic instability common:
  - Usually in first 15min of treatment
  - More likely in patients with compromised cardiac function, sepsis, or MOF.
- There may be a rebound effect secondary to efficient removal of drugs and subsequent redistribution into the circulation from the extra vascular space. Some centres have used IHD for initially removal of drugs/toxins and swap to CVVHDF after initially treatment.

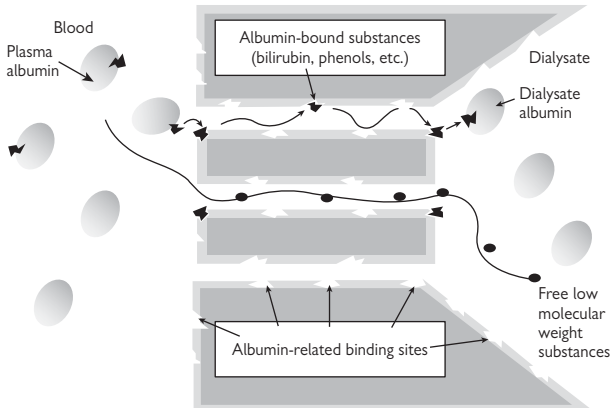

Fig. 14.3 MARs cartridge structure. Reproduced with permission from Mitzner SR, Stange J, Klammt S, *et al.* (2001). Extracorporeal detoxification using molecular absorbent recirulating system for critically in patients with liver failures, *J Am Soc Nephrol* **12**(suppl.17): S75–S82.

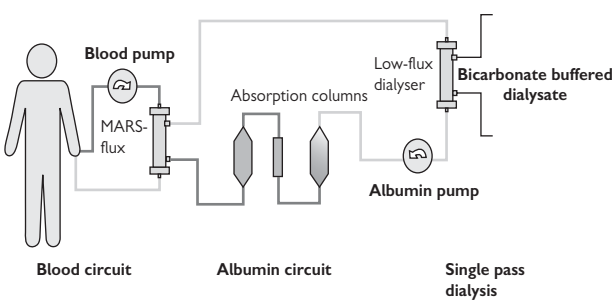

Fig. 14.4 SCHEMATIC of MARs circuit Reproduced with permission from Mitzner SR, Stange J, Klammt S, *et al.* (2001). Extracorporeal detoxification using molecular absorbent rrecirulating system for critically in patients with liver failures, *J Am Soc Nephrol* **12**(suppl.17): S75–S82.

Plasmafiltration

- Uses plasmafilter in a veno-venous circuit to exchange plasma components, such as auto-antibodies, and replace them with albumin or FFP
- Indications:
  - Myaesthenia gravis
  - Guillain–Barré syndrome
  - Goodpasture's syndrome
  - Thrombotic thrombocytopenic purpura
  - Vasculitides, e.g. ANCA, Wegener's
  - Sepsis
  - Antibody mediated haemolysis
- Plasmafiltration removes antibodies in immune mediated disease, albumin bound drugs, and has been employed in some centres in sepsis, although this use remains unproven
- When attempting to remove antibodies or drugs a number of treatments may be necessary because of further production of antibodies or redistribution of drug.

Box 14.6 Advantages and disadvantages of plasmafiltration

Main advantages

- Antibody removal
- Effective albumin bound drug removal
- May have beneficial effect on inflammatory mediators in sepsis.

Main disadvantages

- Access
- Anticoagulation
- Human blood products as replacement
- Removal of immunoglobulins and clotting factors
- Cardiovascular instability
- Large shifts in fluid due to alteration of oncotic pressures
- Arrhythmias secondary to hypocalcaemia.

Box 14.7 Treatment guides

- Blood pump speed 5–9mL/kg/min
- Circuit size <10% of blood volume to avoid the need for blood priming
- Treatment 100mL/kg exchange
- Treatment time no less than 4h
- Replacement fluid 66% albumin and 34% FFP or octoplas
- No fluid removal while on PF
- Plasmafilters have a lower maximum transmembrane pressure, which means higher blood pumps may cause rupture of the membrane.

Chapter 15

Nutrition

Introduction

Nutrition is necessary for the proper growth and development of the healthy child and is essential for adequate wound healing and immune competence in an ill child. An understanding of nutritional requirements of sick neonates, infants, and children is crucial for their management. Equally important is an understanding of the impact of metabolic stress and how this impacts on nutritional requirements in the critically ill child.

Normal nutrition and energy requirements

- Children require nutrition for:
  - Cellular function
  - Growth
  - Activity
- Normal nutrition provides:
  - Water
  - Protein for structure and growth
  - Carbohydrates for energy—disaccharides, lactose (galactose and glucose), sucrose (glucose and fructose), and starch (glucose polysaccharide)
  - Fat for energy, cell membranes, fatty acids, prostaglandins
  - Vitamins and trace elements
- Normal diet provides a mixture of protein, carbohydrate, and fat:
  - In a normal diet carbohydrate constitutes ~70% of calories and fat <30%
  - If inadequate calories from carbohydrate or fat, endogenous protein is catabolized to glucose for energy (gluconeogenesis)
  - Lack of protein leads to malnutrition, wasting despite adequate calories
- The same formula is used for calorie requirements as for fluid requirements (Table 15.1)
- Neonates have an inability to excrete very concentrated urine (max. 600mosmol/L) therefore they may not tolerate feeds with >1kcal per mL (concentrated feed can cause diarrhoea and cause hypernatraemic dehydration)
- Breast milk contains approximately 0.67kcal/mL: thus a term neonate who is breastfeeding will drink about 150mL/kg/day which equates with 100kcal/kg/day
- Older children tolerate more concentrated feeds (1.5kcal/mL) as they can excrete more concentrated urine.

Table 15.1 Energy requirements for age and weight

Age/weight	Calorie requirement
Neonates	100–120kcal/kg per day
<10kg	100kcal/kg per day
10–20kg	1000kcal + 50kcal/kg over 10kg per day
>20kg	1500kcal + 25kcal/kg over 20kg per day

Nutritional assessment

History

PICU patients will generally fall into 2 groups—those who are previously well with normal growth and nutritional status or those with more chronic health issues, often associated with poor growth and nutritional status. A history of poor growth, poor feeding, nausea, vomiting, diarrhoea is important.

Chronic health conditions with poor nutrition include:

- Ex-prematurity:
  - Small for dates
  - Bronchopulmonary dysplasia
  - Sepsis
  - Necrotizing enterocolitis
- Cardiac failure
- Oncological diseases
- Cystic fibrosis
- Chronic GI disorders.

Examination

- Plotting current weight and height as well as head circumference on centile charts is ideal at the time of admission
- A low weight for height is suggestive of acute malnutrition, whereas low weight and height for age is more suggestive of a chronic process.
- If a child has marked capillary leak with generalized oedema, weights need to be interpreted carefully
- As the child's recovers and enters a convalescent phase, monitoring weight gain is an easy way to assess the adequacy of a child's nutritional support
- Anthropometric measurements are often used by dieticians in the outpatient setting for nutritional assessment but have little place in the PICU setting. Generalized oedema in critically ill children is so common as to make measurements of mid-arm circumference and skinfold thickness quite misleading.

Blood tests

- Albumin levels are used to assess nutritional status but can be misleading in PICU. In critical illness the levels are often significantly reduced for non-nutritional reasons:
  - ↑capillary endothelial permeability (seen in infection and SIRS) results in leakage into the interstitial tissue reducing the serum albumin level
  - Dilution from resuscitation fluids
- Proteins such as pre-albumin and transferrin are reduced as part of the body's acute phase response to illness. After the acute phase they are more accurate at reflecting nutritional status.
- Acute phase proteins such as C-reactive protein (CRP) are elevated in the acute hypermetabolic (catabolic) phase of critical illness.

Nutritional requirements

Nutrition and critical illness

Malnutrition, in particular protein energy malnutrition, can be acute or acute-on-chronic. Both are recognized risks of critical illness leading to:

- Muscle weakness
- Growth failure
- Impaired wound healing
- Poor immunity leading to infection
- ↑mortality.

The stress of a major illness frequently renders a patient catabolic, with protein (nitrogen) loss outstripping protein intake. Critically ill patients tend to lose ↑quantities of nitrogen—usually via the urine but sometimes also from the bowel or the skin (for example in burns patients). If they do not receive adequate nutrition they will break down endogenous protein as an alternative source of energy. Whilst it may not be possible to prevent some of the loss of protein due to the acute illness it is possible to minimize the extent of the catabolic state by providing non-protein energy sources early.

Acute conditions associated with poor nutrition include

- Sepsis
- Major trauma, particularly burns
- Gastric stasis, ileus (reduced intake)
- Diarrhoea, fistulae, drain losses (↑loss).

The primary nutritional goal during the acute phase of a critical illness is the provision of sufficient non-protein calories to minimize protein breakdown and adequate protein to aid wound healing and immune function. Provision of calories to allow growth is not a realistic goal acutely but becomes important in the convalescent phase of any illness. To achieve these goals one needs to have an idea of what each patient's total energy expenditure is. Unfortunately this varies enormously from patient to patient and disease state to disease state.

Predicting energy requirement

Energy requirements can be predicted from the equation:

$$TEE = (BMR \times \text{correction factor}) + TEF + AEE$$

where, TEE is total energy expenditure, BMR is basal metabolic rate, TEF is thermic effect of feeding, and AEE is the energy expended in activity. The correction factor for BMR depends on factors increasing or decreasing it (see rest of section).

Total energy expenditure (TEE)

This can be calculated from predictive equations or measured by indirect calorimetry (see Box 15.1) which measures O_2 consumption (VO_2) and CO_2 production (VCO_2).

Box 15.1 Bedside calorimetry

Indirect calorimetry measurement may be inaccurate in the presence of an ETT leak and at high levels of inspired oxygen. It also requires a specific monitor for bedside purposes. Currently its use is not routine (it is largely used in research) but advocates argue that it allows for measurement of energy expenditure and respiratory quotient (RQ = VCO_2/VO_2) and thus allows tailoring of calorie delivery to energy expenditure and avoidance of overfeeding (i.e. when RQ >1).

Basal metabolic rate

- This is defined as the energy consumption in an ideal state of rest and constitutes up to 70% of TEE
- BMR varies with age (see Table 15.2); being maximal for a neonate (energy used for growth) and falling in a kcal per kg basis as a child grows (except during the growth spurt of puberty). A number of equations are available to predict BMR, the most well known being the Harris–Benedict equation
- Factors increasing BMR:
  - Fever/infection/inflammatory response—there is a 12% rise in BMR per 1°C above 37°C
  - Burns
  - Trauma/surgery
- Factors reducing BMR:
  - Sedation, analgesia (5–10% reduction in BMR)
  - Neuromuscular block (up to 40% reduction).
  - Hypothermia (remember, shivering increases metabolic rate in an attempt to conserve heat).

It is clear that in the critically ill patient many of the corrections listed here will need to be applied to get an accurate assessment of BMR. See also Box 15.2

Table 15.2 Basal metabolic rate per kg by age

Age	BMR
1 year	55kcal/kg/day
5 years	45kcal/kg/day
10 years	38kcal/kg/day
Adult	26kcal/kg/day

Thermic effect of feeding

Energy is required to digest and absorb food enterally and this generates heat. This should be accounted for in prescribing enteral feed.

Energy expenditure of activity

This will vary significantly from individual to individual but increases with age. Accounts for 10% of TEE at birth and >25% over 6 months old. This will be ↑ by work of breathing, i.e. when in respiratory distress or on weaning modes on the ventilator. Also ↑ by pain and distress leading to agitational movement.

Box 15.2 Hypermetabolism and overfeeding?

Studies have confirmed that there is little correlation between measured energy expenditure using indirect calorimetry and a number of different predictive formulae used to calculate BMR. Until recent years it was widely believed that critically ill children were invariably in hypermetabolic (catabolic) states, much like adults, and therefore required calories well in excess of those they would need if they were in good health. There are several problems with this:

- There is now a body of evidence that predictive equations (when compared to indirect calorimetry) more often than not overestimated the measured energy expenditure, particularly in infants and small children. Rather than being hypermetabolic, at least in the early phases of illness, many children's energy expenditure was close to or less than the predicted BMR. The catabolic response that can occur in the acute phase of illness will be mitigated by the fact that many children are ventilated, sedated, muscle relaxed, and in a thermoneutral environment (thus reducing energy required for breathing, activity and maintaining temperature)
- Catabolism is typically unresponsive to overfeeding or hormonal manipulation, thus a degree of endogenous protein loss is to be expected in critical illness
- The caloric allotment for growth is not necessary in the acute phase of illness—it is unrealistic to expect children to grow when acutely unwell.

The risks of overfeeding in acutely unwell children are real and can result in:

- ↑work of breathing and ventilator dependency (carbohydrate overfeeding generates CO_2)
- Hyperglycaemia
- Hypertriglyceridaemia, fatty liver, and cholestasis.

Nutritional recommendations

- The recommendation for all centres to measure each patient's energy requirements using indirect calorimetry may not be practical for many units
- Additionally, in practice few intensivists use predictive formulae on a daily basis to determine a patient's nutritional requirements
- The benefit of early enteral nutrition is widely acknowledged and for most, the initial step is to meet the child's fluid requirements with an age-appropriate enteral feed in preference to IV fluids. Thereafter the volume or caloric content of the feed can be adjusted according to the individual case.
- Experienced dieticians (who understand the issues above) are invaluable in advising regarding appropriate goals and often do use various predictive formulae to help them formulate their advice. Where enteral feeding is not tolerated, parenteral nutrition should be introduced.

Calories

- In the acute setting prescribe calories according to BMR (see 📖 Table 15.1, p.276). Take into account fever, disease process, sedation, and paralysis but remember these may cancel each other out (i.e. a septic child who is sedated, ventilated, and paralysed.) Do not give calories for growth
- In the convalescent phase of an acute illness, calorie intake can be increased to take account of:
  - Repair and healing
  - ↑ activity
  - Work of breathing
  - Catch up growth and normal growth
- A recovering child may need >50% increase in calorie intake as he/she heals, wakes up, moves about and weans from the ventilator
- If increasing the fluid allowance is not possible, then additional calories can be added to existing volume (see 📖 Range of enteral feeds p.282).
- Nutritional success in the recovery phase of an ICU admission can be monitored simply by measuring weight gain on a regular basis.

Enteral nutrition

By definition this includes any feed delivered via the GIT. In critically ill children this usually means feed delivered by an oral or nasal feeding tube with its end sited in the stomach or transpylorically in either the duodenum or jejunum. Total or at least partial enteral feeding is the preferred route of nutrition. (See Boxes 15.3 and 15.4.)

Advantages of enteral feeding

- Simple, physiological and cheap
- No venous access required
- Less metabolic disturbance than parenteral nutrition
- Less monitoring and blood tests required
- Maintains gut endothelial integrity
- Possibly reduces bacterial translocation and risk of sepsis
- There is limited evidence that early enteral feeding (within 36h of admission) is associated with improved clinical outcomes.

Disadvantages are few

- Risk of pulmonary microaspiration and infection
- Intolerance—large gastric volumes (See Box 15.5).

Box 15.3 Underfeeding in PICU

Underfeeding in PICU is commonly related to fluid restriction, underprescribing, and from some of the interruptions that occur. This happens regularly for a variety of reasons, many of which are avoidable.

- Arbitrarily deemed 'large' residual gastric volumes
- Prolonged fasting for procedures or nursing cares
- Delays in replacement when tubes are accidentally removed.

- Gastric feeding should always be attempted initially via a NG tube. It is good practice to start feeding with low volumes and slowly grade up if tolerated
- Large gastric residual volumes can be a problem and may lead to malnutrition or aspiration pneumonia
- Gastric emptying varies throughout the day and identifying what is normal from what represents pathological gastroparesis, a common complication of critical illness or injury, can be difficult
- Domperidone, metaclopramide and erythromycin are recommended as gastric prokinetics in the setting of high residual gastric volumes or vomiting. Cisapride is no longer used due to concerns of developing long QT syndrome
- Small bowel motility and absorptive function is often well maintained even in the presence of gastroparesis. Thus small bowel feeding tubes (nasojejunal tubes) may be placed to bypass the stomach. This can be done at the bedside, or endoscopically or under radiological screening
- The introduction of evidence-based feeding protocols improves attainment of caloric goals. Institution involves a multidisciplinary team of dieticians, physicians, and nurses
- There will always be a group of patients in whom enteral feeding will not be tolerated, at least in the short term. Example conditions are:
  - Hypotension with poor splanchnic perfusion
  - Vasopressor-associated splanchnic vasoconstriction
  - Refractory ileus
  - Postop GI patients.

It is important that any protocol recognizes these groups. They should be fed parenterally but introduction of enteral feed should be considered on a daily basis.

Range of enteral feeds

Breast milk should always be encouraged if available. If the quantity is insufficient for calories then fortify it or supplement it with formula feeds. Avoid the use of cow's milk in children under 1 year old.

Formula feeds available include:

- *Normal or polymeric feeds*: these contain a mixture of protein, long chain fatty acids, and complex carbohydrate with vitamins and minerals. They are for children with normal (or near normal) gut function. Examples are breast milk, *Osmolite®, Paediasure®,* and *Ensure®*
- *Pre-digested or elemental feeds*: these may contain amino acids, small peptides, simple carbohydrates (e.g. maltodextrin) and medium chain triglycerides (MCTs) as fat. They are for children with severe GI dysfunction, e.g. short gut or Crohn's disease. Examples are *Pregestimil®* and *Pepdite®*
- *Disease specific diets*:
  - Renal failure—low protein
  - Liver failure—low fat, low sodium
  - Respiratory failure—low carbohydrate
  - Chylothorax—based on MCTs.

Whole protein (polymeric) feeds should be started initially. There is no advantage of peptide (elemental) feeds over polymeric in terms of tolerance, mortality, and infectious morbidity and they are considerably more expensive. To date there is no evidence to support immune-enhancing feeds such as those supplemented with arginine, glutamine, nucleotides, and omega-3 fatty acids (immunonutrition).

Box 15.4 Suggested feeding strategy

How much?: determine the calories and the target volume

Select formula: an age appropriate, polymeric formula. Do not fortify formulas until the patient demonstrates tolerance

Gastric or small bowel feeding: always trial gastric feeding first and only default to small bowel feeding if this fails

Continuous or bolus?: start with continuous feeds. Infants may be more settled after bolus feeding so this can be introduced if continuous feeds are tolerated. Small bowel feeding should always be continuous.

Starting rate:	<6 months	5mL/h
	6 months–10 years	10mL/h
	>10 years	20mL/h

Alternatively start at 25% of target feeding volume

Advancement plan:

1. Check gastric residual volume by aspirating after 4h of feed. Increase by the starting rate (or by 25% of target volume) every subsequent 4h until target volume is reached.
2. If the residual volume is large (i.e. > total volume infused over 4h) then:
   - Return aspirated feed to patient and rest for 1h. Reaspirate again. If feed has been absorbed then continue to increase intake to target volume.
3. If large gastric aspirate is persistent then start trial of prokinetics
   - 1st choice domperidone 0.2–0.4mg/kg 6-hourly enterally
   - 2nd choice erythromycin 2mg/kg 8-hourly enterally
   - Consider metaclopramide intravenously in adolescents
   - If prokinetics are successful continue with 4-hourly increases
4. If there is no improvement with prokinetics after 12h consider placement of small bowel feeding tube (see 📖 p.284).
5. If small bowel feeding fails after 24h consider TPN.

Avoid:

- Unnecessary periods of fasting
- Grading feeds up following a period of fasting—return to the maximal volume the patient was tolerating pre-fasting
- Replace dislodged tubes promptly.

Note: erythromycin interacts with a number of drugs including phenytoin, digoxin, and tacrolimus

Box 15.5 Diarrhoea and enteral feeds

Excessive calorie density can have osmotic effects and cause diarrhoea. This may occur with carbohydrate-rich feeds or with medium chain triglyceride feeds. Stools may be tested for reducing substances (sugars) or for lipid content. Lactose intolerance can be the cause and alternative feeds may have to be sought.

Transpyloric tube placement

- ***Radiological screening:***
  - Under fluoroscopic guidance ± contrast
  - Can be screened well into the small bowel
  - Requires transfer to radiology department and radiation exposure
- ***Endoscopically placed:***
  - Experienced practitioner required (often gastroenterologist)
  - Placement under direct vision
  - Can be done as bedside procedure
  - Requires additional sedation, takes time
  - Difficult to insert beyond duodenum
- ***Blind bedside placement (Box 15.6):***
  - Transpyloric tubes have been developed for quick insertion
  - Avoids transfer, radiation
  - Can be undertaken by PIC nursing or medical staff.

Box 15.6 Suggested technique for bedside placement

- Choose tube-unweighted polyurethane enteral feeding tubes with flexible stylet. 6Fr for <8kg and 8Fr for ≥8kg
- Prepare tube: remove guidewire, flush tube with sterile water, lubricate guidewire with water and reinsert into tube
- Measurements:
  - < 1 year: measure and mark NG length, then measure and mark the jejunal length—from nose to ear to half way to xiphisternum and continuing to the right iliac crest
  - ≥1 year: measure and mark nasogastric length, then measure and mark the jejunal length—from nose to ear to xiphisternum to right iliac crest
- Position patient:
  - Head of the bed at 15–30°
  - Patient lying with left side up (if tolerated)
- Aspirate pre-existing NG tube
- Insert tube to gastric marking:
  - Aspirate gastric contents, confirm with litmus paper (pH 1–5)
  - Flush tube with sterile water
- Continue to advance (whilst slowly rotating it close to the nose) to NJ marking. A small amount of resistance may be felt by experienced practitioners as the tube passes through the pylorus

Box 15.6 Suggested technique for bedside placement (*Continued*)

- Test placement:*
  - Test A: aspirate using 50-mL syringe. Bright yellow aspirates obtained and pH >6. If not passed proceed to test B
  - Test B: 2–10mL of air can be freely bolused in but resistance is met on attempted aspiration back of the air
- Once position confirmed, advance tube further 5–10cm to ensure proximal jejunal placement, secure tube and remove guidewire
- Always leave an NG tube in situ to decompress stomach.

*Note: Some centres require radiographic confirmation of tube position before commencing feeding

Parenteral nutrition

PN is a mixture of protein, carbohydrate, fat, electrolytes, vitamins, and trace elements. PN should be used when enteral feeding is not possible:
- GI disorders, e.g. bowel obstruction, short bowel syndrome, severe inflammatory bowel disease, post laparotomy
- Poor tolerance of enteral feeds in patients with intact GI tracts.

Unlike enteral nutrition, there is no known benefit in starting PN early in the course of critical illness. It is ordered when it is clear the patient will not be tolerating enteral feeds for at least the next 3 days.

Disadvantages to using PN:
- Requires IV access:
  - It can be given peripherally but this compromises the amount of glucose and therefore calories that can be delivered
  - Peripheral IV access is less reliable and can result in breaks in nutrition while new access is established
- Central venous access is more reliable (allows higher glucose concentration) but has greater risks and complications
- Electrolyte and metabolic disturbances such as hyperglycaemia and hypertriglyceridaemia
- Cholestasis is widely reported
- Regular blood monitoring of glucose, triglyceride, liver function
- ↑g ut permeability may lead to bacterial translocation with associated sepsis and multiorgan dysfunction
- PN is relatively expensive.

Prescribing TPN

Goals
- To provide sufficient non-protein calories, as carbohydrate and fat
- To avoid unnecessary catabolism of protein for energy formation
- Total calories should be delivered as:
  - 30–40% fat
  - 50–60% carbohydrate
  - 10–15% protein.

Issues

- The decision regarding how many calories should be decided in close liaison with the dietician and the TPN pharmacist. The requirement is approximately 10% less than in enterally-fed patients as there is no need to allow for the thermic effect of feeding
- The volume of PN is determined by the daily fluid allowance prescribed. If the patient requires strict fluid restriction, the volume of other infusions and IV medications needs to be taken into account in these calculations. If the patient has significant ongoing fluid losses—e.g. vomiting, NG losses, diarrhoea, drain losses—it is unwise to attempt to replace these with PN solutions as the electrolyte composition will not be appropriate. These should be replaced with an appropriate crystalloid solution
- Whenever possible, minimal volumes of enteral feed should be infused in addition to any PN. If tolerated this reduces the incidence of PN related cholestasis and may preserve gut mucosal integrity and function.

Carbohydrates

- Provided as glucose
- Energy content: 3.8kcal/g of glucose
- To avoid hyperglycaemia, start with a solution of 10% dextrose (ie., 10g glucose/100mL) and grade up over 3 days to a maximum of 15%
- Start at 5–10g/kg/day—see Table 15.3
- If the patient's glucose levels rise significantly (≥12mmol/L) an insulin infusion can be commenced (extrapolating from adult evidence some PICUs aim for tighter glycaemic control with insulin)
- Precautions: rebound hypoglycaemia can occur if PN is suddenly stopped (starting a 10% glucose infusion should prevent this).

Fats

- Provided as 'Intralipid®'—an isotonic fat emulsion
- Energy content: 10kcal/g
- It is generally provided as a 20% solution (i.e. 20g fat/100mL)
- Commence at 1g/kg/day and increase to a maximum of 3g/kg/day in 1g/kg increments—see Table 15.3
- Precautions:
  - Thrombocytopenia—lipid impairs platelet function so dose should be limited to 2g/kg/day
  - Hyperbilirubinaemia—fatty acids compete with bilirubin to bind to albumin so dose should be limited in this setting to 1–2g/kg/day.

Protein

- Various amino acid solutions available—usually 10% (i.e. 10g amino acids/100mL)
- Energy content: approximately 4kcal/g
- Start with 1g/kg/day and grade up in 1g/kg/day increments to 2–3g/kg/day
- Precautions:
  - Hepatic and renal impairment—need reduced protein in PN
  - Burns or multitrauma—need additional protein.

Calculation of total calorie intake:
Total kcal/kg/day = (amino acids × 4) + (glucose × 3.8) + (fat × 10)
where the quantity of amino acids, glucose and fat is in g/kg/day.

Electrolytes
- Provided as maintenance but must be adjusted based on blood results
- Precautions: if serum potassium unstable, give potassium free PN and give potassium separately.

Multivitamins and trace elements
- Water and fat soluble vitamins are added routinely
- Trace elements—selenium, iodine, zinc, fluorine, copper and manganese—are added usually when patients are receiving prolonged PN (>2 weeks) or earlier in severe burns or pre-existing malnutrition
- Precaution-early selenium deficiency can cause cardiomyopathy in burns.

Table 15.3 TPN prescriptions for days 1, 2, 3, 4 for water, calorie, protein, carbohydrate, and fat requirements

	Water: mL/kg/day kcal/kg/day	Amino acids: g/kg/day Days:1/2/3+	Glucose: g/kg/day Days:1/2/3+	Fat: g/kg/day Days:1/2/3/4+
Neonates	100	1.5/2/2	10/12/15–20	1/2/3/3
<10kg	100	1.5/2/2	10/10/15–20	1/2/3/3
10–15kg	90	1/1.5/2	5/10/15	1/2/3/3
15–20kg	80	1/1.5/1.5	5/10/10–15	1/2/2/3
20–30kg	65	1/1/1.5	5/10/10–15	1/1/2/2.5
>30kg	50	1/1/1.5	5/5–10/10	1/1/2/2

Note: calorie requirements are the same as water requirements per day.

Adapted from Shann F, Henning R, Shekerdemian L *et al.* (2008) *Paediatric intensive care guidelines*, 3rd edn, Collective Pty. Ltd. Victoria, Australia.

Monitoring TPN

Introduction phase
- Glucose every 6–8h
- U&Es daily
- Triglycerides daily ~accept level ≤4mmol/L if infusing lipid over 24h
- LFTs—twice weekly
- Ca, Mg, PO_4—weekly.

Established
- Glucose daily
- U&Es—twice weekly.
- LFTs weekly
- Trace elements—every 2nd week if burns or chronic malnutrition, otherwise 4-weekly.

Further reading

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Chapter 16

Heat-related illness

Introduction

Heat-related illnesses refer to conditions in which the resulting hyperthermia is due to either ↑heat production or ↓heat dissipation. In these conditions controlling the body temperature by active cooling plays a critical role in the management of these patients.

Heat stroke

High environmental temperature

- The body has different mechanisms to dissipate the heat that is produced by normal metabolic functions:
  - Radiation: transfer from the body to a cooler external surface
  - Evaporation: heat loss from drying of skin or body surfaces
  - Conduction: contact with cooler surface
  - Convection: heat loss when cooler air flows over the body
- Perspiration is the most effective method in the healthy child
- Mechanisms for heat dissipation fail at ↑ temperature and humidity
- Infants are at ↑risk as they sweat less and have higher metabolic rates. They also are too young to control their environment (i.e. remove clothing, get in the shade etc.).

Exertional heat stroke (EHS)

- Results from prolonged physical activity in a hot environment
- Due to a combination of ↑heat production and a ↓heat dissipation
- EHS is the most common form of heat stroke in adults and older children.

Pathophysiology of heat stroke

- In response to heat stress, vasodilation occurs. As peripheral resistance falls cardiac output increases until sweat losses lead to hypovolaemia
- The exact temperature at which cellular damage occurs is not clear. Core temperature may exceed 41°C and cellular damage is believed to be a function of both the maximum body temperature reached and the time of exposure to that temperature.
  - Oxidative phosphorylation fails at 42°C, stopping the production of adenosine triphosphate (ATP) by mitochondria
  - Unchecked, heat stroke will cause multisystem damage characterized by cerebral oedema, hypovolaemia, and renal hypoperfusion
  - Muscle damage (rhabdomyolysis) causes myoglobinuria with resultant renal failure and hyperkalaemia
  - Hepatocellular injury leads to jaundice, encephalopathy, hypoglycaemia, and coagulopathy
  - Endothelial cell damage results in consumptive coagulopathy (disseminated intravascular coagulation).

Clinical presentation

- Symptoms include headache, vomiting, malaise, cramps, and dizziness progressing to confusion, ataxia, and coma
- Symptoms and signs of dehydration and hypovolaemia occur.

Management (Box 16.1)

- Heat stroke should be considered a life-threatening emergency. Aggressive and rapid cooling measures coupled with intravascular volume resuscitation are the mainstay of treatment
- Mechanical ventilation may be required in comatose or cardiovascularly unstable patients
- Antipyretics have no role in the treatment of heat stroke.

Box 16.1 Management key points

- Attend to ***ABCs.*** Give oxygen
- Prepare to cool the patient as soon and as fast as possible
- Aim to reach a temperature below 39°C aggressively. Cooling methods can be stopped when the temperature reaches 38.3°C
- Consider mechanical ventilation in comatose or severely shocked patient
- IV fluids are invariably required—give 20mL/kg 0.9% saline or Hartmann's (Ringer's) as a bolus. Repeat as necessary
- Measure glucose level as hypoglycaemia is common
- Treat heat-producing activity aggressively, e.g. convulsions, agitation or shivering. Sedation and paralysis with muscle relaxants may be necessary
- Check electrolytes—watch for hyperkalaemia and hypo- or hypernatraemia
- Monitor renal and liver function, and coagulation profile
- If patient develops myoglobinuria, keep well hydrated, aiming for a generous urine output. Urine alkalinization and mannitol may be needed (see 📖 Box 31.9 p.665). If renal failure ensues, considered early haemofiltration
- If rhabdomyolysis occurs, IM compartment pressures may need to be measured.

Drug-induced hyperthermia (Box 16.2)

- Rarely, certain drugs can cause an increase in body heat production leading to hyperthermia
- Drugs commonly involved are inhalational anaesthetic agents, sympathomimetics, antipsychotics, serotonin agonists, and drugs with antcholinergic properties
- The resulting hyperthermia is often accompanied by skeletal muscle rigidity, rhabdomyolysis, and hyperkalaemia
- Multiple organ failure; renal impairment, severe metabolic acidosis, cardiac dysfunction, coagulopathy, and death may ensue.

Malignant hyperthermia (MH)

See 🕮 Malignant hyperthermia, p.184.

Sympathomimetic poisoning

- Commonly caused by cocaine and 3,4-methylene-dioxymethamphetamine (MDMA or 'Ecstasy'). This syndrome is caused by an ↑release and disturbed reuptake of serotonin, dopamine, and other catecholamines. (and metabolites)
- The resulting hypermetabolic state may be exacerbated by prolonged physical activity from dancing in a hot environment such as a nightclub or party. In severe cases convulsions, hyperthermia, rhabdomyolysis, and coagulopathy occur
- Associated hyponatraemia may occur from excess water intake
- Treatment includes aggressive cooling and the administration of benzodiazepines and barbiturates to stop the myotonic or hyperkinetic thermogenesis. In severe cases consider sedation and paralysis.

Serotonin syndrome

- Occurs when serotonin agonists are given concurrently with other serotonin releasing agents
- Serotonin leads to an excitatory response characterized by agitation, hyper-reflexia, myoclonus, hyperthermia, diarrhoea, and tachycardia
- The syndrome is self-limiting once the responsible agent is removed
- Treatment is supportive
- The value of antiserotonin agents (chlorpromazine or cyproheptadine) is not known but may be useful in severe cases.

Neuroleptic malignant syndrome

- A rare reaction to antipsychotic therapy, it can occur in any age group (most commonly in young-middle age adults) and normally within 4 weeks after starting therapy
- The pathophysiology is unclear but thought to be related to dopamine receptor blockade
- The syndrome is characterized by muscle rigidity, hyperthermia, and autonomic instability (sweating, tachycardia and labile BP).
- The syndrome can be severe, even lethal. Antipsychotic therapy should be discontinued and dopamine antagonists avoided. The use of dopamine analogues may be useful (bromocriptine 0.025mg/kg orally every 8h). In severe cases, dantrolene 2–3mg/kg may be considered.

As in any other drug-induced hyperthermia, supportive therapy tailored to the patient symptomatology is of paramount importance.

Management (Box 16.2)

Box 16.2 Treatment key points for drug-induced hyperthermia

- Discontinue medication
- Attend to ***ABCs*** and give oxygen
- Stop heat production (agitation, seizures, shivering). Benzodiazepines and, if necessary, non-depolarizing muscle relaxants
- Endotracheal intubation may be challenging due to muscle rigidity
- Mechanical ventilation is often necessary to deal with the ↑CO_2 production and O_2 consumption
- IV fluid replacement as needed. Monitor arterial pressure
- External cooling. Heat production may continue for some time despite stopping offending agent, therefore the chosen cooling method should be able to cool and control body temperature for as long as needed
- Administer:
  - Dantrolene (2–3 mg/kg) IV in MH. Repeat frequently until symptoms under control (up to 10mg/kg)
  - Benzodiazepines and barbiturates for sympathomimetic poisoning
  - Cyproheptadine in serotonin syndrome
  - Bromocriptine (0.025 mg/kg) oral in neuroleptic malignant syndrome
- Watch for signs of rhabdomyolysis, myoglobinuria, and hyponatraemia and hyperkaelemia
- Do not give antipyretic agents.

Practical approach to cooling

Control of body temperature is a common challenge in the PICU. Apart from hyperthermic syndromes there many patients in PICU in whom hyperthermia, even moderate, may be detrimental. The aim of cooling therapy is to reduce or normalize body temperature.

Following improved outcomes in adults (after ventricular arrhythmia induced cardiac arrest) and in newborns (with hypoxic-ischaemic encephalopathy) there is a growing interest in the application of therapeutic hypothermia as a neuroprotective strategy in PICU. If attempted, the aim should be able to maintain body temperature between 33–34°C for 24–48h. Overcooling (<32°C) can cause adverse effects.

There is no clear evidence showing a 'best' method of cooling. All have advantages and disadvantages, and the method used should be based on the particular circumstances of each patient.

Cooling in PICU

- Iced water immersion is popular in field and emergency departments but is impractical in PICU
- Evaporative methods using water and alcohol spray with warm fanning (prevents vasoconstriction) can be used in PICU
- The simplest technique is to use a cooling mattress which can automatically regulate the patient's body temperature to a pre-selected target
- If necessary, other cooling methods can be used in combination (ice packs, cooling blankets, evaporation, fans…) to accelerate the temperature drop.

Box 16.3 Key points for cooling or therapeutic hypothermia in PICU

- Use a cooling mattress
- In most circumstances, the child must be sedated, mechanically ventilated, and paralyzed with muscle relaxants to avoid shivering
- Monitor core temperature with rectal or oesophageal probe
- If rapid cooling is necessary, either:
  - Spray alcohol and water on the child and cool with a fan
  - Place sealed ice packs inside pillow cases over child's exposed body surface (particularly groin, axilla, neck where large blood vessels run) and cover with a forced air cooling blanket
- Once the child's temperature is 1°C above target temperature, stop additional methods and use only cooling mattress
- Avoid overcooling
- If target temperature of normothermia is achieved; stop active cooling and monitor body temperature.

Chapter 17

Prescribing

Introduction

A understanding of basic pharmacological principles is vital to the safe and effective prescription of drugs to patients in PIC. Babies and children handle drugs differently as they grow and the processes involved are often radically altered in critical illness. Children are at particular risk from adverse drug reactions and medication errors.

Pharmacokinetics and dynamics

- Pharmacokinetics is the study of 'what the body does to a drug'
- Pharmacodynamics is the study of 'what a drug does to the body'.

Pharmacokinetics defines the relationship between the dose of a drug and its concentration in different parts of the body (usually plasma) in relation to time. This depends upon:

Absorption If a drug is given IV 100% of the dose enters the bloodstream. If a drug is given orally usually only a fraction is absorbed. Enteral absorption is often compromised in the critically ill child.

Bioavailability is the fraction of drug that reaches the circulation unaltered and is therefore available to reach the target site. A drug given by the IV route is considered to have a bioavailability of 100%.

Volume of distribution (Vd) This is not a physiological volume but the apparent volume into which the drug would have to distribute to achieve the measured concentration. Water-soluble drugs, such as gentamicin, have a Vd similar to extracellular fluid volume. Drugs that are highly bound to plasma proteins have a low Vd.

Clearance Describes the removal of a drug from the body and is defined as the volume (usually of plasma) that is completely cleared of drug in a given time. In children it is described with respect to body weight (mlL/min/kg). Clearance per unit body weight is usually reduced in the neonatal period but may be higher in infants and young children than in adults.

Elimination half-life ($t_{½}$) is the time taken for a drug concentration (usually plasma) to fall to half the original value. It is inversely related to clearance. Therefore 50% of the dose will be eliminated in 1 half-life and 97% of a drug will be eliminated after 5 half-lives. 5 half-lives is also the time required for steady state to be achieved following initial administration of the drug.

In order to shorten the time to reach steady state for drugs with a long half-life a loading dose is typically given.

Concept of multi-compartmental model

Box 17.1

Why does a patient wake up 5min after an injection of thiopentone when we know that it takes several hours to eliminate thiopentone from the body?

Initially the drug is all in the blood and goes to 'vessel rich' organs; principally the brain. After a few minutes the drug redistributes into other tissues (fat, muscle), the concentration in the brain decreases and the patient wakes up.

Represented graphically (Fig. 17.1), there is an initial rapid fall in blood concentration, a plateau, and then a slower gradual fall. The first part is the rapid redistribution phase, the alpha phase. The plateau is the equilibrium phase (where blood concentration = tissue concentration). The slower phase, the beta phase, is the elimination phase where blood and tissue concentrations fall in tandem. This is a simple 2-compartment model. In reality most drugs are much more complicated than this.

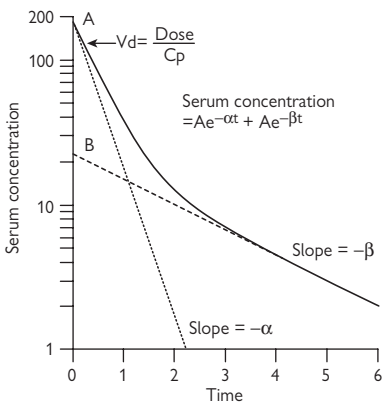

Fig. 17.1 Serum concentration vs time after IV administration. Serum concentration is graphed against time on semilogarithmic graph paper. The heavy and light dashed lines are derived as in fig 9.1. α and β are rate constants for the distribution and elimination phases of a two compartment model. V_d is calculated from the extrapolation intercept as shown. See text. (Adapted from Chernow, B., ed. 1994. *The Pharmacological Approach to the Critically Ill Patient*. 3rd edn. Williams and Wilkins, Baltimore.)

Drug metabolism and excretion

Metabolism

The major pathways involved in drug metabolism are divided into phase I (oxidation, reduction, hydrolysis, and hydration) and phase II (glucuronidation, sulphation, methylation, and acetylation) reactions. In general,

clearance of drugs is reduced in the neonatal period but for many drugs adult clearance values are reached by 2 years of age.

Phase I pathways ('activation')

The major pathway is oxidation which involves the cytochrome P450 enzymes (CYP). The major enzymes are CYP3A4 and CYP1A2.

- CYP3A4: this is responsible for the metabolism of many drugs, including midazolam, ciclosporin, and fentanyl. Activity is reduced in the neonatal period and early infancy. Enzyme activity between individuals varies considerably leading to a large range of plasma concentrations after the same dose of a drug.
- CYP1A2: caffeine and theophylline are metabolized via this pathway. Enzyme activity is reduced in the neonatal period but increases rapidly such that by the age of 6 months activity approaches that of older children and adults.

- ***Pharmocogenomics*** describes the importance of genetic factors, such as CYP enzyme activity levels, in drug handling by an individual.

Phase II pathways ('detoxification')

This involves conjugation to a water-soluble product for biliary or renal elimination. Glucuronidation and sulphation are the 2 major pathways. Glucuronidation is reduced in the neonatal period and there is compensatory sulphation. The development of glucuronidation varies for different drugs. Rates for morphine are similar for a 2-year-old and an adult whilst adult rates for paracetamol are not reached until puberty.

Excretion

Renal excretion is the major route of elimination of water-soluble metablites. Term infants handle drugs that rely on glomerular filtration rate for excretion, such as aminoglycosides, better than preterm infants. Renal tubular secretion reaches adult levels by 6 months of age, until when excretion of drugs through this process, such as penicillins and sulphonamides, will be reduced.

Lipid soluble drugs may be eliminated via the GI tract.

Applications for the intensivist

Absorption

- Slower GI transit time in the PICU patient can delay the rate of absorption of oral drugs
- Conversely the use of prokinetics may increase the rate of absorption
- Practical importance of pH which can vastly affect absorption from the stomach and excretion via the kidneys:
  - Acidic drugs are ionized when the pH is higher than their pKa—the pH at which the drug is 50% ionized. This principle can be applied in the treatment of certain overdoses, e.g. alkalizing the urine will increase the elimination of renally excreted acidic drugs

  - Increasing gastric pH with H_2 antagonists or continuous feeding will increase the ionization of acidic drugs and decrease the absorption via the stomach
  - In contrast, basic drugs will have a higher unionized portion and cross the stomach membrane into the circulation
- The PICU patient with a low cardiac output and therefore blood flow to relevant absorption sites, will have lower rates of absorption of enteral, SC, and IV drugs.

Volume of distribution (Vd)

- A small Vd means that the drug is mainly kept in the intravascular or extravascular space, whereas a large Vd signifies the drug is distributed throughout the tissues of the body
- Children have varying body composition, e.g. neonates have a higher body water content compared to adults
- Vd may be altered by fluid overload, ascities, high output drains, and drugs with a large Vd will therefore require higher doses to achieve adequate blood levels
- Vd is affected by protein binding and the tissue binding of drugs:
  - In general, acidic drugs are bound to albumin and basic drugs are bound to alpha-1 acid glycoproteins
  - Highly protein-bound drugs are mainly contained in the vascular space and have a small volume of distribution.

Metabolism

- The liver is the major source of drug metabolism, but biotransformation can occur in the intestine, kidney, and lungs
- Any orally administered drug will usually pass through the liver and may be subjected to enzymatic processes (first pass metabolism)
  - The drug may be metabolized to an active form or be transformed to an inactive form ready for elimination
  - IV and rectal routes of administration bypass the initial liver metabolism, extensively liver metabolized drugs will have vastly different IV and oral doses, e.g. propranolol.

Clearance/elimination

- The route of elimination of a drug needs to be assessed in the PICU patient:
  - If a drug is secreted into the bile as the main route of elimination but the patient has biliary obstruction then the dose must be ↓ in order to avoid toxicity
  - Conversely, if a drug is eliminated via the kidneys an increase in dose may be required in a patient with improving renal function.
- For most drugs the movement between compartments and out of the body is described by ***'first order'*** kinetics, i.e. a constant fraction of drug is removed per unit time. Therefore the amount of drug removed will depend on its serum concentration
- However in other situations drugs may display non-linear or ***'zero order'*** kinetics.

Box 17.2

Why if I have 10 pints of beer before midnight will I fail a breathalyser test at 8 am the following morning? Either this is due to alcohol having a very long half-life (which it does not) or that alcohol is cleared in a different way.

What happens is that the metabolic pathways responsible for alcohol metabolism are rapidly saturated—the metabolic pathways work to their limit. This is known as *zero order kinetics*: a constant amount of drug is eliminated per unit time rather than a constant proportion as occurs in first order kinetics.

- This form of kinetics occurs with several important drugs at high dosage concentrations: phenytoin, salicylates, theophylline, and thiopentone (at very large doses)
- For such drugs clearance decreases and the half-life increases as the dose is ↑, as the elimination route becomes saturated and cannot increase proportionately
- Careful measurement of drug levels is necessary for many drugs.

Receptor physiology

The purpose of a receptor is to receive a signal, and transduce this signal to produce an effect.

Drug + Receptor ⇆ Drug/receptor complex → Effect

Drugs are ligands which interact with receptors to produce effects:

- ***Agonists:*** interact with the receptor to produce a positive effect:
  - Not all agonists acting on the same receptor will produce the same magnitude of response—this is called *efficacy*
  - Partial agonists do not produce the full response of a 'true' agonist
- ***Antagonists:*** interact with the receptor sites to block the ligand:
  - A competitive antagonist will compete for the receptor site with the ligand, reversibly binding at the site
  - By increasing the agonist the effect can be overcome, e.g. rocuronium is a competitive antagonist for the acetylcholine receptor, by increasing the acetylcholine (the agonist), with anticholinesterases such as neostigmine, the neuromuscular blocking activity of rocuronium can be overcome
  - Non-competitive antagonist effects cannot be overcome by increasing the concentration of the agonist as they irreversibly bind to the receptor or alter the configuration of the receptor, e.g. suxamethonium is not reversed by neostigmine
- A drug's affinity for a receptor is the measure of binding to a receptor
- Continued stimulation of receptors by certain agonists, opioids, or benzodiazepines can result in desensitization (or down regulation) causing an attenuated response to the same dose.

Principles of drug administration

- Enteral dugs are to be encouraged—many common drugs used in PICU have good bioavailability when given enterally. The cost of oral dosage forms is usually a fraction of the parenteral forms as is the sequelae of drug errors.
- If the post pyloric route (jejuna feeding) is used consider:
  - Site of absorption of drug versus position end of feeding tube
  - Osmotic load/sorbitol content/volume of the liquid—administration to the jejunum may cause diarrhoea or local irritation
- The oral/enteral route is not appropriate when rapid blood levels are required; or the gut is not functioning or accessible, e.g. ileus, NEC
- The majority of drugs are given via the IV route in PICU. In the setting of fluid restriction many of the drugs require concentration. The following factors must be considered:
- Solubility of the drug: adequate dilution of the drug is required to prevent the drug coming out of solution
- Access for administration: hyperosmolar solutions or extremes of pH require central venous administration.
  - As a general rule, solutions with an osmolarity above 500mOsm/L are best not administered via a peripheral cannula
  - However, glucose 12.5%, often cited as the highest concentration of glucose to be given peripherally, has an osmolarity of 630mOsm/L.
- Drugs should only be co-infused when absolutely necessary, compatibility is known (see Fig. 17.2), and at the terminal end-site. In practice however, co-infusion is often needed
- The pharmacological action of the drug is equally as important as its chemical and physical compatibility, e.g. an inotrope should not be co-infused with a sedative which requires bolus doses to be given. This will cause a purge of the inotrope and potential haemodynamic instability to the patient.

(a) Vasoactive infusions

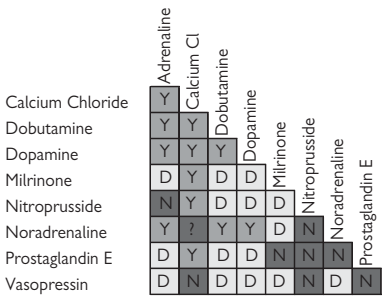

Fig. 17.2 Infusion compatibilities. Adapted from Birmingham Children's Hospital guideline 2009.

(b) Other infusions

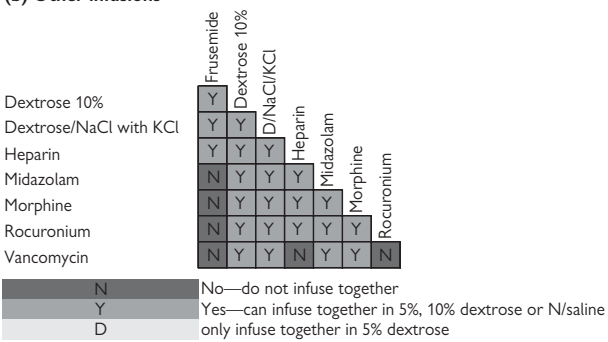

Fig. 17.2 (*Continued*)

Formulations

Solid oral dosage forms

- Tablets can be crushed or capsules opened and dispersed in a small volume of water to give a fraction
- Crushed tablets can block feeding tubes if not adequately flushed
- Accuracy of doses cannot be guaranteed by splitting of tablets
- Effervescent tablets generally contain a high content of sodium
- Lactose, used commonly as filler in tablets and capsules, is problematic in lactose intolerant patients.

Liquid dosage forms

Liquid medicines generally require higher amounts of excipient.

- Ethanol is a common vehicle used which crosses the blood–brain barrier, affects the liver enzymes, causes interactions with common PICU drugs, e.g. metronidazole
- Sugar-containing liquids can cause swings in the blood sugars of a critically ill child
- Aspartame (in sugar-free medication) is used commonly and should be avoided in phenolketonuria
- Sorbitol and mannitol can cause osmotic diarrhoea
- Propylene glycol is used as a solvent for lipid soluble drugs (for oral and parenteral dosage forms):
  - It can cause osmotic diarrhoea, and a risk of hyperosmolality
  - The WHO has set a maximum limit to the intake of propylene glycol to 25mg/kg.
- Some liquid medicines can be used for rectal administration.

Parenteral dosage forms

- Manufacturers' recommendations should be followed for reconstitution and dilution fluids to be used with parenteral injections to avoid precipitation and loss of stability

- The volume for further dilution used in PICU may vary greatly from the manufacturers' recommendations to avoid fluid overload.

Rectal dosage forms

- Suppositories are not dose flexible and should not be cut as uniformity of the drug throughout the unit cannot be guaranteed
- Lubricants used for insertion may affect the release and absorption of the drug.

Other dosage forms

- Transdermal patches may either be of a matrix or reservoir type
- The reservoir type patch should not be cut but partially covered with non-permeable membrane dressing
- With a matrix patch the dose being delivered is proportional to the surface area exposed to the skin
- Eye drops/ointments can be used for non-ocular uses, e.g. gastrostomy sites, as ear drops.

Safe prescribing

Medication errors are a significant problem in PICU and result in preventable morbidity and, occasionally, mortality. In particular 10-fold prescription and administration errors occur, especially in the very young. ***All health professionals will commit a medication error during their career.*** Drug-related errors should be monitored in all PICUs and hospitals through incident reporting and clinical governance systems. Computer-based drug management systems offer huge potential for reducing drug related errors.

Therapeutic drug monitoring

Steady state is the equilibrium that is established between the blood compartment and all the tissues of the body. Steady state is achieved after 4 or 5 half-lives. The longer the half-life, the longer it will take to reach steady state. This can be avoided by giving a large initial loading dose.

$$\text{Loading dose} = Vd \times Cpss$$

where Cpss is the blood level that is desired to produce a therapeutic effect, without toxicity.

Therapeutic drug monitoring (TDM) is of benefit when:

- There is a clinically significant correlation between serum drug concentration and the desired pharmacological effect
- A narrow therapeutic window, i.e. narrow margin between toxic effects and minimum therapeutic effects
- Pharmacological effect is not easily measurable, e.g. some anticonvulsants
- In overdoses/poisoning
- Patients with altered pharmacokinetic handling of a drug, i.e. the PICU patient
- Drug assays are accurate and the result is available in a time frame to inform further dosing.

Drug levels are usually whole serum concentrations and not the free drug fraction.
- For highly protein-bound drugs, the patient with hypoalbuminaemia may experience enhanced effects despite a normal blood level
- Therefore a drug level must be interpreted in the context of the concurrent conditions of the patient.

To ensure correct interpretation of a drug level the following is required:
- Drug dose, frequency, and route
- Drug history: was loading dose given? Is drug at steady state?
- Time sample taken relative to last dose
- Has drug had sufficient time to distribute into correct body compartments?

Box 17.3 Conditions predisposing patients to pharmacokinetic variability and therefore in need of ↑ frequency of TDM

- Fluid overload
- Dehydration
- Acute renal compromise
- Burns
- Liver failure
- Acute cardiac decomposition
- Ascities
- Cystic fibrosis
- Renal replacement therapy
- Patients with high drain losses

Key principles to remember:
- If drug elimination is a problem the same loading dose should be applied but the maintenance dose and/or frequency should be reduced
- Most TDM involves measurement of trough concentration rather than peak concentration
- Where trough levels are higher than range, the dosing interval should be ↑. In general leave the dose unchanged
- Trough levels that are lower than the therapeutic range need more frequent dosing. In general leave the dose unchanged
- A low peak concentration requires a higher dose
- A high peak concentration requires a lower dose (assumes trough level is therapeutic).

Knowledge of a drug concentration at 2 distinct time-points allows an estimation of time to next dose, i.e. when the drug concentration will reach the target trough level. This can be plotted using semi-logarithmic graph paper (Fig. 17.3).

Drug interactions

There is huge potential for drug interaction in PICU at different levels:
- Drugs competing at the receptor site:
  - Aminoglycosides potentiating reversible neuromuscular blockade (see 🕮 p.196)
- Action of 1 drug potentiating the absorption of another:
  - H_2 receptor and proton pump antagonists altering gastric pH
  - Prokinetic drugs or opiates promoting or inhibiting gastric emptying

- Drugs with opposing effects being used together:
  - Inotropes with vasoconstrictor properties alongside vasodilators
- Drugs interacting with each other affecting delivery:
  - Ceftriaxone precipitation with IV calcium.

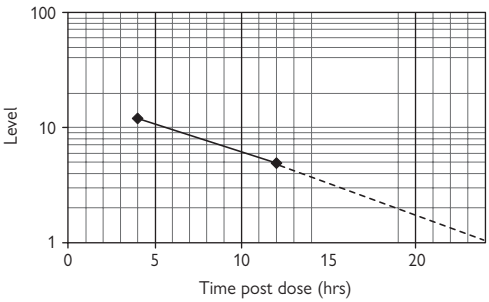

Fig. 17.3 Gentamicin level 4h post-dose of 12mg/L, with a repeat level at 12h of 4.9mg/L. Extrapolation suggests that 24-hourly dosing is appropriate for a target trough level of 1mg/L.

Adverse drug reactions

Around 1% of children in hospital will experience an adverse drug reaction (ADR). Differences in drug metabolism make certain ADRs a greater problem in children, e.g. valpraote hepatotoxicity, or less of a problem, e.g. paracetamol hepatotoxicity following overdose.

The mechanisms of ADR include:

- Impaired drug metabolism: chloramphenicol use in neonates led to the grey baby syndrome. The newborn infant metabolizes chloramphenicol more slowly than adults so a lower dose is required.
- Altered drug metabolism:
  - Children may have reduced hepatic enzyme activity. To compensate they may use other pathways
  - This is thought to be a factor in the ↑risk of hepatotoxicity of valproate in children <3 years old
  - In other children an inborn error of metabolism may potentiate toxic drug effects
- Protein displacing effect on bilirubin: the use of a sulphonamide, sulphisoxazole, in ill neonates in the 1950s was associated with the development of fatal kernicterus.
- Unknown: salicylate and Reye syndrome.

Drug considerations in renal failure

If the renal route is the primary route of clearance of a drug or its metabolites, significant changes must be made to the prescription during renal impairment.

- Plasma creatinine is the best marker of renal function—urea is less useful
- Remember that plasma creatinine is proportional to muscle mass—normal value for a neonate is <30ummol/L compared to 50–80 in an older child
- GFR can be estimated from plasma creatinine (see 🕮 p.652)
- Be aware that plasma creatinine takes time to rise after an acute insult:
  - Assume GFR is compromised in the setting of a low cardiac output
  - Poor urine output may alert you

Prior to prescribing a drug be aware of the route of drug clearance:

- Many drugs are metabolized in the liver to active metabolites that are then excreted through the kidneys—e.g. the active metabolite of morphine, morphine-6-glucuronide, is renally excreted
- Loading doses are mostly unaffected with the exception of drugs where the volume of distribution is reduced where the loading dose should be reduced, e.g. digoxin
- Single or 'stat' doses are unlikely to be problematic in renal impairment as accumulation is unlikely
- Avoid nephrotoxic drugs to prevent further decline in renal function, e.g. NSAIDs.

Antimicrobials are a particularly challenging group of drugs in the patient with impaired renal function.

- An increase in dose above the literature recommendations for that degree of renal impairment maybe required if the patient is not responding
- Aminoglycoside clearance is heavily dependent on renal function
  - Frequent drug monitoring is needed for aminoglycosides
  - In renal impairment revert to using conventional dosing schedules for gentamicin (i.e. 2.5–3.5mg/kg per dose) rather than the newer larger doses—these will produce high levels for several days after a single dose

Drug clearance on renal replacement therapy (see 🕮 p.257)

- PD clearance of drugs is not very efficient and a dose reduction or increase in dosing interval is required
- Drug clearance on CVVH or CVVHD will depend on the ultrafiltration rate employed, on the degree of protein binding of the drug (will not be filtered) and on the sieving coefficient for a particular drug
- In general terms renal replacement therapy should only be considered to be providing the equivalent of a low GFR.

Box 17.4 General rules for prescribing in renal impairment

- Medication should be reduced to a minimum
- Degree of renal impairment should be known prior to prescribing
- Nephrotoxic drugs should be avoided
- Therapeutic drug monitoring should be used where possible to adjust doses
- Dosage regimens for renal failure should be followed
- Signs of toxicity or clinical response should be monitored
- Doses should be re-adjusted as the renal function improves.
- ***Involve a pharmacist!***

Drug considerations in liver disease

The liver is a major site for drug metabolism. Liver disease will affect drug handling in different ways. Drug handling does not readily correlate with traditional liver function tests. Each drug must be looked at individually and in the context of the liver condition affecting the patient.

- Prothrombin (PT) and albumin are the main markers used to reflect hepatic synthesis of the enzymes required for drug metabolism—if these are not synthesized then the enzymes required for drug metabolism are less likely to be fully synthesized or functioning
- Liver blood flow is related to hepatic drug clearance: the greater the flow the more drug that is metabolized—drugs with a high first pass hepatic metabolism are vastly affected by changes in hepatic blood flow
- Drugs that require biotransformation to the active form will have a lower therapeutic response if there is low hepatic blood flow or if the PT and/or albumin are low
- Drugs that are excreted in bile should be avoided in patients with choleastatic jaundice—drugs which are usually absorbed via an enterohepatic recirculation process will show an attenuated response in the patient with impaired bile flow
- Drugs with side effects of bleeding, sedation, itching, hepatoxocity, sodium or water retention should be avoided in severe liver failure as the effects will be enhanced or mask symptoms in the patient.

Dose titration in liver disease

- Drugs with extensive first pass metabolism will require a dose reduction when hepatic blood flow is low, and in the patient with low albumin and elevated PT—consider 50% reduction in dose
- Drugs that are not affected extensively by first pass metabolism but are liver metabolized will required a dose reduction but less than that for high clearance drugs—consider 25% reduction in dose
- Drug levels should be taken more frequently where possible
- Consult a paediatric pharmacist for advice.

Drug considerations in patients on extracorporeal circuits

Continuous renal replacement therapy (CRRT)

Ideally pharmacokinetic studies should be used to guide dosing regimens. However, many drugs have not been studied and drug parameters must be used to estimate clearance and adjust drug dose and interval

Box 17.5 Drug factors favouring removal by CRRT

- Low protein binding
- Molecular size under 1500 daltons
- Small Vd
- High sieving coefficient (~1)
- Anionic drug.

CVVH clearance = sieving coefficient × ultrafiltration rate

- Drugs may be adsorbed onto the filter
- Inotropes, sedation/analgesia, etc. should be titrated according to clinical effect
- Take levels frequently for a drug with a narrow therapeutic index, and dosage regimens should be followed where available
- In the patient on parenteral nutrition increase the protein/amino acid content to take account of filtration losses
- If CRRT indication is acute renal impairment, on stopping CRRT consider whether further dose adjustments are required according to the degree of renal impairment.

Extracoporeal membrane oxygenation (ECMO)

- Little is known about the effect of ECMO on drugs. From the drugs that have been studied it is believed that the half-life and volume of distribution of certain drugs are ↑
- Coexisting renal and/or liver dysfunction will have additional effects
- Drugs can adhere to the circuit components
- As there can be a large volume of blood in circuit, a high proportion of the drug may be lost when circuits are changed
- As with CRRT, drug levels should be used where possible to guide the dosing regimens.

Chapter 18

Transport and retrieval

Introduction

↑centralization of paediatric and neonatal intensive care services means that children with acute injuries and illnesses may present to hospitals that do not have the facilities or skills to maintain intensive care for them. Such patients need to be transferred to intensive care.

In the past, this transfer was undertaken in an ad hoc manner, sometimes by poorly trained staff with inadequate equipment. Patients transported by non-specialist teams suffer an ↑number of avoidable insults.

Patient transport and retrieval is therefore best undertaken by trained and appropriately skilled personnel using dedicated equipment. This may be organized as a stand-alone retrieval service, or one integrated with a PICU.

The principles outlined in this chapter are relevant to both inter-hospital transfers, and to the movement of patients within the same hospital (for example, taking a child from PICU to CT scan). See Table 18.1.

Table 18.1 Transfer types

	Advantages	Disadvantages
One way (patient delivered by referrer)	• May save time • Fewer resources used • Cheap	• Equipment may be inadequate and personnel inexperienced • Base hospital staffing compromised
Two way (patient fetched by receiving team)	• Experienced team • Dedicated equipment • Back up and support	• More expensive • May take longer
Time critical (patient in need of urgent therapy)	• Quickest way to get patient to life saving therapy (i.e. neurosurgery)	• See 'one way transport'
Back transport (patient returned to referring centre after PICU care)	• Frees up PICU bed once patient no longer needs it • Easier for families	• If using full PICU team—expensive • If using referring staff, see 'one way transport'

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The aim of a retrieval service is to commence intensive care as soon as possible, and to continue intensive care until the patient is delivered to an appropriate facility.

Retrieval personnel need the appropriate knowledge and skills to achieve this in the difficult transport environment. The retrieval service establishes the guidelines, policies, and environment in which to facilitate this goal.

Organization of the retrieval service

Retrieval teams are most commonly based on an existing ICU. This provides a body of staff to undertake the retrieval, and allows retrieval staff to support the unit if the retrieval service is not busy.

'Attached' teams also provide continuity of care for the patient, and provide a consistency of approach that stand-alone teams do not. However, taking the retrieval personnel from the ICU may compromise the care of other patients, and the ICU is likely to be busy at the same time of year that inter-hospital retrievals are most needed.

Stand-alone retrieval teams serve a geographical area or number of ICUs and referring centres. They require a minimum number of referrals to remain clinically competent and cost-effective. If this is achieved, the normally small size and 'espirit du corps' of such teams makes skills training and competency retention easier, and such teams can be very effective.

In practice, most 'stand-alone' teams have a close relationship with a small number of PICUs from which they draw their staff on rotation, and with whom they align their policies and guidelines. Teams must ensure that such relationships do not promote inappropriate rivalry and perceptions of elitism from referring hospitals and other ICUs.

Setting up a retrieval service

Retrieval services begin *before* the first telephone call. In setting up a service consider:

- Communication:
  - Liaise with local service providers (both referring centres and local PICUs) and with ambulance services
  - If aeromedical retrievals are likely, appropriate providers need to be approached
  - Advertise widely: details of the service in areas likely to use it—i.e. paediatric wards, emergency departments, neonatal units, outreach care teams (📖 p.35).
- How will people contact the retrieval team?
  - Call centre: dedicated personnel to screen and direct referrers to the most appropriate people. Requires a large volume of referrals to be cost-effective. May handle calls to different teams (ie.. paediatric and neonatal)
  - 'Hot line' on PICU: should be direct to the ICU, rather than switchboard; dedicated to incoming retrieval calls only; accessible to the unit; appropriate paperwork (retrieval forms etc) to hand; well advertised
  - Via the PICU or the PICU registrar: risk of calls getting put on hold, or directed to the wrong person.

Personnel

- Staff need to be selected to oversee the work of the retrieval team (medical and nursing leads) and to undertake the retrievals. As this is often done by trainees, local postgraduate medical education authorities may need to be involved in approving posts
- Nursing staff need to be selected and trained

- The appropriate ancillary and support personnel need to be found
- Training, competency attainment and audit/review systems need to be put in place.

Good personnel are the most valuable part of a transport team.

Safety (see Box 18.1)

- Transfers are high-risk activities for the patient and the team
- Risks of transfer include:
  - Deranged physiology worsened by movement, leading to cardiorespiratory instability
  - Cramped conditions, unfamiliar environment and equipment, professional isolation, temperature, and pressure changes
  - Road traffic accidents involving the ambulance
  - Equipment or resource failure or exhaustion.

Box 18.1 Safety considerations

- Organizational considerations:
  - Clinical protocols
  - Operational protocols and checklists
  - Regular team training
  - Audit and clinical incident monitoring
  - Insurance
- Passenger safety:
  - Passengers must wear seat belts
  - All equipment must be secured
  - Loose objects must be strapped down
  - The ambulance should obey speed restrictions and traffic signs unless there are (rarely) compelling clinical reasons not to
- Patient safety:
  - Pre-departure stabilization and checklist
  - Crash chart
  - Careful monitoring and appropriate intervention throughout
  - The patient must be secured on the trolley or incubator
- Team safety:
  - Team members must wear seat belts
  - The ambulance should stop before team members undertake patient interventions if possible
  - Warm clothing, drinks and snacks, money for emergencies.

Equipment (see Box 18.2)

- Dedicated equipment needed, selected on the basis of the needs of the anticipated population
- Carry all the equipment you are likely to need—do not rely on the referring hospital's supplies
- Equipment bags must be replenished and checked after each retrieval.

Box 18.2 Typical equipment required during transport

- Patient movement:
  - Trolley
  - Incubator for children <5kg
  - System to secure ventilator, pumps, monitors
  - Safety system to secure patient in transfer
  - Equipment bags
  - Multiple compartments to allow access to individual items without unpacking
  - Drug boxes
- Airway management:
  - Equipment to establish and maintain a secure airway
  - Bag-valve device with selected mask sizes
  - ETTs (appropriate sizes), stylet, and Magil forceps
  - Laryngoscopes with appropriate size blades, spare batteries, and bulbs
- Transport ventilator:
  - Small, lightweight, with economical gas usage
  - Capable of ventilating infants and children of all ages
  - Disconnection and high-pressure alarms essential
  - Providing PEEP, facilities for variable FiO_2, I:E ratio, RR, and V_T.
- Portable oxygen supply:
  - Provide high-pressure supply with low-pressure metered flow
  - Sufficient to last twice anticipated duration of transfer
- Suction: portable, battery powered ideally
- IV infusions:
  - Equipment to establish and maintain venous and arterial access
  - Drugs
  - Resuscitation drugs
  - Infusions of sedating and paralysing agents (for ventilated patients)
  - Inotropic infusions
  - Infusion pumps: small, lightweight, long battery life
- Monitoring:
  - Portable, battery powered, monitor, clear illuminated display
  - ECG, oximetry, non-invasive BP, temperature, capnography
  - Invasive channels (preferably 2) for CVP and invasive BP
  - Alarms must be *visible* as well as audible because of extraneous noises
- Document folder:
  - Recording chart, audit form, consent form
  - Infusion charts and crash drug charts—filled in prior to transfer
  - Information for parents, i.e. maps and telephone numbers
- Mobile telephone
- Warm protective clothing for staff.

Members of the retrieval service

The service is normally led by medical and nursing directors, supported by transport fellows and nurses, technical support staff, pilots and drivers, and administrative staff (Box 18.3).

Box 18.3 Typical background and responsibilities of retrieval team members

Medical Director (Typically PICU, NICU, A&E consultant)
- Develop policies and protocols
- Review/approve equipment and medication lists
- Establish and implement outreach programmes
- Review transport cases
- Manage quality improvement programmes.

Retrieval Coordinator (Senior nurse)
- Develop policies and protocols
- Develop/approve equipment and medication lists
- Establish and implement outreach programmes
- Local liaison (e.g. ambulance) and local training
- Review transport cases
- Collect transport data (audit)
- Manage quality improvement programmes
- Budget management.

Transport fellows and nurses
- Experienced in PICU or NICU
- Seniority
- PICU/NICU and resuscitation training
- Availability 24/7
- Competences:
  - Procedural competence to operate independently
  - Operate transport equipment
  - Understand limits of equipment
  - Know supplies.

Tasks
- Nursing and medical care of patient during transport
- Liaison with staff at referring hospital
- Advise about treatment
- Assess need for other specialists e.g. surgeons
- Assess and monitor child's condition
- Keep family informed
- Inpatient care after transfer
- Check and restock kit.

Paramedics/drivers/pilots
- 'Team members'
- Understand needs on call-out.
- Involved in team training
- May need training/skills in PICU/NICU care
- Input into equipment development.

Many of these tasks will vary within different teams according to local custom and practice. Traditional professional boundaries are often crossed in retrievals, and good team members will interchange roles as necessary.

Retrieval team composition

For a particular retrieval this depends on a number of factors:

- Patient's perceived condition:
  - Often difficult to assess over the telephone
  - Anticipate a more rather than a less serious scenario
  - Easier to tell if you know and have an established relationship with the referring team
  - Specific factors may require a team with specific skills (i.e. the child with a known difficult airway)
- Experience of medical and nursing staff:
  - Trainees need to undertake preceptored practice with trainer
  - Consider skill mix of team as a whole—pair junior fellows with senior nurses and vice versa
  - Difficult patients may need 2 experienced medics or nurses, or a combination of skills (i.e. PICU and ENT consultants for a difficult airway)
  - Utilize learning opportunities—take additional trainee for difficult or unusual cases.
  - Nurse-led retrievals
- Staffing practicalities:
  - Time of day.
  - Current staffing levels
  - Patient dependencies and staff skill mix on PICU (for integrated teams)
  - May be necessary to wait for the next shift to come on
- Mode of travel:
  - Special skills and training needed for aeromedical retrievals (see 🕮 p.326).

The retrieval process

Retrievals begin with the first telephone call. From that moment, you have a responsibility to the patient and the referring team.

Triage of referrals

- Obtain the best information available about the patient
- Normally this will mean consultant to consultant referral. In practice the referrer needs to be of sufficient seniority to give a succinct and relevant history, and to act upon requests and suggestions from the retrieval team
- The person taking the call needs to be of sufficient seniority to determine if the patient can be accepted and to give appropriate advice on patient management
- Some teams use a call centre where an administrative assistant takes the initial details, locates a suitable bed, and coordinates a conference call between the referring team, the receiving PICU, and the retrieval consultant. This also allows other experts (such as neurosurgeons) to be included in management discussions.

Determine in the first 2 sentences the patient's current status and what the caller wants from the retrieval team.

There is nothing more frustrating for a referring clinician than spending 10min giving a detailed history to the PICU, only to be told that they have no bed and can't help to take the child anywhere else!

Decide if a retrieval is necessary and possible

- If not, why not?
  - No bed
  - No retrieval team
  - Inappropriate referral (for PICU in general, or for your PICU in particular?)
- Will the situation change in a few hours?
- What are the referring team's options?
  - Is there an alternative PICU? Who calls them? Can the alternative unit collect the patient? Can you deliver the patient from the referring unit to the alternative PICU?
- If a retrieval is necessary and possible, decide:
  - How urgent is the transfer?
  - Is the child in the optimal condition for transfer?
  - Does the benefit of transfer outweigh the risks involved?
  - Who are the most appropriate people to transfer this child?
  - What type and mode of transfer is required for this child?

Document all communication with referring teams and all advice given, even if you cannot take the patient.

Advise on further management

- Give appropriate advice to the referring team to help them resuscitate and stabilize the child

- Resuscitation is the responsibility of the referring team, and urgent interventions that need doing should not be delayed just because the transport team is 'on the way'
- Remember that the referring team may be less experienced at certain interventions, and what seems routine on PICU may be difficult in the referring hospital
- Be prepared to fax or email protocols, and drug or infusion guidelines
- The level of care required may be different for a child undergoing transfer than for a child staying where they are:
  - For instance, a child on CPAP may need to be intubated semi-electively, rather than risking deterioration and emergency intubation in the ambulance
  - The referring team may be able to undertake some of these interventions
- Ask the referring team to prepare photocopies of the notes and copies of X-rays etc., stop feeds, obtain a cross match sample from mother (in the case of neonates).

Activate the retrieval team

- Essential information:
  - Where is the patient (which hospital, which department, which entrance to get in)?
  - What is the required response time?
  - Are there any special considerations?
  - Is a specific type of ambulance needed for the transport equipment?
- Mode of transport:
  - Depends upon geography, distance, priority, and availability
  - Air retrievals considered if road transport time >2h
  - Remember that intervention may be impossible in some helicopter transfers
  - Bad weather may preclude air transfer
- Preparation:
  - Equipment—fully charged and working
  - Sufficient gas supplies for twice the anticipated retrieval time
  - Drugs—appropriate for the retrieval
  - Fluid—adequate amounts and type
  - Team—fed and watered
  - Mobile phone.

Stabilization

- Focuses on an 'ABC' approach
- Before transfer, patients must have:
  - Stable airway
  - Adequate ventilation
  - Adequate circulation
  - Sufficient vascular access (normally at least 2 IV lines)
  - Appropriate monitoring
- Time spent stabilizing the patient reduces instability and physiological deterioration during a transfer (Box 18.4).

Box 18.4

Always stabilize the patient before transfer, unless:

- There is nothing you can do to improve the patient's condition
- The benefits of treatments available on PICU outweigh the risks of transfer—the parents are fully aware of the risks and benefits of transfer

However, this is not an excuse to transfer patients without

- An adequate airway
- Good ventilation and a well filled circulation
- Adequate vascular access.

Packaging

- Secure all arterial and venous access
- Attach chest drains to Heimlich (flutter) valves
- Place NG tube on free drainage
- Identify one reliable secure site of IV access— attach long extension so that you can bolus dugs/fluids without having to expose patient
- Have drugs and fluids that might be needed drawn up (volume, inotropes, arrest drugs)
- Secure patient to trolley or in incubator
- Assign one person to do nothing other than watch the monitor and patient during loading/unloading
- Secure trolley to vehicle.
- See Box 18.5 for departure checklist.

Box 18.5 Checklist for departure

A: airway	• Is the airway secure? If in doubt, intubate • Do you need c-spine control?
B: breathing	• Stabilize patient on the transport ventilator • Check blood gases before departure • Self-inflating bag-valve-mask in the event of a ventilator/gas failure • Suction • Adequate sedation, analgesia, and muscle relaxants • Adequate gas reserves • Insert a chest drain if there is a possibility of a pneumothorax (especially for air transfers) • Insert a NG tube if ventilated.
C: circulation	• Stable circulation with good access • Any bleeding areas controlled • Invasive BP and CVP, when indicated • Inotropes—if in doubt have them prepared and ready to run • Do you have enough pumps and are they fully charged? • Insert a urinary catheter and monitor urine output.

Box 18.5 Checklist for departure (*Continued*)

D: disability	• Pupillary signs • Fits, posturing • Glucose and calcium
E: exposure	• Hypo- or hyperthermia • Warmed incubator and ambulance, activate heating blanket if appropriate. Place hat on patient.
F: finally, don't forget	• All notes, referral letter, results, X-rays • Maternal blood and blood products, if appropriate • Call home just before leaving the referring hospital with a rough ETA • Inform relatives and take contact numbers • Take warm clothing, mobile phone, food, and credit card/money for emergencies • Plan for the return journey.

- Continue care during transfer:
  - Regular observations
  - Note effect of acceleration/deceleration
  - Note trends in vital signs—intervene early
- If you need to undertake interventions during transfer:
  - Stop the vehicle if safe to do so
  - Assess the patient and treat as necessary
  - No interventions in a moving ambulance
- Drive at normal road speed, obeying traffic signs and signals:
  - There is a significant increase in the risk of a motor vehicle accident whilst driving on 'lights and sirens', whilst crossing intersections, and at night
  - 'Lights and sirens' should only be used to get through static traffic, not to go faster
  - Retrievals are different in this respect from primary transport (from the scene of an accident, for instance) or where the patient is being transferred for an urgent or definitive treatment.

Speed kills—even in an ambulance.

Arrival at PICU

- Handover at receiving hospital:
  - Time critical retrievals need a rapid handover and immediate move to the therapeutic intervention
  - Others need a more detailed handover initially – Patient history, interventions, progress, management and observations by the transport team, details of parents, including what has been said to them
- Notify referring hospital of safe arrival
- Notify parents of safe arrival if not accompanying or already on their way
- Clean and pack away kit
- Complete paperwork
- Debrief within team, critical incident forms if appropriate
- Identify topics for training, feedback, and outreach education.

Dealing with parents

It may be your 4th retrieval of the week, but for the parents and family of the child, the situation is a unique, unforeseen crisis of immeasurable proportions. Your dramatic arrival, the physical appearance of the child, and the severity of the illness all heighten the parents' feelings that the child is in imminent danger.

- Parents may exhibit a grief reaction, manifest as feelings of shock and disbelief, accompanied by helplessness
- Coping mechanisms at this stage may include aggression, regression, withdrawal, or repression. Your response to these must enhance the parents' coping strategy
- Parents need information about their child, and reassurance that the retrieval team care for the child as an individual in his or her own right.
  - Take time to speak to the parents in private
  - Make sure that you know the child's name, and give the parents the opportunity to express their fears and ask questions
  - Give the most important information first, and summarize it at the end of the discussion
  - Be realistic and do not be afraid to say that you do not know the answers to certain questions
  - Be careful not to undermine the care given by the team at the referring hospital
- Allow parents to be with their child during the stabilization phase.
  - Loss of physical control for the child's well-being is a major stress for the parents
  - Other major stresses are seeing the child in pain or frightened, seeing the child unable to communicate, and not knowing how best to protect the child
- In many cases, it is not possible for the parents to travel with the child on the return journey to the ICU
  - This is a major source of stress for the parents, who often report feeling that they will never see their child alive again
  - Serious consideration should be made to allow parents to travel in the ambulance with the child if at all possible
  - If not, separate transport should be arranged, or parents should be given specific directions to the hospital, information on parking and directions to get to the ICU.

Transport physiology

Acceleration and deceleration

- Rapid acceleration and deceleration alter cardiac output
- If the patient is lying with their head towards the direction of travel, an acceleration causes venous pooling in the legs and ↓cardiac output
- Baroreceptor-induced vasoconstriction normally ↑systemic vascular resistance, maintaining arterial pressure, but this response is obtunded in children with hypovolaemia, septicaemia or CNS injury
- Deceleration ↑venous return and ↑ICP

- Acceleration and deceleration also affect lung volume by shifting abdominal contents towards the head (reducing lung volume) and by altering V:Q ratios
- NB: sharp braking in ambulance may give a G-force of >7.0!!
- Minimizing affects of movement:
  - Sympathetic driver
  - Position patient across vehicle if possible (rarely possible!)
  - Fluid resuscitation before departure
  - Inotropes/vasoconstrictors should be started early.

Noise and vibration

- Excessive ambient noise:
  - Makes communication difficult and tiring
  - Auscultation with a stethoscope is usually impossible
  - Detection of auditory alarms is inhibited
  - Helmets and ear defenders should be worn in helicopters
  - Ear defenders should be worn by patients where practical
- Vibration:
  - Vehicles transmit vibration to passengers, exacerbating motion sickness
  - Impairs coordination and interferes with the vestibulo-occular and pursuit reflexes, which are important when trying to visualize a monitor display
  - Children with fractures may require additional analgesia
  - Malfunction of pulse oximeter and NIBP
  - Causes displacement of tracheal tubes, chest drains, and venous and arterial cannulae.

Motion sickness

- Caused by the mismatch of afferent visual and vestibular information
- Exacerbated by excessive head movement and reading in transit
- Potentially incapacitating!!
  - Nausea and vomiting—incidence up to 50%
  - 'Sopite syndrome': drowsiness, yawning, ↓mental agility, disinclination to work— incidence up to 100%!
- Antiemetics are generally an effective treatment, but avoid those that also cause sedation.

Temperature changes

- Patients may suffer from heat stress during transfer:
  - Hypothermia most common (see Box 18.6)
  - Hyperthermia due to high environmental temperature and packaging (i.e. vacuum mattress)
  - Monitor temperature continuously.
- Ambulance heating systems are variable. Ensure that the vehicle is warm before the patient gets in to it
- In aeromedical transfers, atmospheric temperature falls by 2°C per 1000 ft of ascent—ensure patient and staff are adequately insulated.

Box 18.6 Heat loss

Heat loss occurs by 4 main mechanisms, and each is accentuated as patient size is reduced:

- By *radiation* to cooler surrounding objects such as ambulance walls and windows. When you are nearly ready to leave the referring hospital, ask the ambulance crew to warm the ambulance up prior to loading the child
- By *conduction* directly from the patient to cold objects placed in contact, such as cold blankets. Transport incubators and blankets should be pre-warmed before use
- By *convection* when cool air flows across the child, for instance when incubator portholes are open, or when the ambulance doors are opened
- By *evaporation* either from the skin, especially in very premature neonates, or from the respiratory tract.

The ambulance environment

Retrieval teams may use a variety of vehicles, including 'rapid response' cars, dedicated retrieval ambulances (Box 18.7), or emergency ambulances used on an ad hoc basis.

Design considerations for intensive care ambulances (from Intensive Care Society, 2002, London UK):

- The vehicle must:
  - Be driven by suitably trained personnel
  - Be able to carry up to 4 members of hospital staff in addition to ambulance crew
  - Staff seats should ideally be rear or forward facing (not side facing)
  - Seats should be fitted with head restraints and seat belts
  - Ramp, winch, or lift system for loading the transport trolley or incubator
  - Patient trolley should ideally be centrally mounted allowing all round patient access
  - Give a stable comfortable ride with minimal noise and vibration levels
  - Have regular service and maintenance contracts
- Ambulance should have a standard 12V DC supply. In addition:
  - 240V 50Hz AC power supply from an inverter or generator sufficient to power a portable ventilator, monitor, infusion pumps, and incubator where appropriate are essential
  - Minimum of two F-size oxygen cylinders in secure housings (the retrieval team must ensure there is sufficient oxygen for twice the anticipated journey)
  - Manifold system with automatic cylinder change over, and audible oxygen supply failure alarm
  - Minimum of 2 wall-mounted outlet valves for oxygen—oxygen concentrators may be an alternative
  - Medical air supply is also desirable, especially for neonatal transfers
  - Adequate lighting, heating, air conditioning, and humidity control.

Box 18.7 Use of a dedicated retrieval ambulance

Advantages

- The vehicle is optimally configured for the transport equipment
- Gas supplies can be ↑ and adapted to the team's needs
- Power supply may be optimized
- Clinical supplies may be stored on the vehicle
- Staff are familiar with the vehicle and its layout
- Reduces reliance on 'front line' ambulances, whose primary purpose is responding to calls from the public.

Disadvantages

- Cost
- Reliance—if the vehicle is broken or being serviced
- Needs a dedicated crew
- May not be the best use of resources, depending on size of retrieval team.

Equipment and monitoring

- Equipment must be:
  - Appropriate and dedicated for transport use
  - Light and easily mobile
  - Secure on the incubator or trolley
  - Robust
  - Have a clear display
  - Familiar and easy to use
  - Suitable for all ages transferred
  - Easy to maintain and cheap to replace
- Power:
  - Most equipment has internal rechargeable batteries
  - Ensure equipment is fully charged before leaving, and is put back on charge after each retrieval
  - Always use external sources of power (ward, ambulance) where these are available
- Gas supply:
  - Compressed gases are a very precious resource. Whenever you can, plug in to someone else's
  - Always make sure you have sufficient gas to cover twice the anticipated journey
  - Make sure you know where the cylinders are on the retrieval trolley and in the ambulance, and how to change an empty cylinder
  - Monitor cylinder contents frequently during a retrieval
  - Cylinders must be secured in the ambulance
  - The content and volume of a cylinder when full is printed on the neck 'collar'
  - Size 'F': 1360L; size 'E': 680L; size 'HX': 2300L
  - Air supply may be obtained from the surrounding atmosphere by entrainment; from air cylinders, or from compressors.

► Don't forget that if you change ventilation mode (i.e. hand bagging the patient), your oxygen consumption (Box 18.8) will also change.

Box 18.8 Oxygen supply

- The oxygen requirements (in litres) of a patient can be estimated from the formula:

  Flow required (L/min) × FiO_2 × estimated journey time (min) × 2
- How long a cylinder will last can be estimated from the formula:

  Cylinder contents (L) / gas consumption (L/min)
- The amount of oxygen available in a cylinder can be estimated from the cylinder pressure:

  [Cylinder pressure (psi) × 0.3) / flow required (L/min)] = Minutes of oxygen available

► Some ventilators have a fixed gas consumption (i.e. Babylog ~10L/min) whilst others vary their gas consumption dependent on the minute volume of the patient.

► Suction equipment may also use the gas supply, and if left on (accidently or, for instance, for a replogle tube) can rapidly deplete gas supplies.

- Humidification:
  - Frequently overlooked during transfer
  - Important to prevent airway damage from desiccation, and airway blockage from dried secretions
  - Disposable heat and moisture exchangers are commonly used, but may increase dead space (and hence $PaCO_2$)
  - Heated water humidifiers are rarely used as they consume power and are easy to spill
- Ventilators:
  - Most commonly gas powered
  - Driven by oxygen and air supply (FiO_2 0.21–1.0), or oxygen plus air entrainment (FiO_2 0.5–1.0)
  - Flow chopping (no flow during expiration, difficult for patient to breathe above ventilator) or continuous flow (uses more gas)
  - Requirements depend on anticipated patient population. Ventilator must:
    —provide IMV and SIMV
    —deliver variable tidal volume and/or variable pressure
    —have an adjustable rate and Ti
    —have visual and audible 'Disconnect' and low/high pressure alarms
    —provide PEEP (appropriate level for patient population)
    —have an airway pressure monitor
    —be cheap, light, robust
- Suction equipment:
  - Electrical or gas powered
  - ⚠ Gas powered systems may deplete gas supplies

- Infusion pumps:
  - Syringe or infusion pumps should be used as gravity-fed drips may be unreliable when moving
  - Pumps should be sited below the level of the patient and be fitted with anti-siphon devices
  - Must have accurate delivery rates within the anticipated range; end of infusion alarms, long battery life
  - Carry at least 6, more may be required depending on anticipated needs of patient
  - Consider which drugs can be given by intermittent bolus, and keeping 1 infusion pump 'spare' if transporting a patient with a critical infusion (prostaglandin, inotropes)
- Defibrillators:
  - Should not be used in the moving vehicle
  - 'Hands-free' systems should be used
  - Automatic external defibrillators are not appropriate for children <1 year of age. Energy attenuating pads should be used in children 1–8 years of age
- Incubators:
  - Small or premature infants <5kg, limited by size of child
  - Controlled thermal environment
  - Compact
  - Confined working environment
  - Large power consumption
- Trolley:
  - Dedicated/ambulance trolley
  - Children >5kg
  - Larger working area, better accessibility
  - Needs safety harness
  - Poor thermal regulation
  - May be problems with ambulance compatibility
- Monitoring:—minimum standards of monitoring include:
  - Continuous presence of appropriately trained staff
  - ECG
  - Non-invasive BP
  - SaO_2
  - $EtCO_2$ in ventilated patients
  - Temperature (preferably core and peripheral)
  - Aim for the same level of monitoring that you would use if the patient was on your unit.

Air transport

- Can greatly reduce transport times compared to ground transfer
- Useful when large distances or difficult terrain are encountered
- Also when specialist treatment such as neurosurgery or ECMO is required urgently
- Air transport is generally considered if the estimated ground transfer time exceeds 2h.

Altitude physiology

Barometric pressure falls with altitude gain. This leads to:

- Reduction in oxygen tension:
  - Oxygen tension falls with altitude (see Table 18.2), and can be calculated from the alveolar gas equation (📖 p.114):

$$PAO_2 = (BP - PH_2O) \times (FiO_2 - (PCO_2 \times 1/R)$$

  - Where BP is the barometric pressure, and R the respiratory quotient
  - 'Pressurized' aircraft are normally only pressurized to ~ 2500m, and an oxygen concentration of 30% is needed to maintain inspired PO_2 at the same level as on the ground
  - In practice, the detrimental effects of hypobaria are limited by the pressurization of the aircraft, the fact that unpressurized aircraft do not normally fly very high, and the awareness of the retrieval team
  - Problems may occur in the sickest patients (i.e. already receiving 100% oxygen at sea level), or if the geography of an area means that substantial ascent needs to be made.

Table 18.2 The effect of increasing altitude on alveolar PO_2

PCO_2 (kPa)	PAO_2 (kPa) (assuming FiO_2 = 0.21)		PAO_2 (kPa) (assuming FiO_2 = 1.0)	
	At 760mmHg	At 500mmHg	At 760mmHg	At 500mmHg
2.5	16.5	10	91.2	66
5.3	13.2	6.5	88	64
8	10	3.3	66	61

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- Expansion of gas filled spaces
  - Boyle's law states that volume is inversely proportional to pressure; so as pressure goes down, volume goes up (see Table 18.3)
  - Enclosed gas filled spaces expand
  - This can cause a small undrained pneumothorax to become a large tension pneumothorax. Pneumothoraces should be drained prior to undertaking an air retrieval
  - Air in the stomach will expand and may interfere with ventilation or predispose to vomiting and aspiration. It should be drained with a nasogastric tube left on free drainage
  - BP cuffs and air-filled bandages or splints may also be affected and should be loosened

- ETT cuffs will also expand and should be deflated or filled with an appropriate volume of saline instead of air
- On descent, Eustachian tube dysfunction may be a cause of severe earache and sinus pain.

Table 18.3 Barometric pressure and approximate gas volumes at different altitudes

Altitude (m)	Barometric pressure (mmHg)	Atmospheres	Relative volume
Sea level	760	1.0	1.0
1500 (unpressurized aircraft may fly at this altitude)	630	0.83	1.2
2500 (commercial aircraft pressurized to this altitude)	560	0.77	1.3
5000	380	0.5	2.0

Equipment

See 🕮 p.323.

The following issues should also be considered in aeromedical transfers:

- Weight and compatibility
- Power and batteries
- Gas must be stowed securely but be accessible if needed
- Vibration
- Safety: aviation approved electronic devices only should be used
- All equipment must be appropriately stowed and restrained.

Choice of aircraft

Both fixed wing and rotary wing aircraft (helicopters) may be used for air transport. For longer journeys (flying time >3h) or over water, fixed wing aircraft are preferred.

- Helicopters:
  - Usually unpressurized
  - Relatively slow: Sea King cruising speed 100 knots; other air ambulance helicopters up to 160 knots
  - Able to land near or at the hospitals at both ends, so often faster than fixed wing aircraft for short journeys
  - May be cramped and limited access to the patient, making intervention difficult
  - Noise makes communication difficult, reduces effects of alarms (must be visual and audible). Staff need to actively listen for alarms
  - Vibration: affects performance and exacerbates motion sickness; children with fractures may require additional analgesia; malfunction of pulse oximeter and NIBP; causes displacement of tracheal tubes, chest drains, and venous and arterial cannulae

- Extreme cold, especially in winter
- High winds may preclude helicopter use
- Ideally the aircraft will take off and land from a landing ground approved for helicopter use adjacent to the hospital. If an impromptu landing area is being used, the transport team should wait 50–100m from the edge of the landing ground until the helicopter has landed. The loadmaster will usually leave the aircraft and instruct the transport team how to proceed
- Helicopters should only be approached from the front in order to avoid the tail rotor (Box 18.9). Smaller helicopters also pose a hazard from the main rotor

Box 18.9 Approaching the helicopter

- Do not go under the rotors until clearly beckoned (or thumbs up)
- Usually the loadmaster (winchman) will come out to you
- In the Sea King, the starboard (rear) cabin door is used for stretchers
- The port (front) door—which has steps—may be used for walking passengers
- Remember that the pilot is still 'flying' the aircraft while still on the ground (unless the rotor has stopped)
- ***Never*** go around the back of the helicopter—touching the tail rotor will kill you
- When ready (loadmaster's decision), with no loose articles, walk—don't run—to the door and load.

- Fixed wing aircraft:
  - May be pressurized
  - Relatively fast air-speed, but long set up times and transfer to/from airport mean that overall, fixed wing retrievals may take longer
  - Use of airports means that multiple load/unloads are needed (hospital to ambulance to aircraft to ambulance to hospital)
  - May be cramped and limited access to the patient
  - Narrow doors may make loading/unloading a trolley/incubator difficult
  - Less noise and vibration than a helicopter, but these can still be a problem.

What to do when it all goes wrong

Inappropriate referrals

- There will be a small minority of referrals where the child does not appear to be 'sick enough' for ICU:
  - Ascertain that you have recorded the history accurately
  - Determine precisely what is giving the referring team concern
  - Is the referring physician of appropriate experience to assess the child? Referrals should ideally be made at consultant level
  - Maintain communication with the referring clinicians, whether or not the child is accepted for intensive care
- Referrals from a 2nd source—i.e. a plastic surgery registrar who accepts a child with burns and who then phones the PICU 'for a bed'—should be discouraged, as there is no opportunity to give advice on stabilizing the child, and important details may be lost or forgotten. The clinicians actually caring for the child at the time of the referral should be contacted for information directly.

Unsalvageable child

Occasionally you will arrive at the referring hospital to find that the patient has deteriorated and is now clearly not going to survive.

- Make a full assessment and aggressively treat immediately remediable problems
- Discuss the situation with base, the referring clinicians, and the parents. Their expectations will guide you
- The situation may be different if the child is referred to a specialist centre, i.e. for ECMO or neurosurgery, where specialist intervention may be life saving
- The potential for organ donation should not be forgotten. If organ donation is a possibility, intensive care will need to be continued.

Death in transit

- This is rare, although there is only anecdotal data on its incidence
- If the child dies in the back of the ambulance, it is best to go to wherever the parents are. If the parents are already on their way to your ICU, you should probably continue there to be with the parents. Alternatively you may need to return to the referring unit
- In general, deaths occurring during retrieval should be referred to the coroner.

Further reading

Barry P, Leslie A (2003). *Paediatric and Neonatal Critical Care Transport*. BMJ Books, London.
Intensive Care Society (2002). *Standards for Intensive Care*. Intensive Care Society, London.
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Chapter 19

Imaging in paediatric intensive care

Standard radiography

Radiological imaging has a major role in patient assessment in PICU, as clinical examination may be limited by patient position, noise from ventilators, alarms, or the environment, and the presence of wounds, drains, or dressings.

Chest X-ray (CXR)

- The CXR is the commonest radiologic modality in use and is suitable for intensive care, offering rapidity, portability, and a reasonable diagnostic yield for most clinical questions raised in critically ill patients
- Bedside chest films should include the upper trachea and larynx, as well as lung bases and upper abdomen. The patient should be well centred and all lines and artefacts should be removed from the surface of the chest. The degree of inspiration and rotation should be considered and the degree of flexion/extension of the neck noted with respect to interpretation of ETT position
  - Neck flexion will advance the ETT down the trachea
- Routine *daily* chest radiography has a high prevalence of findings but less frequently leads to management changes in the absence of clinical signs and is therefore not recommended
- Equally an intubated critically ill patient with lines and tubes should not go for days without a CXR.

Indications

- On admission, particularly following cardiac surgery (Box 19.1)
- Post-intubation or following placement or an internal jugular or subclavian central venous catheter
- To identify position of NG tube if other methods fail
- Investigation of clinical signs (abnormal chest movement, air entry, adventitious sounds)
- Clinical suspicion of pneumothorax
- Following thoracocentesis with or without drain insertion
- Increasing oxygenation or ventilation requirement
- Fever and changes in endotracheal secretions or inflammatory markers suggesting infection
- Follow up of known intrathoracic disease.

Placement of medical devices

- ETTs may be malpositioned in up to 10%. ETT tip should be located midway between clavicles and carina
- Endobronchial intubation may result in overinflation of ipsilateral lung and atelectasis of contralateral lung or in air leak, i.e. pneumothorax, pneumomediastinum, or SC emphysema
- CXR should include upper abdomen to verify intragastric position of NG tubes (NG tubes must have radio-opaque portion)
- Chest drain position after insertion for pneumothorax or effusion may appear acceptable but may be intraparenchymal, in extrathoracic soft tissue, or sandwiched in a lung fissure. Absence of respiratory swing, failure to withdraw fluid, lack of bubbling, and/or clinical signs of ongoing air leak or fluid collection should raise suspicion

- Routine X-ray after removal of chest drains has a low yield in the absence of clinical signs
- Re-expansion pulmonary oedema may be seen after drain placement for effusion or pneumothorax
- Central venous catheter placement may be complicated by pneumothorax (seen with subclavian lines more commonly than jugular), malposition, the wrong trajectory, or haemothorax.

Assessment of airways and lung parenchyma

- *Pneumothorax*: notoriously difficult to identify if anteromedial, subpulmonic, or loculated; the size on plain film correlates poorly with clinical significance. May appear only as sharper cardiac or diaphragmatic outlines and may require CT scan for confirmation. Mediastinal air may cross the midline or extend into the neck or abdomen
- *Effusions*: may be difficult to quantify or localize and may appear only as uniform haze or opacification. Costophrenic angles generally obscured
- *Pulmonary oedema*: cardiogenic is associated with cardiomegaly, vascular prominence, or redistribution, and may be more uniform in appearance. Non-cardiogenic, usually due to ↑capillary permeability (ARDS), is patchy, lacks cardiovascular changes, and may be associated with air bronchograms
- *ARDS*: poor correlation between radiologic changes and clinical condition but useful when new consolidation noted or to follow progress. Alveolar opacification without cardiomegaly is characteristic. Associated findings include atelectasis and barotrauma with evidence of air leak
- *Viral pneumonitis*: interstitial changes common with peribronchial thickening. Commonly associated with atelectasis due to endobronchial plugging and poor collateral air flow
- *Basal opacities* are common but the extent of the abnormality may be underestimated on plain X-rays. Loss of hemidiaphragmatic outline suggests lower lobe pathology
- Whole lung 'white-out' is rarely consolidation; more likely to be atelectasis or effusion/empyema.(but not if develops acutely)
- The majority of air space opacities in ventilated patients are ***not*** pneumonia.

Box 19.1 The postoperative CXR after cardiac surgery

- Provides baseline assessment of mediastinum, heart shape and size
- Identify and localize ETT, central venous and atrial catheters, drains, pacing wires, clips, and other intrathoracic devices
- Assess lung fields for atelectasis, or opacification suggestive of contusion. Infective consolidation unlikely in first 48h
- Pleural fluid likely to be haemothorax in early postoperative period; transudate common when pulmonary venous pressures remain high or fluid overload. Chylothorax should be ruled out when persistent.

Table 19.1 CXR signs

Collapse (atelectasis)	Consolidation
Commonest cause of opacification, especially LLL, RUL	May occur in any lobe
Loss of volume generally secondary to bronchial obstruction	No loss of volume: airspaces filled with exudate, oedema or blood
Mediastinal shift towards collapse	Mediastinal shift uncommon
Segmental, lobar or whole lung	Patchy, homogenous, or irregular; lesions contiguous to heart or diaphragm associated with loss of that border
Central location	Peripheral, abutting fissure or pleura
No air bronchograms	Air bronchograms common as air-filled bronchi outlined against fluid-filled alveolar spaces
Changes evolve rapidly	Changes evolve more slowly

LLL, left lower lobe; RUL, right upper lobe.

Abdominal X-ray

- Relatively few indications on PICU
- Main indication to rapidly rule out perforation or bowel obstruction at bedside but may give insufficient information as an isolated investigation
- NG or nasojejunal tube placement may be confirmed
- Bowel wall thickening non-specific and frequent in critically ill patients
- Gas pattern should be described
- Gastric dilatation frequently seen after mask ventilation or with CPAP
- Air or fluid in the abdomen compress viscera centrally
- Free air suggests bowel perforation but difficult in supine patient. Lateral views ('shoot through') may be required
- Paralytic ileus causes widespread bowel loop distension with loops of colon greater in calibre than small bowel, or can be gasless
- Small bowel distension secondary to obstruction may have a more organized 'stepladder' appearance.

Computed tomography

- Computed tomography (CT) scanning remains one of the most useful modalities in the ICU, due to its availability and ability to provide detailed cross sectional images of the brain, chest, and abdomen. Technological advances with higher resolution and reduced scanning times have made it an integral part of the emergency management of the patient with trauma and other acute intracranial, intrathoracic, and intra-abdominal emergencies
- Multiplanar reconstruction using volumetric data to convert axial to 3D images, is particularly applicable to the study of vascular and tracheo-bronchial structures

- The pitfalls of CT scanning are related mainly to the need for transfer from the intensive care department. In an extremely unstable patient one may have to weigh the risks of transfer against the findings of the scan.

Chest

- Helical CT with rapid multislice systems provides continuous volume data that can then be reconstructed to study mass lesions, vascular anatomy, mediastinal and airway disease, lung parenchyma
- Rapid scanning minimizes or eliminates respiratory artefact
- Most investigations use IV contrast and images acquired within seconds of contrast injection provide angiographic detail and information on anatomy and thromboembolic disease
- CT angiography permits visualization of central and peripheral vascular structures and their relationship to tracheo-bronchial tree and lung parenchyma. Reconstructed images can produce virtual 3D images of vascular tree and may replace the need for conventional angiography
- High-resolution CT with non-contiguous slices is more suitable for diffuse disease and provides detailed images of the lung parenchyma and pleura at lower radiation dose
- May be helpful when oxygenation and ventilatory requirements unexplained by plain X-rays or echocardiography
- Trauma: essential part of the workup of patients with blunt trauma where airways or major vascular structure injury is suspected
- ARDS: demonstrates non-uniformity of disease and changes seen when position changed from prone to supine with associated gravity-dependent atelectasis. New changes identified may signify superimposed infection. Bronchial dilation and subpleural cysts associated with prolonged ventilation may be seen
- Pulmonary oedema: cardiogenic oedema can be differentiated from non-cardiogenic oedema due to capillary leak by the prominent interlobular septal thickening and vascular enlargement seen in the former
- Pleural effusion: size and character of loculated effusions may be better ascertained with CT
- Pneumothorax: if loculated, anterior or subpulmonic, CT provides information to guide drainage
- Pulmonary embolus: CT-angiogram is imaging modality of choice to identify central and segmental emboli which may be missed on US
- Abscess: distribution and character of abscesses well seen, often localized to upper lobes in immunocompetent and more diffuse and multilobar in immunocompromised children. Peripheral lung lesions can be differentiated from empyema
- CT-guided diagnostic and interventional procedures may avoid surgical intervention
- Virtual bronchoscopy: 3D reconstruction provides detailed images of large and small airways and enables highly accurate measurement of airway calibre and visualization of focal stenoses
- 3D-CT has the advantage of non-invasively seeing 'beyond' areas of airway obstruction, unlike bronchoscopy, and examines the relationship of the airways to extra-luminal structures, including mediastinal vessels and lymph nodes.

Abdomen

- Abdominal CT is an integral part of the initial workup of the patient with serious trauma to rapidly identify intra-abdominal injury
  - Haemodynamically unstable patients may not be amenable to CT and require urgent bedside US and/or rapid surgical intervention
- Injury to the liver and spleen are common and easily identified on CT
- Retroperitoneal structures well seen on CT including haemorrhage and pancreatic pathology
- Oral contrast is useful to delineate viscera and IV contrast to identify vascular, infectious, or inflammatory pathology
- Major role in identification of non-traumatic intra-abdominal pathology, generally difficult to assess clinically in the critically ill patient
- CT indicated when intra-abdominal or retro-peritoneal sepsis suspected, i.e. fever, cardiovascular instability, and metabolic acidosis unexplained by clinical examination, plain radiography, and US. Abscesses, ischaemia, or infarction can be ruled out
- CT-guided drainage for diagnosis and treatment may avoid surgical intervention.

Brain

(See 🕮 Chapters 22 and 23.)

CT remains the imaging modality of choice in acute traumatic and non-traumatic brain injury/encephalopathy. Contrast enhancement is not routinely required for acute brain injury but is used to address specific diagnostic questions, i.e. the presence and characteristics of infectious, inflammatory, or malignant lesions. These include meningitis, abscesses, malignancies, and vascular malformations. Further study with MRI or angiography is often required in these cases.

- Major advantages include rapid access and rapid study time to establish intracranial pathology requiring early neurosurgical intervention
- Intracranial haemorrhage, i.e. intraparenchymal, subdural, extradural and subarachnoid haemorrhage are well seen on CT. Basal and orbital skull fractures are also identified
- Raised ICP may be present in severely brain-injured patients even when an early CT scans is reported as 'normal'
  - CT does not necessarily exclude raised ICP.
- ***Routine repeat CT after traumatic brain injury*** is rarely indicated, and is infrequently associated with the need for neurosurgical intervention in the absence of clinical change
- ***Repeat scanning*** should be directed by clinical parameters and ICP monitoring:
  - Changes in level of consciousness
  - Focal or persistent neurological abnormalities
  - Intractable intracranial hypertension
  - Seizures and haemodynamic changes suggestive of raised ICP
- Patients with non-traumatic neurologic pathology presenting with altered level of consciousness, seizures, or focal signs are generally assessed initially with CT scan

- Space-occupying lesions, cerebral oedema, and parenchymal changes associated with metabolic disease may be visible on early CT and direct initial management and the need for further imaging

Box 19.2 Evaluation of the spine in trauma

- Clinical evaluation in the obtunded, intubated child is unreliable and radiographic study essential
- Plain radiography may be limited in detecting cervical spine fractures, especially at the levels of C1–C2 and C7–T1
- Dynamic fluoroscopic examination of the cervical spine is no longer standard practice
- Standard CT studies limited to axial images may potentially miss abnormalities in translation, angulation, and rotation
- CT with reconstructed multiplanar images is the imaging modality of choice to rule out spinal injury with rapid studies readily performed at the time of initial trauma work-up
- 'Reformatted' or reconstructed CT images enable better assessment of these variations and provide indirect evidence of ligamentous injury when bony misalignment or malrotation is present. High resolution images may reveal small avulsion fractures
- MRI is superior at detecting abnormalities of alignment, spinal cord integrity, and ligamentous and soft tissue injuries. However, high sensitivity may make non-specific abnormalities difficult to interpret clinically
- MRI is rarely indicated or available in the emergency situation but may be indicated when clinical examination, X-ray, or CT scanning suggest ligamentous or cord injury, or instability
- Plain radiography is generally adequate for thoracic and lumbar spine but CT scan can image the entire spine rapidly with minimal motion artefact. Axial slices with reformatted and reconstructed views are commonly obtained at the time of initial CT of brain, chest, and abdomen.

Fluoroscopy

- Fluoroscopy has a number of uses—it generally requires transporting the patient to the radiology department, though portable units do exist
- Tracheobronchography with non-ionic water-soluble contrast may provide information about dynamic tracheobronchial disease:
  - The patient must be spontaneously breathing through an ETT or tracheostomy
  - Images are acquired in >1 plane after injection of a small volume of contrast into the trachea
  - Imaging is repeated as different levels of positive pressure are applied, assessed with a manometer incorporated into the circuit
  - The degree of collapse of the trachea and bronchial tree are recorded and the reversibility with PEEP noted
- Screening a post-pyloric feeding tube into position
- Assessing diaphragmatic excursion when paralysis is suspected —US is generally used as first-line investigation (see 📖 p.338).

Ultrasound

US is used as a diagnostic tool and to aid in specific therapy. Echoes or reflections of the US beam from tissues with different acoustic properties yield information on size, shape, and structure of organs and body spaces. US has an increasing role in the early assessment of the unstable trauma patient, with its capacity to examine multiple systems at one time at the bedside. Although less sensitive than CT in trauma and surgical emergencies, it may be useful when CT is unavailable or delayed.

Advantages

- Portability
- Enables rapid bedside analysis in real time and follow-up
- Avoids the risks associated with transporting the critically ill child to the radiology suite
- Increases the yield and decreases the complications of several interventional procedures, e.g. central line placement
- May guide or decrease the need for surgical intervention
- No use of ionizing radiation.

Limitations to optimal acoustic windows

- Inadequate patient positioning
- Dressings, wounds, or drains interfering with probe angle
- Excessive fat
- Air and bone reflect US, limiting use in chest and musculoskeletal system
- Structures surrounded by bone are not generally visible
- Gas in hollow intra-abdominal organs may obscure deeper structures
- Mechanical ventilation with hyperinflation of lungs, pneumothorax, or SC air may obscure views
- Depends on operator experience and skill.

Chest

- Superior to CXR for identification of small or loculated effusions
- Estimates volume of effusion and need for drainage better than X-ray
- Defines the character of the fluid, the presence of loculation and septations, and may suggest aetiology
- Distinguishes between effusion and collapse/consolidation
- Enables some assessment of lung parenchyma deep to effusions or air
- Useful to quantify direction and adequacy of diaphragmatic excursions.

Diaphragm

- Phrenic nerve injury is relatively common after cardiac surgery
- The affected hemidiaphragm may be paralysed, or move paradoxically when lack of tone causes the hemidiaphragm to move cephalad instead of caudad as the rib cage expands in inspiration
- Diaphragmatic weakness/paralysis is also common following liver transplantation, and is seen in a number of neurometabolic and myopathic disorders
- Fluoroscopy provides good images but is limited by need for transport to the radiology department and need for ionizing radiation

- US at the bedside is accessible, makes an immediate diagnosis, and enables simple repeated follow-up—M-mode is preferred, patient must be taken off positive pressure
- Should be investigated when failure to wean, respiratory distress, asymmetric breathing pattern, or paradoxical diaphragmatic movement are noted. CXR may reveal raised hemidiaphragm but this may not be present in a patient on positive pressure ventilation.

Abdomen

- Provides general evaluation of entire abdominal contents including pelvis and retroperitoneum
- Enables assessment of the unstable patient with abdominal trauma for rapid diagnosis of organ or vascular damage
- Has an increasing role in identification of NG and nasojejunal tube position as an alternative to plain X-ray or fluoroscopy
- Solid organs can be assessed for parenchymal changes
- Identifies intraperitoneal or visceral mass lesions but may miss those obscured by overlying organs or air-filled bowel
- Detects even small amounts of peritoneal fluid, e.g. around liver—small amounts of free fluid are common and can be seen in the absence of intra-abdominal pathology, including with generalized capillary leak and/or fluid overload
- Superior to other modalities in imaging of the biliary tree
- Although a good screen for pancreatic disease, CT may be required for diagnosis with US useful for intervention and follow-up.

Renal

- Assessment of the genitourinary tract includes renal parenchyma, collecting system and a 'vascular map' to assess perfusion that measures renal arterial and venous flow
- US is an appropriate study in the evaluation of acute renal failure to distinguish pre-renal, from renal pathology and obstructive uropathy
- ↑echogenicity ('bright kidneys') is seen in conditions where glomerular or tubular disease is present
- ↓renal perfusion may be seen in patients with sepsis and hypotension, and with the use of vasoconstricting drugs—Doppler shows a high resistive index (high systolic/diastolic ratio)
- Calcified lesions are easily identified including stones, or nephrocalcinosis associated with excessive diuretic use
- US may identify adrenal haemorrhage in children with fulminant septicaemia, usually but not restricted to meningococcal disease
- Renal vein flow and patency as well as renal size are assessed to rule out renal vein thrombosis in the patient with haematuria, thrombocytopenia, and an abdominal mass
- Bladder volume estimation is useful in a child with a neuropathic bladder in assessing adequacy of emptying and the need for catheterization.

Venous thromboembolic disease

- Venous thrombosis, particularly of the central veins, is rarely suspected clinically but occurs quite commonly in critically ill children

- Thrombi are most commonly associated with a CVL, and more often seen in lower extremities, reflecting the widespread use of the femoral vein for central catheterization
- Risk factors include young age, recent trauma or surgery, low cardiac output state, systemic infection, malignancy or autoimmune disease, and prolonged immobility
- In the presence of a blocked CVL or positive blood cultures, thrombosis should be strongly suspected and ruled out
- US remains the most common tool for the diagnosis of venous thrombosis. Venography is considered the gold standard but is impractical in the intensive care setting and few studies have compared it to US in children.
- Prophylaxis and treatment of high risk patients with unfractionated or low molecular weight heparin is increasingly common and appears safe and effective in children. Stockings may be a useful adjunct, especially if anticoagulation is contraindicated.

US-guided intervention

- US offers the major advantage of obviating the need to move the patient outside the ICU for interventional procedures
- Imaging in real-time minimizes the risk of damage to vital structures
- US-guided drainage of pleural effusion is associated with a higher yield and fewer complications
- Direct instillation of fibrinolytic agents into empyemas and follow-up imaging are possible at the bedside
- Abscesses and cysts in the chest and abdomen are often diagnosed by CT but drainage may be guided by either modality.
- Abdominal paracentesis and placement of Tenckhoff catheters for peritoneal dialysis may be aided by identifying optimal location for drainage avoiding vital structures
- Emergency paracentesis can be guided at the bedside in cases of rapidly progressive abdominal compartment syndrome.

Vascular access

- US is increasingly used in the placement of CVLs, with NICE recommending its use, though supporting evidence for this is limited
- Evidence for US use is best for internal jugular and subclavian veins
- The traditional 'landmark' technique is still widely practised and associated with well-known complications including haemorrhage, arterial puncture, and wrong trajectory of the catheter
  - Pneumothorax or haemothorax may be seen after internal jugular and subclavian line insertion
- The success of catheter placement is significantly reduced in the presence of venous thrombosis regardless of technique used, so US imaging may be useful as a screen when problems are anticipated.

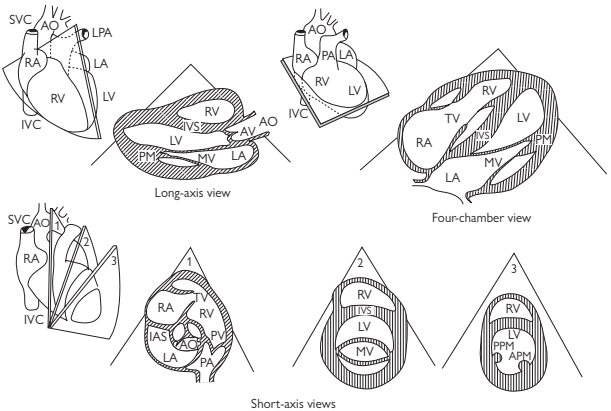
Echocardiography

(See 📖 Chapter 20.)

- Echocardiography assesses cardiac structure and function and has become a major adjunct to clinical examination and to monitoring of the critically ill
- Pre- and postoperative US imaging of the child with congenital heart disease is an essential part of their ICU management
- Transthoracic echocardiography (TTE) is most commonly used for rapid bedside evaluation
- A number of different views are obtained (see Fig. 19.1)
- New diagnosis of previously unsuspected cardiac disease in the critically ill child is not uncommon, particularly in the neonatal period
- Detailed images of cardiac anatomy including atrial and ventricular chambers and septae, valves, vegetations, and thrombi can be obtained
- The configuration of the large vessels draining into and away from the heart can be established
- Doppler technology permits assessment of flow patterns and velocities within the heart and great vessels and the study of intracardiac shunting across valves or septal defects
- Regurgitant flow across the pulmonary and tricuspid valves is frequently seen in critically ill patients enabling estimation of pulmonary arterial pressures (see 📖 p.861)
- Cardiac function can be examined in a qualitative manner as well as with specific measurements of chamber diameters, systolic and diastolic function (see 📖 Chapter 7)
- A major advantage is the ability to sequentially study function to follow the effects of time or specific therapeutic interventions
- IVC assessment may provide information on patient volume status and femoral venous catheter-related thrombosis.

Indications for echocardiography

- Review of anatomy and function following cardiac surgery
- Evaluation when cardiac disease is suspected
- Assessment of myocardial function and regional wall abnormalities, valve function, presence of vegetations or thrombi
- Estimation of intravascular volume status and response to preload
- Clinical suspicion of cardiac tamponade
- Unexplained haemodynamic instability with high inotrope requirement
- Unexplained hypoxaemia where intracardiac shunt suspected
- Clinical evidence suggestive of high pulmonary artery pressures
- Clinical suspicion of proximal pulmonary emboli or with or without presence of deep vein thrombosis
- Identification and quantification of pericardial fluid
- US-guided pericardiocentesis
- Evaluation of the infant with stridor and suspected vascular ring.



AO = aorta; AV = aortaic valve; IAS = interatrial septum; IVC = inferior vena cava; IVS = interventricular septum; LA = left atrium; LV = left ventricle; MV = mitral valve; PM = papillary muscle; RA = right atrium; RV = right ventricle; SVC = superior vena cava; TV = tricuspid valve.

Fig. 19.1 Three major axis views of 2D-echocardiography for defining structural abnormalities. Reproduced from Toro-Figueroa LO, Levin D (1992). *Essentials of Paediatric Intensive Care Manual.* Quality Medical Publishing Inc St Louis, MO.

Limitations

- Images may be limited in mechanically ventilated children by the use of high ventilator pressures, PEEP, and air trapping
- The presence of dressings, drains, large cannulae for assist devices, or when sternal closure after cardiac surgery has been delayed, may all impede optimal imaging
- Right ventricular function is more difficult to assess. RV dilatation and dysfunction is seen in parenchymal lung disease, sepsis, and any condition that increases PVR
- TTE is poor at imaging peripheral vascular structures, including branch pulmonary arteries.

Transoesophageal echocardiography (TOE)

- TOE views the heart from behind and enables highly detailed examination of valves, vegetations and thrombi, particularly within the atria
- Has a major role in intraoperative assessment during cardiac surgery ~assessing repair and any residual intracardiac shunts
- Useful when TTE is limited by poor acoustic windows
- Thoracic aorta well seen, useful in the assessment of trauma
- TOE is superior to TTE at demonstration of endocardial detail
- Provides similar information on haemodynamic status as TTE and may have a role in continuous monitoring—increasingly used during cardiac surgery, particularly in adults

- Complications are uncommon—the intensivist should be present throughout as there is potential for the ETT to be moved or dislodged by the probe.

Pulmonary emboli

- The majority of pulmonary emboli in children originate from CVL-associated thrombi
- Emboli are easy to miss clinically because signs are often ascribed to the patient's underlying illness
- Pulmonary emboli contribute significantly to morbidity and mortality when they are present
- TTE is frequently performed as a first-line bedside investigation and may identify large proximal thrombi
- Diagnosis of the associated acute *cor pulmonale* can be made at the bedside with TTE although right ventricular dilatation and dysfunction may be due to other causes of acute pulmonary hypertension
- Ventilation-perfusion (VQ) scanning has a role in the diagnosis, but is rarely used in the ICU setting due in part to the confounding presence of underlying lung parenchymal disease
- CT angiography is the diagnostic modality of choice to thoroughly assess central and peripheral emboli, and small septic emboli.

Magnetic resonance imaging

MRI is based on the principle that nuclei in hydrogen atoms will align themselves with a strong magnetic field. Radiowaves then applied to the tissue under study are altered by aligned hydrogen nuclei and the signal returned is measured and recorded.

- MRI offers excellent spatial resolution and a high sensitivity for detecting structural lesions in the CNS and cardiovascular system
- It can also provide information on function and perfusion and the status of tissue with respect to ischaemia and vascular patency. In critically ill children the commonest indication is the assessment of intracranial pathology on a non-emergency basis
- Metal-containing medical devices such as infusion pumps and pacemakers can malfunction in the magnetic field.

Advantages of MRI

- No ionizing radiation
- Multiplanar imaging possible
- Provides non-invasive information on function and perfusion
- Better correlation than CT with severity and outcome in brain injury
- Non-iodine based 'paramagnetic' contrast associated with fewer allergic reactions.

Disadvantages of MRI

- Often geographically at a distance from intensive care environment
- ICU equipment often incompatible with MRI environment
- Monitoring and supportive therapy may be suboptimal during study

- Long study times and the numbers of staff involved in transfer make MRI scanning a labour intensive process
- Unstable critically ill children may be unsuitable for scanning. The diagnostic benefit has to weighed against the risk and effort involved
- Metallic devices (pacemakers, wires, clips, spinal rods, ICP catheters) cause significant artefact and may preclude MRI study altogether.

MRI of the central nervous system

- Diffuse axonal injury well detailed with superior grey/white differentiation capabilities to CT
- Provides superior information on white matter and basal ganglia
- Part of work-up in non-accidental injury when brain injury documented
- Useful for study of intracerebral or spinal cord ischaemia, infarction, inflammation, subdural or extradural haemorrhage
- Acute disseminated encephalomyelitis best diagnosed with MRI
- Detailed assessment of demyelination possible
- Useful when suspicion of c-spine cord or ligamentous injury
- Gadolinium contrast primarily used to assess vascular supply of mass lesions or to differentiate tumour from oedema.

MR spectroscopy

- Used to investigate the metabolic activity over an area of interest
- Characteristic 'metabolic profile' may offer diagnostic information
- Lacate peak of interest in metabolic disease and/or ischaemia.

MRI of the cardiovascular system

- Role increasing in the assessment of structural congenital heart disease
- Enables visualization of central and peripheral vascular anatomy and relationships to lungs and airways
- No ionizing radiation in contrast to conventional angiography
- Direction and speed of blood flow as well as shunt can be documented
- Reconstructed images give 3D structural information
- Right and left ventricular volumes and function can be estimated
- Gadolinium contrast may be used to provide magnetic resonance angiogram (MRA) of great vessels.

Further reading

Johnson K, Williams H, Foster K, *et al.* (eds) (2009). *Paediatric Radiology*. Oxford University Press.

Section 3

Specific specialties

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Chapter 20

Cardiac disorders and postoperative care

Applied cardiovascular anatomy

This section describes salient features in a normal heart.

Cardiac anatomy (see Fig. 20.1)

Right heart

- Deoxygenated blood from the systemic circulation returns to the *right atrium (RA)* through the *superior* and *inferior caval veins (SVC* and *IVC)*
- Cardiac venous blood enters the heart through the *coronary sinus* and directly through the *thebesian veins*
- During diastole, blood flows from the RA to the *right ventricle (RV)* through the *tricuspid valve*; this valve has 3 leaflets (*anterosuperior, septal,* and *inferior leaflets*)
- The RV is triangular shaped, and much thinner than the left ventricle (LV). It is heavily trabeculated, and it has a muscular sleeve (*infundibulum*) separating the tricuspid valve from the *pulmonary valve*
- The main *pulmonary trunk* arises to the left and anterior relative to the aorta
- It courses posteriorly before branching into the *left* and *right pulmonary arteries*.

Left heart

- Oxygenated blood from the lungs returns to the *left atrium (LA)* through the *right-* and *left-sided pulmonary veins*
- During diastole, blood enters the *LV* through the *mitral valve*, which is a bicuspid valve (posterior/mural leaflet and anterior leaflet)
- Each leaflet is secured at the base to the mitral annulus, and the free end is linked to the *papillary muscles* via thin tendinous structures (*chordae tendineae*)
- During systole, the papillary muscles contract to increase tension on the chordal apparatus and thus maintain valvar competency
- The *aortic valve* is in fibrous continuity with the mitral valve, and is a trileaflet structure
- 2 of its cusps (left and right) support the origin of the appropriate *coronary arteries*, the 3rd leaflet being termed non-coronary
- The left ventricular wall is 3 times thicker than the RV
- Its fibres are oriented in 3 layers; the inner (subendocardial) layer is the most important in children, and young adults
- The outermost oblique layer, along with the subendocardial layer, have their fibres running longitudinally from the apex to the base, while the middle layer is made up of a radial arrangement of fibres
- Systole involves ventricular contraction which shortens, thickens, and twists towards the apex
- The aorta ascends as a central structure from the heart, and usually arches to the left curving over the heart to descend posteriorly to the left of the spine.

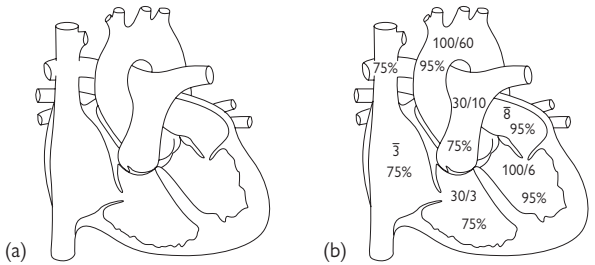


Fig. 20.1 a) Normal heart structures; b) normal O_2 sat and pressure measurements.

Sequential segmental analysis

To evaluate patients with suspected congenital heart disease, it is imperative to analyse the heart in a segmental pattern based on:

- Position of the heart, and other organs (thoracic and abdominal):
  - Visceral sidedness (situs solitus or inversus)
  - Cardiac position (location and orientation)
- Connections between the different regions (veins, atria, ventricles, and arteries)
- Description of a cardiac region based on its morphological characteristics rather than its position, or relation to other structures.

It is also important to understand that:

- *Connection* is an anatomic term showing a direct link between 2 structures; *drainage* a haemodynamic one, referring to flow of blood
- *Single* refers to an absence of a corresponding contralateral structure (single valve in tricuspid atresia); *common* refers to bilateral components with an absent division (e.g. common AV valve).

The ***endocardium*** is the inner layer of the heart, which is metabolically active in contributing to cardiovascular function.

The ***pericardium***, a fibroserous sac consisting of visceral and parietal layers, is a dynamic and adaptive structure which:

- Protects the heart by acting as a barrier
- Reduces friction due to cardiac motion.

Conduction system

Contraction is triggered by electrical impulses which are generated and conducted through a system of specialized cells—the conduction system. The *sinoatrial node* (SA node) generates the electrical impulse which spreads through the atrial chambers.

- *SA node* is situated at the SVC/right atrium junction.

There is a single point of electrical connectivity between the atria and the ventricles; the *atrioventricular node* (AV node)

- *AV node* is situated in the triangle of Koch (near the coronary sinus).

The conduction system then proceeds as the *bundle of His* before dividing into the *left* and *right bundles* and then into various *fascicles*.

Circulation (see also 🕮 Chapter 11)

- There are 2 vascular beds in the circulation—the *pulmonary and systemic* through which the blood is driven by the appropriate ventricles (see Fig. 20.1):
  - The pressure in the pulmonary circulation is significantly lower than that in the systemic circulation
- The vessels become smaller and thinner as they get farther from the great arteries, becoming *arteriole*s, and finally *capillaries* which are the units where gas and metabolic exchange takes place:
  - Arterioles are small arteries with relatively thick muscle and constitute the majority of the resistance to the relevant vascular bed; they regulate blood flow

Applied cardiovascular physiology

(See 🕮 Chapter 7)

Bedside monitoring of the cardiovascular system/circulation

(See 🕮 Chapter 7)

Cardiac arrhythmias

Cardiac arrhythmias can be due to (Box 20.1):

- Disturbances of rhythm (tachyarrhythmia):
  - Supraventricular tachycardia (SVT)
  - Ventricular tachycardia (VT)
- Disturbances of conduction (bradyarrhythmia):
  - Sinus node dysfunction
  - AV dissociations (1st, 2nd, or 3rd degree).

Box 20.1 Cardiac arrhythmias in children can be due to:

- Structural heart disease:
  - Native
  - Postoperative
- Abnormal pathway
- Cardiomyopathy/myocarditis
- Heart failure
- Miscellaneous:
  - Electrolyte imbalance
  - Drugs
  - Systemic disturbance.

Substrates for the genesis of the arrhythmias are:
- Re-entrant mechanisms: these require the presence of 2 electrical pathways separated by an electrically inert tissue, having different properties, setting up an electrical circuit
- Automatic mechanisms: this is due to an abnormally active electrical focus either inherent (atrial ectopic tachycardia) or due to a secondary cause (imbalance, strain)
- Triggered mechanisms.

Presentation
- Palpitations
- Funny turns
- Dizziness
- Syncope
- Cardiac compromise
  - ↓effort tolerance
  - Failure to thrive
  - Breathless, difficulty in feeding
  - Ventricular dysfunction (if prolonged)
- Incidental finding.

Supraventricular arrhythmias
These are conditions that involve structures above the bifurcation of the bundle of His.

Re-entrant tachycardias are the commonest mechanism for arrhythmias seen in children with normal hearts.
- Usually paroxysmal
- Narrow QRS complex
- Regular (constant R–R interval)
- Initiated or terminated by a premature event.

Classically, these rhythms can be terminated with cardioversion. Examples are:
- AV re-entry tachycardia (AVRT)
- AV nodal re-entry tachycardia (AVNRT)
- Wolff–Parkinson–White (WPW) syndrome
- Atrial flutter.

Automatic mechanisms are much less frequently seen.
- Usually incessant
- Can present with cardiomyopathy or cardiac compromise
- Usually have a narrow QRS complex but have varying R–R interval (irregular)
- Do not respond to cardioversion.

Examples are:
- Atrial ectopic tachycardia (AET)
- Junctional ectopic tachycardia (JET)
- Atrial fibrillation.

Diagnosis

- Detailed history
- 12-lead ECG, preferably during an episode (Fig. 20.2)
- Intracardiac electrophysiological studies ('EP study'): an identification of the pathway (or focus) can be made invasively; usually combined with definitive management (ablation) in the same procedure.

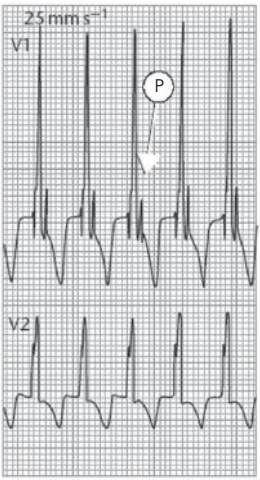


Fig. 20.2 Atrial (V1) and surface (V2) ECGs in nodal rhythm. Reproduced from Mackay J and Arrow Smith, J (eds) (2004) *Core topics in cardiac anaesthesia*, with permission from Cambridge University Press.

Treatment

Based on presentation and identification of the mechanism. Acute management will usually involve IV adenosine or synchronized cardioversion. Specific treatment depends on the mechanism:

- Vagal manoeuvres: Valsalva, diving reflex
- Drug therapy:
  - Re-entry tachycardias will respond to adenosine (200mcg kg^{-1}) given as a fast IV bolus
  - β-blockers (sotalol, propranolol) or digoxin (contraindicated in WPW syndrome)
  - Flecanide
  - Amiodarone reserved for resistant tachycardias
- Definitive therapy:
  - Radio-frequency ablation of the pathway (or focus) by intracardiac mapping has become the mainline of treatment even in children.

Ventricular arrhythmias

VT is defined as at least 3 consecutive beats of ventricular origin with a rate >120beats/min.

- Extremely rare in paediatric practice

- A group of heterogeneous conditions with variable substrates and mechanisms
- As in SVTs the mechanisms involved are re-entrant or triggered automaticity (more common in VT)
- Ventricular fibrillation (VF) is a series of uncoordinated ventricular depolarizations associated with an absence of cardiac output.

Important clues on ECG to help identification (Fig. 20.3):
- QRS axis
- QRS morphology
- Propensity to remain same (monomorphic) or vary (polymorphic).

Box 20.2 Causes

- Primary (idiopathic):
  - RV outflow tract tachycardia
  - Arrhythmogenic RV dysplasia
  - Catecholamine sensitive polymorphic VT
  - Familial (Brugada syndrome, congenital long QT syndrome)
- Myocardial:
  - Cardiomyopathy
  — hypertrophic cardiomyopathy
  — dilated cardiomyopathy
  - Myocarditis
  - Myocardial ischaemia
- Conduction abnormality (heart block)
- Miscellaneous:
  - Structural heart disease (native or palliated)
  - Metabolic derangements
  - Drugs
  - Trauma with myocardial injury.

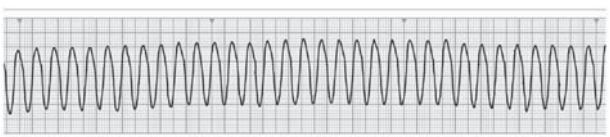


Fig. 20.3 Ventricular tachycardia.

Diagnosis
- A detailed history, with emphasis on family history along with a 12-lead ECG, and identification for a cause should be the primary aim
- ECG monitoring (Holter, loop recorders)
- Specific investigations: genetic testing (long QT syndrome, cardiomyopathy) or cardiac MRI (arrhythmogenic RV dysplasia)
- Invasive EP study will help to map the focus, and ablate it.

Treatment

Acute management of VT depends upon hemodynamic status:

- If the patient is stable, amiodarone can be considered
- If the subject has any evidence of cardiac compromise cardioversion should be used:
  - Synchronized cardioversion for VT
  - Non-synchronized cardioversion for VF.

Specific management of ventricular arrhythmias includes:

- Individuals at risk (previous history, family history):
  - Surveillance
  - Prophylactic measures (ß-blockers, implantable defibrillators (ICDs)
- Pharmacotherapy:
  - Class IA (procainamide), IB (mexiletine) IC (flecanide), β-blockers, Amiodarone
- Definitive management:
  - Ablation of focus (pathway)
  - Implantation of ICD ± pacemaker.

Bradyarrhythmias

These are due to abnormalities in the generation of an electrical impulse or conduction defects. They can be seen in children with structurally normal hearts (complete congenital heart block) or with structural heart disease (ventricular inversion, post surgical).

They can be classified as:

- AV block:
  - 1st degree: prolonged PR interval
  - 2nd degree:
  — Type I (Wenckebach)
  — Type II
  - 3rd degree: complete AV block
- Sinus node dysfunction: bradycardia

Chronotropic incompetence

2nd-degree AV blocks with Wenkebach phenomenon (Type I) is a progressive prolongation of PR interval leading to a blocked impulse. Type II is an abrupt block of an impulse without prolongation of PR interval.

Presentation and coexisting conditions

In children, overt symptoms due to bradycardia are relatively uncommon.

Neonates and infants

- Heart failure (fetal hydrops)
- Apnoea
- Hypoxia
- Gastro-oesophageal reflux with laryngospasm
- Breath holding.

Older children and adolescents

- Heart failure
- Syncope
- ↓effort tolerance
- Easy fatigability
- Sudden death.

Diagnosis

- A detailed history, with emphasis on family history along with a 12-lead ECG, and identification for a cause should be the primary aim
- ECG monitoring (Holter, loop recorders) may identify a long pause, especially at night
- Specific investigations; antibodies (anti-Ro, anti-La) for SLE-related maternal or fetal condition.

Treatment

Fetal management

- Consider the need for early delivery
- Sympathomimetic agents (ritodrine) have been used with limited effect, but are poorly tolerated by mothers.

Acute management of a compromised child

- Chronotropic agents (isoprenaline)
- Atropine
- Temporary pacing.

Pacemakers

- Transvenous (via subclavian vein) or epicardial (surgically implanted)
- In infants a single chamber system (ventricular—VVI) is used, and upgraded to a dual chambered system (DDD) to maintain AV synchrony in older children.

Congestive heart failure

Congestive cardiac failure develops when systemic oxygen supply is inadequate for oxygen demands, or is maintained at the expense of higher atrial filling pressures. In paediatric practice, the cause is frequently a large L-to-R shunt (L→R) (large VSD) with 'preserved myocardial function' as opposed to 'pump failure' as commonly seen in adults.

A range of compensatory mechanisms, initially beneficial, contribute to the pathophysiology. These include:

- Salt and water retention:
  - Aldosternone stimulation (sodium retention)
  - Arginine vasopressin (water and sodium retention)
  - Natriuretic peptides
- Neuro-hormonal changes:
  - Sympathetic stimulation:
  — sympathetic cholinergic fibres (sweating)
  — α-adrenoreceptors (vasoconstriction)
  — β-adrenoreceptors (tachycardia)
  - Renin–angiotensin activation (vasoconstriction)
- ↑red cell mass
- Hypertrophy of cardiomyocytes.

Pulmonary oedema occurs due to a combination of:

- Fluid retention
- ↑filling pressures (left atrium)
- ↑pulmonary blood flow (in L→R shunts)
- Lower oncotic pressures (low albumin concentrations).

Causes

- Volume overload:
  - Intracardiac shunt
  - Extracardiac shunt, e.g. AV malformation, aneurysm of great vein of Galen
  - Valvar regurgitation
- Pressure overload: obstruction—cardiac (aortic stenosis) or arterial (coarctation)
- Intrinsic myocardial contractile dysfunction
  - Myocarditis
  - Cardiomyopathy
- Rhythm disorders:
  - Persistent tachycardia/bradycardia
  - Lack of AV synchrony (heart blocks)
- ↑cardiac output ('high output' states):
  - Sepsis ('warm shock')
  - Severe anaemia
  - Hyperthyroidism
  - Liver failure.

Symptoms and signs

- ↑adrenergic tone:
  - Clammy, pale, vasoconstriction, oliguria
  - Tachycardia

- Impaired myocardial contractility:
  - Poor perfusion, weak pulses
  - Altered sensorium, irritability
  - ↓effort tolerance, chest pain
  - Failure to thrive, breathless on feeding
- Salt and water retention:
  - Cardiomegaly
  - Hepatomegaly
  - Pulmonary congestion
  - Tachypnoea, respiratory distress, frequent 'chest infections'.

Treatment

Box 20.3 Treatment of congestive heart failure

- Specific management of treatable causes, e.g. structural heart disease, myocarditis
- General interventions:
  - Optimize nutrition, haemoglobin
  - Optimize respiratory function
  - — oxygen
  - — respiratory support: CPAP, ventilation
- Impaired myocardial contractility:
  - Inotropes (sympathomimetics, PDEIs)
  - Vasodilators
  - Mechanical support (ventricular assist device, ECLS)
- Compensatory mechanisms:
  - Salt and water retention—diuretics
  - Renin–angiotensin–aldosterone axis—captopril, losartan, spironolactone
- Minimize risk from cardiac impairment:
  - Rhythm abnormalities
  - Thromboembolic phenomena—heparin prophylaxis for severely impaired ventricular function.

Pathophysiology of congenital heart disease

Congenital heart disease lesions can be classified as:

- L→R shunts
- Hypoxaemic lesions
- Obstructive and regurgitant lesions of left and right heart.

Left-to-right shunts

Lesions

- Ventricular septal defect (VSD
- Persistence of arterial duct (PDA)
- Atrial septal defect (ASD)
- AV septal defect (AVSD)
- Aortopulmonary window (AP window).

Clinical manifestations are related to:
- Size of the defect
- Postnatal changes in vascular resistance of the pulmonary and systemic beds.

Following birth, there is a rapid reduction in the pulmonary vascular resistance. This usually takes place over 2-6 weeks following birth; however in the presence of large defects this may be delayed by 1-3 months, and in some cases, there is no significant reduction in the resistance across the pulmonary bed.

Consequences of L→R shunting:
- ↑pulmonary blood flow
- Left atrial dilatation and left ventricular volume overload
- Pulmonary tree:
  - ↑volume and pressure of pulmonary vasculature
  - Large shunts can result in pulmonary vascular disease if not corrected in the 1st year of life
  - Airway obstruction with hyperinflation
- Stretching of oval foramen →↑atrial shunting (L→R).

Hypoxaemic lesions

Cyanosis is defined as the presence of >5g.L^{-1} of reduced haemoglobin. The cardiac causes of hypoxaemia can be classified broadly into:
- Obstruction to pulmonary blood flow
- Transposition physiology
- Common mixing.

Common lesions with obstruction to pulmonary blood flow
- Tetralogy of Fallot
- Pulmonary atresia (with or without VSD)
- Double outlet ventricle with pulmonary stenosis.

Clinical manifestations

The degree of hypoxaemia is determined by the severity of the pulmonary obstruction, and the patency of the PDA. If the obstruction is progressive, there will be a continuing decline in O_2 saturation.
- Adaptive mechanisms:
  - Hyperpnoea
  - Increase in red cell mass—polycythaemia may develop
  - ↑2,3 DPG levels
  - Dilated coronary vessels.

Hypercyanotic spells in tetralogy of Fallot

Characterized by a pronounced fall in O_2 saturation often associated with a manoeuvre causing an increase in intrathoracic pressure, whilst dropping the SVR. Treatment consists of:
- Calm the child
- Oxygen
- ↑SVR:
  - Hip and knee flexion ('squatting')
  - α-receptor sympathetic agent if profound

- Medication:
  - Propranolol (or esmolol in intensive care environment)
  - Morphine.

Initial palliation of any hypoxaemic lesion is to create a stable systemic-pulmonary shunt to replace the PDA.

Transposition physiology

Severity of hypoxaemia is linked to the degree of mixing between the 2 parallel circulations at an intracardiac level.

- Associated lesions:
  - VSD
  - Pulmonary stenosis—quite often complex
- In absence of a significant VSD, neonates are dependent on the size of the atrial communication to maintain adequate oxygen levels.

Immediate management consists of a prostaglandin E infusion and a balloon atrial septostomy

Common mixing

Lesions

- Common arterial trunk (truncus arteriosus)
- Common atrium
- Single ventricle (HLHS)
- Spectrum of hypoplastic RV (tricuspid atresia)
- Anomalies of pulmonary venous return (TAPVD).

Pathophysiology

- Characterized by mixing of systemic and pulmonary blood at some level
- Systemic arterial oxygenation is dependent on the magnitude of the pulmonary venous return relative to systemic venous return
- Manipulation of PVR and SVR can be useful in manipulating the Qp:Qs which will influence O_2 saturation.

Obstruction to systemic output

Can be broadly divided into obstruction to the LV outflow and inflow.

LV outflow tract obstruction

Lesions include:

- Subvalvar, valvar, and supravalvar aortic stenosis
- Aortic arch hypoplasia
- Interrupted aortic arch
- Coarctation.

During fetal development systemic perfusion is not compromised, due to ductal patency, but LV hypertrophy and compromise to LV development can occur to an extent that it is not able to maintain adequate independent systemic circulation (hypoplastic left heart syndrome).

In the postnatal period, ductal patency is essential to maintain systemic flow. The systemic perfusion may be dependent entirely on the ductal flow and right ventricular function (hypoplastic left heart syndrome/ aortic Atresia), or partially (aortic coarctation) where reasonable systemic perfusion can be maintained as long as the aortic end of the ductal patency is maintained.

LV inflow obstruction

Lesions include:

- Mitral stenosis
- Cor triatriatum
- Pulmonary venous obstruction.

The hemodynamic changes in this group cause derangements due to 'back pressure' changes in addition to compromising forward flow. These are:

- Compromised LV output (reduced preload)
- 'Back pressure' changes related to elevated LA pressure:
  - ↑pulmonary venous pressures
  - Pulmonary and RV hypertension
  - Systemic venous congestion (if RV dysfunction).

Regurgitant lesions

Valvar regurgitation is usually associated with other cardiac abnormalities. It can be congenital or acquired—due to an infection or secondary to ventricular dilatation. Symptoms are related to the duration, and severity of the lesions; chronic lesions are better tolerated.

Mitral valve regurgitation (MR) can be due to:

- Isolated (rare)
- Mitral cleft
- AV junction abnormalities (AVSD)
- Papillary muscle infarction (ALCAPA).

Haemodynamic derangements cause:

- Left atrial and ventricular volume overload
- ↑ filling pressures
- Back pressure changes:
  - Pulmonary venous congestion
  - Right heart dilatation and hypertension
- Atrial thrombi
- Atrial dysrhythmias.

Once there is progressive LA dilation, the mitral annulus stretches leading to further ↑ in mitral regurgitation (progressive)

Tricuspid valve regurgitation (TR) *can be due to:*

- Dysplastic tricuspid valve
- Ebstein's anomaly of the tricuspid valve.

Haemodynamic derangements can be similar to discussed earlier, the major differences are:

- Significant instability in neonatal period due to ↑PVR. Haemodynamics improve as resistance ↓
- ↑RA pressures
- R→L shunts → hypoxaemia
- Potential for lung hypoplasia → lung function compromise.

Aortic valve regurgitation (AR) is rarely an isolated anomaly. Haemodynamic derangements include:

- Volume loading of the LV
- LV hypertrophy

- ↑ filling pressures
- Large AR → diastolic runoff → ↓coronary blood flow.

Pulmonary valve regurgitation (PR) can be due to:
- Absent pulmonary valve syndrome
- Following repair/reconstruction of RV outflow tract, e.g. tetralogy of Fallot

Haemodynamic effects:
- RV volume overload
- RV hypertrophy
- Compromised lung perfusion
- LV dysfunction:
  - ↓preload
  - Ventricular interaction.

Pulmonary hypertension syndromes

Pulmonary hypertension (PH) is defined as a mean pulmonary artery pressures of ≥25mmHg.

It can be classified according to aetiology (Box 20.4).

Box 20.4 Aetiology of PH syndromes

- Pulmonary arterial hypertension:
  - Primary PH—unknown cause:
  — familial
  — sporadic
  - Collagen vascular disease
  - Congenital heart disease with systemic-to-pulmonary shunt
  - Miscellaneous:
  — persistent PH of the newborn (PPHN)
  — drugs
  — HIV
  — portal hypertension
- Pulmonary venous abnormalities: left-sided heart disease (mitral stenosis)
- Pulmonary veno-occlusive disease
- Associated with respiratory disease and hypoxemia
- Chronic thrombo-embolic disease: sickle cell disease
  - Other: pulmonary vasculature (e.g. sarcoidosis).

Presentation

- Dependent upon the primary pathology
- Primary PH predominantly affects young people, and has a very aggressive progression
- Diagnosis often delayed in absence of an intracardiac shunt
- Symptoms:
  - Dyspnoea (often diagnosed as ‘asthma’)
  - Frequent respiratory exacerbations (repeated ‘chest infections’)

- Failure to thrive
- Decreasing effort tolerance
- Palpitations, chest pain
- Cyanosis with or without exercise
- Headaches
- Pedal oedema
- Syncope/near syncope.

Diagnosis

- History
- Chest radiograph
- ECG (right-sided changes in 70–80%)
- Echocardiography:
  - Exclude structural heart disease
  - Non-invasive estimation of pulmonary pressure if TR jet is present
- Other investigations:
  - Cardiac catheterization and angiogram
  - Lung perfusion
  - CT scan
  - Lung biopsy.

Treatment

Management of pulmonary hypertensive crises is described on 📖 p.379.

- Treatment of the causative pathology
- Pulmonary vasodilator therapy:
  - Selective type V phosphodiesterase inhibitor (sildenafil)
  - Non-selective endothelin receptor blocker (bosentan)
  - Calcium channel blockers
  - Prostacyclin infusion
  - Inhaled NO
- Home oxygen
- Anticoagulation (aspirin, warfarin)
- Other:
  - Blade atrial septostomy—to allow R→L shunt and preserve cardiac output at the expense of cyanosis
  - Lung transplantation
- Newer therapeutic agents:
  - Vasoactive mediators
  - Potassium channel blockers
  - Serine elastase inhibitors.

Outcome

- Bimodal presentation: aggressive course in infants and adolescents
- Survival:
  - 37% at 1 year following diagnosis
  - 12.5% at 2.5 years
- Lung transplant outcomes (survival):
  - 1 year: 73% (90% for congenital heart disease)
  - 10 years: 30–40%.

Systemic hypertension

Hypertension is uncommon in childhood, but often goes unrecognized for a long time. It is defined as systolic and/or diastolic BP being >95 percentile for age on ≥3 occasions.

Cardiac sequelae of childhood hypertension are uncommon, but acute, severe forms (malignant hypertension) can result in ventricular dysfunction and congestive heart failure. Long standing hypertension can result in:

- Diastolic dysfunction with ↑late filling (prominent 'A' contribution relative to 'E')
- LV hypertrophy
- ↑filling pressures.

Causes

Box 20.5 Causes of hypertension

- Essential (idiopathic)
- Cardiovascular:
  - Coarctation
  - Defects with diastolic runoff (result in *systolic* hypertension):
  — arteriovascular malformation
  — PDA
  — severe AR/MR
- Reno-vascular:
  - Parenchymal renal disease
  - Polycystic kidneys
  - Renal artery stenosis
  - Tumours (Wilms')
- Endocrine:
  - Phaeochromocytoma
  - Congenital adrenal hyperplasia
  - Cushing's disease
- Drugs: steroid therapy.

Presentation

- May be asymptomatic and be detected coincidentally
- Symptoms of primary pathology
- Headaches, visual disturbance
- Encephalopathy (if severe)
- Epistaxis.

Treatment

Hypertensive crisis: after initial resuscitation, aim should be to reduce BP but to avoid a precipitous drop to maintain organ perfusion. Rule of thumb is to reduce BP by no more than 25% in first 12–24H. A quicker reduction is safe if the BP rise is of very recent onset.

Drugs include:
- Nifedepine (oral)
- Labetelol or esmolol infusion
- Sodium nitroprusside infusion
- Hydralazine.

Treatment of primary pathology
- Management of BP:
- Non-pharmacological
  - Weight management
  - Dietary modification (sodium reduction)
- Pharmacological
  - ACE inhibitors (captopril, enalapril)
  - Angiotensin receptor blockers (ARBs) (losartan)
  - β-adrenergic receptor blockers (propranolol, atenolol)
  - Diuretics (frusemide, thiazide)
  - Calcium-channel blockers (nifedepine)
  - Miscellaneous, e.g. minoxidil

Dilated cardiomyopathy and myocarditis

Dilated cardiomyopathy is a group of heterogeneous aetiologies uniformly characterized by ventricular dilatation and impairment of contractility. LV function is usually more affected than RV. Causes are multifactorial, see Box 20.6.

Box 20.6 Causes
- Idiopathic (>50%)
- Myocarditis (10–15%)
- Familial/genetic (20–35%, autosomal dominance is most frequent)
- Autoimmune
- Drug induced (anthracycline)
- Miscellaneous:
  - Persistent arrhythmias
  - Structural heart disease
  - Inborn errors of metabolism
  - Coronary arterial disease (ALCAPA)
  - Neuromuscular disorders.

Myocarditis is an acute process characterized by inflammatory infiltration of the myocardium along with cellular necrosis, and is caused by infectious agents (e.g. enterovirus, coxsacchie), or can be an autoimmune process (e.g. lupus).

Incidence and prevalence are low in children; however there is some evidence of an increasing trend. It is likely that a number of less severe cases of myocarditis associated with a viral infection go undetected.

Presentation

There is a variable period during which the child is asymptomatic as the heart undergoes dilatation and hypertrophy to maintain cardiac output. Cases with a family history may be picked up at this stage on screening. With progression congestive heart failure ensues:

- *Infants*: tachypnoea, feeding difficulties, failure to thrive, sweating
- *Older children*: decreasing effort tolerance with exertional dyspnoea, palpitations, arrhythmias, or syncope (13%).

Diagnosis

- Detailed history including relevant past and family history
- CXR, ECG, and Echo to confirm the diagnosis
- Cardiac catheterization and myocardial biopsy are not routinely performed due to associated high risk
- Cardiomyopathy screen to identify cause—details are available from any paediatric cardiology unit.

Treatment

Acute treatment consists of stabilization and may include inotropes, cautious use of diuretics, and mechanical ventilation if the child has decompensated.

Induction of anaesthesia is high risk if ventricular function is severely compromised:

- Summon expert assistance
- Start inotropic therapy ahead of induction, have epinephrine available
- Use small doses of induction drugs that are unlikely to acutely drop cardiac output or SVR (ketamine, fentanyl, etomidate rather than thiopentone, propofol).

Once stable, management should be aimed towards:

- Identification and treatment of cause
- Decreasing cardiac afterload (ACE inhibitors)
- Diuretics (frusemide)
- Prevention of arrhythmias (digoxin)
- Prevention of thromboembolic phenomena (aspirin or heparin)
- Newer therapies (stable patients in chronic heart failure):
  - β-blockers—carvedilol
  - ARBs—losartan
  - Cardiac resynchronization therapy.

Specific issues

Myocarditis therapy: unproven but used in some centres.

- Immunomodulatory therapy—IV immunoglobulin (IVIG)
- Immunosuppressive therapy—steroids, cyclosporine, azathioprine.

Continuing cardiac instability

- Mechanical support—LV assist device (LVAD), e.g. Berlin Heart Excor® as a bridge to heart transplant, ECLS for myocarditis.

Outcome

- Complete resolution (25–35%)
- Residual cardiac dysfunction (30–35%)
- Deterioration and death/transplant (25–35%).

Poor prognostic factors
- Idiopathic
- Age at diagnosis: <2 years
- First 2 years after presentation.

Prognosis for acute myocarditis in newborns is very poor (up to 75% mortality; highest within 1st week of presentation). Older infants and children bear a better prognosis with 10–25 % mortality, and complete recovery in >50%.

Infective endocarditis

Infection of the endocardium, heart valves, or related structures is known as infective endocarditis. Risk factors include:
- Structural heart disease
- Neonates with invasive procedures or lines
- Prosthetic material in the heart or great vessels

Pathophysiology

The genesis is multifactorial, and difficult to confirm; there is turbulent blood flow leading to endothelial damage. Aggregation of platelets, and fibrin deposition (non-infective thrombotic vegetation) follows. Colonization can occur and is more likely with bacteria producing dextran, in the presence of fibronectin at the local site (Box 20.7).

Infection can damage cardiac structures, vegetations may obstruct blood flow, and occasionally will embolize to other areas, most commonly the lungs (or brain).

Immunological mechanisms are central to pathogenesis, and sequelae of this process, and involves cell-mediated and humoral mediated pathways.
- Hypergammaglobulinaemia:
  - Polyclonal and antigen specific B-cell activation
  - Rheumatoid factors
- ↑levels of:
  - Circulating immune complexes
  - Mixed-type cryoglobulinaemia
- Renal involvement (due to immune complex deposition).

Box 20.7 Commonest organisms include:

- Streptococcus viridians (~40%; commonest)
- Other streptococci
- *Staphylococcus* (most common in postoperative period)
- Gram-negative organisms
- Fungi.

Presentation

- Fever
- Anorexia/weight loss
- Malaise

- Arthralgia
- Chest pain
- Congestive heart failure
- Specific skin lesions less common in children:
  - Petechiae (1/3 cases)
  - Osler's nodes/Janeway lesion/Roth spots/splinter haemorrhage (<10%)
  - Splenomegaly
  - New or changing murmur
- Embolization of infective foci to other organs (e.g. cerebral infarcts).

Investigation (Box 20.8)
- Blood cultures: at least 3–5 samples in the first 24h of presentation (negative in 10–15%)
- FBC: neutrophilia
- Inflammatory markers: very high ESR, raised CRP
- Echocardiography: TTE has 44% sensitivity to detect vegetations
- ECG: ectopic beats, blocks, ST/T changes
- Circulating immunologic complexes (in difficult cases).

Box 20.8 Learning point

Infective endocarditis is a clinical diagnosis confirmed by presence of positive blood cultures. Presence of an echogenic focus (vegetation) on echocardiography supports the diagnosis; however a negative result does not rule out the diagnosis.

Treatment
- Antibiotics for 4–6 weeks (guidance from microbiologists):
  - Usually 2 antibiotics
  - Initial parenteral therapy
- Central venous access only after sterilization of blood and resolution of symptoms: prophylaxis is mandatory for prevention/relapse.

Prognosis
- 20–30% mortality even in the modern era of antimicrobial, therapy
- Always at higher risk for subsequent infection.

Pericarditis and cardiac tamponade

Pericarditis can occur due to:
- Infections:
  - Viral infection:
  — coxsackie, varicella, influenza, infectious mononucleosis, Echo, mumps
  - Purulent infection:
  — *S. aureus* (1/3 cases; 3/4 of those who die)
  — *Haemophilus influenza*, type b
  — *Streptococcus*

  - — *M. pneumonia*
  - — *Candida*, *Aspergillus* (immunocompromised host)
  - TB
  - HIV
- Auto-immune disorders
- Connective tissue disorders
- Malignancy
- Others: drugs, therapeutic procedures.

Presentation

- Clinical manifestations of the primary disorder
- Chest pain
- Pericardial rub
- More severe forms tend to show manifestations of abnormal perfusion:
  - Tachycardia
  - Low volume pulses
  - Pulsus paradoxus
  - Tamponade.

Diagnosis

- Specific investigation for underlying aetiology
- Acute inflammatory markers: CRP/ESR
- Cardiac enzymes (may be elevated)
- ECG:
  - Low voltage complexes
  - Widespread T-wave/ST changes
- Chest radiograph (enlarged heart)
- Echo:
  - Pericardial effusion
  - Echogenic objects (fibrin, clots)
  - Atrial collapse
  - Ventricular function
- Other: cardiac MRI, CT scan, cardiac catheterization.

Treatment

- Treatment of primary cause—antibiotics
- Treatment of haemodynamic alterations:
  - Stabilization of haemodynamics (fluid, inotropes, ventilation if required)
  - Arrhythmias
  - Decompression of pericardial fluid.

Cardiac tamponade

Tamponade occurs when there is sufficient fluid in the pericardial cavity to cause compromise to cardiac filling or contractility, and is not necessarily related to the amount of fluid in the cavity (or size of cardiac silhouette on CXR).

It can be seen as a result of acute pericarditis or in the postoperative period following cardiac (thoracic) surgery.

Presentation
- Dyspnoea
- Tachycardia, small volume pulses
- Narrow arterial pulse, hypotension
- Elevation of systemic venous pressures (CVP, LAP if line present)
- Pulsus paradoxus (decreasing/absent pulses in inspiration).

Treatment
- ABC stabilization—volume, inotropes, ventilation
- Pericardial drainage is the definitive acute management:
  - Needle aspiration can be done as an emergency procedure at the bedside
  - Pericardial tap and insertion of a drain can be done under US or angiographic guidance
  - Surgical drainage, advised if:
  — fluid is posterior
  — adhesions
  — purulent fluid
  — pericardial thickening.

Postoperative care

The practice of cardiac intensive care has evolved considerably over the past 10 years with:
- Greater use of interventional procedures in the catheter lab with device closures of ASD, VSD, PDA, and even percutaneous valve replacements
- Earlier surgical intervention so that postoperative pulmonary hypertension is much less common
- Changes in inotrope and vasodilator therapy
- Greater use of ultrafiltration following bypass and ECLS for children in a low cardiac output state
- Fast-tracking of suitable patients to achieve short PICU and hospital stays.

Cardiac surgical patients epitomize the importance of a multidisciplinary approach in a specialized paediatric or cardiac ICU.

Immediate postoperative care

The major goal is to establish adequate cardiac output to ensure tissue oxygen delivery and end-organ function. This is best addressed with a systematic approach.

Cardiovascular
- Anaesthetic and surgical handovers provide vital information from the operating room whilst the patient was on and off CPB.
  - It is important that both occur as they will provide different information
- Note CPB, aortic cross clamp, and circulatory arrest durations

- Note invasive monitoring lines such as atrial and pulmonary artery lines over and above standard arterial and central venous lines
- If rhythm disturbance is anticipated, attach the temporary epicardial pacing wires to a pacemaker.

Clinical examination on arrival to the PICU is imperative.
- Assess pulses and perfusion and markers of adequate cardiac output including lactate and urine output
- High lactate persistently >5mmol/L is associated with a poor outcome
- Note the type and amount of inotropic support required
- Early Echo is useful to look at ventricular function and postoperative anatomy.
- Low cardiac output state must be anticipated and treated (see 📖 p.373)
- Transfuse blood to keep Hb >10g/dL in those with cyanotic heart disease.

Respiratory

Most patients will return to the PICU intubated and mechanically ventilated until cardiorespiratory adequacy is established.

Uncomplicated cases can often be extubated within a few hours on the ICU if certain criteria are met (Box 20.9).

Box 20.9 Criteria for extubation

- Patient is warm, awake, and calm with intact airway reflexes
- Spontaneous regular breathing
- Haemostasis is achieved
- No significant acid–base disturbance
- Stable haemodynamics on low-level inotropic support
- Satisfactory postoperative CXR and Echo

Continued mechanical ventilation (Box 20.10) may be required for various reasons:
- Airway control
- Unstable haemodynamics with compromised cardiac output
  - To reduce oxygen demand
  - Favourable effects of positive pressure ventilation on cardiac function (reduction in systemic afterload)
- Neurological problems
- Inappropriate level of hypoxaemia, due to V/Q mismatch
- Residual effects of anaesthesia.

Routine post operative CXR to confirm
- Appropriate ETT position
- Location of chest drains and monitoring lines
- To identify lung pathology such as pneumothorax, pleural effusion, or atelectasis
- Look for signs of a widened mediastinum, as this may suggest accumulation of blood within the chest. If drains are not functioning well, this requires further investigation and possible re-exploration (see 📖 p.381).

Box 20.10 Principles of ventilation

- Avoid a high mean airway pressures which will impede systemic venous return, ↑PVR, and reduce cardiac output—especially important after BCPS or Fontan procedure
- Set PEEP ~5cmH_2O unless lung pathology demands a higher PEEP—too high PEEP will ↑ PVR but too low PEEP will result in atelectasis, which will also ↑ PVR
- Use a volume mode with TV ~10mL.kg, limit further if ↑PIP
- Set age-appropriate respiratory rate (12–30 breaths/min) and inspiratory time (0.7–1.5s)
  - Aim for short I:E ratio after BCPS and Fontan as pulmonary blood flow occurs during expiratory phase of ventilation
- Ventilate to a normal $PaCO_2$:
  - Avoid hyperventilation as it causes ↑ SVR and ↓cardiac output
  - Tolerate mild hypercapnia and mild respiratory acidosis.

Infection

Surgery should be deferred if a history of acute illness or infection is obtained in the preoperative assessment.

Infection is uncommon in the immediate postoperative period. However, fever is common and may reflect a systemic inflammatory response to CPB. Patients are routinely covered with prophylactic antibiotics for up to 48h (penicillins/cephalosporins). The optimum antibiotic regimen and duration is unclear for patients with delayed sternal closure and practice varies widely.

- Strict aseptic central venous catheter management is essential with early line removal when possible
- Regular mouth care and oral toilet
- Whilst on antibiotics some prescribe oral fungal prophylaxis
- Screen for infection early and have a low index of suspicion
- Stop antibiotics at 48–72h if cultures are negative
- Fever should be avoided as it causes ↑O_2 demand and may exacerbate brain injury
- Consider fungal infection in the chronic patient.

Renal

Fluid and electrolyte imbalance is common after CPB:

- CPB is associated with a large positive sodium and water balance
- Secondary capillary leak and sodium and water retention following CPB will further augment a positive fluid balance
- Reduced cardiac output will compromise renal blood flow and urine output; secondary release of renin, angiotensin, and antidiuretic hormone will exacerbate fluid overload
- Secondary capillary leak and sodium and water retention following CPB will further augment a positive fluid balance
- Consider diastolic dysfunction and sepsis if oedema persists.

Close attention to strict hourly fluid balance is paramount. Assess patient volume status with clinical examination and pre-load estimates (CVP, atrial pressures).

Box 20.11 Principles of postoperative fluid and electrolyte management

- Restrict fluid therapy to 25–50% maintenance in the initial 24–48h
- Minimal expected urinary output is 0.5mL/kg/h
- Maintain potassium at 3.5–4.5mmol/L to avoid cardiac arrhythmias:
  - *Hypokalaemia*—give 0.5mmol/kg IV KCL infusion over 60min via central line
  - *Hyperkalaemia*—remove K^+ from maintenance fluid. Monitor for peaked T waves on ECG. Give IV insulin/dextrose if present. Consider IV $NaHCO_3$ or CaCl in an emergency. Consider dialysis if hyperkalaemia persists (see 📖 p.257)
- *Hyperglycaemia* is common post CPB:
  - Tight glycaemic control may improve outcome in adults
  - There is no evidence for this in the paediatric cardiac patient
  - Treat with IV insulin infusion if persistently >12 mmol/L or if an associated osmotic diuresis
  - Avoid causing hypoglycaemia
- Diuretics are frequently used to augment urine output:
  - Loop diuretics; furosemide used intermittently at 0.5–1.0mg/kg or continuously as an infusion of 0.1–1.0mg/kg/h
  - Thiazide diuretics (metolazone/chlorothiazide) may be added
  - Aminophylline has diuretic properties
- Oliguria and renal failure may necessitate early institution of peritoneal dialysis or CVVH (see 📖 p.257).

GI/nutrition

Nutrition is an essential part of postoperative management:

- Aim for early enteral feeding in uncomplicated cases
- All patients should have a NG tube—aspirate 4-hourly.

If feeds are not expected to advance, it is important to continue with low volume trophic feeds at 1–5ml/h according to body weight. This may reduce translocation of gut bacteria and decrease the risk of multiorgan failure.

Exercise caution in patients who had prolonged CPB and DHCA times or low cardiac output state pre- and postoperatively as gut perfusion may be affected. In these patients, consider complete bowel rest and institute TPN early to optimize caloric and protein intake. Consult dietician.

- Feeding is routinely stopped for 4h prior to extubation.

Neurological; analgesia, sedation and neuromuscular blockade

Analgesia

Postoperative pain must be anticipated and treated. Most patients will return from the operating room with a continuous opiate infusion.

- Commonly IV morphine sulphate infusion at 10–50mcg/kg/h
- Alternatives are fentanyl (shorter half-life) and remifentanil (very short half-life)
- There is increasing interest in the use of thoracic epidurals in selected cases.

Sedation

IV benzodiazepines (midazolam/lorazepam) may be added for further sedation but are often avoided in the neonatal population because of haemodynamic side effects.

In some centres these drugs are given continuously by infusion, others give intermittent doses as required.

- Oral sedation allows use of lower doses of benzodiazepines.
- Chloral hydrate, triclofos, Vallergan® are examples
- Clonidine (oral or IV) can be used as an alternative to midazolam.

Neuromuscular blockade (NMB)

(Rocuronium/vecuronium/atracurium/cisatracurium) is given intermittently as boluses or as a continuous infusion. Either regimen can be used but adequate sedation is important.

- NMB should be discontinued as soon as possible
- Nerve stimulation ('train of four') should be used to aid titration
- Daily 'holiday' from NMB is helpful not only to titrate drug dose but also to allow neurological evaluation
- In circumstances where patients require heavy sedation and prolonged NMB, EEG may be of benefit.

Drug accumulation is common in the postoperative paediatric cardiac population so drugs need to be weaned as soon as allowed. This will facilitate regular neurological examination required to elicit the possible CNS complications of surgery and CPB. Neurological injury is uncommon, but the risk is ↑ when DHCA is required (see 📖 p.225).

Early postoperative problems

Low cardiac output state (LCOS) (Box 20.12)

Inadequate cardiac output usually indicates abnormal recovery and signs of this need to be monitored vigilantly. Clinical manifestations include:

- Poor perfusion and haemodynamic instability
- High or increasing inotrope requirement
- Oliguria with or without rising serum K levels
- Hyperlactataemia with or without metabolic acidosis.

Although direct measurement of cardiac output is more frequently utilized in PICU, there are additional indirect variables and indicators.

- Declining $ScvO_2$ is suspicious of a LCOS
- Rising lactate implies inadequate DO_2 and predicts a poor outcome.

Box 20.12 LCOS may be caused by:

- Low preload (atrial or central venous pressure)
- Impaired myocardial contractility (RV or LV or both)
- Impaired ventricular relaxation/filling (diastolic dysfunction)
- High afterload (SVR or PVR)
- Rhythm disorder
- Cardiac tamponade
- Residual anatomic defect post-surgical repair.

Preload

- Atrial pressures are directly related to intravascular blood volume status but also related to ventricular compliance
- Fluid administration is guided by LAP and RAP, and the haemodynamic response to a fluid bolus
- Right-sided procedures, such as TOF, often need higher RAP to maintain cardiac output; RV compliance is poor
- Certain left-sided procedures, such as TAPVC, are associated with a higher LAP.

Impaired myocardial contractility

Measures are taken to protect the myocardium during CPB. However, the systemic inflammatory response to CPB induces a spectrum of pathophysiological changes ranging from mild organ dysfunction to multisystem organ failure.

Factors that will depress myocardial performance include:

- Need to perform a ventriculotomy (RV–PA conduits)
- Disturbance to coronary arteries (arterial switch, TOF)
- Air or other emboli
- Metabolic derangements (acidosis, Ca, glucose)
- Epinephrine in high doses may be damaging to the myocardium.

Inotropic support (see 🕮 Chapter 11)

Most patients require inotropic support in the postoperative period. Choice of agent will depend on vascular tone of the pulmonary and systemic circulations and the degree of myocardial dysfunction (see Table 20.1).

Commonly used agents are dopamine, dobutamine, adrenaline but PDEIs (milrinone, enoximone) are increasingly popular for their inodilatory properties. norepinephrine is used for its combined inotropic and vasoconstricting properties. Occasionally vasopressin is used in catecholamine resistant shock. Newer agents are being developed, e.g. levosimenden, but require careful evaluation.

Table 20.1 Vasoactive agents

Drug	Effects	Dose range	Side effects
Dopamine	Dopaminergic	3–20mcg/kg/min	↑HR, arrhythmias, α effect at doses >20mcg/kg/h
Dobutamine	β1, β2	3–15mcg/kg/min	Less arrhythmias than adrenaline but chronotrophy
Adrenaline	α, β1, β2	0.01–1.0mcg/kg/min	↑BP, ↑HR, ↑arrhythmias

Table 20.1 (*Continued*)

Drug	Effects	Dose range	Side effects
Noradrenaline	α and β1	0.01–1.0mcg/kg/min	– ↑SVR, moderate intropy
Milrinone	Phosphodiesterase inhibitor	0.1–1.0mcg/kg/min	Lusitrophy, inodilation, minimal ↑HR

High afterload

- Vasoconstriction and ↑SVR lead to extra LV work and reduced cardiac output
- Reversible causes such as hypoxia, pain, and hypothermia must be identified
- Vasodilation is achieved with sodium nitroprusside (SNP), GTN, or a PDEI (milrinone, enoximone)
- α-blockade with phenoxybenzamine is still used but is difficult to titrate because of its long half-life.

Rhythm disorders (see 📖 p.350)

- Sinus rhythm at normal rate is optimum
- It is essential to determine the cardiac rhythm with a 12-lead ECG
- Maintenance of AV synchrony is vital to maximize cardiac output
- If arrhythmia is anticipated attach temporary epicardial pacing wires to pacemaker
- In some situations an atrial wire ECG may be helpful to differentiate between atrial and ventricular activity especially when rates are rapid:
  - Performed to amplify atrial activity and to define the relationship of P wave to the QRS complex in tachycardias
  - Attach one or both atrial wires to V1 whilst performing a 12-lead ECG
  - If the atrial spike occurs before the QRS complex then sinus tachycardia is likely
  - If the atrial spike is seen within the QRS or just after the QRS then retrograde conduction from a junctional ectopic focus is more likely
  - If dissociation of P and QRS complexes is found the tachycardia is likely to be a His bundle tachycardia

Bradycardia

- Surgery near the conduction system (AVSD) can cause secondary tissue oedema and heart block but this usually resolves spontaneously
- Temporary pacing using epicardial wires may be necessary
- It is uncommon to require a permanent pacemaker
- Consider permanent system if complete block persists at 7 days

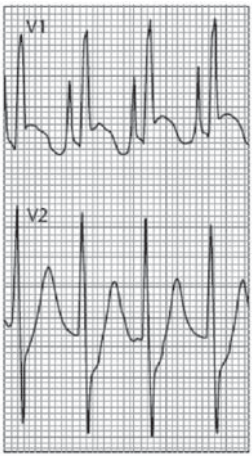


Fig. 20.4 Atrial (V1) and surface (V2) ECGs in NSR—P waves are amplified by atrial ECG. Reproduced from Mackey J and Arrowsmith J (eds) (2004) *Core topics in cardiac anaesthesia* with permission from Cambridge University Press.

Tachycardia

- *Atrial fibrillation* can be treated with digoxin if patient is stable or electrical cardioversion if haemodynamically unstable
- *Atrial flutter* often responds to overdrive pacing but may require electrical cardioversion and digoxin
- SVT is more common:
  - Terminate with IV adenosine which slows or blocks AV conduction
  - Overdrive pacing or synchronized DC cardioversion may be used
- Junctional ectopic tachycardia (JET):
  - Results from abnormal automaticity of the AV node or His bundle
  - More common following TOF, VSD, AVSD, and Fontan procedures
  - Reduce adrenergic agents, correct metabolic disturbance and fever
  - Does not respond to cardioversion, often unresponsive to drug therapy
  - Atrial or dual chamber pacing at a faster rate restores AV synchrony and improves CO
  - Surface cooling to <35°C may be required to slow the junctional rate enough to allow effective pacing
- *Ventricular dysrhythmias* are rare in paediatric practice, but VT or VF needs immediate DC cardioversion.

Temporary pacing

Pacing is indicated when there are manifestations of low cardiac output and cardiovascular compromise:

- ***Atrial*** wires are sited to the right side of the chest
- ***Ventricular*** wires are sited to the left side of the chest.

Pacing modes are described by a standard nomenclature: this describes in sequence:

- The chamber(s) paced:
  - Atrium (A)
  - Ventricle (V)
  - Dual (both) (D)
- The chamber(s) sensed:
  - Atrium
  - Ventricle
  - Dual
  - Neither (O)
- The response to sensing:
  - Triggered (T)
  - Inhibited (I)
  - Dual (T and I) (D).

Other terms that are sometimes used, mapped to the listed nomenclature:

- Fixed rate pacing — AOO or VOO
- Atrial demand pacing — AAI
- Ventricular demand pacing — VVI
- AV sequential pacing — DVI
- AV universal — DDD
- AV demand — DDI.

Modes used

Emergency mode DOO

- Both chambers are paced
- Useful in asystole.

DDD

- Both chambers are sensed and paced
- Used in complete heart block/sinus brady/JET.

AAI

- Only the atrium is sensed and paced
- If the pacemaker senses an atrial impulse, it is inhibited
- Used in sinus bradycardia.

An atrial mode should only be used if AV conduction is intact.

VVI

- Only the ventricle is paced and sensed
- Used in AF with no AV conduction, sinus bradycardia and complete heart block (CHB)

DVI

- Both chambers are paced, ventricle only is sensed
- If pacemaker senses a ventricular impulse then it is inhibited
- Used in sinus brady, CHB, and JET

Rapid atrial pacing

Can be used to overdrive pace an SVT

- Pace above the SVT rate until capture is achieved
- Default rate is 320bpm although this can be adjusted

Pacemaker checks

- Ensure daily pacemaker check and spare battery is available at all times
- Assess pacemaker thresholds daily particularly if patient is pacemaker dependent
  - Gradually lower ventricular output until the ventricular complex is lost; this may result in loss of ventricular output
  - Do the same with the atrial output
  - Record thresholds in mA
  - Return output to a higher setting (threshold + 2mA or twice the threshold are commonly used approaches).

Bleeding and cardiac tamponade (see 📖 p.381)

Residual anatomic defect

- Needs to be considered when LCOS persists
- Consider TOE if TTE inconclusive (better visualization, in particular venous pathways and atrial anatomy)
- Early cardiac catheterization if no progress
- Surgical or catheter intervention correction of residual defect.

Other options in LCOS

- The sternum may be left open to allow myocardial oedema to subside.
- Consider extra corporeal life support (ECLS) (see 📖 Chapter 11)
  - Early referral to an appropriate ECLS centre is recommended
  - Veno-arterial ECLS is required for cardiorespiratory support
  - Commence before irreversible end-organ damage has occurred
  - Cannulation is usually transthoracic but access via neck vessels is also possible if anatomy permits.

Pulmonary hypertension

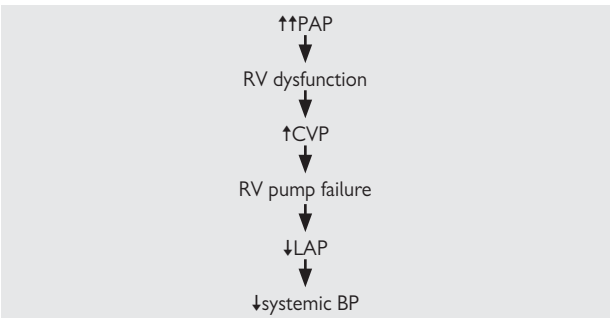
- Seen in lesions with large L→R shunts with chronic high pulmonary blood flow (AVSD, truncus); muscular hypertrophy of PAs
- Pulmonary pressures also increase from any condition that impedes pulmonary venous drainage (obstructed TAPVC)
- ↑PVR may be reactive or fixed
- Assessment of PVR and reactivity to O_2, iNO at cardiac catheterization can identify a high-risk group for postoperative PH
- Postoperative ↑PA and RV pressures may result in RV failure.

Diagnosis of postoperative pulmonary hypertension

- A PA line is inserted via the RVOT in cases judged to be at risk
- Mean PA pressure should be <20mmHg post complete repair
- Ratio of mean PA to mean systemic pressure is a useful measure of the degree of PH; ratio <50% seldom results in RV dysfunction
- Echo can be used to estimate RV pressure if no PA line:
  - Measure peak Doppler velocity (V) of tricuspid regurgitant jet
  - Pressure differential between RA and RV can be estimated = $4 \times V^2$
  - RV pressure = CVP + ($4 \times V^2$)
- RV pressure should equal PA pressure if no RVOTO is present.

Clinical features

- A pulmonary hypertensive crisis can occur if PA pressure increases towards or above systemic level
- Pulmonary hypertensive events are often accompanied by a sudden reduction in lung compliance, which may mimic a blocked ETT



Treatment (see Box 20.13)

- Is aimed at ↓PVR and supporting RV function
- No treatment may be required if ↑PA pressure is well tolerated
- Keep patient well sedated with opiates and benzodiazepines
- Consider muscle relaxant; reduces metabolic demand and facilitate ventilation
- Avoid situations that lead to ↑O_2 demand (fever/pain)
- Ventilate to normal blood gases
  - Oxygen is a pulmonary vasodilator; prevent hypoxaemia but avoid sustained high FiO_2 (pulmonary toxicity)
  - Avoid hypercapnia, do not use hyperventilation to ↓PVR as it causes ↑SVR and ↓CO.
- Inhaled NO (5–20ppm) is a potent selective pulmonary vasodilator and the treatment of choice
  - Acute ↓PAP should be evident immediately
  - Discontinue if no beneficial response within 30min
  - Monitor NO_2 and methaemoglobin levels regularly
  - Be aware of rebound ↑PAP on stopping iNO; slow withdrawal from 2ppm, increase FiO_2, consider covering with sildenafil if on iNO for some time.
- Consider other pulmonary vasodilators
  - Prostacyclin
  - Phenoxybenzamine
  - Sildenafil
  - Bosantan.

Box 20.13 Treatment of a pulmonary hypertensive crisis

- Sedate and paralyse
- FiO_2 1.0, ventilate to low/normal $PaCO_2$
- Correct acidosis with bicarbonate therapy
- Increase inotropic support—epinephrine, milrinone
- Add iNO at 20ppm
- Arrange urgent Echo.

Renal impairment

(See 🕮 Chapter 14.)

Renal impairment is common following cardiac surgery and ranges from mild oligeria (Box 20.14) to renal failure requiring dialysis (Box 20.15).

- Measurement of GFR is complicated so we rely on plasma creatinine as a marker of GFR:
  - GFR ~ 1/creatinine
  - However creatinine does not increase until GFR falls by ~50%
  - Be aware that plasma creatinine is related to muscle mass; normal is <40 ummol/L in an infant, 70–100umol/L in an adolescent male.
- Drug dosing must be modified in the light of renal dysfunction (see 🕮 p.306).

Survival is reduced in patients who require renal replacement therapy after cardiac surgery.

Box 20.14 The oliguric patient

- Assess cardiac output/oxygen delivery—increase inotropic and vasodilator support if LCOS
- Try volume bolus—assess haemodynamic response and urine output
- Rule out catheter problem if oliguria doesn't fit clinical picture
- Consider furosemide if oliguria persists despite optimizing preload—infusion may be needed
- Introduce renal replacement therapy if no response to furosemide infusion or if hyperkalaemia, acidosis.

Box 20.15 Indications for dialysis

- Oligo-anuria
- Uncontrolled hyperkalaemia
- Worsening metabolic acidosis
- Fluid overload with cardiorespiratory compromise
- Rising urea and creatinine.

Renal replacement therapy (dialysis or filtration)

(See 🕮 Chapter 14.)

Commonly used options include peritoneal dialysis (PD) and continuous veno-venous haemofiltration (CVVH) or haemodialysis (CVVHD). Acute haemodialysis is associated with haemodynamic instability so is best avoided.

PD
- Catheter may be inserted at time of surgery to allow drainage of peritoneal fluid and PD to be easily instituted if needed
- Commonly used in neonates and infants undergoing complex repairs
- Techniques are intermittent ('in and out') PD, automated cycling PD, and 'cross flow' PD (requires 2 catheters)
- Limited clearances achieved
- Volumes of 10–30mL/kg used, with 30–60-min dwell time.
- Adjust dextrose concentration ('strength') to achieve fluid balance.

CVVH or CVVHD
- More complex, requiring vascular access and extracorporeal circuit
- Can be run with no anticoagulation but circuit life will be shorter
- More predictable fluid balance, more efficient clearances
- Technique of choice in older child.

Arrhythmias see 🕮 p.350

Bleeding and cardiac tamponade

Box 20.16

- Monitor and replace blood loss
- Correct coagulopathy; aim for platelet count >150
  - Thromboelastography may be useful in addition to conventional tests of coagulation in discerning whether platelets or clotting factors should be given
- If >5mL/kg for consecutive hours consult for surgical exploration
- Aim to re-explore before signs of tamponade
- ECHO does ***not*** exclude a pericardial collection
  - Do not delay chest exploration of you suspect tamponade
- Suspect tamponade if LCOS does not respond to medical management
- Other signs include:
  - Equalization of elevated atrial pressures
  - Sudden drop in chest drainage
  - Widened mediastinum on CXR
  - Pulsus paradoxus
  - New arrhythmias
- Urgent surgical re-exploration is advised.

Necrotizing enterocolitis (NEC)

The risk of NEC in the neonatal cardiac population is substantial. Associated risk factors include prematurity, HLHS, truncus arteriosus, and episodes of low cardiac output and shock.

Clinical presentation varies and diagnosis is often difficult:
- Abdo distension
- Unexplained persistent tachycardia
- Bilious aspirates/vomitus
- Bloody stools
- Dilated bowel loops
- Pneumatosis ~may not be present on AXR

Pneumoperitoneum is a late sign and an absolute indication for laparotomy. Most cases are managed conservatively:
- IV antibiotics (cephalosporin/aminoglycoside/metronidazole) for 7–10 days
- Withold enteral feeds
- Commence parenteral nutrition early.

Have a high index of suspicion and institute treatment promptly as cardiac patients requiring surgery for NEC have a very high mortality rate.

Late postoperative problems

Chylothorax

Accumulation of chyle in the pleural cavity:
- 2% incidence after CHD surgery
- Suspect when there is a persistent pleural effusion often with a creamy yellow appearance
- Confirm with analysis for chylomicrons or lymphocytic predominance on differential cell count.

Causes
- Direct injury to the thoracic duct and accessory lymphatic channels during surgery
- Elevated systemic venous pressures; occurs more commonly with RVOT lesions.

Chronic large losses lead to immune and nutritional deficiencies due to loss of T-lymphocytes, chylomicrons and electrolytes. Monitor IgG levels.

Treatment
- Replace standard feeds containing LCT with MCT preparation
- If persists stop enteral feeding and start parenteral nutrition
- Consider octreotide, a long-acting somatostatin analogue for persistent chylothoraces—exact mechanism unknown but likely related to multiple GI effects including ↓splanchnic blood and thoracic duct flow
- Surgery is indicated when medical therapy fails:
  - Ligation of thoracic duct
  - VATS
  - Pleurodesis
  - Pleuroperitoneal shunt.

Paralysis of hemidiaphragm

- Occurs after 1% of cardiothoracic surgery
- Due to damage to the phrenic nerve:
  - Nerve stretching
  - Blunt trauma
  - Electrocautery/diathermy
  - Ice injury
  - Nerve transection.
- More common on the left side.

Clinical suspicion
- Unable to successfully wean from ventilator
- Unexplained respiratory distress
- Diaphragm sitting high on CXR
- Abnormal breathing pattern; lack of abdominal excursion on inspiration.

Diagnosis
Fluoroscopy or US (M-mode) whilst patient is self-ventilating is diagnostic; important to time inspirations to confirm paradoxical motion.

Management
- Some resolve with conservative management but may require a period of NIV
- Plication of the diaphragm improves FRC and is warranted if unable to wean from mechanical ventilation.

Bilateral diaphragmatic paralysis
- Very rare
- Diagnosis can be missed on screening as both sides may move paradoxically together; careful timing of inspiration will make the diagnosis
- Usually ventilator dependent until recovery of one hemidiaphragm
- Bilateral plication may be of benefit.

Brain injury

The precise incidence of neurological complications following cardiac surgery is unknown as subtle deficits may go undiagnosed. The aetiology is often multifactorial, with a number of considerations (see Box 20.17).

Box 20.17 Aetiology of brain injury

- Genetic factors
- Preoperative factors: periods of profound hypoxaemia, shock, intracranial haemorrhage
- Duration of DHCA
- Adequacy of cerebral neuroprotection
- CO_2 strategy: pH stat or Alpha stat
- CPB haematocrit
- Emboli: air or particulate
- Cerebral perfusion pressure: high SVC pressure will reduce CBF
- Postoperative hyperthermia.

Clinical presentation varies from seizures, encephalopathy, and choreiform movements in the acute setting, to cerebral palsy and learning disorders later on.

Diagnosis
- MRI is the imaging modality of choice; CT is useful but cerebral USS is of limited value in detecting hypoxic-ischaemic injury
- EEG may detect sub-clinical seizure activity.

Staged palliation of a univentricular heart

A number of lesions are not suitable for a 2-ventricle repair and are managed with a series of 2 or 3 palliative procedures. Examples include mitral atresia, tricuspid atresia, some forms of pulmonary atresia, DILV, and HLHS.

In the neonatal period surgery may be required to optimize pulmonary blood flow

- Too little blood flow requires an arterial–pulmonary artery shunt
- Too much blood flow requires a PA band to reduce blood flow.

PVR is high in the newborn period and falls over the first few months of life. Creation of a bidirectional cavopulmonary ('venous') shunt in the newborn period would result in very high SVC pressure and low PBF—hence an arterial shunt is initially needed.

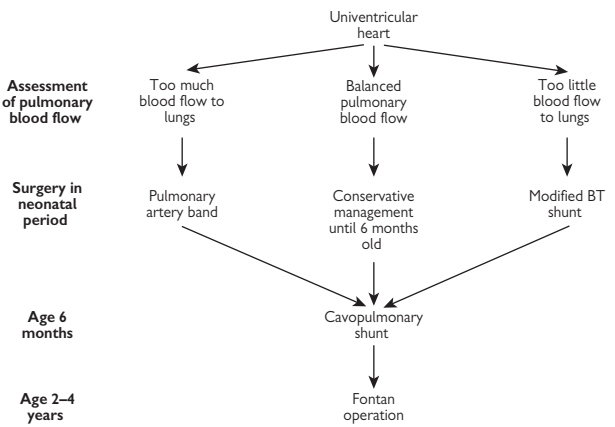


Fig. 20.5 Pathways of palliative operations.

Common surgical procedures (A to Z)

Aortic arch obstruction

Coarctation of the aorta (CoA)

Narrowing of the thoracic aorta, usually distal to the left subclavian artery. Bicuspid aortic valve is common.

Presentation depends on the severity of narrowing.

Neonates with critical narrowing:

- Develop acute LV failure and circulatory collapse when PDA closes
- Resuscitation with ventilation often required; PGE to reopen PDA
- Moderate CoA presents with degree of heart failure.

CoA in the older child:

- Often asymptomatic; upper limb hypertension or murmur
- Male predominance 2:1.

Surgery via left thoracotomy

- Resection with end-to-end anastomosis
- Subclavian flap angioplasty (sacrifices subclavian artery).

Postoperative

- Echo to assess LV function and arch repair
- Hypertension often needs treatment in the postoperative period:
  - To minimize bleeding from the anastomosis
  - To reduce LV afterload
  - Reduce risk of aneurysm formation of dilated post stenotic segment
- Use β-blockers (labetalol, propranolol) ± vasodilators (SNP)
- Long-term antihypertensive medication is rarely needed.

Monitor lower limb function as there is a small risk (0.5%) of spinal cord ischaemia causing paraplegia:

- Felt to be related to intrinsic spinal artery anatomy rather than to aortic cross clamp time.

Post-coarctectomy syndrome is a well described postoperative complication (rare in infants):

- Hypertension accompanied by mesenteric arteritis
- Abdominal pain and fever
- Treatment is good BP control.

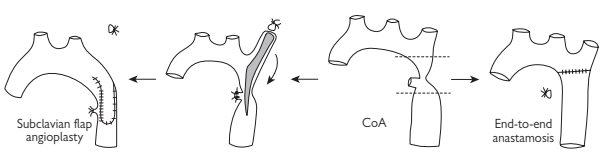


Fig. 20.6 Surgery of coarctation of the aorta.

Interrupted aortic arch

1% of all congenital cardiac defects. This is an extreme form of coarctation where the aortic arch is interrupted or completely atretic causing complete arch disruption or obstruction to luminal flow.

- ***Type A*** (20%) Interruption is distal to the left subclavian artery
- ***Type B*** (75%) Interruption is between the left subclavian and left carotid arteries.
  Associated with DiGeorge syndrome.
- ***Type C*** (5%) Interruption is between the right innominate and left carotid arteries.

All have PDA and most have a VSD. Other associated anomalies include truncus arteriosus, LVOTO, TGA, AP window, bicuspid aortic valve, and anomalous right subclavian artery. 50% have DiGeorge syndrome.

Presentation and management

Most neonates present with acute cardiac failure and signs of circulatory collapse when closure of the ductus occurs:

- Commence PGE1 immediately
- Avoid pulmonary over circulation
- Many require mechanical ventilation and inotropic support.

Surgery

- Single stage total correction is favoured but dependent on the severity of LVOTO
- Median sternotomy, CPB, and DHCA are required
- Recurrent aortic arch obstruction and late subaortic stenosis are uncommon.

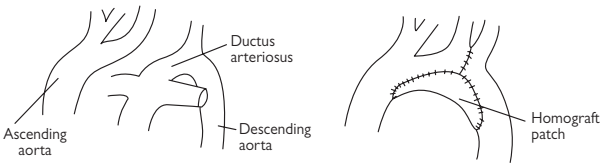


Fig. 20.7 Interrupted aortic arch repair.

Arterial to pulmonary artery shunts

Blalock–Taussig shunt (BT shunt)

- Created in a variety of situations to increase pulmonary blood flow
- Original description—direct anastomosis between the divided subclavian artery and the ipsilateral PA
- Modified BT shunt—places a Gore-Tex® tube between the innominate or subclavian artery and the ipsilateral PA
- Performed via a thoracotomy, usually on the right side
  - 3.5–4.0mm in size but can vary according to size of PA and PVR
  - Flow ~radius^4/length
- Univentricular anatomy (TA/TGA/PS, PA/intact septum) or biventricular lesions (TOF, PA/VSD)

- CPB is not required unless BTS is part of a more complex procedure.

Central shunt

- Involves anastomosis between the aorta and the PAs
- Most common is a Gore-Tex® tube between aorta and central PAs
- Direct anastomosis between aorta and right PA (Waterston) or aorta to left PA (Potts) shunts used in the past: risk of PA distortion and high flow (pulmonary hypertension).

Postoperative

- Generally uncomplicated if biventricular anatomy
- Commence on heparin infusion to prevent shunt thrombosis
- Single ventricle anatomy—need cautious postoperative management of pulmonary and systemic circulations: aim Qp:Qs ~1 with SaO_2 75–85%
- Hypoxaemia may be due to
  - Coexisting lung disease
  - Obstructed or undersized shunt
  - ↑PVR
- CXR, Echo and a trial of iNO should differentiate the aetiology.
- Pulmonary overcirculation arises if the shunt is too large. This is manifested by:
  - Pulmonary congestion
  - High SaO_2—but may not be evident if pulmonary oedema
  - Low diastolic pressure, wide pulse pressure
  - Ventricular volume overload.
- Treatment to ↓SVR (vasodilator) is more effective that attempts to ↑PVR in lowering Qp:Qs.

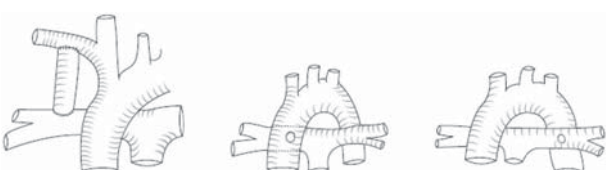


Fig. 20.8 a) Modified BT shunt. b) Waterstone shunt. c) Potts shunt.

Atrial septal defect (ASD)

The atrial septum is formed by a muscular upper aspect (septum secundum) and a thin lower aspect (septum primum), which is connected to the fused endocardial cushions.

Types of ASD

- *PFO* (very common): incomplete fusion of the septum secundum and primum and of no clinical significance
- *Ostium primum* ASD: a type of AV septal defect
- *Ostium secundum* ASD: the commonest defect
- Sinus venosus ASD: defect below the junction of the SVC and RA—associated with TAPVD of the right upper and middle pulmonary veins into the SVC or RA.

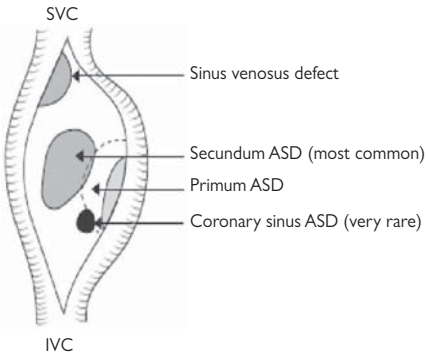


Fig. 20.9 View inside right atrium.

Clinical features

- Most are asymptomatic and ASD is an incidental finding
- High rate of spontaneous closure of small ASDs
- Larger L→R shunt will result in:
  - Volume overload to RA and RV, ↑pulmonary blood flow
  - Recurrent respiratory infections
  - Failure to thrive.

Management

Non surgical closure with a device (Amplatzer septal occluder) placed at cardiac catheterization is now the norm. Complications are rare though significant residual shunt rate.

Surgical closure for

- Qp:Qs > 1.5:1
- Severe congestive cardiac failure in infants
- Small defects may be closed by direct suture but larger defects will require pericardial or prosthetic patch closure.

Postoperative

- Generally uncomplicated cases requiring simple overnight monitoring
- Most patients are extubated after a few hours
- Some units 'fast track' patients and extubate after surgery.

Atrioventricular septal defect (AVSD) (Box 20.18)

(AV canal, endocardial cushion defect, complete AVSD) .

The defect is in the atrial and ventricular septum immediately above the AV valve which is invariably involved (Fig. 20.10a).

40% of children with Down syndrome have some form of CHD of which approximately 50% are AVSDs. Other associations include heterotaxy syndromes (atrial isomerism), tetralogy of Fallot, DORV, TAPVD, and TGA.

- Physiology is dependent upon shunting at both atrial and ventricular levels as well as regurgitation through the AV valve

- Clinically signs of heart failure, failure to thrive, and recurrent respiratory infections are common.

Partial AVSD (ostium primum ASD) See 🕮 p.387.

Complete AVSD a combined defect of both the atrial and ventricular septum with a common AV valve that serves both ventricles:
- Results in a large L→R shunt
- Congestive heart failure develops early in infancy
- Surgery is performed before age 6 months to prevent irreversible PH.

Management

Medical
- Heart failure is treated with diuretics, ACE inhibitor, and digoxin
- Maximize medical therapy in small infants as early surgical mortality is high in this group.

Surgery

PA band—see 🕮 p.394.

Complete surgical repair
- Atrial and ventricular defects are closed with 2 separate patches (see Fig. 20.10b)
- 2 AV valves are recreated by subdividing the common AV valve.
- The left AV valve is not a true mitral valve and care is required during surgery to prevent AV valve regurgitation.
- AV valve competence and function is thought to be superior in those with Down syndrome and surgery in this group less complicated.

Box 20.18 Postoperative key points

- Require close monitoring postoperatively
- LA and PA lines are desirable
- Pulmonary hypertension is common, particularly with delayed closure
- Arrhythmias—heart block or JET can occur
- LCOS:
  - LV no longer ejecting across low resistance created by VSD or MR
  - Dopamine or adrenaline can exacerbate arrhythmias
  - Milrinone is beneficial in this setting of low CO and ↑SVR
- Residual shunts occur less frequently with the advent of intraoperative Echo.

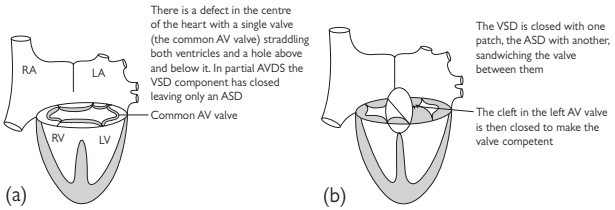


Fig. 20.10 a) Anatomy of AVSD. b) Surgery of AVSD.

Bidirectional cavopulmonary shunt (BCPS)

(Bidirectional Glenn/modified Glenn/hemi-Fontan procedure)

- SVC disconnected from RA and anastamosed to PA:
  - Pulmonary blood flow comprises upper body venous return
  - IVC blood still drains to RA
- Previous arterial shunt is taken down
- Typically ~6 months of age, usually on CPB
- Reduces volume loading of the single ventricle and ventricular work
- Qp:Qs is predictable at ~0.6–0.7
- Patient with bilateral 'disconnected' SVCs may require bilateral BCPS.

In Glenn's original procedure, the SVC was directly anastamosed to the disconnected right PA.

Postoperative key points

- SaO_2 typically ~80–85%
- Systemic hypertension is common:
  - Manage acutely with SNP and ACE inhibitor/β-blocker
  - Rarely requires long-term treatment
- PA pressure is inferred from an SVC central venous line—line should be removed early to prevent clot formation.

Pulmonary blood flow

- Blood flows down a pressure gradient between the PAs and the left (or common) atrium:
  - This is called the transpulmonary gradient (TPG)
  - An IVC central line may be used to infer atrial pressure
- A low TPG (<10mmHg) implies a favourably low PVR
- An elevated TPG (>15mmHg) implies high PVR due to:
  - Anatomically small pulmonary vascular bed (common)
  - Reactive pulmonary arteries (rare)
  - Significant lung/pleural disease, high airway pressures
  - Pulmonary venous obstruction (rare)
- Management of an elevated TPG:
  - Optimize ventilation (see 🕮 p.370)
  - Rule out treatable lung/pleural disease (pneumothorax)
  - Consider trial of iNO to assess reactivity
- A high PA pressure may occur, with a low TPG, as a result of an elevated atrial pressure ('downstream pressure'):
  - Suggests ventricular dysfunction or AV valve regurgitation or stenosis
  - Vasodilator therapy ± inotrope will lower atrial and consequently PA pressures.

Significantly elevated PAP, and consequently SVC pressure, results in facial/upper body venous congestion, pleural effusions (chylous) and headaches.

Consider SVC territory venous collateral drainage, draining directly to the heart, if a patient is inexplicably hypoxaemic.

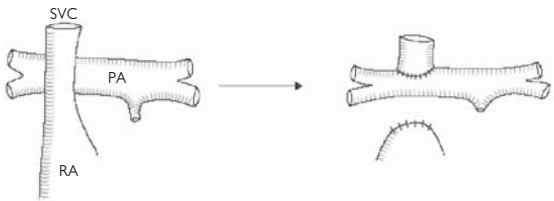


Fig. 20.11 The bidirectional cavopulmonary shunt.

Kawashima variant of bidirectional cavopulmonary shunt

Certain congenital heart lesions are associated with congenital interruption of the IVC with azygous continuation. This results in IVC blood draining via the azygous system into the SVC. Creation of a BCPS in this situation will drain both SVC and IVC blood into the pulmonary circulation.

SaO_2 will typically run ~90%, as hepatic venous blood still drains directly back to the atrium. Lack of hepatic venous blood draining through the lungs may be associated with the development of pulmonary AV communications—resulting in progressive hypoxaemia.

Damus–Kaye–Stansel operation (PA to aortic anastomosis)
Used for single ventricle anatomy with subaortic stenosis with or without distal arch obstruction. PA to Ao shunt provides unimpeded systemic flow and a BT shunt or RV–PA conduit is placed to supply pulmonary blood flow.

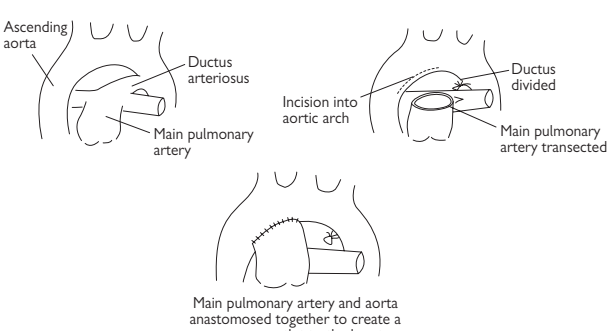


Fig. 20.12 Damus–Kaye–Stansel operation.

Fontan operation

(Total cavopulmonary connection; TCPC.)

- Final palliative stage for univentricular anatomy
- Performed at age 2–5 years
- Connects IVC blood to PA by:
  - Direct anastamosis of RA to PAs (original operation)
  - Creating a 'lateral tunnel' within the RA
  - Use of an extracardiac Gore-Tex® conduit (current)
- Creation of a fenestration between the IVC (or extra-cardiac conduit) and the common atrium:
  - Reduces morbidity and mortality
  - Maintains ventricular preload during times of haemodynamic stress.
  - Creates an obligate R→L shunt—associated lower SaO_2.

Postoperative key points (Table 20.2)

- Low PVR is essential in order that blood flows passively through PA—TPG should be <10mmHg
- Positive pressure ventilation can adversely affect PVR and pulmonary blood flow (see 📖 p.370)
- Encourage weaning to spontaneous ventilation but only wean and extubate if haemodynamically stable
- SVC/IVC pressures are equal and reflect PA pressure rather than ventricular preload—atrial pressure line is essential: often require lots of fluid— titrate to atrial pressure
- Sinus node dysfunction is common: Temporary pacing may be required

The incidence of atrial arrhythmias has reduced with introduction of the extracardiac conduit—related to elimination of atrial suture lines and less atrial distension.

- LCOS needs prompt investigation with Echo to assess ventricular function and evidence of ventricular outflow tract obstruction, and to ensure functioning fenestration:
  - ↓volume loading post-Fontan may unmask outflow tract obstruction
  - Creation or enlargement of a fenestration may improve cardiac output, at the expense of greater cyanosis
- Anticoagulation is initiated early as there is a risk of thrombus formation from slow venous blood flow
- Early cardiac catheterization is warranted for the patient with a 'failing Fontan':
  - High central venous pressure, oedema
  - Pleural effusions (± chylous), ascites
  - Nutritional failure (gut oedema), protein losing enteropathy
- Consider early takedown if no remedial factors are identified.

Table 20.2 Differential diagnosis of low cardiac output after Fontan

CVP	LAP	Cause
Low	Low	Hypovolaemia
High	Low	↑PVR, baffle obstruction, pulmonary artery distortion or branch stenosis
High	High	Ventricular dysfunction, AV valve stenosis or regurgitation, arrhythmia, outflow tract obstruction, tamponade

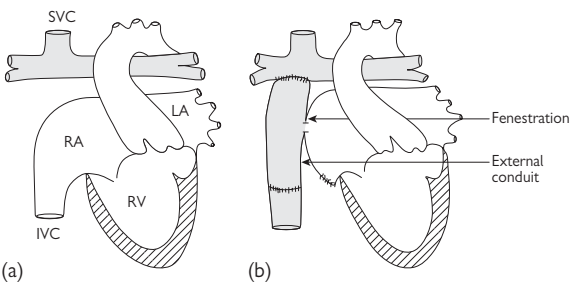


Fig. 20.13 Surgery of total cavopulmonary connection.

Hypoplastic left heart syndrome (HLHS)

Commonest cause of death from heart disease (40%) in neonates. Variety of subtypes with varying degree of hypoplasia of the LV and LVOT—classically occurs with mitral and aortic atresia.

LV is unable to support the systemic circulation which is maintained by RV (via PDA).

- Situation becomes critical after birth when PVR drops and PDA closes
- Systemic output is no longer supported and the neonate presents with circulatory collapse and profound metabolic acidosis.

Management

Need active resuscitation often with ventilation, inotropes, and correction of acid–base abnormalities:

- Commonest problem is excessive PBF and low systemic flow:
  - Aim for a balanced circulation Qp:Qs ~1
  - SaO_2 ~75–85% if no forward flow through LVOT (optimal SaO_2 will be higher if there is forward flow from LV across aortic valve)
  - PGE1 infusion to maintain PDA
- More rarely a restrictive interatrial communication will cause LA distension, pulmonary venous hypertension—results in low SaO_2
  - *Balloon atrial septostomy* will decompress the LA and improve oxygenation prior to surgery.

Surgery

Norwood procedure—first described by Norwood in 1983.

- RV supports both systemic and pulmonary circulations
- Arch reconstruction with aortic or pulmonary homograft
- Main PA used to augment ventricular outflow and ascending aorta
- Pulmonary blood flow via a modified BT shunt (Classical) or RV–PA conduit (Sano modification).

Surgery is high risk and mortality rates of 15–35% reported. Cardiac transplantation is an alternative surgical option.

Postoperative key points

Problems relate to mismatch of pulmonary and systemic blood flow, variable PVR, and myocardial dysfunction.

- Avoid situations that acutely increase PVR
- Sedation and neuromuscular relaxation to reduce metabolic demand
- The sternum is often left open for 24–48h—monitor closely post-closure—can affect RV compliance and ↑SVR
- Aim for SaO_2 75–85%
- Monitor $ScvO_2$—aim for 45–60%.
- Monitor lactate.
- Use volume mode on ventilator: more predictable $PaCO_2$ when lung compliance is changing
- Limit FiO_2 and monitor $EtCO_2$ during manual ventilation: high FiO_2 and hyperventilation leads to pulmonary vasodilation and compromised systemic perfusion.
- Inotropes and vasodilation help augment systemic perfusion
- Optimize Hct
- Echo—monitor for TR, assess arch repair and RV function.

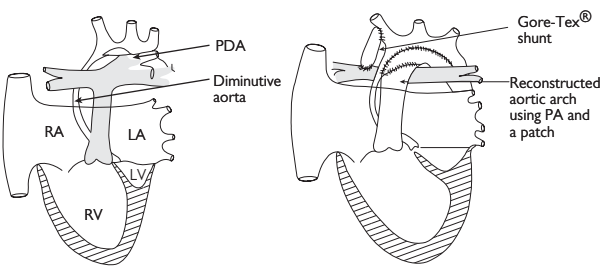


Fig. 20.14 The Norwood procedure.

PA band

Palliative procedure in which the main pulmonary artery is narrowed with a silastic band to increase pulmonary resistance, limit pulmonary blood flow and pressure. Used in a variety of situations:

Biventricular anatomy
- CoA and VSD: where CoA is the critical lesion—both can be performed by thoracotomy with later closure of VSD on CPB if necessary
- Multiple VSDs not suitable for surgical closure
- Where definitive correction of a complex lesion is best delayed.

In these situations, the PA band reduces the L→R shunt across the VSD and consequently decreases heart failure.
- PA band used occasionally to ↑LV afterload and stimulate LV hypertrophy
  - Late presenting TGA where LV mass has regressed
  - Child with congenitally corrected TGA prior to a double switch procedure

'Retraining' of the LV can occur within weeks in an infant but takes much longer in an older child.

Univentricular anatomy
- To limit excessive pulmonary blood flow
- Performed as first part of staged palliation (see 📖 p.384).

Postoperatively SaO_2 will be dependent on the underlying anatomy:
- Biventricular: SaO_2 will remain 95–100%
- Univentricular: SaO_2 75–85%.

Echo (Doppler) to estimate the gradient across the band ($4 \times V^2$) and to evaluate ventricular function and degree of AV value regurgitation—abrupt increase in afterload may cause ventricular failure, AV value regurgitation and LCOS.

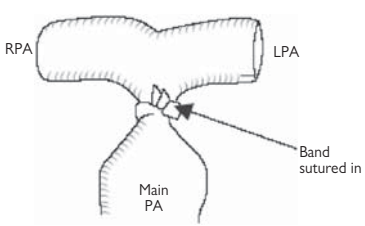


Fig. 20.15 Pulmonary artery banding.

Pulmonary atresia (PA)

Complex group of conditions and may have areas of lung supplied by major aortopulmonary collateral arteries (MAPCAs):
- PA with intact ventricular septum
- PA with VSD (no MAPCAs)
- PA, VSD, and MAPCAS.

Presentation
- Cyanosis is present from birth
- PGE1 infusion is needed to keep PDA open.
- Surgery depends on anatomy and size of the RV
- Associated with 22q11 deletion.

Management

PA intact septum

Dependent on RV size—tricuspid valve standard deviation ('Z') score used in decision-making

- Normal size:
  - Perforation and dilatation of PV (catheter lab) with or without surgical opening of RVOT
  - Ultimately aim for a biventricular repair with RV–PA conduit.

- RV to coronary artery fistulae or sinusoids can form as a result of supra-systemic RV pressures—identified with angiography
- RV dependent coronary circulation occurs in 10%:—relief of RV pressure can reverse coronary flow leading to myocardial ischaemia.

PA with VSD, no collaterals

Effectively an extreme form of tetralogy of Fallot which is duct dependent requiring PGE1 infusion.

Treatment is initially with a modified BT shunt with later complete repair using an RV–PA conduit.

PA, VSD, and MAPCAs

- Pulmonary blood supply is from large collateral vessels arising from the aorta
- Surgery aims to join the MAPCAs together (unifocalization), reconnect them to the native PAs (if present), insert an RV–PA conduit, and close the VSD
- Usually involves a combined thoracotomy and sternotomy
- Surgery may be undertaken in stages—VSD closure delayed until PVR low enough for RV to cope.

Postoperatively

PA/intact septum

- RV dysfunction can lead to a low cardiac output state: this is related to a ventriculotomy, a small RV and occasionally severe PR
- RV is generally less compliant in these patients and this is worsened if a ventriculotomy is performed—milrinone is helpful
- Echo to look for residual lesions.

PA/VSD/MAPCAs (Fig 20.16)

- Echo to look for residual VSD. This is tolerated poorly after relief of RVOTO as RV volume loading can lead to RV dysfunction
- Arrhythmias (heart block, JET) are common in the immediate postoperative period.

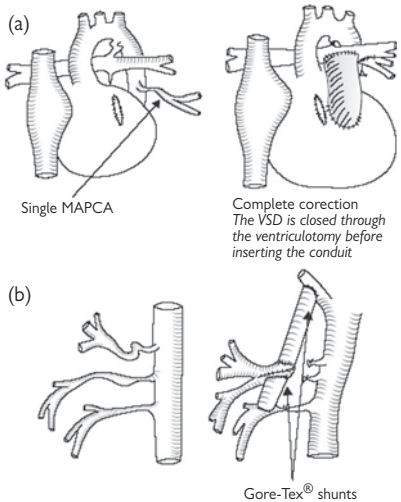


Fig. 20.16 Pulmonary atresia with VSD and MAPCAs. (a) Closure of VSD and conduit formation. (b) Example of unifocalization of 3 major aortopulmonary collateral arteries to the right lung.

Rastelli repair (Fig. 20.17)

Performed in TGA/VSD with significant PS and usually in older infants. VSD is closed with a patch in a way that allows blood to flow from LV through VSD and out to the aorta. Pulmonary valve which comes off the LV is sewn shut. RV–PA conduit is formed using a valved conduit or pulmonary graft homograft.

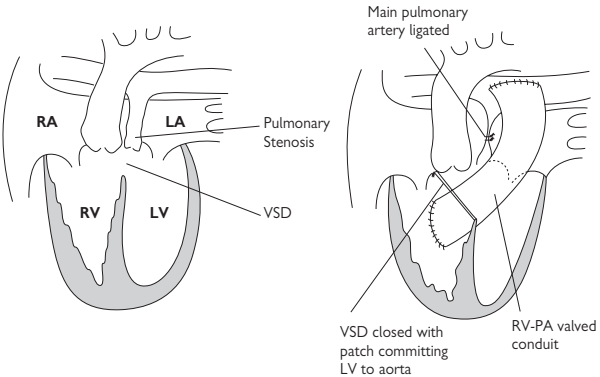


Fig. 20.17 Rastelli operation.

Ross procedure (pulmonary root autograft) (Fig. 20.18)
- Specialized aortic surgery for aortic regurgitation/stenosis
- Diseased aortic valve is replaced with the patients' own pulmonary valve. The pulmonary valve is replaced with a cadaveric or bioprosthetic pulmonary valve
- Longevity of the pulmonary autograft in the aortic position is far superior to currently available bioprostheses and importantly, long-term anticoagulation is not required.

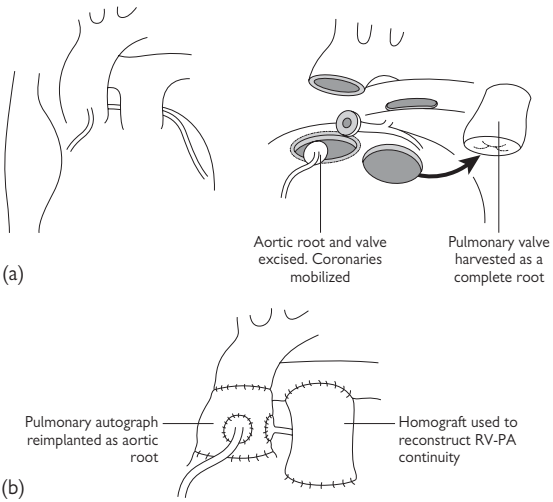


Fig. 20.18 Ross procedure.

Tetralogy of Fallot (TOF)

Described by Fallot in 1888 as a malformation consisting of:
- RVOTO
- VSD
- Deviated overriding of aorta to the right
- RVH (see Fig. 20.19a).

RVOTO can be subvalvular, valvular or in the pulmonary artery and its branches. The pulmonary annulus and the PA are usually hypoplastic, but in the most severe form (10%) is atretic.
- VSD is large and unrestrictive and usually subaortic
- Right-sided aortic arch is seen in 25%
- Abnormal coronary anatomy may coexist—anomalous origin of the LAD from the proximal right coronary (2%) causes the LAD to cross the RVOTO.

Absent pulmonary valve syndrome is a rare form of TOF with similar intracardiac anatomy to TOF but the pulmonary valve is replaced by a membrane leading to:
- Aneurysmal dilation of the pulmonary artery and its branches
- Causes compression of the tracheobronchial tree
- Associated tracheobronchomalacia (TBM) can be severe and compromise respiratory weaning—may require plication of the PAs.

Clinical presentation of TOF
- Cyanosis:
  - Worsens with increasing RVOTO
  - Acute hypoxic 'Tet spell' due to ↑infundibular (subvalvar) 'spasm'
- Clubbing
- Exertional dyspnoea.

Acyanotic TOF occurs when there is mild pulmonary stenosis and a L→R shunt and patients may be asymptomatic.

Box 20.19 Management of TOF

A 'Tet spell' is managed with measures that overcome infundibular spasm and increase PBF:
- Sedation, analgesia (↓catecholamines)
- Oxygen
- Fluid bolus
- ↑SVR; phenylephrine, noradrenaline
- Beta blockade; esmolol (short half life), propranolol.

Surgery (Fig. 20.19b)
Early repair has become standard practice in many centres but primary repair in the symptomatic neonate carries a higher operative mortality. In these patients a staged approach is adopted with initial palliative BT shunt.

Complete repair is carried out on CPB with patch closure of the VSD and enlargement of the RVOT
- Resection of the infundibular muscle tissue and
- Placement of a transannular patch
- RV–PA conduit if RVOT is severely hypoplastic or atretic.

Postoperative
- RV is poorly compliant—exacerbated if repair is via a ventriculotomy.
- RV diastolic dysfunction ('restrictive physiology') not uncommon:
  - Echo shows forward flow in the PA during ventricular diastole
  - Maintain RV preload (CVP >10mmHg), limit catecholamines
  - Milrinone as an inodilator is beneficial
  - Aim to wean positive pressure ventilation.

If RV dysfunction is anticipated, the foramen ovale can be left open to allow R→L shunting at the atrial level and provide greater cardiac output at the expense of oxygen saturation.
- Residual VSD is tolerated poorly

- Arrhythmias:
  - Complete heart block requiring temporary pacing
  - JET—poorly tolerated

In JET there is complete AV dissociation which can be rapidly identified with ECG using the temporary atrial pacing wires (see 📖 p.375). Treatment with IV amiodarone should not be delayed and core body temperature can be cooled to below 36°C

- SIRS and capillary leak following CPB for this lesion is often significant with considerable ascitic losses.

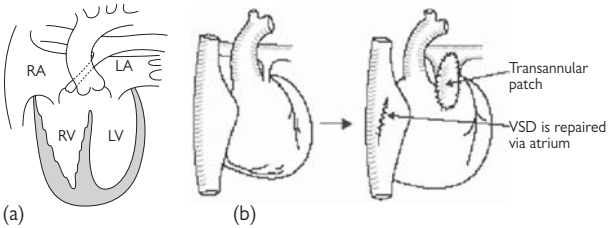


Fig. 20.19 a) Anonomy of tetralogy of Fallot. b) Surgery of tetralogy of Fallot.

Total anomalous pulmonary venous drainage (TAPVD)

30% associated with complex defects and heterotaxy syndromes (atrial isomerism, spleen abnormality, and complex CHD).

Pulmonary veins do not drain into the LA but directly into the RA or via remnants of the embryological venous system. Pulmonary drainage reaches the RA where there is complete mixing with systemic blood before entering LA via ASD.

- All patients are cyanotic
- Survival is dependent on an interatrial communication

Oxygen saturation and clinical status is dependent on whether there is obstruction to the pathway as is usually seen in the infracardiac type.

- Obstructed total anomalous pulmonary veins (TAPVs) lead to pulmonary oedema, pulmonary hypertension and severe cyanosis.

- Supracardiac (50%): drainage into the innominate vein via a left vertical vein
- Cardiac (20%): collecting chamber drains into the coronary sinus
- Infracardiac (20%): drainage into the portal vein, ductus venosus, hepatic vein or IVC
- Mixed 10%: combination of other types.

Management

Patients with severe obstruction need ventilation and stabilization prior to surgery. Strategies to ↓pulmonary hypertension by vasodilating the pulmonary vasculature are often employed—iNO, high FiO_2.

In the setting of pulmonary venous obstruction (TAPVD, mitral stenosis) these manoeuvres can ↑PBF and worsen pulmonary oedema.

- *Balloon atrial septostomy* to enlarge the interatrial communication may provide short-term benefit
- *Surgery* channels pulmonary venous blood to the LA and obliterates anomalous connections under CPB—risk of recurrent pulmonary vein stenosis which has poor outcome.

Postoperative care

- Pulmonary hypertension—monitor PAP:
  - PAP can be suprasystemic and lead to RV (and LV) dysfunction
  - PFO may be left to allow R→L shunting ('blow off')
- LA and LV non-compliant: run higher LAP than expected—sensitive to volume boluses
- Echo—Doppler pulmonary vein flows
- Postoperative arrhythmias (supraventricular)
- Ventricular dysfunction—especially if long CPB.

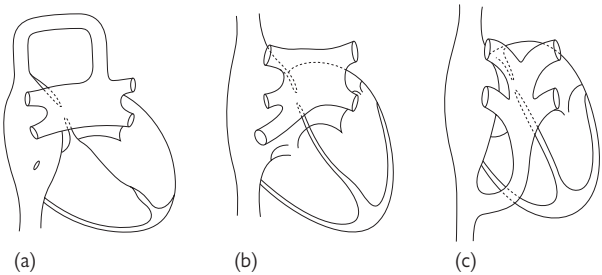


Fig. 20.20 a) Supracardiac: the most common. b) Cardiac: drain to coronary sinus; least likely to be obstructive. c) Infracardiac: less common, but most are obstructive. NB: Confluence lies behind the LA, shown in front of the LA in these drawings only for clarity.

Transposition of the great arteries (TGA)

- Most common variety is D-TGA (Fig. 20.21a)
- L-TGA is a complex condition known also as congenitally corrected TGA (see 🕮 p.402).

D-TGA

Aorta arises from the RV and the PA arises from the LV so that circulations are in parallel rather than in series. Many variants but simple TGA implies ventricular septum is intact.

- Defects that allow mixing (ASD/VSD/PDA) are necessary for survival
- 40% have associated VSD, 30% with PS
- Rare combinations such as TGA/VSD/PS may be balanced and not require immediate intervention
- Patients presenting later, particularly outside the neonatal period and those with abnormal coronary artery patterns create additional risk.

Management

Cyanosis and congestive heart failure occur early in the neonatal period.

- Oxygen may increase mixing by lowering PVR and increase pulmonary blood flow, but the response is variable
- Mechanical ventilation is often required during resuscitation
- PGE1 infusion is commenced to maintain patency of PDA
- Balloon atrial septostomy (Rashkind procedure) will further increase SaO_2 saturation and defer emergency surgery.

Surgery

Arterial switch is the procedure of choice and involves switching of the aorta and main pulmonary artery (see Fig. 20.21b):

- The coronaries are transferred separately onto the neo-aorta
- Lecompte manoeuvre results in the PA lying in front of the aorta.

In the past the Mustard or Senning operations involved switching the right and left atrial inflows to the ventricles—rarely performed now.

Late presentation of TGA with intact septum

- Regression of LV mass occurs when PVR falls so surgery is ideally performed within 10 days of birth
- A PA band may be required to enable ↑LV mass prior to the arterial switch operation.

Postoperative

- The LV is suddenly burdened with a high resistance circuit and needs to adapt to supporting the systemic cardiac output
- This can take time so LV function must be followed with Echo
- Milrinone is often used to help the non-compliant LV to relax
- Coronary ischaemia from malposition of the coronaries is a risk-closely observe ECG changes, especially ST segments
- Other problems include neo-AR and pulmonary artery branch stenosis which occurs later.

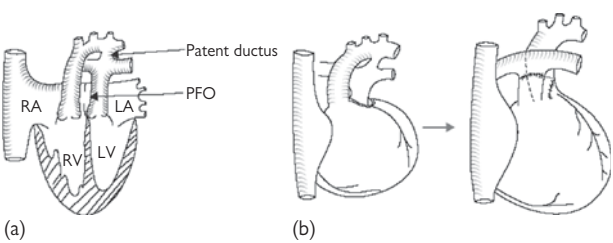


Fig. 20.21 a) Anatomy of transposition of the great arteries. b) The arterial switch procedure.

Congenitally corrected TGA (L-TGA)

Atrial relationship is normal with RA on right of LA. RA empties into a morphological LV via a mitral valve which in turn empties into the pulmonary artery, i.e. the ventricles (and accompanying AV valves) are 'switched'.

The consequences are:
- Normal oxygenation (if no accompanying lesion)
- A morphological RV is the systemic ventricle
- Progressive RV dilatation and TR may develop over time
- Accompanying defects are common such as VSD ± PS and complete heart block—may require a permanent pacemaker.

Surgery
Most centres opt for the 'double switch' procedure in which both an atrial (Senning) and arterial switch are performed:
- An alternative to the arterial switch may be needed if there is significant PS (Rastelli)
- A PA band may be required to re-train the LV prior to the double switch.

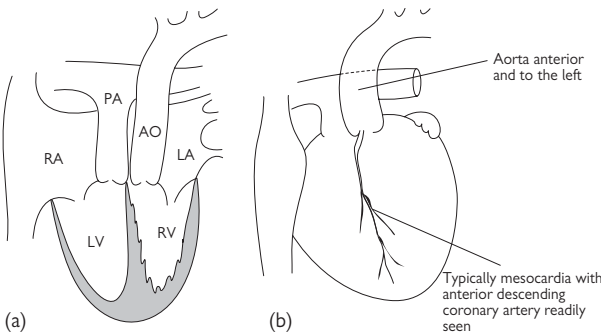


Fig. 20.22 a) Congenitally corrected TGA. b) Double switch procedure.

Truncus arteriosus

- Associated with 22q11 deletion and DiGeorge syndrome
- A single 'trunk' arises from the heart and gives rise to the systemic and pulmonary circulations:
  - VSD present in all
  - 30% have right-sided aortic arch
  - Coronary artery and truncal valve abnormalities are common
  - Can be associated with interrupted aortic arch in a complex form.

Various classifications exist but often is based on the origin of the PAs from the truncal vessel:

I	60%	PAs arise via a main pulmonary artery off trunk
II+III	30%	Separate origins of R and L PAs off trunk
IV	10%	Pseudotruncus. Variant of PA/VSD.

- Unrestricted pulmonary blood flow leads to congestive heart failure but often minimal cyanosis is present
- Delay in surgery leads to irreversible pulmonary vascular disease

- Primary repair includes closure of VSD, disconnection of PAs from trunk and formation of an RV–PA conduit.

Postoperative

- Sternum is often left open to prevent tamponade
- PAP and LAP lines are essential
- Pulmonary hypertension must be anticipated and triggers of pulmonary hypertensive crises must be avoided
- RV dysfunction and failure can occur and lead to LCOS
- For management of pulmonary hypertension see 🕮 p.378
- Truncal valve becomes neo-aortic valve:
  - Variable number of leaflets
  - May be regurgitant.

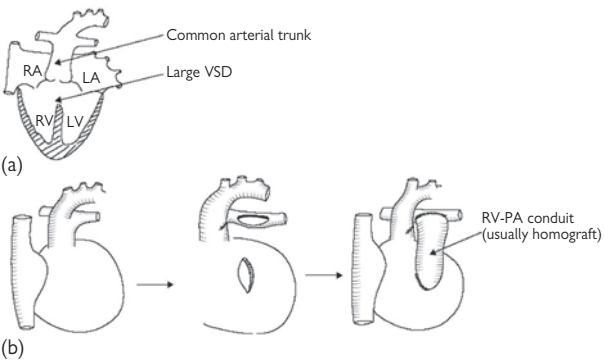


Fig. 20.23 a) Anatomy of truncus arteriosus. b) Surgery of truncus arteriosus.

Ventricular septal defect (VSD)

Occurs in isolation or associated with a variety of anomalies. The ventricular septum consists of a small membranous portion and a large muscular part. VSDs are also described in relation to their position as inlet, outlet, and apical VSDs (see Box 20.19 and Fig. 20.24).

Box 20.19 Types of VSD

Perimembranous VSD

- In the LV outflow tract just below the aortic valve
- Membranous septum but usually also involves some muscular septum
- Extension to non-coronary leaflet of the aortic valve may cause AR.

Muscular VSD

- Often multiple and are entirely bound by muscular septum
- Muscular septum is divided into inlet, infundibular, and trabecular septa
- The term 'Swiss cheese' used to describe multiple muscular VSDs.

Box 20.19 Types of VSD (*Continued*)

Outlet VSD
- Located beneath the pulmonary valve
- Prolapse of the right coronary leaflet of the AV may cause AR.

Inlet or posterior VSD
- AV canal type defects
- Lie posterior to the septal leaflet of the tricuspid valve
- Not associated with defects of the AV valves.

Clinical features
- Dependent on size of L→R shunt
- Can be quantified at cardiac catheterization
- Larger L→R shunt will result in:
  - LA and LV volume overload (and RV when shunt is large)
  - ↑pulmonary blood flow and pulmonary hypertension
  - Failure to thrive and recurrent respiratory infections
  - Longstanding cases lead to fixed pulmonary vascular disease, a R→L shunt and cyanosis (Eisenmenger).

Management
- Spontaneous closure in up to 40% (trabecular [muscular] defects): outlet and inlet defects do not spontaneously close
- Close large VSDs by 12 months of age to prevent pulmonary hypertension.

Medical
- Control heart failure and prevent pulmonary vascular disease: diuretics, ACE inhibitor, and digoxin
- Transcatheter device closure of defect is useful in selected patients:
  - Technique is more complicated than with ASD or PDA
  - Limited by anatomical position of the defect.

Surgical
- Failure of medical management
- Qp:Qs >2:1
- Previous episode of endocarditis
- Defect associated with progressive aortic valve prolapse and AR.

Delay surgery to age ~12 months if symptoms are controlled medically. Asymptomatic patients can be operated later at age 2–4 years.
- PA band—only performed when other lesions make complete repair difficult (see 🕮 p.394)
- Direct surgical closure—with a prosthetic patch on CPB.

Postoperative
- Regular diuretics (lung congestion preoperative)
- Heart block is not uncommon but usually transient: AV node is adjacent to a perimembranous VSD
- Residual defects after surgery are fairly common.

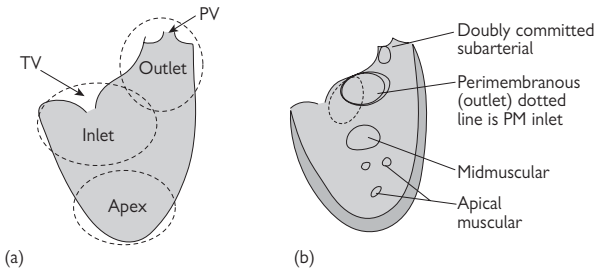


Fig. 20.24 Schematic (a) and ventricular septum (b) viewed from right side.

Further reading

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Chapter 21

Respiratory disease

Structure of the respiratory tree

Fetal lung development is divided into 4 stages:

• Embryonic (0–7 weeks)	Trachea, left and right main stem bronchi
• Pseudoglandular (6–17 weeks)	All conducting (pre-acinar) airways
• Canalicular (16–27 weeks)	Respiratory bronchioli
• Saccular–alveolar (27 weeks–term)	Saccules and alveoli

- Pulmonary blood vessel formation accompanies but lags airway development
- Gas exchange is not possible until the late cannicular—early saccular–alveolar stage of lung development
- Surfactant production begins at about 32 weeks but is not maximal until much nearer term
- During early infancy pulmonary arteries decrease in muscularity accounting, at least in part, for the normal drop in pulmonary vascular resistance that follows birth
- During early childhood alveoli and small blood vessels multiply and all lung structures increase in size.

Upper airway

The upper airway anatomy of babies is different from that of older children and adults (Fig. 21.1):

• Large tongue/high anterior larynx	Difficult to visualize during intubation
• Floppy, U-shaped epiglottis	Obstructs view, greater area for swelling
• Narrowest part of airway at cricoid cartilage	Site for stenosis; limits ET size
• Small tracheal radius	↑airway resistance
• Small tracheal length	Risk of ETT displacement
• Floppy tracheal wall	Risk of airway collapse

- Some infants are obligate nose breathers, and become apnoeic if the nose is obstructed with mucous or an NG tube
- In older children tonsillar hypertrophy may lead to significant airways obstruction.

Lower airway

Infants and young children have a softer, less efficient respiratory engine. Airways collapse occurs more easily, and interruptions to ventilation are less well tolerated:

• Compliant rib cage	Less efficient ventilations and increased work of breathing
• Poorly developed intercostal muscles	Fatigue easily
• Horizontally aligned ribs	Less increase in AP diameter in inspiration
• Protuberant abdomen	Less efficient diaphragmatic contraction;
• Low lung compliance/ high airways resistance	Short lung time constant
• High closing volume	Early airways closure
• High metabolic rate	↑oxygen demands

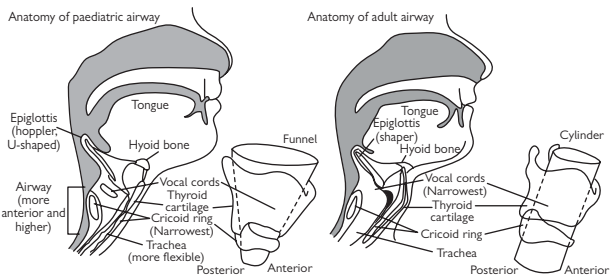

Fig. 21.1 Differences between the paediatric and adult upper airway. Reproduced with permission from http://www.healthstate.ny.us/facilities/hospital/emergency-preparedness/guideline_for_hospitals/section_07/triage.htm

Pulmonary gas exchange

(See 🕮 Chapter 7.)

Disorders in gas exchange are manifest as hypoxaemia and/or hypercapnia which are best evaluated by measuring:

- ***PaO_2***
- ***$PaCO_2$***
- ***Oxygen saturation (SaO_2)***
- ***$P(A–a)O_2$ gradient:***
  - When PaO_2 falls, it is vital to know the difference between alveolar and arterial PaO_2, i.e. A–a gradient
  - A–a gradient is affected by age and position and is a sensitive marker of gas exchange impairment in respiratory disease
  - In air a value of $P(A–a)O_2$ of >3kPa indicates significant pulmonary dysfunction
- ***PaO_2/FiO_2 ratio***: a normal PaO_2/FiO_2 ratio is 300–500mmHg, with values of ≤300mmHg indicating abnormal gas exchange. Values of <200mmHg indicate severe hypoxia

- ***Oxygenation index (OI):*** integrates oxygen requirements, ventilatory requirements, and gas exchange to give an index of severity of lung disease

$$OI = \{\text{mean airway pressure } (cmH_2O) \times FiO_2\ (\%)\} \div PaO_2\ (mmHg)$$

A high OI >30 predicts mortality. In neonates and young children on ventilator support, OI is used to determine intervention such as administration of inhaled NO or commencement of ECMO.

Pulmonary mechanics

(See 🕮 Chapter 7.)

Disorders of pulmonary mechanics result in:

- ***Compliance:*** = volume/pressure, i.e. change in lung volume per unit change in pressure
- ***Resistance:*** = pressure/flow. Varies with airway radius, airway length, flow rate, density and viscosity of gas.
- ***Time constant:*** the time taken for alveolar pressure to reach 63% of the change in airway pressure.

Time constant = resistance × compliance.

Lungs with ↓compliance (e.g. in RDS) have shorter time constants. Very short inspiratory times on a ventilator may lead to incomplete delivery of tidal volume. Short expiratory time may lead to inadvertent PEEP and air trapping.

Control of breathing

Central control

The respiratory centre is in the lower part of the brain stem (the medulla oblongata) and controls normal, rhythmic, cyclic pattern of breathing. Breathing is controlled by:

- Central chemoreceptors:
  - An increase in $PaCO_2$ results in ↑CO_2 and $[H]^+$ in the CSF resulting in an increase in ventilation thereby lowering $PaCO_2$
  - A low $PaCO_2$ level inhibits the respiratory centre
- Peripheral chemoreceptors:
  - Carotid and aortic bodies respond to changes in PaO_2 and $PaCO_2$ by inputting into the central respiratory centre
  - In the presence of hypoxia and hypercapnia there is an immediate increase in breathing
- Brain:
  - Breathing can be influenced by consciousness and this can happen before exercise or be triggered by emotion
- Lung:
  - Receptors in the wall of the bronchi respond to irritant stimuli producing cough, sneezing, and breath hold
  - Stretch receptors prevent overdistention and equally low lung volume cause further inspiration
  - Stretch receptors in the blood vessels in the lung in the presence of heart failure produce hyperventilation.

Respiratory drive

- The efferent nerves pass from the respiratory centre to the diaphragm, intercostal muscles, and accessory muscles of inspiration in the neck

- During normal breathing, inspiration is an active muscular process but expiration is passive reliant on natural elasticity of the tissues
- Any damage to the efferent pathways from the respiratory centre to C3, C4, and C5 and then the phrenic nerve to the diaphragm, may cause severe difficulty in breathing; trauma to the cervical cord, above C3, is normally fatal.

Respiratory failure

Definition: inability for the lungs to perform gas exchange
- PaO_2 <8kPa (60mmHg) and/or with
- $PaCO_2$ >6.5kPa (50mmHg) (see Box 21.1)

Box 21.1 Caveats

- A low PaO_2 is found in children with cyanotic heart disease and does not in itself imply respiratory failure
- A raised $PaCO_2$ may sometimes occur as a compensatory mechanism in metabolic alkalosis (e.g. persistent vomiting). Here, 'central' sensitivity to $PaCO_2$ is not impaired but the threshold is shifted upwards.

- Types: respiratory failure has traditionally been classified as:
  - Oxygenation/type 1 failure (PaO_2 <60mmHg) occurs in the absence of hypercapnia, whereas
  - Ventilatory/type 2 failure occurs when hypercapnia and hypoxaemia coexist
- For management purposes respiratory failure is better classified as either:
  - Acute: rapid respiratory de-compensation
  - Chronic: long-standing inability to perform gas exchange leading to compensatory 'adaptations'. Signs of adaptation include: absence of dyspnoea at rest (altered central chemoreceptor sensitivity); compensated respiratory acidosis (↑HCO_3, normal blood pH); high haemoglobin/haematocrit (untreated hypoxaemia)
  - Acute on chronic: acute respiratory de-compensation in a child with compensated respiratory failure. Commonly presents with profound hypercapnia >12kPa and worsening hypoxaemia.

Presenting features

- Dyspnoea: sub-costal, intercostal, sternal recession, grunting, tracheal tug
- Stridor: upper airway obstruction
- Tachypnoea: not a sensitive sign in young infants
- Apnoea: prominent feature in young infants with RSV bronchiolitis
- Cyanosis: sign of impending de-compensation.

Important not to confuse dyspnoea due to respiratory diseases with Kussmal-type breathing in children with DKA and other syndromes associated with metabolic acidosis.

Other features

- Poor feeding
- Floppiness
- Inability to talk—acute severe asthma.

Causes

Table 21.1 Causes of respiratory failure

	Extra-thoracic airway	Intra-thoracic airway/lung	Respiratory pump
Congenital	• Laryngomalacia • Subglottic stenosis, web or cyst • Tracheomalacia • Vascular ring • Cystic hygroma • Craniofacial anomalies	• Congenital lung disorders, e.g. CDH, congenital lobar emphysema, • CCAM. • Surfactant protein B and C deficiency syndromes • Alveolar capillary dysplasia	• Spinal muscular atrophy • Congenital hypoventilation syndrome • Congenital myotonic dystrophy • Congenital myasthenia gravis • Eventration of diaphragm • Duchenne muscular dystrophy
Acquired	• Infection, e.g. croup, retropharyngeal abscess • Trauma, e.g. foreign body aspiration, burns • 'Other', e.g. hypertrophic tonsils and adenoids	• Bacterial/viral pneumonia, *S. pneumoniae, M. pneumoniae, S. aureus, B. pertussis, RSV,* influenza, adenovirus, bronchiolitis • Heart failure, e.g. TAPVD • Asthma • Near drowning • ARDS • BOOP • Malignancy: e.g. T-cell lymphoma	• CNS infection • Drug overdose • Traumatic brain injury • Guillain–Barré syndrome • Spinal cord trauma • Myasthenia gravis • Kyphoscoliosis • Flail chest • Stroke

BOOP, bronchiolitis obliterans organizing pneumonia.

Investigations

Table 21.2 Investigating respiratory failure

Routine	Indicated by clinical scenario
• Blood gases • CXR • Blood cultures • Non-bronchoscopic BAL: viruses, bacteria, TB culture, and rapid antigen tests • IgM for mycoplasma	• Pernasal swab and PCR for bordetella • Bronchoscopic BAL • Echo • CT chest • CT brain • MRI spine • Lumbar puncture (Guillain–Barré) • Genetics for surfactant protein B • T- and B-cell function studies • Lung biopsy • Bone marrow aspirate and trephine

Note: consider immunological disorders [chronic granulomatous disease, severe combined immunodeficiency disease and human immunodeficiency virus] in cases of suspected or proven opportunistic infection (= CMV, PCP, fungal)

Management

(See 📖 Chapter 8.)

- Attend to ***ABCs***
- Treat cause—see Table 21.1
- The mainstay of management is to ensure adequate oxygenation. SaO_2 >90% should with adequate BP and haemoglobin should ensure adequate oxygen delivery
- Accept a relatively high $PaCO_2$ (8–10kPa) so long as systemic pH is between 7.2–7.3 (permissive hypercapnia)
- Many clinicians use a relatively high PEEP (5–10cmH_2O) and limit peak inflation pressures (30cmH_2O)—as 'lung-protective' strategy in ventilated patients with poor lung compliance
- Start enteral feeding early but watch for overhydrating and overfeeding if ventilated and sedated/paralysed
- Tracheostomy should be considered for children with structural airway abnormalities not immediately amenable to surgery and children needing chronic ventilator support
- ECMO support (see 📖 ECMO p.211) has been shown to be life-saving in neonates and adults with respiratory failure. Early consideration should be given to this treatment option as outcomes for patients referred late (>10 days of ventilation) are no better than using non-ECMO modalities of respiratory support.

Treatment

Table 21.3 Treating respiratory failure

Therapy	Investigations
Antibiotic therapy	• Suspected bacterial infection. ABX choice guided by: • Age; child <3 months consider 'peri-natal' organisms • Immunization status • Community acquired or nosocomial • Suspected opportunistic infection or TB • Blood and lung fluid culture results
Antiviral therapy	• Only in cases where HSV or CMV is proven or strongly suspected • Anti-CD-20 therapy has been used in children with fulminant EBV infection and primary immune dysfunction
Pulmonary vasodilators	• Severe hypoxaemic respiratory failure with high PVR
Thoracic surgery (including tracheostomy)	• Congenital airway and lung parenchymal disorders
Immunoglobulins	• Guillain Barré syndrome, • Primary or secondary Immunoglobulin deficiency
Plasmapharesis	• Guillain Barré syndrome
Corticosteroids	• Asthma • BOOP • Inflammatory muscle disorders (e.g. graft-versus-host disease involving muscle) • Lymphoproliferative disorders
Chemotherapy	• Lymphoproliferative disorders

Pneumonia

(See 🕮 Chapter 25.)

Community-acquired pneumonia (CAP) may be caused by either bacteria or viruses. It remains a serious illness and is associated with severe morbidity and mortality.

Clinical presentation

- Depends on the organism (Table 21.4) and the severity of the illness
- Fever and cough are the commonest symptoms although fever alone may be present without any other symptoms
- Poor feeding, restlessness, or progressive obtundation

- Abdominal, chest, or neck pain
- Tachypnoea is invariably present unless in extremis
- Use of accessory muscles, grunting and nasal flaring indicate respiratory compromise
- Poor colour, low oxygen saturation, and evidence of dehydration and mottling
- Crepitations and bronchial breathing.

Table 21.4 Organisms commonly causing pneumonia in childhood

Neonatal	Older children

• Transplacental/prolonged rupture of membrane:
  • Herpes simplex
  • Toxoplasma
  • Listeria
  • Group B streptococci
	• Viral:
	  • RSV
	  • Influenza A and B, HINI
	  • Adenovirus
	  • Measles

• At birth and nosocomial:
  • Group B streptococci
  • *E. coli*
  • *Chlamydia*
  • *Staphylococcus*
	• Bacterial:
	  • *Streptococcus pneumoniae*
	  • *Mycoplasma, Chlamydia*
	  • *Staphylococcus aureus*
	  • *Haemophilus influenza*
	  • *Group A Streptococcus*

Diagnosis

- A CXR will indicate consolidation, lobar or generalized; coin lesions are commonly seen; however, radiological signs may be delayed
- A blood culture will give positive in approximately 30% of cases
- Respiratory secretions including bronchoalveolar lavage, mycoplasma IgM viral titres, and bacterial and viral PCR studies increase the diagnostic yield.

A patient who fails to maintain SaO_2 with high-flow oxygen, or who requires FiO_2 >0.5, or demonstrates cardiovascular instability should be transferred to HDU or PICU.

Management on PICU

- The child may require to be isolated if a communicable infection is suspected
- Respiratory support with oxygen:
  - In infants nasal CPAP may help in improving oxygenation
  - Chest physiotherapy may worsen the condition especially infants.
- Monitor temperature, respiratory rate and oxygen saturation
- NIV may avoid intubation. If ventilatory support is required (see Box 21.2), RSI should be carried out by a senior physician
- Presence of pleural effusion and empyema will require aggressive treatment (see pleural effusion and empyema)
- IV fluid should be administered with caution as SIADH may occur.

Box 21.2 Decompensation after intubation

Never underestimate how efficient spontaneous breathing is at maintaining adequate gas exchange. It is not uncommon to have a patient who was maintaining SaO_2 >90% on high-flow oxygen to find that once you have intubated them they desaturate significantly. It may take hand ventilation and aggressive ventilation to retrieve the situation. Additionally it is not uncommon for severe hypotension or for pulseless electrical activity to supervene when the effect of anaesthetic induction agent and positive pressure ventilation (reducing venous return) combine. This is not a reason to avoid intubation and ventilation, in fact it is a good reason to intervene earlier. It is recommended to fluid load the patient with 10mL/kg saline prior to intubation if time allows and to have resuscitation drugs at hand.

Treatment

Box 21.3 Medical treatment

- In the PICU, antibiotics are administered intravenously. First-line (empirical therapy) antibiotics in previously healthy children with CAP are:
  - <4 months: cefuroxime
  - >4 months: cefuroxime plus erythromycin
- Treatment with newer generation/ broader spectrum antibiotics and/or antiviral agents should be reserved for children in whom atypical agents are suspected on clinical grounds e.g. immunodeficiency
- Duration of treatment depends on the severity of the child's illness. In most uncomplicated cases, 7–10 days of treatment of intravenous and oral treatment is adequate
- In a child with complications such as empyema, a prolonged course of antibiotic treatment of 4–6 weeks is required. Treatment failure may be caused by resistant organisms or development of empyema or abscess. Drainage of lung abscess could lead to the development of broncho-pleural fistula. It is important to rule out foreign body and immunodeficiency. If there is associated septicaemia metastatic disease may develop
- Discharge to the ward can be arranged once the child is maintaining oxygen saturation >90% in low concentrations of oxygen, has normalized vital signs with minimal tachypnoea and no grunting or accessory muscle use. The child should be feeding orally.

Ventilator-associated pneumonia

Definition

- Nosocomially-acquired (healthcare acquired) lung infection that develops >48h after the initiation of mechanical ventilation
- Associated with ↑morbidity, ↑length of stay, and, in some series, ↑mortality
- Diagnosis is often suspected by a change in the colour and amount of secretions, worsening gas-exchange, and/or a rise in infection markers such as neutrophil count and CRP. However, it can only be truly diagnosed through culture of an infectious agent. The most common bacteria isolated are Gram-negative bacilli (*P. aeruginosa* and *Enterobacter cloacae*) and *Staphylococcus aureus*
- Pneumonia not present at the time of intubation but developing within the first 48h falls outside the definition of VAP. This 'early-onset VAP' may represent a pre-existing but clinically silent infection coming to light as a result of intubation. The organisms most commonly identified in early-onset VAP are *S. pneumoniae*, *H. influenza,* and *M. catarrhalis.*

Management

VAP generally needs treatment with second- or third-line antibiotics. In the absence of confirmatory microbiology, a combination of antibiotics, e.g. vancomycin or teicoplanin and tazocin or ciprofloxacin, should be used in the first instance. Consideration should be given to other sources of sepsis such as central lines.

Risk-reduction strategies

(see 🕮 p.533)

- General infection control:
  - Educate all ICU staff on epidemiology and infection control measures for preventing VAP
  - Maintain strict adherence to hand hygiene, e.g. gloves, alcohol rub
  - Educate parents on infection control measures
  - Rational use of antibiotics
- VAP preventative measures and monitoring:
  - Extubate as soon as possible (risk of VAP increases with duration of intubation)
  - Elevate head of bed (decreases risk for aspiration)
  - Gentle but regular oral hygiene
  - Prevent contamination of ETT by oral or nasal secretions.
    - — sterile procedure using closed systems
    - — ETT suction only as required
    - — mouth before nose
    - — oral suction before ETT and with separate systems
  - Prevent ventilator circuit touching non sterile objects
  - Change ventilator circuit weekly or when visibly soiled
  - Keep circuit dry as possible
  - Monitor secretions (amount and colour)
  - Routine culture of secretions 2-weekly.

Aspiration pneumonia

Aspiration pneumonia can be caused by either inhalation into the lungs of gastric or oropharyngeal contents. These contents produce intense inflammation in the lower airways producing aspiration pneumonia/pneumonitis.

In practice, aspiration events are either:
- Acute and large leading to aspiration pneumonitis
- Sub-acute and minor.

In the latter scenario, there may be no immediate symptoms due to individual aspiration events but repeated lung inflammation lead to damage and symptoms develop over time. The most common aetiology is gastro-oesphageal reflux disease.

Aspiration due to disorders of the upper GI tract/airway

Any condition producing dysphagia may result in aspiration pneumonia. It is estimated that up to 70% of such patients will aspirate silently without any signs and may suffer from recurrent LRTI or pneumonia. See Table 21.5.

Table 21.5 Disorders of the upper GI tract and airway that may increase the risk of aspiration

Abnormality	Conditions
Nasal and oral	Cleft lip, craniofacial syndromes, choanal atresia
Larynx, trachea, oesophagus	Laryngomalacia, laryngeal cleft, tracheo-oesophageal fistula
Major vessels	Double aortic arch; other vascular anomalies
Infection	Tonsillitis, retropharyngeal abscess, epiglottitis, oesophagitis
Neuromuscular	Hypotonia syndromes, neuromuscular junction diseases, muscular diseases
Autoimmune disorders	Scleroderma

Other disorders may increase the risk of aspiration in children due to gastro-oesphageal reflux:
- Head injury/trauma
- Urgent surgery with rapid sequence anaesthesia
- Neuromuscular and neurological disorders associated with laryngeal dysfunction
- Cerebral palsy
- NG tube
- Tracheostomy
- History of seizures
- Obesity
- Hiatus hernia
- Extreme preterm with chronic lung disease.

Community-acquired aspiration pneumonia

Aspiration pneumonitis and pneumonia is prevalent in CAP from causes outlined in the previous sections. Presenting features may be variable and include:

- Fever
- Sudden onset dyspnoea
- Hypoxia and cyanosis
- 'Infiltrations' on CXR and widespread crepitations.

Management and prevention of aspiration

(see Boxes 21.4 and 21.5)

Box 21.4 Management of aspiration

- Airway suctioning especially in infants
- If still cyanosed and not maintaining blood gases with oxygen administered via a rebreathing bag, intubate and ventilate.
- Continue cardiovascular monitoring and transfer to PICU
- Commence antibiotics: penicillin and metronidazole or co-amoxyclav
- Steroids not recommended

Box 21.5 Prevention of aspiration pneumonia in hospitalized patient

- Semi-recumbent position especially obese patients
- The use of promotility agents
- Avoiding excessive sedation
- Avoiding large volume enteral feeding via NG tube.

Pleural effusion and empyema

- The small amount of fluid normally present in the pleural cavity (~0.3mL/kg) contains a few cells and is constantly being generated and absorbed
- Para-pneumonic effusions are accumulations of fluid and inflammatory cells due to an underlying lower respiratory tract infection.
- An empyema is a collection of viscous fluid and cells (pus). The fluid or pus is often loculated (separated by fibrin septae into one or more pockets)
- Non-infective pleural effusions may be secondary to:
  - Congenital heart disease (cardiac failure, post surgery, fontan circulation),
  - Renal disease (nephrotic syndrome, renal failure with fluid overload)
  - Neoplasms
- If the patient is or *is likely to be* clinically compromised by the presence of excess pleural fluid, then it is vital to reduce the size of the effusion for therapeutic purposes. How this is achieved depends on the nature and cause of the effusion.

- If the diagnosis underlying the effusion is unclear, a sample of fluid may be obtained to help to establish it
- Management of pleural effusion is guided by answering the following questions:
  - Is the cause of the effusion known?
  - What are the effects of the effusion on the patient?

Para-pneumonic effusion and empyema

Based on the clinical features (Table 21.6) and CXR findings, decide whether the fluid collection is due to an underlying chest infection.

Table 21.6 Features of pleural effusion

Symptoms/signs	Aetiology	
	Infectious	**Non-infectious**
Fever	+ve	−ve
Chest (pleuritic) pain	+ve	−ve
White cell count	Raised	Normal
Scoliosis (examination/X-ray)	Present	Absent
CRP	Raised	Normal

CXR

- Normal size heart
- Normal mediastinum
- 'Body' of fluid on one side of chest
- Obliteration of the costo-phrenic angle only = a small effusion
- A thick rim of fluid ascending the lateral chest wall = moderate sized effusion
- A dense opacification of involving one or other lower zones = large effusion
- A generalized, unilateral hazy opacification of a lung field may be seen in a young child—difficult to estimate amount of fluid.

US assessment

- A US examination will show the size, position, and presence of the fluid and may determine whether it is loculated
- A small effusion on CXR does not necessarily need US assessment. The child can be managed in the expectation that the effusion will be resorbed
- A moderate to large para-pneumonic effusion or empyema needs US assessment.

A child with a moderate to large effusion on US should be managed in a specialist unit with access to cardiothoracic surgeons. 'Conservative' treatment with antibiotics alone will result in a prolonged illness and hospital stay. There is no place for repeated thoracocentesis in this situation.

If the effusion is not loculated, first insert a chest drain (see 📖 p.422) in the expectation that effective draining of fluid will relieve symptoms and prevent progression of the illness. (Box 21.6)

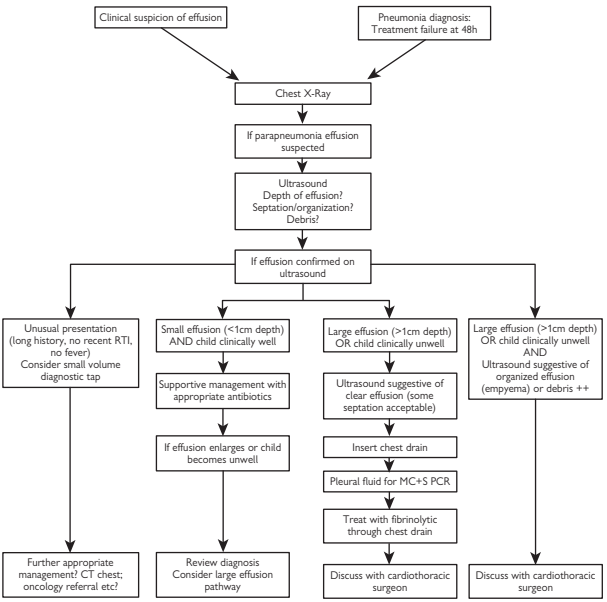

Fig. 21.2 Flowchart for the management of parapneumonic effusions.

Box 21.6 Management of empyema

- High-dose antibiotics IV for 3 weeks (see 📖 Chapter 28)
- Fibrinolysis:
  - Insert small percutaneous chest drain (10–12FG)
  - Urokinase 40,000U in 40mL (10,000U in 10mL if <10kg) given 12-hourly into drain.
  - Clamp drain and encourage mobility 4h after urokinase
  - Drain on suction ($-20cmH_2O$) for next 8h
  - Alteplase is an alternative
  - Do not forget analgesia, e.g. bupivicaine 0.25% 0.5mL/kg into drain and NSAID
- Video-assisted thoracoscopic surgery is gaining popularity for empyema. It has good success with low morbidity.

Chylous effusions

- The lymphatic system transports lymph (a transudate of blood) and lymphocytes. Chyle is lymphatic fluid which has been enriched with fat as a consequence of intestinal absorption. Lymphatic fluid from the left arm, left chest wall, and lower body is transported via the thoracic duct entering the systemic circulation at the left jugulosubclavian venous junction. The course of the thoracic duct in the chest is variable
- Chylous effusions most commonly result from trauma to or obstruction of the thoracic duct in the chest. They are also common in children who have had completion of Fontan circulation where a high venous pressure 'obstructs' lymphatic drainage
- A high fat content and largely lymphocytes in pleural effusion is diagnostic of chyle.

Management

- Since chylous effusions are only diagnosed after obtaining a sample of pleural fluid, it is likely that many children will have a chest drain *in situ*
- If a chest drain has not been placed, then a decision to inset one should be largely based on whether the effusion is interfering with cardiorespiratory function
- Most chylous effusions will resolve over time by reducing the production of lymph
- This can be achieved most simply and safely by using enteral feeds containing 'medium chain triglycerides' as the dietary source of fatty acids
- If this fails to stem lymph flow from the chest tube, then a short course of parenteral-only feeding may be necessary
- Octreotide, a somastain analogue, may be given in addition to parenteral feeds to hasten resolution of the effusion.

Effusions due to renal disease, cardiac failure, or malignancy

Excess pleural fluid in children with renal failure, malignancy, or heart disease should only be drained (pleural 'tap' or chest drain) under controlled circumstances and for very good reasons. Effusions should be drained if there is diagnostic uncertainty (e.g. concerns there may be an empyema or chyle) or if controlled release of fluid may improve gas-exchange and/or cardiac function. Otherwise it is generally better and safer to use therapies directed at the underlying cause of the effusion. This may include fluid restriction, diuretics, corticosteroid (nephrotic syndrome), dialysis (renal failure, severe heart failure), and chemotherapy.

Chest drain insertion

Seldinger (pigtail or straight) or surgical.

Indications

- To drain air or fluid (pleural effusion, blood or pus)
- Pneumothorax:
  - In any ventilated patient
  - Tension pneumothorax after initial thoracocentesis
  - Persistent or recurrent pneumothorax after needle aspiration

- Persistent empyema or parapneumonic pleural effusion (📖 p.420)
- Actual or potential haemopneumothorax:
  - Post traumatic
  - Postoperative.

Landmarks

- Use the triangle of safety, above the 6th rib (roughly at the level of the nipple), behind the pectoralis major muscle and in front of the lattisimuss dorsi muscle which form the borders of the axilla
- Aim for the 4th or 5th intercostal space
- Some children may need a drain placed in a specific place to drain a loculated empyema or pneumothorax. These need specialist referral.

Equipment

- Sterile pack, no. 15 blade, artery forceps, sutures to secure drain, skin prep, gloves, gown, mask and hat, drapes
- Drain selection:
  - Pigtails for simple pneumothorax and pleural fluid
  - Blood and pus need a bigger drain
  - Use smaller size for draining air
  - Larger size for draining blood/fluid
  - Newborn: 8–12 FG
  - Infant: 12–16 FG
  - Child: 16–24 FG
  - Adolescent: 20–32 FG
- EMLA (if time), 1% lidocaine, needles, and syringes
- Underwater seal (or other unidirectional flow drainage system)

Set-up

- Sedation/analgesia/anaesthesia (📖 p.185)
- High-flow O_2
- Monitoring (ECG, SpO_2, and NIBP)
- IV or IO access as indicated
- Patient usually supine with arm behind head
- Full aseptic technique and appropriate anaesthesia.

Technique

Small drains may be inserted by the Seldinger technique. Blunt dissection of the chest wall is not needed. Larger drains require a surgical technique, including blunt dissection.

Technique—Seldinger

- 3-mm skin incision
- Insert Seldinger needle through skin in middle of intercostal space perpendicular to skin
- Once needle is through skin suck on syringe and advance into thorax
- If possible, briefly disconnect the patient from the ventilator and advance the needle through the pleura—a 'pop' may be felt as pleura is breached
- Confirm placement by aspirating air or fluid
- Insert Seldinger wire, soft end first, remove needle
- Reconnect patient to ventilator

- Straighten pigtail with peel-apart sheath, introduce pigtail over wire, don't let go of wire
- Insert pigtail to correct length, peel apart sheath, remove wire
- Stitch and secure drain
- Connect to underwater seal
- Check CXR.

Technique—surgical

- 1–3-cm skin incision. The incision for insertion of the chest drain should be similar to the diameter of the tube being inserted
- Blunt dissection with artery forceps down to pleura
- If possible, briefly disconnect the patient from the ventilator
- Pop artery forceps through pleura; in a big patient confirm by digital exploration
- Remove and discard the trocar from drain
- Grasp drain with artery forceps, and insert through incision
- Reconnect patient to ventilator
- Suture in place
- Stitch and secure drain
- Connect to underwater seal
- Check CXR.

Pitfalls

- Failure to disconnect the ventilator leading to placement in the lung
- Failure of landmarking leading to placement into any and every organ in chest and upper abdomen
- If your knot is loose, wrap some tape around your suture
- If the lung won't re-expand, suspect airway injury in trauma cases, call thoracic surgery
- A loculated empyema needs decortication, if in doubt do a CT scan.

Position of tube

- The position of the tip of the chest tube should ideally be aimed apically for a pneumothorax or basally for fluid
- However, an effectively functioning drain should not be repositioned solely because of its position on X-ray.

How to fix a chest drain (Fig. 21.3)

- Large- and medium-bore chest drain incisions should be closed by a suture appropriate for a linear incision
- 2 sutures are usually inserted—a horizontal mattress suture to assist later closure of the wound after drain removal, and a stay suture to secure the drain
- The wound closure suture should be inserted before blunt dissection.
- 'Purse string' sutures should not be used
- The drain should be secured after insertion to prevent it falling out, and the length of tubing inserted should be noted
- A transparent dressing allows the wound site to be inspected for leakage or infection.

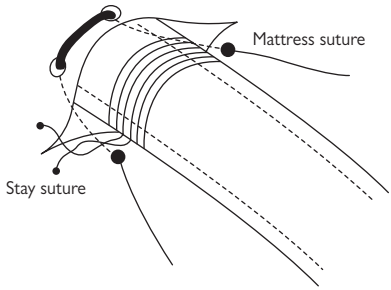

Fig. 21.3 Technique for securing chest drain. The mattress suture is used to facilitate wound closure at chest drain removal. The stay suture is held in place with Sleek or other tape wrapped around the drain. A transparent dressing is placed over the drain site.

Drainage and suction

- Drainage of a large pleural effusion should be slow to prevent discomfort and re-expansion pulmonary oedema. Safe rates are not known in children, but stopping drainage for 1h after draining 1L in adults has been proposed
- 2.5–5cmH_2O of high-volume low-pressure suction is used in most cases (but no evidence that it alters outcome)
- Low-volume suction pumps should not be used (flow too low risking re-accumulation of pneumothorax)
- Unregulated wall suction should not be used (high pressure may traumatize lung)
- Suction should not be used for post-pneumonectomy drains

Clamping the drain

- A bubbling chest drain should not be clamped
- In the management of a pneumothorax, clamping the drain may lead to a tension pneumothorax and should usually be avoided
- In empyema, drains are routinely clamped for 4h after the intrapleural instillation of fibrinolytic agents such as urokinase. There is no need to routinely clamp the drain before its removal in empyema
- If a patient with a clamped drain deteriorates clinically, becomes breathless, or develops SC emphysema, the drain must be immediately unclamped and an urgent medical review undertaken.

Removal

- Once the lung has re-expanded (on X-ray) and there is no further drainage of air or fluid the drain can be removed
- Don't clamp the drain to assess whether an air leak has stopped
- To remove the drain, clamp it and withdraw swiftly whilst the purse string is tied by an assistant
- Ensure adequate analgesia—removal can be painful
- CXR to check that air has not been entrained, leading to pneumothorax.

Management of bronchopulmonary fistula

- Persistent air leak or a failure to re-inflate the lung despite chest tube drainage for 24h due to a communication between the bronchial tree and pleural space
- Causes:
  - Chest trauma
  - Complication of surgery (e.g. thoracic surgery with failure of suture/staple line)
  - Chest drain inserted into the lung parenchyma
  - Complication of mechanical ventilation (rare)
- In the ventilated patient bronchopulmonary fistula may lead to:
  - Loss of delivered tidal volume
  - Loss of PEEP
  - Persistent lung collapse
  - Delayed weaning from mechanical ventilation
- Management strategies include conservative measures such as continued chest drainage (multiple drains may be necessary)
- In mechanically ventilated patients, maintain adequate ventilation and oxygenation while reducing the fistula flow, allowing the leak to heal. This includes:
  - ↓inspiratory pressure,
  - Reduced tidal volumes
  - Reduced respiratory rate, PEEP, and inspiratory times
  - Permissive hypercapnia
  - Tolerating lower oxygen saturations
- Most air leaks will settle spontaneously over a few days if the patient can be weaned onto spontaneous respiration without high levels of PEEP
- The size of the air leak is critical; small fistulae will heal quickly while larger ones, especially if involving a major bronchus will not respond to conservative management
- High ventilatory pressures impair resolution of the fistula
- Other modes of ventilation may be considered, including high-frequency oscillation, and differential lung ventilation through double-lumen tubes
- For proximal leaks, fibreoptic bronchoscopy and direct application of sealants (e.g. cyanoacrylate, fibrin agents, gelform) have been tried with some success
- Refractory cases may need surgical repair of the air leak by thoracoplasty, lung resection/stapling, pleural abrasion/decortication, or other techniques.

See also 🕮 Box 21.6, p.421

Thoracocentesis

- Using a needle (or IV cannula) to tap the chest.
- Diagnostic or therapeutic.

Indication

- Suspected air or fluid within the chest
- Tension pneumothorax.

Landmarks

Will depend on the indication:

- Pneumothorax (including tension): 2nd or 3rd intercostal space, mid-clavicular line, approximately halfway between the clavicle and the nipple in line with the nipple
- Pleural effusion: either at the site of US localization or in the mid-scapular line posteriorly below the upper limit of dullness to percussion. Always stay above the 7th rib
- Diaphragm may be high especially in a newborn.

Equipment

- Sterile pack, skin prep, gloves (gown, mask, and hat), drapes
- IV cannula (20G for a newborn, 14G for adolescent)
- EMLA (if time), 1% lidocaine, needles and syringes
- 3-way tap and closed collection system for large amounts of fluid.

Set-up

- High-flow O_2
- Monitoring (ECG, SpO_2 and NIBP)
- IV or IO access as indicated
- Full aseptic technique
- Local/general anaesthesia or sedation depending on age and cooperation.

Technique

- Mount cannula on syringe,
- Insert needle through skin in middle of intercostal space perpendicular to skin
- Once needle is through skin suck on syringe and advance into thorax
- A 'pop' may be felt as pleura is breached
- Air or fluid should be aspirated into syringe. Advance cannula off needle into chest
- For tension pneumothorax, remove needle and let air woosh out, patient will improve rapidly
- For fluid connect 3-way tap and drainage system and aspirate
- Consider whether a formal chest drain is needed.

Pitfalls

- Bad landmarking
- Suspected tension pneumothorax = needle thoracocentesis.

Bronchiolitis

Bronchiolitis is the most common lower respiratory tract infection in infants requiring admission to hospital and the most frequent cause of respiratory failure requiring PICU admissions. Respiratory syncitial virus (RSV) is the most commonly isolated aetiological agent accounting for ~75% of all cases. Influenza, parainfluenza, coronavirus, enterovirus, metapneumovirus, bocavirus, and rhinovirus viruses account for the remainder.

RSV bronchiolitis—prevention

Passive immunization with humanized monoclonal antibody (palivizumab) significantly reduces RSV-related morbidity (fewer days in hospital, lower incidence of intensive care admission) in infants with BPD and/or haemodynamically significant heart disease

Risk factors

- Prematurity
- Male sex
- Smoking in the home
- Non-breastfeeding
- Low socioeconomic status
- Neurodevelopmental delay
- Chronic lung disease of prematurity
- Age <3 months
- Cystic fibrosis
- Upper airway obstruction
- Congenital heart disease with pulmonary hypertension
- Immunodeficiency.

Clinical features

- Bronchiolitis is a clinical diagnosis
- Antecedent upper respiratory tract infection (URTI) followed by signs of respiratory distress
- Harsh cough
- Bilateral crepitations
- Clinical air trapping and wheezing
- Apnoea especially in preterm infants (20% hospitalized patients).

Indicators of severity

- Ill and exhausted infant
- Sweaty, irritable, and having periods of apnoea
- Barely maintaining oxygen saturation ~90% with a rebreathing bag
- Respiratory rate ≥70 breaths/min
- Mortality in otherwise healthy infants is <1%
- Higher (~3.5%) in infants with underlying conditions such as cardiac or chronic lung disease
- Atelectasis on chest radiograph (up to 30%) or marked overinflation
- Radiological appearances of ARDS are associated with severe disease and may require prolonged ventilation.

Treatment

Box 21.7 Treatment of bronchiolitis

- Monitoring of oxygen saturation, respiratory rate, and heart rate
- Administer oxygen either via nasal canula or headbox to maintain saturation over 90%
- IV fluid may be required if the infant is dehydrated or too sick to take enteral feeds
- Restrict fluids at 2/3 maintenance
- If there is increasing oxygen requirement and signs of fatigue and CO_2 retention, ventilation will be required
- Infants with increasing respiratory distress or apnoea should be managed on PICU. A capillary or arterial gas should be should be measured these infants. Progressive rise in CO_2 is an indication for early ventilatory support.

Pharmaceutical treatment

- No benefit from nebulized salbutamol, ipratropium, or inhaled steroids
- Systemic steroids and antibiotics are not useful
- Nebulized adrenaline may improve oxygenation and clinical signs, but does not improve outcome
- Ribavarin is the only licensed antiviral agent for use in RSV-bronchiolitis but its use is not associated with clinical benefit

Respiratory support

About 2% of infants with bronchiolitis require respiratory support for either apnoea or respiratory failure.

Non-invasive CPAP

CPAP delivered non-invasively via nasal prongs (usually between 5–8cmH_2O) may avoid the need for intubation in many infants.

Mechanical ventilation

- High inspiratory pressure may be required to help oxygenation
- PEEP of 5–10cmH_2O
- Low rates and ↑inspiratory time
- In refractory hypoxia HFOV may be required
- If pneumonia is present the ventilation requirement is prolonged
- Infrequently ECMO may be necessary.

Outcome

- Presence and greater extent of infiltrates on chest CXR
- Majority recover within 2 weeks, many with persistent cough
- An association with subsequent reactive airway disease (RAD) has been found particularly in association with RSV bronchiolitis. However, rhinovirus may have an even stronger association with RAD
- The rate of wheezing following bronchiolitis is between 30–50%
- Follow-up lung function testing demonstrates ↑airways resistance after 10 years.

Acute severe asthma

Asthma is a common reason for admission into PICU and still remains a cause of death, although 1/3 of patients dying from asthma were previously diagnosed as being mild. There has been a steady increase in the number of patients with asthma admitted to PICU. Most childhood (and adult) deaths from asthma occur following pre-hospital cardiorespiratory arrest. Contrary to what is taught, there is no evidence that intubation and ventilation in asthmatics is dangerous—do not delay intubation in an exhausted patient.

Pathophysiology

During an acute attack there is marked airway inflammation with excessive mucous leading to airway plugging. Bronchospasm produces severe airflow limitation leading to progressive respiratory failure. In a small group of children acute anaphylaxis predominates with intense bronchospasm without mucous plugging. In the majority of children there are no specific identifiable precipitating factors. Occasionally, a history of anaphylaxis, e.g. to peanuts, may be obtained.

Differential diagnosis

- Acute infection especially severe pneumonia
- In a child with no previous history, rule out foreign body or mediastinal tumour, e.g. lymphoma.
- Congenital malformation, e.g. vascular ring, tracheal stenosis.

Risk factors

- Previous admission to PICU requiring mechanical ventilation
- History of sudden and rapid deterioration
- Excessive use of β-agonists
- Poor compliance
- Reluctance to accept severity and poor perception of hypoxia.

Management

General points for all asthmatics

- Administer high-flow oxygen with aim of maintaining SaO_2 >94%
- Provide a calm and reassuring environment
- Allow them to assume most comfortable position—often sitting upright reduces distress and improves chest wall movement
- The following clinical signs should be recorded:
  - Pulse rate *(increasing tachycardia generally denotes worsening asthma; a fall in heart rate with signs of life threatening asthma is a pre-terminal event)*
  - Respiratory rate and degree of breathlessness
  - Use of accessory muscles of respiration
  - Amount of wheezing *(might become biphasic or less apparent with increasing airways obstruction)*
  - Degree of agitation and conscious level
  - Clinical signs may correlate poorly with the severity of airways obstruction in some children who may not appear distressed.

- Monitor:
  - Continuous pulse oximetry (falling SaO_2 after bronchodilator therapy may be seen in more severe patients)
  - Continuous ECG
  - BP
  - Serum electrolytes + blood glucose: watch carefully for hypokalaemia
  - Objective measurements of peak expiratory flow (PEF) are essential. However, such measurements may not be tolerated or possible in distressed or young children.

Initial medical treatment

The main points of initial management vary according to severity (Table 21.7).

- Providing high oxygen concentration, if needed, breathing via a reservoir bag
- Continuous nebulized bronchodilator (salbutamol/atrovent) therapy with oxygen
- Early steroid, either orally if tolerated or intravenously
- Sitting the child up to minimise ventilation perfusion mismatch
- Failure to improve with the initial treatment necessitates admission to PICU

Table 21.7 Assessment of asthma severity

Severity	Age	
	<5 years	**>5 years**
Severe	• Too breathless to talk • Too breathless to feed • Respiratory rate >50 • Pulse >130bpm • Significant respiratory distress	• Too breathless to talk • PEFR <50% predicted • Respiratory rate >30 • Pulse >120bpm • Use of accessory muscles
Life-threatening (any of these features)	• *Any age* • Cyanosis • Silent chest • Poor respiratory effort • Fatigue or exhaustion • Agitation or reduced level of consciousness • (PEFR < 33%—measurement may not be tolerated)	

Admission to PICU

- Indications for admission to PICU or HDUs include patients requiring ventilatory support and those with severe acute or life threatening asthma who are failing to respond to therapy, as evidenced by:
  - Deteriorating PEFR
  - Persisting or worsening hypoxia
  - Hypercapnia
  - ABG analysis showing fall in pH
  - Exhaustion, feeble respiration, drowsiness, confusion coma, or respiratory arrest.

- Not all patients with acute severe asthma admitted to intensive care will need ventilation. For pre-intubation treatment see Box 21.8
- Worsening blood gases should not be used on their own in making decisions to intubate (Box 21.9).

Box 21.8 Pre-intubation treatment

- Continuous nebulized bronchodilator therapy
- IV hydrocortisone 4mg/kg
- IV bronchodilator therapy: salbutamol infusion 5mcg/kg/h for 1h then 1mcg/kg/h (continue nebulizers). Watch for hypokalaemia which will almost certainly develop
- If this regimen is not effective, IV aminophylline bolus followed by continuous infusion may also be necessary; a 5mg/kg loading dose should be given over 20min with ECG monitoring (omit in those receiving maintenance oral theophyllines) followed by a continuous infusion at 1mg/kg/h. Aminophylline has a narrow therapeutic range and prolonged therapy carries a risk of adverse effects (tachycardia, arrhythmias, nausea, vomiting, convulsions, hyperglycaemia). Theophylline level (target 60–110mg/L)
- Magnesium sulphate should be administered upon arrival to the ICU: 50mg/kg (0.1mL/kg 50% $MgSO_4$) over 20min followed by infusion (if desired) at 30mg/kg/h (0.06ml/kg/h 50%$MgSO_4$). Aim for serum Mg up to 2.5mmol/L.

NIV may help whilst waiting for medical therapy to work in children not at immediate risk of incipient respiratory collapse. NIV requires a cooperative child and should be discontinued if there is worsening of hypoxia, worsening blood gases or the child is tired and/or at risk of incipient respiratory collapse.

Box 21.9 Criteria for intubation

- Respiratory arrest
- Hypoxia and rising hypercapnia despite maximum oxygen and medical treatment and NIV
- Exhaustion and unable to vocalize
- Altered mental status.

Intubation

- Although intubation does not contribute to mortality, complications do occur commonly during or immediately after intubation. So an ***experienced senior physician must be present:***
  - Worsening bronchospasm ± laryngospasm
  - Worsening hypoxia
  - Barotrauma: greater risk pneumothorax and surgical emphysema
  - Hypotension—positive pressure ventilation causes a decrease in venous return, exacerbated if dehydrated/hypovolaemic + vasodilatation secondary to induction agents.

- For induction:
  - Ensure good IV access
  - Give IV fluid bolus: 10mL 0.9% saline
  - RSI with ketamine (2mg/kg)
  - Use a cuffed ET tube as high PIP may be required
  - Following intubation ***avoid rapid bagging*** (this is often done subconsciously by the intubator due to natural stress/anxiety)—use a slow rate to allow adequate expiration
  - If air trapping is severe: pre-oxygenate then disconnect ETT from ventilator and manually squeeze chest to assist in expiration
  - CXR post-intubation.

Ventilation

- Pressure or volume-controlled:
  - Pressure controlled preferable as it uses a decelerating waveform and so results in lower PIP for given mean airway pressure.
  - If using volume-controlled: aim tidal volume 4–8mL/kg
- Rate:
  - Well below average for age e.g. 5–15. Allow permissive hypercapnia (pH >7.2)
- Inspiratory time:
  - Suggested 1.0–1.5s
- I:E ratio:
  - Long expiratory time to avoid dynamic hyperinflation: 1:3–1:5
  - Possible guides to whether expiration is adequate include improvement in $PaCO_2$
- PIP:
  - Likely to need high pressures—aim to limit PIP <35cmH_2O
  - Note inspiratory plateau pressure may be a more accurate assessment—aim to limit to <30cmH_2O
- PEEP:
  - Avoid high PEEP as this may worsen dynamic hyperinflation
  - Opinion is divided on the benefit of PEEP but moderate PEEP may be beneficial—set to ~ 60% intrinsic PEEP as measured on the ventilator.

Issues during ventilation

- Sedation and paralysis:
  - Adequate sedation is essential to allow permissive hypercapnia, avoiding tachypnoea and patient-ventilator dyssynchrony which can worsen dynamic hyperinflation
  - Morphine/midazolam and/or ketamine (0.5–2mg/kg/h) are appropriate
  - Paralysis should be avoided if possible in acute asthma (risk of critical care myopathy/neuropathy). This may not be possible initially. If required restrict to <48h. Pancuronium or vecuronium are the drug of choice (atracurium releases histamine).
- Bronchodilator therapy:
  - Continue IV bronchodilator infusions.
  - Nebulizers can be inserted into the ventilatory circuit to deliver salbutamol + ipratropium—there is no evidence to suggest which is preferable

- Refractory hypoxaemia:
  - Possible contributing causes include: atelectasis, pneumothorax
  - Hypovolaemia and over-use of β_2-agonists—may worsen V/Q mismatch
  - Some patients may respond to trial of reducing sedation and allowing more patient-synchronized (ASB) breaths
  - If continuing to deteriorate, further measures to consider (limited evidence); ketamine infusion owing to its bronchodilating properties, magnesium infusion, inhalational anaesthetics (isoflurane), BAL or nebulized DNAse to clear mucus plugging, proning and ECMO.
  - Look for lung infection.

Weaning ventilation

- Assessing clinical improvement:
  - Monitor intrinsic PEEP (PEEPi, see Box 21.10 also see 📖 p.123) and the response to therapy
  - Disappearance of pulsus paradoxus
  - Good oxygenation in $FiO_2 < 40\%$
- Continue to aim to minimize patient-ventilator asynchrony during weaning: reduce rate and allow more ASB breaths.

Box 21.10 PEEPi (see also 📖 p.123)

Trend in PEEPi is an excellent way to assess severity of air trapping in asthma. Modern ventilators allow you to measure PEEPi by performing an end-expiratory hold manoeuvre.

PEEPi = PEEP displayed by the ventilator at the end of the expiratory hold *minus* the set (extrinsic) PEEP.

Alternatively, disconnect ETT from ventilator, listen at ETT and count seconds until wheezing stops—this is an indirect measure of gas trapping and will get shorter as the patient recovers

Acute respiratory distress syndrome and acute lung injury

A spectrum of lung diseases associated with a systemic inflammatory response and respiratory failure.

'A syndrome of inflammation and increased permeability that is associated with a constellation of clinical, radiological, and physiological abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension.' See Table 21.8 for some clinical definitions.

Table 21.8 The American-European Consensus Conference definitions of ALI and ARDS

Oxygenation	ALI	PaO_2/FiO_2 <300 (regardless of PEEP)
	ARDS	PaO_2/FiO_2 <200 (regardless of PEEP)
CXR		Bilateral infiltration
Pulmonary artery pressure		<18mmHg if measured, or no evidence of ↑ LAP

Pathophysiology

- Release of pro-inflammatory mediators by an initial insult
- Disruption of the alveolar-capillary unit
- Inactivation of surfactant production
- Activation of the coagulation cascade
- Imbalance between pro-inflammatory and anti-inflammatory mediators, and between pro-coagulants and anti-coagulants
- Abnormalities of clearance of alveolar fluid and transcapillary water transport.

Epidemiology

- Limited data, dependent on definitions, population studied and how hard people look (see Table 21.9)
- Paediatric ARDS:
  - 3.2 cases per year/100,000 population (cf. adults—18–86 cases per year/100,000)
  - 3–4% of all PICU admissions
  - ♂ >♀

Table 21.9 Disorders causing ALI (data relates to adults)

Direct lung injury	Indirect lung injury
• Pneumonia	• Sepsis
• Gastric aspiration	• Severe trauma
Less common	
• Pulmonary contusion	• Cardiopulmonary bypass
• Fat emboli	• Drug overdose
• Near drowning	• Acute pancreatitis
• Inhalational injury	• Multiple blood transfusions
• Reperfusion injury	

Treatment

- Treat hypoxia by oxygen therapy ± mechanical support
- Prevent fluid overload
- Ensure adequate circulation
- Provide sufficient pain relief and sedation
- Early aggressive nutritional support will help early recovery.

Ventilation (see pp.121–2 also p.159)

- Adult data drives treatment recommendations, with few paediatric specific studies to guide us
- Principles of ventilation in ARDS:
  - Prevent atelectasis; re-open atelectatic regions; avoid overdistension—which in a heterogenous lung disease like ARDS is easier said than done!
  - Optimum PEEP—above the lower inflection point (see 🕮 p.121–2)
  - Recruitment manoeuvres
  - Low Vt—5–7mL/kg
  - Avoid PIP >30cm H_2O
  - Permissive hypercapnia with pH support (i.e. bicarbonate administration).

High frequency oscillation

(See 🕮 p.157.)

- Minimizes V_T whilst keeping lung in the 'safe zone' of the pressure volume curve (see 🕮 p.121)
- Often used as 'rescue therapy' when high pressures needed on conventional ventilation, or in ARDS with air leaks
- Although physiological parameters and oxygenation are improved, no convincing population evidence that HFO improves mortality of morbidity in paediatric ARDS.

Prone positioning

- Enhances recruitment of alveoli
- Improves V/Q mismatching
- Reduces RV afterload
- Improves lung compliance
- Most noticeable in an improvement in oxygenation, which occurs in 70–80% of children, is noticed within 1–2h, and is sustained
- However, no evidence of an improvement in survival or reduction in time on the ventilator
- Adult trials suggest that keeping prone for up to 18h is beneficial, but watch pressure areas. Most units turn patients every 8–12h or more frequently.

Inhaled nitric oxide (iNO)

- Should be good—inhaled selective pulmonary vasodilator—it should improve V/Q matching, and treat pulmonary hypertension
- Has been shown to improve outcome in term infants with IRDS
- Majority of adults and children with ARDS will improve oxygen saturations with NO (dose 5–80ppm), but improvements often short lived
- No evidence of improvement in mortality

- Not recommended for routine use, but often added in difficult clinical situations
- Watch methaemoglobin levels.

Aerosolized prostacyclins

- Similar effects to iNO in improving oxygenation, but no evidence of improvement in mortality
- Difficult to deliver correctly—some 'treatment failures' may be delivery failures!

Surfactant

- Surfactant depletion and inactivation occurs in ALI
- Suggestion of mortality improvement from exogenous surfactant administration in one study, but insufficient data to make recommendations
- Choice of surfactant preparation, timing and method of administration may be important variables. Further trials needed.

Steroids

- Steroid therapy suggested because of the presence of pro-inflammatory mediators in ALI/ARDS
- Experimental and animal studies suggest that steroids might reduce fibrogenesis and lung remodelling
- However, no evidence of improvement in survival in adults with ARDS, and some subgroups had a worse mortality
- Steroid therapy not currently recommended unless there is evidence of corticosteroid deficiency.

ECMO

(See 🕮 p.211)

- Used as 'lung rest' in patients otherwise requiring high ventilator pressures, and as 'rescue' in patients deteriorating despite maximal therapy
- RCT-studies in infants and adults with severe respiratory failure suggest that ECMO does reduce mortality, as does a retrospective study of children.

Outcome

Mortality

- Overall mortality in children 18–27% (all ALI); up to 50% (ARDS); 11% (ALI without ARDS)
- Adult mortality ~10% higher
- Worse outcome if pre-existing disease present.

Morbidity

- In adults after ARDS, long-term reductions in health-related quality of life, neurocognitive dysfunction, and abnormal pulmonary function testing seen
- Severity of lung injury and duration of mechanical ventilation correlate with lung function abnormalities
- In children, ALI may interfere with normal lung development leading to chronic lung disease
- Lung function abnormalities occur in almost all children in the year following ARDS, consisting of both restrictive and/or obstructive abnormalities.

Non-cardiogenic pulmonary oedema

Pulmonary oedema occurs when excess fluid enters the alveoli as a result of an alteration in capillary permeability, hydraulic pressure across the alveolar-capillary membrane, oncotic pressure between the blood and alveolar fluid, or disruption of the alveolar capillary unit (see 📖 Box 13.5 p.240).

In *cardiogenic pulmonary oedema*, a high pulmonary capillary pressure (secondary to high left atrial pressure leading to high pulmonary venous pressure) is responsible for the abnormal fluid movement

In *non-cardiogenic pulmonary oedema*:

- Left atrial pressure is normal
- Protein and fluid accumulation in the alveoli is caused by a group of medical and surgical disorders including:
  - ALI/ARDS
  - Reexpansion pulmonary oedema
  - Post-extubation pulmonary oedema
  - Neurogenic pulmonary oedema
  - Reperfusion pulmonary oedema
  - High-altitude pulmonary oedema
  - Opiate overdose
  - Salicylate toxicity
  - Transfusion related lung injury
  - Pulmonary embolism
- The distinction between cardiogenic and non-cardiogenic causes is not always possible, since the clinical syndrome may represent a combination of several different disorders
- Treatment varies depending upon the underlying pathophysiologic mechanisms.

Tracheobronchomalacia

Many paediatric texts use the terms tracheomalacia (TM) and tracheobronchomalacia (TBM) interchangeably. However, TM only refers to accentuated tracheal narrowing during expiration. The degree of narrowing is variable (partial/total) and so therefore is the extent of airway obstruction. TBM should be used if the mainstem bronchi also show excessive narrowing during tidal breathing. Bronchomalacia describes collapse of one or both of the mainstem bronchi without tracheal involvement.

In all forms of TBM, airway narrowing is accentuated during forced expiratory maneuvers (e.g. cough) and is attenuated by positive pressure. Hence, malacic airway segments should only be diagnosed in spontaneously breathing patients.

Aetiology

Table 21.10 Aetiology of TM and TBM

Primary	Secondary

• Idiopathic TM (otherwise normal infants)
• Congenital abnormalities of cartilage
  • Chondromalacia
• Syndromes associated with TM/TBM, e.g.
  • Trisomy 21
  • Absent pulmonary valve syndrome
  • Pierre Robin syndrome
  • CHARGE syndrome
  • VATER anomaly
  • Mucopolysaccharidosis
• Congenital anomalies associated with TM/TBM
  • Tracheo-oesophageal fistula
	• Prolonged intubation
	• Bronchopulmonary dysplasia
	• Tracheotomy
	• Severe tracheo-bronchitis
	• Resulting from cardiac/ vascular compression e.g.
	  • Double aortic arch,
	  • Aberrant right subclavian artery
	  • Left atrial hypertrophy /
	  • enlargement
	• Tumors and cysts:
	  • e.g. teratomas, cystic hygroma, goitre, neuroblastoma
	• Post-traumatic

Presentation

- TM/TBM are associated with substantial morbidity and mortality although the clinical severity of TM/TBM ranges from mild to life-threatening
- It may go unrecognized or misdiagnosed as asthma or other respiratory conditions, thereby contributing to the morbidity of the disease
- Patients with congenital forms of TM/TBM may present at birth but more commonly develop symptoms in the first few months of life
- An array of symptoms depending on the severity and site of airway narrowing may be reported:
  - Stridor: if mainly extrathoracic TM. Airway collapses on inspiration.
  - Wheeze, cough, and air trapping if intrathoracic TM/TBM. Airway collapses on expiration
  - Recurrent episodes of respiratory distress
  - Sternal, substernal, and intercostal retractions
  - Spontaneous hyperextension of the neck
  - Poor feeding and failure to thrive
  - Recurrent acute life threatening events, e.g. apnoea, collapse, bradycardia.

Many of these can be brought on by factors that increase the work of breathing e.g. respiratory tract infections or feeding.

Diagnosis and investigations

Differential diagnoses include:

- Poorly controlled control asthma,
- Intra-luminal obstruction e.g. foreign body and acute pulmonary hypertensive crises.

Table 21.11 Investigations

Investigation	Comment
CXR	Bilateral lung hyperinflation or unilateral lung collapse with contralateral lung hyperinflation
Fibreoptic bronchoscopy (spontaneously breathing)	> 50% collapse of luminal diameter
Bronchography High resolution CT	Bronchography and CT exposes child to ionizing radiation, but can be combined with a pressure gauge to determine 'opening' pressures and so guide management
Thoracic MRI	Investigation of choice for extrinsic intrathoracic compression, e.g. aberrant vasculature

Management of TM/TBM

- On PICU: NIV, CPAP/PEEP (10–15cmH_2O) may prevent a degree of tracheal collapse with TM but has little impact if more distal airways are affected (TBM). Sedation reduces active expiration and worsening air trapping. Improvement may take weeks
- Mild to moderate cases: manage conservatively; expectation child will slowly improve by 2 years of age
- Severe: for children who do not recover spontaneously or who have life-threatening symptoms, a variety of treatment options are available:
  - Tracheostomy ± CPAP support
  - Aortopexy
  - Stent placement.

None of these options is ideal and associated with complications particularly in infants. Therapy must be tailored to the individual patient.

Apparent life-threatening events and sudden death in infancy

Acute life-threatening episodes (ALTEs) and sudden death in infancy (SUDI) are associated rarely. The vast majority of children with ALTE will not become a SUDI statistic and the vast majority of SUDIs will not previously have had ALTEs.

ALTEs

- These are episodes of apnoea and turning blue, generally occur in infants <3 months of age
- All children with ALTE should be admitted to hospital for close monitoring and to exclude infection
- Important causes of ALTE include:
  - TBM
  - Gastro-oesphageal reflux

- Epilepsy
- Brain injury
- Congenital heart disease
- Inborn errors of metabolism
- Non-accidental injury.

A child should be investigated only if the clinical scenario and other findings merit specific tests. For isolated ALTE which resolves in hospital the prognosis is very good. However, parents and carers will often need support and reassurance that this is the case.

SUDI

- SUDI is a tragedy. In most cases, it is generally found that the child dies several hours before being noticed by the parents and seen by para-medical and medical personnel. While it is futile to perform any form of resuscitation under these circumstances, in many instances, advanced life support is attempted as staff are unaware of the scenario leading to death
- Investigation for the cause of a SUDI case often begins in the emergency room. However, it is worth noting that pathologists find it very difficult to separate premorbid findings from postmortem injury caused by attempts to obtain bodily fluids and tissue. Thus many clinicians and pathologists now believe that investigations should be left to specialists with experience and expertise in this area. Inexperienced personnel are best advised to contact forensic teams or strictly follow local policies in relation to obtaining post mortem samples of tissue or fluid. This will optimize the chances of determining the cause of death.

Obstructive sleep apnoea syndrome

- Obstructive sleep apnoea (OSA) (syn. obstructive sleep disordered breathing) describes a syndrome where there is recurrent partial or complete upper airway obstruction during sleep. OSA is associated with a number of signs and symptoms:
  - Sleep arousals and awakenings
  - Hypoxaemia
  - Hypoventilation with CO_2 retention
  - Periodic pauses in breathing
  - Daytime somnolence and fatigue
  - Hyperactivity, poor behaviour and school performance
  - Failure to thrive
  - Snoring
- OSA is most commonly found in children who have insufficient muscle tone or a small airway
- It may also be associated with a variety of relatively common chronic disorders e.g. cystic fibrosis, sickle cell disease and left ventricular failure (LVF).

Causes

Table 21.12 Causes of OSA in children

Insufficient central muscle tone	Relatively small upper airway

• Muscular dystrophy
• Down syndrome
• Myasthenia gravis
• Obesity (Prader–Willi)
• Cerebral palsy
	• Adenotonsillar hypertrophy
	• Cranio-facial syndromes:
	  • Pierre Robin sequence
	  • Crouzons
	  • Aperts syndrome
	  • Treacher Collins
	  • Achondroplasia
	• Tissue infiltration:
	  • Mucopolysacchridoses
	  • Hypothyroidism

Manifestations in intensive care

OSA may present problems in the child in ICU in a number of ways:

- Acute LVF and pulmonary oedema following relief of airway obstruction e.g. post adeno-tonsillectomy
- Recurrent episodes of acute respiratory failure e.g. infant with Pierre Robin syndrome
- Acute on chronic respiratory failure, e.g. teenager with Duchenne muscular dystrophy.

Diagnosis

The differential diagnosis is central hypoventilation syndrome (congenital or acquired). Ideally, polysomnography performed by an experienced sleep service should be used to determine whether a child has OSA. Other types of investigations such as overnight saturations are difficult to interpret and should not be used to exclude the diagnosis or start treatment.

Management

Large adenoids and tonsils should be removed if they are the cause for the OSA. Under other circumstances, the choice lies between tracheostomy and non-invasive (NIV) CPAP support. In children with chronic conditions, NIV-CPAP is the treatment of choice. Tracheostomy is reserved for patients in whom non-invasive CPAP support is not feasible e.g. Pierre Robin syndrome or in whom NIV-CPAP fails.

Airway obstruction

Situations of severe airway obstruction are life-threatening events. Call for senior help and anaesthetic and ear, nose, and throat (ENT) assistance. Stay calm but do not let a child become exhausted.

Acute upper airway obstruction

Upper airway obstruction refers to a restriction of airflow at the level of the pharynx, larynx, or trachea. Clinical symptoms, signs or suspicion

of upper airway obstruction must always be regarded as a life-threatening emergency. A rapid assessment of airway patency and, if necessary, an intervention to secure an airway are the primary goals.

Children with acute airway obstruction often present to emergency department in varying degrees of distress. The parents or carers may report any of the following symptoms:
- Choking
- Sudden and dramatic difficulty in breathing, e.g. sternal recession, tracheal tug, stridor, noisy breathing
- Cyanosis
- Panic, confusion, or agitation which often precedes unconsciousness
- Respiratory arrest following a large or total obstruction.

The history of the illness, particularly its onset, generally points to the correct diagnosis which include any of the following:
- Viral and bacterial infections: croup, abscesses, epiglottitis
- Foreign bodies: peanuts, small coins and items which may or may not be radio-opaque
- Allergic reactions: e.g. bee sting, drugs (penicillin)
- Fire or inhalation burns
- Chemical burns and reactions
- Trauma.

Management
- In a child with a precarious airway, be very wary of inspecting the oropharynx using a tongue depressor or any other equipment as this may induce complete airway obstruction
- Rapid assessment of airway patency
- Discuss/inform ENT and anaesthetic team
- CXR (foreign body)
- Rigid ± flexible bronchoscopy (foreign body, burns)
- Laboratory evaluation of blood samples is generally unhelpful in the acute stages and should only be performed once the airway is secured.

Croup (laryngotracheitis/laryngotracheobronchitis)

- A viral respiratory tract infection affecting the larynx, trachea, and uncommonly the major bronchi. Croup is the most frequent cause for acute onset stridor in a child with fever
- Although most common in children under 2 (see 🕮 p.445), it can affect any age group and may be recurrent.
- The parainfluenza viruses (I, II, III) are responsible for as many as 80% of croup cases; other organisms include adenovirus, metapneumovirus, and influenza A and B. *Mycoplasma pneumoniae* has been found in a few cases.

Presentation and diagnosis
- Fever plus:
  - Hoarse voice
  - Barking (croupy) cough
  - Stridor
  - Respiratory distress (variable degree)

- Stridor may be quiet in the severely affected child corresponding to severe airway obstruction (Table 21.13)
- A child with croup does not look toxic
- Croup has a slow onset compared to acute epiglottitis and is not associated with dysphagia
- Other diagnoses to consider if these symptoms and signs are present include:
  - Foreign body aspiration
  - Bacterial tracheitis
  - Epiglottitis
  - Peritonsillar abscess
  - Retropharyngeal abscess
  - Angio-oedema.

Table 21.13 Assessing stridor in croup

	Mild	Moderate	Severe
Cough	Intermittent	Frequent	Frequent
Stridor	Absent at rest	Audible at rest	Prominent
Retractions	Mild/absent	Visible	Conspicuous
Conscious level	Normal	Minimal agitation	Agitated /lethargic
Pulsus paradoxus*	Minimal	Minimal	Easily palpable
Cyanosis	absent	Absent	Evident

* assessed by palpation. Note: lethargy, cyanosis, and decreasing retractions are harbingers of impending respiratory collapse.

Management

Keep child as comfortable as possible, e.g. allow the patient to remain in a parent's arms and avoiding unnecessary painful interventions. Careful monitoring of the heart rate, respiratory rate, level of respiratory distress, and pulse oximetry are important to detect early hypoxia.

- Moderate to severe disease; evaluate airway patency:
  - Child ventilating effectively: give dexamethasone 0.15mg/kg preferably IV/IM or predisolone 1mg/kg and for symptomatic relief, nebulized epinephrine 0.5mL/kg of 0.1mg/mL solution (i.e 1 in 1000) up to maximum 5mL. Repeat in 30min
    Inhaled budesonide is effective as an alternative to dexamethasone
  - Child not ventilating effectively: do not wait for child to become exhausted. Use high-flow (humidified) oxygen via face mask. Call **experienced anaesthetist and ENT surgeon**. Have emergency drugs, anaesthetic machine and tracheostomy kit available. Gas induction is method of intubation
  - Extubate when leak develops around ETT (2–7 days).

Epiglottitis

- Acute epiglottitis has significant morbidity and mortality and may cause respiratory arrest and death due to upper airway obstruction
- Epiglottitis occurs most commonly in children aged 2–7 years and is generally (>90% cases) due to infection with *H. influenzae* type b (Hib). The incidence of epiglottitis has ↓markedly since the introduction of the Hib vaccine. See Table 21.14 for diagnostic features.
- Airway obstruction in epiglottitis is caused by an inflammatory swelling of supra-glottic structures. Swelling of the epiglottis and ary-epiglottic folds leads to airway narrowing and pooling of secretions
- Aspiration of oropharyngeal secretions or mucous plugging can lead to respiratory collapse.

Table 21.14 Diagnostic features of epiglottitis

Clinical history	Clinical findings
• Abrupt onset, rapidly progressive • High fever up to 40°C • Refusal to eat • Muffled or hoarse voice • Sore throat; cough and ear pain are infrequent • Rapidly progressive stridor • Respiratory distress • Dysphagia.	• Child appears toxic • Marked restlessness, irritability, and anxiety • Sits with chin hyper-extended, body leaning forward (to improve air entry) • Mouth; often wide open wide, tongue may protrude • Drooling child (swallowing difficult/painful) • Stridor with moderate supra-sternal, subcostal, and intercostal retractions • Neck examination may reveal tender adenopathy • Cyanosis, which occurs late in the course of the condition, indicates a poor prognosis.

Investigations

- Differential WCC; blood and secretions should be sent for MC&S
- CXR should be performed as a concomitant pneumonia is commonly present

Management

This should be coordinated and provided by a combination of a **senior anaesthetist and ENT surgeon** (see Table 21.15). Once the airway is controlled, a PIC team is required for inpatient management.

Table 21.15 Managing epiglottis

Dos	Don't
• Keep the patient in view at all times • Sit the child on a parent's or relative's lap • Evaluate of 'Airway, Breathing, and Circulation' • Give the child oxygen using a face mask held by parent/relative • Call the 'airway team' = most experienced on-call anaesthetist and ENT surgeon • Bring the Crash Trolley, anaesthetic machine and tracheostomy kit near the patient.	• Increase the anxiety of the child • Feed the child • Examine the child's upper airway unless in theatre with airway team • Perform X-rays • Give antibiotics, non-urgent medications and perform blood or any other investigations until ***after*** the airway is secure • Give any drug via nebulizer (adrenaline, salbutamol or corticosteroids have no role in the management of epiglottis).

Therapy
- Secure airway:
  - Anaesthetist will use gas induction. Preferably with halothane. If using sevoflurane switch to isoflurane before larygoscopy
- Antibiotics: ceftriaxone or cefotaxime
- With invasive Hib infections all household contacts should receive rifampicin chemoprophylaxis
- Systemic corticosteroid therapy is controversial as they have no proven efficacy in this disease
- Extubate when leak on ETT and patient afebrile.

Bacterial tracheitis and retropharyngeal abscess

Bacterial tracheitis (BT)

- Other terms used to describe this condition include bacterial croup, pseudomembranous croup, and laryngotracheobronchitis
- Majority of children are 8 years of age, mean age 4 years
- Commoner in males (2:1)

Bacteriology
- *Streptococcus pneumoniae* most common organism noted now
- *Staphylococcus aureus*
- α-haemolytic *Streptococcus*
- *Haemophilus influenzae* rare because of immunization
- *Moraxella catarrhalis.*

Presentation
- In primary bacterial tracheitis there is an acute onset of upper airway obstruction, fever, and acute decompensation
- In secondary there is a viral prodrome followed by high fever

- Cough and progressive inspiratory stridor and a typical croupy cough
- May initially be diagnosed as croup; however there is poor or no response to nebulized adrenaline commonly seen in viral croup
- There may be a significant respiratory distress but no drooling
- Positioning does not alter the child's condition, comfortable lying flat
- There may be signs of lower airway involvement such as crepitations and wheezes.

Diagnosis

- The diagnosis is usually clinical
- CXR is usually normal, lateral films are not usually helpful
- Inflammatory markers and WCC will be elevated
- Blood cultures are typically negative, but should be taken
- Diagnosis is usually made by visualizing the supraglottic structures
- Presence of oedema and tenacious secretions is confirmatory of BT
- Culture of tracheal secretions will support the diagnosis.

Management

- Intubation may be necessary. *Senior* help as in croup/epiglottitis
- Indications for urgent intubation and ventilation:
  - Exhaustion (do not wait for this to happen)
  - Marked retraction, poor air entry, poor or absent breath sounds
  - Marked tachycardia
- Following intubation copious purulent secretions will need to be sucked out regularly and high humidification will be necessary
- Tracheal lavage may be required with flexible bronchoscope to remove secretions and membranous films.

Antibiotics

- High-dose IV penicillin is the antibiotic of 1st choice for 1–2 weeks
- Once the sensitivities are available, the antibiotics may be changed
- Complications include:
  - Prolonged ventilation
  - Tracheostomy
  - Systemic sepsis may develop (see 📖 p.569).

Retropharyngeal abscess

- Retropharyngeal abscess is a deep neck infection involving the connective tissue and lymphatics
- The infection is secondary to an URTI or following a penetrating injury of the oropharynx following trauma
- Infection of this space will lead to obstruction of the airway and the upper GI tract. The former is life threatening as it will rapidly produce airway blockage and death
- Majority of children are <6 years of age
- Half of them will present in the 1st year of life
- Commoner in males
- Group A streptococci is the commonest organism. Other organisms include *Staphylococcus*, anaerobes, and *Haemophilus* species

Clinical features
- A URTI
- Fever
- Intense dysphagia
- Drooling
- Odynophagia
- Some respiratory distress, mild stridor, and tachypnoea
- Unwillingness to move neck, holding neck stiffly and even torticollis
- If the oropharynx is examined, it should be done in the operating theatre in a controlled environment so that adequate airway control is maintained
- Examination may reveal a mass, however this is a difficult to feel in an infant
- Be gentle! It is imperative that the abscess does not rupture and empty its contents into the upper airway.

Complications
- Aspiration of abscess contents leading to aspiration pneumonia
- Spread of the infection into the adjacent body of the vertebrae producing osteomyelitis
- The sheath involving the carotid artery sheath may also be involved
- Necrotizing fasciitis.

Investigations
- Retropharyngeal thickening is seen in >80% of cases on lateral neck X-ray
- A CT scan of the neck is helpful in differentiating an abscess from cellulitis as well as demonstrating extension of the abscess into the contiguous spaces.

Treatment
- Retropharyngeal abscess is a life-threatening condition and all children should be admitted to PICU for monitoring and management
- If there is any respiratory compromise, the child should be intubated and surgical drainage performed
- Antibiotic therapy should be initiated in all patients once the diagnosis is suspected. 1–2 weeks
- The antibiotics of choice are either co-amoxyclav or clindamycin.

Sequelae of intubation

- Laryngeal oedema
- Granulomas are common in long-term intubated patients but are also seen after short periods of intubation particularly after septic shock. They have been described following surgery
- Sub-glottic and tracheal stenosis are particularly common in preterm infants
- Vocal cord paralysis can be bilateral or unilateral which be due to nerve injury or due to mechanical injury of the vocal cords. The paralysis usually resolves spontaneously over months.

Congenital lung abnormalities

Congenital tracheal stenosis

Patterns of tracheal stenosis

- 4 different anatomic patterns have been described:
  - Short segment stenosis of the upper (subglottic) airway
  - Progressive narrowing (carrot-shaped)
  - Intermediate length (hourglass), common in Down syndrome
  - Distal segmental (funnel-shaped).

Clinical features

- Hourglass type often asymptomatic—detected during cardiac surgery
- Mild—1–3months, respiratory difficulty with URTI
- Stridor (biphasic), cyanosis, feeding difficulty, noisy breathing
- Multiple episodes of croup, failure of medical treatment
- Difficulty in passing suction catheter.

Investigations

- Plain CXR: air bronchogram, barium swallow, arteriogram—need to rule out other causes, e.g. oesophageal pouch, vascular ring
- Chest CT/ spiral CT/MRI: sedation may further compromise the airway
- Tracheobronchograms : with non-ionic contrast media
- Bronchoscopy with direct visualization and dynamic assessment, it will also allow evaluation of any intra/extraluminal compression.

Treatment

- In mild stenosis there is a need to treat any URTI aggressively with antibiotics
- Short segment narrowing will require either balloon dilatation or stent placement. If this fails resection and end-to-end may be required
- Long segment narrowing will need anterior and/or posterior wall division with autologous tissue grafts using pericardium, costal cartilage. Slide tracheoplasty may be required.

Pulmonary sequestration

- Mass of non-functioning lung tissue separated from the normal broncho-pulmonary tree and vascularized by an aberrant systemic artery
- 0.15–6.45% of all pulmonary malformations; 2 variants are present, extralobar sequestration (ELS) and intralobar sequestration (ILS).
- ELS has its own pleural lining whilst ILS has no separate pleura.

See Table 21.16.

Table 21.16 Problems and complications of lung sequestration

Problems	• Recurrent pulmonary infections secondary to fistula between the sequestration and the airway or GI tract	• Usually asymptomatic • Usually found on CXR as mass
Complications	• Systemic: chills, fever, weight loss • Respiratory: cough, haemoptysis, haemothorax, pleural effusion, pyoptysis, abscess	• Rare • Usually asymptomatic • Abscess/ TB/GI tract communications necessary for infections

Investigations and management

- CXR, bronchography and MRI/CT with angiography to delineate the vascular supply
- Antibiotics to treat chest infection but surgery is usually required
- Indications for surgery are severe symptoms, recurrent chest infections, failure to thrive, dysphagia, and respiratory distress

Congenital cystic adenomatoid malformation (CCAM)

- 50% present with severe respiratory distress in the newborn period
- The rest will present beyond the neonatal period with recurrent pneumonias
- It occurs with equally in the right and left lungs and in any lobe but more so in the lower lobes
- 3 types have been described:
  - Macrocystic—associated with best prognosis
  - Microcystic
  - Solid—often stillborn or early neonatal death.

Further reading

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Chapter 22

Neurocritical care

Acute neurology

The field of acute neurology in intensive care holds an important place in the historical development of paediatric critical care. Polio, Reye's syndrome and head trauma management, for example, have shaped our present practice of emergency support and interventions.

Clinical history and examination

Presenting history

The presenting pattern of illness often provides clues to the diagnosis.

- ***Acute central deterioration*** is associated with:
  - Metabolic disturbance
  - Ingestions and poisoning
  - Cerebrovascular accidents
  - Trauma
- ***Cerebral deterioration*** over days or weeks is more compatible with:
  - Infection
  - Chronic intoxication
  - More slowly developing raised ICP
- ***Focal neurological abnormalities*** before central disturbance suggests:
  - Cerebrovascular disease
  - Intracranial mass
  - Focal encephalitis.

Past medical history may provide vital clues of recurrent disorders:

- Seizures
- Migraine
- Sickle-cell disease.

Family history of epilepsy or TB may be discovered, or the report of previous stillbirths or deaths in infancy may indicate inherited metabolic disease.

Social history may suggest non-accidental or inflicted injury, lead poisoning, brucellosis, or the family may recently have arrived from the tropics, introducing the possibility of a wide variety of intracranial infectious pathology.

General examination

- After initial resuscitation, a focused assessment is needed
- The ***size and weight*** of the child might indicate failure to thrive, suggesting a long-standing metabolic disease, or emotional deprivation
- ***Check for breath odours***—these might suggest DKA, solvent abuse, or one of the rare aminoacidopathies
- ***Inspect skin and scalp***
  - For bruises, abrasions or evidence of inflicted trauma
  - Examine the mouth for trauma or a torn frenulum
  - Examination of the skin might suggest a neurocutaneous disorder (e.g. neurofibromatosis, tuberous sclerosis) or sepsis, (e.g. minor abrasion leading to staphylococcal toxic shock, the petechial haemorrhages of meningococcaemia and, where prevalent, rickettsial disease)

  - Bleeding into the skin or from any of the orifices might suggest a bleeding diathesis
- ***Head examination***, particularly in infants and young children.
  - Fontanelles and sutures should be palpated
  - Listen for bruits
  - Head circumference should be measured and recorded. Comparison with earlier records should be made, if possible
  - Ventricular shunt or reservoir in situ: assess ventricular CSF pressure if the child is obtunded
  - Look for signs of meningeal irritation: these may be absent in the very young infant or in the critically ill child, even in the presence of subarachnoid haemorrhage or meningitis
- ***Nose, mouth, pharynx, and external auditory meati*** might demonstrate abnormalities such as CSF rhinorrhoea or otorrhoea
- ***Lumbosacral region and spine:*** for evidence for spinal dysraphism:
  - Meningocele
  - Myelomeningocele
  - Spina bifida occulta
  - Skin dimple, pit, sinus, local patch of hair, naevolipoma
- Also look for signs of raised ICP (see Box 22.1).

Box 22.1 General signs of raised ICP

- Reduced conscious level
- Abnormal respiratory pattern
- Unequal or unreactive pupils
- Impaired or absent oculocephalic or oculovestibular responses
- Systemic hypertension, bradycardia
- Tense fontanelle
- Abnormal body posture or muscle flaccidity.

Disorders of breathing

Cheyne–Stokes (alternating apnoea and hyperpnoea) can be seen with metabolic disturbance, bilateral cerebral hemisphere dysfunction, and insipient temporal lobe herniation.

Central neurogenic hyperventilation (deep rapid respiration) can occur with hypoxia-ischaemia, hypoglycaemia, or lesion between low midbrain and midpons. In traumatic brain injury it may be caused by damage in the rostral brainstem or tegmentum.

Post-hyperventilation apnoea may indicate forebrain damage.

Ataxic respiration (irregular depth and rate) can be caused by abnormality of the medulla and impending respiratory arrest.

Apneustic breathing (gasping, respiratory arrest in inspiration) indicates pontine involvement.

Synchrony and strength of chest and abdomen during breathing should also be assessed:

- Paradoxical movement or posturing with preference for particular side may suggest diaphragmatic weakness

- In those receiving ventilatory assistance, the work of breathing with different levels of ventilatory support is a helpful guide to overall muscle strength.

Temperature should be measured and recorded.

- ***Hyperpyrexia*** may be central in origin, but is most likely to be due to infection or dysautonomia (only after excluding infection)
- ***Hypothermia*** may result from shock, hypothalamic disturbance or inadequate measures for warming, possibly during transfer.

Circulation

- ***Pulse, BP*** should be measured and recorded
- ***BP*** changes are frequent in neurological illness:
  - Hypertension may be a cause or consequence of acute neurology
  - Hypertension and/or bradycardia may be a result of ↑ICP
  - Hypotension may be due to shock or central/spinal causes
- ***Palpate major vessels*** and auscultate them, especially over the neck, for a bruit which may indicate arterial stenosis.

Eye examination

Ocular responses

- Position of the eyes at rest: note any deviation (conjugate or dysconjugate) or any spontaneous eye movements such as roving eye movements or nystagmus
- Corneal reflex: its absence relates to the depth of coma
- Ocular motility: assess the 'doll's eye manoeuvre' (see Box 22.2).

Box 22.2 Brain stem reflexes

Only test if the neck is stable and the patient is comatose.

(See 🕮 p.725.)

Oculocephalic reflex (Doll's eye manoeuvre):

- Make sure that the neck is stable and is cleared of injury
- Hold the child's eyelids open and briskly rotate the head first to one side and then the other
- Positive response: full conjugate eye deviation to the ***opposite*** side (i.e. if the head is rotated to the right, the eyes deviate to the left). This indicates an intact pathway in the brain stem
- Vertical eye movements: test by briskly flexing and extending the neck. Positive response is observed when the eyes deviate upward with neck flexion and downward with neck extension.

Oculovestibular response (calorics):

- Make sure that the child is in deep coma; (the test will cause discomfort and lead to distress and vomiting if conscious)
- Ensure that the tympanic membranes are intact before starting to instil up to 60mL of iced saline
- Normal response: conjugate deviation of the eyes to the side of irrigation.

Pupils

- Pupillary size at rest and in response to light should be assessed
- The light reflex consists of an afferent pathway through the optic nerve and an efferent pathway involving both sympathetic and parasympathetic fibres
- Transtentorial herniation causes compression of the parasympathetic fibres along the 3rd cranial nerve (CN III) and results in ipsilateral pupillary dilation with no response to direct or consensual stimulation
- If not due to medication or poisoning, bilateral unresponsive dilated pupils reflect bilaterally compressed CN III or severe cerebral hypoxia-ischemia.

Pupillary size at rest:

- Pin-point pupils due to pontine lesions are uncommon in comatose children
- Consider poisoning with opiates, phenothiazines, alcohol, barbiturates, or sodium valproate when miotic (constricted) pupils are present
- Ipsilateral pupillary constriction associated with ptosis and anhidrosis (i.e., Horner's syndrome) may be an early sign of transtentorial herniation or damage to the hypothalamus with interruption of sympathetic pathways.

Pupillary responses and the corneal reflex

- Correlate with the severity of coma
- Impaired extra-ocular movements and preserved pupillary reflexes occur in disorders of neuromuscular transmission
- Toxic levels of phenytoin may be associated with ophthalmoplegia
- Asymmetrically reacting pupils: no specific diagnostic importance unless unilateral fixed dilated pupil (see Box 22.3).

Box 22.3 Unilateral dilated pupil

- Unilateral pupil dilation unreactive to direct stimulation but consensually reactive is caused by absent light perception in that eye or a problem with the afferent limb of the reflex (optic nerve or tracts)
- Fixed dilated pupil requires urgent intervention. Its presence strongly suggests transtentorial herniation
- If unexplained unilateral (or bilateral) fixed and dilated pupil(s) is present consider as causes topical or systemic administration of anticholinergics or sympathomimetic drugs, or the presence of an eye prosthesis!

Fundoscopy

The fundi need careful examination and this is best left until other ocular signs and responses have been documented.

- On occasions adequate fundal examination may only be achieved by the use of short-acting mydriatrics: record this in the notes and label the patient—don't be caught out by iatrogenic fixed and dilated pupils!
- Retinal haemorrhages: if present suspect other intracranial haemorrhages and the possibility of inflicted traumatic brain injury. Request ophthalmologist to perform formal examination

- Papilloedema:
  - Single most reliable sign of intracranial hypertension
  - ⚠ Rarely seen in the first 24–48h of acute elevations in ICP
  - Its absence should not lull you into a false sense of security
- Papillitis is difficult to distinguish from papilloedema. It is sometimes seen in encephalitis (especially that due to varicella and mycoplasma).

Neuromuscular examination

Examination of the peripheral nervous system and muscle strength and tone is essential in the assessment of the weak or unconscious child.

Head and neck

- Note any asymmetry of the face
- In the comatose child, use firm supraorbital or suprasternal pressure to assess power/response in the facial distribution
- Elicit and assess the gag reflex
- Look at the tongue for wasting and fasciculation.

Limbs

- Focal weakness or laterality usually implies a structural lesion
- May rarely result from a metabolic disorder
- Look for wasting of muscle groups, particularly the small muscles of the hand—may suggest critical illness polyneuropathy.

Power

Know the commonly used 5-point scale for describing power (Box 22.4).

Box 22.4 5-point scale

0 = no contraction
1 = flicker or trace of contraction
2 = active movement with gravity eliminated
3 = active movement against gravity
4 = active movement against gravity and resistance
5 = normal strength.

Tone

- Assess all 4 limbs
- Extensor hypertonus should be closely looked for, since such spasms may be unilateral or bilateral, occur spontaneously, or occur only after stimulation.

Extensor hypertonus: the lower limbs are extended, with internal rotation and, often, plantar flexion and scissoring.

Decorticate rigidity: the arms are flexed across the chest—in general, decorticate posturing is associated with cortical or hemisphere dysfunction.

Decerebrate rigidity: the elbows are extended—

- May result from structural lesions or metabolic dysfunction. Often associated with a rise in ICP
- The brain stem is often damaged in children whose upper limb movements show decerebrate patterns.Abnormal movements
- Extrapyramidal signs such as dystonia (distorted posture of the limbs and trunk resulting from excessive muscular tone) may occur in both

the conscious and unconscious child and should suggest the possibility of drug toxicity (e.g. phenothiazine poisoning)
- Repetitive or rhythmic movements may suggest seizure activity
- Look for obvious generalized tonic–clonic episodes or myoclonic jerks which are usually easily identified
- Subtle seizure-related phenomena in infants, such as chewing movements and cyanosis from chest rigidity, are less readily recognized.

Deep tendon reflexes
- Use a peripheral nerve stimulator to check that the peripheral nervous system is intact and not pharmacologically blocked
- Areflexia and flaccidity in the unconscious child is a grave sign. Exclude generalized peripheral neuropathy and muscle relaxant use
- Asymmetric reflexes may be helpful in lateralizing any injury
- Bilateral ↑ reflexes may be due to traumatic brain or spinal cord injury.

Clonus: rapid sustained dorsiflexion of the ankle should be performed by pushing up on the sole of the foot:
- Clonus involves a sustained rhythmical muscle contraction felt against the palm of the hand pushing up on the sole of the foot. It reflects hypertonia.

Plantar (Babinski) reflex: Stroke the lateral aspect of the sole of the foot from back to front with a firm object. Normal response is a downward movement of the great toe (flexor plantar response).
- A positive Babinski reflex (extensor plantar response) occurs when there is dorsiflexion of the great toe, typically with fanning out of the other toes:
  - Seen with corticospinal tract damage (intracranial or spinal cord)
  - May be observed during sleep and deep coma of any cause
  - Often present for a short time after a generalized convulsion
  - Usually present in normal infants when corticospinal tract fibres are incompletely developed.

Glasgow coma scale (GCS) score

The GCS should be used as a summary of conscious state. It is a useful tool for monitoring change. A number of modified versions of the GCS have been developed for use in infants and children (see Tables 22.1 and 22.2).

Table 22.1 GCS scoring in infants

	Response	Score
Eye opening (E)	• Spontaneous	4
	• To speech	3
	• To pain	2
	• None	1
Best verbal (V)	• Coos and babbles	5
	• Irritable cries	4
	• Cries to pain	3
	• Moans to pain	2
	• None	1

(*Continued*)

Table 22.1 GCS scoring in infants (*Continued*)

	Response	Score
Best motor (M)	• Normal	6
	• Withdraws to touch	5
	• Withdraws to pain	4
	• Abnormal flexion	3
	• Abnormal extension	2
	• None	1

Table 22.2 GCS scoring in children

	Response	Score
Eye opening (E)	• Spontaneous	4
	• To verbal stimuli	3
	• To pain	2
	• None	1
Best verbal (V)	• Oriented	5
	• Confused speech	4
	• Inappropriate words	3
	• Non-specific sounds	2
	• None	1
Best motor (M)	• Follows commands	6
	• Localizes pain	5
	• Withdraws to pain	4
	• Flexes to pain	3
	• Extends to pain	2
	• None	1

A score ≤8 is used as a criterion for endotracheal intubation in the head-injured child, in whom severe injury is defined as GCS ≤8, moderate injury GCS 9–12, and mild injury GCS 13–15.

The motor component of the score is the most discriminatory component with which to assess depth of coma.

AVPU scale

An abbreviated scale to assess conscious state has been developed in relation to making a quick assessment in the emergency situation. This has been popularized by the Life Support Courses.

- It is a 4-point scale
- It provides a 'quick and dirty' initial assessment
- It should ***NOT*** be seen as an alternative to the Glasgow Coma Scale
- Any child with a score below 'A' should have a GCS score carried out

- A= ***A***lert
- V= Responds to ***V***oice
- P= Responds to ***P***ain
- U= ***U***nresponsive to painful stimulus.

Neurological investigations

The initial investigation of the child with an acute neurological problem falls into 2 broad categories:
- Diagnostic investigations
- Supportive investigations: i.e. those that may provide information about optimum supportive therapy during the child's illness.

Investigations must be tailored to the individual child's history and examination. As a general rule, the following investigations should be carried out on admission:
- Blood gas
- Point of care glucose measurement (glucometer)
- Blood glucose, U&Es, and serum osmolality
- Liver function tests, FBC, assessment of coagulation
- Blood culture, CRP.

Lumbar puncture (LP)

Bacterial meningitis is an important cause of childhood mortality:
- Traditional teaching was to undertake an LP if there was the slightest suspicion of meningitis
- However there have been a number of reports of brain herniation following LP in children with meningitis
- It is difficult to predict which children are at particular risk of tentorial herniation
- If the child has been ill for several days or certain features are present (Box 22.5) it is advisable to treat with antibiotics and postpone obtaining confirmatory spinal fluid findings.

Box 22.5 Relative contraindications to LP in the comatose child

Impaired consciousness and signs of:
- Raised ICP or cerebral oedema
- Focal neurology or space-occupying lesion on CT
- Incipient 'coning' (e.g. pupillary changes)
- Unstable BP and HR
- Infection of the skin at the proposed LP site
- Evidence of coagulopathy
- Acute meningococcal disease before adequate stabilization.

Characteristic LP findings in a number of neurological conditions are summarized on 🕮 p.552.

Cranial imaging

(See also 🕮 Chapter 19.)

Cranial imaging studies are indicated when the initial biochemical studies have failed to clarify the diagnosis, or if a structural lesion is suspected.

Cerebral US scan: for detecting major intracranial abnormalities in young infants, particularly intraventricular haemorrhage and hydrocephalus.

Not as sensitive as cranial CT scan in detecting smaller (but still clinically significant) lesions such as focal infarcts, small parenchymal haemorrhages, subdural collections, or features of diffuse hypoxic ischaemic injury.

Cranial CT scan

In the comatose patient, emergency CT scan is particularly useful for:

- Identifying pathology needing urgent surgery (e.g. space-occupying lesion, acute hydrocephalus)
- Evaluating the presence of cerebral oedema and likely ↑ICP:
  - The latter is assessed by reviewing the presence or absence of CSF spaces both above and below the tentorium
  - Loss of spaces below the tentorium (i.e., the basal cisterns) is indicative of severe swelling
  - *CT scan is not a reliable investigation to identify or exclude ↑ICP.*

MRI

MRI has advantages over CT scan:

- Lack of ionizing radiation
- Greater sensitivity to changes due to blood flow, oedema, haemorrhage, and myelination
- Easier differentiation between grey and white matter
- Better anatomy of posterior fossa lesions
- Ability to discriminate cytotoxic from vasogenic oedema
- Possibility of combining with magnetic resonance spectroscopy (MRS) to measure brain metabolites.

Neurophysiology

Electroencephalography (EEG)

EEG assessment is particularly useful when clinical evaluation is unreliable because of treatment with sedatives, hypnotics, or muscle relaxants. During the acute phase of illness it may provide information about the severity and distribution of altered cerebral function of the cortex, presence of discharges (seizure activity), and even a clue to diagnosis.

EEG during an acute encephalopathic process usually shows varying degrees of slow activity. The relationship between increasing severity of encephalopathy and worsening EEG changes can be graded as:

- Normal for age
- Borderline normal for age
- Abnormal for age: graded according to frequency and amplitude of slow activity (as patients deteriorate, predominant EEG activity becomes slower—4–6 cycles/s to 0.5–2 cycles/s—and of lower amplitude, <μV, then intermittent)
- Suppression-burst pattern—alternating periods of activity and suppression/silence
- Electrocerebral silence—no discernible electrical activity.

Continuous EEG is particularly useful in intensive care:
- To detect events occurring intermittently such as seizure activity
- To determine if abnormal movements are related to EEG abnormality
- To titrate barbiturate therapy to a target level of brain suppression.

Simplified systems have been developed that either incorporate fewer EEG leads, or utilize standard monitoring leads but produce summary readouts that enable interpretation by intensive care staff. These are sometimes referred to as cerebral function analysis monitors (CFAM).

Evoked potential studies

These are used in a similar manner to EEG, for assessing the severity of brain injury in global insults as well as the potential cumulative detrimental effects of secondary cerebral injury.

The range of studies, with examples, includes:
- Brainstem evoked potentials—auditory EPs
- Sensory evoked potentials—somatosensory (SSEPs)
- Motor evoked potentials—rarely used in intensive care.

SSEPs have been shown to be useful in predicting prognosis after diffuse brain injury. They are produced by stimulation of the upper limb in the median nerve territory and recording of electrical transmission at both the cervical spinal cord level (Erb's point) and over the contralateral cerebral hemisphere.

Bilateral absence of a cortical SSEP response on 2 occasions following traumatic or hypoxic-ischaemic brain injury is associated with death or severe disability (>98% positive predictive value)

⚠ The presence of a subdural collection, a focal brain lesion or recent decompressive craniectomy may occasionally create false positives.

General neurocritical care practice

The intensivist is frequently involved in emergency department care, or in interhospital transfer to the PICU or CT scanner. On first seeing the patient make sure that the ABCs of resuscitation are dealt with. Specific factors worth considering at an early stage of assessment and admission are as follows:

Airway and breathing (Box 22.6)

- Respiratory failure can be a major cause of morbidity and death in the acute phase of brain injury
- Patients can present with respiratory impairment secondary to loss of airway protective reflexes, muscular weakness, and alteration in the ventilatory drive or signs of aspiration
- Rapid assessment of airway patency and reflexes, respiratory effort, and gas exchange is essential
- Oxygen must be delivered at high flows via a face-mask during the initial assessment.

Box 22.6 Respiratory care

Indications for endotracheal intubation
- ↓level of consciousness (GCS <9)
- Deteriorating level of consciousness
- Signs of ↑ICP
- Loss of airway protection reflexes
- Hypoxaemia
- Hypoventilation
- Shock.

Endotracheal intubation
- Should only be attempted by a skilled operator
- Avoid delays that could precipitate hypoxaemia or increase ICP, and consequently worsen brain injury
- Use rapid sequence induction (RSI) in all patients.

Initial targets with mechanical ventilation
- Avoid hypoxaemia
- Achieve normocapnia
- Use standard doses of analgesics, sedatives and neuromuscular blocking agents.

Tracheostomy
- Long term endotracheal intubation may be necessary
- Indications for tracheostomy vary, but it should be considered in all patients receiving prolonged ventilation.

Fluid therapy

Close control of serum sodium concentration and plasma osmolarity is essential.
- Both SIADH and cerebral salt wasting can occur in brain injury—both will result in hyponatraemia but their management is very different (see 🕮 p.685).

Excessive fluid administration, especially when hypotonic, may exacerbate brain oedema; however, fluid restriction per se has not been shown to improve outcome in general neurocritical care. A drawback of fluid restriction is loss of intravascular volume, lowering of arterial pressure and consequent lowering of cerebral perfusion pressure. The type of fluid to be administered may vary with age:
- **Infants: glucose containing normal (0.9%) saline**
- **Older children: isotonic saline fluid.**

Monitoring
- Close control of fluid balance
- Frequent serum electrolyte measurements (minimum 12-hourly)
- Haemodynamic monitoring to ensure normovolaemia
- Blood glucose levels should be monitored closely in severely ill patients:
  - Hypoglycaemia may be present in the acute phase, especially in neonates, and it can further complicate the neurological condition
  - Hyperglycaemia may be present as a response to stress; it is associated (not necessarily in a causative way) with worse neurological outcome in traumatic brain injury

- Tight glycaemic control (insulin to maintain blood glucose 4–7mmol/L) is not recommended.

Nutrition

Nutrition should be started as soon as possible. Ideally the enteral route should be used within 24–48h of admission. A NG tube should not be used in the head-injured patient; use an orogastric tube. Gastroparesis is common in patients with acute brain injury; consider prokinetic agents or post-pyloric feeding early on. If the enteral route is not tolerated parenteral nutrition should be considered.

Acute brain injury

The brain can be injured in many ways (Box 22.7). Its responses to injury, however, are uniform and include any combination of:

- Altered level of consciousness
- Change in behaviour
- Seizures
- Respiratory dysfunction
- Loss of autoregulation
- Cerebral swelling and raised ICP
- Syndrome of inappropriate antidiuretic hormone secretion.

In generalized insults these features fall into one of the following 4 categories:

Generalized depression of cerebral hemisphere function

- Consciousness is depressed
- Motor tone becomes diminished
- Pupils are small but reactive
- Reflex eye movements are prominent
- Asterixis (palmar 'flapping tremor'), one of the hallmarks of metabolic and hepatic encephalopathy, may relate to intermittent depression of motor function.

Heightened excitability of neural tissue

- Results from direct lowering of the threshold for neuronal excitability or because of a selective depression of inhibitory influences on neuronal function
- Cheyne–Stokes respiration may result from bilateral hemispheric inhibition
- Seizures may result from excitability.

Selective vulnerability

- Focal involvement of a specific brain region to a systemic metabolic insult.
  - This may be due to regional differences in tissue metabolic requirements for oxygen, glucose, or amino acids or, alternatively, regional differences in neurotransmitters and receptors
- It is not uncommon for focal findings to remain unexplained e.g. those occurring during hypoglycaemia, hyperglycaemia, uraemia, and hypercalcaemia.

Progressive deterioration

- Features and signs indicative of raised ICP and central syndrome
- Brain tissue shifts and herniation
- Cytotoxic cerebral oedema.

Box 22.7 Causes of brain injury

Infection and inflammatory conditions

- Meningitis and encephalitis
- Toxic shock
- Subdural empyema and cerebral abscess
- Toxins.

Poisoning

Neoplasm

- Brain tumours.

Trauma

- Head injury: concussion or contusion
- Haemorrhage: epidural, subdural, parenchymal.

Vascular causes

- AV malformation
- Cerebrovascular stroke and aneurysm
- Venous thrombosis.

Metabolic causes

- Hypoglycaemia
- DKA
- Electrolyte abnormalities
- Inborn errors of metabolism
- Hepatic encephalopathy
- Hormonal abnormalities: thyroid, adrenal, pituitary
- Uraemic encephalopathy.

Other

- Hypothermia or hyperthermia
- Seizures and postictal state
- Hypertension
- Hydrocephalus
- Hypoxia-ischaemia
- Sepsis
- Perioperative cardiac surgery.

Raised intracranial pressure

In the absence of an intracranial space-occupying lesion or hydrocephalus, raised ICP can result from:

- ↑venous pressure (as in dural sinus thrombosis)
- ↑resistance of arachnoid villi to resorption of CSF (in meningeal inflammation)
- Hypersecretion of CSF (in certain endocrine abnormalities)
- Cerebral oedema due to toxins, infection, ischaemia, or trauma.

Cerebral oedema

Cerebral oedema is defined as an increase in brain volume due to an increase in its water content.

- Localized oedema may merely result in altered cerebral function with no change in brain tissue and fluid dynamics
- CT scanning may show diffuse or localized low attenuation as a result of high water content
- T2-weighted MRI will show an intense signal.

The forms of cerebral oedema are:

Vasogenic oedema

- ↑cerebral capillary endothelial permeability resulting in an exudate of proteinaceous fluid in surrounding cerebral white matter
- Focal or global cerebral oedema will be determined by the cause of change in cerebral vascular permeability (e.g. infection, trauma, toxins, focal seizures, and hypertension).

Cytotoxic oedema

- Brain cells undergo rapid swelling as a result of membrane ionic pump failure secondary to intracellular energy failure
- May be due to hypoxic-ischaemic insult, severe infection, toxins, status epilepticus, and low cerebral blood flow.

Hypo-osmotic oedema

- Osmotic dysequilibrium between a low osmolality plasma compartment and higher osmotic pressure within glial cells will result in astrocytic water accumulation, and brain tissue oedema
- May occur with hyponatraemia, excessive fluid resuscitation for DKA, and dialysis dysequilibrium syndrome.

Interstitial oedema

- In patients with raised ICP and hydrocephalus, periventricular interstitial oedema may occur
- Caused by transependymal resorption of CSF into the extracellular space.

Hydrostatic oedema

- ↑intravascular pressure is transmitted to the capillary bed with the net efflux of water into the extracellular space
- Seen in states of deranged autoregulation, as occurs in malignant hypertension.

Meningitis and ICP monitoring (see also 📖 p.95 for intracranial pressure monitoring)

Some centres recommend monitoring and aggressive management of ICP because:

- Death in meningitis is usually associated with ↑ICP
- ICP cannot reliably be estimated non-invasively—neuroimaging (CT/MRI) does not reliably identify ↑ICP
- Bacterial meningitis results in loss of cerebral autoregulation—estimates of cerebral perfusion pressure require knowledge of ICP
- ICP therapies have been shown to lower ICP
- Insertion of an external ventricular drain can be used both to measure ICP and to treat raised ICP by draining CSF
- Drainage of CSF is highly effective at lowering ICP as a result of the relative 'hydrocephalus' that results from impaired CSF reabsorption.

However there is currently no evidence to support this approach.

Clinical features at various stages of raised ICP

Transtentorial herniation

Many of the clinical signs observed are secondary to direct compression of structures or due to angulation of nerves or arteries against normal structures in the area.

Herniation can cause increasing coma, with distortion of the brainstem leading to midbrain and pontine haemorrhages, midbrain or medullary compression, and death. Signs include:

- ↑BP, ↓ or ↑ in pulse, irregularity in respiratory rhythm
- Temperature irregularities and diabetes insipidus may develop
- Episodes of decerebrate rigidity
- Eventually cardiorespiratory arrest.

Unilateral herniation occurs when intracranial hypertension is more marked in the supratentorial compartment, e.g. acute intracranial haematoma with the affected side displaced into the tentorial notch:

- Uncal herniation: occurs when unilateral transtentorial herniation is more marked anteriorly. (Posterior hippocampal herniation may also occur.)
- Clinical manifestations of uncal herniation include: respiratory irregularities and ultimately cardiorespiratory arrest; ipsilateral CN III palsy, contralateral hemiparesis, deepening coma with decerebrate posturing.

Cerebellar herniation occurs when the increase in ICP is maximal in the posterior fossa. Such herniation occurs more commonly downwards, squeezing one or both of the cerebellar tonsils through the foramen magnum, compressing the medulla and leading to:

- Respiratory irregularities or sudden cardiorespiratory arrest
- Neck stiffness and head tilt; lower CN palsies
- Upward herniation of the cerebellum through the tentorial notch, causing midbrain compression leading to paralysis of upward gaze, dilated and/or fixed pupils and respiratory abnormalities.

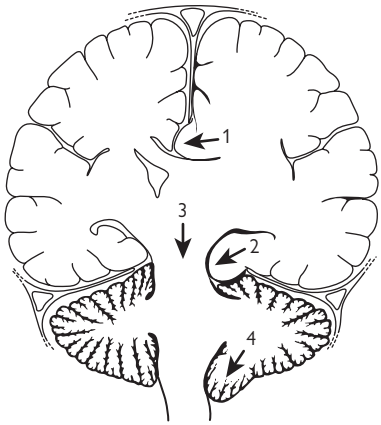


Fig. 22.1 Patterns of brain herniation. (1) Cingulate herniation under the falx. (2) Uncal herniation through the tentorial incisura. (3) Central transtentorial herniation through the incisural notch. (4) Cerebellar tonsillar herniation through the foramen magnum. Reproduced with permission from Wilkins RH and Rengachary SS (eds). *Neurosurgery*, 2nd edn, volume 1, © McGraw-Hill.

Seizures and status epilepticus

Status epilepticus (SE) is a prolonged seizure that lasts >30min, or recurrent seizures during which the patient does not regain consciousness within a 30-min period. The success of treatment depends on prompt recognition and treatment.

Status epilepticus is classified as convulsive or non-convulsive. Non-convulsive status epilepticus (NCSE), also known as sub-clinical status epilepticus, is diagnosed with EEG, and should be considered in the comatose patient. The common causes and initial investigations are shown in Box 22.8.

Convulsive status epilepticus (CSE)

Generalized CSE

- Episodes may be tonic–clonic, clonic, or tonic in character
- Often starts with a series of seizures in known epileptics
- In between seizures there may be coma, dysautonomia, cyanosis, and hypotension.

Clonic SE

- Episodes may persist for hours
- Seizures are predominantly unilateral, but may alternate between sides
- Consciousness may be normal
- Post-ictal hemiplegia may occur.

Tonic SE
- Less common than tonic–clonic or clonic SE
- Seen in children and adolescents with known epilepsy
- Duration of tonic SE may be much longer than that of other types of CSE.

Focal motor SE
- May be seen in children with acute brain injury or epilepsy.

Myoclonic SE
- Characterized by repeated myoclonic jerks
- Most commonly due to hypoxic-ischemic encephalopathy
- Other causes: hypoglycaemia, hepatorenal failure, heavy metal intoxication.

NCSE

NCSE should be considered in children with prolonged post-ictal state or unexplained alterations in consciousness.

The features of NCSE are:
- Alteration in level of consciousness >30min or complex partial seizures without full recovery of consciousness
- Epileptiform discharges on EEG
- Clinical and EEG response to IV anticonvulsants.

Box 22.8 Common causes and initial investigations

The common causes of childhood seizures include:
- Fever
- Epilepsy
  - 1st presentation
  - Difficult seizure control
  - Subtherapeutic anticonvulsant levels
- CNS infections
- Trauma
- Poisoning
- Metabolic abnormalities.

After emergency therapies, useful diagnostic tests include:
- Brain imaging: CT, MRI
- EEG
- LP
- Blood: magnesium, electrolytes, calcium, glucose, and creatinine
- Blood gas
- Toxicology: blood and urine
- Metabolic investigations: ammonia
- Anticonvulsant levels in those on anticonvulsants
- FBC and white blood cell differential.

Initial treatment of status epilepticus

Anticonvulsant treatment is needed in a timely manner (Box 22.9). At any stage, if there is significant respiratory compromise, proceed to intubation and support breathing.

Box 22.9 Timing of anticonvulsants in status epilepticus

0 to 5min: ABCs of resuscitation
- Monitor vital signs, give oxygen via mask, establish IV access.

5 to 10min: start anticonvulsants
- Use IV lorazepam (0.05–0.1mg/kg, up to 6mg) ***or*** rectal diazepam (0.5mg/kg, up to 10mg). If there is no response, repeat the dose after 5–10min.

15 to 20min: if seizure persists
- Load with IV phenytoin (15–20mg/kg, at rate <1mg/kg/min) or IV phenobarbitone (15–20mg/kg, at rate <1mg/kg/min) (if patient already on phenytoin)
- Give rectal paraldehyde (0.4mL/kg PR).

>30min: refractory seizure
- APLS guideline: call anaesthetist, consider RSI with thiopentone
- Consider load with IV phenytoin or phenobarbitone (whichever not given as listed here) if some break in seizure activity and ABC stable.

Refractory status epilepticus

Working definition of refractory status epilepticus (RSE)

RSE has been defined in various ways:
- Seizure that is unresponsive to an adequate dose of a first-line parenteral antiepileptic drug
- Seizure that is unresponsive to at least 2 doses of diazepam (IV or rectal) in succession followed by phenytoin/phenobarbitone (20mg/kg), or both, given over 30min as an infusion, or failure to respond to the latter alone or in combination.
- Seizure that continues for 60–90min after initiation of treatment.

Box 22.10 Consequences of prolonged seizure activity

- Early phase:
  - Cardiovascular: tachycardia, hypertension, ↑CVP
  - Metabolic: hyperglycaemia, lactic acidosis
  - Respiratory: mild hypoxaemia and hypercapnia
  - Autonomic: sweating, hypersecretion, dilated pupils
- Late phase:
  - Cardiovascular: hypotension,
  - CNS: loss of cerebrovascular autoregulation, cerebral oedema, absent pupillary and corneal reflexes
  - Metabolic: hypoglycaemia, rhabdomyolysis, hyperkalaemia, hepatic failure, disseminated intravascular coagulation
  - Respiratory: hypoxia and hypercapnia, apnoea, aspiration
  - Autonomic: hyperpyrexia, vomiting.

Management

There are few guidelines on how to treat seizures that do not respond to initial anticonvulsants. Anaesthesia may be necessary, but also consider:

- Has pseudo-status epilepticus (i.e. factitious seizures) definitely been excluded?
- Has appropriate drug therapy been used?
- Has maintenance antiepileptic therapy been initiated?
  - Check that long-term maintenance treatment has been started.
- Have all systemic and metabolic derangements been excluded and appropriately controlled?
  - Correct hypoglycaemia, hyponatraemia, hypocalcaemia, metabolic acidosis, and dehydration. Exclude hyperammonaemia
  - Reverse significant hyperthermia with active cooling
- Has a treatable underlying structural, metabolic, or infective aetiology been missed?

Anticonvulsant options in RSE

There are 3 anticonvulsant strategies reported for RSE:

- Midazolam
- Very-high-dose phenobarbitone
- Thiopentone/pentobarbital.

Midazolam

- Loading dose 0.15–0.50mg/kg
- Start continuous infusion and increase rate in increments up to 30mcg/kg/min (median 10mcg/kg/min)
- Achieve acute seizure control and maintain stability
- May be tolerated without the need for ventilation and/or inotropic support
- Give the minimum dose necessary for control
- Wean therapy with consultation with neurologist.

Very-high-dose phenobarbitone

- Repeated bolus doses of 10mg/kg every 30min until seizures controlled
- Monitor blood levels
- Maximum total dose in 24h ranges from 30–120mg/kg (median 60mg/kg), achieving median blood level 114mcg/mL).

Thiopentone/pentobarbital

- Loading dose of 4–8mg/kg
- Start continuous infusion and increase rate up to max 10mg/kg/min if required to control seizures—give the minimum dose necessary for control
- Achieve acute seizure control and monitor continuous EEG—aim for suppression-burst pattern, avoid complete suppression
- Maintain haemodynamic stability with inotropes if necessary
- Watch out for hypothermia, ileus, and VAP. Be aware that pupillary reflexes can be lost.

Surgery for RSE

Very occasionally RSE does not respond to anticonvulsants. Neurosurgery is rarely indicated. However, in cases with Rasmussen's encephalitis or other forms of acute, focal pathology it may be beneficial (e.g. epilepsia

partialis continua). The preoperative evaluation will include detailed neuroimaging, surgical implantation of subdural grids, as well as neurology/neurosurgery assessment. Surgical options include:
- Lobar or multilobar cerebral resection
- Hemispherectomy
- Subpial transection
- Corpus callosotomy
- Implantation of a vagal nerve stimulator.

Infection and inflammatory conditions

A number of infectious organisms can affect the CNS and, from the perspective of neurocritical care, each has the potential for generating distinctive clinical syndromes (Box 22.11).

Box 22.11 CNS infection and inflammatory 'critical care' syndromes

- Purulent meningitis (see 📖 p.550)
- Aseptic meningitis (see 📖 p.550)
- Acute encephalitis (see 📖 p.550)
- Paralysis and weakness syndromes:
  - Transverse myelitis
  - Poliomyelitis
  - Gullain–Barré syndrome
  - Botulism
- Acute disseminated encephalomyelitis
- Tetanus-like illness
- Neurosurgical conditions
  - Ventriculitis and infected shunts
  - Brain abscess
  - Subdural effusion
  - Spinal abscess.

Infective paralysis and weakness syndromes

A detailed history of the progression of symptoms helps to determine the likely cause, including:
- Viral:
  - Poliovirus
  - Coxsackie
  - Rabies
  - HSV
  - Influenza
  - Epstein–Barr virus
  - St. Louis encephalitis virus
- Non-viral:
  - *Clostridium botulinum*
  - *Campylobacter*
  - *Mycoplasma pneumoniae*
- PICU treatment is usually supportive with mechanical ventilation.

Transverse myelitis

Myelitis is inflammation of the spinal cord, usually involving both grey and white matter. When limited longitudinally to a few segments it is described as transverse myelitis. When it spreads progressively upwards it is described as ascending myelitis.

Aetiology

- Often unknown
- Viral
- Bacterial or tuberculous infection
- Part of demyelinating disorder
- Acute demyelinating encephalomyelitis
- Acute from of multiple sclerosis.

Clinical features

- Fever
- Back pain
- Flaccid paralysis, loss of reflexes
- Sensory level
- Loss of sphincter control.

Diagnosis

- Based on clinical features
- MRI appearance
- LP:
  - Raised protein
  - Some cells—neutrophils, lymphocytes, or mixed.

Treatment

- Supportive
- Antibiotics to cover bacterial aetiology
- Steroids are often used
- IVIG may be considered in refractory cases.

Poliomyelitis

The course of severe forms of poliomyelitis may vary:

- Poliovirus typically produces aseptic meningitis alone or in association with asymmetric flaccid paralysis
- Severe forms with paralysis are caused by destruction of the anterior horn cells of the spinal cord
- Sometimes compromise in bulbar and airway function may be present because of involvement of motor nuclei of CNs.
- Different degrees of functional recovery usually begin after some weeks and continue for the 1st year after onset.

Diagnosis

- CSF: elevated protein and pleocytosis
- Culture of virus: isolation from oropharynx and stools
- Serology

Guillain Barré syndrome (see 🕮 p.487).

Botulism

Botulism is produced by *Clostridium botulinum* toxin. Toxin may enter the blood because of:

- Ingestion of botulism toxin, usually from home canned foods
- Ingestion of *Clostridium botulinum* and production of toxins in the GI tract
- Entry from a wound

Clinical course

- Symptoms may start as early as 6h after exposure to toxin, or some time later, up to 6 days
- Cranial nerves are usually involved first: swallowing is often affected as well as speech and eye movement
- Other signs and symptoms include nausea, vomiting, dry mouth, and abdominal cramps
- As the disease progresses it causes weakness or paralysis of the extremities and respiratory muscle involvement
- In infants the disease may be mild with only hypotonia.

Diagnosis

- Electromyography with repetitive nerve stimulation is the best diagnostic tool during the initial period of the disease
- Recovery of *Clostridium botulinum* toxin from stool
- Serology

Disease-specific therapy

- Antitoxin is useful to remove circulating toxin but it does not affect toxin already at the neuromuscular junction. In infants botulism antitoxin is not recommended because of good prognosis
- Antibiotics are used to eradicate the source of toxin production. Penicillin and metronidazole is effective. Aminoglycosides may worsen the neuromuscular transmission defect.

Acute disseminated encephalomyelitis (ADEM)

ADEM is an inflammatory demyelinating disease of the CNS:

- Monophasic evolution (differentiating it from multiple sclerosis)
- Parainfectious disease: precipitated by viral exanthems (e.g. measles, mumps, rubella, and chickenpox), Epstein–Barr virus, influenza, group A *Streptococcus* and *Mycoplasma* infections; occasionally by vaccination
- Prognosis is usually good and many children may recover spontaneously in days to months.

Clinical findings

Acute presentation:

- ↓level of consciousness
- Behavioural changes
- Focal or multifocal neurological deficits:
  - Pyramidal tract signs
  - Ataxia
  - Cranial neuropathy
  - Optic neuritis

  - Seizures
  - Sensory abnormalities
- Other signs and symptoms: fever, headache, malaise, meningism.

Neuroimaging:
- CT scan is usually normal
- Demyelination on MRI in the absence of direct infection
- MRI T2 and FLAIR sequences frequently show multiple, disseminated asymmetrical lesions that affect the white matter throughout the CNS including the spinal cord. Occasionally single lesions might be seen.

CSF:
- LP should be performed to exclude direct infection of the CNS
- CSF may show: normal WCC to mild pleocytosis (100–200 cells/mm^3); mild protein elevation
- Cultures and virology should be negative.

Management
- Antibiotics: usually started because of suspected meningitis or encephalitis. These can be stopped once the diagnosis is confirmed
- Supportive mechanical ventilation in children with rapid deterioration or signs of bulbar compromise
- General care: seizure control, physiotherapy, and adequate nutrition
- Steroids are currently used in most cases. Regimens include: methylprednisolone 30mg/kg/d (maximum 1g) for 3 days, followed by oral prednisolone 2mg/kg/d during 2 weeks, and a 4-week wean
- Plasma exchange or IV immunoglobulin have been used in relapsed or refractory ADEM.

Tetanus-like illness

Tetanus is a neurological syndrome caused by a toxin that is produced by *Clostridium tetani*. Toxins act by disabling central inhibitory neurotransmission in the anterior horn cells. This lack of inhibition to excitatory impulses produces characteristic:
- Muscular rigidity
- Episodes of muscular spasms

Clinical findings
- In many developing countries tetanus is endemic and still produces high mortality, especially in newborns of non-immunized mothers
- In older children, most cases are secondary to trauma and infection with dirty objects, animal bites, burns, or chronic ulcers
- Trismus is a typical early sign
- Generalized muscular spasms produce a posture that resembles decorticate posturing
- Generalized seizures may occur after an episode of rigidity.

Management
- Supportive care:
  - Control motor symptoms
  - Support organ systems
- Specific therapy:
  - Human tetanus immunoglobulin as a single dose of 3000–6000 units given intramuscularly to neutralize toxins that are still being released

- Antibiotics to eradicate *Clostridium tetani*
- Metronidazole 30mg/kg/day in 4 divided doses; alternatively, penicillin 100,000–250,000 units/kg/day.

Ventriculitis and infected ventriculoperitoneal shunts (VPS)

Inflammation of the ventricles is usually associated with ventricular shunt devices but it may also be secondary to meningitis or rupture of a cerebral abscess into the ventricular system.

Clinical features

- Symptoms of shunt infection include headache, bulging fontanelle, poor feeding, nausea, vomiting, lethargy, exacerbation of strabismus, seizures, and signs of meningeal irritation. CN VI palsy may be present
- Fever is present in most instances. Any patient with a VPS developing fever should be assessed for possible infection. Exclude otitis media, viral upper respiratory infection, and urinary infection
- CT scan may show ventricular enlargement

- Infection often coexists with a blocked VP shunt

Diagnosis

- Ventricular CSF: >25 leucocytes/mm^3, or a positive culture
- Pathogens: coagulase-negative *Staphylococcus* species, *Staphylococcus aureus* and Gram-negative rods

Management of VPS infection

- Remove VPS and send 2 sets of CSF for culture
- Antibiotics: consult local microbiology specialist

Box 22.12 Initial empiric treatment

- Vancomycin: covers *S. aureus* and coagulase-negative *Staphlococcus:*
  - Can be combined with rifampicin which has better penetration of the blood–brain barrier
- ***And*** 3rd-generation cephalosporin: Gram-negative infections.

Definitive treatment

- Dictated by culture, sensitivities, and blood–brain barrier penetration.

Intrathecal treatment

- This should only be performed with neurosurgical and microbiological supervision: it requires a preservative free preparation of the antibiotic.

A patient with a VPS presenting with headache, vomiting, fever, or a reduced level of consciousness has a blocked ± infected shunt until proven otherwise. This is a neurosurgical emergency.

Brain abscess

Brain abscess is a severe and potentially fatal condition. It may rupture into the ventricular system or lead to tentorial herniation. Most cases occur in children with congenital heart disease, sinusitis, otitis media,

or mastoiditis. Other causes include trauma, local instrumentation, and rarely meningitis. The most frequent causative bacteria are streptococci, staphylococci, enterobacteriaceae, and anaerobes. Mixed infections are common. Fungal infections are very rare.

Clinical features

- Presentation depends on size, position, infecting organism, and host response
- Signs: fever, raised ICP, and focal neurology
- Imaging: CT scan showing a hypodense area surrounded by a ring that is enhanced with contrast ('ring enhancement'). MRI allows earlier identification of the initial lesion and may show multiple small lesions
- LP is dangerous: risk of herniation and it should not be performed if brain abscess is suspected
- Laboratory tests: WBC usually ↑ but can be ↔; CRP usually ↑.

Management

- Empiric antibiotic treatment depends on the likely source of infection and causative organisms, including anaerobes (see 📖 p.590).
- Later treatment should be guided by culture results
- Surgical excision and drainage
- Steroids: controversial.

Spinal abscess

Spinal epidural abscess can lead to paraplegia. Early recognition and treatment are essential if severe consequences are to be avoided. Abscess may arise from local infection or after haematogenous dissemination, penetrating injuries, or local invasive procedures, like LP.

Spinal abscess may produce problems such as direct compression of the spinal cord, mechanical compression of the blood vessels, or vasculitis with compromise of local blood flow. *Staphlococcus aureus* is the most frequent cause of spinal abscess, followed by *Streptococcus viridans*, *Streptococcus pneumoniae*, *Salmonella enteritidis* and other Gram-negative bacilli. Rare causes may be *Mycobacterium tuberculosis* and fungi.

- Early clinical features: non-specific, e.g. fever or irritability
- Later features: localized pain, weakness, and paralysis
- Imaging: urgent MRI should confirm the diagnosis when present
- Treatment: laminectomy with or without an epidural drain and antibiotics. The initial empiric treatment should cover *Staphylococcus aureus* (i.e., flucloxacillin) together with a 3rd-generation cephalosporin to cover Gram-negative organisms.

Subdural empyema

Subdural empyema may be a complication of meningitis.

- Infecting organisms depend on the source
- Clinical findings: signs of ↑ICP, nuchal rigidity, seizures or focal neurology, fever not resolving
- Antibiotics may include: continuation of treatment for meningitis; empiric treatment similar to that used in brain abscess
- Surgical drainage.

CNS tumours

Brain tumours are the most common solid tumours, accounting for 25% of all childhood malignancies. There are many histological subtypes, each with different features, management and outcomes (Box 22.13).

The neurosurgical emergency presentations associated with CNS tumours are:

- Deteriorating conscious level with:
  - Raised ICP
  - Papilloedema
  - Cranial nerve deficits from direct tumour involvement
  - False localizing signs: III & VI CN palsies (mass effect from raised ICP)
  - Unexplained seizures, particularly if focal
  - Increasing head size (infants)
  - Acute hydrocephalus
- Spinal cord compression with:
  - Back pain
  - Gait, sensory, bladder and bowel disturbance.

Consult a neurosurgeon immediately. High-dose dexamethasone may be needed preoperatively.

Postoperative care

The PICU may be involved in the early postoperative care of patients with CNS tumours. This may include management after:

- VPS insertion
- Tumour resection

In general, standard care with neurological observations should be all that is required, with attention to postoperative wounds and drains, haemoglobin level, and electrolytes. **Avoid hypotonic IV fluids**. Chemotherapy and radiotherapy are usually started after discharge from PICU.

Of particular concern, though, are the complications that may occur in patients with either brainstem glioma or craniopharyngioma.

Brainstem glioma and abnormal control of breathing

A glioma growing in the region of the pons is usually high grade and considered inoperable. The diagnosis is based on characteristic MRI appearances, and, very occasionally, biopsy. Median survival <1 year. In those undergoing surgery there is the risk of peri-surgical oedema impairing the normal drive to breathing, particularly when the patient is asleep. Intubated patients will require careful weaning and tracheostomy may need to be considered.

Craniopharyngioma and damage to hypothalamic-pituitary structures

Acute hypopituitarism (see 📖 p.683) may present preoperatively or postoperatively—diabetes insipidus may develop. Urine output, blood chemistry (sodium), and haemodynamic state must be followed closely. A paediatric endocrinologist should be involved with endocrine assessment and treatment.

Box 22.13 Brain tumours

Low grade glioma (Grade 1, 45% CNS tumours)
- Common sites are cerebellum and optic pathway
- Posterior fossa lesions can be cured with surgery
- Most are pilocytic astrocytomas.

High grade glioma (grade III/IV, 10% CNS tumours)
- Occur in older children and teenagers
- Mainly supratentorial
- Often difficult to resect completely.

Primitive neuro-ectodermal tumours (PNETs, 25% CNS tumours)
- The most common group of malignant brain tumours of childhood
- They are known as a medulloblastoma if present in the cerebellum
- Tumours metastases (mainly via the CSF) 10–15% of cases.

Ependymoma (10% of CNS tumours)
- Presentation with obstructive hydrocephalus if periventricular lesion
- 10% metastasis to spine
- Histological grading (I to IV) does not correlate with prognosis.

Germ cell tumours (5% of CNS tumours)
- Rare, more commonly seen in teenage boys
- Usually occur in the midline (suprasellar or pineal).

Craniopharyingioma (10% of CNS tumours)
- Slow growing midline epithelial tumours arising in the suprasellar area from remnants of 'Rathke's pouch'
- Benign on histology but difficult to resect completely
- Associated with hypopituitarism.

Stroke in childhood

Cerebrovascular stroke is rare in childhood, but it does cause significant morbidity. The cause can be ischaemic, haemorrhagic, or venous in origin. The majority of cases will have a likely cause identified on history and examination, and the main causes are:
- Sickle cell disease
- Congenital cardiac defects
- Cerebral infection
- Cerebral vascular abnormality:
  - Aneurysm
  - AV malformation
- Trauma (arterial dissection).

Management
- Initial attention to ABC
- Treatment of acute conditions such as meningitis
- Early transfer to a specialist unit—should be carried out within 4h since there may be neuroprotective thrombolytic therapies that can be given
- Decompressive craniectomy may be an option.

The field of 'adult stroke' is rapidly changing and it is important that children receive the benefits of new therapies.

Investigation

A full list of investigations is shown in Box 22.14. Once stable, all children will also require:

- Brain imaging using MRI and angiography rather than CT scan—although this will show the distribution of injury
- Even with a known condition such as trauma, all children require screening for underlying thrombophilia as these conditions may coexist.

Treatment

After stabilization, treatment should be undertaken in a specialist centre.

- Insertion of an external ventricular drain should be considered if there is subarachnoid haemorrhage accompanying intracranial haemorrhage associated with an aneurysm or AV malformation
- In adults with subarachnoid haemorrhage HHH (hypertension–hypervolaemia–haemodilution) therapy is used to prevent vasospasm—there is limited evidence to support its use in paediatric practice
- Definitive management of aneurysm or AV malformation will be either neurosurgical or interventional radiology (coil or glue occlusion)
- The role of anticoagulation/thrombolysis in cerebral venous sinus thrombosis is debated; low-dose heparin is generally recommended
- In the critically ill ICP monitoring and decompressive craniectomy may be considered after CT and neurosurgical evaluation—this includes assessment of type of lesion, and volume and distribution of infarction or haemorrhage.

Box 22.14 Investigations for acute stroke

Blood: haematology

- FBC, ESR: polycythaemia, leukaemia, inflammation
- Thrombophilia screen, fibrinogen: thrombophilia.

Blood: biochemistry

- Electrolytes, magnesium
- Liver function tests
- CRP: inflammation
- Plasma lactate and CSF lactate: mitochondrial disorders
- Fasting glucose: diabetes
- Fasting lipid screen: dyslipidaemias
- Thyroid function tests: Hashimoto thyroiditis and encephalopathy
- Ammonia: urea cycle disorders
- Homocysteine (free and total): methyltetrahydrofolate reductase (MTHFR) deficiency
- Serum Iron, total iron binding capacity, ferritin, red cell folate, and vitamin B12: iron deficiency and other nutritional disorders
- Plasma amino acids: aminoacidurias
- Carnitine (acyl, free and total): β-oxidation defects.

Urine: biochemistry

- Urine organic and amino acids: homocystinuria, MTHFR deficiency.

(*Continued*)

Box 22.14 Investigations for acute stroke (*Continued*)

Imaging studies
- MRA and MRA: vascular disease
- Doppler angiography: carotid stenoses
- Echo: endocarditis and other cardiac disease.

Neurometabolic disorders

(See also 🕮 Chapter 33.)

The neurological presentations to PICU of inherited metabolic disease (IMD) may include:

Acute encephalopathy

Deterioration in level of consciousness resulting from IMD:
- May occur in a previously healthy child
- Usually shows no focal features but ataxia may be present
- May start with unusual behaviour
- Progresses rapidly even to the stage of coma.

The likely causes are hyperammonaemia, amino acidopathy, organic aciduria, fatty acid oxidation defect, mitochondrial defect, hypoglycaemia.

Chronic encephalopathy with acute deterioration

Grey matter: developmental delay, psychomotor retardation

Developmental delay is a common problem, but the features that warrant investigation for IMD include:
- Global delay affecting all areas of development
- Progressive course with loss of developmental milestones
- Objective evidence of neurological dysfunction (e.g. special senses, pyramidal tract, extrapyramidal, cranial nerves)
- Severe behaviours including irritability, impulsiveness, aggressiveness, and hyperactivity
- Seizures (complex partial or myoclonic) originating early in life that are resistant to usual therapy.

Causes include: vitamin B6—dependency, biotinidase deficiency, neuronal ceroid-lipofuscinosis, GM2 gangliosidosis, Cherry-red spot-myoclonus syndrome (sialidosis type I), Leigh disease, Alpers disease, mitochondrial encephalopathy-lactic acidosis syndrome (MELAS) and stroke-like episodes.

White matter: gross motor delay, weakness, and incordination
- Central involvement only:
  - Canavan disease, Alexander disease, GM2 gangliosidosis, GM1 gangliosidosis, X-linked adrenoleucodystrophy (ALD), amino acidurias, organic acidurias
- Central and peripheral involvement:
  - Metachromatic leukodystrophy (MLD), Krabbe leucodystrophy, peroxisomal disorders.

Chronic encephalopathy with abnormalities outside the CNS
- Muscle: mitochondrial myopathy

- Hepatosplenomegaly ± bone:
  - Gaucher disease, Niemann–Pick disease, mucopolysaccharidosis (MPS) I–IV (Hurler disease, Hunter disease, Sanfilippo disease, Sly disease), GM1 gangliosidosis, sialidosis II, Zellweger
- Skin ± connective tissue:
  - Homocystinuria, Menkes, fucosidosis, multiple sulfatase deficiency, galactosialidosis, prolidase deficiency.

Stroke

The IMD associated with stroke or stroke-like episodes are:

- Homocystinuria
- Fabry disease
- Organic acidopathy: methylmalonic acidaemia, propionic acidaemia, isovaleric acidaemia, glutaric aciduria I and II
- Ornithine transcarbamoylase deficiency
- MELAS
- Congenital disorder of glycosylation type 1A
- Familial hemiplegic migraine.

Myopathy

- Acute intermittent muscle weakness: hyperkalaemic periodic paralysis, paramyotonia congenita, hypokalaemic periodic paralysis
- Progressive muscle weakness: glycogen storage disease II (GSD, Pompe disease), GSD III
- Myopathy as a manifestation of multisystem disease: mitochondrial myopathies.

Investigations (see Box 22.15)

Box 22.15 Investigations for myopathy

- Imaging: MRI of head—basal ganglia ± midbrain /brainstem changes typical
- X-rays of hands, chest, lateral spine
- Blood: FBC, serum electrolytes with urea and creatinine, glucose, liver function, plasma amino acids, ammonia, lactate, acylcarnitines, blood gas
- Urine: amino acids, organic acids, and mucopolysaccharide and oligosaccharide screen
- Electrophysiology: auditory brain stem reflexes, visual-evoked potentials, somatosensory evoked potentials, nerve conduction, EMG, EEG

Postmortem protocol

In the event of a child dying, adequate diagnosis is important for family genetic counselling if an underlying neurometabolic disorder is suspected. A postmortem protocol should be discussed with your local laboratory so that items such as biopsy needles (e.g. liver, kidney, and skin), dry ice, and culture media, can be made readily available and samples can be appropriately stored at any time. After obtaining parental consent collection should include:

- Urine and serum samples
- Fibroblast (skin) culture
- Muscle and liver biopsies (3 or more specimens stored frozen on dry ice or in liquid nitrogen at −20°C).

Post-resuscitation disease

Acute neurological complications may occur after successful cardiopulmonary resuscitation, irrespective of the underlying cause.

Cerebral oedema after cardiac arrest

This complication is more likely to occur in patients who have had a cardiac arrest following a period of hypoxia.

Imaging

CT scan is most likely to show changes on day 3 post-resuscitation. An earlier scan may be helpful though for excluding other intracranial pathologies that may have precipitated the arrest. MRI will identify regional differences in oedema and may provide prognostic information if performed within ~5 days.

PICU management

Supportive care and prevention of secondary insults is the mainstay of treatment post-resuscitation. The specific issues (and their priority) needing to be addressed after admission are best remembered by considering the following questions:

Has the patient been adequately resuscitated?

- An intubated and ventilated post-resuscitation patient needs to have, at least, normal BP, normal oxygen saturation, and normal biochemistry.

Has a post-resuscitation neurological examination been documented?

- Undertake a formal assessment after 6h of adequate BP, oxygenation, and biochemistry. Subsequent examination should be determined by ones initial findings and the patient's progress

Is there evidence of systemic post-resuscitation disease?

- Hypoxic-ischaemic insult is not solely restricted to the CNS. Over the first few days after resuscitation there is a time course of injury affecting renal function (acute tubular necrosis), hepatic function (transaminitis and coagulopathy), GI function (mucosal injury with feed intolerance), and haematology. Each of these systems may need supporting.

Has the patient developed any post-resuscitation CNS 'symptoms'?

The most frequently seen 'symptoms' relate to specific patterns of injury and their time course in severe injury:

- Seizures often refractory to treatment: can be multifocal and are seen more frequently in comatose infants
- Decorticate, decerebrate, and opisthotonic posturing: abnormal motor posturing associated with raised ICP and severe injury
- Myoclonic jerks: more often seen in the older deeply comatose child in association with intermittent EEG activity; episodes can be initiated by, and in time with, each ventilator breath
- Basal ganglia movement disorder: this can range from overt hemiballismus to near-continuous athetoid movements in the severely obtunded patient; episodes become obvious once neuromuscular

blockade has been discontinued and should be differentiated from seizures. These movements will require specific drugs in discussion with a paediatric neurologist.

Does the patient have intact control of breathing?

- There are a variety of patterns of abnormal breathing occurring in brain injury (see 📖 p.453). At an early stage a patient may have respiratory drive that later becomes absent as their condition evolves.

Therapeutic hypothermia

The value of mild, induced hypothermia has been assessed in adults and neonates with hypoxic-ischaemic insult. The American Heart Association suggests *considering* induced hypothermia (32° to 34°C for 12–24h) for comatose children after cardiac arrest, though there is currently no level I evidence to support this.

Further studies are needed to define optimal timing, duration, degree of cooling, re-warming intervals, and benefit from hypothermia.

Outcome

The likelihood and quality of survival after resuscitation from a period of hypoxia-ischaemia are the subjects of much literature. Survival may be as low as 5% and in those who do survive >50% may have multiple disabilities.

Prognostic assessment

It is important to have a realistic idea of likely outcome when discussing your treatment with the family. Patients should be assessed regularly over the first few days of admission. At 24h after resuscitation, the clinical features associated with poor outcome are:

- Abnormal pupillary response
- Abnormal motor response
- Bilaterally absent somatosensory evoked potentials
- Electrocerebral silence or intermittent EEG activity (suppression-burst)
- MRI changes indicating injured cerebral cortex and basal ganglia

Brain death (see 📖 p.723)

Neuromuscular disorders

A variety of disorders that affect the neuromuscular system may result in respiratory failure.

Cerebral insult

Any brain insult may make a child unreactive and move less. In these children there may be obvious signs of cerebral dysfunction such as encephalopathy. Facial movement and peripheral power are good if the child is able to follow commands. However, they may have low tone in the trunk, with relatively better tone at limb extremities. Reflexes should be present.

Central hypoventilation syndrome (CHS)

- Characterized by respiratory depression during sleep, more marked during the non-rapid-eye-movement state
- Can progress to hypoventilation during all sleep and awake states
- Reversible disorders of hypoventilation and apnoea (e.g. sepsis, hypothermia, hypocalcaemia, hypoglycaemia, seizures) should be excluded.
- Congenital: onset in the perinatal period. Require long-term nocturnal ventilatory support or equivalent alternative such as phrenic nerve pacing. This is best undertaken in specialist centres
- Acquired: associated with conditions such as posterior fossa tumours, encephalitis, hypoxic-ischaemic encephalopathy, metabolic disorders, and idiopathic hypothalamic dysfunction.

Spinal cord lesions

Spinal tumours and transverse myelitis should produce a horizontal level, below which there will be upper motor neuron signs or a sensory level, or both.

Anterior horn cell disorders

These produce a flaccid, areflexic limb, normally sparing the face.

Spinal muscular atrophies

Confirmation of these conditions includes fibrillation on electromyography and genetic homozygous deletion of the survival motor neuron gene.

- Type 0 (neonatal form): very severe, often with arthrogryposis related to paucity of *in utero* movement
- Type 1 (Werdnig–Hoffman): severe with onset in the first months of life. Typically there are 'bright eyes', severe hypotonia, 'frog-like posture', areflexia, and weakness that is present more in the legs than arms
- Type 2: onset in the first years of life with low tone, peripheral weakness, absent reflexes, and scoliosis
- Type 3: adolescent onset with progressive weakness and gait disturbance, loss of reflexes, and low tone.

Critical illness polyneuropathy, myopathy and related disorders

Prolonged neuromuscular blockade

We use neuromuscular blocking agents in PICU in order to promote better ventilatory management in some patients. These drugs can be given intermittently or by continuous infusion. The modern trend in using continuous infusions makes long-term drug administration easier and it minimizes haemodynamic and ventilatory fluctuations due to rapidly changing drug levels. However, this practice may come at a significant cost—occasional prolonged neuromuscular blockade despite drug discontinuation. The causes of this problem can be divided into 2 types of problem (Box 22.16).

Box 22.16 Causes of prolonged neuromuscular blockade

Pharmacokinetically based

This is usually a short-term problem that is attributable to altered hepatic or renal clearance because of end-organ dysfunction. Peripheral neurophysiology will confirm persistent neuromuscular blockade.

Neuromuscular function based

This is usually manifested as prolonged paralysis in patients with normal end-organ function. Electromyography will show neuromuscular defects.

The aim whenever neuromuscular blocking agents are used must be to avoid these prolonged problems. We can do this by making sure that we include in our practice:

- Peripheral nerve stimulation monitoring
- Periodic drug discontinuation or 'drug holiday': every 24h make sure that the infusion is turned off and only restarted if indicated, and when the patient starts to move.
  - Reduce the infusion rate if recovery is delayed by several hours
- Recognition of interacting drug therapy (Box 22.17)
- Attention to electrolyte and acid–base management.

Critical illness polyneuropathy, myopathy

Despite the approaches described, other peripheral neurological problems may still occur in certain high-risk groups. Risk factors include:

- Asthma
- Steroid therapy, or drugs containing a steroid ring
- Sepsis syndrome
- Multiple-organ system dysfunction

In adults, entities called critical illness polyneuropathy and critical illness myopathy have been well described in those requiring mechanical ventilation for >3 days of critical illness. The key features are:

- Failure to wean from mechanical ventilation in an expected time
- Limb weakness
- Impaired deep tendon reflexes
- Intact sensory function

- Normal CSF
- Abnormal peripheral neurophysiology.

Critical illness neuromyopathy also occurs in children but does not occur as frequently as in adults:

- Diagnosis is based on clinical findings though abnormalities of creatine kinase (CK), electromyography (EMG), and nerve conduction may be present
- It should be considered where there is difficulty in weaning mechanical ventilation or reduced movement/muscle strength
- Although use of muscle relaxants is a risk factor it can occur in children who have not received muscle relaxants
- The treatment is essentially supportive once it has been recognized:
  - Respiratory support may be required for weeks
  - Good skin and pressure area care
  - Optimize nutritional support
  - Regular neurophysiotherapy
  - Splints/orthoses may be required to optimize joint position.

Box 22.17 Drugs that interact with neuromuscular blockade

Drugs that shorten duration of action

- Frusemide
- Methylxanthines
- Phenytoin (not with atracurium)
- Carbamazepine
- Azathioprine.

Drugs that potentiate blockade

- Other neuromuscular blocking agents
- Antibiotics, in particular, aminoglycosides and clindamycin
- Antiarrhythmic agents
- Midazolam
- β-adrenergic receptor blockers
- Calcium channel blockers
- Cyclosporin
- Combination of steroids and steroid-based neuromuscular blocking agents (e.g. vecuronium and pancuronium).

Guillain–Barré syndrome

An acute demyelinating polyneuropathy. It often follows an intercurrent infection, classically *Campylobacter enteritis*. Initially, there are motor signs that progress up the body. Typically there is gait disturbance, which then progresses to involve the arms, and then respiratory and bulbar muscles in severe cases. Children may complain of muscle pain, which can mask the weakness. Sensory involvement also occurs, but this feature may be overlooked.

Aetiology

- Epstein–Barr virus
- Cytomegalovirus
- Measles
- Mumps
- Eneteroviruses
- *Mycoplasma pneumoniae*
- *Borrelia burgdorferi*
- *Campylobacter*.

Differential diagnosis

The differential diagnosis includes:

- Myasthenia gravis
- Poliomyelitis
- Spinal cord compression
- Transverse myelitis
- Botulism.

Diagnostic features (see Box 22.18)

- ***Clinical picture***: muscle weakness, with loss of reflexes in an ascending fashion, dysaesthesia/pain
- ***Nerve conduction studies:*** characteristic features
- ***CSF:*** elevated protein, but this does not occur at onset
- ***Serology:*** antiganglioside antibodies (anti-GQ1b, anti GM1 in AMAN); antibodies to agents listed in 'Aetiology'.

Clinical course

- ***Onset:*** starts 1 to 2 weeks after an antecedent illness
- ***Ascending weakness:*** initial deterioration normally lasts <2 weeks
- ***Plateau phase:*** in regard to the symptoms
- ***Recovery:*** Should begin within 2–4 weeks, in a descending manner, with full recovery some times taking months—reflexes are the last to recover.

Management

- Monitor respiratory state every few hours initially: lung function including forced or crying vital capacity and/or maximum negative inspiratory pressure
- Autonomic involvement: dysautonomia leads to tachycardia, fluctuating BP, and GI disturbance.

- Mechanical ventilation should be considered if the forced vital capacity falls below 15–20mL/kg, if the maximum negative inspiratory pressure falls below 20–30cmH_2O, or if the patient is too fatigued to be tested.
  - **It is important to remember that suxamethonium is contraindicated since it is likely to result in hyperkalaemia**
- Early introduction of physiotherapy and occupational therapy to avoid joint contracture
- Control dysaesthesia/pain: tricyclic agents and gabapentin may be useful
- Immunoglobulin: IV treatment (total dose 2g/kg over 2–5 days) is normally used initially, with plasma exchange reserved for refractory cases
- Consider tracheostomy if recovery is slow and a significant period of ventilation is anticipated

Box 22.18 Clinical variants of GBS

Acute inflammatory demyelinating poliradiculoneuropathy (AIDP)
- Ascending hypotonic paralysis and areflexia
- Usually affects the lower extremities; less frequently symptoms may present in the upper extremities or in the face
- Sensory loss in a glove-stocking distribution may be present
- Autonomic disturbances may be present.

Acute motor-sensory axonal neuropathy (AMSAN) and the acute motor-axonal neuropathy (AMAN)
- Immune response against the axons instead of the myelin sheath
- Usually more severe than AIDP.

Miller Fisher syndrome
- Antibodies affect the oculomotor nerves, dorsal-root ganglion cells and cerebellar neurons
- Ophthalmoplegia, ataxia and areflexia

Autonomic dysfunction

Dysfunction of the autonomic nervous system is seen in children with GBS, especially those that require mechanical ventilation:
- Sphincter disturbance: requires catheterization of the bladder
- Sweating and hypersalivation: can cause loss of fluid and electrolytes requiring changes in IV fluid therapy
- Ileus: rare but can cause loss of large amounts of GI secretions and inadequate enteral feeding
- Cardiac dysrhythmias and BP disturbance:
  - Periods of instability with hypo- or hypertensive episodes and tachy-bradyarrhythmias.
  - α-agonists and β-blockers can therefore be dangerous
  - Cardiac pacing may be necessary.

Myasthenia gravis

The cardinal clinical feature of MG is fatigability. Difficulties range in severity from mild ptosis to respiratory difficulty. Childhood cases can be categorized as:

Transient neonatal MG

This is found in babies of mothers with MG and is due to placental transfer of maternal anti-acetylcholine-receptor antibodies or maternal immunocytes which then compromise the infant's receptors.

- Impairment is usually evident within hours of birth but may be delayed for a few days
- Early findings are weak suck, poor swallowing, muscle weakness, paucity of spontaneous movements, respiratory inadequacy, and ptosis.

Persistent neonatal (congenital) MG

These infants have acquired the autoimmune or non-autoimmune hereditary type of disease. Their mothers do not have MG.

- Symptoms are usually evident on the first day of life, but like the transient neonatal form of MG they may appear days later
- Respiratory function may be so involved that ventilatory support is required and as the disease progresses bulbar dysfunction may be more obvious
- Contractures similar to those associated with arthrogryposis multiplex congenita may also be present.

Juvenile MG

This condition is very similar to the adult form of the disease. Features usually appear after the age of 10 years. It is more common in girls. The disease waxes and wanes with exacerbations that sometimes necessitates mechanical ventilation. Affected children have serum IgG antibody to nicotinic acetylcholine receptors less frequently than do adult patients.

Diagnosis

Evaluation for probable MG consists of a trial of edrophonium chloride (Tensilon®) or neostigmine. Evaluation in infants is best done with oral neostigmine because of the difficulty in assessing weakness over a short period and because of poor cooperation. Peripheral neurophysiology, change in ventilatory requirement and video is also informative in the clinical assessment.

Treatment

Virtually all forms of MG are treated with 1 or more of the following:

- Anticholinesterases
- Prednisolone
- Immunosuppressants
- Thymectomy
- Plasmapheresis.

The specifics of when, what and how much to use are best left to consultation with paediatric neurology specialists.

Myasthenic crisis versus cholinergic crisis

In some patients, despite seemingly optimal drug therapy, there is an inability to maintain basal ventilation needs or effective swallowing of oropharyngeal secretions. These problems may occur when the patient is receiving concurrent antibiotics, narcotics, barbiturates, tranquillizers, or antiarrhythmics (e.g. lignocaine, quinidine, procainamide and propranolol). Hypokalaemia may also cause similar symptoms.

It is important in such cases to consider both a myasthenic crisis and a cholinergic crisis (Box 22.19).

Box 22.19 Myasthenic crisis vs. cholinergic crisis

Myasthenic crisis

This is manifested by:

- Progressive and profound weakness
- Results from too little treatment.

Cholinergic crisis

This looks similar to a myasthenic crisis but is also accompanied by:

- ↑sweating
- Profuse formation of saliva
- Vomiting, abdominal colic, and diarrhoea
- Results from administration of greater than optimal dosing of anticholinesterase medication.

Differentiating between these crises is very difficult. If there is doubt, the patient should first receive edrophonium chloride intravenously during the period when the optimal effect of the ongoing anticholinesterase therapy is anticipated.

- Improvement in weakness indicates a *myasthenic crisis* and the need for larger doses of long-acting anticholinesterase drugs
- If the edrophonium injection is not effective then a *cholinergic crisis* is probably present. This condition requires the withdrawal of anticholinesterase therapy. Atropine may be required to reduce perspiration, vomiting, colic. and diarrhoea.

Catastrophic brain injury

Persistent vegetative state (PVS)

PVS is the term used to describe a clinical syndrome following brain damage in which, after an initial comatose period, patients:

- Pass into a state of 'wakefulness without awareness'
- Never regain recognizable mental function.

Children in the PVS have suffered destruction of the cerebral cortex and/or its integrating connections, although brainstem function is preserved. They will survive when ventilation is withdrawn, spontaneously open their eyes, regain sleep–wake cycles and sometimes chew and swallow. They may grind their teeth and scream for protracted periods of time. Unfortunately the appearance of these signs of 'awakening' in a previously deeply unconscious child may deceptively suggest the onset of improvement. Such children may remain in this condition for many years provided they receive nutrition and good nursing care.

The diagnosis of the PVS has profound implications for the child and their family. Up to 10% of adult survivors of hypoxic-ischaemic encephalopathy have this outcome. The proportion in children is ~3%. Early reliable indicators of such an outcome would therefore be of immense value in the PICU. They would facilitate the option of withdrawing/limiting futile therapy (see Box 22.20 and 📖 p.723).

Box 22.20 Ethics Advisory Committee of the RCPCH: withholding and withdrawing treatment in children

Brain Death: mechanical ventilation in such circumstances, where specific criteria are met, is futile and the withdrawal of intensive care ICU treatment is appropriate.

Permanent and PVS: *it may be appropriate to withdraw or withhold life-sustaining treatment.*

No Chance: the child has such severe disease that life-sustaining treatment simply delays death without significant alleviation of suffering. Treatment to sustain life is inappropriate.

No Purpose: the child may be able to survive with treatment, but the degree of physical or mental impairment will be so great that it is unreasonable to expect them to bear it.

Unbearable: the child or family consider that in the face of progressive and irreversible illness further treatment is more than can be borne. They wish to have a particular treatment withdrawn or to refuse further treatment irrespective of the medical opinion that it may be of some benefit.

Brain death

(See 🕮 p.725.)

The diagnosis of brain death should be considered in all deeply comatose children who are being mechanically supported, where there is evidence of brain stem damage.

The task of the clinician is to attempt to distinguish those children in whom there is the possibility of recovery from those where no such possibility exists. Where the brain stem is dead, widespread clinical experience has established that somatic death inevitably follows.

In 1976 and 1979 the UK medical Royal Colleges and their Faculties issued criteria for the diagnosis of brain death in which they emphasized that the permanent functional death of the brain stem constitutes brain death. In practice, the absence of brainstem function after excluding hypothermia and drug and metabolic intoxication, in the presence of irremediable structural brain damage, is sufficient to make the diagnosis.

The diagnosis is thus a clinical one and, at least in the UK, does not require EEG or other ancillary tests for evidence of absent cortical function. For details of the UK practice see 🕮 p.725.

In the USA, the President's Commission Guidelines for the Determination of Death in 1982 differed fundamentally from the UK criteria in that evidence of the cessation of higher cerebral function as well as brainstem function was advocated. They also acknowledged the criteria might be different in children, particularly those <5 years. They recommend that the interval between first and second tests be more prolonged the younger the patient.

Chapter 23

Trauma and burns

Overview of trauma

Epidemiology

Trauma is the leading cause of death in children >1 year of age in the developed world.

- 2/3 of major paediatric injury consists of isolated head injury (TBI)—in the UK, 5.4 per 100,00 children are admitted to PICU with TBI/year
- Motor vehicle accidents and falls account for 80% of multiple trauma
- Most paediatric trauma is blunt trauma, penetrating trauma is more common in areas of the world with greater levels of gun crime
- Deprivation increases the risk of a severe TBI
- Peak time for injury is mid-late afternoon—hospital trauma services should be organized for ↑ arrivals in emergency departments in late afternoon and early evening

Pathophysiology of injury

Injury is a result of:

- Direct trauma, blunt, penetrating, and from resultant shock waves
- Hypoxia: common in multiple trauma victims because of reduced chest wall compliance, CNS depression, airway obstruction and hypovolaemia
- Shock:
  - Leads to tissue hypoxia
  - Haemorrhagic shock commonest type in trauma
  - Sympathetic tone will maintain BP, until the child has lost 60% of their blood volume
- Neurohumeral response:
  - Hypoxia and direct trauma to tissues → systemic inflammatory response syndrome
  - Causes myocardial depression, vasodilatation, and direct injury to certain tissues (glutamate release in brain)
- All of the above → hypoxia of major organs (especially brain and heart), abnormal cellular metabolism, cell ischaemia, multiorgan failure and death.

Presentation

History to note

- Mechanism of injury; blunt, penetrating, shock waves, deceleration
- In RTA: speed of vehicle, thrown from vehicle, fatalities
- Loss of consciousness, seizures.

Examination

- *Respiratory:* airway patency, tracheal position, respiratory distress, respiratory noises, hypoxia, evidence life-threatening injuries
- *Cardiovascular:* tachycardia, capillary refill time, hypotension, evidence of bleeding, neck veins, skin temperature
- *Neurological:* GCS/AVPU, pupillary signs, evidence of raised ICP, evidence of localizing signs, evidence of spinal cord injury—need to log-roll patient to feel down length of spine and do rectal examination
- *Abdomen:* loss of bowel sounds, bruising over abdomen (tyre/seatbelt mark), guarding, rigidity
- *Pelvis:* spring test, urethral injury—gross haematuria, perineal bruising
- Very important to look for other major injuries that could adversely affect outcome especially long bone injuries, burns.

Investigation

Level of investigation depends on indications, these may include: 📖 p.503 (see also 📖 pp.336–7).

- ABG and lactate
- Biochemistry including glucose
- FBC
- Cross-match
- X-ray (trauma series): c-spine views, chest, pelvis
- CT scan of head
- CT scan of c-spine, chest, abdomen if appropriate
- Abdominal US is widely used in adult practice.

Management ('in a nutshell')

Organization

- Excellent management of the multiple trauma victim is based on the multidisciplinary team approach.
- All trauma calls should be 'run' by an experienced team leader
- Management should carried out simultaneously, rather than sequentially, and coordinated by the team leader.

Airway

- Maintain patent airway with in-line cervical spine immobilization
- If need to open airway use jaw thrust with c-spine immobilized
- If GCS <9, or responding to pain only, or unresponsive (PU on AVPU)—intubate.
- Once airway stabilized, immobilize c-spine with collar, sand bags, and tape.

Breathing

- 100% oxygen by non-rebreathe mask initially
- Intubate if any sign of hypoxia—at induction, be aware undiagnosed hypovolaemia might worsen dramatically
- Ensure cardiovascular status assessed and resuscitated
- Monitor end-tidal pCO_2—maintain $PaCO_2$ 4.5–5kPa
- Maintain PaO_2 above 12kPa
- Keep sedated and muscle relaxed to decrease oxygen demand
- Orogastric tube essential to decompress stomach—improves ventilation especially in toddlers. Do not insert a NG tube if there is concern about base of skull fracture
- Treat all life-threatening thoracic complications (see 📖 p.510).

Circulation

- Ensure 2 large-bore cannulae or central venous line
- If difficult access, insert 2 intraosseous needles
- Volume resuscitate as required. First 4 boluses 10mL/kg normal saline
- If still evidence of shock, treat with blood
- Obtain arterial access
- If cardiovascularly unstable, it is essential to find source of bleeding and treat. This may mean surgery
- Vasopressor (i.e. norepinephrine) may be required in a severe traumatic brain injury to maintain cerebral perfusion pressure (CPP)

- Inotrope (epinephrine) may be required if cardiac contusion suspected or in the setting of pulmonary oedema (see 🕮 Box 13.5, p.240).
- Catheterize patient to quantify urine output.

Disability

- Neuroprotect if evidence of severe traumatic brain injury—control $PaCO_2$, to within lower end of the normal range, maintain well oxygenated, maintain mean arterial pressure at a level appropriate for age and to maintain estimated CPP (see 🕮 pp.505–7, also pp.95–100)
- Keep head in midline and bed angled at 30° head-up
- Manage spinal trauma appropriately if present
- Treat evidence of raised ICP—mannitol (0.5g/kg), increase CPP, normalize PaO_2 and $PaCO_2$, consider brief hyperventilation in the setting of fixed dilated pupils

Exposure

- Maintain normothermia.
- Prevent hypothermia especially during resuscitation.
- ***Do not actively rewarm the patient with severe brain injury***
- Maintain euglycaemia.

Secondary survey

- Should be performed by an experienced person
- Methodical examination of all systems looking for further non life-threatening injury—see appropriate sections in rest of chapter.

Transfer (see 🕮 Chapter 18)

- Patient should not be transferred until cardiovascularly stable—even if this means operating within a non-trauma centre
- Patients with expanding cranial mass lesions need definitive neurosurgery and should be transported as soon as cardiovascularly stable
- Patients should be transferred by experienced doctors and nurses, who are competent at managing airways, as well as life-threatening complications of trauma
- Before moving a patient, ensure:
  - Patient stable, and sufficiently sedated and muscle-relaxed
  - Sufficient IV access, urinary catheter, orogastric tube
  - Full monitoring commenced—ECG, pulse oximetry, end tidal pCO_2, invasive BP
  - There is sufficient oxygen, batteries for monitor, and pumps fully charged
  - Sufficient anaesthetic and resuscitation drugs and fluids (including blood)
  - Discussed with PICU and neurosurgery
  - Discussed with parents
  - All notes, X-rays, and CT scans copied.

Head injury (traumatic brain injury)

Presentation

- Head injury is a common problem, in UK 1 million patients present to hospital, 50% of them <16 years old (see Box 23.1)
- Severe traumatic brain injury (GCS <9) is a common cause of death in children, accounting for 15% all deaths in 1–15-year-olds and 25% of deaths in 5–15-year-olds
- Minor head injury is usually uncomplicated; <1 in 800 admissions admitted for observation develop serious complications; however, subtle long-term sequelae are common in mild and moderate TBI
- Causes of TBI vary in different age groups
- Injury prevention is important and there has been a major effect from seat belts with more recent concentration on child-seat designs, wearing a cycle helmet, producing >80% reduction in risk of head injury.

Causes

- Road traffic accident most common cause of severe injury (commonest pedestrian, followed by cyclist, passenger in vehicle)
- Falls (domestic for younger child—furniture, stairs, windows, trees, walls and buildings)
- Recreational/sports injury
- Non-accidental injury—important in children <2 years of age
- Gunshot/penetrating injury—relatively uncommon in UK

Box 23.1 Head injury patterns

Blunt head injury

- Head comes into forcible contact with a flat, smooth surface
- At point of impact there is a steep rise in pressure, with a fall at the opposite pole which can equal a negative pressure of 1 atmosphere
- The positive pressure may have little effect on the brain. The negative pressure may produce small areas of cavitation and focal haemorrhages in the superficial cortex.

Sharp head injury

- There may be laceration of the scalp, local depression or fragmentation of the skull, dural tearing and bruising, and laceration of the underlying brain
- Intracerebral haemorrhage usually arises from torn superficial vessels of the cortex.

Compression head injury

- Severe injuries may occur without initial loss of consciousness. Fractures involve the foramina at the base of the skull, producing CN palsies
- Can also result in vascular complications, e.g. dissection
- Side-to-side compression causes fractures through the middle fossa. In these cases the pituitary is at risk.

Types of intracranial injury

3 main mechanisms of intracranial damage:

- Focal lesions, that mainly involve the cortical grey matter
- Diffuse traumatic axonal injury (TAI)
- Secondary injury caused by oedema, space-occupying effects, reduced cerebral perfusion.

Hemorrhage and other focal brain tissue effects

- Epidural or extradural haematomas (EDH) complicate 2–3% of all head injury admissions in children:
  - In infants, EDH of venous or bony origin is found in the posterior fossa adjacent to the venous sinuses. They often have a delayed presentation because the infant has significant intracranial reserve with open fontanelles
  - In older children EDH arises from arterial bleeding. There may be a short lucid interval after injury, but patients will deteriorate rapidly
- Subdural haematoma (SDH) is common in children, especially in non-accidental TBI:
  - It is the associated brain injuries that account for immediate unconsciousness at the time of accident and any focal neurologic deficits (e.g. hemiparesis, pupillary abnormalities, and seizures)
- Traumatic intraparenchymal haematomas or contusions are less common in children.

Diffuse traumatic axonal injury (TAI; also known as DAI)

- TAI may vary from small foci of axonal injury to a more severe form of diffuse TAI, in which there is widespread injury throughout the brain, including the brainstem
- CT imaging may miss TAI; a MRI is the investigation of choice. (see 🕮 p.503)

Diffuse swelling of the cerebrum

- Cerebral swelling develops during the early phase of post-traumatic coma and peaks between 24–72h after injury
- Focal injury may occur in combination with diffuse injury—high-speed impact and acceleration–deceleration forces make the medial temporal lobe particularly vulnerable because of its position in the middle cranial fossa.

Spinal cord injury

SCI in children is uncommon. In Europe, the incidence of non-fatal SCI is 0.09–2.12 per 100,000 children, per year.

Traumatic SCI is the result of primary and secondary injury mechanisms:
- In cases of vertebral column injury spinal cord injury occurs in < 50%
- Complete SCI is seen in < 25% cases
- SCI is an easily overlooked complication of non-accidental head injury.

Clinical patterns

Damage from acute SCI evolves over hours or days. Post-SCI ischaemia—related to failing autoregulation, BP, cardiac output, and oxygenation—may contribute to worsening injury.

Pattern of SCI in the child's developing spine differs from that in adults.
- In children <9 years of age, spinal injuries are more frequently seen in the atlas, axis, and upper cervical vertebrae
- Ligamentous injuries leading to atlanto-occipital dislocation are more common than bone injuries
- An adult pattern, with less frequent involvement of the cervical spine, is seen in older children
- SCI may be seen in the absence of abnormality on plain X-rays—SCI without radiographic abnormality (SCIWORA)

SCIWORA

The clinical features range from tingling dysaesthesias or numbness to frank weakness or paralysis. MRI demonstrates 5 classes of post-SCI-WORA cord findings and are highly predictive of outcome:
- Complete transection: very poor outcome
- Major haemorrhage: very poor outcome
- Minor haemorrhage
- Oedema only
- Normal: all of these patients make complete recovery.

Thoracic SCIWORA

Consider in accidents involving high-speed direct impact, distraction from lap seat-belts, and crush injury by slow moving vehicles.

Traumatic atlanto-occipital dislocation

Disruption of the supporting ligaments leads to displacement in either transverse or vertical direction. Rare in children and adolescents. Most do not survive initial cardiac arrest and apnoea. Combined high SCI and brainstem injuries must be suspected in this group.

Functional integrity of the spine and spinal cord

Complete injury is signified by loss of motor function, segmental reflexes, and sensation below a given level.

Flaccid arreflexic paralysis and anesthesia to all modalities characterize spinal shock. This problem is found in half of SCI patients and resolves within 24h in >90% of cases.

Assessment of the patient with TBI/SCI

Airway and breathing

► ***Hypoventilation due to brain injury or c-spine injury is common.***

Intubation is often mandatory (Box 23.2).

TBI

- Hypercapnia is a potent cerebral vasodilator and ↑ICP
- Hyperventilation leading to hypocapnia may cause cerebral vasoconstriction → cerebral ischaemia, particularly early post-injury when cerebral blood flow is ↓.
  - If clinical suggestion of brainstem compression, hyperventilation may be indicated, but for a brief period only.

SCI

Pattern of respiratory dysfunction depends on the level of injury:

- Complete injury above C3 causes respiratory arrest and death unless immediate ventilatory assistance is given.
- Injury at the C3-C5 level (phrenic nerve innervation of the diaphragm) leads to respiratory failure.

Box 23.2 Indications for intubation in TBI and SCI

- Loss of airway protective reflexes
- Uncontrolled seizures
- Chest wall dysfunction
- Respiratory muscle dysfunction
- Apnoea
- $PaCO_2$ >6kPa (45mmHg) or <3.3kPa (25mmHg)
- Unreactive pupil(s)
- GCS <9 or fall in score >3 irrespective of initial score.

C-spine

Injury to the c-spine must be assumed to have occurred in any head-injured patient until such time as neck soft tissue or bony injury has been ruled out.

- The neck should be immobilized in an appropriately-sized collar and manipulation should be kept to a minimum
- If the collar is removed for any reason, the neck should be held in midline position and gentle axial traction applied by single operator.

Circulation: causes of hypotension

- Hypovolaemia secondary to blood loss:
  - Blood loss sufficient to cause hypotension is rarely due to bleeding in the cranium except in small infants where subgaleal haematomas can be life threatening.
- Cardiogenic shock, arrhythmia, and pulmonary oedema occur (Box 23.3):
  - Due to cardiac contusion from direct trauma or
  - Due to acute myocardial dysfunction in the setting of severe brain injury
- Neurogenic shock in cases of cord injury above T4: reflects sympathetic denervation of the heart (T1–T4) and vasculature with resulting ↓contractility, ↓HR, and arterial and venous dilatation.

Box 23.3 Neurogenic pulmonary oedema

So called 'neurogenic pulmonary oedema' is thought to be mediated through acute left ventricular dysfunction, with an abrupt increase in left atrial pressure resulting in pulmonary oedema. It is therefore more 'cardiogenic' than 'neurogenic'. The acute ventricular dysfunction is thought to be mediated through a surge or 'storm' of catecholamine release in patients with severe subarachnoid haemorrhage or traumatic brain injury. Exogenous catecholamines are often needed to support myocardial function despite being implicated in causation.

Neurological assessment

Rapid neurological examination (Coma score + pupillary reaction, presence of any lateralizing signs) should only take a few minutes and will determine most appropriate management:

- Assess GCS to classify severity of injury (severe traumatic brain injury GCS <9, moderate GCS 9–13, mild GCS 14–15)—the motor score is the most useful discriminator
- The AVPU system (***A***wake, responds to ***V***oice, responds to ***P***ain and ***U***nresponsive) provides a quick initial assessment of conscious level but is not an alternative to the GCS
- Note pupillary reaction—size in millimetres, shape, reaction to light and equality
- Assess motor function and any asymmetry
- Signs suggesting brain stem compression or impending herniation (Cushing's triad—bradycardia, hypertension, and abnormal respiration, usually in the setting of fixed dilated pupils).

Clinical management

- The vast majority of children attending hospital can be discharged after initial assessment as the head injury is mild. They should be given written instructions for reattendance
- If there are suspicions of a possible non-accidental injury the child must be admitted and child protection procedures followed (see 📖 p.849)
- Children with a history of loss of consciousness, vomiting, skull fracture, or headache must be admitted for neurological observation in an appropriate children's ward
- Children with moderate and severe head injury, or polytrauma with any severity of head injury, should be managed according to ATLS/APLS guidelines with:
  - Appropriate resuscitation
  - C-spine immobilization
  - Repeated neurological assessments
  - A detailed secondary survey to determine the extent of injuries and the nature and speed of general and specific management
  - Urgent CT scan.

Initial management of severe head injury

Aims

To prevent secondary injury by preventing and avoiding:

- Hypoxia
- Hypotension
- Raised ICP.

► It is essential this is done continually, including whilst undertaking x-ray examinations, CT scan and during all transfers.

Urgent management (GCS <9 or rapidly falling GCS)

- Intubation and ventilation:
  - RSI with c-spine stabilization (see 📖 p.132)
  - Cuffed ETT preferable
- Sedate and initiate neuromuscular blockade
- Monitor $EtCO_2$ to ensure adequate ventilation and avoid hyperventilation, aim for $PaCO_2$ 4.5–5.0kPa
- Monitor arterial BP via arterial line. Aim to keep MAP:
  - >50mmHg for <1 year
  - >60mmHg 1–5 years
  - >70mmHg 5–12 years
  - >80mmHg >12 years
- Give volume boluses initially, add vasopressor (i.e. norepinephrine) or inotrope (i.e. dopamine, epinephrine) if MAP not responsive—vasopressor first line unless clinical suspicion of impaired myocardial function, e.g. pulmonary oedema
- C-spine immobilization (triple—collar, sand bags and tap) and log roll for any subsequent examination
- Treat any life-threatening injuries
- Urgent CT scan of head (full trauma series if indicated).

After admission, the clinician plans investigations to try and answer the following 4 questions:

- Is there intracranial pathology that requires emergency surgery?
- Should we monitor ICP?
- Is the spine unstable and therefore needs fixation?
- Does this patient require full investigation for suspected NAII?

Neuroimaging

Indications for head CT scan in TBI

- (NICE guideline; based on Canadian CT Rules, see Box 23.4)
- GCS <13 at any time since injury
- GCS = 13–14, 2h post injury
- Suspected/proven open or base of skull fracture
- Post-traumatic seizure
- Focal neurological deficit
- Dangerous mechanism of injury.

Box 23.4 NICE guideline on CT scanning

The NICE guideline on CT scanning is intended to exclude significant intracranial injury in children who would previously have been admitted to hospital for observation without having a CT scan, allowing early discharge in those with a normal CT scan. Application of the guideline results in significantly more head CT scans being undertaken. A challenging group are those with mild injury (GCS >12) who require a general anaesthetic in order to undertake a CT scan—some centres opt to observe this group in the first instance.

C-spine films, CT scan and MRI (see 🕮 p.336)

- C-spine X-ray films (AP, lateral ± odontoid peg view) unless plan is to include CT scan of c-spine in a patient having a CT head:
  - This is becoming more standard practice but involves a significant radiation exposure
  - CT patients with severe TBI or those with a history suggestive of c-spine/spinal cord injury, e.g. apnoea at scene
  - Also CT if plain X-rays are abnormal or inadequate
- If C-spine films taken ensure adequate exposure (all 7 c-spine bodies visible as well as C7–T1 junction):
  - Check alignment: anterior and posterior vertebral bodies, posterior margin spinal canal, and spinous processes
  - Check contours: vertebral bodies and spinous processes
  - Check odontoid
  - Check soft tissue: space between anterior vertebral body and posterior pharyngeal shadow
- If in doubt get expert radiological review as soon as possible; for all CT scans a radiological review should be standard
- Spinal MRI is highly sensitive to changes in the spinal cord, haemorrhage, and ligamentous injury. It is indicated if there are cord-related neurological symptoms or signs.

Clearance of the c-spine (see 🕮 p.337)

Clearance of the c-spine, as being stable, is an area of controversy and debate. There are no formal guidelines and each unit should discuss its management with neurosurgery, and neuroradiology colleagues.

- In the conscious child, immobilization can be discontinued when there is a full range of pain-free movement and normal c-spine imaging.

In children with significant TBI it is much more difficult. Approaches that may be employed include:

- Maintain cervical spine immobilization until an MRI can be performed to exclude ligamentous and cord injury
- Maintain c-spine immobilization until the patient can be assessed for pain, limitation of movement (can be weeks in the most severe cases)
- Remove the collar if radiology of c-spine (plain films or CT) is normal and the patient is moving all limbs.

Further management

- If further management is to be undertaken at PICU or the neurosurgical centre, transfer must be arranged according to clinical need for surgical intervention (Box 23.5)
- Whilst awaiting transfer undertake regular and frequent neurological observations as well as HR, BP, saturations, $EtCO_2$, blood gas, blood glucose, FBC, clotting studies, electrolytes
- Use PEEP (physiological ~5 cmH_2O) to prevent atelectasis and hypoxia
- All patients should have a minimum of 2 large-bore cannulae or a central line. (Avoid internal jugular lines if possible spinal injury.)
- Treat ongoing bleeding
- Treat hypotension with fluid to normovolaemia and then use pressors
- If cardiovascular instability remains consider other sites of bleeding: this includes long bone fractures, abdominal viscera, chest, pelvis, and in infants the scalp
- Place urinary catheter
- As part of 'neuroprotection' place head in midline, elevate head 15–30°, load with IV phenytoin, keep serum sodium >135 mmol/L (give 2–4mL/kg of 3% saline), maintain serum glucose in normal range, maintain normothermia (avoid hyperthermia)
- Treat raised ICP
- Keep in close liaison with PICU and Neurosurgeon.

Box 23.5 Primary transfer or retrieval?

Significant delays are introduced if the patient is first taken from the accident scene to a non-neurosurgical hospital. Where possible pre-hospital teams should transfer directly to a trauma centre.

If a transfer between the first hospital and the neurosurgical centre is needed, the use of a retrieval service may add further delays.

However the imperative is that an appropriately trained and equipped team transport a child with severe TBI—the best model will vary from one location to another (see 📖 Chapter 18).

ICP monitoring and treatment in TBI

ICP monitoring (📖 p.95) is indicated in:

- Children with severe TBI (GCS <9) and a mass lesion:
  - Remove the mass lesion and insert an ICP monitor at surgery
- Severe TBI (GCS <9) plus any CT abnormality:
  - Early CT may miss features of TBI and small contusions. Some guidelines recommend ICP monitoring in any child with a GCS <9, regardless of CT appearance
- CT evidence of intracranial hypertension (e.g. swelling, shift, or cisternal compression) regardless of GCS
- In moderate head injury (GCS 9–12), deterioration warrants repeat head CT to rule out interval development or enlargement of a mass lesion, and consideration for placement of an ICP monitor.
- Normal ICP is usually <10mm Hg in adults, between 3–7mmHg in younger children, and <6mmHg in infants
- In adults, the threshold for initiating treatment of intracranial hypertension is taken as 20–25mmHg.

CPP (see 📖 pp.97–100)

CPP is calculated as the difference between the MAP and the mean ICP. Reductions in CPP below specific threshold values are associated with poor outcome.

In severe TBI, recent studies suggest that the level of CPP associated with poor outcome is between 40–65mmHg. As MAP increases with age an age-related CPP target should be used:

- 40–50mmHg in infants and toddlers
- 50–60mmHg in children
- >60mmHg in adolescents.

ICP-directed therapies

If ICP increases to >20mmHg a systematic approach should be followed. Before considering specific ICP therapies ensure that there isn't a simple explanation:

- Adequate sedation and analgesia
- Adequate ventilation ($PaCO_2$ 4.5–5.0kPa)
- Adequate oxygenation

If ICP remains elevated consider the therapies described (Box 23.6)

- The evidence base for these is poor so the order with which the interventions are applied will vary from centre to centre
- First-tier therapies should be used before second-tier therapies, which in general have greater potential adverse effects
- Consider the need for repeat CT scan if increasing intervention is needed to control ICP, particularly if the initial CT revealed haemorrhage
- Children with most severe TBI will have a second CT scan undertaken within 48h of injury.

Box 23.6 First- and second-tier ICP-directed therapies

First-tier therapies

- Elevate the head to 30° and position in the midline
- If ventriculostomy /EVD is in place, then CSF can be drained.

Hyperosmolar therapy

- Mannitol (0.25–0.5 g/kg over 5–15min): withhold if the serum osmolality is above 320mosm/L,
- Hypertonic saline: (see Box 23.7)
  - Continuous infusion of 3% between 0.1–1.0mL/kg/h or
  - 2–4mL/kg bolus of 3% saline
  - Few adverse reactions with sodium levels as high as 160mmol/L.

Mild hyperventilation ($PaCO_2$ 4.0–4.5kPa)

Second-tier therapies

Lumbar drain

- Requires open basal cisterns on CT scan and no significant mass or midline shift, preferably with EVD in place.

Barbiturates:

- Thiopentone (or pentobarbital) loading dose of 5–10 mg/kg over 15–30min, followed by infusion of 1–10mg/kg/h:
  - Titrate to ICP response, support BP as required
  - Titration to burst suppression with EEG monitoring is ideal.

Decompressive craniectomy

- If there is evidence of brain swelling on CT scan with ICP that is difficult to control on medical management.

Hypothermia

- Titrate degree of hypothermia to ICP response
- Lowest temperature 32–33°C
- Patient may be unstable during rewarming phase.

Moderate/severe hyperventilation

- Risk of inducing cerebral ischaemia through vasoconstriction
- Do not use unless monitoring cerebral perfusion/brain oxygenation.

Box 23.7 How to make hypertonic (3%) saline

- To prepare 50mL of 3% saline: take 5mL of 30% sodium chloride and dilute with 45mL of water for injection
- To prepare 500Ml: take a 500mL bag 0.9% sodium chloride, remove 36Ml and add 36mL of 30% sodium chloride.

Ongoing PICU management

ICP monitoring

- Continue ICP monitoring until baseline ICP can be kept <20mmHg without intervention
- In most (but not all) patients the duration of ICP monitoring will be <7 days:
  - Risk of ventriculitis increases after 7 days
  - Monitor serial CSF white cell count and culture
- If multiple therapies used to control ICP, withdraw these one at a time
  - Start with second-tier therapies, then first-tier
  - Allow $PaCO_2$ to normalize
  - Lift muscle relaxation (if used)
- Remove ICP monitoring if ICP remains under control (<20–25mmHg).

Respiratory support

- The risk of atelectasis and VAP is very high (Box 23.8) as a result of:
  - Maintaining the patient supine with minimal lateral movement
  - Heavy sedation ± muscle relaxation
  - Risk of aspiration around time of accident
- Ensure effective physiotherapy is employed—may require pre-physiotherapy boluses of analgesia/sedation to blunt ICP rise
- Consider possibility of infection—send modified BAL or ET secretions
- Use PEEP as required to maintain adequate end-expiratory lung volume

Classical teaching was to avoid using PEEP in patients with cerebral oedema for fear it would compromise cerebral venous drainage by increasing intrathoracic pressure. There is no evidence that use of physiological levels of PEEP does this. Use of no PEEP or inadequate PEEP will certainly cause atelectasis which will impair gas exchange and will exacerbate ICP.

Nutritional support

- Encourage early enteral nutrition
- Trauma patients often develop gastroparesis:
  - Add pro-kinetics
  - Consider post-pyloric feeding.

Other

Pressure areas

- Risk of pressure area breakdown is high (Box 23.8)—vulnerable sites include back of scalp, sacral area, and heels:
  - Regular observation of pressure areas
  - Cycle areas exposed to pressure as much as can be tolerated.

Box 23.8 Immobility and complications

There are significant benefits to early clearance of the spine in patients with severe head injury:
- The ability to move the patient from the supine position decreases the risk of atelectasis/VAP and pressure area breakdown
- Early MRI scanning may be used to 'clear' the spine without needing to wait until the patient can undergo a clinical assessment
- A normal high resolution CT scan of the c-spine may be accepted, given the problems and risks of taking an unstable patient to MRI.

Antibiotics
- No role for prophylactic antibiotics in TBI patients unless there is a contaminated penetrating injury or a compound skull facture
- Antibiotic therapy for potential VAP should be guided by microbiology findings on BAL/ET secretions
- Post-traumatic meningitis is rare but can occur in the patient with a skull fracture, or the patient with an infected ventricular catheter:
  - CSF should be sampled to confirm the diagnosis and to allow antibiotics to be tailored
  - Prophylactic antibiotics are ***not*** routinely indicated in a patient with a base of skull fracture or an ICP monitor or ventricular catheter.

Temperature control
- Pyrexia is common after severe brain injury of any cause:
  - It is associated with worse neurological outcome
  - Pyrexia is associated with a rise in ICP
- Temperature should be kept normal for the first 72h—longer if ICP control is difficult
- Routine early use of hypothermia does not improve outcome
- Use of titrated hypothermia as a second-line ICP intervention is used in some centres but there is no evidence that it is safe or effective
- Neurogenic hyperthermia may continue late after head injury in association with dysautonomia and 'catecholamine storming episodes'.

Anticonvulsants
- Overall early seizures (in first 7 days) occur in ~15%
- The risk of long-term seizures in these patients is about 15%
- The more severe the injury, the higher the incidence:
  - GCS <9: 27% risk
  - GCS 9–12: 2 % risk
  - GCS 13–15: 2% risk
- Seizures are more common after SDH or a depressed skull fracture
- Prophylactic anticonvulsants are recommended in adults with severe TBI, based on trials showing reduced *early* seizures—their role in paediatric management is controversial since there are no prospective controlled trials in children
- Phenytoin is the most frequently used agent
- Duration of optimal treatment is uncertain—consider stopping after 7–10 days if no evidence of seizure activity.

Management of spinal injury

Skeletal injury

- Consult a neurosurgeon and/or orthopaedic/spinal surgeon—local policy may vary as to who is responsible for spinal injuries
- Establish whether the injury is stable or unstable—maintain spine precautions and immobilization if any uncertainty
- Options for ongoing stabilization include halo traction for c-spine injuries and body cast for thoracolumbar injury
- Occasionally surgical fixation will be required.

Cord injury

High-dose methylprednisolone became standard therapy in adults with non-penetrating acute cord injury in 1990s:

- Current uncertainty over study design and safety doses of used
- No studies in children
- The authors favour the use of steroids
- Start within 8h of injury:
  - Methylprednisolone 30mg/kg bolus over 15min followed by infusion at 5.4mg/kg/h for 23h
  - If the patient starts treatment between 3–8h of injury, the infusion is continued for 48h.

Orthopaedic injury

Injuries to be aware of are fracture of long bones and pelvic fractures:

- These are painful:
  - Requiring opiates and splinting/immobilization
  - Femoral nerve block may be useful for a femoral fracture
- Can → significant blood loss into the tissues → hypovolaemic shock
- Diagnosis is made on plain X-rays. Additional information about pelvic fractures can be obtained from a CT through the pelvis.

Complications

- Consider bladder or urethral injury with pelvic fractures
- Compartment syndrome may develop after a long-bone fracture:
  - Monitor distal perfusion and CK
  - Measure compartment pressures if concerned
  - Early fasciotomy to release affected compartment
- Fat embolism is a theoretical complication occurring days after injury.

Management

- Involve orthopaedic team early
- A complicated fracture will require early fixation
- In the patient with coexisting severe head injury surgery is ideally delayed until concerns about raised ICP have subsided
- In coexisting head injury ICP should be monitored in the operating room and neuroprotective measures should be continued.

Thoracic injuries

- Thoracic injury occurs in 10% of paediatric trauma patients and 25–50% of patients suffering multisystem injury
- 5% mortality, ↑ to 35% in multi-system injury
- 85% of thoracic injury caused by blunt trauma, most due to RTAs.

Pathophysiology

- The paediatric rib cage is compliant due to incomplete costal ossification, elastic cartilageneous joints, and thin intercostal musculature
- The compliant ribs do not dissipate the force of impact → widespread intrathoracic injury ***without*** rib fracture or signs of external injury
- When >2 ribs are fractured in 2 or more places, a flail segment occurs → compromised breathing and ventilation-perfusion mismatch
- The mobility of the mediastinal structures ↑ risk of thoracic injury, e.g. tension pneumothorax and injury to the trachea and great vessels.

Presentation

History to note

- Blunt vs penetrating trauma
- Penetrating injury more likely to be associated with life-threatening blood loss
- Thought regarding mechanism of injury can help determine likely life-threatening injuries.

Examination

- Respiratory: tachypnoea, respiratory distress, wheeze, stridor, unilaterally ↓air entry, hypoxia, evidence of a flail chest
  - Respiratory injuries can initially be asymptomatic even if serious injury
- Cardiovascular: tachycardia, hypotension, prolonged capillary time
- It is critical to detect and treat life-threatening injuries immediately
- Associated injuries occur in the following order:
  - CNS
  - Soft tissue
  - Skeleton
  - Abdomen.

Investigations relevant to thoracic injury

- CXR: should not delay treatment if the child is unstable
- ABG
- Hamoglobin/haematocrit
- CK/troponin if cardiac contusion expected
- ECG
- Echo: if cardiac contusion is suspected
- Bronchoscopy: if airway injury suspected
- MRI/MRA/CT angiogram/angiogram: if great vessel injury suspected.

Specific management

- Support airway, breathing, and circulation
- Intubate and ventilate if necessary:
  - Be aware that children may tolerate intubation poorly due to poor lung compliance (pulmonary contusion), and chest wall elasticity

- An initial normal CXR does not rule out serious lung injury
- If there is any suspicion of a tension pneumothorax, needle thoracocentesis should be performed immediately
- Almost all patients with a flail segment will require ventilatory support
- If haemodynamically unstable it essential that you rapidly determine source of loss. This may require a surgical intervention.

Potentially life-threatening thoracic injuries and specific management

Pneumothoraces

- Tension pneumothorax:
  - Diagnosed on clinical suspicion
  - Respiratory distress, hypoxia, unilaterally ↓air entry on affected side, hyper-resonant on affected side, tracheal deviation to opposite side
  - Immediate needle thoracocentesis: mid-clavicular line, 2nd intercostal space, followed by formal intercostal chest drain (see 🕮 p.426)
- Open pneumothorax:
  - Sucking chest wound with signs of pneumothorax
  - Cover wound and insert intercostal chest drain (see 🕮 p.422).

Massive haemothorax

- Large blood loss of >20mL/kg blood loss immediately or >2–3mL/kg/h for 3 consecutive hours after insertion of intercostal drain
- Management: clamp ICD, volume resuscitate
- Will probably require intubation and ventilation
- May require open thoracotomy.

Injury to the airway

- Can be partial or complete
- Presents with pneumothorax with persistent air leak, subcutaneous emphysema (especially if worsened by positive pressure ventilation), ↓air entry, wheeze, increasing ventilatory requirement
- Diagnosed by bronchoscopy
- Management: incomplete disruption to smaller bronchi is often conservative with ICD insertion and high frequency, low mean airway pressure ventilation
- If air leak persists or is complete will need surgical repair through a median sternotomy.

Rupture of the diaphragm

- More common on left than the right
- Suspect clinically if increasing respiraory distress, bowel sounds in chest
- Confirmed by CXR with elevated left hemidiaphragm
- Need to suspect abdominal pathology if present
- Management: ventilate. Surgery when stable.

Oesophageal perforation

- More common in penetrating injury
- Suspect from history and especially if develop mediastinitis. Air present in prevertebral space on lateral c-spine X-ray

- Diagnosed by oesophogram with water soluble contrast or at endoscopy
- Management:
  - If asymptomatic, place patient nil by mouth with orogastric tube placed under direct vision to decompress stomach
  - If symptomatic, surgical exploration may be necessary. Gastrostomy at this stage may be useful for healing.

Cardiac contusion

- Presents with signs of ↓cardiac output, features of ischaemia on ECG, or dysrhythmia
- Confirmed by abnormality in ventricular wall motion
- Increased troponins are diagnostic
- Important to rule out as continuing volume replacement may worsen myocardial function.
- Management: supportive with ventilation and inotropes.

Cardiac tamponade

- Diagnosis is made clinically by muffled heart sounds, signs of ↓cardiac output and distended neck veins (and raised CVP if CVL present).
- CXR shows a globular heart shadow and tamponade can be confirmed on Echo
- If the patient is in extremis management should be instigated immediately rather than waiting for investigations
- Management: volume resuscitation and pericardiocentesis initially, followed by emergency surgery
- **Pericardiocentesis should be performed with a cannula inserted below the xyphisternum and directed at a 45° angle toward the left scapula, aspirating as you insert until blood is withdrawn.**

Great vessel injury

- Very rare in children, typically in rapid deceleration injuries
- If presenting symptomatically, these injuries are often fatal
- Can present with hypertension in the upper limbs, ↓/absent pulses, interscapular murmur
- The most common presentation is a radiographic finding in a stable patient
- Radiographic signs include a widened mediastinum, depression of the left main bronchus, right shift of orogastric tube, apical capping, left pleural effusion, and fractures of 1st and 2nd ribs
- Diagnosed with MRA or angiography
- Management: resuscitation followed by surgery.

Abdominal trauma

Presentation

- Children more vulnerable to serious intra-abdominal injury than adults:
  - The organs are relatively large, the abdominal wall is thin, and the musculature less developed
  - The liver and spleen are more anterior
  - The ribs provide less protection to liver and spleen, the ribs are more compliant and easily compressed allowing the solid organs underneath to be compressed
- Development of hypovolaemia, peritonism, and abdominal pain may be delayed by many hours—admission for observation may be indicated

⚠ Rupture to liver, spleen, kidney and bowel may not immediately produce symptoms, especially if the injury is retroperitoneal.

Causes

- Blunt trauma
  - RTAs: pedestrians, bicycle, passenger
  - Falls at home: down stairs, from windows, onto solid objects
  - Falls out of the home: from trees, equipment in playgrounds, onto bicycle handlebars
  - Direct blow to abdomen: deliberate or accidental (punch, kick during sports, kick from horses)
  - Direct blow to the back – deliberate or accidental
- Penetrating injury
- Direct blows may result in injury to solid organs, bowel or mesentery due to compression against rigid structures, i.e. the spine or the ground
- Deceleration injuries occur due to shearing forces exerted on mobile parts of the GI tract moving away from their point if fixation, i.e.:
  - Sigmoid colon
  - Ileocaecal junction
  - Duodenojejunal flexure.

Assessment

- Assessment and management should follow advance life support principles (APLS, EPLS and ATLS i.e. **ABCs**)
- Accurate history will aid in the rapid diagnosis and management
- Fluid resuscitation according to cardiovascular assessment
- Ongoing hypotension and hypovolaemia raise the possibility of significant abdominal and/or thoracic injury
- A surgeon should be present immediately to assess the abdomen
- Bloods for amylase, liver function tests.

Investigations

Laparotomy may be indicated as an emergency before investigations if the patient remains cardiovascularly unstable and you are unable to maintain circulation with fluid resuscitation—this must be decided by consultation with the surgical consultant.

- Double contrast (IV and intragastric) CT scan—gold standard and should be undertaken in severe cases once cardiovascularly stable
- Abdominal US offers the potential advantage of being accessible in the emergency department; however serious injury including solid organ rupture, retroperitoneal haematoma, haemorrhage, and bowel rupture can all be missed even by experts
- Abdominal X-ray is of minimal use except to identify position of NG tube and possible free air following a perforation
- Diagnostic peritoneal lavage (DPL) should not be done as it is of little value, and hinders ongoing assessment
- Magnetic resonance cholangiopancreatography (MRCP) may be useful if CT scan and serum amylase suggests a significant pancreatic injury and direct urgent partial pancreatectomy.

Management of intra-abdominal bleeding

- Intraperitoneal bleeding with hypovolaemia:
  - Fluid resuscitation
  - Blood and clotting factors if necessary
  - Conservative non-surgical management with bed rest, analgesia, and fluids will be successful in the majority of cases
  - Manage in a specialist centre with paediatric surgery and PICU
- Mesenteric bleeding with hypovolaemia
  - Less likely to be manageable conservatively
  - Laparotomy either immediately or after resuscitation.

Further management

Liver/spleen injury

- Preferably managed conservatively, but if urgent laparotomy needed in referring hospital, a conservative approach may be adopted with packing of abdomen rather than definitive surgery
- If significant liver injury refer to centre with hepatobiliary surgery.

Duodenum

- Commonly injured following direct blows to the abdomen (such as on bicycle handlebars)—a fixed retroperitoneal structure compressed against the vertebral bodies
- May be due to non-accidental physical child abuse
- Presentation may be delayed and manifest as feed intolerance
- Surgical intervention may be required or feeding via jejunostomy may be successful whilst more minor injuries repair.

Renal injury

- Ruptured kidney can be managed conservatively with fluid resuscitation and bed rest, occasional laparotomy is necessary for severe uncontrollable haemorrhage
- Loss of perfusion to a kidney will be evident on CT scan with contrast.

Lumbar spine

- Chance fracture of the lumbar spine should be looked for (crush fracture) as it may be associated with injury to the duodenum or pancreas and in severe cases with a spinal cord injury.

Maxillofacial and ophthalmologic injury

- The majority due to motor vehicle, motorbike, or bicycle accidents
- Also occur in falls and in NAI
- 50% of patients presenting with maxillofacial injuries will suffer from multiple trauma.

History to note

- Mechanism of injury
- Visual disturbances, flashes of light, photophobia, diplopia, blurred vision, pain, or change in vision present with eye movement
- Change in hearing present, tinnitus, or vertigo
- Trouble breathing through the nose?
- Bloody or clear-fluid discharge from the nose or ears
- Difficulty opening or closing the mouth, pain on biting or muscle spasm, history of teeth malalignment
- Areas of numbness or tingling present on the face.

Examination

- Facial asymmetry, swelling, or haemorrhage
- CSF leak from nose or ear, Battle sign (bruising of mastoid)
- Bony crepitus especially along orbital rim, zygomatic arch, at the articulation of the zygoma with the frontal, temporal, and maxillary bones
- Palpate mandible and condyle
- Look for missing, mobile, fractured, or malocclusion of the teeth
- Inspect for exophthalmos or enophthalmos, fat protruding from the globe and ptosis. Evert eyelids and check for foreign bodies or lacerations. Check for corneal abrasions with fluorescin staining
- Assess visual acuity, abnormality of ocular movements, pupillary size, shape, and reactivity to light, both direct and consensual
- Thorough cranial nerve examination, evidence of facial parasthesia
- Evidence of other injuries.

Investigation

- For upper and mid-facial injuries: axial and coronal CT scan
- For lower facial injuries: panographic X-ray of mandible. If mandibular fracture suspected, but X-ray negative:perform condylar CT scan.

Management

- Manage airway and ventilation
- If evidence of serious maxillofacial injury, patient should be intubated early as oedema will make a delayed intubation difficult.
  - Nasotracheal intubation is contraindicated
- Manage circulation: do not remove any extruding foreign particle without the presence of a surgeon
- Pain relief
- Ophthalmology consultation: treat any corneal injury
- Maxillofacial surgeon review and surgery if necessary
- If multiple fractures, tracheostomy may be required.

Urological trauma

Renal injury

- The kidney in a paediatric patient is more vulnerable to injury relative to an adult as it sits in a more superficial position and is less protected by muscle and fat. Trauma can be secondary to blunt injury or acceleration/deceleration forces
- Renal injury may be masked by more pressing clinical problems. The child with multiple trauma should have the urinary tract investigated as a matter of routine by a contrast-enhanced CT scan or US scan, particularly if there is loin pain, haematuria, bruising over the renal angle, or haemodynamic compromise with no obvious cause
- One should suspect renal injury if there is evidence of bony injury to the lumbar vertebral bodies
- Renal injury can also occur following a relatively minor injury (e.g. sport or play injury) if there is a pre-existing renal anomaly such as hydronephrosis or ectopic kidney
- The kidney may sustain any of the following injuries , which are graded according to severity:
  - Grade 1: contusion
  - Grade 2/3: laceration
  - Grade 4: transection
  - Grade 5: renal pedicle injury leading to damage to the renal vasculature
- Management is primarily conservative and general principles include close observation for haemodynamic instability and falling haemoglobin concentration. More severe injuries can be associated with urinoma formation with leakage of urine into the perirenal area. Surgery is indicated on a case by case basis As much renal tissue/function should be preserved as possible. Irreversibly damaged renal tissue will require resection in time in order to prevent complications such as renal induced hypertension. Small localized urionomas can be left to settle spontaneously or drained percutaneously.

Ureteric injury

Rare in children and more likely to be iatrogenic following surgery, e.g. appendicectomy or hernia repair

Bladder injury: seat belt injuries and pelvic fractures can be associated with bladder trauma. Management is usually formal repair after a period of continuous catheterization and drainage.

Urethral injury: more common in boys following a straddle injury or pelvic fracture. If urethral or bladder injury is suspected specialist help will be necessary with regard to catheterization. Suprapubic catheterization is the preferred route.

Burn injury

Presentation

- The majority of burns in children occur in toddlers and pre-school children and the burns usually occurs as result of their behaviour involving scalds
- Scalds follow pulling down containers, or being in the way of adults when they spill hot liquids
- Immersion injuries are likely to be more extensive and deeper due to longer time of contact
- Older children are more likely to have flame burns and the risk taking behaviour of males results in a greater incidence
- House fires have become less common in developed countries and depend on the use of building materials, presence of smoke alarms, and cooking on open fires
- In the younger child you must consider the possibility of a NAI due to immersion, cigarette burn, or as the result of neglect.

Key actions on presentation

- Weigh patient or perform accurate estimate
- Assess burn surface area use 'rule of nine' ± chart (see Fig. 23.1)
- Establish time and mode of burn injury, and note time presentation
- Resuscitate according to APLS, EPLS guidelines i.e. **ABCs**
- Establish access rapidly
- Give analgesia
- Contact Burn Surgeon
- Consider need to protect airway and intubate
- If housefire or possibility of inhalation give 100% O_2 and measure carboxyhaemoglobin level.

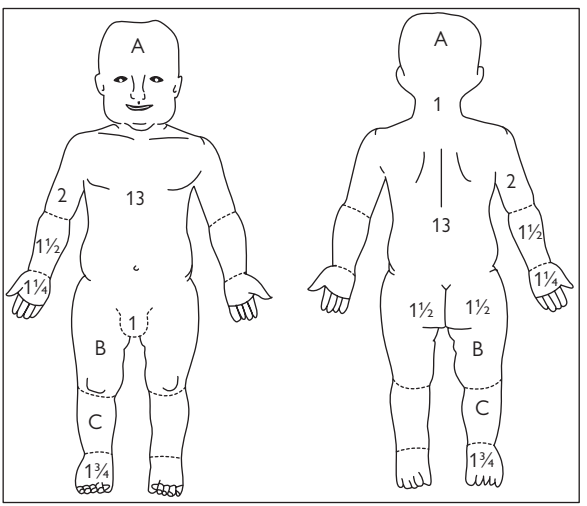
Causes and pathophysiology

- Burn may result from thermal (water, other liquid, contact with hot object, and flame) or chemical injury
- This results in a local and potentially systemic response depending on size of injury (more than 20–25% body surface area (BSA) involvement likely to produce major systemic effects)
- Following thermal or chemical injury to skin 3 zones of injury are produced
  - *Zone of coagulative necrosis:* tissue necrosis at the time of burn, the depth is determined by temperature and length of exposure
  - *Zone of stasis:* severe inflammation occurs adjacent to area of necrosis with ↓blood flow leading to extension of necrosis over 12–24h (can be modified by treatment or worsened as a result of poor perfusion)
  - *Zone of hyperaemia:* less severe inflammation not likely to progress to necrosis unless super added infection.

Assessment

- Assessing body surface area—percentage body surface area (% BSA)
- Use rule of nines or specific diagrams (Fig. 23.1)

- Older child:
  - Head 9%; torso – front 9%, back 9%
  - Arms 9% each; legs 19% each
  - Groin 1%
- Toddler
  - Head 18%; torso—front 18%, back 18%
  - Arms 9% each; legs 14% each
- Ignore simple erythema.



Area	Age (years)				
%	0	1	5	10	15
A	9	8.5	6.5	5.5	4.5
B	3	3	4	4.5	4.5
C	2.5	2.5	3	3	3.5

Fig. 23.1 Calculation of BSA (%) at different ages.

Aims of early management (in a nutshell)

- Accurate assessment of extent and severity of burns
- Good analgesia
- Adequate fluid resuscitation (see 📖 p.520)
- Identification of any complicating factor (carbon monoxide poisoning, inhalation injury, burn to area such as head, neck, groin that makes management more complicated, circumferential burns)
- Intubate early patients at risk of airway difficulty and respiratory failure.

Always use a cuffed endotracheal tube, regardless of age, as chest wall compliance may become severely reduced, resulting in a significant leak. You don't want to have to change the ETT 24h later when the head and neck have swollen and visualization of the airway is difficult.

- Establish early contact with Burn Service and agree management plan
- Ensure safe and appropriate transfer to Burn Centre in timely manner.

Urgent management

- Cooling the burn wound—use cold running water 15°C (8–25°C) for 15–20min but avoid making patient hypothermia, cooling must take place as soon as possible within first 3h, also has some useful analgesic effects for smaller burns (5–10%)
- Prevent hypothermia—even without cooling effect of water there is disruption to thermoregulation with a significant burn, remove damp clothing, cover burn and use blankets, measure core temperature and use warming devices if needed
- Give 100% oxygen to all except minor burns—in addition always give 100% oxygen to the patient from a house fire or other enclosed space, even if minor burn
- Insert minimum of 2 peripheral cannula in unburnt skin if possible—give fluid resuscitation according to protocol
- Insert urinary catheter in all patients > 20% BSA—also in burns to perineum—use urinary output figures to guide adjustments to fluid therapy
- Fast and make nil by mouth until after consultation with Burn Surgeon
- Insert NG tube for all patients with burn >20% BSA, all intubated patients, head and neck burns, younger children with burn >10% BSA
- Give adequate analgesia—IV opoids (usually morphine)
- Emergency wound management—once patient stable cover wound with cling film wrap or clean non-adhesive dressing, only use alternative dressings as directed by Burn Surgeon
- If indicated perform escharotomy after discussion with Burn Surgeon—indicated if circumferential burns could compromise the viability of a limb or trunk burns could compromise chest wall compliance
- Elevate limbs and avoid constrictive dressings
- Sit patient up if burn to head and neck to help reduce swelling
- Tetanus prophylaxis—assess tetanus status in all patients and give booster + tetanus toxoid as indicated.

Investigations

- FBC
- Clotting studies
- Electrolytes, renal function, liver function tests, albumin
- CK if suspicion of significant tissue damage
- Cross-match blood products if early surgery anticipated.

Indications for intubation

- Evidence of possible airway compromise:
  - Burn to head and neck with swelling
  - Stridor, hoarse voice, swollen lips

  - Singed facial, nasal or head hairs
  - Carbonaceous material in or around mouth or nose or in sputum
- Unconscious
- If complex/severe burns and will require significant interventions, with or without transfer to PICU/Burn Centre.

Fluid resuscitation

- Modified Parkland Formula to estimate the volume of resuscitation fluid to administer in the first 24h following burn:
  = 3–4mL Hartmann's (or Ringer's lactate solution × body wt (kg) × % total BSA affected (see Box 23.9)
- Use 3mL/kg if early presentation and more minor burn
- Fluid resuscitation is required to maintain circulation and urine output
- Measure urine output and aim for at least 0.5–1.0mL/kg/h
- If evidence of severe deep burns with extensive tissue damage resulting in haematuria, haemoglobinuria, or rhabdomyolysis a higher urine output of 1–2mL/kg/h may be desirable and aided by diuretics as well as fluid resuscitation
- The volume to be given calculated from the modified Parkland formula should be given over the 24-h period ***from the time of the burn*** and not from the time of presentation:
  - Give the first 50% of the calculated volume in the first 8h and the remaining 50% over the next 16h
- Monitor the serum electrolytes carefully and watch out for hyponatraemia that is more likely to occur in younger children
- In younger children you will also need to calculate the normal maintenance fluids they will require using standard formula then add this to the resuscitation fluids (after the initial period this maintenance fluid may be give as feeds).

Box 23.9 Example:

25kg 3-year-old with 25% full thickness burn.

Modified Parkland formula:

- 4mL × 25kg × 25% = 2500mL in 24h
- 1st 8-h period 1250mL = 156.3mL/h
- 2nd 8-h period 625mL = 78.1mL/h
- 3rd 8-h period 625mL = 78.1mL/h

Subsequent management of the child with severe burns

Surgery and dressings

- Escharotomy may be needed for circumferential burns to affected limbs, neck, or trunk
- Early surgical debridement of necrotic tissue is preferred as early grafting is associated with improved outcome
- Scrubbing of affected skin is also frequently undertaken
- A significant number of general anaesthetic episodes accumulate in a patient with severe burns—for debridement, scrubbing, dressing changes, and skin grafting

- Grafting uses either split skin grafts from the patient's own unaffected skin, donor skin grafts, or 'experimental skin'
- Blood loss during operative sessions can be large
- Ideally enteral nutrition is continued and the patient is not fasted for surgery or gas: insertion of a nasojejunal tube with post-pyloric feeding allows this.

Airway/ventilation

- Consideration should be given to early tracheostomy in a child with very large burns:
  - Fixation of an ETT may be difficult and unstable with facial burns—wiring to the maxilla or to permanent teeth is an option
  - Prolonged ventilation is often required
  - Extremely high levels of analgesia and sedation are needed in the intubated burns patient—lower levels suffice after tracheostomy
- Ventilation should follow the principles used in any patient with lung injury—HFOV may be useful in severe inhalational injury
- Practice varies widely with respect to pulmonary management after inhalational injury:
  - In adults frequent bronchoscopy is employed, not so in children
  - Various agents have been employed to suppress the inflammatory response—typically applied by nebulization or instillation
  - N-acetylcysteine, sodium bicarbonate are examples (no evidence).

Nutrition

- Early enteral feeding, ideally post-pyloric
- Aim for high calorie, high protein intake
- Indirect calorimetry very helpful as predictive energy expenditure equations are not reliable
- Supplement with parenteral nutrition if enteral feeding is not well tolerated
- Add trace element supplements—zinc, selenium, monitor levels
- If severe burns to perineum consider creation of an abdominal stoma to prevent faecal contamination (assumes abdominal wall is ok)

Antibiotics

- Do not give prophylactic antibiotics—will encourage resistant organsims
- Fever is universal after a severe burn and does not mean infection—monitor WBC and left shift, check frequent cultures
- Regular skin surveillance swabs will identify colonizing organisms but should not be treated unless suspicion of bacteremia/invasive infection
- Use narrow spectrum agent where possible
- There is no evidence to support routine line changes unless there is clear suspicion of line-related sepsis.

Miscellaneous

- Suxamethonium is best avoided from 5–150 days post burn because of the risk of severe hyperkalaemia
- There is some evidence that β-blockade may improve outcome in children after severe burns—endogenous catecholamine levels are high in this population

- Heat loss is massive through burned skin—increase ambient temperature
- Risk of stress ulceration is signifiacnt—use a drug to suppress acid production and early enteral feeding.

Smoke inhalation and carbon monoxide poisoning

Smoke inhalational injury

- Smoke inhalation is implicated in 75% of all fire-related deaths, although many of these patients will have suffered burns as well
- Signs and symptoms can take 24–36h to develop
- Mortality rate for smoke inhalation alone is 7%. This rises to 22% if carbon monoxide (CO) poisoning is simultaneously present.

Pathophysiology

There are 3 ways in which injury can occur

- Heat damage: restricted to the oropharynx as heat rapidly dissipates
- Asphyxiation resulting in hypoxia:
  - The fire consumes oxygen, which means the FiO_2 of the surrounding atmosphere is reduced to 10–12 %. This more than halves the PaO_2.
  - CO decreases the oxygen-carrying capacity of the blood further
  - Combustion of substances such as plastic, polyurethane, rubber, and paper produces cyanide gas. Cyanide causes myocardial and neurological toxicity
- Pulmonary irritation:
  - Direct irritation to the parenchyma and bronchial tree leads to activation of the inflammatory cascade, which causes wheeze, pulmonary oedema, and ARDS.

Presentation

History to note

- Whether in enclosed space—increases risk of smoke inhalation
- Time trapped in the fire
- Presence of particular materials such as polyurethane, plastic etc.

Examination

- Respiratory: soot in around nares, carbonaceous sputum, stridor, wheeze, respiratory distress, ↓air entry in atelectatic areas, respiratory failure, and hypoxia
- Cardiovascular: tachycardia, signs of shock due to SIRS from upper airways burns or other injuries
- Burns: site (especially if facial burns), % surface area, thickness
- Look for signs of other injury

Investigations

- CXR: early CXR is often normal
- Pulse oximetry: unreliable in methaemoglobinaemia
- ABG: metabolic acidosis, respiratory failure, hypoxia

- Carboxyhaemoglobin (HbCO) level:
  - Co-oximetry is available on most modern blood gas analysers
- Lactate: suggests prolonged hypoxia or secondary to cyanide/methaemoglobin
- Renal function and CK in large burns: suspicion of rhabdomyolysis
- Bronchoscopy in severe airway burns and atelectasis.

Management

- Manage airway: early intubation in facial burns due to likelihood of worsening oedema
- Protect c-spine in all cases unless precise mechanism of injury is known
- Intubate in respiratory failure: suxamethonium can be used in the immediate post-burn period
- Obtain IV access. Volume resuscitate if necessary
- Treat HbCO if present
- Initially assume HbCO in all patients, therefore treat with 100% oxygen via a non-rebreathe mask if not intubated
- In severe respiratory failure due to inflammatory response and atelectasis, consider nebulized heparin or N-acetylcysteine
- The value of repeated bronchoscopy to assess the airways and provide pulmonary toilet is not proven but is widely practised in adults
- Mechanical ventilation should incorporate a high PEEP, low tidal volume 'protective strategy', with HFOV needed in severe cases.

CO poisoning

CO is a colourless and odourless gas caused by the incomplete combustion of organic matter including fossil fuels.

Pathophysiology

CO affects the body in 2 main ways:

- Tissue asphyxia:
  - CO decreases the oxygen carrying capacity of Hb. It has a 200 × greater affinity for binding to haem than oxygen
  - CO shifts the haemoglobin dissociation curve to the left, inhibiting the release of oxygen to the tissues
  - Directly acts on the mitochondrial electron-transport chain by binding mitochondrial cytochromes. Decreases ATP and increases free oxygen radical production
- Inflammatory activation:
  - Free radicals activate inflammatory response
  - Perivascular changes cause neutrophil sequestration and activation
  - Releases reactive oxygen species that cause brain lipid peroxidation
  - Byproducts alter immunologic recognition of myelin basic protein and start autoimmune cascade against cerebral proteins causing direct damage.

Presentation

History to note

- History of exposure especially fire
- Duration of exposure
- Neurological symptoms: headache, dizziness, loss of consciousness, shortness of breath, loss of muscle control, nausea, amnesia.

Examination

- Signs of smoke inhalation
- Cherry-red skin
- Hyperthermia
- Respiratory: tachypnoea, hypoxia, crackles (non-cardiogenic pulmonary oedema), abnormally high pulse oximetry in the face of hypoxia
- Cardiovascular: tachycardia, hypo or hypertension, dysrhythmias, myocardial depression, and vasodilation
- Neurological: reduced conscious level, rigidity, brisk reflexes, hearing and visual loss, movement disturbances, seizures
- Ophthalmology: retinal discolouration, flame-shaped haemorrhages, papilloedema.

Investigations

- ABG with co-oximetry
- HbCO level (%)
- FBC—haemoglobin
- Lactate and acid–base status: correlated with degree and duration of hypoxia
- Creatine kinase—rules out rhabdomyolysis
- CXR
- Head CT scan—if evidence of cerebral damage.

Management

- Manage airway, breathing, circulation
- All patients with expected HbCO should receive 100% oxygen:
  - Half-life HbCO decreases from 320min in air to 30–90min in 100% oxygen.
- Treat burns if indicated
- Treat brain injury if indicated
- Consider hyperbaric oxygen therapy especially if HbCO is >25%, and if evidence of cerebral injury or myocardial dysfunction.

Lightning injuries

8 million lightning strikes occur each day worldwide, of which 20% strike the earth. Mortality worldwide is 1000 deaths per year (0.05 deaths per 100,000 population), with roughly 3× that many surviving a lightning strike.

Pathophysiology

- Only 3–5% of injuries are due to a direct strike. The majority of injuries are due to ground strikes nearby with spread of current or side-splash
- Each lightning flash is the equivalent to a direct counter current shock of 12–200mA. Currents of 20–50mA lead to respiratory arrest and >60mA to VF.

Presentation

Most deaths occur either due to primary cardiac arrest or hypoxia due to paralysis of respiratory muscles or failure of the respiratory centre:

- Cardiac arrest from VF or asystole (20%), myocardial dysfunction (direct current, hypoxia, or arrhythmias), arrhythmias esp. VF (10%)
- Hypoxia , respiratory arrest
- Neurological (70% of patients) with loss of consciousness , confusion, aphasia, neurological deficit (direct injury or hypoxia), transient paraplegia, spinal cord necrosis with permanent cord damage, cataracts, seizures
- Musculoskeletal (5% of patients) with muscle necrosis, rhabdomyolysis, compartment syndrome
- Renal failure and myoglobinuria
- Burns (60% of patients). Superficial burns over body, especially torso, linear superficial burn markings that are pathognomonic and occur in 30% of cases. Deep burns are rare.

Management

- Supportive therapy including cardiopulmonary resuscitation (i.e. **ABCs**)
- Treatment of respiratory depression and myocardial dysfunction with intubation and inotropes
- Active management of rhabdomyolysis and myoglobinuria may be necessary, but is rarely needed
- Development of compartment syndrome may require fasciotomies
- Cerebral protection may be required if primary or secondary CNS injury
- Burns should be treated dependent on their thickness and size.

Outcome

- Survival of cardiac arrest from lightning strike is far higher (30%) than for most other causes of cardiac arrest in children. This is even the case when there is prolonged resuscitation
- The majority of morbidity is neurological with 70% of survivors suffering some transient sequelae. Persistent neurological damage is rare
- Renal failure, compartment syndrome and ongoing cardiac abnormalities occur in <5% of patients.

Drowning and near-drowning

Definition

- ***Drowning***: death from suffocation as a result of submersion in liquid
- ***Near-drowning***: submersion episode of sufficient severity to warrant medical attention and which is not immediately fatal.

Presentation

- Second leading cause of death in childhood, ♂ >♀
- High rate of severe neurodisability in survivors.

Causes

- Outdoors: pools, lakes, rivers sea
- Domestic: baths
- >50% victims unintentionally entered water—falls, lack of supervision, lack of safety devices, alcohol
- Seizure disorder ↑risk of drowning in all water environments
- Infant /toddlers: often found submerged after a period of inadequate supervision, e.g. in bath or garden pond
- Older child, teenager, and young adult—poor decision-making:
  - Under estimate risks and over estimate their abilities
  - Alcohol may be involved, hypothermia may contribute to drowning.

Urgent management

- Resuscitation (**ABCs**): as soon as possible at the scene, effective CPR at this time will have the biggest effect on the possibility of good outcome
- Transfer to emergency department rapidly
- Limit further hypothermia
- Consider other injuries: spinal or head injury following dive into shallow water or fall.

Further management

- If return of spontaneous circulation is achieved a range of supportive measures are appropriate:
  - Active rewarming if the patient is hypothermic
  - Ventilatory support, inotropes
  - Neuroprotection to prevent secondary brain injury
  - Other individual organ support depending on injury
- Little real difference in management of salt versus fresh water drowning—most important factor is the duration of hypoxia
- ARDS: may develop in survivors
- Child protection concerns may need to be addressed.

Outcome

- Outcome poor if no spontaneous cardiac output on arrival at hospital—except good outcome from prolonged resuscitation ***may*** occur if submersion in cold water (<5°C) and patient hypothermic (central temperature <32°C)
- Other indicators of poor outcome: submersion >9min; CPR in ED; CPR >25min; fixed dilated pupils; seizures after 24h

- Favourable factors: <3 years, short submersion (<3min), conscious on arrival in hospital, pulse present on arrival in hospital, submersion ice cold water, core temperature <32°C.

The role of post-resuscitation therapeutic hypothermia is uncertain in children following cardiac arrest. Extrapolation of findings from adults post VF arrest out of hospital has resulted in therapeutic hypothermia being used in some PICUs. Trials are needed to determine whether outcomes are improved.

Cold injury

Causes of hypothermia

- Heat loss by radiation, convection, conduction, and evaporation
- Most commonly due to drowning or environmental exposure
- Less commonly secondary to injury (i.e. burns) or poisoning.

Presentation

- Normal core temperature 36.5–37°C.
- Symptoms occur <35°C; conscious level falls ~33°C; serious risk of cardiac arrest <32°C; vital signs may be undetectable <30°C.

Assessment

- Continuous measurement of core temperature is essential
- Care interpreting a sudden increase in temperature—local measures to rewarm may affect the accuracy of temperature measurement.

Management

- Rewarm. Options include:
  - External heating devices, e.g. water blanket, warm air
  - Warmed inspired gases
  - Warmed IV fluids
  - Peritoneal dialysis with warmed dialysis fluid
  - Gastric lavage with warmed saline
  - Extra-corporeal support—haemofiltration or ECLS
- Identify and treat complications/effects of hypothermia
- If core temperature <32°C and VF, raise temperature before drugs or defibrillation as VF will be refractory to treatment
- Maintain circulation with CPR until return of rhythm and output

Further management

- Intensive Care Support as necessary, directed at underlying cause
- Mild hypothermia usually has no long term sequelae
- Complications including arrhythmias, renal failure, muscle damage, and pancreatitis described following severe hypothermia.
  - Maintaining the patient at 33°C for 48h following severe hypothermia may reduce complications.

Near-hanging and choking

- Near-hanging is defined as non-judicial hanging that is not immediately fatal
- Complete (suspended above the ground) or incomplete (postural asphyxiation)
- Mechanism of injury is age dependant. In toddlers postural asphyxiation (especially in cribs) is commonest, while in adolescents attempted suicide and accidental strangulation is commonest.

Pathophysiology

- Classically death due to judicial hangings is due to disruption of the spinal cord, due to distraction of the skull from the spinal column with a C2 spinal fracture
- In near hangings (even complete) the distance of fall is normally not great enough and there are normally no cervical spine fractures
- Death is not normally due to airway compromise, but due to:
  - Venous obstruction, with cerebral stagnation and hypoxia. This causes loss of consciousness and airway compromise
  - Arterial spasm due to carotid pressure, resulting in cerebral hypoxia
  - Vagal collapse due to carotid sinus pressure and parasympathetic stimulation.

Presentation

History

- Mechanism of injury
- Intentional vs unintentional
- Loss of consciousness at scene
- Loss of cardiac output at scene.

Examination

- Respiratory: stridor, muffled voice, weak cough, respiratory distress, hypoxia
- Cardiovascular: cardiovascular compromise due to hypoxia, cardiac arrest
- Neurological: evidence of hypoxic cerebral injury, subconjunctival haemorrhages, evidence of spinal cord injury
- Musculoskeletal: abrasions, lacerations to neck, evidence of spinal column injury.

Investigations

- ABG: level of hypoxia, respiratory compromise
- Lactate
- C-spine X-ray: anterior, lateral and odontoid peg views
- CT scan neck: looking for bony injury
- MRI neck: to evaluate ligamentous injury and cord injury
- CT scan or MRI head: if evidence of cerebral injury
- Doppler vessels: if evidence of venous or arterial injury.

Management

- C-spine immobilization
- Airway management: be aware intubation may be challenging due to laryngeal injury and oedema
- Manage circulatory failure if present
- Manage hypoxic brain injury if present
- Manage spinal column/cord injury if present
- Look for evidence of other injuries and manage accordingly.

Outcome

Mortality: strangulation accounts for 2.5% of all worldwide trauma deaths. Mortality predictors are loss of cardiac output at scene, and GCS <9 at scene.

Morbidity: tracheal stenosis, spinal column injury (very rare), spinal cord injury, hypoxic brain injury, psychological trauma

Further reading

Adelson PD, Bratton SL, Carney NA, *et al.* (2003) Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents. *Pediatr Crit Care Med* **4**(Suppl): S1–S71.

NICE (2007). *Head injury: triage, assessment, investigation and early management of head injury in infants, children and adults.* NICE clinical guideline 56. National Institute for Health and Clinical Excellence, London.

Parslow RC, Morris KP, Tasker RC, *et al.* (2005) Epidemiology of traumatic brain injury in children receiving intensive care in the UK. *Arch Dis Child* **90:** 1182–7.

Stiell IG, Wells GA, Vandemheen K, *et al.* (2001). The Canadian CT head rule for patients with minor head injury. *Lancet* **357:** 1391–6. [TBI guidelines]

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Chapter 24

Infection control policies and PICU

Introduction

In the PICU it is estimated that 12% of patients suffer a healthcare associated infection (HCAI). This encompasses what is known as hospital associated or nosocomial infection. Until relatively recently there has been a degree of complacency associated with the spread of HCAIs. A change of mindset is required to reduce this:

- Infection must be viewed as a failure in patient management
- Preventing infection is the responsibility of all healthcare professionals and is integral to patient safety.

Infection control measures

Hand hygiene

This the most critical element in controlling the spread of infection. It is important that appropriately designed sinks and alcohol gel dispensers are readily available at the point of use and that an appropriate handwashing technique is used (e.g. Ayliffe–Taylor technique).

Hands must be washed:

- Before touching a patient
- Before any aseptic task
- Immediately after any exposure to body fluids (and after glove removal)
- After touching a patient and his or her immediate surroundings when leaving
- After touching any objects or furniture in the patient's immediate surroundings- even without touching the patient.

Other important areas of Infection Control Policy

- ***Design and construction***:
  - Adequate hand washing facilities
  - An environment that is easily cleaned
  - Sufficient space for patient care, and
  - Adequate provision of isolation rooms
- ***Cleanliness of the unit***
- ***Decontamination of equipment***: this is critical and items that are single-patient use must not be re-used
- ***Written guidance/policies*** on the measures needed to minimize the risk of infection to patients. Examples are:
  - Towards antibiotic resistant bacteria such as *MRSA*.
  - Policy on isolation of patients and precautions with particular infections, e.g. *varicella-zoster, pertussis*
  - Policy toward staff protection and immunization
  - Advice on what to do following a needlestick injury (including post exposure prophylaxis (PEP) if the child has HIV or is thought to be at high risk of HIV)
  - Policies specific to the paediatric setting include the use of toys on the unit
- ***Surveillance for healthcare associated infection***: these may be related to specific infection types (such as bloodstream infections) or specific

organisms (MRSA) or incorporate clinical information (ventilator associated pneumonia)
- ***Antibiotic** use* should also be monitored and audited
- All Infection Control Policies need regular review and compliance with policy needs to be audited.

The intensive care unit infection control policy can be 'wrapped up' in a structured and systematic approach known as a *care bundle*. This been shown to effectively reduce the incidence of HCAI. Care bundles use checklists and audit to regulate compliance and all recommendations should be evidence based.

Ventilator associated pneumonia (VAP)

(See 🕮 p.417.)

VAP accounts for a significant proportion of healthcare-associated infections on the PICU. VAP increases length of stay, hospital costs, and may increase mortality rate. An example of a VAP care bundle and checklist are given in Boxes 24.1 and 24.2.

Box 24.1 Example of a VAP care bundle[1]

Prevention of bacterial colonization of oropharynx, stomach, and sinuses
- Change ventilator circuit and in-line suction catheters when visibly soiled
- Drain condensate from ventilator circuit at least every 2–4h (use heated wire circuits to reduce rainout)
- Store oral suction devices (when not in use) in non-sealed plastic bag at the bedside. Rinse after use
- Hand hygiene before and after contact with ventilator circuit
- When soiling from respiratory secretions is anticipated, wear a gown before providing care to patient
- Follow unit mouth-care policy—every 2–4h

Prevention of aspiration of contaminated secretions
- Elevate head of bed 30–45°, unless contraindicated and by written order
- Always drain ventilator circuit before repositioning patient
- When possible, for children >12 years, use ETT with dorsal lumen above endotracheal cuff to help suction secretions above the cuff.

[1] Adapted from Bigham MT, Amato R, Bondurrant P, *et al.* (2009). Ventilator associated pneumonia in the pediatric intensive care unit: Characterizing the problem and implementing a sustainable solution. *J Pediatr* **154:** 582–7.

Box 24.2 Ventilator care checklist—VAP prevention

Patient Name_____ Unit Number_____

Check if completed (Y/N)

Date/Time				
Hand decontamination before & after contact with ventilator				
Ventilator circuit inspected and changed when visibly soiled				
Condensate drained at least every 4h and before turning				
In-line suction device changed when soiled				
Oral suction device stored in un-sealed plastic bag				
Mouthcare complete every 4h				
Head of bed at 30–45°				

If any answer no or unable to complete please add comments below:

Catheter-related bloodstream infection

Bloodstream infections, of which the majority are related to the presence of a IV catheter, again cause a significant number of all healthcare-associated infections on the PICU (approximately 25%).

An example of measures designed to produce a sustained reduction in catheter related blood stream infections (CR-BSIs) are shown in Box 24.3.

Comprehensive, sustained approach to reducing CR-BSIs

Box 24.3 Implemented unit-based safety culture and daily goal sheet

CR-BSI intervention

- Handwashing
- Full barrier precautions during line insertion
- Chlorhexidine (2%) cleaning of the skin
- Avoiding the femoral site
- Removing unnecessary catheters
- Education on infection control practices
- Facilitators – central-line carts, checklists, ability to stop the procedure if practices not adhered to.

Adapted from Pronovost P (2008). Interventions to decrease catheter-associated bloodstream infections in the ICU: The Keystone Intensive Care Unit project. *Am J Infect Control* **36:** S171.e1–5.

Further reading

Pratt RJ, Pellowe CM, Wilson JA, *et al.* (2007). National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England. *J Hosp Inf* **65S**: S1–S64.

Chapter 25

Immunity and infection

Introduction

For more than 150 years man has waged war on infection:

- In much of the developed world there have been profound improvements in living standards accompanied by better hygiene, cleanliness, and access to clean water.
- The advent of antibiotics meant for the first time we could actively target bacteria and thus rendered previously untreatable infections treatable.
- The introduction of childhood immunizations have reduced and, in some cases, eradicated many previously fatal infections
- Consequently, in the developed world there has been a significant reduction in mortality and morbidity from infectious disease in children
- Despite this, infectious disease is still the leading cause of death of children throughout the world
- The recognition of viruses and fungi as pathogens and the recent rise of the multiresistant organism have acted as reminders that although some battles have been won, the war against infection is far from over.

Infection may be the primary cause bringing a child to paediatric intensive care or it may supervene after admission. Either way, infection, be it community or hospital acquired represents a considerable (and potentially avoidable) economic burden to the nation's health resources.

Host response to infection

Recognizing infection (Box 25.1)

Most babies will be colonized with commensal bacteria within 24h of birth. The distinction between colonization and infection (microbial overgrowth) is one of magnitude (number of colony forming units per gram or millilitre of tissue) accompanied by clinical symptoms and signs.

Microscopy or growth of organisms in sterile sites means either infection or contamination. Sterile sites are:

- Blood
- Urine
- Lower respiratory tract (BAL or brush specimen)
- CSF
- Pleural, peritoneal fluid.

Fever

- Body temperature has a normal diurnal variation (peaks at midday and midnight):
  - Rectal temperature approximates core temperature and is 0.5°C higher than readings from mouth or ear and 1°C higher than axilla (peripheral)
  - Normal temperature depends on where it is read. Normal core temperature is 36.5–37.4°C
  - Toe: core temperature difference is a marker of perfusion but is influenced by ambient temperature (falls when warm)

- Fever is an adaptive process caused by circulating cytokines and is a sign of inflammation ***not*** necessarily infection
- Non-infective causes of fever include:
  - Systemic inflammatory response syndrome
  - Transfusion reactions
  - Neoplasms, e.g. lymphomas
  - Tissue damage, e.g. postoperative, post trauma, crush injury
  - Kawasakis disease, pancreatitis (inflammation)
  - Porphyria, thyrotoxocosis.

Fever is to be expected in the first 48h following major surgery, particularly after cardiac and major abdominal surgery. This rarely signals infection but reflects the inflammatory response to surgery. Conversely this means that postoperative infections are difficult to diagnose with certainty.

Box 25.1 Markers of infection

- White cell count:
  - Leucocytosis: usually raised in acute and chronic bacterial (rather than viral) infection
  - Neutropenia may be a sign of overwhelming infection (sepsis) and reflects neutrophil migration to areas of infection (from the circulation) and bone marrow depression. Counts vary with age.
  - Lymphocytosis: raised in acute bacterial and viral infections. Particularly in severe *Bordatella pertussis* infection
- Platelets and clotting factors. Reduced in overwhelming sepsis. Usually due to consumption (particularly at endothelial level) and dilutional secondary to fluid resuscitation
- Liver function tests. Altered transaminase and low albumin levels may reflect underlying inf:ection
- CRP: non-specific acute phase protein raised in infection/ inflammation. Acts as opsonin to aid phagocytosis. Often raised in bacterial rather than viral infections.
- Procalcitonin- probably a more specific indicator of bacterial infection than CRP (i.e. less influenced by inflammation), making postoperative bacterial infection easier to diagnose.

The immune system

- The immune system defends the body against infection and consists of layered defences of increasing specificity.
- Physical barriers such as skin prevent pathogens from entering the body. If a pathogen breaches these barriers, the innate immune system provides an immediate non-specific response
- The adaptive immune response, activated during infection, results in specific immunological memory, improving host defence in the event of a future encounter with the same pathogen

Components of the immune system (Table 25.1)

Table 25.1 The immune system

Innate immune system	Adaptive immune system
• Non-specific response • Exposure leads to immediate maximal response • Cell-mediated and humoral components • No immunological memory	• Pathogen and antigen specific response • Lag time between exposure and maximal response • Cell-mediated and humoral components • Exposure leads to immunological memory

Adapted from Janeway CA and Travers P (2005) Immunobiology: the immune system in health and disease (6th edn) © 2005, from Janeway, CA *et al. Immunobiology 6th edn*, reproduced by Garland Science/Taylor and Francis Ltd.

Innate immunity

Microorganisms which enter the body will encounter cells and humoral components of the innate immune system. Innate immune defences are non-specific. The innate immune response does not confer long-lasting immunity against a pathogen.

Inflammation

- The first response of the immune system to infection or injury
- The symptoms of inflammation are redness and swelling, caused by ↑blood flow into a tissue
- Inflammatory mediators are released by injured or infected cells and recruit immune cells to the site of infection
- When the inflammatory response spills over into the general circulation the 'systemic inflammatory response syndrome' (SIRS) results (see 📖 Chapter 26).

Complement system

- Complement is the major humoral component of the innate immune response.
- Complement is an opsonin that is deposited on the surface of microorganisms:
  - Thus enabling immune cells to bind to the organism prior to phagocytosis
  - Complement kills microorganisms directly via cell lysis
  - Acts as a chemotactic signal, enhancing recruitment of immune cells.

Cellular components of the innate system

The cells of the innate system comprise:

- Neutrophils: important for phagocytosis of bacterial and fungal pathogens
- Macrophage/monocytes: responsible for killing of intracellular pathogens, e.g. mycobacteria and fungi
- Natural killer cells (NK): these are lymphocytes with the ability to kill virus infected cells
- The vascular endothelium is also an important part of the innate immune response, directing inflammatory cells to sites of injury and inflammation.

Adaptive immunity

The adaptive immune system is concerned with developing immunological memory consisting of:

- Antigen-specific memory T and B lymphocytes (cellular compartment)
- Specific antibodies (humoral and mucosal compartments).

Immune function disorders

Children with primary immunodeficiencies (Table 25.2) and ↑susceptibility to infection present to PIC with infection and organ failure. Particularly:

- Overwhelming bacterial sepsis and shock
- Interstitial pneumonitis.

Infants

Often present with severe combined or T-cell immune deficiency usually present with:

- Interstitial pneumonitis due to:
  - *Pneumocystis jerovici*
  - *Cytomegalovirus (CMV)*
  - *Respiratory syncytial virus (RSV)*
  - Disseminated enteroviral infection
  - Invasive fungal infection
  - Severe viral infections including *Epstein–Barr virus (EBV)*
- Leucocyte adhesion deficiency may also present in early life with severe bacterial infections.

Children from 6 months and 5 years

After placentally transferred maternal IgG has declined, children are more likely to have an antibody disorder.

- Patients with antibody deficiencies, complement deficiency, or asplenia may present with infections due to encapsulated bacteria such as
  - *Haemophilus influenzae* type B
  - *Neisseria meningitides*
  - *Streptococcus pneumonia*
- Typically these infections affect the chest, sinuses, and ears (sinopulmonary infections), but other bacterial infections may include meningitis and septic arthritis/osteomyelitis. Repeated infections can lead to organ damage, particularly bronchiectasis.

Children requiring admission to intensive care for a first infectious insult are unlikely to have an underlying immune defect. However, if the infection is severe, unusual (e.g. *Pneumocystis jerovicii*) or if there is a history of recurrent infections, GI symptoms, or failure to thrive, the child should be screened for primary and secondary immunodeficiency.

Diagnosis

Immunology

Immunological investigations are always best performed after discussion with a paediatric infectious disease and immunology. Bear in mind that many investigations require immediate processing. Some tests are difficult to interpret during acute illness or if blood products have been administered and are sometimes best deferred until after PICU discharge.

Management

- General supportive treatment, including management of airway, breathing, and circulation
- Specific treatment and prophylaxis of infection (should be determined in consultation with paediatric infectious diseases and paediatric immunology departments)
- Immunological interventions (should be determined in consultation with paediatric immunology team—see Table 25.3)
- Curative treatment—following acute episode, e.g. bone marrow transplantation where appropriate.

Table 25.2 Primary immunodeficiency syndromes*

Deficiency syndrome	Abnormality	Defect	Susceptibility to infection
Severe combined immune deficiency	Various	Absent T and B cells	Fungal, bacterial and viral infection causing recurrent *Candida* infection, chronic diarrhea, failure to thrive or interstitial pneumonitis
DiGeorge syndrome	Thymic aplasia, associated with 22q deletions (CATCH-22), 10p deletions or CHARGE association	Variable T and B cell deficiency	Fungal, bacterial and viral infection

Table 25.2 Primary immunodeficiency syndromes* (*Continued*)

Deficiency syndrome	Abnormality	Defect	Susceptibility to infection
MHC Class I deficiency	TAP mutations	No CD8 T cells	Viruses
MHC Class II deficiency	Unknown	No CD4 T cells	Fungal, bacterial and viral infection
Wiskott–Aldrich syndrome	X linked: faulty WASP gene causing thrombocytopenia, eczema, and recurrent infections usually affecting the sinopulmonary system.	Reduced polysaccharide antibody responses	Encapsulated and intracellular bacteria
Common variable combined immunodeficiency	Unknown: MHC linked	Defective antibody production	Extracellular bacteria
X-linked hypogamma-globulinaemia	Loss of Btk tyrosine kinase	No B cells	Extracellular bacteria, viruses
X-linked hyper IgM syndrome	Faulty CD40 ligand	No isotype switching	Extracellular bacteria
IgA/IgG deficiency	Unknown: MHC linked	No IgA synthesis	Recurrent sinopulmonary infections
Phagocyte deficiencies	Numerous, including leucocyte adhesion defects, defects of phagocytosis and chronic granulomatous disease	Loss of phagocyte function	Extracellular bacteria, fungal infection
Congenital neutropenias	Various, including congenital and cyclical neutropenia and Schwachmann-Diamond syndrome	Reduced/absent neutrophils	Extracellular bacteria, fungal infection

(*Continued*)

Table 25.2 Primary immunodeficiency syndromes* (*Continued*)

Deficiency syndrome	Abnormality	Defect	Susceptibility to infection
Complement deficiencies (including MBL deficiency)	Numerous	Loss of complement components	Extracellular bacteria esp. *Neisseria* spp.
Natural killer cell defect	Unknown	Loss of NK cells	Herpes viruses
X linked lymphoproliferative syndrome	X-linked—mutation in T cell regulatory protein SAP	EBV triggered lymphoproliferative disease, EBV triggered haemophagocytic syndrome	EBV
Ataxia-telangiectasia	Chromosome breakage disorder	T cells reduced	Recurrent sinopulmonary infections

*Adapted with permission from Janeway CA, Travers P. (1997) *Immunobiology – the Immune System in Health and Disease*, 3rd edn. Churchill Livingstone, London.

Table 25.3 Possible immunological interventions on PICU

Infection/underlying defect	Possible intervention
Neutropenic sepsis	G-CSF, granulocyte infusions
Sepsis with neutrophil defect, e.g. CGD	Interferon-γ, G-CSF
Sepsis in complement deficiency	Fresh frozen plasma
Immunoglobulin deficiency with bacterial infection	Intravenous immunoglobulin (IVIG)
Viral infection in immunoglobulin deficient patients	IVIG, Anti-CD20 antibody (if EBV infection)
Cell-mediated immune deficiency—viral infection	Adoptive immunotherapy with specific cytotoxic T lymphocytes
Cell-mediated immune deficiency—opportunistic infections	Interferon-γ
Cell-mediated defects	Bone marrow/T-cell infusion from matched sibling donors
Lymphoproliferative disease	EBV cytotoxic T lymphocytes, anti-CD20 antibody

Acquired immunosuppression

The immune system may become suppressed by a variety of different factors including disease states, trauma, and medical treatments. *Secondary immunodeficiency is common in PIC patients.*

Causes of secondary immunodeficiency

- Associated with intercurrent illness
- Malnutrition
- Drugs : immunosuppressive (e.g. steroids) and cytotoxic chemotherapy
- Malignancy
- GI and metabolic disease
- Post splenectomy

Immunosuppression from intercurrent illness

- Stress such as that which occurs after trauma, burns, and surgery, can lead to suppression of immune function. In full-blown form, these responses can lead to SIRS
- Infection itself can also lead to immunosuppression through the nonspecific effects of stress discussed earlier.

Immunosuppression from pre-existing condition

- Some micro-organisms, e.g. HIV can suppress the immune response
- Other causes of secondary immunodeficiency include malnutrition, particularly protein energy malnutrition and trace element deficiencies
- Malignancy and metabolic disorders can also depress immune function
- Excessive plasma protein loss as in nephrotic syndrome, protein losing enteropathy, or chylous leaks can lead to very low immunoglobulin levels
- Patients with hyposplenism are susceptible to overwhelming sepsis particularly with *Pneumococcus* and other capsulated organisms.

Iatrogenic immunosuppression

- Corticosteroids have a range of immunosuppressive effects
- Chemotherapy and radiotherapy also affect predominantly T cells but can also cause neutropenia leading to:
  - Fungal infections
  - Pyogenic bacterial infections
  - Viral infections
  - Pneumocystis
  - Intracellular bacteria such as *Mycobacteria* and *Salmonella* spp.
- Purely immunosuppressive agents, e.g. ciclosporin and tacrolimus, lead predominantly to problems with T-cell pathogens.

'At risk' as a consequence of PICU treatment

- Indwelling arterial and venous catheters bypass the physical barrier of the skin and may become infected, commonly with coagulase-negative staphylococci.

- Tracheostomized patients commonly become colonized or infected with *Pseudomonas* or *Staphylococcus aureus*.
- Pressure areas, resulting from prolonged immobility, may break down resulting in localized or systemic infections.

Management of the child with secondary immunodeficiency

- Recognition that a child is at risk of infection
- Attention to routine procedures for minimizing nosocomial infection, e.g. hand washing, barrier nursing when appropriate (see also 📖 p.532)
- Early aggressive treatment for suspected infection, whether viral, bacterial, or fungal
- Prophylactic antimicrobials, e.g. antifungals in patients with neutropenia, penicillin in hyposplenic patients, and cotrimoxazole in those with persistent CD4 lymphopenia
- Immunizations, e.g. pneumococcal and meningococcal vaccination in splenectomized individuals and varicella vaccine in patients prior to solid organ transplantation
- IVIG as prophylaxis or treatment is of uncertain value in secondary immunodeficiency.

Human immunodeficiency virus infection

Worldwide over 40 million people are infected with HIV, with 640,000 children newly infected in 2004, the majority living in sub-Saharan Africa. By contrast, paediatric HIV infection is relatively rare in Europe and North America, with only about 1500 cases reported to the National Survey of HIV in Pregnancy and Childhood in the United Kingdom.

Clinical features of children presenting with HIV

HIV is a human retrovirus:

- Principally infects CD4-positive T-helper lymphocytes (CD4 cells)
- Generally infects children in the perinatal period (mother-to-child transmission). Most children acquire infection perinatally
- Destruction of CD4 cells leads to ↑susceptibility to infection
- The clinical manifestations of HIV are due to infection and the direct effects of HIV
- Up to 20% of children born with HIV infection present with severe symptoms or die in infancy
- This pattern of early progression of disease in infancy, with severe immunodeficiency and opportunistic infection, leads to the majority of admissions of HIV infected children to PICU.

Presentation to PICU

The most common reason for PICU admission is acute respiratory failure (Box 25.2), which usually presents in previously undiagnosed, rapidly progressing infants.

- The most common cause is Pneumocystis pneumonia (PCP), caused by *Pneumocystis jirovecii* (previously known as *P. carinii*). This usually occurs in infants from around 3 months of age and presents as progressive

respiratory distress leading eventually to hypoxic respiratory failure. This presentation is commonly misdiagnosed as bronchiolitis
- Respiratory failure may also present in older children, or in those already known to have HIV, especially if their disease is advanced
- Failure of any organ system may occur in HIV, resulting in PICU admission. Some reasons for PICU admission are listed in Box 25.3
- Older children who present with HIV may have had mild symptoms for many years without HIV being diagnosed. They may present with more serious infection (e.g. pneumonia, meningitis, osteomyelitis)
- Children may also present with more severe manifesations of common childhood infections, such as chickenpox
- Lymphoid interstitial pneumonitis (LIP) occurs in up to 20% of children with HIV, and is a condition characterized by chronic lymphoid infiltrates within the lungs. It is often symptomless, being only evident on chest radiography. Children with LIP usually also have hepatosplenomegaly, lymphadenopathy, and often parotitis.

Diagnosis of HIV

- Any child with suspected immunodeficiency should have HIV infection ruled out
- <18 months—HIV serology in the child may reflect passive transfer of HIV antibody from an infected mother and may not necessarily reflect infection in the infant
- >18 months, serology represents true infection
- The gold-standard test is HIV DNA PCR in the child's blood
- Investigation of the cause of disease depending on symptomatology.
- FBC: haemoglobin (anaemia), neutrophils (may be low), platelets (thrombocytopenia)
- CD4 lymphocytes
- Liver function and renal function tests are often deranged
- For PCP, non-bronchoscopic BAL and Grocott stain of secretions is required.

Management

- The presenting complication should be treated, e.g. antibiotics
- Supportive PICU care for organ failure

Box 25.2 Respiratory problems in HIV

- Respiratory problems are common in HIV, often characterized by dry cough and progressive breathlessness and hypoxaemia. Causes range from persistent viral pneumonitis, e.g. RSV, influenza, CMV through bacterial pneumonia to TB and lymphoid pneumonitis.
- PCP is caused by *Pneumocystis jirovecii* (previously *P. carinii*) which is an opportunistic unicellular fungal pathogen. CXR show diffuse bilateral interstitial infiltrates and effusions are rare. Organisms can be seen with Grocott stain done on BAL or lung biopsy. Treatment is with high-dose co-trimoxazole IV or pentamidine IV (if resistant). Steroids improve outcome in adults but CMV needs to be excluded before starting them in children.

Box 25.3 Presentation to PICU with HIV

Respiratory
- PCP
- CMV pneumonitis
- Pneumonitis due to common respiratory viruses (respiratory syncytial virus, influenza, parainfluenza, adenovirus)
- Bacterial pneumonia
- TB
- LIP (rarely)
- Airway obstruction.

Cardiovascular
- Cardiomyopathy.

Neurologic
- HIV encephalopathy
- Encephalopathy due to other causes
- Bacterial meningitis
- Cryptococcal meningitis
- Cerebral toxoplasmosis.

Gastrointestinal
- HIV enteropathy
- Gastroenteritis
- Acute abdomen
- Hepatitis and liver failure
- Pancreatitis.

Renal
- HIV nephropathy
- Renal failure
- Hyponatremia

Severe infection
- Sepsis
- Disseminated mycobacterial infection
- Disseminated varicella

Immune reconstitution

Iatrogenic
- Complications of antiretroviral drugs

Malignancy
- Lymphoma
- Kaposi's sarcoma
- Investigations.

Outcome

- Since the advent of effective combination antiretroviral therapy in 1997, both mortality and morbidity for children with HIV have altered dramatically.
  - Mortality declined from 9.3 per 100 child years in 1997 to 2 per 100 child years in 2001–2002
  - Progression to AIDS also declined significantly as have admissions to hospital
- Infants are the only group in which there has been little improvement in outcome. Infants present with severe disease before antiretroviral therapy can begin. This emphasizes the importance of antenatal diagnosis of maternal HIV, to enable interventions to reduce the risk of perinatal infection (e.g. antiretroviral therapy, planned Caesarean section, and avoidance of breastfeeding).

Nosocomial infection

Nosocomial infections (NIs) or healthcare associated infection (HCAI) are caused by organisms acquired while the patient is hospitalized (see 📖 Chapter 24):

- The PICU is one of the most important and common hospital locations for the development of NI (see Box 25.4)
- Children <5 years of age, particularly those <1 year, have the highest incidence of NI.

Risk factors

- Invasive procedures and devices
- Immune suppression due to:
  - Young age
  - Underlying disease
  - Chronic stress
  - Steroid use
  - Lack of mobility
- ↑physical contact between patients and healthcare workers
- Frequent and prolonged use of broad-spectrum antibiotics allows selective pressure on microbes that facilitates the development or selection of drug-resistant organisms, which are more difficult to treat and control
- Parenteral nutrition
- Antacid use (histamine receptor-2 blockade).

The overall mortality attributable to NI in the PICU is estimated to be between 10–15%. Patients with NI have an increased risk of death. It is believed that at least 1/3 of all NIs could be prevented through stringent implementation of hospitals' infection control programmes.

Box 25.4 NIs in PICU

Most frequent NIs in PICU are:
- Primary bloodstream infections
- Pneumonia
- Urinary tract infections
- The mean overall rate is around 6 infections per 100 patients, or 14 per 1000 patient-days.

The most common organisms isolated from PICU-acquired NI are:
- Coagulase-negative staphylococci
- Enterococci
- *Staphylococcus aureus*
- *Enterobacter cloacae*
- *Candida* spp.
- *Pseudomonas aeruginosa*
- *Klebsiella* pneumonia
- *Acinetobacter* spp.

Definitions and diagnosis

- NI is traditionally defined as any infection not present or incubating at the time of the patient's admission. Differentiation between microbial colonization and infection is vital to reach a proper diagnosis and avoid unnecessary use of antimicrobial treatment. A pragmatic definition may be: infection diagnosed >48h after hospital admission
- Because patients on PICU are subjected to multiple invasive procedures and artificial devices (e.g. vascular lines, pressure-monitoring transducers, urinary tract catheters, intracranial pressure sensors, dialysis devices, respiratory therapy equipment), clear definitions are critical to diagnose infection rather than colonization
- Potential catheter-associated bloodstream infections should be evaluated with a minimum of 2 blood cultures taken before institution of initial or new antimicrobial therapy, including at least 1 blood sample drawn by venepuncture and another obtained through the central line.

Antimicrobial management

Organisms causing NI depend on:
- Prevalent organisms
- Antimicrobial susceptibility patterns.

Both of which are particular to each PICU.
- Empiric antimicrobial choice will vary from unit to unit but depend on:
  - Severity of clinical disease
  - Type and site of infection
  - Nature of the underlying morbidity
  - Knowledge of the relative frequency and local susceptibility patterns of hospital-acquired pathogens
- 'Blind therapy' should cover:
  - Gram-positive bacteria including coagulase-negative staphylococci, enterococci, and MRSA (if common)
  - Gram-negative bacteria, including *Pseudomonas*

- Vancomycin combined with piptazobactam, ceftazidime, or meropenem is a reasonable choice if 'blind antibiotics' are indicated
- Empiric antifungal therapy can be initiated in situations in which suspicion of fungemia is very high (i.e. a severely ill patient who is colonized with *Candida* or a neutropenic subject who is not responding to ongoing broad spectrum therapy)
- Once culture information becomes available, treatment can be tailored to specific pathogens isolated, or discontinued if no infection is identified. This is essential to avoid prolonged use of unnecessary antibiotics that may lead to ↑resistance among the nosocomial pathogens in the PICU.

Preventive measures

- Important general principles for reduction of NI within PICUs include avoidance of patient crowding, adequate staff-to-patient ratios, and optimal methods of infection control
- There is currently not enough evidence to recommend the use of a selective decontamination antibiotic policy.

1. Sinusitis
2. Intravascular catheter infection
3. Wound infection
4. Pneumonia empyema
5. Endocarditis pericarditis pericardial effusion
6. Acalculous cholecystitis
7. Perforated ulcer perforated bowel/infracted bowel pancreatitis necrotizing enterocolitis
8. Sanitary towel/tampon
9. Urinary tract infection
10. Deep vein thrombosis

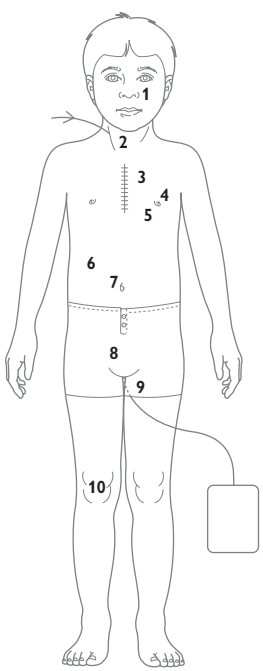

Fig. 25.1 Common causes of nosocomial fever in ICU.

Meningitis/meningoencephalitis

Meningitis and meningoencephalitis may be caused by bacterial or viral infection.

Bacterial meningitis

Infection is acquired from:

- In neonates via
  - The maternal placenta: *Listeria monocytogenes*
  - The maternal vagina: Group B *streptococcus*, *Escherichia coli*
- The community: *Streptococcus pneumoniae*, *Neisseria meningitidis*
- (Rarer causes of neonatal meningitis may also include staphylococci, enterococci, and viridans streptococci).

In countries with effective vaccination policies against *Haemophilus influenzae* type b, *Streptococcus pneumoniae* and *Neisseria meningitidis*, the epidemiology of childhood meningitis is changing, with most cases now being caused by organisms or strains not covered by the vaccines.

Aseptic meningitis

Aseptic meningitis refers to meningitis where no bacteria are isolated. Viruses are the commonest causes of aseptic meningitis:

- Enteroviruses: the commonest cause, being more frequent in the summer and early autumn (echovirus, coxsackie, polio)
- Less frequent viral causes include adenovirus, mumps, measles, Epstein–Barr virus (EBV), and arbovirus

Other causes include:

- *Mycoplasma pneumoniae*, Lyme disease, cat-scratch disease, *Chlamydia psittaci*, and leptospirosis
- Fungi (e.g. *Cryptococcus*, *Candida albicans*, coccidioidomycosis, aspergillosis, histoplasmosis, and mucormycosis) are seen in immunosuppressed children.

Noninfectious causes of aseptic meningitis include

- Spinal anaesthesia
- Chemicals injected into the subdural space for diagnosis or therapy
- Intracranial bleeding
- Vasculitides
- Cerebral neoplasm
- Kawasaki disease can also present with CSF pleocytosis.

Acute meningoencephalitis

Acute meningoencephalitis can be differentiated from aseptic meningitis by the presence of severe disturbances of consciousness, but symptoms overlap. Acute meningoencephalitis should also be differentiated from non-infectious encephalopathies (e.g. metabolic, vascular, demyelinating disease, Reye syndrome):

Acute meningoencephalitis in children include

- Herpes simplex virus 1 and 2 (most common in UK)
- Enterovirus
- Mycoplasma pneumonia

- Varicella zoster, EBV, adenovirus, and influenza virus
- Arboviruses are major causes of meningoencephalitis in many areas of the world and should be routinely screened for in endemic areas
- Rarer causes include TB and rabies.

Pathogenesis

Usually bacteria gain access to the CSF via:

- Nasopharynx
- Bloodstream
- Leptomeninges
- Fractures
- Neurosurgical procedures (e.g. CSF shunts)
- Cochlear implants
- Rupture of an intracranial abscess.

The local inflammatory response results in an alteration in the CBF, vasculitis, obstruction to CSF outflow and reabsorption, all leading to an increase in ICP.

Viral infection may cause meningitis, meningoencephalitis, or encephalitis. Differentiation from bacterial infection of the CNS is made on the basis of signs and symptoms, including clinical epidemiology and CSF changes. Clinical symptoms consistent with meningeal involvement are milder but overlap with those of bacterial infection, whereas in meningoencephalitis, the cerebral symptoms and signs predominate with variably associated meningeal involvement.

Clinical features

Meningitis/meningoencephalitis leading to PICU admission is often associated with complications and poor outcome.

Clinical features vary:

- In infants diagnosis can be particularly difficult:
  - Bulging fontanelle, neck stiffness (often absent)
  - Fever, lethargy, irritability, apnoea, and poor handling
  - Seizures with slow recovery and coma occur
- In the older children:
  - Fever, headache, and vomiting at an early stage
  - Irritability, photophobia, altered mental state, and neck stiffness later on
  - Focal neurological signs,seizures and coma occur
  - Kernig's and Brudzinski's signs are often absent in young children
- At any age, signs of systemic sepsis or shock may be present:
  - Tachycardia
  - Poor perfusion
  - Hypotension
  - Tachypnea
  - Purpura, or petechiae.

Diagnosis (Table 25.4)

Bacterial meningitis

- The diagnosis of bacterial meningitis is confirmed by recovering bacteria from the CSF
- Lumbar puncture (LP) invariably has to be postponed due to the risks of tentorial herniation (Box 25.5)
- Gross elevation of inflammatory markers in the serum, such as CRP, may be helpful for diagnosis.

Viral meningitis/encephalitis

- Clinical features vary from mild focal neurological symptoms and signs to severe generalized encephalopathy (coma). Diagnosis particularly in meningoencephalitis can be very difficult.

Box 25.5 Lumbar puncture (LP)

Positive results from CSF obtained from LP represents the gold standard for a diagnosis of meningitis. Unfortunately many patients with bacterial meningitis or conditions mimicking it have raised ICP. If there is suspicion of raised ICP then LP should be deferred until raised ICP can be excluded.

Contraindications to LP are:

- Signs or suspicion of raised ICP
- Coagulopathy
- Cardiovascular instability
- Infection at LP insertion site.

Table 25.4 Diagnosis of meningitis

	Cerebrospinal fluid	Notes
Bacterial meningitis	Cloudy,turbid 100–>1000 polymorphs/mm^3 Low glucose <1/2 plasma High protein <1.5g/dL	Oral antibiotics can make diagnosis difficult If bacteria not cultured perform rapid antigen PCR
Tuberculous meningitis	Fibrinous 100–500 mononuclear cells (mainly lymphocytes)/mm^3 Very low glucose <1/2 plasma Very high protein 1–5g/dL	Mantoux up to 60% +ve Low sensitivity for culture and PCR RAS available CXR: 1° focus 50–90% CT/MRI meningeal enhancement, hydrocephalus and infarction Treat if clinically suspicious

Table 25.4 Diagnosis of meningitis (*Continued*)

	Cerebrospinal fluid	Notes
Viral meningitis	10–1000 and mononuclear/mm^3 (early in illness can be >1000 neutrophils/mm^3) Normal glucose >1/2 plasma Normal or mildly elevated protein<1g/dL	Viral antigen detectable Viral specific antibodies in CSF
Meningoencephalitis	Normal–>10 mononuclear/mm^3 Normal-low glucose Normal-high protein (up to 6g/dL)	PCR of CSF can detect virus or *Mycoplasma* CT scan, MRI, or EEG may aid in diagnosis. Brain biopsy may be necessary

Management (Table 25.5)

Antimicrobial therapy (Box 25.6)

- Early diagnosis and appropriate parenteral antimicrobial therapy are essential. The specific choice of antibiotics depends on the age of the patient, the likely cause, local epidemiology, and antibiotic sensitivities
- In infants <3 months old, a combination of ampicillin/amoxicillin (<7 days old: 60mg/kg 12-hourly; 7–21 days: 60mg/kg 8-hourly; >21 days 50mg/kg 6-hourly IV) and ceftriaxone (80mg/kg once daily IV) or cefotaxime (<7 days old: 50mg/kg 12-hourly; 7–21 days: 50mg/kg 8-hourly; >21 days: 50mg/kg 6-hourly IV)
- After age 3 months, treatment with ceftriaxone (80mg/kg once daily or 2–4 g once daily IV) or cefotaxime (50mg/kg 6-hourly IV) alone is adequate. If there is suspicion of cephalosporin-resistant *Pneumococcus*, or in cases where LP has been deferred, addition of vancomycin or rifampicin should be considered
- If TBM is considered possible, anti-TB therapy with at least 4 drugs (isoniazid, rifampicin, pyrizinamide, and ethambutol) should be started empirically
- The duration of antibiotic therapy depends on the infecting organism-Meningococcal meningitis is treated for 7 days, Hib meningitis for 10 days, and pneumococcal meningitis for 14 days
- If viral meningoencephalitis is considered, empirical aciclovir (1500mg/m^2/day tds) should be commenced
- Antibiotics should always be started when meningitis is suspected, and the treatment modified when results from the LP (when judged safe to perform) are available. Negative CSF cultures should prompt a search for other treatable causes (e.g. TB, *Mycoplasma*, Lyme disease), and a 2nd LP may be necessary. In cases where viral infection is confirmed, antibiotics can be stopped. Fungal meningitis is treated with amphotericin.

Table 25.5 Treatment of meningitis

Diagnosis	Age	Treatment	Notes	Duration of treatment
Bacterial	<3 months	Ampicillin/ amoxicillin and cefotaxime/ ceftriaxone	If there is a suspicion of cephalosporin-resistant *Pneumococcus* consider adding vancomycin or rifampicin	*Neisseria menigitidis*: 7 days. *Haemophilus influenza B*: 10 days. *Strep. pneumonia*: 14 days
	>3 months	Cefotaxime/ ceftriaxone Consider steroids (Box 25.7)		
Tuberculous		Isoniazid Rifampicin Pyrazinamide Ethambutol Steroids (Box 25.7)	Consult with infectious disease/ microbiology	Up to 1 year (2 months for pyrazinamide, ethambutol)
Viral	<1 year	Aciclovir 60mg/kg 8-hourly	Consult with virologist	3 weeks
	>1 year	1500mg/m^2/day Steroids		

Box 25.6 Antiviral therapy

- Aciclovir has changed the previously, often fatal, course of HSV encephalitis.
- There should be no delay in starting this treatment whenever HSV is suspected.
- The dose of aciclovir is 60mg/kg per day, given at 8-hour intervals, for 10 days in infants <1 year or 1500mg/m^2/day for older children.

Box 25.7 Steroids

- Early use of dexamethasone has been shown to reduce risk of hearing loss in children with Hib meningitis and to improve outcome in adults with pneumococcal meningitis
- The role of steroids in the treatment of other types of meningitis in children is less clear but we recommend its use in all bacterial meningitis
- Dexamethasone must be administered with or before the 1st dose of antibiotics to get maximum benefit. Therapy should be discontinued if the patient does not have bacterial meningitis. The recommended dose is 0.15mg/kg every 6h for 4 days or 0.4mg/kg every 12h for 2 days.

Complications

Cerebral oedema

Raised ICP is invariable in bacterial meningitis and may result in

- Coma
- Brain stem dysfunction
- Death.

Seizures

- Convulsions that occur in the earlier stages of meningitis are usually generalized, and have less prognostic significance than those occurring later
- Brain swelling, diffuse ischemia, cerebral inflammation, hyponatraemia, subdural effusion, or focal infarction may cause seizures in meningitis.

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) (see also 📖 p.234)

Fluid management is complex with competing demands for fluid restriction and circulatory support—attention to detail is necessary to control plasma sodium and maintaining oxygen delivery to the brain

Subdural effusion

- Up to 50% of children with meningitis develop subdural effusions
- Subdural effusions usually occur several days after the onset of illness, but they may be present from admission
- They often resolve spontaneously
- However, if the effusion is large or associated with seizures or focal signs, or if there is raised ICP, then surgical drainage should be considered.

Obstructive hydrocephalus

- Obstructive hydrocephalus occurs when pus in the ventricles blocks the outflow of CSF, and is more frequent in small infants
- Communicating hydrocephalus is caused by inadequate absorption of CSF, and it may develop >2 weeks after the onset of illness
- Patients with tuberculous meningitis (TBM) often have signs of hydrocephalus on presentation

Meningococcal disease

Meningococcal infection remains a major health problem in children, with a significant mortality and morbidity. Prompt recognition and aggressive early treatment are the only effective measures against invasive disease. This requires immediate administration of antibiotic therapy, and the recognition and treatment of patients who have complications such as shock, raised ICP, or both.

Epidemiology

Approximately 10% of the population carry meningococci in the upper respiratory tract at any time, with higher rates amongst teenagers and young adults. Disease usually occurs after colonization.

Risk factors for disease include
- Younger age
- Winter or dry season
- Close contact with a carrier or case
- Moving into new communities
- Active or passive smoking
- Exposure to respiratory infection.

Factors increasing susceptibility and severity of disease include
- Complement deficiency
- Hypogammaglobulinaemia and hyposplenism
- Variations in cytokine responses
- Variation in coagulation pathway control.

Of children who progress to invasive meningococcal disease
- 30–50% have meningitis alone (mortality 5%)
- 7–10% have features of septicaemia alone (mortality 5–40%)
- 40% present a mixed picture of meningitis with septicaemia.

Clinical features

The classical presenting features of meningococcal disease include
- Fever
- Characteristic haemorrhagic rash
- Meningitis
- Septicaemia
- Early, less-specific features of sepsis such as leg pain, cold hands, and feet and abnormal skin colour are commonly reported.

Symptoms and signs of meningitis

In patients with meningococcal meningitis the following symptoms and signs predominate
- Headache, fever, vomiting, photophobia, neck stiffness, positive Kernig's (when hips and knees are flexed, subsequent knee extension is painful), and Brudzinski's signs (involuntary lifting of legs when the neck is flexed), and lethargy
- In infants and younger children, poor feeding, irritability, a high pitched cry, and a bulging fontanelle are typical findings
- Seizures may occur in up to 20% of cases.

Symptoms and signs of septicaemia

Meningococcal septicaemia may present with:
- Fever, rash, headache, flu-like symptoms (especially myalgia), vomiting, or abdominal pain
- Clinical signs of shock: tachycardia, poor peripheral perfusion, tachypnoea, oliguria, confusion, and hypotension may be present
- Rarely, invasive disease may take the form of focal infection, such as arthritis, pneumonia, conjunctivitis, pericarditis, or endophthalmitis.

Rash

The presence of a characteristic haemorrhagic rash is highly variable; however, most proven cases develop a rash at some stage in their illness. Typically this is:
- Haemorrhagic (petechial or purpuric)

- ~15% of patients will present with an atypical, blanching, maculopapular rash, which may evolve into the more typical non-blanching form over anything from minutes to hours
- <10% never develop a rash and their presentation is indistinguishable from other causes of sepsis
- Petechial rash is usually due to enterovirus or other viral infection
- Rarer diagnoses such as Henoch–Schönlein purpura, connective tissue disorders, haematological disorders (e.g. protein C or S deficiency), platelet disorders (e.g. ITP), drug effects, bone marrow infiltration, etc.), and trauma (including NAI), need to be considered. However, a significant minority (around 10%) will turn out to have meningococcal infection

Fever and a non-blanching haemorrhagic rash should always prompt a serious consideration of the diagnosis of meningococcal disease and lead to empiric antimicrobial therapy unless another diagnosis is apparent.

Diagnosis

- Clinical features.

Laboratory

- Elevated WCC or neutropenia
- High CRP
- However, these acute phase reactants may take 12–24h to respond following the onset of meningococcal infection and may be relatively normal early in the course of the disease

Microbiological confirmation is important for guiding public health management for exclusion of other possible causes.

Cultures include:

- Blood
- Throat secretions
- CSF (in the absence of contraindications)
- Skin lesion aspirates may confirm a diagnosis and allow for antimicrobial sensitivity testing
- PCR from blood, skin, or CSF is now routinely used to detect meningococcal DNA.

Progression of disease

Meningococcal disease may progress rapidly, even after appropriate antimicrobial treatment has commenced. All children admitted to hospital with suspected meningococcal disease should be closely monitored for signs of deterioration.

Outcome may critically depend on the prompt recognition of 2 important complications

- Shock (Box 25.8)
- Raised ICP.

Box 25.8 The presence of shock

Shock in meningococcal disease is multifactorial and results from:
- Hypovolaemia caused by capillary leak syndrome
- Myocardial dysfunction
- Vasodilatation
- Impaired cellular metabolism.

Patients present with:
- Cold peripheries, prolonged capillary refill time
- Tachycardia, hypotension
- Impending or established respiratory failure
- Oliguria and renal dysfunction leading to renal failure
- In the most severe cases, ischaemia of the skin or even a whole limb may occur
- Despite severe shock, preservation of brain perfusion is often present until decompensation occurs, A child's relatively alert state may make observers underestimate the degree of cardiovascular collapse. Signs of cerebral impairment with irritability or reduced level of consciousness indicate a loss of cerebral vascular homeostasis and reduced brain perfusion
- Development of hypotension signifies a failure of compensatory mechanisms. It should be remembered that the diagnosis of shock in children is not dependent on the presence of arterial hypotension
- Coagulopathy is universal in severe sepsis, regardless of the cause. Both pro-coagulant and anticoagulant pathways of haemostasis are dysregulated, resulting in the clinical syndromes of DIC and purpura fulminans.

Management of meningococcal septicaemia

Initial assessment

The use of prehospital parenteral antibiotic therapy is recommended following a provisional diagnosis of meningococcal disease:
- Attend to **ABCs**
- The child may be shocked and hypoxaemic (pulmonary oedema).

Shock

- The goal of circulatory support in shock is the maintenance of oxygenation and adequate tissue perfusion
- The priority is fluid resuscitation to restore intravascular volume. Early and aggressive fluid resuscitation improves survival in paediatric septic shock
- Inotropic support is frequently necessary in order to maintain cardiac output and organ perfusion
- The establishment of central venous access is a priority in the critically ill patient. This will aid and guide fluid resuscitation

- Central venous oxygen saturation ($ScvO_2$) has been a useful guide to the adequacy of oxygen delivery in shock, with the goal of achieving a CVP of 8–12mmHg, and $ScvO_2$ >70%
- Arterial access should also be established as a priority, particularly whilst a pulse can be felt. This will allow accurate BP readings and blood gas analysis.

An initial bolus of 10–20mL/kg of fluid should be given over 5–10min to children with signs of shock. The expected response to volume replacement is reduction in HR, warming of the peripheries, and decrease in capillary refill time. Repeated review is mandatory as the disease may progress due to ongoing capillary leakage.

- Bladder catheterization should be performed early to allow urine output accurately assessed
- When signs of shock persist after an initial 20mL/kg of fluid, further 20mL/kg fluid boluses should be given until signs of circulatory compromise improve
- If shock persists after 40–60mL/kg of fluid resuscitation, there is a significant risk of pulmonary oedema developing. Elective tracheal intubation and mechanical ventilation is recommended at this stage, even in the absence of overt signs of respiratory or neurological failure
- Fluid resuscitation should be monitored continuously using:
  - HR, BP, CVP, core–peripheral temperature difference
  - Urine output
  - pH, base excess, and lactate measurements from blood gases
- As myocardial depression is invariably a contributory feature of persistent shock, inotropic support with adrenaline, dopamine or noradrenaline should be initiated early, via a central vein.

Respiratory support

- Face mask oxygen should be delivered from the outset
- Indications for immediate endotracheal intubation are:
  - Hypoxia, with severe respiratory distress indicating a progression of pulmonary oedema
  - Severe persistent shock
  - Fluctuating or decreasing conscious level (GCS <8, or a decrease of 3 points within 1h)
  - Signs of raised ICP.

Biochemistry

Profound derangements in blood chemistry including:

- Metabolic acidosis and lactataemia:
  - This reflects severity of shock and will respond to fluid management, inotropes, respiratory support
  - Management with alkalinizing agents, e.g. sodium bicarbonate or THAM is rarely indicated but may become necessary to maintain pH >6.9
  - Consider renal replacement therapy

- Hypoglycaemia, hypocalcaemia, hypokalaemia, hypomagnesaemia, or hypophosphataemia. These can be detected by repeated blood testing and treated if present. Hyperglycaemia may occur following resuscitation and stabilization
- Creatine kinase may indicate muscle necrosis. Myoglobinuria may occur.

Haematology

- DIC (i.e. consumption coagulopathy) is common and is exacerbated by dilutional coagulopathy from IV fluid therapy
- There may be bleeding from mucosal surfaces and venepuncture sites
- Spontaneous pulmonary, gastric, or cerebral haemorrhage may occur, particularly if there is associated thrombocytopenia
- Correction of coagulopathy with blood products may prevent life-threatening haemorrhage.

For skin manifestations see Box 25.9

Box 25.9 The skin in meningococcal disease

The skin may be severely compromised in meningococcal disease through inadequate perfusion as a result of vasoconstriction and DIC. ↓skin perfusion may predispose pressure areas to ischaemic damage, and tissue oedema from capillary leak may cause a compartment syndrome. The role of fasciotomy to treat ischaemic limbs is not clearly established, but has been used in circumstances where there is clear evidence of a compartment syndrome. Multidisciplinary input from orthopaedic, vascular, and plastic surgeons may be needed for limb salvage. Amputation should not be considered until it is felt to be absolutely necessary and only performed following extensive discussion.

Raised ICP

Although most critically ill children with meningococcal infection have shock as their primary clinical problem, a small proportion present primarily with signs of raised ICP due to inflammation of the meninges and capillary leak → cerebral oedema:

- The signs of raised ICP are:
  - ↓level of consciousness
  - Focal neurological signs including unequal, dilated, or poorly responsive pupils, relative hypertension, and bradycardia
  - Papilloedema is a late finding in acutely raised ICP
- If raised ICP is suspected, an IV infusion of mannitol (0.25–0.5g/kg over 5min, or 3% saline 3mL/kg over 5min), may prevent brainstem herniation. Urgent tracheal intubation is indicated
- If raised ICP coexists with shock then the priority is to correct the shock before addressing specific measures to control the ICP. An adequate or high BP is necessary in order to maintain cerebral perfusion, thus fluid resuscitation may result in improved levels of consciousness
- In the absence of shock, cautious fluid restriction may be useful, but fluid balance requires careful monitoring.

Antibiotic therapy

- Cefotaxime (50mg/kg 6-hourly IV) or ceftriaxone (50–80mg/kg once daily) for 5–7 days for both meningitis and septicaemia
- Remember that purpura fulminans can be caused by (rare) *Streptococcus pneumoniae*, *Staphylococcus aureus*, and other Gram-negative bacteria.

Steroids

- High dose dexamethasone (0.15mg/kg 4 times daily for 4 days or 0.4mg/kg twice daily for 2 days) given with or before the 1st dose of antibiotics appears to reduce the incidence of neurological sequelae in bacterial meningitis and should be used in cases of suspected meningococcal meningitis without shock
- High-dose steroid use is contraindicated in meningococcal shock, as this has been shown to worsen the outcome of adults with septic shock
- Low-dose steroids (0.5mg/kg hydrocortisone) may be of some benefit in refractory shock but is not proven

Pneumococcal disease

Streptococcus pneumonia is an encapsulated Gram-positive diplococcus that is found in the nasopharynx of up to 40% of healthy children. In PICU *Pneumococcus* commonly presents as bacteraemia, pneumonia, and/or meningitis (📖 Meningitis p.550).

Epidemiology

- Infection with *S. pneumoniae* is usually droplet spread and more prevalent in winter when it can be associated with viral illness such as influenza
- It is more common in neonates and children up to 2 years old
- Most younger cases present with bacteraemia, older children are more likely to have pneumonia.

Clinical features

- Bacteraemia can progress to septic shock and spread to pleura, bones, and joints
- 40% of pneumococcal pneumonia have bacteraemia
- Pneumococcal pneumonia presents as fever, cough, malaise and respiratory failure
- 50% is multilobular and 40% have pleural effusions.

Diagnosis

- WBC $>15 \times 10^9$, neutrophils $>10 \times 10^9$
- *S. pneumonia* can be isolated from blood, pleural fluid
- BAL may be diagnostic (nasopharyngeal culture may reflect only colonization)
- Pneumococcal rapid antigen testing and PCR can be useful if antibiotics have been given.

Management

- Initial resuscitation as necessary—***ABCs***
- Supportive PICU, including mechanical ventilation, high-frequency oscillation, fluid resuscitation, inotropes/pressor, and renal support
- Do not wait for cultures, start antibiotics if *Pneumococcus* is suspected
- With bacteraemia start with ceftriaxone or cefotaxime. In classic pneumonia start cefuroxime 25mg/kg, 8-hourly
- If antibiotic resistance or immunosuppression is suspected consider vancomycin 10mg/kg, 6-hourly
- If *Pneumococcus* is confirmed consider benzylpenicillin
- Treat bacteraemia for 10 days and pneumonia for 14 days
- Effusions/empyema may require drainage.

Toxic shock and soft tissue infection (necrotizing fasciitis)

Both *Staphylococcal aureus* and Group A β-haemolytic *Streptococcus* (GABHS) are Gram-positive bacteria that can cause *toxic shock syndrome* (TSS) and soft tissue infection.

Necrotizing fasciitis is extensive local infection leading to necrosis of soft tissue and skin. (Box 25.11)

Epidemiology

- In GABHS toxic shock syndrome:
  - The condition is probably toxin induced (stimulating massive cytokine release and tissue damage and shock)
  - 50% of cases associated with necrotizing fasciitis
  - Risk factors include varicella infection, wounds, immunosuppression
  - Mortality is lower in children than in adults (5–10%)
- Staphylococcal TSS:
  - Toxin mediated cytokine release leads to shock and capillary leak
  - Can occur in adolescent girls with tampon use and with skin lesions (infections, insect bites, scalds, burns, surgery).

Clinical features of TSS

- Abrupt onset 'flu-like' symptoms
- High fever and diffuse macular rash (later becomes desquamating) and mucous membrane breakdown
- Rapid onset hypotension and shock
- Multiple organ failure:
  - ARDS
  - Encephalopathy
  - Renal/hepatic failure
  - Severe coagulopathy and thrombocytopenia (DIC)
- Necrotizing fasciitis classically presents on trunk and spreads down to perineum and legs. Skin is erythematous and swollen. Vesicles and bullae can appear and skin can become anaesthetic.

Diagnosis (Box 25.10)

- Diagnosis is on clinical features and cultures may be negative
- WBC is often not excessively raised but inflammatory markers, e.g. CRP can be very high (>100)
- Creatine kinase monitors muscle necrosis
- GABHS isolated (Gram stain and culture) from normally sterile site, e.g. blood, CSF, skin/tissue
- *Staphylococcus* isolated from blood culture or skin/tissue
- Toxin assays are not useful
- MRI can help confirm necrotizing fasciitis in deeper tissues.

Box 25.10 Differential diagnosis of TSS

- Staphylococcal TSS
- GABHS
- Meningococcus
- Salmonella
- Measles
- Leptosprosis
- Rocky Mountain spotted fever
- Stevens–Johnson syndrome
- Kawasaki's disease.

Box 25.11 Causes of necrotizing fasciitis

- GABHS
- Enterococci
- Coagulase-negative *S. aureus*
- Clostridium
- Gram-negatives, e.g. *E. coli*, *Pseudomonas*, *Enterobacter*.

Management

TSS and necrotizing fasciitis carry a high mortality and require prompt and aggressive treatment in the same manner as meningococcal disease:

- Immediate attention to ***ABCs.*** Do not hesitate to intubate and ventilate
- Aggressive fluid resuscitation, invasive monitoring, and inotropic support. Bear in mind that pressor agents such as norepinephrine and vasopressin can compromise circulation to at-risk tissues
- Immediate high-dose broad-spectrum IV antibiotics, e.g. ceftriaxone 50–80mg/kg once daily or cefotaxime 80mg/kg 8-hourly and flucloxacillin 50mg/kg 6-hourly
- When diagnosis confirmed consider changing to benzylpeniciilin in GABHS or
- Add clindamycin (suppresses toxin synthesis) in severe TSS or necrotizing fasciitis
- IVIG may help reduce toxin effects.

In cases of necrotizing fasciitis prompt surgical intervention is mandatory

- The infection/necrosis can spread in hours
- Involve general and plastic surgeons

- 'If in doubt-debride!'. It may be difficult to preserve viable tissue early in the disease process
- Aggressive debridement removes infected and necrotic tissue and limits spread
- Fasciotomies can prevent compartment syndrome
- Amputation may be necessary earlier rather than later
- Daily 're-look' visits to theatre may be necessary until spread is controlled (daily photographs or using a marker pen to delineate limit of inflammation can be useful in assessing spread)
- Hyperbaric oxygen therapy is as yet unproven.

Viral infection in PICU

Young children and those with suppressed or deficient immune systems are at risk of life-threatening viral infections. There is a spectrum of illness including:

- Myocarditis (see 📖 p.364)
- Hepatitis (see 📖 p.632)
- Pneumonia/pneumonitis (see 📖 p.414)
- Meningoencephalitis (see 📖 p.550).

Viral myocarditis

- Generally caused by enteroviruses (particularly coxsackie B) but also by any respiratory viruses (including CMV) and HIV
- Often presents with prodrome of fever, malaise, poor feeding progressing to congestive cardiac failure
- Older children complain of chest pain, dyspnoea, and palpitations
- Raised WCC, ESR, and CRP as well as creatine kinase (MB) and troponin I
- ECG shows small complexes and ST abnormalities as well as arrhythmias
- Cardiac Echo reveals hypokinesis, dilatation, and pericardial effusions
- Mortality is high and approaches 75%.

Viral pneumonia/pneumonitis (Box 25.12)

- Common cause of death in the developing world and commonest in infants and young children
- Lower respiratory tract infection scan involve co-pathogens (particularly with parainfluenza pneumonia)
- Influenza can cause both laryngotracheobronchitis and pneumonia often mimicking bacterial sepsis in infants
- Parainfluenza causes larygotracheitis and pneumonia (in the immunocompromised)
- Cytomegalovirus is relatively benign in the immunocompetent but can cause fatal pneumonitis in the immunocompromised
- Hanta virus can cause pneumonia and haemorrhagic fever but is rare in the UK
- SARS is a life-threatening atypical pneumonia caused by coronavirus.

Diagnosis

Nasopharyngeal swabs and wash, BAL, CSF, urine, faeces, serum, or tissue can be used. Techniques involved are:

- Immunofuorescence and enzyme-linked immunosorbent assays
- Microscopic identification of viral inclusion bodies
- Early antibody rise in IgM and later rise (10–14 days) in IgG
- DNA or RNA amplification (PCR).

Box 25.12 Common causes of viral lower respiratory tract infection

- Adenovirus
- Cytomegalovirus
- Herpes simplex virus 1 and 2
- Influenza A (B less likely), H1N1 (swine flu)
- Metapneumovirus
- Parainfluenza 1, 2 ,and 3
- RSV.

Management of serious viral illness

- Death from viral causes has fallen without specific therapy. Most cases are self-limiting
- Supportive ICU care is mainstay of treatment including mechanical cardiac support (ECMO, LVAD) for myocarditis and mechanical ventilation for pneumonia
- Effective antiviral agents incude: ribavarin and palivizumab for RSV (if immunocompromised), ganciclovir for CMV, aciclovir for Varicella and HSV (see 📖 p.600).

Tuberculosis

Tuberculosis is uncommon in developed nations but is still prevalent in the developing world. In developed nations it is often seen in immigrant communities and in communities with a poor standard of living.

It is caused by *Mycobacterium tuberculosis*, an aerobic Gram-positive bacillus. There are also *atypical mycobacteria* which may cause human infection, although infection with these organisms is unlikely to result in admission to PICU.

Epidemiology

- Infection is normally contracted by inhalation, and the primary lesion is almost always in the lungs
- Primary infection of the gut may also occur if the organism is ingested. Gut infection is unlikely to result in admission to PICU

Clinical features

Presentations to PICU

Primary pulmonary TB is unusual in PICU, but TB may present as a lobar or generalized pneumonia or as lymphadenitis causing airway obstruction.

Spread of infection

- TB may spread either via the lymphatics or via the bloodstream
- Acute military TB is uncommon
- Tuberculous meningitis causing obstructive hydrocephalus may require urgent external ventricular drainage
- Spread can occur to pleura, pericardium or peritoneal cavities, bone, and kidneys.

Diagnosis

All cases

- Chest radiograph
- Mantoux test
- Sputum/EETT secretions × 3 for auramine staining and TB culture
- Gastric washings × 3 for for auramine staining and TB culture
- PCR.

Pulmonary TB on PICU

- Bronchoscopic BAL for acid-fast bacilli and TB culture
- CT chest if symptoms or signs of airway obstruction.

TB meningitis

See 🕮 Table 25.4 p.552.

Consider

- Investigating for immune deficiency, particularly if infection is disseminated or caused by atypical or vaccine strains. (Defects of the interferon-γ/interleukin-12 system result in a profound defect of cell-mediated immunity to mycobacteria, including environmental mycobacteria and bacille Calmette-Guérin [BCG])
- Bone marrow aspirate if signs of marrow suppression and to exclude haematological malignancy

Management

Treatment should be commenced following consultation with the Paediatric Infectious Diseases team. Current NICE guidelines were published in 2006.[1]

Management of active TB

6-months of isoniazid and rifampicin supplemented in the first 2 months with pyrazinamide and ethambutol.

Children with active meningeal TB should be offered:

- 12 months of isoniazid and rifampicin supplemented by pyrazinamide and ethambutol for the first 2 months
- A glucocorticoid at the normal dose range equivalent to prednisolone 1–2mg/kg, maximum 40mg with gradual withdrawal starting within 2–3 weeks of initiation.

Reference

1. NICE (2006). *Clinical diagnosis and management of tuberculosis, and measures for its prevention and control*. National Institute for Health and Clinical Excellence. London.

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Chapter 26

Sepsis and multiple organ failure

Introduction

- Sepsis can be defined as the *systemic response to infection*
- Sepsis may lead to:
  - Shock
  - Multiorgan dysfunction
  - Multiorgan failure
- Sepsis and its consequences are major causes of morbidity and mortality on PICUs
- Despite great advances in our understanding of sepsis, the pathophysiology of this process can be bewilderingly complex
- No single intervention has been shown in a randomized trial to be of benefit in sepsis.

There has been a dramatic improvement in outcome for children with sepsis in PICU in recent years, neither because of new drugs nor new technology but because of high quality basic supportive care and regular review of the patients and their response to intervention.

Definitions

Sepsis and the systemic inflammatory response (SIRS)

By the 1980s, physicians in adult intensive care suggested that patients with certain clinical characteristics represented an important category of patients:

- Altered temperature (fever or hypothermia)
- Tachycardia or bradycardia (in <1-year-olds)
- Tachypnoea
- ↑Raised or low WCC
- The presence of infection.

Formal criteria based on these suggestions were proposed in 1991 (and updated in 2001) providing a basis for inclusion criteria into clinical trials. Since then terms such as ***SIRS, sepsis,*** *and* ***septic shock*** have become synonymous with intensive care medicine (see Box 26.1)

SIRS is the same response as sepsis but in the absence of proven or suspected infection. Multiorgan dysfunction can be associated with SIRS, sepsis, or septic shock.

Box 26.1 Definitions of SIRS, infection, sepsis, severe sepsis, and septic shock

SIRS

The presence of at least 2 of the following 4 criteria, one of which must be abnormal temperature or leucocyte count:

- Core temperature of ≥38.5°C or ≤36°C.
- Tachycardia, defined as a mean heart rate ≥SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; ***or***
- Otherwise unexplained persistent elevation over a 0.5–4-h time period.

Or for children <1 year old: bradycardia, defined as a mean heart rate <10th percentile for age in the absence of external vagal stimulus, β-blocker drugs, or congenital heart disease, or otherwise unexplained persistent depression over a 0.5-h time period.

- Mean respiratory rate ≥2SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anesthesia
- Leucocyte count elevated or depressed for age (not secondary to chemotherapy-induced leucopenia) or ≥10% immature neutrophils.

Infection

A suspected or proven (by positive culture, tissue stain, or PCR test) infection caused by any pathogen ***or*** a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g. white blood cells in a normally sterile body fluid, perforated viscus, CXR consistent with pneumonia, petechial or purpuric rash, or purpura fulminans)

Sepsis

SIRS in the presence of, or as a result of, suspected or proven infection.

Severe sepsis

Sepsis plus one of the following: cardiovascular organ dysfunction ***or*** acute respiratory distress syndrome ***or*** 2 or more other organ dysfunctions. Organ dysfunctions are defined in Box 26.2

Septic shock

Sepsis and cardiovascular organ dysfunction as defined in Box 26.2

Box 26.2 Organ dysfunction criteria

Cardiovascular dysfunction

Despite administration of isotonic IV fluid bolus ≥40mL/kg in 1h

- Decrease in BP (hypotension) ≤5th percentile for age or systolic BP ≤2SD below normal for age ***or***
- Need for vasoactive drug to maintain BP in normal range (dopamine ≥5 mcg/kg/min, or dobutamine, epinephrine, or norepinephrine at any dose) ***or***
- 2 of the following:
  - Unexplained metabolic acidosis: base deficit >5.0mEq/L
  - ↑ arterial lactate >2 × upper limit of normal
  - Oliguria: urine output <0.5mL/kg/h
  - Prolonged capillary refill: >5s
  - Core to peripheral temperature gap >3°C

Respiratory

- PaO_2/FiO_2 <300 in absence of cyanotic heart disease or preexisting lung disease ***or***
- $PaCO_2$ >72 torr or 20mmHg over baseline $PaCO_2$ ***or***
- Proven need for >0.5 FiO_2 to maintain saturation >92% ***or***
- Need for non-elective invasive or non-invasive mechanical ventilation.

Neurologic

- GCS ≤11 (57) ***or***
- Acute change in mental status with a decrease in GCS ≥3 points from abnormal baseline.

Hematologic

- Platelet count <80,000/mm^3 or a decline of 50% in platelet count from highest value recorded over the previous 3 days (for chronic hematology/oncology patients) ***or***
- International normalized ratio >2.

Systemic inflammatory response syndrome (SIRS)

Common causes

- Trauma
- Major surgery
- Cardiac bypass
- Pancreatitis
- Burns and other insults

It is important to note that clinically it is often difficult to distinguish between *SIRS* and *sepsis* and thus both conditions are regularly treated as the same. This gives an important insight into the host immune response—there is a 'final common pathway' of severe inflammation in response to any insult as long as that insult is sufficiently severe enough.

Box 26.3 PIRO

Recently a new framework known as ***PIRO*** has been proposed for describing sepsis. This system is thought to be more subtle with better disease specificity:

- ***P***redispostion (prior diseases, e.g. immunodeficiency)
- ***I***nsult (type of infection)
- ***R***esponse (type of host response)
- ***O***rgan failure (pattern and severity of organ dysfunction)

As yet this has not been adopted internationally.

Epidemiology

Defining the true incidence of sepsis is difficult because most uncomplicated cases will never present to hospital. Additionally many children will be admitted to PICUs with diagnoses of respiratory failure, status epilepticus, DKA etc. associated with underlying infection and whilst fulfilling the criteria for sepsis it is not recorded.

- A landmark study of *severe sepsis* in the US recorded an annual incidence of 0.56 /1000 children (<19 years) or more than 42000 cases per year (Fig. 26.1). The rate was highest in infants (5.2/1000) who comprised 48% of the total cases
- In North London, UK, of about 1200 children referred each year with a primary diagnosis of 'sepsis', 47% were <1 year old.

Until there are objective biomarkers of degrees of systemic inflammation we should make efforts to use existing terminology accurately. The term ***sepsis-induced multiorgan failure*** is probably the most appropriate description for a child requiring intensive care admission receiving artificial ventilation, and fluid and vasoactive drug haemodynamic support.

Outcome

- Overall in developed counties a case-fatality rate of around 10–20% is typical, though amongst the increasing proportion of cases with significant underlying disease this value is higher (Fig. 26.2)
- Survival rates quoted for paediatric severe sepsis vary widely depending on the population studied
- PICU mortality for sepsis-induced multiple organ failure has fallen in the UK
- A higher proportion of deaths now occur in the immediate early resuscitation phase at local emergency rooms and during transport to regional units
- The recent global RCT of activated protein C in 474 children with severe sepsis suggested an overall PICU case fatality rate of 17% although the range was from 0–40% between countries
- Cases with lung as the presumed site of infection had worse outcomes than did those with primary septicaemia (22% vs. 11% mortality, p=0.01).

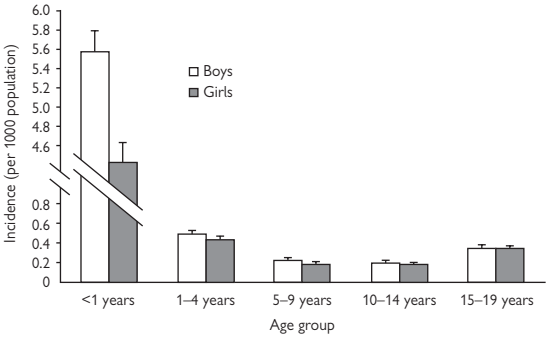

Fig. 26.1 Incidence of severe sepsis by age and sex. The incidence is highest in the youngest patients and decreases until late adolescence (15–19 years old). A total of 48% of all patients are <1 year old, and 27% are admitted at birth. 95% confidence intervals are shown by error bars. Reproduced from Scott Watson R, *et al.* (2003). The epidemiology of severe sepsis in children in the United States. *Am J Respir Crit Care Med* **167:** 695–701, copyright American Thoracic Society.

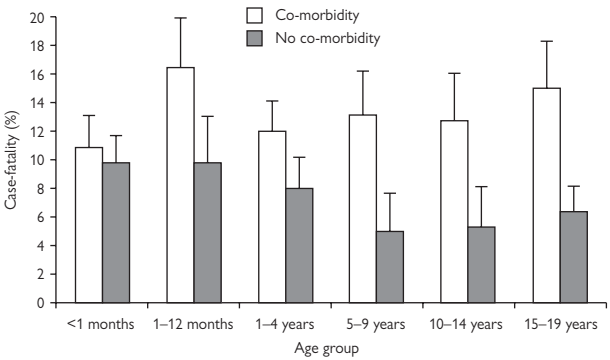

Fig. 26.2 Case fatality of children with severe sepsis by age and comorbidity. Case fatality is highest in children 1–12 months old and is significantly higher among children with any underlying disease. 95% confidence intervals are shown by error bars. Reproduced from Scott Watson R, *et al.* (2003). The epidemiology of severe sepsis in children in the United States. *Am J Respir Crit Care Med* **167:** 695–701, copyright American Thoracic Society.

Box 26.4 'Magic bullets and modern machines'

Research in sepsis in intensive care medicine has a short and rather chequered history. On the one hand it cannot be denied that research is absolutely necessary to further our understanding of disease and to evaluate new and established therapies. On the other, it has to be acknowledged that enormous amounts of time and money have been spent evaluating pharmaceutical 'magic bullets', many of which have little or often undesired effects. Similarly many new expensive technologies have been introduced with little or no evidence that they have improved patient outcome. Much of this has distracted ICU physicians from concentrating on basic principles of management. It is generally acknowledged that most of the reductions in ICU mortality rates have come from an improvement in basic management rather than through an introduction of any single intervention.

Fortunately, it appears as if lessons have been learnt from past mistakes and now new therapies or protocols of management are subject to large multicentre randomized and controlled trials before being adopted.

Certain principles have come to light:
- The heterogeneity of patients included in clinical trials of sepsis is likely to have a contributed to the many of the negative results of clinical trials of ICU therapies
- Definitions such as SIRS, sepsis, and septic shock which were introduced to help with clinical trials of therapies in ICU may be too loose. They lack specificity (is it really correct to include a patient with sepsis from pneumonia in the same group as a patient with sepsis having previously suffered major trauma?)
- Therapies or practices that are successful in adult ICU patients will not necessarily have the same effects in PICU patients
- Similarly, therapies or practices in babies may not be applicable to larger children or adolescents
- Drugs that target the immune or inflammatory response can have unforeseen and undesirable results
- Pressure must be applied to publish the negative results of trials.

Examples of interventions or therapies that have come and gone for the treatment of sepsis in recent years are:
- Goal-directed therapy guided by pulmonary artery catheters in adults
- Monoclonal antibody to endotoxin (HA1A)
- NO synthase inhibitors
- Ibuprofen (prostaglandin inhibition)
- Steroids (high and low dose, although low dose not evaluated in children)
- Bradykinin inhibitors
- Elastase inhibitors
- Activated protein C (in children).

New therapies that are currently looking doubtful are:
- Vasopressin: appears to offer no advantage over high dose norepinephrine in sepsis in adults
- Intensive insulin therapy for tight glycaemic control: the incidence of hypoglycaemia is high.

Pathophysiology

The pathophysiology of sepsis and multiple organ dysfunction is extremely complex but involves interactions between the stimulus (e.g. infecting microorganism) and the hosts immune and inflammatory responses.

The inflammatory response

- Is an evolved, vital, protective reaction that is designed to recognize and to kill invading pathogens and to mop up any resulting debris
- It can be a non-specific innate immune reaction as seen with the complement cascade
- It can be a coordinated, targeted, adaptive immune response that is responsible for the generation of immunological memory specific to individual antigens
- An effective acute inflammatory response will prevent a local insult spreading from the site of injury and becoming a systemic insult.

Unfortunately the same molecules responsible for the inflammatory response may also be harmful when disseminated more widely. For example:

- Beneficial secretion of tumour necrosis factor (TNF) facilitates local bacterial killing by increasing local blood flow and aiding phagocytic action
- Harmful excess systemic levels of TNF or related molecules, as seen in sepsis can cause widespread endothelial dysfunction with vasodilatation, capillary leak, phagocyte activation, and coagulopathy.

Humans appear to have evolved a counter-balancing anti-inflammatory response, which keeps to inflammatory response in check by preventing systemic overflow of local inflammation and to close down systemic inflammation once it has occurred. Not surprisingly, any therapy aimed at inhibiting the pro-inflammatory response runs the risk of leaving this anti-inflammatory response unbalanced and potentially harmful (see Fig. 26.3).

The principal mechanisms by which the inflammatory response causes harm is ***failure of vital organ perfusion*** resulting from 3 main processes

- Endothelial dysfunction
- Thrombosis and bleeding
- Myocardial dysfunction.

Endothelial dysfunction

- Acute inflammation affects all major functions of the vascular endothelium (Box 26.5)
- Blood vessels typically become dilated regardless of the impact on local blood flow and pressure
- The thromboresistant (and fibrinolytic) properties of the endothelium are reduced, causing a tendency for clot formation to occur regardless of whether it is required or not
- The capillaries become more permeable to fluid as a result of changes in charge and adhesion molecule configurations
- Inflammatory cells are widely recruited to the tissues by the expression of activated forms of endothelial adhesion molecules.

Thrombosis and bleeding (Box 26.5)

- Systemic inflammation lowers the threshold for clot formation (and slows the rate at which clots are broken down)
- This consumption of coagulation factors and platelets is called DIC or consumptive coagulopathy and results in bleeding as there are no longer enough clotting factors to form subsequent blood clots
- Virtually all aspects of the coagulation and fibrinolytic pathways are disrupted during sepsis
- Obstruction of small blood vessels with unwanted thrombosis is a contributing factor in failing organ perfusion
- Therapeutic administration of molecules that have anticoagulant and profibrinolytic effects such as activated protein C have been shown to provide some benefits in adults but not in children with severe sepsis.

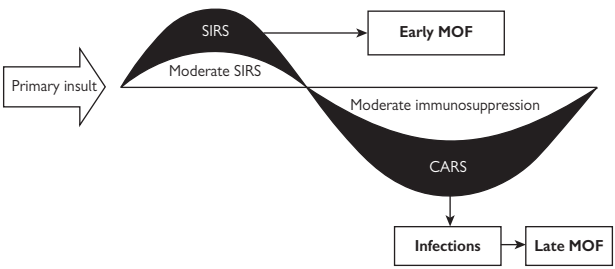

Fig. 26.3 Immune response in critical illness. Following a primary insult such as exposure to invading micro-organisms, the patient mounts both proinflammatory and anti-inflammatory responses. A severe systemic proinflammatory response—evident as SIRS can cause rapid multiple organ failure. The balancing counterinflammatory acute response syndrome (CARS) may similarly be excessive leading to an inability to defend against subsequent infectious insults.

Myocardial dysfunction

- Acute inflammation typically causes a decrease in myocardial contractility secondary to direct inhibition of myocyte function by inflammatory mediators including TNF, interleukin-6, platelet activating factor and NO
- Without aggressive fluid resuscitation tissue hypoxia, acidosis, poor coronary perfusion, and reduced pre-load from capillary leak all lead to reduced cardiac output
- In response to fluid resuscitation (increasing pre-load) the heart dilates thus enabling stroke volume to be maintained. Combined with a moderate tachycardia this will result in a higher than normal cardiac output.

In practice we observe a range of haemodynamic states in paediatric sepsis on presentation. Recent consensus guidelines highlight the need to titrate

the resuscitation given to the haemodynamic pattern observed in the individuals but also to consider the adequacy of the oxygen delivery to the state of tissue demand as represented by a central venous saturation.

Box 26.5 Inflammatory mediators, coagulation, and the microcirculation

There are a myriad of mediators involved in the inflammatory response that lead directly or indirectly to widespread tissue injury. Bacteria, viruses, and fungi have unique cell-wall molecules which are recognized by receptors on immune cells (toll-like receptors) and induce transcription and release of cytokines from these cells. Cytokines can be pro or anti inflammatory and can activate endothelial cells in the microcirculation (via adhesion receptors) and injure endothelial cells by inducing neutrophils, monocytes, macrophages, and platelets to bind to them. In turn, NO (a potent vasodilator) is released (via inducible NO synthase) as well as proteases, oxidants, prostaglandins, and leukotrienes.

Coagulation is activated via the endothelium and fibrinolysis is impaired. Widespread microthrombi further amplify injury leading to distal ischaemia and tissue hypoxia.

All in all this potent combination can overwhelm the microcirculation leading to widespread vascular permeability (capillary leak), vasodilatation and DIC.

Proinflammatory molecules:	**Procoagulants:**
Interleukin-1β	↓ Protein C
Interleukin-6	↓ Protein S
TNF-α	↓ Antithrombin 111
Prostaglandins, leukotrienes, kinins and proteases (eg elastase)	
Anti-inflammatory molecules:	**Antifibrinolysis**
Interleukin 10	↑plasminogen activator inhibitor

Management of sepsis and sepsis shock

Consensus guidelines for the management of severe sepsis have been produced as 2 initiatives 'Surviving Sepsis' and The American College of Critical Care Medicine (ACCM) clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock. Both have been updated in 2008 and are essential reading for anyone involved in the care of cases of septic shock (see 📖 p.583).

Resuscitation

- The quality of the immediate care of a child presenting in shock due to sepsis is ***the*** major factor determining outcome
- Each additional hour in unresolved shock at least doubles the risk of death
- Resuscitation should follow the standard algorithm of assessment of ***Airway***, ***Breathing***, and ***Circulation***.

In practice the overwhelming priority is support of the circulation.

The ACCM guidelines recommend resuscitation to end-points that reflect the adequacy of organ perfusion rather than simply BP as suggested by:

- Capillary refill of <2s
- Normal pulses and warm extremities (with no differential between peripheral and central pulses)
- Urine output >1mL/kg/h
- Normal mental status

Resuscitation should be undertaken in a structured manner with attention to the time elapsed and the individual patient's responses (see Fig. 26.4)

Fluid therapy

- Aggressive volume expansion in aliquots of 20mL/kg should be administered over 5min and repeated promptly if there is any suggestion of persistent perfusion abnormalities
- There is little evidence to support the use of one kind of IV fluid over another
- Colloids used in children:
  - Human albumin 4.5% (molecular weight 66,000)
  - Gelatin solutions such as Gelofusine® (succinylated gelatin mwt 30000) or Haemaccel® (polygeline mwt 35,000)
- Crystalloid solutions used in children are:
  - Normal saline 0.9%
  - Hartmanns or Ringer's lactate solutions
- Colloids contain larger molecules and are less prone to endothelial leak thus staying in the circulation for longer. This is not the case in severe sepsis with massive capillary leak
- Gelatins have an incidence of anaphylaxis (~0.1%) and can worsen coagulopathy
- Crystalloids are cheap and safe but may cause more tissue oedema.
- There is no place for larger molecular colloids, e.g. hydroxyl ethyl starch (mwt 200,000) in paediatric resuscitation
- There is no place for hypotonic crystalloids (e.g. glucose/saline) in paediatric resuscitation.

Inotropic/pressor support

- Inotropic support should be considered early in the care of such cases if shock is not reversed with rapid fluid administration
- Again there is little consensus as to the choice of first-line inotrope. Epinephrine seems the obvious candidate but dopamine or dobutamine can be used
- Norepinephrine is the obvious choice in the vasodilated patient, i.e. warm shock. Vasopressin can be useful in catecholamine resistant shock.

Goal-directed therapy

- Studies that have investigated 'fine-tuning' of aggressive resuscitation ***early*** in septic shock to the responses of individual patients have shown dramatic benefits in adults and in children
- Monitoring superior caval vein oxygen saturation ($ScvO_2$) with a target of >70%, in addition to standard perfusion and BP targets generally results in more aggressive resuscitation which may improve outcome.

Induction of anaesthesia in septic shock

Timing

- Consider semi-elective intubation and ventilation after 40–60mL/kg IV fluid, particularly if signs of abnormal perfusion persist
- Ongoing resuscitation of the circulation is essential while preparations are being made for induction
- Consider starting inotropes pre-intubation
- Dilute strength epinephrine can be given via a peripheral cannula in the short term if central access is not available
- Multiple team members aid in the process.

Induction agents

- Ketamine 1–2mg/kg IV and fentanyl 2–5mcg/kg IV cause little cardiovascular depression and are probably the safest agents to use in septic shock
- Thiopentone, propofol, benzodiazepines, and inhalational anaesthetic agents all carry risks of significant myocardial depression and systemic vasodilatation. These agents are not recommended in septic shock
- Etomidate is associated with an ↑risk of death in septic shock. Administration of hydrocortisone does not avoid this risk.

ETT leak

Lung compliance will deteriorate in many cases that present in septic shock—ETT leakage should be minimal.

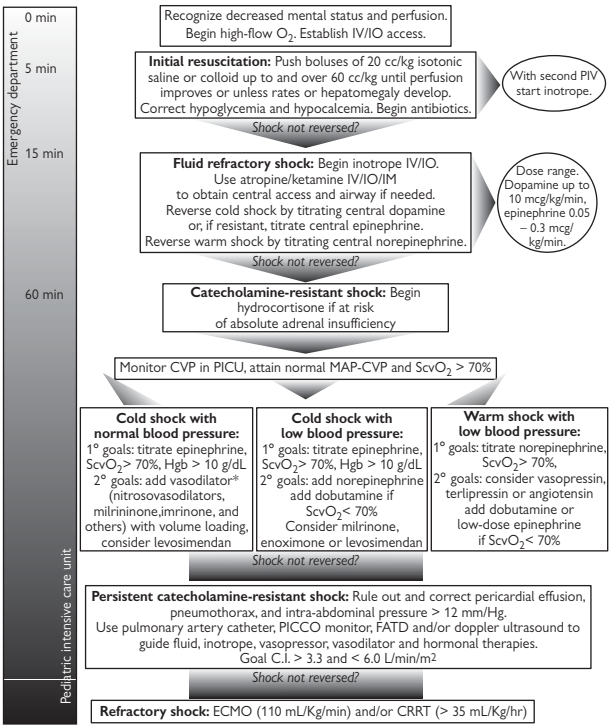

Fig. 26.4 2008 ACCM algorithm for stepwise management of haemodynamic support for infants and children with septic shock. Reproduced with permission of the publisher copyright 2008, Society of Critical Care Medicine.

Dealing with the cause of sepsis

- During resuscitation attention must also be paid to the likely cause of the sepsis and specific action taken to deal with this. In most cases candidate organisms and appropriate antibiotics will vary by age and country
- Surgery may be indicated, e.g. abscess drainage, debridement, or laparotomy for ischaemic bowel.

Supportive care

Essentially all PICU treatment of sepsis-induced multiple organ failure is supportive and is aimed at maintaining organ perfusion. Despite this, one must not forget to:

- Evaluate and re-evaluate antibiotic therapy, particularly in light of microbiological culture data

- Consider the possibility of nosocomial superinfection (including fungal) at all times
- Consider the possibility of surgical or radiological intervention.

A full description of ICU care cannot be summarized here but some priorities will be highlighted in each organ system.

Respiratory

- *Pulmonary oedema is common in sepsis-induced MOF both as a result* of myocardial failure but also capillary leak (ARDS)
- Use of PEEP, e.g. 8–12 cmH_2O) and relatively long inspiratory times (1.0–1.5s) are often effective in maintaining lung volumes without excessive PIP
- Minimize barotrauma and volutrauma by avoiding PIP >30cm and tidal volumes of >7mL/kg
- High frequency oscillation is valuable if a PIP/plateau pressure >30cmH_2O or mean airway pressure >16 cmH_2O and FiO_2 >0.6 is required
- There is no consensus on target blood gases, but an arterial of pH 7.25 or above can be tolerated (particularly with permissive hypercapnia) and indeed may be optimal for oxygen delivery
- Arterial saturation (SaO_2) > 90% usually ensures adequate oxygen delivery if cardiac output is maintained
- Reduce PEEP with care to avoid sudden de-recruitment of alveoli
- After shock has resolved, a conservative fluid strategy (i.e. drying the patient out) is associated with a shorter days on a ventilator.

Cardiovascular

- Consider milrinone (inodilator) if patient persists with poor peripheral perfusion (cold shock) despite fluid and inotropes
- Beyond the early resuscitation phase there are no clear recommendations for ongoing cardiovascular support
- Patients may become less sensitive to catecholamines after a few days through a process of receptor downregulation and tachyphylaxis
- Never stop high-dose catecholamines suddenly. Always begin by weaning with care, then speed up if tolerated.

Renal

- Pre-renal failure leading to ATN is common in septic shock (~25%) but this risk can be much reduced by aggressive resuscitation
- Anuric renal failure causes acidosis, electrolyte disturbances, and fluid overload making patient management very difficult
- Consider early CVVH to provides control of these parameters in addition to possible disease-modifying effects

Coagulopathy

- Coagulopathy is caused by consumption (DIC) and dilution (volume resuscitation) and is a sign of severe sepsis
- Effective resuscitation specifically reduces the risk of coagulopathy
- Transfusion of FFP 20mL/kg provides around 30% of typical levels of many of the coagulation factors and fibrinolytic proteins

- There is a body of opinion in intensive care medicine that believes that aggressive FFP resuscitation combined with high-volume haemofiltration or plasmafiltration/plasma exchange improve survival in severe sepsis.

Endocrine

- Relative adrenal insufficiency does occur in septic shock
- Always consider the use of hydrocortisone in patients that have recently been on steroid treatment (3–6 months), e.g. oncology patients with septic shock
- Administration of low-dose hydrocortisone improves shock but not survival in adults. It is not clear if the same applies to children
- Most clinicians give physiological replacement hydrocortisone (2.5–5mg/kg/day 6-hourly) to children with catecholamine refractory shock
- Tight glycaemic control is not recommended in children—there is no evidence to support its use and episodes of hypoglycaemia may be harmful.

Metabolic

- Electrolyte abnormalities are common in sepsis
- Hypokalaemia can exacerbate myocardial function and precipitate arrhymias
- Hypomagnesaemia can cause myocardial dysfunction and refractory hypokalaemia
- Hypocalcaemia and hypophosphataemia can occur and affect myocardium and muscle function
- Abnormalities should be corrected carefully in the acute setting via a central line if possible but can be given peripherally.

Further reading and information

Brierley J *etal.* (2009). Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med* **37**(2):666–88.

Surviving Sepsis Campaign website: wwwsurvivingsepsis.org

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Chapter 27

Laboratory investigations for infectious disease

Introduction

Infections account for a large proportion of admissions to PICU and having an understanding of diagnostic methods as well as available tests is useful for any clinician working in the PICU setting.

Principles

Microorganisms are detected either directly or by culture. The pathogen suspected will direct the clinician towards the most appropriate test(s).

Direct detection methods include

- Microscopy
- Identifying toxin
- Antigen detection
- Molecular assays e.g., polymerase chain reaction (PCR).

Almost any body fluid and tissue can be cultured. As a general rule the larger the sample sent for culture the greater the yield.

Culture techniques

- Using special media
- Identifying biochemical reactions (e.g. coagulase)
- Identification using special antisera (e.g. latex agglutination)
- Molecular methods (e.g. DNA sequencing/PCR).

Bacteria

- Ideally, specimens for bacterial identification should be taken prior to the administration of antibiotics
- Bacterial pathogens are isolated on agar plates
- Various techniques are used for identification:
  - Appearance both macro- and microscopically
  - Staining responses (e.g. Gram stain)
  - Use of biochemical tests (e.g. coagulase)
  - Use of antisera for confirmation (e.g. agglutination tests, detection of specific antibodies)
- Once a bacterial organism is identified it can be cultured in the presence of antibiotics to assess if it is susceptible to that agent or not
- Serology can be used to diagnose certain bacterial infections but results may be slow for PICU.

Viruses

- Viruses can be directly identified using molecular methods such as PCR (which is expanded on next) or by electron microscopy
- Intracellular viral culture can be used but PCR is a more sensitive and effective diagnostic tool
- Viral specimens should be collected as early as possible after onset of symptoms before viral shedding stops
- Serology may also be used to identify viruses.

PCR

The ability to amplify specific DNA sequences has revolutionized diagnostic pathology. It is now routinely used in the diagnosis of infectious diseases as well as analysis of oncogenes, haematological malignancies, general paediatrics, and many other specialities. PCR amplifies DNA by up to a million-fold and as a result very little DNA is required. Drawbacks are the expense and the fact that minimal contamination can lead to false positive results.

Serology

- Diagnosis is made by either detecting antibody or antigen in blood and other body fluids
- Active disease versus carrier or previous infection may be differentiated, e.g. in hepatitis B infection
- Methods include immunofluorescence, agglutination, ELISA, and complement fixation. Detecting antibody in viral infections can be particularly useful because once viral shedding has ceased, viral culture is of no value
- Antibodies tests include testing for HIV, hepatitis A–E, CMV, EBV, RSV, mumps, measles, rubella, influenza, yellow fever, and many more

General principles

- Rising IgM indicates 'new' infection
- Rising IgG levels indicates 'new' or a 'previous' infection or immunity as a result of vaccination
- Increasing IgG (rising titre) when 2 samples are taken with a reasonable interval between the samples (paired sera) indicates a 'new' infection or re-infection.

Fungi

- Direct microscopy is often used to diagnosis fungal presence. Histopathological diagnosis should however be confirmed on culture
- Fungal infection can only be diagnosed with evidence of tissue invasion. Invasive aspergillosis can be diagnosed with the measurement of galacotomanon which is an antigen released in blood or with PCR
- Both fungal culture techniques and serological methods can be used in diagnosis.

Protozoa

The most important protozoan infection is malaria. This is usually identified using direct microscopy. Alternative methods include antigen detection as well as culture which is rarely used.

Specimen collection

More common specimens collected in PICU

Surface specimens

- Skin specimens may be sent as surveillance for organisms such as MRSA or from obviously infected sites such as abscesses
- Petechial rash aspirates or scrapings may be particularly useful in suspected meningococcal disease especially if antibiotics were administered prior to taking blood cultures
- Indwelling vascular catheters are often colonized by bacteria which are normally non-virulent such as coagulase –ve staphylococci. If the catheter is thought to be the source of the infection, then blood cultures should be taken and the catheter removed and sent for MC&S.

Respiratory tract specimens

The most common specimens sent are those looking for viral pathogens including specimens from the upper respiratory tract.

- Nasopharyngeal aspirates (NPA) are particularly useful for diagnosing RSV, parainfluenza, or influenza using immunoflurescence
- Pharyngeal, nasal, and throat swabs are used to diagnose bacterial pathogens such as meningococci, staphylococci, streptococci, and pertussis.
- Viral pathogens such as adenovirus, influenza, parainfluenza, rhinovirus, RSV, and metapneumovirus are usually diagnosed using PCR or electron microscopy
- Sputum may be spontaneously coughed, suctioned, or induced by physiotherapy. BAL will provide a specimen in a ventilated patient. Both may be investigated for bacteria, viruses and fungi. Cytology provides cell counts on BAL specimens.

Blood

- Normally sampled from a sterile venepuncture site. May require multiple samples from numerous sites of the body at different times, e.g. in endocarditis
- Can be used to identify bacteria, viruses, and fungi using a variety of techniques as already discussed. Certain organisms will require prolonged culture in order to isolate the pathogen.

Other sites where specimens may be obtained include:

- Urine: microscopy and culture
- Cerebrospinal fluid: microscopy, culture, PCR, cells, glucose, protein
- Pleural effusion: microscopy, culture, PCR (pneumococcus), pH, LDH
- Pericardial effusions: microscopy, culture, PCR.

Futher reading

Provan D (ed) (2005). *Oxford Handbook of Clinical and Laboratory Investigation*. Oxford University Press.

Chapter 28

Antimicrobial use on the PICU

Introduction

- Inappropriate use of antimicrobials is associated with the emergence of resistant micro-organisms which are a significant challenge on PICU. Organisms such as methicillin-resistant *Staphylococcus aureus (MRSA)*, glycopetide-resistant enterococci, extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae and carbapenem resistant *Acinetobacter* may cause significant problems, particularly if they become embedded within a unit
- The mechanisms involved with the emergence and spread of these organisms on an individual unit are complex but include the overuse and misuse of antibiotic agents. Examples include:
  - Prolonged use of surgical antibiotic 'prophylaxis'
  - Continued use of IV broad spectrum agents despite the identification of the aetiological agent of infection
- Broad-spectrum antibiotic use is related to the emergence of fungal infections which in general have a higher morbidity and mortality
- Infections due to antibiotic resistant bacteria are associated with ↑length of stay on the PICU and ↑mortality.

Antimicrobial stewardship programmes focus on ensuring the proper use of antimicrobials to provide the best patient outcomes, lessen the risk of adverse effects, promote cost-effectiveness, and reduce or stabilize levels of resistance. They usually involve a number of strategies:

- Educating physicians in the appropriate use of antibiotics
- Hospital/ICU guidelines for antibiotic prescribing
- Restriction on the use of antibiotics
- Daily review of antibiotic prescriptions and feedback to prescribers on inappropriate therapy to modify future prescribing
- Computer-assisted prescribing
- Antibiotic cycling—scheduled rotation of antibiotics may reduce resistance.

Antibiotics (antibacterials)

Resistance amongst bacteria varies greatly from institution to institution, Table 28.1 gives a rough guide to susceptibility. The intensivist should discuss resistance patterns with their local microbiologist.

Table 28.1 lists bacteria commonly seen on PICU, either acquired in the community or acquired as a consequence of healthcare, together with a list of widely available antibiotic options.

Table 28.2 lists possible first-line antibiotics for specific infections, broken down by system or site or infection, whilst waiting for culture and sensitivities. Note this may need modification according to local sensitivity profiles.

Antituberculous agents are out with the scope of this text and expert advice should be taken when prescribing these agents on PICU.

Table 28.1 Antibacterial agents

	Antibacterial agent																	
Selected bacteria	**Metronidazole**	**Clindamycin**	**Linezolid**	**Vancomycin**	**Erythromycin**	**Flucoxacillin**	**Polymyxin (Colistin)**	**Trimethoprim**	**Ciprofloxacin**	**Meropenem**	**Piperacillin-tazobactam**	**Gentamicin**	**Ceftazidime**	**Ceftriaxone/Cefoatxime**	**Cefuroxime**	**Co-amoxiclav**	**Amoxicillin**	**Benzylpenicillin**
Group A streptococcus	R	S	S	S	s	S	R	S	s	S	S	c	s	S	S	S	S	S
Group B streptococcus	R	S	S	S	s	S	R	S	s	S	S	c	s	S	S	S	S	S
Streptococcus pneumoniae	R	S	S	S	s	S	R	S	s	S	S	c	s	S	S	S	S	S
Staphylococcus aureus (MSSA)	R	S	S	S	S	S	R	S	c	S	S	S	R	S	S	S	R	R
Staphylococcus aureus (MRSA)	R	R	S	S	R	R	R	S	R	R	R	S	R	R	R	R	R	R
Coagulase negative staphylococci	R	R	S	S	R	R	R	R	R	R	R	S	R	R	R	R	R	R
Enterococcus spp.	R	R	S	S	R	R	R	R	S	S	s	c	R	R	R	R	s	R
Enterococcus spp. (VRE)	R	R	S	R	R	R	R	R	S	S	s	c	R	R	R	R	R	s
Listeria monocytogenes	R	s	S	S	S	R	R	*	s	S	s	c	R	R	R	S	S	R
Neisseria meningitides	R	R	R	R	R	S	S	R	p	S	S	R	S	S	S	S	S	S
Haemophilus influenzae	R	R	R	R	R	R	S	S	S	S	S	S	S	S	S	S	S	R
Escherichia coli	R	R	R	R	R	R	S	S	S	S	S	S	S	S	S	S	s	R
Escherichia coli (ESBL+)	R	R	R	R	R	R	S	S	s	S	R	S	R	R	R	R	R	R
Klebsiella spp.	R	R	R	R	R	R	S	S	S	S	S	S	S	S	S	S	R	R
Enterobacter spp.	R	R	R	R	R	R	S	S	S	S	S	S	R	R	R	R	R	R

S = usually sensitive; s = some resistance reported; c= only in combination therapy; p = used as prophylaxis; R = resistant; underlined options are agents of choice.

*Co-trimoxazole is active against *Listeria monocytogenes*

Table 28.2 First-line antibiotics

Infection	Likely organisms	Suggested 1st line	Comments
Bloodstream infection			
Septicaemia (neonate) <48h old	Group B streptococcus *Escherichia coli* *Listeria monocytogenes*	Benzylpenicillin + gentamicin or amoxicillin + cefotaxime	Consider disseminated HSV and enterovirus infections
Septicaemia (neonate) >48h old	As above + *Staphylococcus aureus* Enterobacteriaceae	Flucloxacillin + gentamicin or amoxicillin + cefotaxime	Coagulase-negative staphylococcus may need to be covered if CVC *in situ*
Septicaemia (hospital acquired)	Anti-pseudomonal cover also required	Meropenem or tazocin	
Septicaemia (indwelling line)	Need to cover coagulase-negative staphyloocci	Vancomycin + cefotaxime (community) or meropenem (hospital)	
Septicaemia (immuno-compromised)	Anti-pseudomonal cover also required	Meropenem	Consider fungal and viral infections
Septicaemia (suspected meningococcal)	*Neisseria meningitidis*	Cefotaxime or Ceftriaxone	
Respiratory system			
Pneumonia (neonate)	Group B streptococcus *Escherichia coli* *Listeria monocytogenes*	Benzylpenicillin + gentamicin or amoxicillin + cefotaxime	Consider viral pneumonia Consider *Chlamydia trachomatis* and *Bordatella pertussis* —— macrolide indicated
Community-acquired pneumonia (CAP)	*Streptococcus pneumoniae* *Haemophilus influenza* *Mycoplasma pneumoniae*	Cefuroxime +/- clarithromycin	
Pneumonia (hospital acquired)	Enterobacteriaceae *Pseudomonas aeruginosa*	Meropenem or tazocin	CAP organisms may cause infection too.
Epiglottitis Bacterial tracheitis	*Haemophilus influnzae* *Staphylococcus aureus*	Cefotaxime or ceftriaxone	

Table 28.2 First-line antibiotics (*Continued*)

Infection	Likely organisms	Suggested 1st line	Comments
Intracranial infection			
Meningitis (neonate)	Group B streptococcus *Escherichia coli* *Listeria monocytogenes*	Benzylpenicillin + gentamicin or cefotaxime + amoxicllin	
Meningitis	*Neisseria meningitidis* *Streptococcus pneumoniae*	Cefotaxime or ceftriaxone	
Encephalitis	Above + herpes simplex virus	Add IV aciclovir	
Brain abscess	*S. anginosus* *S. pneumoniae* Anaerobes Enterobacteriaceae	Cefotaxime or ceftriaxone plus metronidazole	
Meningitis (post neurosurgery)	Enterobacteriaceae *P. aeruginosa* *Staph. aureus*	Meropenem	
Meningitis complicating ventriculoperitoneal shunt	Coagulase-negative staphylococci	Vancomycin plus Cefotaxime or Ceftriaxone	If diagnosis confirmed remove shunt + intrathecal antibiotics
Skin and soft tissue infection			
Cellulitis	*Staph. aureus* *Strep. pyogenes*	Flucloxacillin or erythromycin	
Cellulitis (immunocompromised)	Above + *Pseudomonas aeruginosa*	Meropenem or tazocin	Consider fungal infection
Surgical wound infection	*Staph. aureus*	Flucloxacillin or erythromycin	Consider organisms relevant to site of surgery if deep seated infection

Continued

Table 28.2 First-line antibiotics (*Continued*)

Infection	Likely organisms	Suggested 1st line	Comments
Renal tract infection			
<3 months of age	*Escherichia coli* Enterobacteriaceae *Enterococcus* spp.	Amoxicillin + gentamicin or cefuroxime	Consider cefotaxime if possible meningitis
Uncomplicated renal tract infection (>3mths)		Trimethoprim or cefalexin	
Pyelonephritis (>3mths)		Amoxicillin + gentamicin or cefuroxime	
Intra-abdominal infection			
Necrotizing enterocolitis in neonates		Benzylpenicillin + gentamicin + metronidazole or amoxicillin + cefotaxime + metronidazole	
Community-acquired peritonitis	*Escherichia coli* *S. anginosus* *Bacteroides fragilis*	Cefuroxime + metronidazole	
Secondary peritonitis	Enterobacteriaceae *P. aeruginosa* *Enterococcus* spp.	Meropenem or tazocin	Consider antifungal cover. Agents may depend on previous antibiotic exposure
Cardiovascular infection			
Endocarditis (native valve)	*Staph. aureus* *Streptococcus* spp.	Flucloxacillin + gentamicin	Add amoxicillin if symptoms subacute
Endocarditis (prosthetic valve or conduit)	As above plus Coagulase-negative staphylococci	Vancomycin + gentamicin	

Penicillins

- Selectively binds bacterial cell wall
- Facilitate the activity of other agents such as gentamicin so they can reach their targets within the bacterial cell
- Side effects include hypersensitivity, leucopenia and with high doses, sodium overload.
- Flucloxacillin is stable to a penicillin degrading enzyme commonly produced by staphylococci
- Amoxicillin has a broader spectrum of activity, although resistance amongst *E. coli* is now exceptionally common
- Most penicillins are excreted via the renal route and in order to avoid CNS toxicity doses should be modified accordingly
- Flucloxacillin may be associated with cholestatic jaundice and hepatitis and should be used with caution in this group.

Co-amoxiclav

- A combination of amoxicillin with the beta-lactamase inhibitor clavulanic acid
- Increases the spectrum of activity to include anaerobes, *S. aureus,* and resistant *E. coli.*

Piperacillin-tazobacatam

- A combination of a ureidopenicillin and a β-lactamase inhibitor
- Has a broad spectrum of activity as indicated in Table 28.1 and is excreted in both urine and bile.

Meropenem

- A carbapenem antibiotic with a wide spectrum of activity
- Resistance amongst Enterobacteriaceae is uncommon in the UK but a steady stream of isolates is being identified in patients returning from abroad
- Resistance amongst other bacterial groups such as *Pseudomonas aeruginosa* and *Acinetobacter* spp. is more commonly seen.

Cephalosporins

- Spectrum of activity varies between different classes
- Ceftriaxone is of particular note because of its use in meningococcal disease and suspected meningitis
- Ceftriaxone should not be given concomitantly with IV calcium preparations
- Overuse of cephalosporins may be associated with the emergence of extended spectrum β-lactamase producing Enterobacteriaceae
- In adults cephalosporins are increasingly avoided due to their association with *Clostridium difficile* infection
- 3–9% of individuals are cross allergic to penicillins and *cephalosporins* although specific allergy also occurs.

Ciprofloxacin

- Has a broad spectrum of activity
- Resistance can rapidly emerge if use as monotherapy against *S. aureus* and it should not be used for pneumococcal infections

- Is widely distributed in tissues and achieves good concentrations in the CSF in the absence of meningeal inflammation (unlike β-lactams).
- There is concern about its use in children in view of arthropathy detected in animal studies
- May cause haemolysis in children with G6PD deficiency
- Convulsions may also occur particularly with concomitant non-steroidal agents
- Some authorities have associated the emergence of MRSA with high levels of ciprofloxacin use.

Polymyxin

- Is listed as it is one of the few agents active against resistant Gram-negative bacteria
- Can be used systemically for the treatment of such infections but due to nephro- and neurotoxicity should only be used when isolates are resistant to alternative agents.

Gentamicin

- An aminoglycoside with a wide spectrum of activity
- Activity is diminished under anaerobic conditions
- May be used in synergistic combination with β-lactam agents
- Intracellular organisms are resistant to it as it does not enter cells
- Concentration in tissues varies but rises in the presence of inflammation
- Is excreted via the renal tract and may cause oto- and nephrotoxcity, particularly with prolonged use (>7 days)—ototoxicty may be exacerbated by ototoxic diuretics (furosemide).
- Once daily dosing (extended interval dosing in neonates) is the preferred method of administration—apart from in endocarditis, extensive burns, or in the setting of renal dysfunction
- Serum levels must be monitored and local guidelines followed
- Less common side effects include neuromuscular blockade and hypomagnesaemia, particularly in patients on cytotoxics.

Trimethoprim

- Infrequently used on the PICU apart from in combination with sulfamethoxazole for the treatment and prophylaxis of *Pneumocystis jiroveci* pneumonia.

Erythromycin

- A macrolide
- Used to treat Gram-positive infections when patients are allergic to β-lactam agents
- Also used in the management of infections due to intracellular bacteria
- Newer agents are better tolerated and can be given less frequently
- Macrolides interact with many immunosuppressive agents and should be used with extreme care in transplant patients.

Clindamycin

- A lincosamide
- Active against staphylococci and streptococci
- Rapidly and widely distributed

- Inhibits protein synthesis by binding to the 50S subunit of susceptible bacterial ribosomes
- *In vitro* suppresses toxin production in TSS (TSS toxin 1) and severe staphylococcal necrotizing pneumonia –Panton–Valentine leucocidin (PVL)
- Isolates that are erythromycin resistant must be tested for inducible resistance to clindamycin
- Side effects include diarrhoea and skin rashes
- Clindamycin is associated with *C. difficile*.

Metronidazole

- Principally used for treating anaerobic infection
- Dose should be reduced in severe liver disease and renal impairment
- Peripheral neuropathy may occur with prolonged therapy as can convulsions.

Glycopeptides (vancomycin, teicoplanin)

- Widely used in the ICU setting
- Active against coagulase-negative staphylococci, a frequent cause of central-line related infection
- Rapid infusion of vancomycin may cause histamine release, the 'red-man syndrome'. This is less common with teicoplanin
- Resistance to tecicoplanin may develop amongst certain strains of staphylococci
- Although oto- and nephrotoxicity to vancomycin is recorded this is uncommon with the highly purified current preparation of the drug and blood level monitoring.

Linezolid

- An oxazolidinone antibiotic
- Bacteriostatic activity against resistant Gram-positive infection
- Achieves high tissue concentrations
- Similar to clindamycin inhibits toxin production and therefore is recommended in particular for suspected PVL infections which might be due to clindamycin-resistant staphylococci
- Side effects include blood disorders and optic neuropathy, particularly with prolonged therapy
- Resistance has been reported in certain Gram-positive organisms such as enterococci.

Antifungals

Increasingly antifungal therapy is being tailored on the basis of identification and susceptibility testing. Table 28.3 gives an outline of the spectrum of activity of those antifungal agents currently available

Table 28.3 Antifungal agents

	Antifungal agent						
Selected fungi	**Amphotericin (Ambisome)**	**Caspofungin**	**Micafungin**	**Posaconazole**	**Voriconazole**	**Itraconazole**	**Fluconazole**
Candida albicans	S	S	S	S	S	S	S
Candida parapsilosis	S	R	R	S	S	S	S
Candida glabrata	S	S	S	S-R	S-R	R	R
Candida tropicalis	S-R	S	S	S	S	S	S-R
Trichosporon beigelii	R	R	R	S	S	S	S
Cryyptococcus neoformans	S	R	R	S	S	S	S
Aspergillus fumigatus	S	S	S	S	S	S	R
Aspergillus tereus	S-R	S	S	S	S	S-R	R
Mucor spp.	S	R	R	S	R	R	R
Scedosporium	S	R	R	S	S	R	R
Fusarium	S-R	R	R	S-R	S-R	R	R

S= sensitive; R = resistant; underlined options are agents of choice.

Triazole antifungal agents

- Triazoles include fluconazole, itraconazole, voriconazole, and posaconazole
- Act by inhibiting the fungal cytochrome P450 enzyme, 14α-demethylase
- Also has some activity against the related mammalian enzyme; therefore these agents interact with a range of drugs including phenytoin, protein pump inhibitors, cyclosporine, tacrolimus, sirolimus, statins, and antiretrovirals
- Related compounds (imidazoles) are used for superficial mycoses.

Fluconazole

- Available in oral and IV formulations. It has >90% oral bioavailability
- Widely used on PICU as prophylaxis, pre-emptive therapy or treatment

- Half-life of 24h, protein binding 11% and >80% is excreted unchanged in urine
- Penetrates well into tissue and the CSF
- Main side effects are GI upset and hepatotoxicty.

Voriconazole

- Undergoes extensive metabolism in the liver
- Half-life is ≥24h, protein binding 58%, renal excretion <2%
- Penetrates well into tissue and CSF
- Main side effects are GI upset and visual disturbances
- Less commonly hair loss, electrolyte disturbance and QTc prolongation are seen
- IV vehicle may accumulate in renal failure and not removed by dialysis.

Itraconazole and posaconazole

- Used much less frequently on PICU
- Posaconazole is only available orally and principal use is in haematology/oncology patients and/or zygomycetes infection.

Amphotericin B

- Acts by binding ergosterol, disrupting fungal cell membrane function—it therefore displays fungicidal activity *in vitro*
- IV liposomal amphotericin (ambisome) is the predominant amphotericin formulation used in paediatrics in developed countries—renal toxicity and infusion related adverse effects are less common
- Amphotericin is extensively bound to tissue and although it has poor CSF penetration it is effective in treating cryptococcal meningitis.

Echinocandins

- 3 clinically available E*chinocandins*:
  - All available as IV preparations
  - ***Micafungin*** has a paediatric licence.
- Act by inhibiting the enzyme, beta-(1,3)-D-glucan synthase: present in many but not all fungi
- Fungistatic against molds but increasingly used as first-choice therapy in patients with candidaemia or invasive candidiasis.

Antivirals

Treatment of HIV with antivirals is outside the scope of this text and specific expert advice should be obtained.

Table 28.4 Antiviral agents

	Antiviral agent							
Selected viruses	**Ribavirin**	**Amantidine**	**Pleconaril**	**Oseltamivir**	**Cidofovir**	**Foscarnet**	**Ganciclovir**	**Aciclovir**
Herpes simplex	S	R	R	R	S	S*	S	S
Varicella zoster	S	R	R	R	S	S*	S	S
Cytomegalovirus	S	R	R	R	S	S*	S	R
Adenovirus	S	R	R	R	S	R	S	R
Influenza A	S	S	R	S	R	S	R	R
Influenza B	S	R	R	S	R	R	R	R
Parainfluenza	S	R	R	R	R	R	R	R
RSV	S	R	R	R	R	R	R	R
Measles	S	R	R	R	R	R	R	R
Enterovirus	S	R	S	R	R	R	R	R
Polyomaviruses (JC & BK)	R	R	R	R	S	R	R	R
Poxviruses (incl. orf and molluscum contagiosum)	S	R	R	R	S	R	R	R
Haemorrhagic fever viruses (e.g. Lassa fever)	S	R	R	R	R	R	R	R

S= sensitive; R = resistant; underlined options are agents of choice.

*Including aciclovir resistant strains (HSV & VZV) and ganciclovir resistant strains (CMV)

Aciclovir

- A nucleoside analogue available in a number of oral and IV forms
- Poorly absorbed and therefore severe infections need to be treated with IV therapy
- Used in PICU mainly for suspected encephalitis, disseminated HSV infection in neonates and severe varicella zoster
- Used prophylactically in certain transplant groups
- Resistance may occur after prolonged therapy particularly in the immunocompromised
- Renal dysfunction may occur and can be avoided with reducing rate of infusion, adequate hydration, and dose modification in renal failure.

Ganciclovir

- A nucleoside analogue with specific activity against CMV
- Also active against HSV and VZV but toxicity precludes use as first-line therapy for these infections
- Usually given intravenously but a prodrug is available than can be used orally
- Side effects include bone marrow suppression, CNS abnormalities such as confusion, convulsions, hallucinations and tremor occur in 5% of recipients, liver function abnormalities, fever, and rash occur in 2%.

Foscarnet

- A non-nucleoside pyrophosphate analogue
- Has a broad spectrum of activity but limited because of toxicity—mainly used to treat CMV disease in patients for whom ganciclovir therapy fails or is contraindicated
- Renal toxicity is common, chelation of metal ions may cause hypocalcaemia, hypomagnesaemia, hypokalaemia, and hypophosphataemia.
- Other side effects include anaemia, genital ulceration, nausea, vomiting, headache, convulsions, tremor, and pancreatitis
- Is sometimes used at lower doses in combination with ganciclovir in order to avoid toxicity.

Cidofovir

- An acyclic cytosine analogue
- Has a broad spectrum of activity but limited by nephrotoxicity
- For systemic infections is usually given intravenously—e.g. for systemic adenovirus or JC/BK virus infections
- Can also be used topically for example against pox viruses.

Oseltamivir

- A selective neuramidase inhibitor
- Only available orally and for use in children >1 year
- Is active only against influenza A and B and should be used as per NICE guidelines
- Resistance is increasingly reported.

Pleconaril

- An oxadiazole
- Active against most enteroviruses and rhinoviruses
- Some evidence that may of benefit in severe neonatal enterovirus infection.

Amantidine

- Inhibits influenza A replication by preventing virus acidification—required for fusion of the viral envelope to cells
- Resistance can emerge rapidly
- No longer recommended for use in influenza A cases but may have a role in combination therapy.

Ribavirin

- A synthetic nucleoside
- Wide viral spectrum of activity *in vitro*
- Common side effects include headaches and anaemia, it is teratogenic and embryotoxic
- Despite its wide spectrum of activity its use has declined particularly for RSV.

A number of other agents such as immunoglobulins are used for the prevention and treatment of viral infections.

Newer antimicrobial agents

Daptomycin

Daptomycin is mentioned as resistant Gram-positive infections are an increasing problem on PICU. This is a lipopeptide with better bactericidal activity than glycopeptides. Its main side effect is muscle toxicity that may be irreversible at high doses.

Further reading

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Chapter 29

Neonatology

Neonates in PICU

Despite there being considerable variation between countries and institutions in the way patients are distributed between PICU and NICU (neonatal intensive care or special care baby unit), knowledge and expertise in neonatology is essential for any paediatric intensivist. This chapter is a brief excursion into the world of neonatology and is not intended to offer comprehensive knowledge. For further information please consult a specialist neonatal textbook.

Generally neonates that are admitted to PICU are comparatively mature (many PICUs have minimum weights, e.g. 2.5kg) and have specific indications:

- Surgical:
  - Congenital heart disease
  - Diaphragmatic hernia
  - Tracheo-oesophageal fistula
  - Gastroschisis/exomphalos
  - Airway abnormalities
  - Other congenital anomalies
- Infection:
  - Neonatal sepsis
  - Metabolic disease
  - Bronchiolitis.

Definitions

- The neonatal period is defined as the first 28 days of life
- Sometimes it is broken down into early (<7 days) and late (8–28 days).

Pre-term baby terminology

- Prematurity: <37 complete weeks of gestation
  - Extreme prematurity: <28 weeks
- Low birth weight: <2.5kg
  - Very low birth weight: <1.5kg
  - Extremely low birth weight: <1kg

Neonatal circulation and ventilation

It is important to understand the changing anatomy and physiology around the time of birth and to apply this understanding when a neonate becomes unwell.

Features of fetal circulation (Fig. 29.1)

- High PVR. The lungs are not inflated
- Low SVR. Umbilical arteries connect the systemic circulation to the low pressure placenta
- Gas exchange occurs in the placenta.
- Almost all 'venous blood' from the SVC enters the right ventricle and travels to the aorta via the pulmonary trunk and the ductus arteriosus. Less than 10% enters the branch pulmonary arteries.
- Oxygenated blood from the placenta passes to the IVC via the ductus venosus, portal vein, and hepatic veins

- 30% of IVC blood traverses the foramen ovale and enters the left ventricle via the left atrium. This blood preferentially perfuses the coronary arteries and brain with oxygen-rich blood.

Changes in circulation at birth

- First breath expands the lungs
- PVR falls and pulmonary blood flow increases
- Pulmonary venous return rises and causes an increase in left atrial pressure

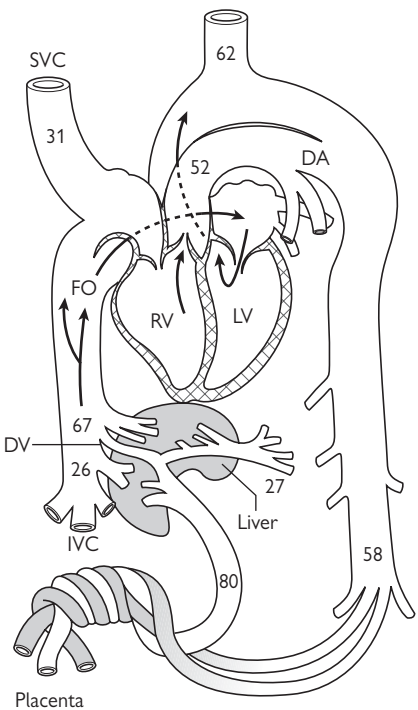

Fig. 29.1 The fetal circulation. Mean oxygen saturations are given in the relevant sites. DA, ductus arteriosus; DV, ductus venosus; FO, foramen ovale; IVC, inferior vena cava; LV, left ventricle; RV, right ventricle; SVC, superior vena cava. Reproduced from Baker E (1993). Congenital heart disease in the neonatal period. In Rennie, JM, Robertson, NRC (eds) *A Manual of Neonatal Intensive Care*, 4th edn. Edward Arnold, London with permission.

- Foramen ovale closes due to the pressure differential between left and right atria. This can be reversed if right atrial pressure rises (secondary to a rise in PVR and right ventricular pressure) causing a R→L shunt
- The rise in oxygen tension closes the ductus arteriosus (prostaglandin inhibition) and reduces PVR over the coming months (pulmonary arteriole smooth muscle regression).

Fetal lungs

- Fetal lung fluid is produced at 12 weeks' gestation
- Absence of fetal breathing is associated with lung hypoplasia.

Changes in lungs at birth

- Decrease in lung fluid production
- Drainage and resorption (via lymphatics) of lung fluid in birth canal
- Caesarean section is associated with tachypnoea of newborn (poor fluid clearance)
- High negative intrapleural pressures (40cmH_2O) lead to lung inflation
- Regular respirations are established
- The diaphragm is main respiratory muscle
- Lung compliance increases and airway resistance decreases over first few days
- Neonates are obligate nasal breathers
- Ventilation/perfusion mismatch improves as PVR decreases.

Neonatal issues

There are a number of issues that are particular to neonates (and younger infants) and should be considered when treating them in PIC.

Minimal handling

Neonates need treating with care. This is particularly true of pre-term babies. They do not respond well to rough or excessive handling and become easily stressed:

- Stress can lead to hypoxia, apnoea, vasoconstriction, and bradycardia
- Stress can be provoked by pain, cold, overstimulation
- Do not persist in technically difficult procedures, e.g. siting of lines, give the baby and yourself a rest or get a senior colleague involved.

Temperature control

Babies lose heat rapidly (see Box 29.1) and have reduced ability to generate it. Cold babies become ill babies and have ↑mortality. They lose the ability to increase their ventilation in response to hypoxia. They increase their oxygen consumption in response to a cold environment, develop respiratory distress and coagulopathy. Vascular access is difficult in cold babies.

- Babies lose heat due to minimal subcutaneous fat, thin skin, high surface area to body weight ratio, and large heads
- Neonates cannot shiver and use sympathetically mediated brown fat—non-shivering thermogenesis—to generate heat. This is about 6% of birth weight at birth but is limited in preterm neonates

- Sedation and paralysis inhibit heat production
- Shocked babies become cold babies.

Box 29.1 Iatrogenic hypothermia is avoidable

- Avoid wet babies. Minimize antiseptic solutions and dry them immediately
- Minimize exposure during procedures
- Minimize procedures. Get senior assistance. Does this baby really need central venous access or can we wait and warm it up first?
- Watch for heat loss in transfer situations, e.g. retrieval or return from theatre
- If hypovolaemic then resuscitate promptly with 10–20mL/kg boluses of normal saline 0.9% or colloid
- Incubators and overhead heaters reduce radiant heat loss
- Polythene wrapping, hats, clothing and reflective material reduce heat loss.

Jaundice

Physiological jaundice is common in the first days of life in term infants (and up to the first 2 weeks in preterm infants) and is due to immaturity of hepatic enzymes. It is characteristically unconjugated.

- Up to 66% of normal newborns become jaundiced
- Jaundice is more common in breast-fed than formula-fed babies (breast milk inhibits bilirubin glucuronidation)
- Infants, especially preterm infants, have higher rates of bilirubin production than adults
- The predominant source of bilirubin is the breakdown of hemoglobin (red blood cells have shorter lifespan in neonates, 40–70 days)
- Obstructive jaundice (e.g. biliary atresia and hepatitis) does not usually present in the early neonatal period
- Risk factors for the neurotoxic effects of hyperbilirubinaemia, i.e. kernicterus (yellow staining of basal ganglia) include:
  - Unconjugated bilirubin level (conjugated does not cross the blood–brain barrier)
  - Longer duration of exposure
  - Younger gestational age
  - Younger age of baby
  - Sick baby with other organ dysfunction.

Initial investigations (Fig. 29.2)

- Split bilirubin to determine unconjugated and conjugated fractions
- FBC and reticulocytes
- Blood group and Coombs' test
- Thyroid function tests
- Blood, urine, and surface swab cultures
- Liver function tests, renal function, glucose.

Further tests

- Galactosaemia, G6PD, tests for inborn errors of metabolism and serology for congenital infection and hepatitis.

The reader should refer to a specialist neonatal text for full list of investigations for prolonged jaundice.

Treatment for jaundice

The vast majority of babies require no treatment. Well term babies do not require phototherapy until bilirubin exceeds 350micromol/L (see Table 29.1).

- Phototherapy converts unconjugated bilirubin into water soluble components (excreted in urine and bile) and has remained the standard of care for the treatment of unconjugated hyperbilirubinaemia. Treatment may cause:
  - Loose stools (↓gut transit time)
  - ↑ fluid loss through skin. Watch fluid balance and give additional fluids (~30mL/kg/day)
- Extreme or rapidly rising hyperbilirubinaemia requires exchange transfusion
- Thresholds for both phototherapy and exchange transfusion are available, though local practice may vary (Box 29.2)
- Do ***not*** give phototherapy for conjugated jaundice. It turns babies a deep brown colour.

Box 29.2 'Rule of thumb'

Threshold for phototherapy

- Unconjugated bilirubin (umol/L) = > [(10 × gestational age) −100]

Threshold for exchange transfusion

- Unconjugated bilirubin (umol/L) = > (10 × gestational age).

Table 29.1 Management of jaundice in the healthy full term baby*

Age in hours†	Bilirubin level in µmol/L	
	Phototherapy	**Exchange transfusion**
25–48	260	340
49–72	310	430
>72	340	430

†Below 24h jaundice must always be investigated as it is usually due to a haemolytic process. Whether to use phototherapy or to carry out an immediate exchange is a matter for clinical judgement and depends on the rate of rise, the absolute level, and the condition of the baby.

*Reproduced from Rennie, JM, Robertson, NRC (eds) Congenital heart disease in the neonatal period. In Renne JM and Robertson NRC, *A Manual of Neonatal Intensive Care*, 4th edn. Edward Arnold, London with permission.

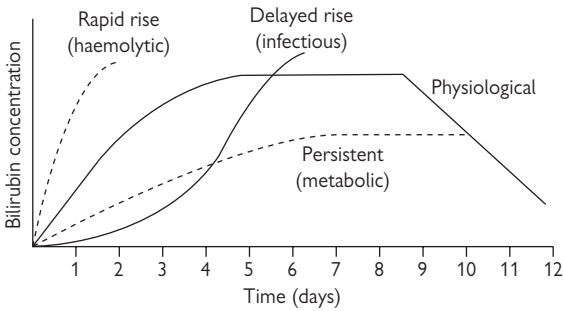

Fig. 29.2 Patterns of neonatal jaundice.

Glucose control

Hypoglycaemia is common in the newborn infant:

- Serum glucose levels <2.2mmol/L in the first 24h of life and 2.6mmol/L thereafter are considered hypoglycaemic
- 4–6mmol/L is considered normal
- There is a normal dip in blood glucose 2–4h postnatally
- Babies particularly at risk of hypoglycaemia are:
  - Preterm
  - Small for gestational age
  - Macrosomic babies (may have hyperinsulinism)
  - Infants of poorly controlled diabetic mothers
  - Infant who suffers perinatal asphyxia.

Treatment

Box 29.3 Treatment of hypoglycaemia

(See also 📖 p.681)

- Bolus 5mL/kg of IV glucose 10% slowly, follow up with infusion of 10% glucose at 3mL/kg/h (equivalent to 5mg/kg/min or 72mL/kg/day glucose 10%)
- Repeat glucose level after 30–60min
- Increase the infusion as necessary to 4mL/kg/h (i.e. 6.6mg/kg/min or 100mL/kg/day G10%)
- If infection is suspected or there is no alternative explanation for hypoglycaemia take blood cultures and treat with broad-spectrum antibiotics
- When blood glucose normalizes, feeds can be reintroduced gradually and infusion tailed off
- If hypoglycaemia persists then increase the rate of glucose or consider increasing glucose concentration (12.5% or 15%) if volumes are large.
- If concentration of 12.5% or above required then infuse through a central line/peripheral long line (PICC)
- If resistant consider glucagon 20mcg/kg IV/IM 12-hourly.

Renal function/fluid balance

(See also 📖 p.648)

The neonatal kidney has a limited ability to concentrate urine or to excrete a water or sodium load. Thus neonates are particularly vulnerable to both dehydration and fluid overload

- Nephrogenesis and glomerulogenesis is complete by 35 weeks of gestation but glomeruli are immature
- Neonates concentrate urine to a maximum 600–800mosmol/kg (older children and adults achieve 1500mosmole/kg)
- First few days of life characterized by adaptive diuresis/natriuresis (leading to initial weight loss).

Analgesia and sedation

Neonates suffer pain and discomfort although this may not always be obvious. Thus, both analgesia and sedation are mandatory for many neonates in PICU.

- All neonates require hypnotic (and often analgesic) drugs before intubation. Awake intubation is to be avoided. See Box 29.4
- Analgesics (both systemic and local) are necessary for many practical procedures, e.g. arterial lines, chest drains. Try to coordinate procedures in order to minimize distress
- The onset of action for many drugs can take several minutes—wait for them to work before embarking on a painful or stimulating procedure
- Morphine is the most frequently used analgesic with neonates and has sedative properties thus making it appropriate as a sole agent
- Morphine half-life is up to 9h in the preterm and up to 7h in the term baby but falls to 3h in infants

- Neonates can be very sensitive to morphine (immature blood–brain barrier). Watch for respiratory depression
- If rapid analgesia is required consider fentanyl (quicker onset and shorter acting than morphine)
- Midazolam is the most appropriate hypnotic for neonates (short-acting and water soluble) and can be given as bolus or infusion
- ❗ Midazolam can cause hypotension in neonates particularly in combination with fentanyl
- Midazolam accumulates quickly and can cause withdrawal symptoms when stopped. Long-term infusions should be tapered off over several days and symptoms of withdrawal looked for (regurgitation, agitation, sweating, tachycardia, seizures)
- Oral sedation can be used but chloral is often avoided in neonates (displaces bilirubin from albumin and has toxic metabolites)
- The effects of analgesics or sedation during the neonatal period on long-term neurodevelopment and psychological outcome has not been well studied.

Box 29.4 Intubating neonates

The combination of morphine (opioid), midazolam (benzodiazepine), and muscle relaxant is often used for intubation of neonates. Unfortunately morphine and midazolam take up to 5min or longer to have appreciable sedative effects. Ensure that adequate doses are given and that care is taken to ensure that they have taken effect before attempting intubation. Alternatives include using fentanyl instead of morphine (bolus 1–3mcg/kg) which has a rapid onset. Anaesthetic agents such as thiopentone, propofol, or ketamine with suxamethonium or rocuronium give the best conditions for intubation. Units should have an intubation protocol with use of standard drugs.

Drug handling

(See also 🕮 Chapter 17.)

Care must be taken in administering drugs to premature babies and neonates as they are generally more sensitive to the effect of a drug and also more likely to have adverse effects.

- Neonates have less protein binding of drugs than infants (less albumin and α-1 acid glycoprotein) resulting in more free drug and thus ↑effect
- Neonates have a greater proportion of body weight that is water. Thus water soluble drugs have a greater volume of distribution. Many drugs may need a greater loading dose (mg per kg) in neonates than in infants, e.g. muscle relaxants and aminoglycosides
- Preterm and term neonates have less fat and muscle and therefore drugs may redistribute less resulting in greater plasma levels for longer, e.g. opioids and barbiturates
- Hepatic drug metabolism is not fully developed in neonates:
  - Phase 1 reactions (oxidation, reduction, hydrolysis) are reduced. Reduced cytochrome P450 can lead to prolonged action of theophylline, benzodiazepines, and barbiturates

  - Phase 2 reactions (conjugation through glucuronidation, sulfation and acetylation) are reduced affecting morphine and paracetamol clearance
- Renal function is less in neonates and can affect drug excretion: aminoglycosides and cephalosporins have prolonged half-life
- Closure of a patent ductus can affect drug delivery.

Specific neonatal conditions

Respiratory distress in the neonate

The commonest causes of respiratory distress in the neonatal period are
- Infant respiratory distress syndrome (IRDS)
- Transient tachypnoea of the newborn (TTN)
- Persistent pulmonary hypertension of the newborn (PPHN)
- Meconium aspiration syndrome.

IRDS

IRDS affects newborns, usually preterm, and is characterized by ↑work of breathing and hypoxia secondary to a lack of surfactant production.
- Babies present within the first 4h of birth with grunting respiration, subcostal, intercostal, and sternal recession
- CXR appearances depend on the severity of the disorder with poorly inflated lungs and a 'ground glass' appearance
- Extensive atelectasis occurs secondary to surfactant deficiency
- The production of pulmonary surfactant is necessary to maintain alveolar stability and normal lung function
- Surfactant is produced in the 3rd trimester
- The incidence and severity of RDS has ↓ with the administration of steroids to mothers presenting in premature labour
- IRDS can be effectively treated with exogenous surfactant preparations (Curosurf®, Survanta®) given down the ETT (followed by bag ventilation). This can be repeated at 8–12h
- Can be complicated by pneumothorax, pulmonary haemorrhage, and pulmonary hypertension
- Can lead to chronic lung disease.

TTN

Under normal circumstances, labour and delivery will result in clearance of lung fluid. Failure to do so will result in excess lung liquid resulting in non-compliant lungs and ↑airways resistance.

Features:
- Tachypnoea as a result of ↑ airways resistance and stiff lungs, occurs within a few hours after delivery
- Tachypnoea exceeds 60 breaths per minute with nasal flaring, use of accessory muscles and grunting
- Air trapping due to reduced expiratory time and largish lung volume on CXR
- Cyanosis responding to oxygen
- May require CPAP or even rarely invasive ventilation but recovery is quick.

PPHN

PPHN occurs when there is a failure of the expectant fall in pulmonary arterial pressures with birth (see Box 29.5). PPHN occurs in 1–6/1000 live births and is a major cause of morbidity and mortality (20–25%) in the term and near term infant.

Box 29.5 PPHN can be precipitated by

- Maternal drugs such as aspirin
- Pulmonary hypoplasia
- Congenital malformations, e.g. congenital diaphragmatic hernia
- Developmental/iNO disorder, e.g. alveolar-capillary dysplasia
- Meconium aspiration syndrome
- Group B strep infection
- Hypoglycaemia.

Pathophysiology

- After birth, PVR remains equal to or greater than SVR and blood continues to flow R→L across the foramen ovale/ductus arteriosus
- The lungs continue to be bypassed and severe hypoxaemia ensues
- Elevated PVR leads to right heart dilatation and failure.

Diagnosis

- Usually presents within a few hours of birth with cyanosis, respiratory distress, and hypotension.
- CXR may be normal or compatible with meconium aspiration, IRDS or diaphragmatic hernia.
- Echocardiography confirms pulmonary hypertension.

Treatment

- The aim of treatment is to improve alveolar oxygenation, minimize pulmonary vasoconstriction, and maintain systemic pressure and perfusion
- Treatment initially involves good supportive intensive care:
  - Ventilation should aim for normal oxygenation (SaO_2 >95%) with (low) normal CO_2. Avoid significant hyperventilation. High frequency oscillation may be considered
  - Combining inhaled NO and HFOV is more successful than either alone
  - Paralysis with sedation is often necessary
- Inotropes (dobutamine ± adrenaline) and inodilators (milrinone) may help
- iNO is a selective pulmonary vasodilator without significant systemic effects and is a useful adjunct to therapy
- Prostacyclin may help, however the non-specific vasodilatation of both pulmonary and systemic circulations can limit use
- ECMO is the recommended treatment for PPHN when other therapies have failed. An oxygenation index of >30 if NO is being used or >40 without NO should be a trigger for considering ECMO
- Spontaneous resolution of this syndrome may occur 36h to several days after birth

- Follow-up of survivors has revealed few abnormalities of pulmonary and circulatory systems with 15–25% neurological sequelae.

Meconium aspiration

Meconium aspiration syndrome (MAS) occurs when a neonate inhales meconium and induces 3 major pulmonary effects: airway obstruction, surfactant dysfunction, and a chemical pneumonitis. The incidence is 1–5/1000 live births. Mortality is <5%. Risk factors for mortality include resuscitation outside hospital, first-born babies, shock, pneumothorax, pulmonary hypertension, and renal failure. Meconium aspiration is a trigger for PPHN.

- Depending on the degree of respiratory distress, respiratory support should be provided with oxygen via a nasal cannula, continuous positive pressure ventilation, conventional mechanical ventilation, or high-frequency oscillatory ventilation
- Paralysis with muscle relaxants may be necessary
- Inotropes can reduce R→L shunt and improve oxygenation
- Exogenous surfactant may be beneficial
- Inhaled NO may be useful in the management of the pulmonary hypertension associated with MAS. It may be more effective when combined with high-frequency oscillatory ventilation
- ECMO is used when other therapies have failed to result in improvement.
- Respiratory distress usually subsides in 2–4 days, although tachypnoea can persist for longer.

Chronic lung disease (CLD)

CLD is a general term for long-term respiratory problems in premature babies. It is also known as bronchopulmonary dysplasia (BPD). CLD generally results from lung injury to newborns that needed ventilator support.

- Risk factors for lung injury include:
  - Immature lungs
  - Surfactant deficiency
  - Presence of a L→R shunt through a PDA
  - Oxygen toxicity
  - Baro and volume (stretch) trauma from mechanical ventilation
- It is diagnosed when a premature baby continues to need additional oxygen after reaching 36 weeks gestational age
- The CXR of lungs with CLD often shows a bubbly, sponge-like appearance
- Treatment of CLD may include:
  - Steroids (dexamethasone, see Box 29.6)—shorten ventilator dependence but long-term benefits are unclear. There are some concerns about adverse neurodevelopmental outcome. Useful if started between day 7 and 14 (Cochrane review)
  - Bronchodilators
  - Fluid restriction and diuretics
  - PDA ligation if PDA fails to close with medical management
  - Good nutrition
  - Immunization against lung infection by respiratory syncytial virus (RSV) and influenza

- Oxygen therapy to prevent hypoxia—maintain SaO_2 > 95% to reduce risk of pulmonary hypertension
- Screening and treatment of retinopathy of prematurity.

Box 29.6 Dexamethasone in CLD

Example of weaning regimen for dexamethsone
- 250mcg/kg/dose 12-hourly for 3 days
- 150mcg/kg/dose 12-hourly for 3 days
- 100mcg/kg/dose 12-hourly for 3 days–1 week
- 100mcg/kg/dose 24-hourly for 3 days–1 week
- 100mcg/kg/dose 48-hourly for approx 4 weeks.

Side effects
- Concerns about long-term neurological sequelae
- Hypertension, irritability
- Hyperglycaemia
- ↑risk of infection, particularly oral candida
- Reduced growth and bone mineralization.

Hypoxic ischaemic encephalopathy (birth asphyxia)

Hypoxic ischemic encephalopathy (HIE) is the term for damage to cells in the CNS from inadequate oxygen delivery to the brain. HIE may cause death in the newborn period or result in developmental delay, seizure disorder, and/or cerebral palsy. Very often the injury occurs during difficult birth but can occur *in utero*. In many instances the cause is never determined.
- Severe asphyxia can result in hypotension, acidosis, and organ failure
- Children who are diagnosed with HIE can range from mild to severe in the amount of damage that has occurred.
- EEG, MRI and CT scans are used to determine the severity and location of the brain injury
- Therapeutic hypothermia for 72h looks promising as a neuroprotective strategy
- Longer-term treatment is mainly supportive and aimed at controlling seizures and managing ↑ muscle tone.

Retinopathy of prematurity (ROP)

ROP is an abnormal vascular proliferative disorder of the immature retina aggravated by high oxygen levels. It can acutely threaten vision.

ROP is prevented by ABG monitoring and keeping PaO_2 <12kPa (10kPa in VLBW). ROP is rarely a problem in PICU although inadequate attention to detail may put a pre-term baby at risk. Set SpO_2 target at 91–96% to prevent hyperoxia.

Screening is carried out by experienced paediatric ophthalmologist in at risk babies.
- Premature babies <31 weeks or <1500g
- Others considered at risk
- Screening is carried out at 6–7 weeks of age and repeated every 2 weeks

- Screening identifies babies who require laser treatment to treat vascular proliferation and prevent retinal detachment and blindness

Intraventricular haemorrhage (IVH)

Again, rarely a problem in PICU but a significant cause of morbidity and mortality in infants who are born prematurely. Neurological complications include life-long seizures, developmental delay, and cerebral palsy. IVH is uncommon in term neonates but occurs in 60–70% of neonates weighing 500–750g and 10–20% of those weighing 1000–1500g. There is an inverse relationship between the severity of the haemorrhage and the likelihood of survival.

- IVH is classified on radiological appearance on cranial US (Box 29.7).

Box 29.7 Grading of IVH

- Grade 1: subependymal haemorrhage
- Grade 2: intraventricular haemorrhage (IVH)
- Grade 3: IVH + ventricular dilatation/hydrocephalus
- Grade 4: IVH with parenchymal extension/periventricular leucomalacia (PVL).

- Grade 1 is of little or no neurodevelopmental significance
- Infants with massive IVH often rapidly deteriorate and die
- Significant proportion of survivors show motor and cognitive deficits
- Extremely low birth weight infants with IVH have poorer neurodevelopmental outcomes at 20 months than infants with normal cranial US
- 10–15% get hydrocephalus that may not appear for 2–4 weeks and may require shunting—serial (weekly) US scans are important to follow progress

Necrotizing enterocolitis (NEC)

Can be a life-threatening condition for premature neonates.

- Multifactorial aetiology which may include bowel ischaemia, rapid advancement of feeding, compromised immunity, and overcolonization of the bowel with enterotoxin-producing bacteria
- Mortality is higher in low birth weight infants and an associated perinatal hypoxic event
- Clinical picture may include abdominal distension, bilious vomiting, and blood in the stools and/or signs of systemic sepsis
- May be so extensive as to cause intestinal failure; either secondary to massive surgical resection or to severe mucosal damage despite an apparently adequate length of remaining bowel.

Investigations

- Blood picture: FBC, coagulation screen, U&Es, CRP
- Radiology: abdominal films when indicated to rule out perforation, assess bowel dilatation and presence of intramural or portal tree gas.

Treatment

- Antibiotics: benyl peniciilin, aminoglycoside and metronidazole for 7–10 days.
- Nil by mouth

- NG free drainage
- Fluid resuscitation, inotropes, and ventilation if indicated
- Blood products if required
- Surgical intervention in severe cases
- TPN.

Neonatal sepsis

Neonatal sepsis is invasive infection occurring in the first 4 weeks of life (Box 29.8). Neonatal sepsis occurs in 0.5–8.0/1000 births. It is a low incidence but high-risk problem. The highest rates occur in low birth weight infants, those with respiratory failure at birth, those with maternal perinatal risk factors, and prolonged rupture of membranes. The risk is greater in males (2:1) and in neonates with congenital anomalies.

Because diagnosis can be difficult many neonates who do not have the disease will by necessity be treated for sepsis (Box 29.10).

Box 29.8 Organisms causing neonatal sepsis

The major bacterial pathogens are (80% of infections):
- Escherichia coli (E. coli)
- Group B β-haemolytic *Streptococcus*
- Coagulase-negative *Staphylococcus* (CONS).

Other causes include:
- Pseudomonas aeruginosa
- Gram negative bacilli- Klebsiella, Proteus, Enterobacter, Haemophilus.
- Staphylococcus aureus
- *Pneumococcus* and other streptococci
- Listeria monocytogenes
- Fungi
- Viruses.

Early-onset sepsis (within 7 days of birth)
- Usually results from organism's acquired intrapartum
- Risk factors are prolonged membrane rupture (>24h), prolonged labour, pre-term, multiple pregnancy, and maternal infection (urinary, enteral, foul liquor)
- 85% of cases occur within 24h of birth
- Group B *Streptococcus* and *E. coli* account for 70% of early-onset sepsis.

Late-onset sepsis (after 7 days)
- Both intrapartum and environmental organisms may be responsible
- Risk factors include prolonged use of intravascular catheters, pre-term, ETTs, malformations (GI, spinal, urogenital)
- *S. aureus* and CONS account for many late onset cases
- Group B *Streptococcus* and *E. coli* do still occur

- Fungal sepsis is an increasingly important cause of sepsis in hospitalized neonates
- Disseminated herpes simplex virus (HSV) sepsis in the neonate can present in a similar manner to severe bacterial sepsis.

Box 29.9 Immunity and the neonate

Neonates, particularly premature ones, have a relative immune deficiency and are prone to infection. They lack both the physical barrier to infection and have deficiencies in both cellular and humoral immunity:

- Neonates in PICU are especially susceptible—they have thin and easily damaged skin, and often have tubes and lines inserted
- Neonates have normal lymphocyte numbers but relative T and B lymphocyte dysfunction. B lymphocytes require adequate IgG levels to synthesize antibodies.
- The bacteriocidal capacity of neonatal polymorphs are reduced
- Neonates have adequate IgG from placental transfer but this falls to a trough after about 3 weeks. Neonates are born deficient in immunoglobulins- IgA, IgD, IgE, IgM. Thus after 3–4 weeks all neonates have transient hypogammaglobulinaemia
- Maternal IgG confers immunity for certain infections but not for *E. coli* or TB
- Neonates have low complement levels.

Box 29.10 Symptoms and signs of neonatal sepsis

- Lethargy, poor feeding, irritability
- Pallor, mottling
- Tachypnoea (>60/min), apnoea, respiratory failure
- Abdominal distension, vomiting, regurgitation
- Seizures
- Temperature instability (↑↓), widening toe-core difference
- Tachy- (>160/min) and brady- (<80/min) cardia
- ↑capillary return time
- Full fontanelle
- Blood glucose instability (hypo- and hyperglycaemia)
- Acidosis

Investigations:

- FBC, differential and clotting profile
- Blood glucose
- Liver and renal function
- CRP and/or procalcitonin
- Blood culture, urine culture, swabs of nose, throat, ear, umbilicus, and any skin lesions, and maternal high vaginal swab
- Culture of removed vascular catheter
- Lumber puncture
- CXR, AXR if indicated
- ABGs.

Treatment

- ABC:
  - Respiratory support; oxygen, CPAP, ventilation
  - IV volume resuscitation
  - Cardiovascular support, e.g. inotropes; dopamine, norepinephrine, and epinephrine
- Antibiotics (see Box 29.11 and 📖 p.590)
- Antivirals (aciclovir)
- Antifungals (fluconazole or amphotericin)
- Correct coagulopathy
- IV immunoglobulin. Consider in severely unwell cases or in infants at risk of 'relative hypogammaglobulinaemia'.

Box 29.11 Empirical treatment for bacterial neonatal sepsis

Any neonate with suspected bacterial infection should receive antibiotics. Babies deteriorate too quickly to withhold treatment. These can be stopped if the baby improves, cultures are negative, or if there is an alternative diagnosis. Most cases of proven infection should be treated for 14 days (or 21 days in meningitis).

Antibiotic treatment should be given according to culture results but empirical treatment is the norm.

Every hospital has different likely pathogens and patterns of resistance so antibiotic choice has to be tailored to each unit.

However some recommendations can be made:

- Early onset sepsis (<48h from birth) give penicillin and aminoglycoside (e.g. gentamicin, amikacin, netilmicin)
- Later onset (>48h) consider flucloxacillin and aminoglycoside
- If meningitis suspected give 3rd generation cephalosporin for CSF penetrance (cefotaxime, ceftriaxone) and ampicillin for listeria
- If IV catheter infection suspected give flucloxacillin or vancomycin if resistant organisms are likely, e.g. CONS or resistant *S. aureus*
- If NEC or intra-abdominal sepsis suspected add metronidazole
- Consider fungal infection (particularly) in late onset neonatal sepsis.

Seizures

(See also 📖 p.467)

Seizures during the neonatal period occur in ~1% of all neonates and are considered to be in a separate category from epilepsy. Neonatal seizures frequently are a non-specific sign of underlying disease. Neonatal seizures can be benign but overall 10–50% of patients with neonatal seizures die during the neonatal period, and 50% of survivors develop long-term neurological complications.

- Neonatal seizures are usually divided into 4 main categories:
  - Clonic seizures are characterized by rhythmic, repetitive shaking of isolated parts of the body which can be multifocal and migrate

  - Myoclonic seizures represent very brief isolated jerks
  - Tonic seizures can be focal or generalized.
  - Subtle seizures consist of eye deviation, oral-buccal movements, or patterned movements of the extremities like bicycling
- Causes of neonatal seizures include birth injury (hypoxia, haemorrhage), congenital abnormalities, metabolic disorders
- Investigations include glucose, electrolytes (including Mg, Ca), renal and liver function tests, ammonia, clotting studies, toxicology, septic screen, TORCH screen, urine/blood organic and amino acids
- EEG may be diagnostic
- Imaging includes cranial US and CT/MRI scan.
- ***Management***: supportive (ABC), correct any metabolic abnormality and control seizures (usually with IV benzodiazepine).

Congenital and neonatal bowel disorders

Congenital bowel anomalies commonly present soon after birth, and often require emergency or urgent surgical intervention. Postoperative ventilation may be required, particularly if the surgery is extensive with a long anaesthesia time or the neonate is premature. The neonate may have other associated anomalies, which require support from the PICU. See Box 29.12.

Box 29.12 Principles of postoperative care in neonates

Analgesia
- In most cases IV morphine infusion will suffice
- NG/rectal paracetamol can be used for morphine-sparing effects
- Avoid non-steroidal analgesics.

Sedation
- When muscle relaxants are used for postoperative ventilation, use morphine and consider adding midazolam infusion. Use a lower infusion rate than older infants and watch for accumulation
- Preferred muscle relaxants for infusion are atracurium, vecuronium, and rocuronium. It is advisable to stop infusions every day to prevent accumulation, assess effect of sedatives, and neurology.

IV fluids
- Obtain excellent IV access early (preferably preop or theatre). IV access may be a problem later with an oedematous neonate. Consider peripheral feeding line, central line, or Hickman line (for fluids and TPN).
- Fluid requirements for neonates:
  - Day 1 of life — 2mL/kg/h (50mL/kg/day)
  - Day 2 — 3mL/kg/h (75mL/kg/day)
  - Day 3 and thereafter — 4mL/kg/h (100mL/kg/day)

Box 29.12 Principles of postoperative care in neonates (*continued*)

- For first 24h restrict postoperative IV maintenance fluids to a percentage of normal, e.g. 60–80% of calculated maintenance for age to account for stress response (AVP)
- Restrict IV maintenance to 75% maintenance for paralysis and ventilation, unless volume is required to deliver TPN
- *Maintenance solutions*: use10% glucose solutions without electrolytes for first 48h of life then add sodium and potassium as per daily requirements. 0.45% saline combined with glucose 5% (with added potassium) is appropriate for older neonates (>2 weeks)
- Intravascular volume/filling boluses are given as:
  - Isotonic crystalloid: 0.9% saline or Hartmann's (Ringer's lactate)
  - Colloid (human albumin 4.5% or gelufusine)
- Blood products if indicated
- Replace all NG, stoma, and drain losses with 0.9% saline
- Watch for large 'third-space losses' into abdominal cavity and from capillary leak—replace as boluses in first instance
- Renal perfusion may be reduced by raised intra-abdominal pressure
- Check daily electrolytes and renal function tests
- Urine electrolyte concentrations may give objective evidence of losses if electrolyte balance is a problem
- Check daily weight if possible.

Nutrition

- TPN may be required
- Enteral feeds should not be started without surgical consultation.

Oesophageal atresia and tracheo-oesophageal fistula

Preoperative

- Incidence 1:3500 live births. 5 anatomical variations
- Diagnosis: feeding failure and inability to pass a feeding tube into the stomach
- Other cardiac, GI, skeletal, or urogenital anomalies in 50% of cases—Echo should be undertaken before surgery
- Aim to avoid positive pressure ventilation before surgery—babies ventilated preoperatively require urgent surgery and gentle ventilation to prevent gastric distension and perforation.

Perioperative

- Surgical retraction can compress/bruise lung. Pleura may be opened by mistake
- Long gap atresia may require feeding gastrostomy and cervical oesophagostomy or staged approach.

Postoperative

- At risk of anastomotic leak and stricture
- Postoperative ventilation and muscle relaxation may be requested if the oesophageal anastomosis is under tension.
- Ensure secure transanastomotic tube (effectively NG tube).

Diaphragmatic hernia

Preoperative

- The incidence is 1:3000. Commonly left sided. Associated with cardiac anomalies in 20% of cases. The diagnosis is usually made in the antenatal period
- The severity of the underlying lung hypoplasia determines the outcome. Problems are mainly respiratory:
  - Characterized by hypoxia and pulmonary hypertension from birth
  - Ventilation and muscle relaxation may be required preoperatively
  - Aim for adequate gas exchange without inducing lung injury
  - Minimize ventilator peak pressures (<25) and PEEP: aim for preductal SaO_2 >85% and allow permissive hypercapnia (pCO_2 8–8.6kPa)
  - HFOV may be required and may avoid the use of ECMO. iNO often used for severe pulmonary hypertension
  - Frequent Echos to assess pulmonary hypertension (from TR jet), right ventricular dilatation, response to iNO
  - Inotropes, e.g. dopamine should be used to maintain adequate blood pressure (MAP >40 mmHg) and reduce R→L shunt
  - ECMO should be used for severe cases: oxygenation index >40, high mean ventilator pressures, cardiovascular instability
  - Not a surgical emergency: optimally neonate should be stabilized and weaned from HFOV and ECMO prior to surgical intervention
  - If gas exchange is severely impaired, morbidity and mortality can be high ~also relates to the size of the defect

Perioperative

- May require surgery on PICU if unstable. Surgery can be done on HFOV.

Postoperative

- May have initial 'honeymoon period' before worsening of gas exchange
- Same ventilatory problems as preop. Avoid barotrauma—use HFOV.
- Improvement with time reflects alveolar growth and improving pulmonary hypertension.

Gastroschisis/exomphalos

Preoperatively

- Incidence 1:3000. Gastroschisis is usually an isolated anomaly. Characterized by defect in abdominal wall and herniation of abdominal contents without covering sac. Exomphalos has membrane covering visera and has occasional cardiac anomalies associated—Echo
- Large evaporative fluid losses—over abdominal contents with cling film or equivalent. Prone to infection and hypothermia.

Perioperative

- It may be difficult to return abdominal contents
- Abdominal silo (silastic pouch) may be used rather than primary abdominal closure
- Consider 'surgical' line (Hickman, Broviac) for prolonged TPN.

Postoperative

- Place slightly head up
- 'Third space' fluid is considerable. Hypothermia can occur
- May require postoperative ventilation
- After primary repair the abdomen may be tense and distended. Abdominal compartment syndrome (see 📖 Box 30.5 pp.637–8) can occur and lead to bowel ischemia, renal insufficiency, and vena caval occlusion. Abdominal pressure should be monitored and if compartment syndrome is suspected the abdomen should be surgically re-opened and a silastic pouch used. Sedation and paralysis should be used until abdominal distension is reduced and the process of ventilator weaning can be started
- Placement of a silo allows for gradual return of contents and avoids many of these problems. Classically the contents of the silo are reduced manually every 12–24h. This may take up to 10 days
- Controversy about best intensive care course in this situation:
  - Option A: sedation and paralysis are continued until all the bowel is within the abdomen and the abdomen has been closed surgically
  - Option B: early weaning of sedation and ventilation—ongoing reduction of the silo continues back on the ward. This approach is associated with fewer complications, e.g. nosocimial infection
- TPN should be started early
- Long-term feeding problems are common—long-term TPN may be required and even small bowel transplantation in the worst cases

Further reading

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Chapter 30

Gastroenterology and hepatology

Introduction

The gut is a sensitive gauge to an individual's general state of health. This is particularly relevant in children where a diverse range of diseases can result in abdominal pain, constipation, diarrhoea, or vomiting. Consequently disturbances of the GI or hepatobiliary systems are frequently seen in PICU. These may represent primary GI disease, e.g. volvulus or pancreatitis, or may be secondary to systemic disease, e.g. sepsis.

Development of gastrointestinal and hepatobiliary system

- The major GI structures have developed by the end of the first trimester. However functional maturity continues throughout childhood
- The newborn gut is capable of absorbing nutrient but has little reserve
- Infants have immature villi and lower luminal surface area and reduced secretion of pancreatic digestive enzymes (amylase, lipase)
- Absorption of fat, glucose, and protein are all impaired compared to older children but absorption of (maternal) immunoglobulins occurs.
  - Breast milk should be the first-line feed offered to all newborns

The liver is relatively large in a newborn but has immature function:

- Reduced bile acid production—hence ↓fat absorption
- Reduced enzyme activity: reduced drug metabolism and bilirubin conjugation
- Reduced synthetic function, e.g. albumin production
- Rapidly depleted glycogen stores
- Liver function develops rapidly after birth

Gastrointestinal structure, function, and applied physiology

All functions of the GI tract can be disrupted to varying degrees in the critically ill child. These can be summarized as:

- Digestion and absorption of nutrients and drugs
- Fluid and electrolyte balance
- Neuroendocrinological control
- Host defence.

Digestion, absorption, and intermediary metabolism

Nutrients are

- Digested (mechanically and enzymatically broken down)
- Absorbed across the enterocyte
- Transported via the portal vein or thoracic duct (long chain triglycerides) to the liver, where they undergo intermediary metabolism.

Critical illness leads to a reduced intake of all nutrients as well as an alteration of the body's nutrient requirements (see 📖 p.278):

- The stress of critical Illness (cytokine mediated) via glucagon, catecholamine and cortisol secretion leads to:
  - ↑metabolic rate
  - Gluconeogenesis
  - Proteolysis and peripheral oxidation of amino acids
- Consequently tissue breakdown and malnutrition may occur in the critically ill child.

See Box 30.1

Regulation of water and electrolytes

- The small intestine both secretes and absorbs water and electrolytes
- This process is regulated by hormones acting on the gut both locally, including serotonin and substance P, and systemically, e.g. aldosterone
- Diarrhoeal diseases can damage the Na/K ATPase mechanism leading to torrential, and sometimes life-threatening, fluid and electrolyte loss. Causes include:
  - Cholera
  - *E. coli*
  - *Salmonella*
  - *Campylobacter*
  - *Clostridium* spp.
- Systemic acidosis increases the absorption of Na and Cl from the gut
- Drugs commonly used in the PICU also influence this function:
  - Opiates increase Na and Cl reabsorption
  - Spironolactone blocks the reabsorption of Na
  - Laxatives and antacids increase secretion of electrolytes and fluid.

GI neuroendocrine control

Coordination of secretion and motility is controlled by paracrine and neuroendocrine systems.

Gut motility is affected by:

- Changes in autonomic tone
- Stimulation or manipulation by peptides, drugs, or infectious processes
- Hypoxaemia and acidosis directly reduce gut motility in PICU.

Hydrochloric acid

- The stomach has an acid environment, which prevents bacterial colonization and promotes enzyme activity
- Acid production is stimulated by acetylcholine, gastrin and most importantly histamine (via H1 and H2 receptors)
- Gastric distension stimulates the production of gastrin and histamine
- H_2 receptor antagonists (e.g. ranitidine) block histamine mediated acid production
- Proton pump inhibitors (e.g. omeprazole) irreversibly block the acid production mediated by histamine, gastrin and acetylcholine.

The pancreas

- Endocrine function regulates blood glucose levels via the islets of Langerhans:
  - A cells: glucagon

  - B cells: insulin
  - D cells: somatostatin
  - PP cells: pancreatic polypeptide
- Exocrine function:
  - Digestive enzymes and bicarbonate from the pancreatic duct
  - Pancreatic secretion is phased and is responsible for secondary digestion, and solubility of bile salts
  - It is inhibited by somatostatin and pancreatic polypeptide
- Octreotide (a synthetic somatostatin) is used in the treatment of the complications (pseudocyst, fistula) of pancreatitis.

Hepatobiliary system

Portal circulation

- Liver has a high blood flow (>25% of resting cardiac output).
- Portal venous obstruction (chronic liver disease) leads to portal hypertension (10–15mmHg), which results in ascites and GI dysfunction.

Hepatic function

- Produces and excretes bile for lipid emulsification
- Breakdown of haemoglobin to bilirubin and biliverdin (added to bile)
- Carbohydrate metabolism
  - Synthesis of glucose—gluconeogenesis from amino acids, lactate and glycerol
  - Storage of glycogen and breakdown to glucose—glycogenesis and glycogenolysis
- Lipid metabolism:
  - Cholesterol synthesis
  - Triglyceride production
- Protein metabolism:
  - Synthesis of unique protein substances, e.g. albumin, transferrin, and coagulation factors including proteins C, S, and antithrombin
  - Converts ammonia to urea (urea cycle)
- Degradation and elimination of products (mainly lipid soluble).

Host defence (immunology and microbiology)

- The gut is the largest immune organ in the body
- The integrity of intestinal mucosa is an important barrier in the defence against infection
- The mouth and upper GI tract are predominantly colonized with gram-positive organisms, while the lower tract and colon are colonized with anaerobes and Gram-negative organisms, particularly coliforms
- The colon is the most heavily colonized part of the gut
- Antibiotics drastically reduce the number of anaerobes and coliforms
- Bacterial translocation refers to movement of bacteria from inside the gut via the portal circulation and liver to the general circulation causing bacteraemia or septicaemia
- Mechanisms of host defence:
  - Gastric acid prevents bacterial colonization
  - Routine use of antacids, e.g. H_2 antagonists can increase upper GI bacterial colonization with subsequent upper airway colonization with Gram-negative organisms. This increases the risk of nosocomial pneumonia

- Motility is important for clearing bacteria from the gut lumen, reducing overgrowth, and improving absorption.
- Gut-associated lymphoid tissues (GALTs), which include Peyer's patches and single lymphoid nodules in the intestinal mucosa and appendix are important to gut immune function
- Kupffer cells in the liver phagocytically mop up portal venous bacteria. They also trigger cytokine (TNF, IL1) release in sepsis.

Box 30.1 The gut and the systemic inflammatory response

It has been postulated that the gut is the 'engine' of the SIRS. The theory goes something like this: the splanchnic circulation contains about 30% of circulating blood volume. In shock states the splanchnic circulation is sacrificed (catecholamine and vasopressin mediated) in order to preserve flow to the brain, heart, and lungs. This, coupled with inadequate fluid resuscitation, leads to intestinal underperfusion and subsequent mucosal ischaemia and damage. This in turn allows bacterial translocation from the gut lumen across the bowel wall to the portal circulation. Kupffer cells and neutrophils are then activated leading to a generalized cytokine response, SIRS and shock.

This mechanism was postulated >20 years ago and has generated bookshelves of research. A monitoring device, 'the tonometer', has even been developed to monitor gut mucosal pH. As is often the case, despite this being an attractive proposition, there is still no convincing evidence that this process genuinely occurs.

Evaluation of gastrointestinal and liver function

Clinical examination (see 🕮 Chapter 4)
Clinical examination is mandatory but unfortunately often overlooked if the child is sedated and ventilated. As with all examination start with general observation. Examine the hands, head, neck, and chest.

Observation
- General signs: dehydration, malnutrition, pallor, jaundice, irritability, drowsiness, stigmata of chronic liver disease
- Abdomen: look for distension, veins, scars, stomas, obvious masses
- Nasogastric aspirate: yellow, green, blood stained.

Palpation
- Tenderness and guarding (signs of peritonism) are limited if the patient is sedated and/or paralysed (surgeons often need reminding!)
- Palpate for masses and organ enlargement
- Liver tenderness may indicate stretching of the liver capsule.

Percussion
- Dullness will establish the liver and splenic contours
- Detection of fluid (e.g. ascites).

Auscultation for peristaltic sounds
- High pitched and frequent bowel sounds are common with enteritis or obstruction
- Absent bowel sounds (listen for 60s) suggests paralytic ileus and/or peritonitis.
  - However, absence of bowel sounds per se is not a reliable indicator of whether enteral feeds will be tolerated

GI function

Laboratory testing
- Raised amylase in upper GI perforation
- Raised lipase and amylase in pancreatitis
- Hypocalcaemia (30% of patients) in pancreatitis
- Electrolyte disturbance in secretory diarrhoea
- Raised inflammatory markers in acute inflammatory bowel disease.

Stool and aspirate examination
- Stool microscopy, culture and sensitivity for detection of bacteria, toxin (particularly *C. difficile*) and viruses
- Faecal calprotectin (if available) is a sensitive but non specific marker of bowel inflammation.

Gastrointestinal endoscopy
- *Diagnostic:* varices, erosions, ulceration, inflammation, angiodysplasia
- *Therapeutic*: injection therapy, photocoagulation, thermocoagulation, band ligation of varices. Placement of post-pyloric feeding tubes, percutaneous gastrostomy tube and stents in pancreatic/biliary tract.

GI reflux monitoring
- 24-h oesophageal pH probe—may be helpful in cases of recurrent pneumonia, wheezing/stridor, or abnormal head and neck posturing
- Multiple monitoring sites if bile reflux is suspected.

Hepatic dysfunction

Hepatic dysfunction is common in PICU, more often secondary to systemic illness (e.g. shock, trauma, sepsis or cardiac failure) than to primary liver disease.

Primary liver problems include:
- Biliary atresia
- Intrahepatic cholestasis
- Familial and metabolic disorders
- Viral infection
- Fulminant hepatic failure of any cause.

Laboratory testing (Box 30.2)
Hepatic dysfunction is suggested by:
- Markers of reduced synthetic liver function:
  - Prolonged prothrombin function via liver and vitamin K-dependent clotting factors (I, II, V, VII, IX, and X)

  - Hypoalbuminaemia
  - Hypoglycaemia
  - Raised ammonia
- Markers of hepatocellular injury and/or cholestasis:
  - Raised bilirubin, alkaline phosphatase (ALP), gamma glutaryl transferase (GGT), 5' nucleotidase (5-NTD) indicate cholestasis.
  - Raised transaminases; alanine transaminase (ALT) and aspartate transaminase (AST) indicate hepatocellular injury.
    — ALT has high specificity for liver damage compared to AST which is released after myocardial, renal, pancreatic damage or haemolysis (from erythrocytes).

Box 30.2 Liver function tests

Liver function tests, e.g. ALT, ALP, are poor indicators of hepatic function (synthetic, metabolic, immune, nutritional). Liver enzymes can appear normal in the early phase of acute liver injury and the extent of the rise depends on the number of functioning hepatocytes. Generally prothrombin time is the best test of 'synthetic' activity and bilirubin (conjugated /unconjugated mixed) gives a guide to metabolic activity.

Many children in PICU, particularly with shock, sepsis or heart failure have grossly altered liver function tests and coagulopathy. This reflects reduced liver blood flow and corrects when the patient recovers.

Hyperbilirubinaemia
- Conjugated is assessed by direct reaction
- Unconjugated is the difference between the total and conjugated.

Unconjugated hyperbilirubinaemia is caused by:
- ↑bilirubin production—haemolysis
- Reduced uptake and intracellular transport—hepatocellular dysfunction
- Reduced conjugation—prematurity, hepatocyte dysfunction.

Conjugated hyperbilirubinaemia (cholestasis) is caused by:
- Impaired intrahepatic transport of bilirubin—sepsis, cell death, structural anomalies, biliary atresia and cystic fibrosis
- Impaired extrahepatic transport of bilirubin to the gut—gallstones, perforation of bile duct, choledochal cyst, or extrinsic compression.

Neonatal hyperbilirubinaemia: see 🕮 Chapter 29.

Imaging the GIT/hepatobiliary system

(See 🕮 Chapter 19.)
- X-rays:
  - Plain abdominal film can demonstrate radiopaque objects (NG/gastrostomy tubes), perforation (abnormal air distribution), ischaemia ('thumbprinting'), ileus, and mechanical obstruction
  - Film with contrast (water soluble or barium sulphate) will demonstrate atresia, stricture, intussusception, Hirschprung's disease

- Ultrasonography:
  - May provide information in patients who are too unstable to transport to radiology
  - Useful for imaging vascular structures and blood flow analysis (Doppler)
  - Liver size can be estimated as well as abnormalities in structure and architecture
  - Tumours, abscess, haematoma, and dilated ducts can be imaged
  - Portal vein gas bubbles may be visualized in a patient with enterocolitis without any evidence on plain AXR.
- CT scan with both IV and gut contrast will often provide additional information over and above plain films and US.

Liver failure

Fulminant hepatic failure (FHF)

FHF is characterized by severe hepatic dysfunction and hepatocellular necrosis in the absence of chronic liver disease:

- It has a high mortality rate (60–80%) without transplantation
- Results in multiorgan failure
- Frequently is associated with encephalopathy
- Management is supportive with consideration for transplantation.

Aetiology

- Infection: hepatitis (A, B, C, E), HSV, EBV, CMV, dengue, leptospirosis, malaria
- Toxic: paracetamol overdose (FHF following paracetamol in children is rare, but reflects a very high dose), idiosyncratic reactions
- Metabolic (e.g. galactosaemia), infiltrative (e.g. leukaemia, haemophagocytic lymphohistocystosis), autoimmune, vascular.

Clinical presentation

- Malaise, anorexia, and nausea
- Jaundice
- Bleeding and bruising (unresponsive to vitamin K administration)
- Encephalopathy
- Rapid onset with profound metabolic disturbance:
  - Hypoglycaemia
  - Hyperammonaemia
  - Metabolic acidosis.

Investigations

- FBC: ↓platelets
- U&Es: hypernatraemia, hypokalaemia, hypoglycaemia, renal dysfunction
- Coagulation screen: ↑prothrombin time
- LFTs: ↑transaminases, hypoalbuminaemia, hyperbilirubinaemia
- Hyperammonaemia

Box 30.3 Treatment of FHF

See 🕮 p.734 for indications for urgent liver transplantation.

- ***Fluids/cardiovascular:***
  - Restrict IV maintenance fluid whilst maintaining normoglycaemia (use 10% glucose if required)
  - Do not allow hypovolaemia to develop (use colloids but watch for fluid overload with oliguria)
  - Hypotension is usually secondary to low SVR (use α agonists such as norepinephrine)
- ***Coma:***
  - Exclude hypoglycaemia, seizures. Brain CT scan to exclude cerebral haemorrhage
  - Early intubation and ventilation (grade III/IV encephalopathy) with invasive cardiovascular monitoring
  - Consider ICP monitoring (correct coagulopathy)
  - Preserve cerebral oxygen delivery with maintenance of cerebral perfusion pressure (>50mmHg) with pressors if required
  - Reduce ICP with head-up tilt, muscle relaxants (prevents coughing) and mannitol/3% saline
  - Reduce cerebral oxygen consumption with profound sedation (consider thiopentone infusion with burst suppression on cerebral function monitor) or mild therapeutic hypothermia.
- ***Renal:***
  - Renal failure and oliguria are common and can lead to fluid overload and worsening cerebral oedema
  - Early haemofiltration to create space for fluid/blood products
- ***Coagulation:***
  - Coagulopathy is typical
  - Use FFP, cryopreciptate and platelets (keep >40 × 10^9/L)
- ***Lactulose*** and ***neomycin:*** suppresses the production of ammonia by bowel flora and hence reduces serum ammonia
- ***N-acetyl cysteine*** in all cases:
  - Replenishes glutathione in paracetamol overdose
  - Has antioxidant (free radical scavenging) and anti-inflammatory effects
- Consider ***MARS*** (molecular adsorbent recirculating system). Removes lipophilic albumin bound molecules (e.g. bile acids, bilirubin, cytokines, fatty acids, drugs)
- Consider plasmafiltration if MARS not available:
  - Removes circulating mediators and metabolic toxins
  - Improves coagulation avoiding fluid overload and increases fibrinogen, factors II, V, VII, and IX
- Early communication with and consideration of transfer to supraregional paediatric liver transplant unit for extracorporeal liver support and transplantation.

Chronic liver disease

A child with chronic liver disease may present to PICU with:

- Sepsis
- Variceal or non-variceal bleeding

- Spontaneous bacterial peritonitis
- Acute-on-chronic liver disease
- End-stage liver disease—gross ascites, multiorgan dysfunction.

Liver transplantation

(See 🕮 p.734)

Overall outcome has improved steadily in all paediatric age groups over the past 20 years. The limiting factor is the scarcity of suitable organs for transplant, but organ splitting and living related donation are methods increasingly used by transplant centres.

Intestinal failure

Intestinal failure (IF) is defined as a reduction of functional gut mass below that required for the digestion and absorption of nutrients and fluids to allow normal growth. In general patients with IF require protracted or indefinite PN.

Aetiology

- Short bowel syndrome:
  - Bowel atresias, gastroschisis, NEC, mid-gut volvulus
  - Arterial thromboses
  - Severe Crohn's disease (in older children)
- Neuromuscular disease: chronic intestinal pseudo-obstruction syndrome or Hirschsprung's
- Congenital: microvillus inclusion disease or intestinal epithelial dysplasia.

Complications

- Related to the presenting condition:
  - Deficiencies of nutrient, vitamin, mineral, and trace elements
  - Subsequent bone disease and growth failure
  - Gastric acid hypersecretion
  - Pancreatic insufficiency
  - Water and electrolyte loss
  - Hyperoxaluria and biliary lithiasis
  - IF-associated liver disease
  - Small-bowel bacterial overgrowth
- Related to therapy:
  - Central venous line sepsis
  - Vascular thrombosis
  - PN-related liver disease.

Management

- Early management is concerned with restoration of fluid and electrolyte balance and commencement of PN via appropriate venous access.
- Once stabilized, enteral feeding is begun to initiate enteral adaptation and prevent mucosal atrophy—it may take many months before the child comes off PN (often home PN), child usually remains on a combination of both

- Admission to PICU is often due to sepsis, liver dysfunction or excessive fluid and electrolyte losses from jejunostomy or ileostomy
- A child with chronic IF and liver disease should have an assessment in a supraregional liver/intestinal transplant centre.

Intestinal obstruction and ileus

Mechanical ileus

- Obstructive ileus
- Strangulation, e.g. volvulus, intussusception, incarceration.

Functional (postoperative, paralytic, localized) ileus

- Is commonly associated with abdominal surgery and disruption of normal bowel motility but is also commonly seen with critical illness unrelated to the GI tract
- Is most profound in the colon, followed by small bowel, least in the stomach. It can have serious consequences for neonates and infants.

Types

- Postoperative or paralytic ileus: usually lasts for a few days
- Acute pseudo-obstruction/localized ileus. This is a condition associated with a wide variety of states encountered in the PICU:
  - Shock states: blood is preferentially diverted to brain, heart, and lungs leaving the gut relatively ischaemic. In extreme cases discrete areas of gut /mesentery may become necrotic
  - Electrolyte disturbance, e.g. hypokalaemia, hyponatraemia
  - Cholecystitis, pancreatitis, lower lobe pneumonia.

Clinical presentation

- *Obstructive ileus* (gradual onset): vomiting, mild/moderate pain, distended abdomen, increasing constipation/altered stool pattern, ↑peristalsis (↑bowel sounds). It may be associated with other illnesses or intra-abdominal adhesions
- *Strangulation* (sudden onset): vomiting, moderate/severe pain, abdomen can be distended, mucous and possibly blood in stool, ↑peristalsis (increased bowel sounds). ***The child may present in a collapsed shocked state.*** Strangulation may be spontaneous or secondary to hernia, surgery, or acute enteritis
- *Functional (paralytic) ileus/pseudo-obstruction* (can have an insidious onset): mild/moderate pain, distended abdomen, ↓bowel sounds.

Investigations

- FBC, coagulation screen, U&Es, CRP, amylase, lipase, serum glucose
- Radiology: plain and lateral abdominal films (fluid levels, distribution of gas, 'free air'), chest film
- Ultrasonography: free fluid, tumour, cysts, abscess, intussusception
- Contrast studies, from top and/or bottom ends
- CT scan of abdomen with contrast.

Treatment

- Early surgical referral if acute abdomen suspected
- Nil by mouth
- Nasogastric tube on free drainage
- Correction of hypovolaemia and electrolyte disturbance
- X-rays/US/contrast studies looking for underlying cause.

Box 30.4 The acute abdomen in PICU

There are few more challenging conditions than a child with an acute abdomen. Resuscitation, diagnosis, and treatment occur concurrently and rapid intervention is often necessary to prevent the case 'running away from you'. These cases are often characterized by:

- Massive fluid losses (third space loss /capillary leak) leading to shock
- Respiratory failure with diaphragmatic splinting and possibly ARDS
- Abdominal hypertension and compartment syndrome: abdominal distension and raised intra-abdominal pressure with compression of intra-abdominal vasculature and viscera and resultant renal failure
- Metabolic acidosis, and raised lactate
- Anaemia, thrombocytopenia and coagulopathy from both consumption (DIC) and dilution.

A diagnosis of acute abdomen is suggested by:

- Abdominal pain, distress, agitation, confusion, lethergy
- Increasing (often bile-stained) NG aspirates
- Abdominal distension and tachypnoea
- Signs of fluid depletion:
  - Signs of dehydration
  - Tachycardia
  - Metabolic (↑anion gap) acidosis with increasing base excess and raised lactate
  - Oliguria.

Resuscitation: *often requires several experienced personnel*
(Airway, Breathing, Circulation)

- Oxygen: early intubation and ventilation (RSI may be appropriate for full stomach—see 🕮 p.132).
- Ventilation: high PEEP (> 8cmH_2O) may be required as the abdomen distends and 'splints' diaphragm. If the lungs are non-compliant then minimize baro and volu-trauma with small tidal volumes (5mL/kg) and allow permissive hypercapnia if pH allows (>7.1)
- Volume resuscitation needs to be aggressive:
  - Fluid requirements can be enormous and may require 'syringing' in. Remember that short cannulae allow for more rapid flow than longer CVP lines. Titrate fluid challenges against clinical response
- Venous access and invasive monitoring can be difficult, Try to site 'lines' as soon as possible before swelling makes it impossible
- Ideally central lines should be internal jugular or subclavian:
  - Femoral (intra-abdominal) CVP readings may reflect intra-abdominal pressure
- Oliguria, anuria may also occur secondary to intra-abdominal swelling and pressure (compartment syndrome)—monitor renal function

Box 30.4 The acute abdomen in PICU (*Continued*)

- Coagulopathy and thrombocytopenia are common and should be corrected prior to surgery or large catheter insertion. Blood products are good colloids for resuscitation
- ABGs provide the best way to monitor progress of resuscitation:
  - Worsening metabolic acidosis and rising lactate are poor prognostic signs
- Watch for hypoglycaemia, particularly in neonates. Correct calcium if low and watch for hyperkalaemia with renal shutdown.

Diagnosis/treatment

Early diagnosis is imperative. Aggressive resuscitation is pointless if a correctable intra-abdominal lesion (e.g. volvulus) is being missed.

- This is a multidisciplinary emergency. Call for experienced surgical input immediately
- Remember that tenderness cannot be elicited if the patient is sedated and paralysed!
- Check amylase and lipase
- AXRs should be performed. Remember free gas (from perforation) may only be identified on the supine patient with a 'lateral shoot through'. US (by experienced operator) or CT scan may help with diagnosis (see 🕮 Chapter 19)
- If a laparotomy is to be done remember to have blood and other products available. Inform an experienced anaesthetist as soon as possible
- Surgical decompression of the abdomen can relieve intra-abdominal compression and help with ventilation, circulation, and renal perfusion and may save a deteriorating child
- In the setting of gross free intra-abdominal air a cannula or drain may be sited to decompress the abdomen and buy time before laparotomy.
- Bear in mind that critical surgical procedures or drain placement may have to occur on the PICU.

Box 30.5 Abdominal compartment syndrome (ACS)

Intra-abdominal pressure may be raised from intra-abdominal pathology (e.g. volvulus, perforation), following abdominal surgery (e.g. gastroschisis, laparotomy), following trauma or burns or secondary to fluid resuscitation and intra-abdominal sequestration (e.g. sepsis).

Normal intra-abdominal pressure (IAP) in a ventilated child is between 1–8mmHg. IAP >12mmHg can be defined as intra-abdominal hypertension. Abdominal compartment syndrome (ACS) develops when raised IAP is sustained and organ dysfunction and failure (usually renal) ensues. It can be seen with IAP >15–20mmHg.

Raised IAP leads to organ failure by direct compression of organs and by compressing abdominal veins and arteries. Splinting of the diaphragm leads to increased intrathoracic pressure, alterations in V/Q mismatch and contributes to development of ARDS.

(*Continued*)

Box 30.5 Abdominal compartment syndrome (ACS) (*Continued*)

Measurement of IAP

IAP can be measured directly with an intraperitoneal catheter or indirectly from intravesical (bladder) pressure measured from a urinary catheter. Gastric pressure can be measured if there has been bladder trauma:

- Various systems have been used to measure bladder pressure
- These involve integrating a fluid-filled flush solution and a standard pressure transducer into the urinary catheter system
- To measure intra-abdominal/vesical pressure the urinary drainage tubing is clamped and sterile saline is flushed through the urinary catheter into the bladder
- Installation volumes are 1mL/kg <20kg and 25mL >20 kg.

Management of raised IAP

- Serial monitoring of IAP to identify and quantify problem
- Optimize systemic perfusion pressure—fluid resuscitation may aggravate IAP but should not be withheld
- Consider diuretics and haemofiltration for renal failure
- Percutaneous decompression can be achieved with use of a peritoneal dialysis catheter if there is lots of ascites
- Surgical abdominal decompression may be necessary. The abdomen may need to be left open or a silastic pouch created as for gastroschisis.

Box 30.6 Diplomacy and the surgeon

As is often the case, it is not always obvious if the critically ill child has a genuinely acute abdomen or has gross septic shock with capillary leak, i.e. the massive volumes of fluid resuscitation that you have been administering end up sequestered as ascites, causing abdominal tamponade. Resuscitating such a child in PICU without a definite diagnosis can be disheartening.

On the other hand, performing a laparotomy on a critically ill child with an acute abdomen is a daunting prospect for any surgeon and anaesthetist. Add inotropic support, high ventilator pressures, anuria, acidosis, and coagulopathy into the mix and it is understandable why many surgeons are reluctant to take such a child to theatre—the mortality rate is appreciable. If laparotomy is not feasible, then surgical decompression and drainage of ascites may be an alternative—this allows for easier ventilation and may restore renal perfusion.

Management of difficult cases requires good communication with the surgical team. Points to concentrate on include:

- Most coagulopathy is correctable in the short term, particularly if products are given just prior to surgery
- A trip to CT scan (to get a diagnosis) is often as complex as going to the operating theatre and may not give a clear diagnosis

Box 30.6 Diplomacy and the surgeon (*Continued*)

- A laparotomy may decompress the abdominal tamponade and give the kidneys a chance to recover
- A negative laparotomy, with no pathology to be found, may therefore be helpful in itself.

Gastrointestinal bleeding

Whilst GI bleeding as a primary diagnosis rarely necessitates PICU admission, prompt or massive GI bleeding may require haemodynamic monitoring and aggressive resuscitation. Many PICU patients are at risk of GI bleeding.

Acute bleeding

Aetiology

- Erosions from viral illness or drugs (e.g. NSAIDs)
- Gastric or duodenal ulceration
- Portal hypertension leading to oesophageal and gastric varices
- Mallory–Weiss or vascular lesions
- Stress ulcers.

Clinical presentation

- Overt: haematemesis, brisk NGT blood loss, malaena (2% loss of blood volume)
- Lower GI bleeding (neonates): aetiology is diverse and may be associated with pain, diarrhoea.

Management of severe acute GI bleed

This should involve a multidisciplinary team of PICU staff, gastroenterologist, paediatric surgeon, radiologist, operating theatre staff.

Resuscitate

- ABC: oxygen, early tracheal intubation, urinary catheter, invasive arterial monitoring
- Haemodynamic resuscitation with fluid, colloid, and blood
- Correct coagulopathy with FFP, cryoprecipitate, and platelets as necessary
- Consider NG lavage with saline and norepinephrine.

Diagnosis

- Upper GI endoscopy for location and control of haemorrhage, collect biopsies
- Arteriography to locate site of bleeding—requires a brisk bleed to be positive

Treatment

- Omeprazole raises gastric pH (>6) and prevents dissolution of clots
- Endocsopic injection or banding of varices

- Medical management: vasopressin, somatostatin and its analogue octreotide (1mcg/kg/h) all reduce splanchnic blood supply and hence may reduce variceal bleeding
- Balloon tamponade of varices via Sengstaken–Blakemore tube
- Surgical intervention may be necessary if medical management does not stop bleeding.

Stress ulcers in PICU

Stress ulcers in intensive care are more common in adults than children and classically were described following head injury (*Cushing's ulcer*) or burns (*Curling's ulcer)*. Now recognized as a complication of any critical illness. They are usually upper GI but can be associated with patches of gastric mucosa in a Meckel's diverticulum.

Aetiology

- Mucosal damage and ulceration occur secondary to poor splanchnic perfusion (shock and acidosis)
- ↑acid production, loss of mucosal integrity (when not being fed), and motility are also implicated
- High risk groups include:
  - Significant burns, head injury, sepsis, shock and multiple organ dysfunction syndrome (MODS)
  - Failure to establish enteral feeding, severe GI reflux, previous acute GI bleeding.

Prophylaxis

Prophylaxis with drugs should be used in high-risk groups (discussed earlier). However most patients on PICU (who are enterally feeding) do not require prophylaxis.

Other measures include:

- Establish enteral feeding early, especially protein-based feeds (increases gastrin which improves cell turnover)
- Minimize use of drugs that reduce motility
- Improve gastric emptying with prokinetic agents (e.g. erythromycin, domperidone).

Drug prophylaxis

- Protein pump inhibitors (e.g. omeprazole) block the effect of histamine, gastrin, and acetyl choline (Ach), resulting in the most effective control
- H_2 blockade (e.g. ranitidine) can be used for patients with lower risk.
- Sucralfate does not affect gastric pH and is not as efficacious if given in addition to H_2 antagonists.

Lower GI bleeding

This can be defined as bleeding distal to ligament of Treitz (junction of duodenum and jejunum).

Causes of massive bleeding include:

- Meckel's diverticulum (sudden, painless) or intussusception (pain, redcurrant stool)
- Ischaemic bowel or volvulus (pain, acidosis, shock)
- Inflammatory bowel disease (bloody diarrhoea ± mucus)
- Vascular malformations (sudden, painless) and Henoch–Schönlein purpura (abdominal and joint pain, smoky urine)

Treatment
- As previously discussed for upper GI bleeding
- Further tests involving radiology (angiography, radionucleotide scan)
- Exploratory laparotomy or laparoscopy.

Acute pancreatitis

Although a common condition in adults this is a rare condition of childhood. The severest form of the disease is associated with pancreatic necrosis and multiple organ failure. Mild pancreatitis has mild organ dysfunction and usually recovers uneventfully.

Aetiology
- Idiopathic
- Congenital (structural anomalies): choledochal cysts, intrapancreatic ductal duplications, duodenal diverticulum, stricture of the common duct
- Acquired obstructive causes (gallstones)
- Trauma, e.g. acceleration/deceleration injury (car accident), particularly in younger children
- Viral infection: mumps, coxsackie B
- Background illness: cystic fibrosis, burns, hepatitis, drug reaction.

Clinical presentation
- Abdominal tenderness and/or pain
- Nausea & vomiting
- Fever
- Initially tachycardia progressing to hypotension and shock.

Investigations
- FBC, U&Es, LFTs, amylase, lipase, arterial blood gases, CRP
- US/CT images.

Diagnosis
- Raised amylase, raised lipase (neither is specific though lipase may be more sensitive)
- Raised CRP
- US: enlargement of pancreatic gland, altered echogenicity of pancreas, dilated pancreatic duct and free fluid
- CT: more useful later on to show the presence of necrosis, abscess or pseudocyst

Scoring system (validated in children)
The presence of 3 or more criteria indicates a severe attack of acute pancreatitis:

On admission:
- <7 years of age
- Weight: < 23kg
- WBC: >20
- LDH: >2000 IU

Initial 48h:
- Calcium: <0.75mmol/L
- Albumin: <26g/L
- Fluid resuscitation: >75mL/kg/48h
- Blood urea: >20mmol/L

Complications
- Pancreas: pseudocyst abscess, necrosis
- Bowel: ileus or obstruction
- Hepatobiliary: cholestasis
- Shock and multiple organ failure including ARDS, hypotension, renal failure, and coagulopathy.

Treatment
- ABC
- Nil by mouth and NG tube
- Analgesia
- Antacids
- Octreotide (somatostatin analogue) which inhibits pancreatic exocrine secretion, and may be specifically useful in chronic complications, e.g. pseudocyst, fistula
- Consider glucagon and trasylol
- TPN:
  - There is controversy about whether to introduce early enteral nutrition in adults with acute pancreatitis or whether to rest the gut and use PN
  - Conisder trial of jejunal feed.

Gastrointestinal reflux

Gastro-oesophageal reflux is common in neonates and rarely leads to serious consequences in this group. In its severest form however reflux can lead to oesophagitis, aspiration pneumonia, and failure to thrive. Occasionally reflux can cause severe vagally-mediated reactions that are life threatening including apnoea, laryngospasm, and bradycardia. It has been implicated as a cause of cardiac arrest and sudden infant death syndrome.

Obviously reflux is more likely if a child is horizontal/supine (gravity prevents some reflux) and thus the incidence of severe reflux falls as children develop and learn to sit, stand and walk. Children with delayed development who stay supine (e.g. with neurological disorders) often have severe reflux and can present with airway oedema, stridor or recurrent pneumonia. Reflux can also be secondary to dysmotility disorders of the gut.

PICU patients are at risk of reflux for various reasons:
- Supine position
- Inappropriate oesophageal sphincter relaxation due to coma and drugs
- Mechanical ventilation, coughing and suctioning
- Critical illness with ileus (see 📖 p.635)
- Postoperative abdominal surgery (high intra-abdominal pressure, ileus and reduced gastric emptying).

Diagnosis
Clinical history, barium swallow, pH probe and bronchoscopy with BAL (fat-laden macrophages would support the diagnosis but are also seen in other conditions).

Treatment

- *Medical:* nasojejunal feeding (if gastrointestinal dysmotility is the underlying cause), thickened feeds
- *Pharmacological:* Gaviscon®, H_2 antagonists (ranitidine), proton pump inhibitors (omeprazole) will reduce gastric acidity and prokinetic agents (e.g. domperidone, erythromycin) will encourage gastric emptying
- *Surgical:* Nissen's fundoplication ± gastrostomy. This is the option for repeated episodes of aspiration.

Miscellaneous gastrointestinal problems

Caustic injury to the oesophagus

- Rare cause of oesphageal injury
- Usually sodium hydroxide or hypochlorite (caustic soda or bleach)
- Can cause deep oesophageal burns, which can lead to perforation, or, in the long-term, strictures
- *Symptoms:* chest pain, drooling, inability to swallow secretions and stridor (if the upper airway is damaged)
- *Treatment:*
  - Prompt management of ABC
  - If there are signs of airway compromise (e.g. severe stridor): do not delay, get skilled help with intubation and make sure an emergency trans-tracheal ventilation set is available
  - Consider detailed ENT examination prior to extubation
  - Perform upper GI endoscopy after 24h when injury has demarcated and staged. A NG tube should be placed for feeding
  - Follow-up endoscopies will be needed to monitor and treat strictures

Inflammatory bowel disease including toxic megacolon

- IBD (Crohn's disease, ulcerative colitis, or infective colitis, including *C. difficile*) may present with diarrhoea, bleeding, toxic megacolon, or even bowel perforation.
- Main issues are those of analgesia, fluid balance, and transfusion
- As with diarrhoea, careful attention to fluid balance and acid–base status
- Increasing abdominal distension may compromise respiratory function
- Patient with IBD may need steroid treatment:
  - Additionally remember to use steroid cover if patient has been on long-term steroids (pituitary-adrenal suppression). Hypotension which is fluid/inotrope insensitive may be the clue
- Treatment of severe *C. difficile* colitis includes oral ± IV vancomycin, metronidazole, and immunoglobulin therapy
- Surgery with partial or total colectomy may be needed in severe cases.

Further reading

Beattie M, Dhawan A, Puntis JWL (eds) (2009). *Paediatric Gastroenterology, Hepatology and Nutrition.* Oxford University Press, Oxford.

Kelly DA (ed) (2008). *Diseases of the Liver and Biliary System in Children*, 3rd edn. Wiley-Blackwell.

Chapter 31

Nephrology

Introduction

Patients with intrinsic renal disease are not common in PIC. However, many PIC patients have some degree of renal involvement in their disease process.

Generally, patients will have *pre-renal* involvement, manifest as oliguria. They will require monitoring and manipulation of their fluid and electrolyte balance, acid–base status, and drug prescriptions. Some may require some form of renal replacement therapy or associated procedure such as plasmafiltration.

Renal structure and function

Anatomy

The kidney is divided into 2 zones; the outer renal cortex and an inner renal medulla (see Fig. 31.1). Microscopically, the renal cortex contains the nephron and the renal medulla contains the loop of Henle, the vasa recta, and the distal portion of the urinary collecting system.

- The nephron is the basic structural and functional unit of the kidney and when nephrogenesis ceases (at about 34 weeks) there are approximately 1 million nephrons in each kidney. The nephron consists of:
  - A network of capillaries, called the glomerulous, surrounded by a membrane called Bowman's capsule through which the blood is filtered
  - An afferent arteriole supplying it and an efferent arteriole draining it
  - The renal tubular system consisting of: proximal tubule, loop of Henle, distal tubule, and collecting duct
- Most nephrons (85%) are found in the outer cortex
- Juxtamedullary nephrons (15%) are found at the corticomedullary junction and have a longer loop of Henle, enabling them to concentrate the urine more effectively via the countercurrent mechanism.
- The juxtaglomerular apparatus (JGA) consists of a combination of specialized tubular and vascular cells which help regulate glomerular filtration and renal blood flow.

Function

- Urine production begins when blood is filtered through the Bowman's capsule (there are 3 layers: the endothelium, the basement membrane, and the epithelium)
- Substances are filtered according to their molecular size and electrical charge
- The glomerular filtrate passes through the renal tubules where its volume is reduced and composition altered by tubular reabsorption of water and solutes and tubular secretion of solutes
- Most solute reabsorption takes place in the proximal tubule and loop of Henle. This is an active ATP-consuming process. Sodium, potassium, calcium, phosphate, glucose, amino acids, and bicarbonate are reabsorbed

- The active transport of sodium and chloride out of the ascending limb of the loop of Henle (which is relatively impermeable compared to the descending loop) creates a hypertonic environment within the medullary interstitium which drives water reabsorption from the descending limb and the medullary collecting duct (countercurrent mechanism).
- 99% of the glomerular ultrafiltrate is reabsorbed. The remainder of the filtered fluid becomes urine which enters the renal pelvis and drains into the ureter.

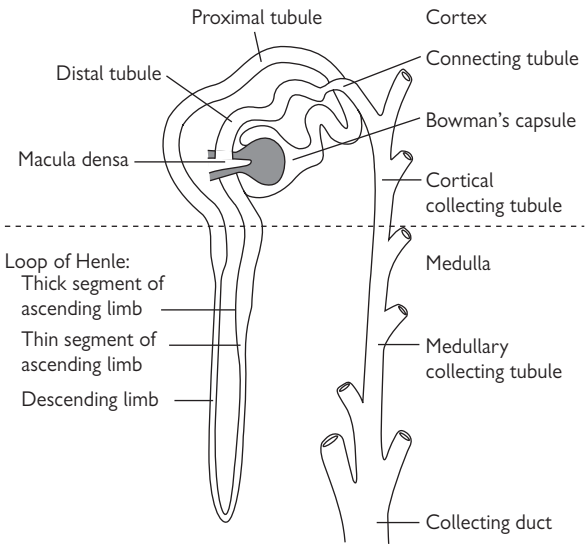

Fig. 31.1 Basic tubular segments of the nephron. The relative lengths of the different tubular segments are not drawn to scale. Reproduced from Guyton AC, Hall JE (2006). *Textbook of Medical Physiology*, 11th edn, Elsevier, Philadelphia.

Hormones produced by the kidney.

- ***Renin:*** released by the juxtaglomerular apparatus. Leads to the formation of angiotensin 2 which promotes sodium retention via a direct action on the tubule and aldosterone
- ***Prostaglandins (PGE_2, PGI):*** regulate renal blood flow via vasodilatation of afferent and efferent arterioles
- ***1,25 dihydroxycholecalciferol:*** the active metabolite of vitamin D. Principal action is to promote Ca^{2+} and PO_4^- absorption from the gut
- ***Erythropoietin:*** ↑RBC production in the bone marrow.

Hormones acting on the kidney

- ***ADH or vasopressin (AVP):*** promotes water reabsorption in the collecting ducts. Released by the posterior pituitary gland in response to ↑osmolality of the blood and to volume depletion. It is a stress hormone and is released in response to surgery, hypoxia, and pyrexia
- ***Aldosterone:*** promotes sodium reabsorption in the collecting ducts. Produced by the adrenal gland
- ***Atrial natriuretic peptide (ANP):*** lowers SVR and causes natriuresis. Produced by cardiac atrial myocytes. ANP counters the increase in BP and blood volume caused by the renin–angiotensin system. Brain natriuretic peptide is released by the cardiac ventricle myocytes in response to stretch and has similar actions
- ***Parathyroid hormone (PTH):*** promotes renal phosphate excretion, calcium reabsorption and vitamin D production. Produced by the parathyroid glands.

The renin–angiotensin system

- Renin is released in response to a fall in BP, either as a consequence of hypovolaemia or poor cardiac output
- Renin leads to the production of angiotensin I, converted by ACE to angiotensin II, mainly in the lung.
- Angiotensin II is a potent vasoconstrictor, by which it acts to maintain BP
- Within the kidney the vasoconstrictor effect is greater on the efferent arteriole than the afferent arteriole, resulting in a greater net perfusion pressure across the glomerulus. Thus, the glomerular filtration rate (GFR) is maintained despite a fall in renal blood flow
- As an adequate GFR is essential to maintain acid–base and electrolyte balance in the body, the renin–angiotensin system aims to preserve renal function even when the patient is haemodynamically comprised.

Renal blood flow

- The kidneys receive about 20% of the cardiac output—by weight this is 4× the blood flow of the liver and 8× that of the heart
- Blood enters the kidney via the renal artery which branches into multiple afferent arterioles and enters the glomerulus. Blood exits via the efferent arteriole. Efferent arterioles form peritubular capillaries and dip into the medulla to facilitate the countercurrent concentrating mechanism. Blood drains from the kidneys in the renal veins
- Renal blood flow is autoregulated and is maintained over a wide range of blood pressures
- The kidneys extract a disproportionately high quantity of oxygen from the blood per gram of tissue to meet their high metabolic demand. Much of this energy is used for the active transport of sodium
- Low PO_2 in the renal medulla make the kidney extremely sensitive to hypoxic damage in low cardiac output states.

Neonatal kidneys

- Renal blood flow increases after birth, doubles after 2 weeks, and triples by 1 year old

- GFR (mL/min/1.73m^2) is 15–20 at term, doubles after 2 weeks, and reaches adult levels of 80–120 by 2 years
- Maximal urine concentration is low at birth (600mOsmol/kg) and increases over the first year of life to >800mOsmol/kg
- Maximal adult values are 1500mOsmol/kg.

Evaluation of renal function

Clinical history

Take note of:

- History of recurrent urinary tract infections
- Haematuria
- Proteinuria
- Bloody diarrhoea
- Large fluid loss due to:
  - Diarrhoea and vomiting
  - Haemorrhage following trauma
  - Insensible losses following thermal injury
- By far the most typical picture on PICU is the child with ARF from septic, cardiogenic, or hypovolaemic shock. ARF presents with oliguria, i.e. urine output <0.5mL/kg/h (<1mL/kg/h in neonates).

Practical points with oliguria

- Catheterization is mandatory if urine output is in question. It is better to catheterize the bladder and confirm that urine output is adequate rather than 'wait in the dark'
- If urine output falls abruptly when catheterized, ***always*** check for a blocked catheter (flush with 1mL/kg sterile saline)
- The priority is to measure the blood potassium immediately to ensure it is not dangerously high. Do not prescribe potassium supplements in IV fluids until level is known
- Commence a strict input and output fluid balance chart
- If practicable an accurate body weight should be obtained
- Do not prescribe any potentially nephrotoxic drugs, e.g. aminoglycosides and non-steroidal anti-inflammatories until the level of renal impairment has been established.

Investigations of renal function

Biochemistry (Table 31.2)

- *Urea:*
  - Urea is ***not*** a good index of renal function
  - It is typically raised with both pre-renal (dehydration, hypovolaemia) and renal causes of renal failure
  - This can be both delayed or consistently low in patients with poor dietary intake of protein (malnutrition)
  - ***Urea is low*** in those who are overhydrated or have liver disease
  - Urea results from ammonia breakdown and requires adequate liver function for synthesis. It accumulates in the blood when renal excretion is impaired

- Raised urea can occur following GI haemorrhage, after a high protein meal, with corticosteroid therapy and in severely catabolic states
- Ratio of urine:plasma urea can help distinguish pre-renal (dehydration and hypovolaemia) from renal causes of oliguria. Higher ratios (>10:1) are seen in pre-renal conditions whereas low ratios (<4:1) are seen with renal causes.

- *Creatinine:*
  - Creatinine is produced at a constant rate from skeletal muscle breakdown (creatine, creatine phosphate). Values rise with growth
  - Plasma levels are raised when renal function is severely impaired
  - Creatinine of 60μmol/L refects a significant fall in glomerular filtration rate in a neonate (see Table 31.1)
  - Ratio of urine:plasma creatinine can help distinguish pre-renal from renal causes of oliguria. Higher ratios (>40:1) are seen in pre-renal conditions and lower ratios (<20:1) are seen in renal causes.

Table 31.1 Urea and creatinine in the first month of life*

	Urea (mmol/L)	Creatinine (μmol/L)
Term	1.6–10	35–115
1 week	1.6–5	14–86
1 month	1.9–5.2	12–48

*Adapted with permission from Baker E, Congenital heart disease in the neonatal perioid. In: Rennie JM, Roberton NRC (2002). *A Manual of Neonatal Intensive Care*, 4th edn, Edward Arnold (Publishers) Ltd, London.

Creatinine is a product of skeletal muscle (creatine) breakdown—be aware of children with a low muscle mass and renal failure in PICU, e.g. neuromuscular disease or the chronically malnourished or cachexic patient with severe growth failure. They can have low serum urea and creatinine levels even in the face of severe renal impairment.

- *Urinary sodium:*
  - When renal blood flow falls, sodium resorption increases and urinary sodium falls
  - Intrinsic renal disease (e.g. tubular disease) may impair sodium resorption and result in ↑urinary sodium
  - Urinary sodium may help distinguish renal from pre-renal causes of oliguria. Pre-renal <20mmol/L. Renal >40mmol/L
  - Diuretics cause a natriuresis and confuse the factors listed previously.
- *Fractional excretion of sodium (FE_{Na}):*
  - This is the equivalent of sodium clearance divided by creatinine clearance, expressed as a percentage

$$FE_{Na} = \frac{\text{Urine [Na]} \times \text{Plasma [Cr]} \times 100}{\text{Plasma [Na]} \times \text{Urine [Cr]}}$$

(Note: express Na and creatinine in same units—mmol or μmol)

- May help distinguish pre-renal from renal oliguria. FE_{Na}<1% suggests renal hypoperfusion. FE_{Na}>2.5% suggests acute tubular necrosis. Again, this test is not useful after diuretics.

Table 31.2 Biochemical renal assessment

	Pre-renal causes	Renal causes
Urine osmolality (mOsmol/kg)	>500	<400
Urine Na (mmol/L)	<20	<40
Urine:plasma urea	>10:1	<4:1
Urine:plasma creatnine	>40:1	<20:1
FE_{Na} (%)	<1	>2.5

- *Renal imaging* (see 📖 p.339):
  - Ultrasonography of the kidney and renal tract can be conveniently performed at the bedside of a critically ill child and provides information on renal size, position, and gross anatomy. Urinary tract obstruction can be detected and Doppler studies can assess renal blood flow and detect thrombosis in renal arteries and veins.
  - 'Bright' kidneys on US may be an indication of acute tubular necrosis (ATN see 📖 p.659) although its detection is seldom of diagnostic or therapeutic value
  - Small kidneys on US often reflect chronic renal failure.

GFR

Definition

- The volume of fluid (in mL) filtered from the renal glomerular capillaries into the Bowman's capsule per unit time (in minutes)
- Measured, or estimated (eGFR), to provide an indication of overall renal function. Many of the functions of the kidney are related to the GFR:
  - Excretion of nitrogenous waste, sodium, potassium, phosphate, free water and water soluble drugs e.g. gentamicin
  - BP control
  - Acid–base balance
  - Erythropoietin secretion and activation of vitamin D1
  - Gluconeogenesis

GFR is 'autoregulated' over a range of renal blood flow by alterations in afferent and efferent arteriole tones:

- Afferent arteriole dilatation and efferent arteriole constriction increase filtration (and GFR)
- Afferent constriction reduces filtration and GFR

GFR is estimated on PICU when potentially nephrotoxic drugs are used. Dose adjustment according to the estimated GFR can reduce the risk of further renal damage and prevent toxic levels of renally excreted or metabolized drugs.

Box 31.1 GFR and renal reserve

GFR does not fall until 'renal reserve' of nephrons is reduced by 80% or more (i.e. <20% functional). As more nephrons are lost, GFR plummets resulting in renal failure and need for renal support (95% loss of nephrons).

In practical terms GFR measurement rarely influences the decision to implement renal replacement therapy (see 📖 Chapter 14). Acidosis, hyperkalaemia, oliguria, and/or fluid overload resistant to other therapies are the usual indications for this.

Measurement or estimation of GFR

- On PICU, the GFR is usually estimated rather than measured according to the Haycock- Schwartz formula:

$$pGFR = (k \times ht) / P_{cr}$$

Where

- pGFR is the predicted glomerular filtration rate (ml/min/1.73m^2)
- k is a constant, an empirically derived value relating height to muscle mass
- ht is height (in cm) and
- P_{cr} is plasma concentration of creatinine in micromol/l
- k is usually taken to be 40 (for creatinine in μmol/L) or 0.45 (for creatinine in mg/dl). It varies with age, reflecting the changes in relative muscle mass
- In the malnourished, k of 40 will lead to an overestimate of GFR
- This formula is accurate enough for most clinical scenarios and will help ensure safer prescribing for critically ill patients on PICU.

Other methods of measuring GFR include:

- *Inulin clearance:* the gold standard, expensive almost never done on PICU
- *Creatinine clearance* = $(U_{creat} \times V) / P_{creat}$

The volume of creatinine cleared from the plasma per unit of time in (mL/min) can be used to estimate the GFR. The value is corrected for size by conversion to surface area (mL/min/1.73m^2). U_{creat} is urine concentration of creatinine, V is volume of urine over period of time and P_{creat} is plasma concentration of creatinine Again rarely performed due to the necessity of an accurately timed urine sample.

Box 31.2 Conversion factor to change from North American units (mg/mL) to SI units

	Conversion factor
• Creatinine	88.4
• Urea	0.357
• Calcium	0.2495
• Phosphate	0.3229
• Glucose	0.05551

Water and electrolytes

Renal handling of water

- The kidney regulates water and sodium levels in parallel to maintain homeostasis and blood osmolality within the normal range (270–295 mmol/kg)
- Water is absorbed in the proximal tubule by osmosis, following the active reabsorption of ions
- AVP or ADH increases the permeability of the collecting ducts to water allowing the production of smaller volumes of concentrated water
- Fractional excretion of water is calculated from

$$FeH_2O = Pcr/Ucr \times 10$$

where Pcr and Ucr are plasma and urine creatinine. FeH_2O <1% in prenal failure and SIADH.

Renal handling of sodium

- The sodium concentration in the glomerular filtrate is similar to that in the blood
- ~65% of the filtered sodium is reabsorbed in the proximal tubule
- 25% of the filtered sodium is reabsorbed in the loop of Henle. This is inhibited by loop diuretics
- 5% of the filtered sodium is reabsorbed in the distal tubule. This is inhibited by thiazide diuretics
- 2–5% is reabsorbed by the collecting ducts. This is inhibited by amiloride and spironolactone
- ANP decreases sodium reabsorption in the proximal convoluted tubule. It also inhibits renin and reduces aldosterone secretion by the adrenal cortex.

Renal handling of potassium

- Potassium is the major intracellular cation. All cells use the Na^+/K^+ ATPase pump to actively transport K^+ into the cells
- Potassium is freely filtered at the glomerulus but almost all the filtered potassium is reabsorbed before the filtrate reaches the collecting tubule
- Potassium is then secreted into the collecting duct.

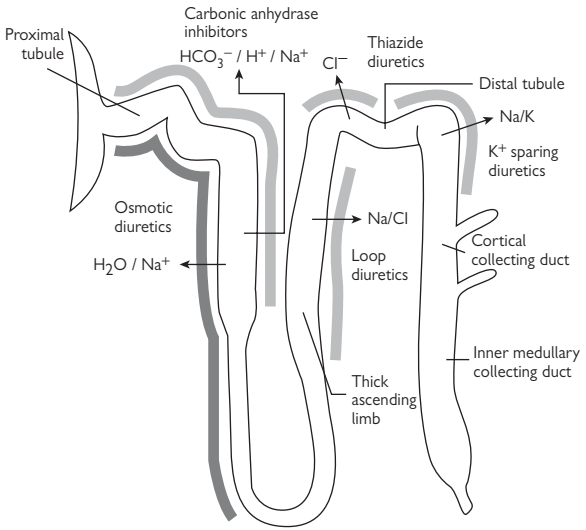

Fig. 31.2 Diagram of kidney physiology and diuretics.

Diuretics

All diuretics increase urine output but differ in their mechanism of action (see Box 31.3). The majority of diuretics exert their effect in by inhibiting sodium reabsorbtion in different parts of the nephron. They are used for renal failure, heart failure, liver cirrhosis, and hypertension. The antihypertensive actions of diuretics are often independent of their diuretic effect. See Box 31.4 for side effects.

Box 31.3 Types of diuretics

Loop diuretics
- Can cause substantial diuresis, e.g. up to 20% of the filtered sodium and water load
- Examples are furosemide, bumetanide, ethacrynic acid
- Inhibit active chloride and thus sodium reabsorption in the ascending loop
- Water follows sodium and thus urine output increases
- Cause hypokalaemia and metabolic alkalosis.

Thiazides
- Examples include hydrochlorthiazide and metolazone
- Inhibit sodium-chloride reabsorption and metabolic acidosis in distal tubule
- Cause hypokalaemia.

Potassium sparing
- Spironolactone is an aldosterone antagonist.
- Other examples are amiloride and triamterene.

Others
- Mannitol is an osmotic diuretic that is freely filtered but not reabsorbed. To maintain osmotic balance water is retained with it in the urine
- Acetazolamide is a carbonic anhydrase inhibitor that alkalinizes urine and may be used for chronic metabolic alkalosis
- Xanthines such as aminophylline, theophylline, and caffeine inhibit sodium reabsorption and thus act as diuretics.

Box 31.4 Side effects of diuretics

Diuretics have a range of side effects more commonly seen with chronic use:
- *Hypokalaemia*: loop diuretics, thiazides and acetazolamide
- *Hyperkalaemia*: spironolactone, amiloride
- *Hyponatraemia*: furosemide, thiazides
- *Metabolic alkalosis*: loop diuretics and thiazides
- *Metabolic acidosis*: amiloride, acetazolamide
- *Neonatal rickets*: thiazides
- *Hypercalcaemia*: thiazides
- *Hypomagnesaemia*: loop diuretics and thiazides
- *Hyperuricaemia*: loop diuretics and thiazides.

The kidney and acid–base balance

- Acid production and intake must be balanced by acid excretion
- Ventilation controls the CO_2 level and the kidney controls the bicarbonate level
- Buffers are necessary to prevent dangerous swings in hydrogen ion concentration:
  - Bicarbonate is the major extracellular buffer
  - Phosphate and proteins are the major intracellular buffers.

Metabolic acidosis

- The renal response to metabolic acidosis is to produce ammonia ions (NH_4^+) for excretion and to generate new bicarbonate
- Acidosis increases H^+ ion secretion and bicarbonate reabsorption in both the proximal and the distal tubules
- Renal compensatory mechanisms take time to become effective (at least 12h)
- H^+ ions enter cells and K^+ ions exit cells to maintain electrical neutrality leading to hyperkalaemia
- Anion gap (AG) differentiates types of metabolic acidosis:
  - AG = ([Na] + [K]) – ([Cl] +[HCO_3])
  - AG is normally 10–14
  - Hyperchloraemic acidosis has normal AG
  - Raised AG metabolic acidosis is seen in shock (lactic acidosis), diabetic ketoacidosis, poisoning or overdose, e.g. aspirin, cyanide, ethylene glycol (see 🕮 Chapter 36).

Metabolic alkalosis

- In conditions of hypochloraemia, e.g. following vomiting or diuretic therapy, bicarbonate secretion in the collecting tubule is inhibited as there is reduced chloride available for exchange, leading to alkalosis
- Alkalosis can cause hypokalaemia.

Renal tubular acidosis

- Failure of H^+ ion secretion in the distal tubule or reabsorption of bicarbonate in the proximal tubule leads to failure of the kidney to acidify the urine appropriately. The net effect is metabolic acidosis
- The term RTA is usually reserved for patients with otherwise normal renal function but poor or inadequate urinary acidification
- Patients with RTA have a normal anion gap
- The chronicity of the problem usually means the child has profound metabolic bone disease (poor growth and fractures) secondary to the severe phosphate wasting and acidosis
- There are several different forms of RTA including:
  - *Type 1 or Distal RTA*: characterized by failure to secrete H^+ in the distal tubule (i.e. cannot lower urine pH to <5.5) and hyperchloraemia
  - *Type 2 or Proximal RTA*: characterized by failure of the proximal tubule to reabsorb bicarbonate from the glomerular filtrate and ability to lower urine pH to <5.5

- The acidification test (to differentiate RTAs) involves the administration of furosemide and repetitive and timed urinalysis. Renal specialists should be involved
- The mainstay of treatment for both type 1 and 2 is bicarbonate supplementation to control the acidosis.

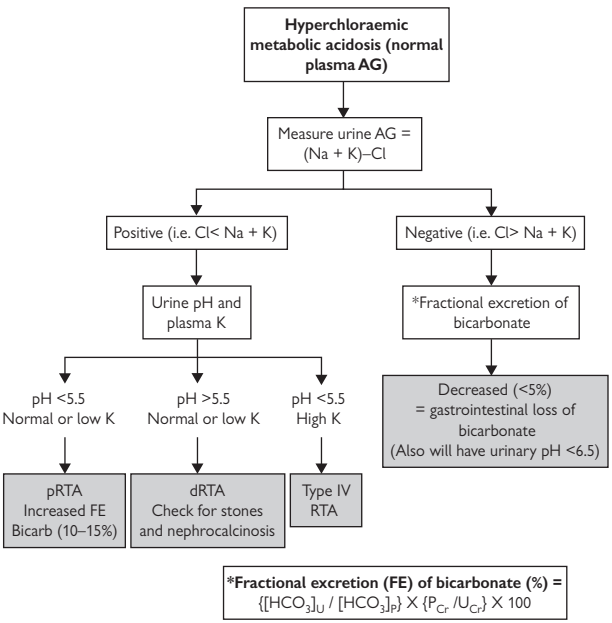

Fig. 31.3 Approach to diagnosis of hyperchloraemic metabolic acidosis. Adapted with permission from Herrin JT (1999). Renal tubular acidosis. In Barratt TM *et al.* (eds) *Paediatric Nephrology*, 4th edtn. Lippincott Williams and Wilkins, Baltimore.

Acute renal failure

Definition

Potentially reversible inability of the kidney to maintain normal body chemistry and fluid balance. It is usually characterized by:

- ***Uraemia:*** reduced consciousness, vomiting, twitching, raised plasma creatinine, hyperkalaemia and metabolic acidosis.
  In PICU it is associated commonly with:
- ***Oliguria:***
  - <1.0mL/kg/hr in neonates and infants
  - <0.5mL/kg/hr in children
  - <400mL/day in adults or older teenagers

  (polyuric acute renal failure occurs rarely in PICU).

Aggressive therapy to correct hypovolaemia, hypotension and hypoxia may lead to spontaneous recovery of renal function without the need for renal replacement therapy. Other important practical points include

- Most oliguria responds to IV fluid challenge. Never use diuretics before adequate volume replacement has been given
- Measure serum potassium: institute aggressive therapy if serum potassium high >6.5mmol/L
- Assess acid–base balance: arterial sample if possible otherwise central venous or free flowing capillary blood gas. Respiratory compensation (by hyperventilation) of a metabolic acidosis associated with ARF takes time and the critically ill child may be unable to achieve it at all
- Consider intubation and ventilation early if hypoxia and/or hypercapnia are severe
- Consider IV bicarbonate if acidosis persists despite correction of hypovolaemia and hypotension. Be aware that bicarbonate may worsen hypercapnia in the unwell but spontaneously breathing child
- Check ionized calcium level (usually with blood gases) and treat levels < 1.0mmol/L before giving bicarbonate—correction of acidosis further lowers the ionized calcium levels
- Always remember to exclude urinary tract obstruction as the cause of oliguria. Flush the urethral catheter to ensure it is not blocked (1mL/kg saline). US scan of the renal tract to exclude bladder clots, hydronephrosis or posterior urethral valves in a boy.

Differential diagnosis of cause of ARF

The causes of ARF can be divided into:

- ***Pre-renal:***
  - Hypovolaemia
  - Capillary leak in sepsis (common in PICU)
  - Haemorrhage following trauma or surgery
  - Burns (high insensible loss and capillary leak)
  - Severe diarrhoea and vomiting
  - Cardiogenic shock
- ***Renal:***
  - ATN secondary to prolonged pre-renal causes of ARF
  - Haemoglobinuria and myoglobinuria seen in trauma and crush injury

  - Renal arterial or venous thrombosis (venous more common in the neonatal period)
  - Haemolytic uraemic syndrome
  - Glomerular disease e.g. acute glomerulonephritis
  - Pyelonephritis
  - Drugs: see Box 31.5
- ***Post-renal:***
  - Obstruction of the renal tract from raised intra-abdominal pressure (trauma, abdominal pathology) or tumours compressing the ureters, posterior valves, bladder clot
  - Neuropathic bladder e.g. spina bifida, spinal cord injury.

Box 31.5 Nephrotoxins

- *Antibiotics*: aminoglycosides, cephalosporins, penicillins, sulphonamides, tetracyclines, vancomycin.
- *Diuretics:* furosemide, thiazides
- *Anticonvulsants:* phenytoin, sodium valproate
- *Immunosuppressants:* ciclosporin, tacrolimus
- NSAIDS, amphotericin, radiographic contrast, herbal remedies, paraquat, antifreeze, heavy metals.

Acute tubular necrosis

- Most ATN in PICU is secondary to low renal blood flow associated with hypotension, hypovolaemia, and shock
- ATN ensues when pre-renal causes of ARF are not corrected promptly
- The kidney requires and receives 20–25% of the cardiac output in order to support normal renal function. As the renal blood flow is reduced the kidney's auto-regulatory mechanisms fail and the renal parenchyma is rendered susceptible to hypoxic damage
- This is particularly so in the region around the proximal renal tubule and the ascending limp of the loop of Henle (the juxtamedullary region) where active, energy-dependent sodium reabsorption occurs
- Acute tubular cell death and necrosis ensue
- Renal tissue swelling occurs leading to further compression of blood vessels and further reduction in GFR
- Cellular debris occluding the renal tubules causes further oedema within the renal cortex and yet further reduction in the GFR
- Kidneys may appear bright on US scan.

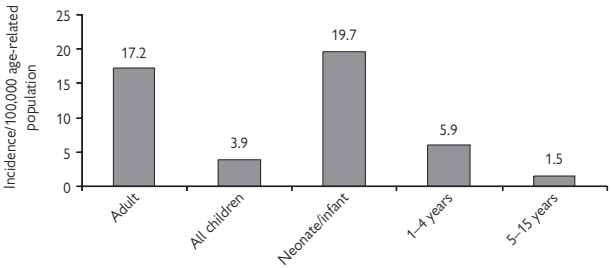

Fig. 31.4 Effect of age on incidence of ARF. Reproduced from Feest TG, Round A, Hamad S. (1993). Incidence of severe acute renal failure in adults: results of a community study. *Br Med J* **306**: 481–83, with permission from *BMJ* Publishing Group Ltd.

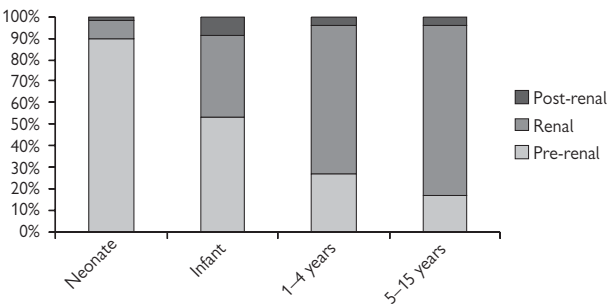

Fig. 31.5 Aetiology of ARF in children by age. Reproduced from Moghal NE *et al.* (1998). A review of acute renal failure in children: incidence, etiology and outcome. *Clin Nephrol* **49:** 91–5, Dustri-Verlag.

Box 31.6 Neonatal renal failure

Neonates are particularly at risk of renal failure due to relatively reduced renal blood flow (15% of cardiac output increasing to 25% when older) and glomerular filtration rate. It is commonly associated with hypoxia and the causes of pre-renal failure listed earlier.

Urine Na <20mmol/l, FeNa <2.5 and osmolality >400mOsmol/kg are suggestive of pre-renal ARF in neonates.

Box 31.7 Management of oliguria in PICU

- Confirm diagnosis, i.e. catheterize if not already
- Exclude blocked catheter
- Fluid challenge to ensure renal blood flow. Oliguria is usually due to pre-renal causes:
  - Give bolus of fluid 10–20mL/kg normal saline over 30min or shorter
  - Assess response (HR, capillary refill time core–peripheral temperature difference, change in CVP) and repeat fluid challenge if necessary
  - After 20–40mL/kg of normal saline (crystalloid) consider colloid: 4.5% human albumin solution or gelofusine
  - If response is poor start CVP monitoring and invasive arterial BP monitoring
  - Use blood or appropriate blood products for fluid boluses if haemoglobin is low or falling or the patient is thrombocytopenic or coagulopathic
- Distinguish between pre-renal and renal disease (urine Na, FeNa, urine osmolality, urine urea and creatinine ratios)
- Start inotropes/inodilators if cardiogenic component is suspected (post-cardiac surgery, sepsis).
- Try furosemide 1–2mg/kg as a bolus or infusion 0.2–1.0mg/kg/h after the fluid challenge if cardiovascularly stable (this may not improve renal function but may increase urine output and thus fluid balance)
- Monitor urea and creatinine, electrolytes, acid–base, serum lactate and blood gases
- Acute hyperkalaemia can be life threatening and levels >6.5mmol/L should be treated:
  - Ensure no potassium is given either in IV fluids or enterally, including feeds and supplements
  - Start emergency management of hyperkalaemia (see 📖 p.244)
- Consider renal replacement therapy.

Emergency treatment of hyperkalaemia (K^+ >6.5mmol/L)

(See 📖 p.224)

Management of established ATN

- Fluid management:
  - Daily weight and hourly input/output monitoring are the best indicators of fluid balance
  - Consider restriction to insensible losses (330mL/m^2/day or 10mL/kg/day) plus urine output and other measured losses
- Electrolyte imbalance:
  - Daily monitoring of U&Es, creatinine, bicarbonate, calcium, and phosphate. More frequent monitoring may be required according to clinical picture
  - With careful attention to fluid balance and diet (often with the help of a renal dietician) it is possible to avoid fluid overload, hyperkalaemia and acidosis

- Acidosis: try sodium bicarbonate slowly (over 30min) IV as a half correction either:
  - 1–2mmol/kg of sodium bicarbonate (8.4% = 1mmol/ml)

  or
  - according to the formula: Dose (mmol) = BE × Wt/4 <10kg
    = BE × Wt /6 >10kg

  (this is because ECF volume falls with age. BE is base excess and Wt is weight in kg)
  - CO_2 generated by the bicarbonate can cause hypercapnia.
- Consider renal replacement therapy.

Renal dopamine

There is no evidence that low-dose dopamine prevents renal failure or improves renal function. Dopamine may increase renal blood flow and thus urine output but appears to have no other advantages over other inotropes in hypotensive patients. Drugs that maintain a diuresis have a useful role in avoiding fluid overload in ARF.

Glomerulotubular dysfunction

In the PICU setting, acute severe glomerulotubular dysfunction usually manifests itself as ARF with the associated disturbances of electrolyte and acid–base balance.

Acute disturbances in the normal function of the nephron can also lead to hypertension, haematuria, RTA and renal Fanconi syndrome.

Glomerular disease

Proliferative glomerulonephritis and glomerulonephropathies associated with multisystem or autoimmume disease are rare conditions. Management will involve supportive care in PICU with careful attention to the management of fluid balance, electrolyte and acid–base problems as well as specialist advise from a Paediatric Nephrologist.

Tubular disease

- ***Rhabdomyolysis:*** causing myogobinuria and haemoglobinuria. Usually caused by crush injury, trauma with compartment syndrome, burns, hyperthermia syndromes, epilepsy, asthma, dystonias, or drug reactions. Life-threatening hyperkalaemia and hypocalcaemia can occur secondary to massive muscle damage. Myoglobin and uric acid are released which can precipitate/accumulate in renal tubules causing renal failure. Management includes aggressive fluid therapy and diuresis (see Box 31.8)
- ***Tumour lysis syndrome***: when large tumours or rapidly proliferating tumours (T-cell leukaemia) respond to chemotherapy, uric acid and calcium phosphate can precipitate in the renal tubules. This can be avoided by using rasburicase or allopurinol and diuresis as in rhabdomyolysis.

- ***Tubulointerstitial nephritis***: this condition is the result of a type of allergic reaction which leads to interstitial inflammation and tubular damage. Mainly secondary to drugs, e.g. phenytoin, rifampicin, immunoglobulins, and non-steroidal anti-inflammatories. Occasionally due to infection or associated with autoimmune disease and vasculitic syndromes. Treatment includes discontinuation of all suspect drugs and is otherwise supportive
- ***Non-steroidal anti-inflammatory drugs (NSAIDs)***: normally renal arterioles vasodilate under the influence of prostaglandins. NSAIDs inhibit prostaglandin synthesis leading to vasoconstriction and reduced renal blood flow. This can cause a fall in the GFR and is exacerbated by volume depletion, diuretic therapy, pre-existing renal impairment and the concomitant use of other nephrotoxic agents. Special attention to fluid balance and renal function during the use of these agents should be exercised
- ***Renal Fanconi syndrome***: dysfunction of the proximal tubule leading to abnormalities in the reabsorption of water and electrolyte (RTA, rickets, glycosuria, hypophosphataemia, aminoaciduria). The causes can be congenital or acquired and include galactosaemia, tyrosinaemia, drugs, and toxins.
- ***Hepatorenal syndrome***: this occurs in previously normal kidneys in association with hepatic failure. It may be secondary to redistribution of renal blood flow possibly due to the local action of prostaglandins. Despite ascites many patients are hypovolaemic. It should be suspected in liver disease with oliguria, raised urea and creatinine, high urine osmolality with high urine to plasma creatinine ratio and low urine sodium (<10mmol/L). Management requires CVP monitoring.Treat with fluid challenge—Hartmann's, gelofusine, or salt poor albumin can be used to raise CVP between 3–8mmHg. Avoid CVP >10mmHg which may lead to more hepatic damage and pulmonary oedema.

Box 31.8 Treatment of rhabdomyolysis (crush injury) and tumour lysis syndrome

- Anticipate problems. For tumour lysis, start allopurinol and or rasburicase before chemotherapy and continue for 5–7 days
- Reduce IV and oral potassium and phosphate supplements
- Aggressive fluid therapy for diuresis. Aim for urine output >2mL/kg/h by using 1.5–2× maintenance fluid, i.e. half normal saline 0.45% with glucose 2.5% or normal saline 0.9% or Hartmann's or Ringer's solution
- Consider replacing urine losses
- Diuretics: IV furosemide 1mg/kg, or IV mannitol 0.5–1g/kg
- Monitor electrolytes, particularly potassium, calcium and phosphate.
- Check for fluid overload (including CVP)
- Keep urine pH >6.5. Use bicarbonate if necessary (add 25mmol sodium bicarbonate to each 500mL of maintenance fluid)
- CVVH is effective at removing myoglobin.

Haemolytic uraemic syndrome

First described in 1955, HUS consists of:
- Microangiopathic haemolytic anaemia
- Thrombocytopenia
- ARF.

It is the most common cause of ARF in children. HUS has a wide clinical spectrum from subclinical to life threatening and has 3 broad categories:
- Diarrhoea positive (D+ or typical HUS, 90% cases in UK)
- Diarrhoea negative (D− or atypical HUS)
- Secondary HUS (HIV, malignant hypertension, chemotherapy drugs, malignancy, total body irradiation)

Typical D+ HUS

- Peak incidence between 6 months and 4 years. Most cases are <3 years
- Typically, the child presents after a history of bloody diarrhoea associated with verotoxin producing *Escherichia coli* (VTEC), strain 0157:H7, also called shiga toxin. The commonest source is the cow and children are infected from eating under cooked beef or drinking unpasteurized milk or from contaminated water
- Other symptoms include vomiting and abdominal pain which can be due to bowel perforation, toxic dilatation or intussusception
- Clinical signs include dehydration, hypovolaemia, extreme pallor and jaundice (due to haemolytic anaemia), petechie (due to thrombocytopenia) and hypertension
- Extra renal manifestations include:
  - Seizures
  - Altered conscious state and focal neurological signs
  - Cranial nerve palsies
  - Encephalopathy with decerebrate posturing, coma and in extreme cases tonsillar hernation and brainstem death
- 5–10% die during the acute phase, usually as a consequence of intestinal or cerebral complications.

Atypical D– HUS

- Atypical HUS occurs in <10% of cases but is commonly due to *Pneumococcus*, i.e. causing meningitis, empyema, or pneumonia
- Pneumococcal HUS. *Streptococcus* pneumonia produces neuraminidase which cleaves n-acetylneuramic acid from cell-surface glycoproteins and exposes the normally hidden T antigen (Thomsen-Freidenreich) on RBCs, platelets, and glomeruli. The exposed T antigen reacts with anti-T immunoglobulin in plasma resulting in a thrombotic microangiopathy. Plasma should be avoided as much as possible and RBCs and platelets washed before transfusion, to remove anti-T immunoglobulin
- Atypical HUS and the rare genetic causes have a worse prognosis, both in terms of mortality and the need for ongoing renal replacement therapy
  - Plasma exchange has been advocated for neurological signs.

Endothelial damage

Whatever the cause of HUS, the ultimate result is widespread endothelial damage in the kidney, brain, and intestine. This microangiopathy causes haemolytic anaemia with fragmented red cells on the blood film, platelet aggregation leading to thrombocytopenia and localized intravascular thrombosis. The coagulation screen is normal in HUS. The haemolysis and thrombocytopenia precede the onset of oliguria and ARF.

Box 31.9 Thrombotic thrombocytopenia (TTP)

This is a rare disorder of the coagulation system associated with deficiency or inhibition of the enzyme ADAMTS 13. This enzyme cleaves von Willebrand factor and is also known as von Willebrand factor-cleaving protease. Inhibition or deficiency of the enzyme leads to formation of platelet microthrombi in small blood vessels causing haemolysis and end-organ damage particularly:

- Brain—stroke, altered behaviour, fluctuating neurological signs
- ARF
- Fever
- Petechiae and bruising due to thrombocytopenia
- Microangiopathic haemolytic anaemia

HUS and TTP therefore have similar presentations with neurological signs and symptoms predominating in TTP, although the distinction is not clear cut.

Investigations

Basic investigations include:

- FBC, blood film
- U&Es, creatinine, liver function, LDH, glucose, urate, lipase, amylase
- Clotting screen, group and save
- Urinalysis for blood, protein, and microbiology
- VTEC serology
- Stool microscopy and culture
- Sputum microscopy and culture
- Blood culture
- Direct Coombs test (usually positive if T antigen present)
- HIV test
- ADAMTS13 enzyme activity (if available)

Selective investigations include:

- CXR, AXR
- Renal and abdominal US
- CT abdomen, brain if indicated.

Treatment

- HUS:
  - Treatment is largely supportive with blood transfusion for anaemia and RRT for ARF
  - Ventilatory support is indicated for respiratory failure associated with fluid overload and severe neurological comprise

- TTP:
  - Plasmaphoresis to remove the inhibitor of ADAMTS13 and replace the patient's plasma with FFP or cryosupernatant
  - Untreated, mortality is high with high morbidity for neurological sequelae
  - Patients can be critically ill and frequently require PICU care.

Hypertension

The exact incidence of hypertension is unknown, but it is probably not as rare as once thought. Measurement of the child's BP should be part of the routine physical examination.

General points

- Girls have a higher BP than boys before puberty but thereafter the reverse is true
- Measurement in the young child can be difficult and should be repeated to avoid spurious results

Definition

- Average systolic BP and/or diastolic BP >95th percentile for age, sex, and height on >3 occasions (i.e. 5% of population are hypertensive)
- Consult charts for normal data and percentiles of children's BP.

Causes

- Essential (primary) hypertension. Usually the case in post-pubertal children (particularly if obese)
- Secondary hypertension. Usually the case in younger children
- 60–80% due to renal parenchymal abnormality
- 5–25 % due to renovascular disease, coarctation of the aorta or phaeochromocytoma.

Measurement and techniques (see 🕮 p.67)

Signs and symptoms of hypertension

Most children who come to the attention of the paediatric intensivist will have hypertensive crisis with encephalopathy and cerebral oedema (irritability, seizures, reduced GCS) or pulmonary oedema secondary to cardiac failure.

Clinical assessment and investigations

- The aim is to look for evidence of end-organ damage and search for the cause
- Seek specialist advice from a Paediatric Nephrologist
- Family history (stroke, myocardial infarction, renal failure)
- Physical examination including femoral pulses for radio-femoral delay (coarctation of the aorta).
- Physical stigmata of neurofibromatosis (café au lait spots) and other syndromes associated with renal abnormalities/hypertension e.g. Bardet–Biedl, von Hippel–Landau, Turner's, Noonan's, Williams syndromes

- Virilization or ambiguity of the genitalia may indicate adrenal hyperplasia
- Evidence of chronic renal disease (polyuria, dysuria, enuresis, failure to thrive, bone disease)
- Fundoscopy and echocardiography/12-lead ECG to assess severity and longevity of systemic hypertension
- Urine for blood and protein
- Spot urine albumin:creatinine ratio
- Baseline bloods including FBC, U&E, creatinine, LFTs
- Exclude prescription and recreational drugs as a possible cause—amphetamines, ecstasy, cocaine, oral contraceptives
- CT scan or MRI indicated in acute encephalopathy.

Box 31.10 Drug therapy for hypertensive crisis.

Labetolol infusion: start at 0.5mg/kg/h increasing as necessary to 3mg/kg/h. Labetolol is best given diluted with glucose 5% to give a 1mg/mL solution. It can be given neat (5mg/mL) but this gives less control and takes longer to clear the dead space of the cannula/catheter

Sodium nitroprusside infusion: start at 0.5mcg/kg/min increasing to 8mcg/kg/min. Watch for rebound tachycardia. Always dilute in glucose 5%, i.e. 50mg SNP in 250mL glucose 5%. Never mix with other drugs and protect from sunlight (wrap in silver foil provided and use opaque infusion set). SNP is converted to cyanide and thiocyanate. Blood cyanide levels must be checked after 3 days and should be <100mcg/100mL. Do not use in patients with vitamin B12 deficiency or impaired liver function.

Box 31.11 Management of hypertensive crisis.

- This is an emergency with a high risk of morbidity and mortality
- Intubation and ventilation will be required for patients with severe encephalopathy or pulmonary oedema secondary to congestive cardiac failure
- Care must be taken during induction of anaesthesia to prevent dangerous swings in BP. Expert anaesthetic help should be sought:
  - Site large-bore IV cannulae
  - Anaesthetic induction agents (e.g. propofol or thiopentone) or sedatives (midazolam, diazepam) can cause hypotension. Doses should be given slowly and titrated against the patients response (loss of eye lash reflex) before muscle relaxants are given. If BP falls precipitously, give rapid saline 0.9% infusion 10–20mL/kg to restore BP
  - Conversely intubation can be very stimulating and can aggravate the hypertension significantly. Fentanyl 1–3mcg/kg and/or lignocaine 1mg/kg given with induction of anaesthesia can obtund the hypertensive response

(*Continued*)

Box 31.11 Management of hypertensive crisis (*Continued*)

- Hypertensive encephalopathy is due to raised ICP either as a consequence of an intracerebral bleed or cerebral oedema. ICP can be measured but is not recommended as BP should be controlled over the following 24–48h. Neuroprotective strategies should be followed until the patient is normotensive (see 📖 p.465)
- The preferred drug for management of hypertensive crisis is IV labetolol (α- and β-blocker) infusion
- If contraindicated (e.g. asthma, heart failure), use SNP (a direct vasodilator)
- Hydralazine (vasodilator) by slow IV injection can achieve rapid control of BP if necessary
- BP must be brought down slowly in order to avoid end-organ damage. Too precipitous a reduction in the BP can be associated with infarction of the optic nerve head and other potentially irreversible neurological complications
- In general, the more acute the onset, the faster the BP can be normalized. However, in most situations the duration of hypertension is unlikely to be known and it is generally accepted that the goal BP should be the 90th–95th percentile for age, sex, and height and the aim should be a 25% reduction in first 8h with further control achieved over the next 16–48h

Further reading

National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (2004). The Fourth Report on the Diagnosis, Evaluation, and treatment of high blood pressure in children and adolescents (2004). *Pediatrics* **114**: 555–76.

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Chapter 32

Diabetes and endocrinology

Diabetic ketoacidosis

Diabetes ketoacidosis (DKA) is a serious complication of untreated diabetes mellitus and the leading diabetes related cause of death in childhood. DKA is characterized by:
- Hyperglycaemia (blood glucose >11mmolL^{-1})
- Metabolic acidosis (pH <7.3)
- Bicarbonate <15mmol.L^{-1}
- Urinary ketones.

DKA is an medical emergency which if left untreated will lead to death. Patients with >5% dehydration or altered consciousness should optimally be treated in a high dependency setting (HDU).

Patients should be admitted to PICU with:
- Severe dehydration or shock (cardiovascular instability)
- Severe acidosis (pH≤7.1)
- Depressed or falling level of consciousness that puts child at risk of aspiration
- Age <2.

Epidemiology

- The incidence varies widely, with significant differences reported by different countries
- Predominantly a complication of type 1 diabetes mellitus (T1DM), rarely seen in type 2 patients
- DKA is often the first presentation of T1DM particularly if <4 years
- DKA is seen in established T1DM (1–10% per patient per year):
  - Accidentally interruption of insulin administration (i.e. malfunction of insulin pumps)
  - During intercurrent illness, e.g. sepsis
  - Intentional interruption of insulin secondary to multiple reasons, i.e. family discord, adolescent risk taking, diabetorexia (omission of insulin to achieve weight loss)
- Mortality from DKA varies from 0.15–0.3% of cases
- Causes of death include:
  - Cerebral oedema
  - Hypovolaemic shock
  - Hypokalaemia.

Aetiology and pathophysiology

DKA is caused by a relative insulin deficiency. This leads to hyperglycaemia, hyperosmolality, and ketone production secondary to:
- ↑glycogenolysis and gluconeogenesis (in liver and kidney)
- ↓glucose utilization peripherally (muscle and other organs)
- ↑lipolysis and activation of the β oxidation pathway, leading to ketogenesis (β hydroxybutyrate and acetoacetate) and metabolic acidosis.

The problem is exacerbated as hyperglycaemia exceeds the renal threshold for glucose (8.9–11mmol/L) which results in glycosuria and osmotic diuresis, progressive dehydration, further acidosis and electrolyte inbalance.

A vicious circle ensues where stress stimulates counter-regulatory hormones further stimulating ketogenesis, hyperglycaemia, and increasing the peripheral resistance to insulin.

Metabolic acidosis

- Primarily caused by the accumulation of the ketoacids; acetoacetate and β-hydroxybutyrate
- Osmotic diuresis leads to dehydration, and in severe cases hypovolaemia and hypoperfusion. The resulting lactic acidosis exacerbates the metabolic acidosis
- Hyperchloraemia occurs mostly due to the IV fluid resuscitation which usually contains generous quantities of chloride, e.g. normal saline, gelofusin.

Hyperosmolality

This is caused by hyperglycaemia and raised plasma urea from dehydration.

Dehydration

- Dehydration is primarily from the intracellular space due to the elevated plasma osmolarity
- Dehydration is often overestimated so a maximum of 8% dehydration should be used.

Electrolyte imbalance

Vast amounts of electrolytes are lost in the osmotic diuresis:

- *Sodium*: although true hyponatraemia may occur, a falsely low sodium reading (pseudohyponatraemia) may occur in DKA. This is due to hyperlipaemia (decreasing the aqueous proportion of the blood) and hyperglycaemia (diluting the sodium due to volume shifts from the intracellular to extracellular space). Pseudohyponatraemia is less common with modern blood analysers
- *Potassium*: serious disturbances in plasma potassium occur commonly within a few hours in DKA. Whether high, normal, or low there is always total body depletion of potassium.
  - Initially hyperkalaemia reflects acidosis and hyperosmolality as potassium moves from the intracellular to the extracellular space. As osmotic diuresis progresses, significant amounts of potassium are washed into the urine and depletion of body of potassium occurs. Insulin administration and the normalization of the blood glucose and pH causes potassium to move back into the cells, resulting in hypokalaemia
- *Phosphorus and magnesium*: it is common for both to be significantly reduced.

Clinical features

- Classically, the patient presents with a history of polyuria, polydipsia, and polyphagia
- Nocturia and enuresis are common presentations
- Other symptoms includes dehydration, vomiting, abdominal pain, hyperpnoea (Kussmaul breathing), often with a fruity smell caused by acetone, and drowsiness.

Diagnosis

DKA describes the patient that presents with:

- Blood glucose concentration >11mmol/L,
- Blood pH <7.3
- Bicarbonate level <15mmol/L
- Plasma ketones >3mmol/L
- Urinary ketones.

Investigations

Blood

- FBC and differential
- Electrolytes and urea and creatinine
- Glucose
- Liver function tests (transaminases and clotting screen)
- ABGs
- Lactate and ketones
- Blood cultures.

Urine

Urinalysis including ketones.

Management of DKA

- Please refer to British Society of Paediatric Endocrinology and Diabetes guidelines (www.bsped.org.uk) or International Society of Pediatric and Adolescent Diabetes guidelines (www.ispad.org)
- Involve a specialist with an interest in diabetes as early as possible.

Box 32.1 In a nutshell:

- Initial assessment
- ABC of resuscitation including reliable venous access
- Blood gase
- Institute monitoring, e.g. pulse oximetry, ECG, (arterial line and central line only rarely if indicated)
- Blood and urine tests
- Fluid therapy
- Insulin therapy
- Antibiotics if indicated
- Watch for and minimize sudden changes in plasma sodium, osmolality, and potassium
- Watch for signs of cerebral oedema and treat if necessary (see 📖 p.465).

Airway and breathing

- The majority of patients with DKA will not require intubation—remember to use humidified oxygen via a facemask
- Beware the agitated patient who becomes quiet without lucidity
- Indications for endotracheal intubation (Box 32.2) are:
  - Respiratory failure including fatigue (hyperventilation is necessary to compensate for metabolic acidosis; respiratory compromise from whatever cause can lead to acute worsening of acidosis)

- Loss of airway reflexes (aspiration of gastric contents is a real risk with DKA)
- Worsening conscious state. Occasionally an extremely confused and agitated patient is easier to manage when intubated.
- Ensuing coma (electively intubate at GCS ≤8).

Box 32.2 Endotracheal intubation

Endotracheal intubation in severe DKA can be challenging and the strategy will need to be adjusted depending on the clinical situation. As a guide, the main points would be:

- Always consider a RSI as the risk of aspiration is high (see 📖 p.132)
- If cerebral oedema is suspected then treat with mannitol 0.5–1.0mg/kg or hypertonic saline 3% 4mL/kg
- The induction agents should be chosen with neuroprotection in mind, unless the patient is shocked with hypotension; in which case cardiovascular stability should take priority
- Initial ventilation should be aimed to maintain similar CO_2 levels that the patient was achieving prior destabilization—usually hypocapnic (this avoids acute increase in CBF and thus ICP). EtCO_2 monitoring is an invaluable tool to continuously assess these patients
- The degree of ventilation should be decreased as the pH recovers with the administration of insulin. pH levels between 7.1–7.2 are usually well tolerated and the clinician should avoid correcting fully the pH solely at the expense of a low CO_2
- Nurse head-up (15°) and maintain sedation and paralysis if cerebral oedema is suspected.

Circulation

- In severe DKA the patient may present with ***shock***:
- Replenishing the intravascular volume should be done by administering intravenous fluid boluses (10–20mL/kg)
- Use Normal saline (0.9%) or Hartmann's solution (Ringer's lactate). Colloids such as gelofusine or human albumin solution can be used but should be limited to 5–10mL/kg aliquots because they stay in the circulation
- Senior advice should be sought if >30mL/kg IV is indicated. Tachycardia may take up to 12 hours to normalize
- Restoring circulating volume alone will bring down blood glucose significantly
- In the comatose child with suspected cerebral oedema care should be taken not to overhydrate in order to avoid exacerbating neurological complications.

Rehydrate (Box 32.3)

- Rapid rehydration is unnecessary once shock has been treated
- Estimate dehydration bearing in mind that it is often overestimated
  - 4% or
  - 8%

- Do not estimate >8% dehydration for deficit calculations
  - Deficit should be replaced over 48h:

$$\text{Hourly rate} = \frac{(\text{48h maintenance} + \text{half deficit} - \text{resuscitation fluids})}{48}$$

  - Calculate maintenance at 80% of normal requirements
  - Exclude colloid from resuscitation volumes
  - Do not include ongoing urinary losses
- Normal saline should be used but Hartmann's solution considered if chloride levels are high
- When blood glucose falls to 15mmol/L switch to half Normal saline 0.45% and glucose 5% combined (with 40mmol/L potassium)
- If urine losses are persistent and >3mL/kg/h then consider replacement on an hourly basis with normal saline 0.9%

Box 32.3 Which fluid and when?

- There is some evidence that solutions such as Hartmann's (Ringer's) solution that contain less chloride than saline (0.9%) are less likely to cause hyperchloraemic acidosis. If problems are encountered with large volumes of saline then Hartmann's solution is an alternative
- If blood glucose falls to less than 15mmol/L within 6h or by more than 5mmol/L/h after treatment has commenced then there is probably still a sodium deficit. If this is the case we suggest using 0.9% saline and 5% glucose combined rather than saline 0.45% and 5% glucose combined. These can be made up by removing 100mL from 500mL of 0.9% saline and replacing it with 100mL of 50% glucose. Again Hartmann's solution can be substituted for saline.

Insulin

- Insulin should be given via a continuous IV infusion. Typically, a dose of 0.1U/kg/h is sufficient to re-establish glucose as a source of energy and in turn, stop ketogenesis
- To make an infusion: Add 50U short-acting insulin (e.g. Actrapid® or humulin R®) to 50mL Normal saline 0.9% making 1U/mL. Label clearly
- Changes in the glucose concentration should be closely monitored and hourly measurements will be required in the initial stages of DKA management
- If blood glucose continues to rise then fluid replacement may be inadequate
- Rarely does the insulin rate need to be ↑ but if the reduction in blood glucose is <2.5mmol/L/h and/or acidosis persistent, then increase the infusion rate to 0.15–0.2U/kg/h
- As blood glucose reaches 15mmol/L glucose should be added to the IV fluids to avoid excessive hypoglycaemia
- The insulin infusion should not be reduced until pH normalizes and the ketone bodies have been metabolized
- If available a ketone meter allows for bedside plasma ketone measurements on a regular basis (12h)

- Finally, IV insulin infusion can be converted to subcutaneous insulin when:
  - pH>7.3,
  - Bicarbonate over 18mmol/L
  - Anion gap is normal
  - Enteral feeding is established
- Consider reducing insulin infusion to 0.05U/kg/h. Stop IV infusion 60min ***after*** converting to subcutaneous insulin.

Electrolytes

Sodium

- Hyponatraemia should be treated aggressively even if the low level of sodium is thought to be only artificially low. Particularly if the patient develops signs of neurological compromise
- The therapeutic goal should be to achieve and maintain a plasma sodium level in the high normal range (145mmol/L). Consequently all hypotonic solutions should be avoided. Saline 0.9% is recommended
- As glucose and pH normalize the plasma sodium may increase to a moderate supranormal levels (150–160mmol/L). This sodium level is normally well tolerated and may provide some protection against neurological complications like cerebral oedema
- Sodium may be artificially depressed by the effects of glucose and lipids. Sodium can be tracked through the corrected sodium.

$$\text{Corrected Na} = \text{Na} + 0.3 \times (\text{glucose} - 5.5)$$

Potassium

- Hyperkalaemia:
  - Normally seen on presentation in association with severe acidosis and hyperglycaemia (and possibly impaired renal function)
  - Plasma potassium should normalize quickly with insulin therapy. However if ECG changes consistent with hyperkalaemia are present then manoeuvres to lower potassium should be taken immediately, particularly with renal impairment (see 📖 p.243)
  - In the severely acidotic patient the classic hyperkalaemic treatments aimed at shifting potassium into the intracellular space are unlikely to work and emergency haemodialysis should be considered early
- Hypokalaemia:
  - Total body potassium is reduced in DKA
  - Replacement potassium chloride (KCL) should be started as soon as resuscitation is completed and fluid replacement begins
  - Start KCL at 40–60mmol/L.

Bicarbonate

- Bicarbonate should be avoided in the majority of DKA. It can exacerbate hypokalaemia, prolong ketoanion metabolism, and cause intracellular acidosis. Furthermore, bicarbonate will produce an $\uparrow CO_2$ load for a respiratory system already at its limits
- Bicarbonate maybe considered in cases of extreme acidosis not responding to fluid and insulin therapy (pH <6.9 when the low pH may interfere with organ function). If used, bicarbonate should be infused

slowly at a rate 0.5–1mmol/kg/h. The pH and CO_2 should be closely monitored and the infusion stopped when the pH reaches 7.0.

Monitoring

- Document fluid balance carefully (include oral intake)
- Hourly observations including level of consciousness and pupil size (neurological observations)
- We recommend a DKA flow chart when on an insulin infusion:
  - Hourly blood glucose and 2-hourly plasma ketones (6-hourly urine ketones)
  - 2–4-hourly venous or ABGs, sodium, potassium, chloride, and urea.
  - Calculate effective plasma osmolality 2–4-hourly

  Plasma osmolality = $(2 \times Na) + (2 \times K)$ +glucose
- Keep a very close eye on changes in the sodium, corrected sodium, and osmolality, which are critically important in anticipating complications of DKA.

Complications of DKA (Box 32.4)

Cerebral oedema

- The most serious complication of DKA
- More common in children than adults, particularly <5 years old
- Clinical cerebral oedema has a prevalence of 1–2% and carries a significant mortality rate (21–25% of cases)
- Risk factors for development of cerebral oedema are:
  - Younger age
  - Newly diagnosed
  - Longer duration of symptoms
  - More severe acidosis at presentation
  - Higher plasma urea at presentation
  - Greater hypocapnia adjusting for degree of acidosis
  - Over rapid fluid hydration
- Usually manifests itself 4–12h into the DKA treatment when the patient's metabolic derangements start to recover. There is evidence that many more patients have subclinical cerebral oedema. In the majority of cases, cerebral oedema is idiosyncratic and unpredictable.

- There is increasing (but not yet overwhelming) evidence that the fall in plasma sodium concentration during treatment may be associated with the development of cerebral oedema. It is vital that plasma sodium (and corrected sodium) concentration as well as plasma osmolality are monitored carefully
- Warning signs of cerebral oedema include:
  - First presentation, history of poor control, failure of sodium to rise during initial treatment, initial low osmolality, headache, irritability, falling level of consciousness
  - Bradycardia, hypertension, and respiratory embarrassment are late signs of cerebral oedema and imply brainstem herniation

- If cerebral oedema is suspected then rapid osmolar changes should be minimized. Consider reducing the insulin rate to 0.05U/kg/h

- Treat suspected cerebral oedema with:
  - Mannitol 0.5–1g per kg that can be repeated every 2–4h
    And/or…
  - Hypertonic saline 3%. Assuming a volume of distribution of 60% of body weight for sodium, then 1mL/kg (0.5mmol/kg) of hypertonic saline 3% raises plasma Na by 0.8–1mmol/L. Thus giving 4mL/kg slowly should raise plasma Na by 3–4mmol/L
  - Aim to maintain a plasma Na between 150–160mmol/L
  - Reduce maintenance fluid to 2/3 and replace calculated deficit over 72h
- The classic measures of neuroprotective intensive care (i.e. head elevation, ventilation, sedation, paralysis etc.) should also be implemented

Box 32.4

The pathophysiology of cerebral oedema in DKA is not completely understood. Suggested factors include the rate of correction of blood glucose and acidosis, and the presence of 'idiogenic osmoles' within brain cells. These are substances formed within brain cells when the extracellular fluid (ECF) becomes hyperosmolar (e.g. hyperglycaemia and hypernatraemia) in order to prevent intracellular dehydration. Unfortunately when the ECF is being rehydrated these osmols persist (at least for a while) and draw water from the ECF into the brain cells and lead to cerebral oedema. Other factors implicated are changes in plasma sodium, administration of bicarbonate, low $PaCO_2$, high urea, hypoperfusion and interleukin release by the action of ketones.

Cardiac arrhythmias

Related to electrolyte disturbances, in particular hyperkalaemia. The ECG may provide the earliest of warning of disturbances in the conduction system of the heart.

Pulmonary oedema

- Thought to be related to changes in osmolality
- May compromise the ability to clear CO_2 in severe metabolic acidosis.

Hyperosmolar hyperglycaemic non-ketotic coma

- Extreme hyperglycaemia and hyperosmolality can occur without ketosis in diabetic patients
- Extremely rare in childhood, it is more common in adults and in patients with type 2 diabetes
- There some evidence that the mortality rate is higher than DKA (14%)
- Always seek management advice from a paediatric endocrinologist if possible.

Hyperglycaemic hyperosmolar states without ketosis occurs when the patient retains enough insulin production to inhibit ketosis but not to control hepatic glucose production. Extreme hyperglycaemia induces hyperosmolality and osmotic diuresis, which in turn causes dehydration and electrolyte imbalance.

Diagnosis

Criteria include:
- Blood glucose >33mmol/L
- Plasma osmolality >330mOsm/L
- No significant ketosis.

Management

- There is little data regarding the best therapeutic approach in children
- Fluid administration alone significantly reduces blood glucose
- Saline 0.9% is recommended for fluid replacement instead of hypotonic solutions. Hypernatraemia may occur as glucose declines. If hyperchloraemia is a problem consider Hartmann's solution
- As there is no ketosis insulin therapy should be delayed—a smooth and gradual decline in blood glucose and plasma osmolality is the aim
- Insulin, if necessary, should be prescribed at no more than 0.05U/kg/h as glucose may fall precipitously

Blood glucose

Requirements

Neonates: Between 6–8 mg/kg/min (think ↑insulin if >12mg/kg/min)
Infants: Normally <10mg/kg/min
Children: Normally <8mg/kg/min

Glucose intake in mg/kg/min = (%dextrose × rate mL/h) / (weight × 6)

- Neonates and Infants are more vulnerable than older children to lack of glucose as they have higher requirements and less glycogen
- If children are catabolic/stressed they assimilate less glucose
- High glucose content in TPN leads to ↑ production of CO_2.

Choice of fluids

- 10% dextrose is the strongest concentration that can be given safely in peripheral IV lines:
  - Even then extravasation can cause tissue injury, so care is needed
  - Remember concerns about using hypotonic solutions as maintenance therapy (see 📖 p.231)
- 5% dextrose with 0.45% or 0.9% saline as maintenance usually provides enough dextrose for infants and older children.

Measurement

Blood glucose measurement is affected by sample type, processing delay, and method used.

- Plasma glucose is 12% higher than whole blood glucose
- Samples should not be taken from a central line that has been used to infuse glucose solutions; nor from a line (or lumen) that is proximal to another one infusing a glucose solution
- Lab-based measurements are affected by delay in sample processing as red cells continue to metabolize glucose in the sample after it is taken
- Well maintained blood gas machines generally produce lab standard accuracy for blood glucose measurements
- Bedside stick testing usually underestimates blood glucose. Stick Test <3.5 should be checked with an urgent lab/gas machine sample.

Definition

- There is no universally accepted definition of hypo or hyperglycaemia
- Glucose control varies with age (particularly in the newborn and preterm) and is affected by sickness and medication
- Suggested definitions of hypoglycaemia range from 1.7mmol/L (in neonates) to 3.5mmol/L (30–63mg/dL)
- Suggested definitions of hyperglycaemia range from 6.1–15mmol/L (110–250mg/dL)
- Pragmatically, we suggest normal plasma glucose in children >1 month is 3.5–5.5mmol/L (63–100mg/dL); that hypoglycaemia is <2.5mmol/L (45mg/dL); that hyperglycaemia is >8mmol/L (140mg/dL)

► ***But*** we always interpret glucose measurements in the light of the child's clinical condition, current symptoms and likely course.

Hyperglycaemia in PICU

- Hyperglycaemia in critically ill children is common. It may be related to the child's illness or their treatment:
  - May be seen in conditions associated with an inflammatory response, e.g. sepsis, pancreatitis, following major surgery or trauma
  - May be secondary to glucose in maintenance fluids; endogenous or therapeutic catecholamines and corticosteroids
- Currently it is not known if critically ill children have a relative insulin deficiency or resistance
- Hyperglycaemia is associated with a worse outcome in PICU but it is not clear whether this is a causative relationship

See Box 32.5

Box 32.5 Tight glycaemic control in PICU

There has been a recent interest in controlling glucose to physiological levels—known as 'tight glycaemic control'. There is some evidence that this benefits critically ill adults with sepsis and burns. Retrospective studies in children suggest they may benefit. Multi-centre prospective trials in paediatric intensive care are currently underway in UK, USA, and Canada.

While awaiting the outcome of these studies, it is reasonable to adopt a pragmatic approach which balances good glycaemic control with safety. Increases in hypoglycaemic events associated with tight blood glucose control must be avoided.

Locally agreed protocols are often employed to guide staff in this balancing act. A general policy of maintaining blood glucose in a target range of 5–10mmol/L with a minimum of 4-hourly checks may safely achievable. In some children, a higher target range may be more appropriate.

In any case, it might be the glucose variability, or the time spent at high glucose levels, which is the prognostic indicator for outcome, rather than the absolute level.

Management of hyperglycaemia

- There are insufficient data to provide clear guidelines of when to start treatment:
  - Insulin infusions are not without complications—generally as a patient gets better the stimulus for hyperglycaemia is removed
  - Blood glucose may fall rapidly and the consequences of hypoglycaemia can be severe
- If blood glucose is consistently above 10mmol/L an insulin infusion at a rate of 0.05U/kg/h may be started. Monitor glucose 1/2-hourly for the first 2h on insulin then 1-hourly
- If any repeat glucose <10mmol/L wean insulin infusion by 50% and recheck glucose after 20min
- Exciting developments in continuous glucose monitors and closed loop Insulin delivery systems promise to revolutionize this area of care.

Hypoglycaemia in PICU

Hypoglycaemia is one of the more common metabolic disturbances seen in childhood and can be defined as blood glucose <2.5mmol/L or <4mmol/L in children with diabetes. As glucose is the main energy substrate for the brain hypoglycaemia can have devastating consequences.

- The underlying mechanisms behind hypoglycaemia are:
  - Poor glucose supply (e.g. low glycogen stores in preterm babies, poor feeding and malabsorption)
  - ↑glucose consumption (e.g. sepsis, excess insulin)
  - Abnormalities in hormonal control of glucose metabolism resulting in reduced gluconeogenesis or glycogenolysis (e.g. endocrine and metabolic diseases and drug related).

See Box 32.6

Clinical features

- Initially due to activation of the adrenergic autonomic nervous system (tachypnoea, tachycardia, vomiting, and sweating)
- Progressive hypoglycaemia results in neurological symptoms of lethargy, deteriorating consciousness, and seizures
- Neonates may only display jitteriness, poor feeding, and hypotonia.

Diagnosis

Necessary samples should be collected for laboratory analysis while the patient is hypoglycaemic. Once taken glucose administration should proceed immediately.

Box 32.6 Aetiology and investigations for hypoglycaemia

Hypoglycaemia is the sign of an underlying disease process. Causes of hypoglycaemia include

- *Neonatal*: preterm, IUGR, maternal diabetes mellitus (hyperinsulinism), fetal alcohol, Beckwith–Wiedemann syndrome
- *Endocrine*: hyperinsulinism, hypopituitarism, growth hormone deficiency, congenital adrenal hyperplasia, hypothyroid
- *Metabolic:* glycogen storage, galactosaemia, organic acidaemia, carnitine deficiency, Acyl CoA dehydrogenase deficiency
- *Toxic:* salicylates, alcohol, insulin, β-blockers, valproate
- Sepsis, starvation, malnutrition.

Tests include:

- Blood glucose, urea, electrolytes, liver function tests, arterial gases
- Septic screen, toxicology
- Plasma lactate, pyruvate, ketones, free fatty acids, total and free carnitine levels, amino acids, insulin, C-peptide, ammonia, and acyl carnitine
- Plasma hormones: insulin, cortisol, growth hormone.

Box 32.7 Treatment of hypoglycaemia

Treatment should start as soon as blood samples have been collected. ***Hypoglycaemia warrants treatment if blood glucose < 2.6mmol/L.***

Asymptomatic child

- Enteral administration of glucose, either orally or via NG tube is very effective particularly if there is no venous access.

Symptomatic child

- Slow IV bolus of 5mL/kg of 10% glucose (0.5g/kg) or 2mL/kg of 25% glucose in older children
- To avoid a surge in insulin secretion (and further hypoglycaemia), follow this with a glucose infusion:
  - 10% glucose with saline 0.9% or 0.45% at 5mL/kg/h (i.e. 500mg/kg/h of glucose)
  - Make 10% glucose with saline 0.9% or 0.45% by removing 100mL from a 500mL bag of 0.9% or 0.45% and replacing it with 100mL of 50% glucose
- If glucose requirements are higher or fluid volumes need restriction then insert a central venous catheter to deliver more concentrated solutions (12.5 or 20% glucose).
- If hypoglycaemia persist despite glucose treatment, glucagon (0.1–0.2mg/kg and up to 1mg) may be helpful as long as the patient has adequate glycogen stores.
- Hydrocortisone, 2–3mg/kg or 25–50mg/m^2, may be useful in refractory hypoglycaemia.

- Hyperinsulinism
  - Due to hypersecretion of insulin by the islet cells in the pancreatic islets of Langerhans
  - Results in recurrent hypoglycaemia, requiring high glucose intake often over 10mg/kg/min.
- *Treatment*
  - Give adequate glucose intake to maintain normoglycaemia; this may require a central line
  - Consider adding continuous infusion of glucagon (10–50 mcg/kg/h) or octreotide (1–5mcg/kg/h) in difficult cases
  - Once glycaemic control has been achieved, oral diazoxide (5mg/kg 3 times a day) is commenced for maintenance treatment
  - Diazoxide should be used in conjunction with chlorthiazide—additive effect and reduces fluid retention
  - After starting diazoxide aim to gradually introduce bolus feeding
  - Continuous feeds may be helpful in severe hypoglycaemia
  - Blood glucose levels should be checked before and after feeds and kept >3mmol/L at all times. If this can not be achieved, consider surgical option (subtotal pancreatectomy) for resistant cases.

Diabetes insipidus: central or neurogenic

Whilst water balance can be affected by multitude of factors, we shall concentrate on those secondary to alterations of arginine vasopressin (AVP), formerly known as antidiuretic hormone (ADH). AVP is a major determinant of renal water excretion.

- Central DI describes a syndrome of inadequate endogenous AVP secretion characterized by uncontrolled hypotonic polyuria despite a hyperosmolal state (urine osmolality <300mOsmol/L)
- DI is responsive to exogenous AVP administration
- DI in PICU is commonly secondary to:
  - Suprasellar tumour (craniopharyngioma)
  - Surgical removal of supresellar tumour
  - Severe traumatic brain injury (where it is a poor prognostic sign, often preceding brain death)
  - Cerebrovascular accidents, ischaemic/hypoxic brain injury or may be idiopathic
- Insufficient secretion of AVP leads to:
  - ↑loss of free water in urine
  - The water loss in turn causes an elevation of plasma osmolality and sodium.

Clinical features

- A urine osmolality <300mOsm/L and a plasma osmolality >295mOsm/L are diagnostic
- Hypernatraemia Na >150mmols/L
- Dehydration
- Haemodynamic instability in the setting of brain death.

Where mannitol has been administered in traumatic brain injury to control the ICP, the resulting diuresis may obscure the clinical picture. Osmotic diuresis generally leads to a more concentrated urine (higher urine osmolality) than that seen in DI.

Box 32.8 Treatment of diabetes insipidus

- Patients with severe dehydration or shock should receive 20mL/kg IV isotonic fluid (e.g. saline 0.9%, Hartmann's, Ringer's lactate) to maintain intravascular volume
- Once the circulating volume has been re-established, the excessive water loss must be replaced
  - Urine output should be replaced with hypotonic solutions
  - Glucose 5% or glucose 4% with saline 0.18% combined may be used
  - Watch for secondary hyperglycaemia and subsequent osmotic diuresis from glucose containing solutions
  - In most PICU patients, IV AVP (at least in the acute phase) will be required to control the urine output.
  - Intranasal or subcutaneous AVP may be used later
  - Infusion of AVP between 0.05–2mU/kg/h, carefully titrated, is sufficient to control the plasma sodium and urine output
- AVP is a potent vasoconstrictor—watch for lactic acidosis or myocardial ischaemia (ST depression on ECG).

Nephrogenic diabetes insipidus

- Is a rare condition, characterized by a state of uncontrolled hypotonic polyuria, insensitive to the administration of AVP
- Is either secondary to a relative resistance to AVP in the kidney or a primary disorder in the concentration gradient of the medullary tubule
- A wide array of renal disorders can cause nephrogenic DI (chromosomal abnormalities, lithium, hypokalaemia, hypercalcaemia, radiation, and sickle cell anaemia)
- Treatment includes a combination of hydrochlorothiazide (1–3mg/kg/daily) or amiloride (0.2–0.7mg/kg/daily) with indomethacin (0.5–3mg/kg daily).

Arginine vasopressin or antidiuretic hormone disorders

Syndrome of inappropriate antidiuretic hormone (SIADH)

SIADH is characterized by:

- Hypotonic hyponatraemia
- ↑AVP (ADH) secretion without stresss, hyperosmolar, or hypovolaemic stimulation
- Water retention and reduced urine output

It is important to stress that AVP (ADH) is a stress hormone and thus ↑AVP levels are part of normal homeostatic mechanisms. Many so-called causes of SIADH are in fact appropriate causes of ↑AVP secretion:

- CNS pathology (incidence of up to 15%):
  - Trauma
  - Infection: bacterial meningitis, encephalitis
  - Cerebrovacular bleeding
  - Tumours
  - Guillain–Barré
- Lung pathology:
  - Bacterial pneumonia
  - Bronchiolitis
  - Asthma, pneumothorax
- Drugs: morphine and NSAIDs. vincristine, and cyclophosphamide

Care should be taken not to confuse SIADH with other conditions (Box 32.9) that promote excessive sodium losses like adrenal insufficiency, hypothyroidism, diuretics, or cerebral salt wasting syndrome. In these conditions, sodium deficit, not water retention, is the primary reason for the hyponatraemia.

Box 32.9 Diagnosis of SIADH

SIADH is frequently overdiagnosed. Many cases in PICU are in fact 'appropriate'. The diagnosis can only be made when clinical criteria are met and when appropriate causes are excluded:

- Na <135mmol/L
- Hypotonic plasma (osmolality <270mOsmol/kg)
- Excess renal sodium loss (>20mmol/L) and concentrated urine (>600mOsmol/L)
- Normal renal, adrenal, and thyroid function
- ↑plasma ADH (AVP)
- Absence of oedema
- Absence of appropriate cause.
- Absence of diuretics.
- Exclusion of fluid overload.

Cerebral salt wasting

Severe hyponatraemia may occur secondarily to cerebral salt wasting (CSW). This can develop suddenly (possibly with delayed onset) with few clues to herald it. It is seen following subarachnoid haemorrhage and traumatic head injury but may occur with any intracranial pathology. The characteristic excessive natriuresis is probably mediated by an ↑release of atrial and brain natriuretic peptides. CSW is characterized by:

- Hyponatraemia
- Renal wasting of sodium and chloride. Inappropriately high fractional excretion of sodium
- Dehydration from excess water loss
- Note-sodium loss is greater than water loss.

See Boxes 32.10 and 32.11

Box 32.10 CSW or SIADH?

CSW must be differentiated from SIADH as they have different treatments and misdiagnosis can be catastrophic. Unfortunately laboratory findings can be remarkably similar in both conditions:

- Hyponatraemia
- High urine osmolality compared with plasma.

Careful clinical assessment (including CVP) and fluid balance should reveal the diagnosis:

- CSW is characterized by volume depletion and natriuresis (fractional excretion $FE_{Na} > 1$)
- SIADH there is ↑total body water and lower urine output.

Box 32.11 Management of CSW

- Adequate water and sodium replacement is the mainstay of the treatment of these patients
- Monitoring urine sodium concentrations will provide a useful guide to the required sodium intake
- If the diagnosis is uncertain a temporary strategy would be to change the patient's fluid intake to replace the urine output (mL per mL), with 0.9% saline or an intravenous fluid containing a sodium amount above the urine sodium concentration. This is a simple way to manage these patients until the diagnosis is confirmed
- If the patient is frankly hyponatraemic and/or symptomatic with plasma Na<125mmol/L give sodium replacement IV as 3% saline. Lower concentrations may not be able to compensate for the ongoing sodium loss
- Once plasma sodium is normalized the sodium in the fluids may be reduced
- It reported that the use of steroids, i.e. methylprednisolone or fludrocortisone, may help to control persistent natriuresis.

Adrenal disorders

Adrenal insufficiency

- Primary adrenal insufficiency describes a syndrome where there is an inadequate secretion of mineralocorticoids (aldosterone) and glucocorticoids (cortisol) by the adrenal gland. Adrenocorticotrophin levels are elevated due to reduced cortisol negative feedback control
- Secondary adrenal insufficiency is due to ↓corticotrophin releasing factor or ACTH levels (or both) (see Box 32.12)
- Inadequate secretion of glucocorticoids causes a wide range of symptoms but it is the development of hypoglycaemia and cardiovascular compromise that bring these children to the attention of the Paediatric Intensivist
- The shock state observed in these patients has some unusual features in that it can be quite unresponsive to traditional therapies like volume resuscitation and catecholamine administration
- Reduction in mineralocorticoid secretion leads to hyponatraemia and hyperkalaemia. The excess sodium in the urine also causes excessive water loss and dehydration that may contribute to shock.

This condition is rare and the symptoms are subtle. The treatment is specific so timely diagnosis is essential.

Clinical presentation

Although presentation of adrenal insufficiency may vary from a subacute onset to adrenal crisis the clinical features in PICU are:

- Hypoglycaemia (↓glucocorticoid)
- Hypotension: often unresponsive to IV fluid and catecholamine secretion (↓glucocorticoid)
- Hyponatraemia, hyperkalaemia and dehydration (↓mineralocorticoid)
- Wasting, hyperpigmentation, virilization.

Box 32.12 Causes of adrenal insufficiency

Primary

- Congenital adrenal hyperplasia and hypoplasia
- Autoimmune adrenalitis (Addison's disease)
- Adrenal infection (TB) or infarction/haemorrhage
- Post adrenalectomy, drug induced

Secondary

- Hypothalamic/pituitary pathology:
  - Intracranial tumours, e.g. craniopharyngioma, glioma
  - Pituitary hypoplasia
  - Infection, inflammation (Langerhans histiocytosis)
  - Trauma, post neurosurgery, post radiotherapy
  - Post-steroid therapy (hypothalamic–pituitary–adrenal suppression).

Diagnosis

- Random basal cortisol levels may be normal and are rarely useful, although a 09:00h cortisol <100nmol/L is abnormal
- The short Synacthen test to assess the response of the adrenal gland (see Box 32.13)
- Further tests should involve an endocrine specialist.

Box 32.13 The short Synacthen test

Synthetic adrenocorticotrophin (Synacthen) is administered IV (dilute in 2mL normal saline and give slowly over 2min). Anaphylaxis has been reported, but it is extremely rare.

Age	Dose
<6 months	62.5mcg
6–24 months	125mcg
>2 years	250mcg

Sample: serum cortisol is measured at 0, 30, and 60min. If primary adrenal insufficiency is suspected, ACTH should also be measured at the start of the test.

- A normal response is a cortisol level of >550nmol/L.

Management (Box 32.14)

Adrenal (Addisonian) crisis demands immediate treatment and should not be delayed for diagnostic purposes. Characteristics of adrenal crisis are:

- Nausea, vomiting and abdominal pain
- Decreasing level of consciousness
- Hypotension and shock.

Box 32.14 Management of adrenal crisis

- Stabilize airway if necessary (i.e. comatose patient). Mechanical ventilation if necessary
- Restore the IV volume with IV saline boluses in 20mL/kg aliquots
- If hypotension and shock persist despite IV fluids, catecholamines (e.g. epinephrine infusion) should be started
- Check blood glucose. Give 5mL/kg glucose 10% if hypoglycaemic. Appropriate maintenance fluid would be 0.9% saline and 5% glucose combined. Glucose should be checked regularly and the glucose concentration of fluid ↑ (10% glucose with saline) if necessary. Central venous access may be necessary for higher glucose concentrations
- Give hydrocortisone as a slow IV injection; neonate 10mg then 100mg/m^2/day; child 1 month–12 years 2–4 mg/kg every 6h; child >12 years 100mg every 6h

Box 32.14 Management of adrenal crisis (*Continued*)

- Correct electrolyte disturbances. Hyperkalaemia may improve with the initial resuscitation as any acidosis is corrected. Sufficient IV sodium should be given to normalize the plasma level at the appropriate speed. Hypertonic saline (3%) may be needed in the floppy severely hyponatraemic patient (see 📖 p.238). Urine sodium concentration will provide an indication of the concentration needed in the intravascular fluid to maintain plasma sodium
- Perform short Synacthen test (Box 32.13) once the child is stable (stop hydrocortisone 12 h beforehand). Steroid cover can be provided with dexamethasone (which does not affect the cortisol assay) if needed
- Restart hydrocortisone replacement once the Synacthen test is completed
- As shock improves and patient's stress levels decreases, the hydrocortisone may be tapered towards normal maintenance doses of 15–20mg/m^2/day orally
- Adrenal crisis can be precipitated by an underlying stress. Infection should be actively investigated and antibiotics administered if indicated.

Patients with adrenal insufficiency presenting with intercurrent illness should have their hydrocortisone dose doubled. Following major surgery or serious illness the dose should be increased by 3–4-fold. IV glucocorticoid administration may need to be considered.

Patients persistently losing salt may benefit from fludrocortisone (150mcg/m^2 in a single a.m. dose). Sodium chloride supplements (2–8mmol/kg/day) will be needed (depending on plasma electrolytes and renin levels) for at least the first year of life.

Box 32.15 Adrenal insufficiency and sepsis

Children with septic shock may have adrenal insufficiency. The data from clinical trials has not produced clear evidence of benefit for steroid replacement therapy in sepsis. A 'common sense strategy' would be the sensible approach:

- If time allows perform baseline cortisol levels and a short Synacthen test (see Box 32.13). If the baseline is <550nmol/L then consider a short course of hydrocortisone (2.5–5mg/kg/day 6-hourly IV)
- In cases of shock unresponsive to fluid or inotropes give low-dose hydrocortisone (as in Box 32.14).

Phaeochromocytoma

- Neuroectodermal tumour of chromafin cells usually located within the adrenal medulla and sympathetic ganglia
- They secrete epinephrine and norepinephrine. Norepinephrine secretion is greater in childhood. If epinephrine predominates then tachyarrhythmias are more likely
- Children present with sustained rather than with paroxysmal crisis
- Classic symptoms are hypertension, headache, sweating, nausea, vomiting, disturbed vision, and weight loss. Haematocrit may be elevated. Hypertensive crises, hypertensive encephalopathy or cardiac failure may occur.

Diagnosis

- Raised plasma and urine catecholamines; Plasma metanephrine is a more sensitive test
- Catecholamine metabolites can be found in the urine: vanillymandelic acid (VMA)
- Imaging studies directed to identify the site of the tumour will follow.

Treatment

Antihypertensive treatment in preparation for surgical excision of the tumour, is crucial in the management of these patients.

- α_1-adrenergic blockade with phenoxybenzamine is the treatment of choice. The starting dose is 5 or 10mg twice daily depending on the age of the child. This dose is increase slowly 2–3 times per week until normotension is achieved
- If the tumour is known to release adrenaline or the patient shows tachydysrhthmias, β-adrenergic blockade should be considered once adequate α_1-adrenergic blockade has been achieved . Urgent treatment options include propanolol (0.01–0.1mg/kg) via a slow IV injection or esmolol (25–100mcg/kg/min) as a IV infusion, if careful titration is required. ECG and BP should be monitored throughout. Once control is achieved the patient can be changed to oral propanolol
- In the event of severe hypertensive crisis sodium nitroprusside (0.5–10mcg/kg/min) is very effective. It has a rapid onset and achieves rapid control. Thiocynate and cyanide levels should be monitored, especially if it is used for >24h or at a rate >4mcg/kg/min
- In severe chronic hypertension beware of reducing BP too rapidly. Allow several days for cerebral circulatory autoregulation to adapt to the lowering BP.

Thyroid disorders

Thyrotoxicosis

- Thyrotoxicosis is unusual in PICU patients
- Thyroid storm (Box 32.16) is a rare disorder that presents with extreme thyroid symptomatology including high fever, tachycardia, and neurological changes. It can be easily confused with sepsis, malignant hyperthermia, anticholinergic poisoning, transfusion reaction, and adrenal crisis. Thyroid storm may be precipitated by stress such as intercurrent infection, surgery or trauma.

Diagnosis

- Thyroid function tests; namely raised free T_4, free T_3 and low TSH (thyroid stimulating hormone)
- Defining individual diseases will depend on the type of antibody identified and the results of the technetium isotope scan.

Treatment

Hyperthyroidism should be managed by a paediatric endocrinologist.

There are currently 2 strategies:

- Block and replace: carbimazole (blocking agent) and thyroxine
- Dose titration: carbimazole is titrated until patient is euthyroid
- Dose titration with propylthiouracil if carbimazole is not tolerated.

Box 32.16 Thyroid storm

Attention to ***ABCs***

- Oxygen. These patients have ↑oxygen consumption
- Secure airway and sedate, paralyse, and ventilate if indicated, e.g. severe shock or those that require active cooling
- Hypovolaemia should be rapidly treated with IV boluses of 0.9% saline (20mL/kg) until resolved. Hartmann's or gelofusine (10mL/kg) are excellent alternatives and have the advantage of buffering capacity
- β-blocking agents are used to control the sympathetic overdrive. Propanolol (0.01mg/kg/dose) is given slowly every 10min until symptoms are under control (recommended maximum 5mg). Monitor ECG. Once control is achieved, the patient can be treated with oral propanolol at a dose of 0.25–0.5mg/kg 3 or 4 times daily (monitor glucose)
- Fever should be reduced with active cooling (when sedated, paralysed and ventilated) and antipyretics. Salicylates should be avoided as they displace the thyroid hormones from protein-binding sites
- Antithyroid treatment with propylthiouracil (200–300mg/kg 6-hourly) may be used
- Dexamethasone 1–2mg 6-hourly
- In neonates use propylthiouracil 0.5–1.5mg/kg/day single daily dose and prednisolone 2mg/kg/day.

Hypothyroidism

- Hypothyroidism is commonly a coexisting problem rather than a primary cause for admission to PICU
- Congenital hypothyroidism may occasionally be missed in neonatal screening as the assay only measures TSH
- Hypothyroidism can occur with:
  - Iodine deficiency (commonest cause worldwide)
  - Amiodarone therapy
  - Secondary to intracranial tumours, post surgery, or radiotherapy
  - Post irradiation (bone marrow transplant).

The sick euthyroid syndrome

- This is a thyroid hormone disorder characterized by normal thyroid function (normal thyroid stimulating hormone response to TRH stimulation) and low circulating T_3 and T_4 levels
- It is often seen with stress and associated with many conditions seen on PICU, e.g. trauma, sepsis, cardiac surgery, malignancy
- Currently there is no evidence that patients with sick euthyroid (low T_3) benefit from thyroid replacement therapy.

Further reading

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Chapter 33

Metabolic disorders

Introduction

The clinical presentation of metabolic disorders varies widely and establishing the clinical diagnosis can be complex and challenging. However, early recognition and treatment of metabolic disease presenting as critical illness can prevent death and neurological consequences (Table 33.1). In this chapter a systematic clinical and diagnostic approach is given, guiding the paediatric intensivist in the initial stabilization, diagnostic workup, and further treatment of a patient with suspected metabolic disease. Team work and early liaison with the local metabolic disease service are of great importance in the successful management of these conditions.

Table 33.1 Examples of metabolic disorders that may require intensive care

Disorder	Presentation	Investigations
Organic acidaemias		
Proprionic acidaemia Methylmalonic acidaemia Isovalaeric acidaemia	Encephalopathy	Hyperammonaemia Metabolic acidosis Urine organic acids
Aminoacidopathies		
Maple syrup urine disease	Encephalopathy	Ketosis (sig. metabolic acidosis rare) Plasma and urine amino acids
Tyrosinaemia	Liver/renal disease	↑ transaminases, jaundice Renal tubular disease Plasma and urine amino acids
Urea cycle disorders		
CPS deficiency OCT deficiency AS deficiency AL deficiency	Encephalopathy	Hyperammonaemia Urine organic acids Urine orotic acids Plasma and urine amino acids
Disorders of glucose and galactose metabolism		
Glycogen storage disease Type 1	Failure to thrive Hepatomegaly	Hypoglycaemia Lactic acidosis Enzyme analysis (liver)
Fructose 1,6-biphosphate deficiency	Encephalopathy	Hypoglycaemia Lactic acidosis Urine organic acids Enzyme analysis (liver)

Table 33.1 Examples of metabolic disorders that may require intensive care (*continued*)

Disorder	Presentation	Investigations
Disorders of mitochondrial energy metabolism		
Pyruvate dehydrogenase deficiency	Neurological disease Dysmorphism in some	Lactic acidosis Enzyme analysis (fibroblast) Urine organic acids
Pyruvate carboxylase deficiency	Neurological disease	Hyperammonaemia Lactic acidosis Enzyme analysis (fibroblast)
Disorders of fat oxidation		
MCAD; VLCAD; LCHAD Carnitine transport defect	Encephalopathy Liver disease Cardiomyopathy (except MCAD)	Hypoketotic hypoglycaemia ↑transaminases ↓plasma carnitine; urine organic acids; acylcarnitines DNA analysis Assays on skin fibroblasts

CPS, carbamoyl phosphate synthase; OCT, ornithine carbamoyltransferase; AS, argininosuccinate; AL, argininosuccinate lyase; MCAD, medium chain acyl-CoA dehydrogenase; VLCAD, very long chain acyl-CoA; LCHAD, long chain hydroxy acyl-CoA dehydrogenase.

Acute metabolic encephalopathy

Organic acidaemias, certain amino acid disorders and urea cycle and fatty acid oxidation defects may present as an acute life-threatening encephalopathy. Presentation is usually in infancy but may occur in an older child and occasionally even in adulthood.

Invariably infants are normal at birth, due to the protection of the placenta, washing out toxic metabolites. Over subsequent days to weeks symptoms develop due to accumulation of toxic metabolites and their effects on the CNS.

History, symptoms, and signs

- Family history of sudden death in infancy
- History of previous early fetal loss or history of HELLP syndrome (Haemolytic anaemia, Elevated Liver enzymes, Low Platelets) or acute fatty liver of pregnancy in the mother:
  - Most metabolic disorders have autosomal recessive inheritance and sudden infant deaths may occur in consanguineous families
  - Ornithine transcarbamylase deficiency and certain other disorders have X-linked inheritance and may be associated with history of unexpected death in male infants
- Symptom-free period lasting hours to months
- Symptoms triggered by illness, immunization or change in diet
- Lethargy and poor feeding, vomiting
- Drowsiness progressing to coma—may be accompanied by seizures or hypotonia. Symptoms may progress rapidly
- Central apnoea or tachypnoea and respiratory distress
- Respiratory alkalosis is frequently seen in urea cycle disorders as ammonia is a very potent central respiratory stimulant
- Unusual odours: sweaty feet smell of isovaleric acidaemia or classical maple syrup urine disease
- Disproportionate severity of illness—patient seems to be more severely affected than expected.

Differential diagnosis and causes see Boxes 33.1 and 33.2

Box 33.1 Differential diagnosis of acute encephalopathy

- 1. Sepsis
- 2. Acquired brain injury (infective, vascular, traumatic)
- 3. Poisoning
- 4. Drug withdrawal
- 5. Endocrine disorders: e.g. adrenal insufficiency.

Box 33.2 Causes of acute metabolic encephalopathy

With normal ammonia

With metabolic acidosis and ↑anion gap

- Normal or elevated lactate and ↑urinary organic acids:
  - Organic acidaemias or
  - Fatty acid oxidation defects (carboxylic aciduria present)
- Normal lactate and abnormal plasma amino acids:
  - Maple syrup urine disease
- ↑lactate, normal urinary organic acids, and normal glucose:
  - Respiratory chain defects
  - Pyruvate carboxylase deficiency
  - Pyruvate dehydrogenase deficiency
- ↑lactate, normal urinary organic acids and hypoglycaemia:
  - Glycogen storage disease type I
  - Fructose-1,6-diphosphatase deficiency
  - PEP carboxykinase deficiency.

No acidosis, abnormal plasma amino acids

- Non-ketotic hyperglycinaemia
- Maple syrup urine disease.

No acidosis, normal amino and organic acids

- Molybdenum cofactor deficiency
- Fatty acid oxidation defects.

With high ammonia

Symptoms in first 24h:

- Transient hyperammonaemia of the newborn (THAN)
- Organic acidaemia.

Symptoms after 24h with metabolic acidosis:

- Organic acidaemias:
  - Methylmalonic acidaemia
  - Proprionic acidaemia
  - Isovaleric acidaemia.

Symptoms after 24h without metabolic acidosis:

- Urea cycle defects:
  - Carbamyl phophate synthethase (CPS) deficiency
  - Ornithine transcarbamylase (OTC) deficiency
  - Argininosuccinic acidaemia
  - Citrullinaemia.

Acute metabolic encephalopathy: investigations

Laboratory

- FBC with differential
- Coagulation profile: PT, APTT, fibrinogen
- Urinalysis
- Blood gas and anion gap
- Serum electrolytes: Na, K, Ca, phosphate, Mg, urea, creatinine
- Blood glucose, plasma ammonia, and lactate
- Plasma carnitine and acylcarnitine profile
- Liver function tests
- Urine reducing substances
- Urine ketones if acidosis or hypoglycemia present
- Plasma and urine amino acids, quantitative
- Urine organic acids.

Other investigations

- Brain imaging for cerebral oedema and haemorrhage
- CT or MRI; US less reliable
- EEG: slow wave suppression and burst suppression frequently seen.

Plasma ammonia should be checked in any child, regardless of age, with unexplained CNS disease (coma, seizures, cerebral oedema).

Ammonia in the newborn

- Samples for ammonia measurement should be free-flowing, sent on ice and processed immediately: a 'difficult' sample or delay in reaching the laboratory will result in an inappropriately elevated level
- Normal value for plasma ammonia is 65μmol/L. Values up to180μmol/L may be seen during any acute illness (Box 33.3)
- Values >200μmol/L require urgent investigation to rule out metabolic disorder
- All ammonia levels >200μmol/L should be immediately repeated to confirm the trend and rate of increase. This will also unmask sampling or analysis errors
- Values >500μmol/L require urgent treatment and may need haemofiltration or dialysis if no response to medical therapy (see 📖 p.266)

Box 33.3 Differential diagnosis of raised ammonia in the newborn

- Sepsis or any other severe illness
- Birth asphyxia
- Parenteral nutrition
- Herpes simplex infection
- THAN.

Acute metabolic encephalopathy: management (Box 33.4)

Removal of toxic metabolites

The level of hyperammonaemia and duration of exposure determine neurological outcome. If organic acidaemia or urea cycle defect is suspected immediate treatment should be started in close collaboration with metabolic specialist.

- Monitor blood gases, electrolytes, and ammonia levels frequently
- Intubate and ventilate early if significant encephalopathy, respiratory failure, or need for renal replacement therapy
- Treat suspected urea cycle defect and high ammonia (see Box 33.4)
- In suspected organic acidaemia consider carnitine supplementation as this promotes excretion of organic acids.
- Note: this is not safe to use when a fatty acid oxidation defect is suspected—may induce arrhythmias.
- In critically ill infants with ammonia >500μmol/L, or rising ammonia despite drug treatment or display symptomatic cerebral oedema urgent removal of ammonia is required by:
  - High-flux continuous veno-venous haemofiltration (CVVH), targeting >100mL/kg/h ultrafiltration rates, or
  - If this does not control ammonia start continuous veno-venous haemodiafiltration (CVVHDF))
  - if cardiovascularly stable with good venous access consider continuous veno-venous haemodialysis (CVVHD) or acute haemodialysis
  - PD or exchange transfusion does not achieve adequate clearance rates of toxic metabolites or ammonia.

Removal of precipitating nutrients, prevention of catabolism, and general support

- Discontinue milk feeds
- Provide high-energy IV intake using glucose (rate >6 mg/kg body weight/min)
- Hyperglycaemia (blood glucose >12 mmol/L) should be treated with low dose insulin (0.05U/kg body weight/h) under close monitoring. This may also promote anabolism
- Correct acidosis aggressively with IV bicarbonate infusion and correct electrolyte abnormalities.
  - Potassium bicarbonate or potassium acetate may be used in cases of persistent metabolic acidosis and hypokalaemia
- Haemodynamic support with fluids and inotropes as necessary. These patients can be extremely unstable
- Provide sedation and analgesia if suspected cerebral oedema. Consider muscle relaxants but beware undetected seizure activity
- After improvement within 48–72h, consider re-introducing protein intake at 0.5g/kg body weight/day and increase gradually to 1g/kg body weight/day. Input from metabolic specialist and dietician is required.

Box 33.4 Drug treatment of hyperammonaemia

- Loading doses (intravenously over 90min):
  - Arginine hydrochloride 250mg/kg
  - Sodium benzoate 250mg/kg
  - Sodium phenylbutyrate 500mg/kg
- Continuous infusions (to follow and run over 24h):
  - Arginine hydrochloride 250mg/kg
  - Sodium benzoate 250mg/kg
  - Sodium phenylbutyrate 250mg/kg.

These drugs promote nitrogen excretion through conjugation to glycine and glutamate. The infusions should be continued until final diagnosis is made and are compatible to be run together on a single infusion line. They are not compatible with sodium bicarbonate. They contain sufficient sodium to meet daily requirements but can cause severe hypokalaemia—early supplementation and frequent monitoring is needed.

Metabolic acidosis

(See also 🕮 p.247.)

In children where metabolic acidosis is unexplained, particularly severe, or persistent, or where there is a large anion gap, the possibility of an inborn error of metabolism should be considered.

Metabolic acidosis occurs commonly in:
- Cardiac disease (particularly low output states)
- Tissue hypoxia
- Poor tissue perfusion from any cause, such as septic shock
- Inborn errors of metabolism (🕮 see Table 33.1, p.694)
  - Defects of pyruvate metabolism and functional defects of the mitochondrial electron transport chain
  - Organic acidaemias
  - Defects of glucose and galatose metabolism.

Investigations
- Blood:
  - Glucose
  - Lactate
  - Ammonia
  - Aminoacids
- Urine:
  - Ketones
  - Aminoacids
  - Organic acids.

Hyperlactataemia

(See also 📖 p.90)

Suspect a metabolic disorder if a child has a high blood lactate in the setting of a normal cardiac output—with good volume pulses, warm peripheries, normal BP.

Many inborn errors of metabolism are associated with increases in measured serum lactate (Table 33.2) but as this is a very non-specific finding it should not be used as an only marker for these disorders. Many raised lactates are due to difficulty in trying to obtain the sample from children, or venostasis due to the use of a tourniquet.

Table 33.2 Major causes and some individual examples of hyperlactataemia. This is not a complete list

Inborn errors of metabolism	Other causes
Disorders of carbohydrate metabolism • Glycogen storage disorders—type 1 • Fructose metabolism disorders • Hereditary fructose intolerance • Fructose 1,6 bisphosphatase deficiency	*Tissue hypoxia* • Asphyxia, ischaemia, shock • Exercise • Seizures
Disorders of mitochondrial energy metabolism • Disorders of pyruvate metabolism: pyruvate carboxylase deficiency, pyruvate dehydrogenase complex deficiency • Disorders of respiratory chain enzymes: MELAS, MERRF, NARP, SURF, POLG • Disorders of mitochondrial fatty acid metabolism: LCHAD,VLCAD • Disorders of ketogenesis and ketolysis: • 3-hydroxy-3-methylglutaryl-CoA Lyase deficiency	*Drugs:* • Aspirin • Cocaine • Dinitrophenol • Metformin • Nitroprusside • Valproate in overdose • Catecholamines • Salbutamol • Theophylline
Disorders of amino acid metabolism • Branched-chain organic acidurias: • Maple syrup urine disease, propionic aciduria, isovaleric aciduria, methyl malonic aciduria	*Sepsis* • Multi organ failure • Hyperventilation
Vitamin responsive disorders • Holocarboxylase synthetase deficiency • Biotinidase deficiency	Sampling error

Congenital lactic acidaemias

- Pyruvate carboxylase deficiency
- Pyruvate dehydrogenase deficiency
- Glycolytic and mitochondrial respiratory chain disorders.

These conditions are characterized by failure of mitochondrial ATP production, which is an essential energy substrate for efficient functioning of

cellular metabolic pathways. These disorders can affect either glycolysis or mitochondrial oxidative phosphorylation (respiratory chain defects). In the latter conditions ATP production is severely impaired. Presenting symptoms can range widely depending on organ involvement including muscle weakness, encephalopathy, stroke and liver failure.

Hypoglycaemia

(See also 🕮 p.681.)

Most infants and children who present with hypoglycaemia do not have metabolic disease. Other causes such as low calorie intake, exposure, sepsis, adrenal failure, or hypopituitarism should be excluded.

Clinical features of metabolic conditions associated with hypoglycaemia

- Failure to thrive
- Lactic acidosis: differentiate from hypoxia, low cardiac output state, and drugs
- Encephalopathy, stroke: congenital lactic acidosis
- Muscle weakness: congenital lactic acidosis
- Cardiomyopathy, cardiac failure, conduction defects, circulatory collapse:
  - Fatty acid oxidation defects
  - Mitochondrial disorders
- Sudden infant death
- Dysmorphic features; high forehead, large bulbous nose with short columella, smooth philtrum, and thin upper lip in hyperinsulinism.

Metabolic causes of hypoglycaemia

- Hyperinsulinism and hypopituitarism—see 🕮 p.681
- Glycogen storage disease type I:
  - Inability of the liver to release glucose from glycogen, resulting in hypoglycaemia during fasting, lactic acidosis, hepatomegaly, and failure to thrive.
  - Neutropenia also occurs in glycogen storage disease type Ib & 1c
- Disorders of gluconeogenesis : fructose 1,6-biphosphatase deficiency
- Fatty acid oxidation (FAO) disorders:
  - Infants with FAO are unable to use stored fat and quickly deplete glycogen stores during fasting
  - Children with FAO are unable to synthesize ketones and typically present with non-ketotic hypoglycaemia. This can be associated with signs of liver dysfunction (Reye-like syndrome) with metabolic acidosis, raised ammonia, and transaminases
- MCADD (medium chain acyl Co-A dehydrogenase deficiency) is the most common FAO disorder. This can present as an acute life-threatening event or sudden infant death. There may be a family history of sudden infant death.
- MCADD is associated with the presence of the acylcarnitine octanoyl carnitine (C8) in plasma: this test is now part of the neonatal screening programme in the UK and other countries

- Encephalopathy precedes hypoglycaemia in younger children and may be the only presenting feature in adolescents
- Any sign of encephalopathy/irritability should be treated aggressively.
- VLCADD (very long chain acyl Co-A dehyrogenase deficiency): in addition to a presentation with hypoglycaemia or Reye-like syndrome, VLCADD can be associated with dilated or hypertrophic cardiomyopathy
- Any child who dies unexpectedly with evidence of fat accumulation in the liver or muscle, should be suspected to have a FAO disorder.

Any child presenting with cardiomyopathy or conduction defects with associated arrhythmia should be investigated for FAO disorders.

Investigations (Table 33.3)

- Paired plasma and cerebrospinal fluid glucose and lactate
- Pre- and post-prandial free fatty acids and 3-hydroxybutyrate levels
- Plasma carnitine and acylcarnitines
- Urinary organic acids
- Insulin and C-peptide levels taken when blood glucose <2.5mmol/L
- Mutational analysis is available for many of the glycogen storage disorders with liver biopsy seldom needed to exclude these disorders
- Plasma for carbohydrate metabolism enzyme essay
- Muscle biopsy for respiratory chain enzymes
- MRI brain to assess for typical changes associated with Leigh's encephalopathy (progressive encephalopathy due to cerebral mitochondrial cytopathy)
- ^{31}P MRI spectroscopy: detects defects of oxidative phosphorylation

Table 33.3 Emergency investigations for hypoglycaemia

Sample	Investigation
1mL (in fluoride bottle)	Glucose, lactate
2mL (in heparin bottle) separated and frozen immediately	Free fatty acids, 3-hydroxybutyrate, carnitine
3mL (in heparin bottle) separated and frozen immediately	Insulin, C-peptide, cortisol, growth hormone
1mL EDTA	DNA analysis
First urine after hypoglycaemia (freeze if delay in transfer to lab)	Organic acids

Treatment of hypoglycaemia related to inherited metabolic disorders (IMD)

- Ensure adequate glucose intake: calculate required intake to maintain normoglycaemia
- Glycogen storage disease:
  - Avoid fasting
  - Provide frequent carbohydrate intake using corn starch and overnight feeds

- Fatty acid oxidation defects:
  - Avoid fasting
  - Provide frequent carbohydrate intake with corn starch
  - Restriction of dietary fat intake
  - ⚠ Carnitine supplementation—only in consultation with metabolic specialist. In some disorders may precipitate fatal arrhythmias
- Congenital lactic acidaemias:
  - Correct acidosis
  - Low carbohydrate, high fat diet
  - Minimize exposure to precipitating factors such as fasting, exposure to cold, sedatives, anaesthesia and infections
  - No specific treatment available—dichloroacetate may lower lactate concentration but there is no evidence that it alters outcome.

Metabolic disease presenting as acute liver failure (ALF)

This group of conditions presents with the following symptoms: jaundice, ascites, oedema, bleeding tendency, hepatic encephalopathy (see 📖 p.632).

Laboratory test findings in acute liver failure (see Box 33.5):
- Hypoglycaemia
- Prolonged prothrombin time
- Raised transaminases
- High bilirubin
- Lactic acidaemia
- Elevated methionine levels.

Practice point: seek urgent specialist advice from a metabolic expert and hepatologist in any child presenting with acute liver failure.

Metabolic causes of ALF in the newborn period or infancy

- Tyrosinaemia type I: disorder of amino acid metabolism characterized by high plasma methionine and tyrosine levels and generalized aminoaciduria with disproportionately high urinary tyrosine
- Galactososaemia:
  - Presents with liver failure, vomiting, and poor feeding
  - Affected infants may have cataracts
- Infantile haemochromatosis: characterized by hepatic and extra-hepatic parenchymal iron deposition. It is a cause of FHF in newborn infants
- Hereditary fructose intolerance: onset after introduction of fructose or sucrose in diet
- Mitochondrial disease.

Metabolic causes of ALF in the child >2 years of age

- Wilson's disease:
  - Abnormality of copper metabolism
  - Rare before 3 years of age

  - Older children may have Kayser–Fleischer rings of cornea or sun flower cataracts
  - Associated with renal tubular acidosis, cardiomyopathy, cardiac arrhythmias, haemolyis, and neuropsychiatric symptoms such as mood swings, dementia, psychosis and dyskinesia.
- Tyrosinaemia type I (as for the newborn period/infancy)
- Fatty acid oxidation disorders with Reye-like syndrome.

Investigations

- Plasma and urinary aminoacids: elevated tyrosine and methionine in tyrosinaemia
- Urinary succinylacetone: diagnostic for tyrosinaemia (elevated)
- Urinary reducing substances: positive in galactosaemia
- Red blood cell galactose-1-phosphate uridyl transferase assay:
  - Deficiency diagnostic of galactosaemia
  - Common mutations are present in some populations and may be preferred method of confirmation
- Plasma ferritin: very high levels in neonatal haemochromatosis
- Liver biopsy for fructose 1,6- phosphate aldolase and copper:
  - Elevated in Wilson's disease
  - Confirmation of Wilson's disease by mutational analysis
- Serum caeruloplasmin and copper levels: low in Wilson's disease
- Urinary copper: raised in Wilson's disease

Management

For detailed management advice for acute liver failure see 🕮 p.633.

General measures

- Eliminate galactose, fructose, and protein from diet until diagnosis is confirmed
- Maintain adequate energy intake with IV glucose
- Monitor progression of acute liver failure and consider liver transplant assessment if poor prognostic indicators present. Seek specialist advice.

Specific treatment

- Lactose-free diet in galactosaemia (soy-based formula can be used)
- Sucrose-free diet in congenital fructose intolerance
- Tyrosinaemia:
  - Treatment with nitisinone (NTBC) rapidly stabilizes the condition
  - Coagulopathy improves within hours of first dosage
  - Liver transplantation may be required at later stage
- Wilson's disease:
  - Chelating agents such as penicillamine are used to remove tissue copper but can precipitate acute neurological disease
  - Trientene is not associated with this phenomena but does not work well in the presence of liver failure
  - Low copper diet and vitamin B6 supplements
  - Zinc acetate reduces intestinal copper absorption.

Box 33.5 Poor prognostic indicators in acute liver failure

- Prothrombin time >60s
- Bilirubin >300micromol/L
- Severe metabolic acidosis
- Hypoglycaemia
- Acute renal failure with serum creatinine > 300micromol/L
- Moderate to severe encephalopathy

Decompensation of the child with IMD

Children with known metabolic disorders should have an emergency management plan. It is important to enquire if such a plan is available. If this is not available some general rules may help once the child has been made safe.

- Manage airway, breathing, circulation, and neurological disability according to standard guidelines
- Treat sepsis or cause of decompensation according to standard paediatric guidelines
- Promote anabolism by giving IV 10% glucose with added electrolytes as required. ⚠ Except in mitochondrial disease where extra glucose will be converted to lactate, making acidosis worse
- Check for and treat hyperammonaemia, hypoglycaemia, and acid–base disturbance
- Provide alternative pathway therapies, usually as drug treatment. Previous history of management will be important to plan interventions. Discuss early with the department usually caring for the child
- Many of the disorders will need reintroduction of a specialized diet usually within 48h as prolonged delay may cause catabolism of body protein and fat.

Investigation of the dying child with suspected IMD

Metabolic disorders are a relatively rare cause of sudden, unexpected death in infancy. However, an appropriate diagnostic workup is vital to establish the cause of death and for genetic counselling of the family. Conditions prone to present as sudden unexpected death in infancy are fatty acid oxidation disorders and glycogen storage disorder type I.

Practice points

- Involve a metabolic specialist at the earliest opportunity to guide the investigation.
- Have a pre-made kit available in the PICU, for collection of appropriate samples out-of-hours.

Collect the following samples during life

- Heparinized blood: separate in the laboratory and store at −20°C
- Blood spots on filter paper for acylcarnitines
- Blood for DNA analysis in EDTA bottle—store at −20°C
- Urine: in plain tube, store at −20°C. If urine is not available CSF can be collected and stored at −20°C
- Skin biopsy:
  - Collect full thickness biopsy of 2 × 2mm under aseptic technique to avoid bacterial contamination.
  - Store at 4–8°C in tissue culture medium or sterile saline
  - Transport to metabolic laboratory at earliest opportunity
- Liver biopsy: fine needle biopsy stored in cryotube and snap frozen in liquid nitrogen or dry ice. If this is not available store in sterile container at −20°C.
- Muscle biopsy may be indicated in specific cases. Store in cryotube and snap freeze at −70°C or in plain container stored at −20°C. Discuss with metabolic specialist.

Note: skin, liver and muscle biopsies may be taken post-mortem with appropriate consent from the family. This should be done as soon as possible after death and ideally within 12h, to avoid bacterial contamination and deterioration of the samples.

Postmortem examination

After unexplained death of a child when a metabolic disorder is suspected, the family should be offered the opportunity of a full postmortem examination and appropriate local consent procedures for this should be followed. The benefits of making every effort to establish a definitive diagnosis should be explained in terms of genetic counselling and possible antenatal diagnosis in future pregnancies. If the family declines the offer of a full postmortem examination, permission should be sought for postmortem skin and liver biopsies.

Further information and reading

British Inherited Metabolic Disease Group: www.bimdg.org.uk/guidelines.asp

Burton BK (1998). Inborn errors of metabolism in infancy: a guide to diagnosis. *Pediatrics* **102;** e69.

Fernandes J, Saudubray J-M, van den Berghe G, *et al.* (2006). *Inborn Metabolic Disorders – Diagnosis and treatment*, 4th edn. Springer.

Leonard JV, Morris AM (2006). Diagnosis and early management of inborn errors of metabolism presenting around the time of birth. *Acta Pædiatrica* **95:** 6–14.

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Chapter 34

Haematology

Anaemia

Reduced Hb concentration; normal Hb concentration varies with age dependent on RBC production, and change from HbF to HbA. Normal erythropoiesis is dependent on adequate intake of iron, folate and vitamin B_{12}, erythropoietin production and stem cell function.

Change in haemoglobin concentration with age

Age	*Hb (g/dL)*
• Newborn	13.5–19.5
• 3 months	9.5–13.5
• 1 year	10.5–13.5
• 5 years	11.5–13.5
• 10 years	11.5–15.5
• 15+ years: ♀	12–16
• 15+ years: ♂	13–16

Causes

Blood loss
- Sampling
- GI haemorrhage
- Surgery
- Trauma.

Impaired RBC production
- Marrow failure, e.g. shock, chemotherapy, nutritional deficiency, poisoning
- Erythropoietin deficiency, e.g. renal failure
- Disorders of Hb synthesis, e.g. sickle cell disease, thalassaemia.

Abnormal RBC maturation
- Infection, e.g. parvovirus B19.

↑ RBC destruction
- Mechanical, e.g. cardiopulmonary bypass, HUS, DIC
- Immune-mediated, e.g. ABO, Rh, autoimmune
- Toxins, e.g. drugs (penicillin, quinidine), snake venoms
- Membrane defects, e.g. hereditary spherocytosis
- Metabolic defects, e.g. glucose-6-phosphate deficiency.

In critically ill children, a number of these causes may overlap as part of the anaemia of acute inflammation, e.g. in severe infection due to *Streptococcus penumoniae*: ↑sampling, bone marrow failure, and haemolysis.

Investigation

Initial FBC, including MCV, and blood film for cell morphology, e.g. spherocytes, red cell fragmentation.

Further investigations

- Check for signs of bleeding e.g. wounds, haematuria, occult faecal loss
- Reticulocyte count: ↓ suggests impaired RBC production; ↑ suggests ↑RBC destruction
- Ferritin: indication of iron stores if MCV↓ but note ↑ in acute inflammation may be misleading
- Serum B12 and red cell folate levels if MCV↑
- Bilirubin and serum LDH: ↑ suggests ↑RBC destruction
- Haptoglobins: absence suggests ↑RBC destruction
- Direct antiglobulin test (DAGT); previously known as direct Coombs test: sensitive to red cell bound antibody, e.g. ABO, Rh as cause of increased RBC destruction
- Investigation of DIC (see 📖 p.716).

Management

1. Treat underlying cause where possible

2. Blood transfusion:

Ideal Hb level for optimal oxygen carriage and blood viscosity controversial. Usual target 10–12g/dL. (For packed cell transfusion volumes see 📖 p.719.)

Consider packed cell transfusion:

- If Hb <7g/dL
- If Hb <10g/dL in pre-term neonate or 1st week of life
- If Hb <10 g/dL in child with uncorrected cyanotic congenital heart disease
- Higher transfusion thresholds may be needed in children with cardiothoracic disease, or those requiring significant cardiopulmonary support.

Also see 📖 p.719.

Sickle cell disease

A chronic, hereditary disease most common in the populations of Central and West Africa and their descendants in North America and the Caribbean. It is the most common haemoglobinopathy and its inheritance is autosomal recessive. Due to a single amino acid substitution on the β chain of haemoglobin, HbS replaces HbA in the red cell. When exposed to hypoxia, cold, or dehydration these cells become rigid, sickle, and assume other bizarre shapes. Sickling results in erythrostasis, occlusion of blood vessels, thrombosis, and tissue infarction, particularly of the bones, lung, brain, and spleen.

Infection

Children with sickle cell disease are functionally asplenic, so are at particular risk from encapsulated organisms e.g. *Haemophilus influenze* type B, *Streptococcus pneumoniae, Salmonella*. Immunizations must be kept up to date. Infections can occur suddenly and are the leading cause of death, so any febrile illness is a medical emergency.

Sickle cell crises

Management must include:

- Appropriate resuscitation with high-flow oxygen, e.g. 15L/min with reservoir
- IV rehydration fluids
- Broad-spectrum antibiotics, e.g. cefotaxime 50mg/kg 6-hourly
- Adequate analgesia, including use of opiate infusions, e.g. morphine

Acute chest syndrome

Presenting signs of cough, pleuritic chest pain, and tachypnoea. CXR shows pulmonary infiltrates and pleural effusion. Secondary chest infection or ARDS may supervene. Treatment as outlined earlier, plus partial exchange transfusion if severe hypoxaemia, e.g. PaO_2 <10kPa (75mmHg) despite FiO_2 >0.6, with or without ventilatory support. Add macrolide to antibiotic cover. Bronchodilators may also be useful in some cases.

Thrombotic stroke

Usually due to occlusion of large vessel e.g. middle cerebral or internal carotid artery. Sudden onset with seizures and hemiparesis without preceding headache. Partial occlusion often causes silent watershed infarcts. Intubate, ventilate, and perform CT scan to rule out treatable lesions, e.g. subdural haematoma. Load with anticonvulsants, e.g. phenytoin 18mg/kg. Consider ICP monitoring. Early partial exchange transfusion essential and may need to be repeated. Anticoagulation should be avoided.

Acute splenic sequestration

Uncommon but fatal in up to 35% of cases. Usually occurs between 10–30 months and virtually never after 5 years of age. Acute drop in Hb (>4g/dL) associated with shock and splenomegaly. Urgent treatment of hypovolaemia needed with repeated 20mL/kg fluid boluses plus early packed cell transfusion.

Partial exchange transfusion

Required to reduce HbS level. Diminishes risk of sickling and increases oxygen-carrying capacity without volume overload. Requires use of large bore access × 2. Indications include:

- Severe infection
- Acute chest syndrome, particularly if ventilated
- CNS signs, particularly if suggestive of thrombotic stroke
- Acute priapism.

A 2-volume exchange (i.e. 150mL/kg) of reconstituted red cells (50% packed cells/50% FFP) performed over 4–6h should reduce HbS level to <30%. Essential to monitor fluid balance and avoid hypovolaemia.

Neutropenia

Most common form of compromised immunity in children. Generally associated with cancer and its treatment. Infection risk and severity of infection related to absolute neutrophil count. Potentially life-threatening infections usually occur when neutrophil count $<0.5 \times 10^9$/L, and risk increases dramatically when count $<0.1 \times 10^9$/L. Risk also greater when rapid drop in neutrophil count or prolonged neutropenia.

Causes

- Reduced bone marrow production
  - Leukaemia, lymphoma
  - Aplastic anaemia
  - Chemotherapy, radiotherapy
  - Severe bacterial and viral infections
- ↑ use or destruction, e.g. severe bacterial infections, hypersplenism
- Hereditary, e.g. cyclical neutropenia

Management

General

- Isolate children with neutrophil counts $<1 \times 10^9$/L in positive pressure high efficiency particulate airflow (HEPA)-filtered rooms to prevent nosocomial infections, particularly *Aspergillus* species, and strict infection control procedures
- Minimize invasive procedures
- Maintain good oral hygiene with mouthwashes
- Prophylactic cotrimoxazole, acyclovir and fluconazole to prevent PCP, HSV reactivation, and fungal infection

- Broad-spectrum aggressive antibiotic cover (e.g. piptazobactam plus an aminoglycoside), for both Gram-positive organisms e.g. staphylococci, and Gram-negative organisms e.g. *Klebsiella penumoniae*. Also early use of antifungal agents, e.g. liposomal amphotericin, caspofungin
- Granulocyte colony stimulating factor (G-CSF) given if severe infection and/or neutropenia particularly severe or protracted to stimulate bone marrow.
- White cell transfusions sometimes used if life-threatening infection.

Specific

- Pulmonary infiltrates. Ventilatory support started as necessary, often non-invasive initially. If intubated for early BAL. Add macrolide cover for atypicals e.g. *Mycoplasma*, *Legionella*. Normal CXR does not exclude diagnosis. Treatment dose co-trimoxazole and steroids if PCP isolated; if no response consider pentamidine.
- Septic shock. Often related to indwelling intravascular catheters, so add vancomycin early to cover for coagulase-negative *Staphylococcus*. If no response or concern regarding methicillin-resistant staphylococci, replace vancomycin with linezolid.

Platelet disorders

Thrombocytopenia

Platelet count $<150 \times 10^9$/L, but rarely symptomatic until $<50 \times 10^9$/L. Spontaneous bleeding is more likely to occur when the count $<20 \times 10^9$/L; often minor, e.g. skin petechiae, oozing at intravascular catheter sites, but can be potentially life-threatening, e.g. pulmonary or intracranial haemorrhage.

⚠ Platelet clumping can cause apparent thrombocytopenia. Excluded by examination of blood film.

Causes

- Sepsis; commonest cause in PICU, often related to severity of illness e.g. meningococcaemia; may provide indicator of outcome and response to treatment
- DIC (see 📖 p.716)
- ITP
- Anti-platelet antibodies:
  - Frequent platelet transfusion
  - Drugs e.g. unfractionated heparin → heparin-induced thrombocytopenia (HIT), usually occurs 5–10 days after 1st administration; amiodarone, captopril, carbamazepine, phenytoin, vancomycin
  - Systemic lupus erythematosis (SLE)
  - Infections, e.g. infectious mononucleosis, malaria
- HUS, TTP
- Bone marrow failure, e.g. tumour infiltration, leukaemia, aplastic anaemia
- Bone marrow suppression, e.g. chemotherapy
- Dilutional following massive transfusion for bleeding
- Sequestration, e.g. splenomegaly.

Management

- Treat underlying cause, e.g. antibiotics for sepsis, stopping suspected drugs, plasma exchange for HUS/TTP
- For HIT, if suspected test for HIT antibody; if confirmed or evidence of thrombosis, stop heparin and anticoagulate with danaparoid, or direct thrombin inhibitors e.g. argatroban or lepirudin
- Platelet transfusions if count $<20 \times 10^9$/L, or if count $<50 \times 10^9$/L and active bleeding or undergoing invasive procedure. ABO-matched platelets improve platelet survival.
- For ITP, if actively bleeding in addition to platelet transfusion, treat either with steroids, e.g. prednisolone 2mg/kg daily for 2–3 weeks, or IVIG for 5 days. If these treatments fail, splenectomy may be necessary.

⚠ Avoid platelet transfusions in HUS/TTP unless active bleeding

Thrombocytosis

Platelet count $>500 \times 10^9$/L; relatively common on PICU, particularly in infants, ♂ >♀, with extreme thrombocytosis ($>1000 \times 10^9$/L) occurring in 1% of all admissions. Almost always reactive, usually secondary to inflammation.

Causes

- Infection:
  - Bacterial e.g. *Staphylococcus aureus*
  - Viral e.g. RSV
- Pneumonia, particularly with empyema
- Previous episode of bleeding and thrombosis.

Management

Even in children with extreme thrombocytosis, there is no evidence for ↑risk of thrombosis or the use of prophylactic anticoagulation, unless other risks for thrombosis.

Disorders of coagulation

Disseminated intravascular coagulation (DIC)

Commonly occurs in critically-ill children and if severe may be life-threatening. There is simultaneous generation of thrombin and activation of fibrinolysis, plus consumption of platelets.

Excess thrombin cleaves fibrinogen to fibrin, which is polymerized to form microvascular thrombi that trap platelets. Excess thrombin also assists conversion of plasminogen to plasmin, which cleaves fibrinogen leading to the generation of breakdown products i.e. fibrin degradation products (FDPs) that inhibit polymerization of fibrin and worsen the bleeding tendency.

Causes

- Sepsis, particularly with release of endotoxin e.g. Gram-negative bacterial infections, meningococcaemia. Commonest cause in PICU
- Other infections:
  - Malaria
  - Rickettsial infections
  - Viral haemorrhagic fevers
- Traumatic tissue damage, e.g. burns, head injury
- Liver failure
- Severe transfusion reactions/GVHD
- Snake envenomation.

Investigation

- FBC: platelet count $<100 \times 10^9$/L, often $<50 \times 10^9$/L; Hb possibly ↓
- Blood film; fragmented RBCs, ↓platelets
- aPTT: prolonged
- PT: prolonged
- Fibrinogen: <1.0g/L
- Fibrin degradation products (FDPs): >40mcg/mL
- D-dimers: present.

Signs and symptoms

- Purpura, leading to digital or limb necrosis (purpura fulminans)
- Oozing from previous puncture sites, gums, nose
- End organ failure secondary to microvascular thrombi causing iscahemic damage, e.g. renal failure, encephalopathy.

Treatment

- Support and treatment of underlying condition, e.g. ventilation, inotropic support, renal replacement therapy, antibiotics, antivenom
- Replacement of depleted blood components:
  - Platelets: 10mL/kg repeated as necessary (see 🕮 p.720)
  - FFP: 20mL/kg repeated as necessary, if bleeding and PT and APTT prolonged
  - Cryoprecipitate; 5mL/kg if bleeding and fibrinogen <1.0g/L
- Heparin infusion: sometimes used, especially if major intravascular occlusion; may increase risk of haemorrhage
- Antithrombin III: increases anticoagulant effect of heparin.

Thrombosis

Venous thrombosis of some degree may occur in up to 10% of all PICU patients. Usually associated with presence of central venous catheters, particularly in infants in part due to occlusion of the lumen of the vessel and also due to developmental changes in balance between pro- and anticoagulant factors. Infection of indwelling intravascular catheters is an additional risk factor. Dehydration also increases the risk of thrombosis secondary to central venous catheters, e.g. in children with DKA. In older children, the major risk is of deep vein thrombus secondary to immobility and paralysis.

Hypercoagulable states due to inherited deficiencies of protein C, protein S, or antithrombin III occasionally present in childhood.

Thrombosis may also occur as part of HIT (see 🕮 p.714).

Signs of venous thrombosis include swelling, discolouration and pain in the affected limb. In SVC syndrome, there is also oedema of the face and upper chest, cyanosis, and sometimes chylothorax.

Investigations

- Doppler ultrasonography should identify or exclude large vein thrombosis in the majority of cases
- Venograms are very occasionally used if doubt remains, particularly in neonates
- If suspicion of hypercoagulable state, check protein C, protein S, and antithrombin III levels.

Management

Prevention

- Use of TED compression stockings on older and/or immobile children
- Use of prophylactic LWMH, e.g. enoxaparin SC, particularly for immobile children
- Intermittent pneumatic compression of lower limbs
- Early ambulation whenever possible

Treatment

- Elevation of affected limb
- Thrombolysis using fibrinolytic agent, e.g. tissue plasminogen activator (rt-PA), preferably as an infusion directly into the thrombus via catheter at 0.05mg/kg/h, as dose $1/10^{th}$ of systemic treatment dose, reducing risk of haemorrhage. Continue for at least 48–72h regardless of outcome. Maintain fibrinogen level >1.0g/dl and platelets $>100 \times 10^9$/L. If using rt-PA systemically, e.g. for arterial thrombus or major pulmonary embolism, consider neuroimaging before starting infusion at 0.5mg/kg/h for 6h only. Contraindications to thrombolysis include active bleeding, general surgery within 10 days or neurosurgery within 3 weeks. ⚠ If severe bleeding occurs, stop infusion and administer cryoprecipitate 5mL/kg. If bleeding life-threatening, also infuse tranexamic acid 15mg/kg over 10min
- In addition to thrombolysis, to prevent clot extension systemically anticoagulate with heparin infusion (20–30U/kg/h) to keep aPTT × 2–3 normal value. Continue for at least 48h after thrombolysis.

- For thrombus secondary to HIT, treat with danaparoid or direct thrombin inhibitors e.g. argatroban or lepirudin
- Surgical thrombectomy may be necessary if thrombolysis unsuccessful.

Anticoagulants and antithrombotics

The haemostatic system changes with age in children, affecting thromboembolic events, response to therapeutic agents, and the pharmacokinetic parameters of agents affecting coagulation. A thrombus is a fibrin net trapped with platelets and red blood cells, which is more likely to occur when blood flow is sluggish and clotting factors are allowed to accumulate.

Anticoagulants and anti-platelet agents commonly used in PICU
- Unfractionated heparin
- LMWH
- Epoprostenol (also known as prostacyclin)
- Citrate
- Aspirin.

Unfractionated heparin catalyses the ability of anti-thrombin to inactivate certain coagulation enzymes, especially thrombin.
- Antithrombin levels are particularly low in neonates and remain ~25% lower in children compared to adults
- Children need for higher doses due to greater clearance
- Close monitoring of the aPTT is essential in any patient. Protamine can be used to reverse heparin.

LMWHs increase the action of anti-thrombin on factor Xa but not on thrombin.
- LMWH requires monitoring of anti-Xa levels
- Monitor closely in renal impairment.

Epoprostenol, in addition to causing vasodilation of the pulmonary and systemic arterial vascular beds, inhibits platelet aggregation.

Citrate binds with calcium which is required at various stages of the coagulation cascade. Citrate is mainly used to provide anticoagulation of extracorporeal circuits.

Aspirin exerts its antiplatelet action by inhibition of thromboxane A_2 synthesis in platelets. Used infrequently due to risk of Reye syndrome. It is used widely for children with prosthetic material *in situ* following cardiac surgery

Thrombolytic/fibrinolytics used in PICU

These are agents that lyse thrombus by activating plasminogen to form the proteolytic enzyme plasmin, which degrades fibrin.
- Urokinase is a directly acting plasminogen activator, often used in lines blocked with a thrombin sleeve
- Alteplase is a recombinant tissue type plasminogen activator (tPA) whose activity is enhanced in the presence of fibrin and is therefore more clot specific. Due to a short half-life, must be given as an infusion.
- Recent surgery and internal bleeding are contraindications to the use of fibrinolytics.

Product transfusions

Blood and blood product transfusion carries potential risk for the patient in terms of anaphylactic reactions, incompatibility reactions, and infection. Conversely, blood transfusion can be life saving, and many procedures in intensive care would be impossible without it. Blood and blood products are donated by volunteers in the UK, and are a limited resource. Product transfusions must be used knowledgeably, and not wastefully.

Blood products

Transfusion compatibility (Table 34.1)

- Blood should be cross-matched before transfusion and only compatible products transfused:
  - In an emergency, i.e. massive blood loss that threatens life, Group O, Rhesus-negative blood can be given
  - A blood sample for full cross-match should be taken before O negative blood transfusion
- O negative blood should be readily available within minutes in critical care areas
- Group-specific (ABO matched) blood should be available in ~10min
- Fully cross-matched blood should be available in ~30min.

Table 34.1 Transfusion compatibility

Blood group	Blood	Platelets	FFP	Cryoprecipitate
O	O	O	Any	O
A	A or O	A or O	A or AB	A
B	B or O	B or O	B or AB	A
AB	Any	Any	AB	A

Products

Red cells

- Whole blood or packed cells used to treat major blood loss, anaemia (in the context of ICU), haemoglobinopathies
- Contain additives to maintain cells in optimum condition
  - CPDA—citrate, phosphate, dextrose, adenine
  - SAGM—sodium chloride, adenine, glucose, mannitol
  - May cause biochemical problems, especially during large or rapid transfusion
- Blood products deteriorate with storage
  - Oxidant damage of cells
  - Microaggregate formation
  - ATP and 2,3DPG depletion
  - Blood for transfusion should be as fresh as possible
- Volume for top up transfusion:

  (Desired [Hb] – actual [Hb]) × weight (kg) × 5

  - 15mL/kg works well for most cases

  - Check [Hb] at end of transfusion, and if lower than expected give a little more from the same bag to minimize donor exposure
  - Diuretic therapy during transfusion may be considered, but is not routinely required
- Normal maximum rate (for routine top-up transfusions) 5mL/kg/h. May be given more quickly for acute replacement of blood losses or hypovolaemia

FFP

- Produced from plasma from a single donation
- Contains all clotting factors, albumin, and gamma-globulin
- Must be used immediately after thawing and must be ABO compatible
- Rh-D negative females must receive Rh-D negative FFP
- Indications:
  - Bleeding, where INR or APTT >1.5
  - Prophylaxis before invasive procedures if INR or aPTT >1.5.
- Dose 10–20mL/kg which raises the coagulation levels 12–15%
- May cause anaphylaxis
- Does not transmit CMV
- Does not contain leucocytes—does not need to be irradiated.

Cryoprecipitate

- Prepared from a single donation
- Contains high levels of factor VIII, fibrinogen and von Willebrand factor (>140mg/unit fibrinogen and >70IU/unit factor VIIIc)
- Cryoprecipitate from ABO compatible units should be used (although the risk of incompatibilities is small)
- Indications:
  - Bleeding, where fibrinogen <2g/dL
  - Prophylaxis before invasive procedures if fibrinogen <2g/dL
- Dose 10–20mL/kg
- Rarely causes anaphylaxis
- Does not transmit CMV
- Does not contain leucocytes—does not need to be irradiated.

Platelets

- Contains platelets and small volume of plasma
- ABO and RhD compatible units preferred
- Indications:
  - Thrombocytopenia secondary to marrow failure or peripheral consumption
  - Stable patient with no risk factors for bleeding, keep platelet count $>10 \times 10^9$/L
  - Critically ill patient or bleeding, keep platelet count $>50 \times 10^9$/L
  - Severe bleeding, following cardiac surgery or while on ECMO, keep platelet count $>100 \times 10^9$/L
  - Prophylaxis before invasive procedures, keep platelet count $>100 \times 10^9$/L
  - Seek the advice of a haematologist before treating TTP, ITP, or HIT
- Initial dose 10–20mL/kg
- May causes anaphylaxis, especially if given too quickly
- Must be irradiated if patient at risk of developing GVHD

CMV negative products

- Given to patients at risk of transfusion-acquired CMV infection
- Order CMV negative blood products for:
  - All products for children <1 year of age
  - Patients requiring intrauterine transfusion
  - CMV-negative patients who are bone marrow or organ transplant recipients (assuming the marrow or the organ donor is also CMV negative)
  - CMV-negative patients who may be going for organ transplant; who have an acquired or congenital immunodeficiency; who are undergoing splenectomy.
  - CMV-negative pregnant women
  - HIV-positive patients.

Irradiated products

- Used to prevent transfusion-related GVHD (TR-GVHD):
  - Occurs in immunocompromised recipients
  - Transfused lymphocytes proliferate and damage recipient organs especially bone marrow, skin, liver, and GI tract
  - Fever, skin rash, pancytopenia, abnormal liver function, and diarrhoea
  - Fatal in >80% of cases.
  - Onset is ~8–10 days post transfusion, longer in infants
- Prevented by gamma irradiation of cellular blood products—whole blood, packed cells, platelets, white cell transfusions
- Order irradiated blood for:
  - Patients with suspected or likely congenital cellular immunodeficiency
  - Patients with acquired immunodeficiency
  - Patients with Hodgkin's disease
  - Intrauterine and subsequent transfusions
  - Exchange transfusions
  - Stem cell and bone marrow transplant recipients
  - Patients receiving HLA matched products, or products from biologically related family members.

Hazards of transfusion

Immediate transfusion reactions include:

- Febrile reactions
- Minor allergic reactions
- Severe allergic reactions (anaphylaxis)
- Acute haemolytic reactions
- Bacterial contamination leading to bacteraemia
- Transfusion-related acute lung injury (ALI) (see 🕮 p.434)
- Fluid volume overload
- Citrate toxicity
- Hyperkalaemia.

Delayed adverse outcomes of transfusion include:

- Delayed haemolysis due to red cell antibodies
- Transfusion related GVHD

- Iron accumulation with recurrent transfusions
- Infectious disease transmission.

Management of suspected transfusion reaction

- Evaluate ABC—commence resuscitation if required
- Stop transfusion
- Flush IV line with N saline
- Check blood product prescription, blood product label and patient are all correctly identified
- Minor reactions (such as mild fever or urticaria) may be treated symptomatically, and the transfusion completed at a slower rate (assuming the blood product is the correct one for the patient)
- In more severe reactions, the transfusion must be stopped
- Investigation:
  - The blood pack must be retained and returned to blood bank
  - Post-reaction blood sample (EDTA)
  - Post-reaction urine sample
- The following may also be required—discuss with haematologist:
  - Blood cultures
  - HLA or neutrophil antibodies
  - Anti-IgA antibodies
  - HLA typing.

Further reading

British Committee for Standards in Haematology Transfusion Task Force: Writing Group (2004). Transfusion guidelines for neonates and older children. *Br J Haematol* **124:** 433–53.

Lacroix J, Hébert PC, Hutchison JS, *et al.* (2007). Transfusion strategies for patients in pediatric intensive care units. *N Engl J Med* **356:** 1609–19.

Chapter 35

Brain death, organ donation, and transplantation

Introduction

It is the job of the intensivist to identify suitable candidates for organ donation as well as looking after the brainstem dead child and their family.

This can represent a considerable challenge in the face of the inevitable total body failure and cardiac arrest that follow brainstem death (BSD). A knowledge of the pathophysiological processes involved and attention to detail are often necessary in order to maintain organ viability and ultimately transplant success.

Death and organ donation are difficult and emotional issues. The death of a child is just about the worst thing that can happen to a parent. Both medical and nursing staff can be very affected. It is vital that the intensivist bears this in mind in all dealings with family and staff. Treat the patient with the dignity that they deserve.

- Although expensive, paediatric organ transplantation is a successful treatment option for children with end-stage organ failure
- The first attempted paediatric organ transplant was in 1952, an ultimately unsuccessful kidney transplant. Following this, immunosuppression therapy was introduced to prevent transplant rejection
- After initial trials with total body irradiation, azothioprine and prednisolone were introduced with great success in the early 1960s
- In 1979, the calcineurin inhibitor ciclosporin revolutionized paediatric transplantation: immunosuppression was achieved without high-dose steroids. Negative side effects, particularly on growth and development, were avoided
- Improvements in survival have been achieved with improved general care and the introduction of drugs such as tacrolimus (calcineurin inhibitor) and mono- and polyclonal antibody treatment for acute rejection
- Although it may be life saving, transplantation is no 'cure' and condemns the recipient to a lifetime of medication and medical input
- Most cases of heart, lung, and liver transplants rely on donated organs from brainstem dead children, generally following traumatic brain injury (TBI)
- Not surprisingly there is a worldwide shortage of such organs.

Brain death

- Death can be defined as the irreversible loss of the capacity for consciousness combined with irreversible loss of the capacity to breathe. Without brainstem function both of these are lost
- Children with severe irreversible brain damage who have no brainstem function may survive for days or weeks if mechanically ventilated
- Criteria for brain death have therefore been developed. Patients who fulfil these, even if ventilated, will eventually develop cardiovascular collapse and cessation of heartbeat
- BSD tests (Boxes 35.1 and 35.2) can confirm to relatives that death has occurred and allows them the opportunity to grieve
- Once BSD is confirmed mechanical life support should be withdrawn unless donation is occurring. The timing of the approach to relatives regarding organ donation is contentious; many units start discussion before BSD tests
- Brainstem death tests are not necessary for withdrawal of life support (see 🕮 End of life care, p.828).

Box 35.1 Criteria for undertaking brainstem testing

At the time of assessing the patient, the examiners ***must*** satisfy themselves that:

- The mechanism of injury or diagnosis resulting in irrecoverable coma is known
- The rectal temperature is above 35°C
- Adequate haemodynamic function is present with no hypotension
- The biochemistry is normal (glucose and sodium particularly)
- There are no metabolic or endocrine causes of coma present
- There is no evidence that drugs able to cause impaired consciousness or respiratory depression have been given and that sedative drugs used in ICU have worn off completely
- Neuromuscular blockade is excluded by the presence of peripheral reflexes or neuromuscular conduction on nerve stimulation
- Blood levels of barbiturates and benzodiazepines are needed if these drugs have been used:
  - High levels of thiopentone can mimic brainstem death
  - Levels of thiopentone and phenobarbitone must be monitored and be <25mg/L before tests are undertaken.

Tests of brainstem function (Box 35.2)

- The absence of brainstem function can be reliably determined by careful neurological examination and by addition of specific manoeuvres
- Tests should be by 2 medical practitioners, registered for >5 years and competent in the field. It is recommended that at least 1 is a consultant, 1 a paediatrician, and 1 not primarily involved the case. They must never be members of the transplant team
- Allow at least 4h observation of absent brainstem activity before undertaking tests (longer if aetiology is a hypoxic ischaemic insult)

- 2 sets of tests performed: separately or together (interval between is matter of clinical judgement). Death not pronounced until 2nd set of tests satisfied, but legal time of death is at the first test.

If these preconditions for testing cannot be met then 4-vessel angiography or radionuclide scanning should be considered to demonstrate absent CBF above carotid siphon.

Box 35.2 BSD tests

All brainstem reflexes should be absent

- No motor response to painful stimulation bilaterally in supraorbital nerve area and lateral condyles at level of temperomandibular joint (testing CN V and VII)
- Absent corneal reflex—no response when cornea is touched (CN V and VII)
- Absent pupillary reflex—both pupils fixed and unresponsive to light (CN II and III)
- Absent oculovestibular reflex—no deviation in eyes when 20mL ice water instilled in each ear. Clear access to tympanic membranes ensured (CN III, VI, and VIII)
- Absent gag reflex or cough reflex when suction catheter passed into trachea (CN IX and X)
- Apnoea test (testing brainstem respiratory centres):
  - Ventilate child with 100% oxygen for 10min
  - Before test begins reduce minute ventilation to achieve $PaCO_2$ (from ABGs) of 5.3–6KPa (40–45mmHg)
  - To achieve apnoeic oxygenation: disconnect ventilator and administer 100% oxygen at 2–4L/min via a tracheal catheter or CPAP re-breathe circuit
  - Observe child for 10min. $PaCO_2$ should trigger respiratory centre in brainstem if it is functioning
  - Repeat blood gases and confirm $PaCO_2$ is >8 KPa (60mmHg) or >1.5KPa from baseline.

Note:

- Absent 'doll's eyes' movement (oculocephalic reflex) are not an essential part of BSD testing.
- If there is chronic compensated respiratory acidosis it will be necessary to allow a rise in pCO_2 sufficient to reduce pH to <7.2.

Age and BSD testing

In the UK death is a clinical diagnosis. The 1991 British Paediatric Association guideline still applies:

- >2months: use the same criteria as in adults
- 37 weeks–2 months:
  - Infant brains have ↑resistance to brain damage and may recover substantial function following unresponsiveness compared to adults. It is rarely possible to confidently diagnose BSD
- <37 weeks' gestation: the development of brainstem reflexes in pre-term infant are not well defined. BSD tests cannot be used.

There is however international variation in practice:
- In other EU countries different age group stratifications exist
- In US *whole brain death* is used. This necessitates the need for other tests:
  - Cerebral angiography confirms no CBF and thus death
  - EEG showing electrocortical silence may be valuable when combined with examination, but is not diagnostic
  - Some states use different guidelines for <1 year and >↑1 year old.

This is a very distressing period for any relatives. Keep them fully informed of any actions or procedures that you are planning. It is very easy for the medical staff on a busy unit with many urgent tasks (contacting the transplant team, chasing up blood results) to forget the sheer magnitude of what is happening. Treat all relatives with empathy and understanding. It is mandatory to treat the patient with dignity and respect at all times. Nursing and other staff often have a very close relationship to both child and relatives and despite professional appearances they may be very emotional as well. Keep this in mind.

Some parents and even siblings may want to be present during BSD tests. Indeed, this may remove any doubts they have, and helps with grieving. The process should be explained and performed in a compassionate manner. The possibility of spinal reflexes should be explained beforehand. Once BSD certified either proceed to organ donation or withdrawal of life-sustaining treatment.

Organ donation and the organ donor

There are 3 main types of solid organ donation in the UK
- Live related: children are not ethically or legally accepted as donors
- Cadaveric heart beating donation after BSD
- Cadaveric non-heart beating: after withdrawal of life-sustaining treatment on PICU.

In the UK, transplants are the responsibility of the National Health Service special health authority.[1] Donor transplant coordinators are crucial partners in this process, and should be contacted with any potential donation on PICU.
- In some units a collaborative approach of the family is made by both the ICU consultant and the donor coordinator
- In other units the donor coordinator may only become involved once the family has given consent for organ donation.

Non-heart beating donation

- Organ donation after death following withdrawal of life support is increasingly practised

- Usually occurs following catastrophic brain injury when BSD criteria cannot be met but life support in PICU is no longer in the child's best interests
- Requires careful consideration of potential suitability:
  - Death must occur following withdrawal of ventilation without a prolonged period of hypoxia or hypotension
  - The surgical team must be standing ready to operate at the time ventilation is withdrawn
- Withdrawal of ventilation either in the operating theatre, anaesthetic room, or in ICU if in close proximity.

Reference

1. http://www.uktransplant.org.uk

Donor workup

- A comprehensive list of tests will be requested by local transplant coordinator
- Detailed past and current medical history are necessary to evaluate current organ function and suitability (see Box 35.3)
- Timescale, treatment, and response to events such as cardiac arrest, hypotension, or hypoxic episodes are essential for donor assessment
- HIV, CJD (Creutfeldt–Jakob disease), disseminated malignancy (although not primary brain tumours), and systemic sepsis are absolute contraindications to organ donation
- Certain inborn errors of metabolism will be contraindications to organ donation
- Relative contraindications exist, e.g. viral infections or infection or functional impairment in donor organs but this will need evaluation by the transplant team
- Blood for viral serology should be sent immediately, e.g. HIV, human T-lymphocyte virus 1, hepatitis B and C, cytomegalovirus
- Being a Coroner's case is not an absolute contraindication to any form of organ donation, but permission ***must*** be gained prospectively.

Box 35.3 Requirements of recipient transplant teams

- ***Kidney:*** age, hypotension, high-dose inotropes, serum urea, creatinine, electrolytes
- ***Liver:*** age, weight, hypotension, inotrope dose, use of vasoconstrictors including vasopressin, electrolytes, LFTs, clotting profile, glucose.
- ***Pancreas:*** age, hypotension, high dose inotropes, blood glucose, serum amylase, abdominal trauma
- ***Heart:*** age, weight, hypotension, high-dose inotropes, cardiac Echo, ECG, CXR
- ***Lungs:*** age, size, weight, hypotension, high-dose inotropes, cardiac echo, bronchoscopy, ECG, CXR, ABG on 100% O_2 with PEEP 5.

Care of the paediatric organ donor

Evidence shows that BSD patients will eventually suffer cardiac arrest, preceded by increasing physiological instability. Whilst waiting for the transplant team to get consent from the relatives and to evaluate the child for donor suitability, the intensivist must optimize the brain dead child for organ harvest.

Problems following brainstem death

The incidence of complications increases with time from BSD.

Hypotension

- Mostly secondary to hypovolaemia and myocardial dysfunction
- Hypovolaemia secondary to:
  - Therapy for ↑ICP (e.g. mannitol, fluid restriction)
  - Relative hypovolaemia from loss of vasomotor control and ↓sympathetic tone leading to vaso/venodilatation and peripheral pooling.
  - Diabetes insipidus which leads to further hypovolaemia
- Microinfarcts in the myocardium occur.

Arrhythmias

- Both brady- and tachyarrhythmias occur
- Sudden unheralded cardiac arrest.

Pulmonary complications

- Pulmonary oedema can occur with:
  - Fluid overload (particularly when trying to keep kidneys perfused)
  - Neurogenic pulmonary oedema (sudden massive ↑ in SVR with brainstem herniation)
  - ARDS and capillary leak
  - Cardiac failure
- Lung infection and/or aspiration
- Baro/volu-trauma and oxygen toxicity
- All these factors can cause significant hypoxaemia.

Metabolic disturbance

- Hypotension and/or hypoxaemia can lead to metabolic acidosis
- Hypernatraemia, hypokalaemia, hypocalcaemia, and hypomagnesaemia can occur secondary to diuretic therapy (for ↑ICP) and/or diabetes Insipidus.

Endocrine disturbance

- Diabetes insipidus is common following BSD:
  - Either secondary to hypothalamic-pituitary dysfunction or absence of CBF (which normally transports ADH)
  - See 🕮 p.683
- Hyperglycaemia:
  - Brain death and thus ↓brain glucose utilization
  - ↓insulin secretion
  - Secondary to catecholamine infusions
  - Can cause osmotic diuresis and aggravate hypovolaemia and electrolyte disturbance
- Thyroid and steroid secretion can be altered and should be considered if there is cardiovascular instability of unknown cause.

Hypothermia
- Temperature maintenance is essential for BSD tests
- Loss of central control leads to poikilothermia and heat loss
- Hypothermia can ↓oxygen delivery to tissues (oxyhaemoglobin curve is shifted to the left).

Coagulopathy
Plasminogen activators and fibrinolytic compounds are released from injured brain tissue and may cause DIC.

Infection
Be vigilant for VAP, line sepsis, or urinary tract infection.

Management of the organ donor
As in most critical care the overall goal is for adequate tissue oxygen delivery with minimal organ support.

IV fluids
- Maintenance fluids should be limited to insensible losses and urine output, e.g. 25–50% of 'normal' maintenance fluid
- Minimal glucose required in maintenance fluids (avoid hyperglycaemia)
- Hypotonic fluid may be indicated, particularly if serum sodium is high. (e.g. 4% glucose/0.18% saline, 5% glucose)

Diabetes insipidus (📖 p.683)
Replace 100% of previous hour's urine output with IV 4% glucose/0.18% saline containing 2u/L of aqueous vasopressin (or desmopressin acetate DDAVP).

Cardiovascular
- If not already present, start invasive monitoring of arterial and central venous BP
- Cardiac Echo needed to evaluate anatomy and to assess function
- If there has been a period of hypoxia and/or hypotension then troponin levels and ECG will be useful
- Arrhythmias should be treated. If possible ↓ or stop arrhythmogenic inotrope/pressor infusions. Correct electrolytes and acid/base if abnormal
- Inotropes: use minimum necessary to maintain systolic BP at a low normal for age. Avoid high doses of any agent.

Pulmonary
- Watch for overventilaion and hypocapnia: minimal alveolar ventilation is required to maintain normocarbia (reduced CO_2 production due to diminished metabolic rate)
- Minimize baro/volu-trauma by avoiding large tidal volumes and excess pressures
- Avoid excess PEEP to maintain venous return
- Minimize FiO_2 to avoid oxygen toxicity, particularly if lungs are to be donated
- Careful fluid management (do not overhydrate) with invasive haemodynamic monitoring should avoid pulmonary oedema

- If infection is suspected perform BAL and send secretions for Gram-stain, culture and sensitivity (including viral immunofluorescence/PCR)
- Postural drainage and chest physiotherapy can be helpful
- Bronchoscopy may be necessary for severe mucous plugging.

Endocrine/metabolic

- Treat diabetes insipidus as previously described (📖 p.683)
- Treat hyperglycemia with insulin infusion at 0.05–0.1U/kg/h and strict glucose monitoring. Aim for nomoglycaemia. Minimize catecholamine infusions if possible
- In case of refractory hypotension consider hydrocortisone and/or triiodothyronine (📖 p.689)

Renal

- Adequate urine output (1mL/kg/h) is helpful but can be misleading in BSD patients with many confounding factors
- Remember that mannitol, hyperglycaemia, radiological contrast can all cause an osmotic diuresis
- If oliguria persists despite restoration of circulating volume and good BP consider use of frusemide (bolus or infusion).

Temperature homeostasis

- Warming blankets and radiant heaters are required to keep core temperature above 35°C
- Consider warming all IV infusions.

Blood and products

- Minimize use of blood if possible—accept Hb 7g/dL (transfusion can expose donor to new antigens)
- Platelets, FFP, and vitamin K may be indicated in DIC.

Withdrawing life support

(📖 See End of life care p.828.)

Process of withdrawal of care

Brainstem dead donor

- ICU notified of anticipated theatre time
- Give sufficient notice to prepare the child and the family
- Family and friends say their goodbyes in the ICU
- Child (donor) is fully monitored for transfer to theatre
- The order of harvesting organs decided by surgical teams
- Drugs usually given include heparin, methylprednisolone, and antibiotics
- At the end of the procedure the donor is returned to ICU where the family may attend.

Non-heart beating donor

- Death is anticipated quickly after withdrawal of ventilation
- Surgical team is waiting in operating theatre:
  - Ventilation is withdrawn in theatre (anaesthetic room) or in the ICU if nearby

- The child remains monitored after withdrawal of ventilation so that duration and severity of hypoxia or hypotension can be recorded
- After onset of asystole the child is observed for any evidence of cardiac, respiratory, or muscle activity (beyond agonal gasping)
- The child is certified dead by the ICU doctor
- A period of time is allowed for further observation and to allow the family to say their goodbyes
- This varies but in many centres is between 5–10min
- This results in a predictable *warm ischaemic* time
- The donor is transferred into theatre where the organs are harvested as quickly as possible
- After donation the body is returned to ICU to allow the family to attend.

Transplantation and transplant rejection

Matching donor to recipient can depend upon the organ being transplanted, the urgency of clinical need, and the background disease of the recipient. Waiting lists exist for all solid organs in the UK.

The major difficulty in transplantation is preventing the new host from rejecting the organ by an immune process. Every individual has a highly variable number of antigens expressed on their cells. The only organs that would not be rejected without immunosupression are those from a site without immune surveillance such as the cornea or organs from an identical twin.

Matching donor and recipient

- Match blood group type
- Match histocompatability loci antigens (HLA) as much as possible.

Rejection

- Transplantation of an organ, tissue, or cells between genetically different individuals (known as allografts or homografts) will result in graft rejection unless the immune response triggered immediately post transplantation is controlled (Box 35.4)
- Rejection:
  - Is main cause of late mortality in recipients of organ transplantation
  - May present with deteriorating organ function or with non-specific symptoms such as fever, poor appetite, irritability, or fatigue
- Monitoring of graft function is by:
  - Organ function measurements, e.g. Echo, GFR
  - Biopsy and histological examination
- The degree of rejection depends upon:
  - The nature of tissue transplanted
  - Donor/recipient genetic disparity

  - Site of transplantation
  - The immune status of recipient
- In general PICU management is basically supportive whilst the rejection response is managed by the transplant team.

Hyperacute rejection

- Humoral mediation
- Complement-mediated response in recipients with pre-existing antibodies to donor (e.g. ABO)
- Occurs in minutes and transplant must be removed to prevent SIRS and death.

Acute rejection

- Cellular mediation
- Mediated by T-cell responses to proteins in donor organ and characterized by mononuclear cell infiltration in organ
- Occurs several days post transplant if not on immunosuppressants
- Since development of powerful immunosuppressive drugs incidence of acute rejection has greatly ↓.

Chronic rejection

- Chronic alloreactive immune response
- Irreversible and cannot be treated effectively
- Only definitive treatment is re-transplantation.

Box 35.4 Immunosuppressant drugs and transplantation

Drugs used include:

- Calcineurin inhibitors (inhibit IL-2): ciclosporin, tacrolimus
- mTOR inhibitor (inhibit IL-2): sirolimus, everolimus
- Antiproliferatives: azathioprine , mycophenolic acid
- Corticosteroids: prednisolone, hydrocortisone
- Antibodies:
  - Monoclonal anti-IL-2R receptor antibodies (basiliximab, daclizumab)
  - Polyclonal antibodies: antithymocyte globulin (ATG) and antilymphocyte globulin (ALG)
- Generally triple therapy regimen of calcineurin inhibitor, an antiproliferative, and a corticosteroid used
- Antibody inductions are added for high-risk patients.

Side effects

- Ciclosporin:
  - Hypertension, renal dysfunction, tremors, seizures, hyperuricaemia, hyperglycaemia, hirsuitism.
- Tacrolimus:
  - Encephalopathy, pupillary changes.
- Azothiaprine:
  - Bone marrow suppression—pancytopenia, infection, nausea and vomiting, mucosal ulceration

(*Continued*)

Box 35.4 Immunosuppressant drugs and transplantation (*Continued*)

- Corticosteroids:
  - Hypertension, sodium and water retention, hyperglycaemia, infection, muscle weakness, growth inhibition, and bone abnormalities
- Antibodies:
  - Anaphylaxis, rash, thrombocytopenia, renal impairment.

Liver transplantation

Indications

- Chronic progressive liver disease e.g. biliary atresia
- Hepatic tumors
- Acute fulminant hepatic failure (FHF).

Criteria for predicting death and need for liver transplantation (from King's College Hospital, London, UK)

Paracetamol poisoning

- pH <7.3 irrespective of grade of hepatic encephalopathy (HE)
- PT >100s.
- Serum creatinine >300μmol/L with grade III/IV HE.

All other aetiologies

- PT >100s (irrespective of HE grade)
- Or 3 of:
  - Age <10 years or >40 years
  - Aetiology of non-A, non-B hepatitis, halothane, or idiosyncratic drug reaction
  - Jaundice for >10 days prior to HE
  - PT > 50s
  - Serum bilirubin >300μmol/L.

Status 1: most urgent level

- Rapid development grade III/IV HE
- PT >25s
- On vasopressors or ventilatory support
- Have primary graft non-function
- Expected to live <7 days without transplant
- Inborn error of metabolism with CNS toxic metabolites.

Contraindications

- Uncontrolled sepsis/multi-organ system failure
- Irreversible brain damage:
  - By neurologic examination
  - Imaging studies
  - Sustained ICP >50mmHg
  - Cerebral perfusion pressure < 40 for 1–2h.

Modes
- Auxillary liver transplant or hepatocyte transfusion can act as 'bridge to recovery of own liver'
- Transplant can be whole, segmental, or live related lobe donation.

Reasons for PICU management
- Pre-transplant:
  - For FHF (📖 see p.632)
  - Extracorporeal liver assist device (ELAD). (📖 see p.272 and p.633)
- Post-transplant:
  - For glucose control
  - For haemodynamic stability—vasopressors may be required
  - FHF care continued including anticoagulant optimization to prevent graft thrombus
  - To continue renal support (CVVH) as liver function improves
  - To optimize immunosuppression
- Complications include:
  - Arterial or venous thrombosis or stenoses, e.g. hepatic artery, portal vein, or IVC—usually early postoperative period
  - Biliary complications of obstruction, leak, or stones
  - Abnormalities of the liver parenchyma such as infarct or abscess
  - Graft rejection
  - Extrahepatic fluid collections
  - Post-transplantation lymphoproliferative disease.

Transplant outcome
- For FHF: 60%
- For chronic liver disease: 75%.

Renal transplantation

- Renal transplant is the commonest solid organ transplant carried out in children and is considered the optimal treatment for end-stage renal disease
- Survival at 3 years with either living donor or cadaveric donor transplantation is markedly superior to dialysis
- PICU admission is rarely necessary.

Reasons for PICU admission
- Very large graft e.g. from parent in small child
- Electrolytes disorders
- ARF due to graft dysfunction—may require dialysis
- Bleeding from the anastomoses
- Arterial or venous thrombosis/stenoses
- Urologic complications such as ureteric obstruction or leak
- Graft rejection (acute or chronic).

Outcome
- 5-year graft survival: live donor—80%; cadaveric—70%
- Rates are not as high and renal function somewhat poorer if organ source is a non-heart beating donor.

Heart transplantation

Indications

- Isolated heart:
  - Severe congenital malformations e.g. hypoplastic left heart (HLHS)
  - Myocarditis/end stage cardiomyopathy
  - Myocardial tumors.
- Heart/lung transplant (HLT):
  - Eisenmenger's syndrome
  - Congenital defects with pulmonary vascular disease
  - Congenital defects with inadequate pulmonary vessels (not surgically correctable).

PICU management

- Pre transplant: heart transplant is often performed in children already on ICU with irreversible myocardial failure, often on mechanical support e.g. ECMO/VAD
- Post-transplant: most children need a period of ventilation, haemodynamic support, and general intensive care
- Early complications include:
  - Primary graft failure-: the most severe complication of heart transplantation and the commonest cause of death in first 30 days
  - Risk factors are infancy, larger donor–recipient weight mismatch, long donor ischaemic time, anoxia as cause of donor death, and need for ECMO (in recipient) pre transplantation
  - Hyperacute (antibody mediated) rejection now ↓ due to HLA matching.
- Acute re-transplantation for primary graft failure has a high mortality but early ECMO support allows graft recovery of 50% (to discharge)
- Late complications include:
  - Acute rejection: commonest cause of death between 30days–3 years
  - Chronic rejection or post-transplantation coronary arterial disease
  - Infectious complications
  - Epstein–Barr virus infections and PTLPD
  - Auto-immune cytopenias
  - Side effects of immunosuppression (see 🕮 Box 35.4).

Outcome

- Survival rates are improving (as with other transplants)
- Survival approximately 85% at 1 year and 65–80% at 5 years.

Heart/lung and lung transplantation (HLT and LT)

Results of HLT and LT almost identical. The prognosis in HLT depends largely on presence of lung allograft. Due to low donor availability and fewer indications LT/HLT are relatively rare.

Indications

- HLT (see 'Indications')
- LT: primary lung disease or pulmonary vascular disease with preserved LV and recoverable RV function

- Infants/young children: pulmonary alveolar proteinoses, pulmonary venous obstruction, infantile interstitial pneumonitis, and primary pulmonary hypertension
- Older children: cystic fibrosis.

Mode
- Single lung transplantation: rare in children
- Double lung transplants are usually bilateral sequential single lung transplants as tracheal anastomoses are prone to dehiscence
- Living-lobar lung transplantation usually involves 2 separate adult (relative) donors and is controversial.

PICU management
- Pre-transplant: mechanical ventilation is currently a contraindication to lung transplant
- Post-transplant:
  - Gentle ventilation required
  - Triple drug immunosuppression (cyclosporine, tacrolimus, and IV corticosteroids)
  - Late complications carry a poor prognosis and include respiratory infection (often viral), acute or chronic rejection, and lymphoproliferative disease.

Outcome

Currently outcome is poor even in cystic fibrosis and there are calls for a major RCT for lung transplantation.

Bone marrow transplantation

Haematopoietic stem cell transplantation from blood or bone marrow (BMT) are being used as treatment for an increasing variety of diseases of childhood.

Indications for BMT

- To replace diseased, non-functioning marrow, e.g in leukaemia
- Following high-dose chemotherapy or radiotherapy to replace bone marrow, e.g. rescue treatment for recurrent lymphoma
- To replace bone marrow with genetically healthy functioning marrow to prevent progression of a genetic disease e.g. Hurler's syndrome
- For immunodeficiency syndromes, e.g. severe combined immunodeficiency.

Types of BMT

These are classified by the donor type
- Autologous: stem cells are harvested from the patient themselves from bone marrow or apheresis (peripheral blood stem cells) and returned after treatment
- Allogeneic: the donor shares genetic type with the child, e.g. a sibling or parent or unrelated match from bone marrow register
- Umbilical cord blood transplant: stem cells from the umbilical cord immediately after birth are tested, typed, counted, and frozen until

used. Cord recipients have ↓risk of severe graft-versus-host disease (GVHD) as T lymphocytes function poorly

Bone marrow transplant and PICU

Up to 40% need PICU due to complications which have a high mortality rate and high cost. BMT occasionally occurs in a child already in PICU, usually those with newly diagnosed severe immunodeficiency or in a child being conditioned for BMT who gets an infection or fluid overload. Reasons for PICU admission include:

- Toxicity of conditioning regimen
- GVHD in allogenic grafts
- Opportunistic infections, septic shock, line infection
- GI irritation, e.g. severe mucositis, vomiting, diarrhoea
- Severe bleeding from low platelets, e.g. intracranial or GI
- Seizure disorders
- Drug reactions
- Liver/kidney failure
- Veno-occlusive disease.

Respiratory distress and fluid overload after BMT

- Causes of respiratory distress can occur concurrently and mimic one another:
  - Infection- bacterial or viral
  - Pneumonitis and GVHD
  - Airway inflammation
  - Fluid overload
  - Pulmonary haemorrhage
  - All are serious lung complications of BMT that mimic each other.
- All present with hypoxia and reduced lung compliance. CXR shows bilateral infiltrates.

Treatment

- Targeted at several causes concurrently
- Consider antibiotics (often already started), antiviral and antifungal therapy with targeted investigations, e.g. PCR
- Optimize immunosuppression—for interstitial pneumonitis and GVHD
- Fluid overload may lead to pulmonary oedema, liver dysfunction, hypertension, and ventilator-associated lung injury. The primary cause is the large volumes needed in the form of medications, nutrition, and blood products coupled with renal dysfunction due to disease/medications, infection, chemotherapy or radiation. Use aggressive diuresis with furosemide infusion or boluses (start at 0.05–0.1mg/kg/h IV) and consider CVVH
- Interstitial pneumonitis classically presents within 2 months of bone marrow transplant. It is associated with GVHD and may be a heralding feature. Increasing immunosuppression and steroids are required
- UK standard practice is non-invasive ventilation and deferring invasive investigations (BAL, high-resolution lung CT and lung biopsy) unless intubation is necessary—no benefit of such tests on survival has been demonstrated. Mechanical ventilation may be necessary and has a significant mortality associated with it.

Organ dysfunction

- Hepatic and cardiac impairment common due to transplant process.
- Damage may result from infection, GVHD, chemotherapy, radiation, fluid overload or veno-occlusive disease

Graft failure

- Can result from infection, recurrent disease, or if the stem cell count in the donated marrow was insufficient to engraft
- Infection can prevent/delay engraftment and/or cause permanent organ damage. Antibiotics, antifungal, and antiviral therapy are given to prevent serious infection in the immunosuppressed child
- Graft failure may be treated with a repeat BMT if source is available.

GVHD

- Often a serious and life-threatening complication following BMT. Occurs when donated cells do not recognize recipient's cells
- Most common sites: skin, GI tract, liver, and lungs
- Symptoms can be acute or chronic (graded 1 to 4) and include diarrhoea, fever, skin changes, abdominal pain, respiratory complications, and ↓liver function
- GVHD is treated with escalating immunosuppression using steroids and ciclosporin depending on the response.

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Chapter 36

Poisoning

Introduction

<1% of cases of childhood poisoning are fatal. Aggressive management regimens are therefore inappropriate for the majority of children. However, 5–10 children die each year in the UK from poisoning. Good history taking and careful patient assessment are key to ensuring the correct level of intervention (Box 36.1).

Box 36.1 Principles of management

- Assessment and resuscitation
- Clinical history and identification of poisoning agent
- Prevention of further absorption of poison
- Protection of end organs from toxic effects
- Elimination of poison from body
- Prevention of further episodes of poisoning
- Continuation of monitoring until child fully stabilized.

Resuscitation

Airway

Many drugs/toxins cause CNS depression leading to impaired airway patency and ventilation. Careful monitoring is required, with a view to achieving airway control before deterioration occurs. Intubation is indicated if airway patency is not maintained, airway reflexes are poor and the patient is vomiting, and if respiratory support is required.

Breathing

Hypoxia and acidosis secondary to hypoventilation may exacerbate the toxicity of some poisons.

- Administer oxygen if the child shows any signs of impairment
- Assess respiratory rate, air entry, and pattern of breathing (acidosis may lead to Kussmaul breathing)
- Have a low threshold for ABG analysis if the child has any impairment in level of consciousness.

Circulation

- Check rate and rhythm of pulse
- If any signs of impairment attach ECG monitoring
- Assess perfusion and BP
- Fluid resuscitation and inotropic support may be necessary in some forms of systemic poisoning.

Disability

- CNS depression is a common symptom of poisoning.
- Level of consciousness and pupillary reactions should be assessed.

Drugs causing dilated pupils include:

- Anticholinergics (e.g. atropine, older antihistamines, tricyclic antidepressants)
- CNS stimulants (e.g. amphetamines, LSD)
- Theophylline (and its derivatives).

Drugs causing pupillary constriction include:
- Opioids (morphine, heroin)
- Cholinesterase inhibitors (organophosphate and carbamate insecticides).

Clinical history and identification of poison

General background medical history
- Potential poison taken (if medicines, include other medicines in house)
- Quantity
- Time of ingestion
- Vomiting or other symptoms.

Unknown tablets can be identified using electronic databases such as TICTAC. Information on the management of specific poisons should be obtained from the poisons information service, online (see 📖 p.753) or from local policies.

Gastric emptying
- Particular value if poison not adsorbed by activated charcoal (iron salts, fluorides, potassium salts, lithium, methanol, ethylene glycol)
- Contraindicated after ingestion of strong alkalis, strong acids, and hydrocarbons
- Induced vomiting is of limited value
- Syrup of ipecac should not be used
- Use gastric lavage only if a life-threatening amount of poison ingested in the last hour. Airway protection needed if ↓ consciousness.

Activated charcoal
- May reduce drug absorption—but effect decreases with time
- Occasionally may enhance drug elimination
- Dose 1g/kg
- Add to soft drinks to increase palatability if patient conscious
- Antiemetics may be necessary
- Give via NG tube if unconscious
- Repeated doses (1g/kg 4-hourly) may enhance elimination of some drugs.

Haemodialysis
Consider if:
- Poisoning clinically severe, with coma, respiratory depression, hypotension, and hypothermia
- The patient's condition fails to improve or continues to deteriorate despite intensive supportive measures
- Plasma drug level high
- Serious complications such as hepatic/renal failure whilst patient still unconscious
- Drugs/poisons that may be removed by haemodialysis include:
  - Ethanol, methanol, ethylene glycol, phenobarbitone, phenytoin, salicylates, β-blockers, organophosphates, digitalis, paraquat, amanita mushrooms.

Specific poisons

Alcohol

- 90% absorbed from GI tract in 1h
- Moderate intoxication (plasma conc. 1.8-3–5g/L)
  - Slurred speech, diplopia, blurred vision, ataxia, incoordination, blackouts, sweating, tachycardia, nausea, vomiting, and incontinence
  - Acidosis, hypoglycaemia (may be delayed up to 36h if fasted), and hypokalaemia may occur
- Severe intoxication (plasma conc. 3.5–4.5g/L)
  - Cold clammy skin, hypothermia, hypotension, stupor, coma, dilated pupils, depressed or absent tendon reflexes
  - Severe hypoglycaemia, convulsions, respiratory depression, and metabolic acidosis may occur
  - Cardiac arrhythmias such as atrial fibrillation and AV block.

Management

- Ensure patent airway and adequate ventilation
- Observe for at least 4h if >0.4mL/kg body weight of absolute ethanol had been ingested (i.e. 1mL/kg 40% spirit, 4mL/kg 10% wine, or 8mL/kg 5% beer)
- Monitor vital signs and blood glucose
- Correct hypoglycaemia with oral or IV glucose (dependent of level of consciousness). Glucagon is usually ineffective
- Correct hypotension with volume expansion and inotropes
- Treat seizures as per usual algorithm (benzodiazepines and phenytoin)
- Consider haemodialysis if blood ethanol conc. >5g/L or pH <7.0.

Amphetamines and derivatives (including 'Ecstasy')

- Street drug content varies—usually ~5%
- Individual response varies
- Faster, intensive effects with snorting or IV use than ingestion
- Large doses cause:
  - Sweating, confusion, and anxiety
  - Vomiting and abdominal pain
  - Hallucinations, seizures, and coma
  - Chest pain, palpitations, dyspnoea, and hypo/hypertension may occur
  - Cerebral vasculitis or haemorrhage, rhabdomyolysis, DIC, and ischaemia may occur
  - Crystal methamphetamine can cause pulmonary oedema.

Serious prognostic signs include marked hyperpyrexia, coma, seizures, or focal neurological signs

Management

- Consider activated charcoal if presentation within 1h
- 12-lead ECG and vital signs
- U&Es, LFTs, and CK if signs of toxicity
- Benzodiazepines to control agitation and seizures

- If metabolic acidosis despite correction of hypoxia and fluid resuscitation, give correction of sodium bicarbonate
- Hypertension usually resolves with benzodiazepines to treat agitation. Occasionally treatment with GTN infusion is required
- In serious overdose intubation should be early
- Treat hyperthermia aggressively. Sedation and active cooling may be needed. Water sprays, CVVH, CP bypass, and peritoneal lavage have been used to promote cooling. If temperature exceeds 39–40°C consider dantrolene (1mg/kg to max. 10mg/kg).

Aspirin/salicylates

Severe toxicity if >500mg/kg ingested.

Symptoms/signs

- Nausea, vomiting, tinnitus, lethargy, dehydration, restlessness, sweating, hyperventilation, haematemesis, hyperpyrexia, hypoglycaemia, hypokalaemia, thrombocytopenia, DIC, renal failure, non-cardiogenic pulmonary oedema
- Confusion, disorientation, coma, and convulsions are more common in children than adults
- Acid–base status: metabolic acidosis ± respiratory alkalosis
- Metabolic acidosis, plasma level >350mg/L and neurological impairment suggest severe toxicity.

Management

- Consider activated charcoal if >125mg/kg ingested in last 1h (and later if enteric coated)
- Measure plasma salicylate concentration at least 2h after ingestion (peak occurs later if enteric coated)
- Repeat every 3h until levels falling
- Take a blood gas (arterial, capillary or venous)
- Check U&Es, clotting, and glucose
- If level >350mg/L alkalinize urine (aim pH7.5–8.5) with 40–80mmol/L sodium bicarbonate in 5% dextrose at maintenance rates
- Urine output should be >2mL/kg/h
- Beware of hypokalaemia and hypernatraemia
- Consider haemodialysis if: renal failure, heart failure, non-cardiogenic pulmonary oedema, coma or convulsions, severe acidosis, persistent high salicylate concentrations after urine alkalinization, plasma level >700mg/L.

Benzodiazepines

Symptoms/signs

- Drowsiness, ataxia, respiratory depression, hypotension, coma.

Management

- Maintain airway and adequate ventilation
- Consider activated charcoal if taken>1mg/kg in last hour
- Treatment should mainly be symptomatic
- If severe symptoms consider flumazenil 10mcg/kg
  - May be repeated and infusion 10mcg/kg/hr continued)
  - Shorter half-life than many benzodiazepines

  - Not licensed for acute benzodiazepine overdose
  - Do not use if combined overdose suspected (especially tricyclic antidepressants) or known epilepsy
- Treat hypotension with fluids/inotropes.

β-blockers

Symptoms/signs

- Bradycardia, hypotension, pulmonary oedema, syncope, drowsiness, seizures, dilated pupils, coma, bronchospasm
- Symptoms more likely if other cardioactive drugs also ingested.

Management

- Consider activated charcoal if within 1h ingestion
- Maintain airway and ventilation.
- 12-lead ECG. Check U&E and glucose
- Large doses of atropine (0.04mg/kg) may be helpful in bradycardia
- Treat hypotension with fluids/inotropes
- Treat severe cardiac signs with glucagon: 50–100mcg/kg bolus followed by 50mcg/kg/h infusion
- If no improvement, use isoprenaline (0.02–0.5mcg/kg/min)
- Pacing may improve heart rate but not hypotension
- Dobutamine may work better than other inotropes
- Bronchospasm should be treated with salbutamol or aminophylline
- Mechanical cardiac support may be required if unresponsive to drug therapy and pacing.

Cocaine

Symptoms/signs

- Euphoria, agitation, tachycardia and tachypnoea, ataxia, dilated pupils, nausea and vomiting, headache, hallucinations
- Can be complicated by hypertension, myocardial ischaemia, dysrhythmias, aortic or coronary artery dissection, cerebral infarcts/haemorrhage, hyperpyrexia, rhabdomyolysis, metabolic acidosis and hypokalaemic paralysis.

Management

- Ensure patent airway and adequate ventilation
- Consider activated charcoal if ingestion in last hour
- Benzodiazepines may be used to control agitation and convulsions (more effective than phenytoin)
- Treat hypertension unresponsive to benzodiazepines with IV GTN, SNP or phentolamine (avoid β-blockers)
- GTN should be used to treat chest pain which may be due to coronary artery spasm
- Treat metabolic acidosis/broad complex tachycardia with sodium bicarbonate
- Hyperpyrexia should be treated with benzodiazepines and cooling. Consider dantrolene (1mg/kg to max. 10mg/kg) if temp exceeds 40°C
- Give fluid to maintain good urine output if CK rises

Iron

Serum iron level 4h post ingestion is best indicator of severity (>5mg/L = severe toxicity).

Symptoms/signs

- Nausea and vomiting and abdominal pain are common in 1st 6h.
- Early haematemesis, coma and convulsions, shock, or metabolic acidosis suggest severe poisoning
- Hepatocellular necrosis with hypoglycaemia and encephalopathy occur after 12h.

Management

- Replace lost fluid and blood
- Give desferrioxamine 15mg/kg/h (usual max 80mg/kg/day may be exceeded) if serum iron >350mg/L, >100mg/kg elemental iron ingested, hyperglycaemia, acidosis, or encephalopathy. Continue until urine loses its pink/red colouration, or serum iron<100mg/L
- Whole bowel irrigation or endoscopic removal may be useful if large number of iron tablets ingested.

Methanol

Symptoms/signs

- Ataxia, drowsiness, dysarthria within 30min of ingestion
- Metabolic toxicity due to metabolism to formaldehyde and formic acid occurs 12–24h later: blurred vision (optic disc oedema), extrapyramidal signs, coma, pancreatitis, severe metabolic acidosis (methanol increases anion gap).

Management

- Support airway and ventilation as needed
- Gastric aspiration if within 1h of ingestion (no role for charcoal)
- Monitor vital signs and U&E, LFTs, glucose, amylase, and ABG
- Measure methanol levels
- Treat seizures with phenytoin or lorazepam (exclude hypoglycaemia)
- Specific treatment with ethanol or fomepizole (blocking alcohol dehydrogenase) is indicated if:
  - Plasma methanol conc. >200mg/L at any time
  - Recent history of large ingestion (>10mL) and osmolar gap>10
  - Clinical suspicion of ingestion with Ph <7.3, HCO_3^- <20, osm gap >10
  - *Contact Poisons Information Service for dosing advice*
- Give folinic acid hourly for 48h
- Haemodialysis if methanol conc. >500mg/L, CNS toxicity, acidosis, renal failure, deterioration despite supportive measures. Continue until plasma methanol level is undetectable.

Opiates

Symptoms/signs

- Varying degrees of coma and respiratory depression
- Pupils usually pin-point
- Hypotension, tachycardia, hallucinations, rhabdomyolysis, non-cardiogenic pulmonary oedema.

Management

- Support airway and ventilation if necessary
- Naloxone 0.01mg/kg IV (repeat after 2min if no response), followed by IV infusion if large doses have been required
- Failure to respond to naloxone suggests another CNS depressant drug has been taken, or cerebral damage has already occurred
- Some opioids (i.e. buprenorphine) only partially reversed by naloxone
- If sustained release preparation ingested, consider charcoal
- Monitor for at least 6h after last dose of naloxone
- Methadone has long duration of action—may outlast effects of naloxone—monitor for longer following large overdoses.

Paracetamol

Severe liver damage likely if >250mg/kg ingested (unlikely if <150mg/kg).

Symtpoms/signs

- Initial anorexia and vomiting
- 24–72h—right upper quadrant pain
- 72–96h—vomiting, symptoms of hepatic/renal failure and pancreatitis.

Management

- Activated charcoal if >150mg/kg ingested in last 2h (75mg/kg if high risk—e.g. on drugs inducing liver enzymes, cachexia, CF)
- Take plasma paracetamol levels at 4h (not before)
- Use nomogram (see Fig. 36.1) to determine need for N-acetylcysteine (NAC) therapy (should be started within 8h for maximal effect).
  - If >150mg/kg ingested up to 24h previously—start NAC therapy without waiting for levels
  - NAC dose: 150mg/kg over 15min, 50mg/kg over 5h, then 100mg/kg over 16h (give in 5% dextrose)
  - If anaphylactoid symptoms occur, pause infusion, give antihistamines (steroids if severe). Recommence infusion when symptoms settled
- Recheck INR/PT, creatinine, ALT, glucose and bicarbonate after therapy
- If results abnormal continue NAC infusion at 6mg/kg/hr and discuss with hepatology service. Repeat bloods at least 12-hourly
- Discuss with regional hepatology service if:
  - Acidosis
  - Rising creatinine/oliguria
  - Encephalopathy
  - PT >50s
  - Ingestion >150mg/kg
  - If presenting >15h post ingestion.

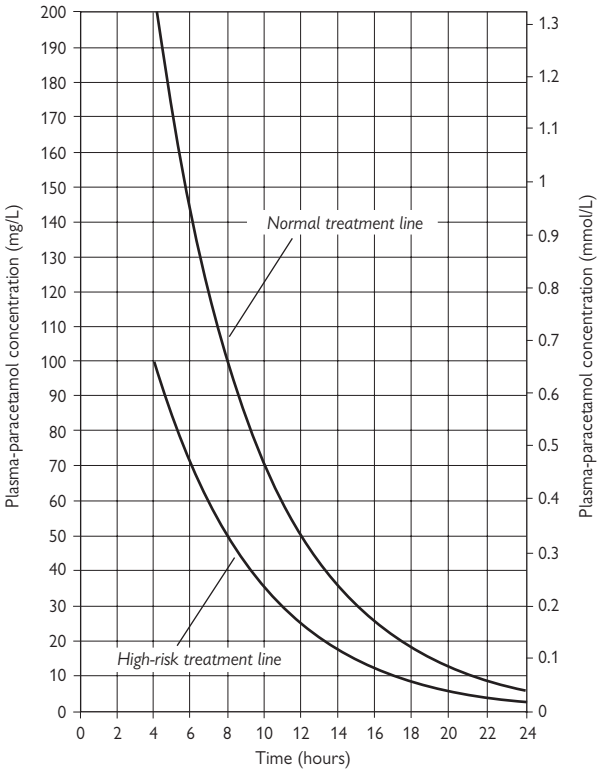

Fig. 36.1 Paracetamol normogram. Patients whose paracetemol levels are above the normal treatment line should be treated with NAC. Patients who are malnourished or who are on liver enzyme-inducing drugs should be treated if the paracetemol levels are above the high risk treatment line. Reproduced from Ramrakha P, Moore K (2004) *Oxford Handbook of Acute Medicine*, 2nd edn. Oxford University Press, Oxford.

Phenytoin

Intervention only required if >20mg/kg ingested.

Symptoms/signs

- Nausea, vomiting, ataxia, nystagmus, divergent gaze, hypotension, respiratory depression usually occurs within 4h
- Bradycardia and hypotension usually only follow rapid IV injection.

Management
- Activated charcoal if within 1h of ingestion (consider repeated doses)
- Check plasma levels. Symptomatic usually >20mg/L; >40mg/L suggest serious toxicity
- Treat hypotension with fluids and inotropes.

Tricyclic antidepressants

Symptoms/signs
Sinus tachycardia, dry mucous membranes, dilated pupils, urinary retention and ileus, ataxia, ↑tone and hyper-reflexia, convulsions, and coma. Prolonged PR, QRS and QT intervals with T-wave changes and AV block.

Management
- Maintain airway and ventilation/oxygenation
- Give activated charcoal if >5mg/kg ingested in last hour (consider 2nd dose)
- Perform ECG—treat arrhythmias with correction of hypoxia and acidosis (with bicarbonate or hyperventilation). Avoid pharmacological therapy. If other measures fail, amiodarone or phenytoin may be useful. Torsades de pointes may respond to slow magnesium infusion
- R-wave >3mm in aVR is 81% specific for development of arrhythmias and seizures
- Correct hypotension with fluid. If pH <7.1, or arrhythmias develop give bicarbonate and maintain pH 7.45–7.5. Hyperventilation to $PaCO_2$ of ~4kPa may be of benefit
- Epinephrine is more effective and less arrhythmogenic than dopamine or norepinephrine. Glucagon may be of benefit
- Control seizures with benzodiazepines
- ECMO may be necessary to support cardiac output.

Newer antidepressants
- Usually do not cause severe symptoms, although can cause bradycardia, hypertension, and junctional rhythms.
- 'Serotonin syndrome' (due to SSRI ingestion) can cause hyperpyrexia, rhabdomyolysis and renal failure
- Treatment is symptomatic.

Environmental poisons

Carbon monoxide
- Acute symptoms include headache, nausea, weakness, angina, dyspnoea, and coma
- Diagnosis is by history and measurement of carboxyhaemoglobin levels—severe symptoms usually if >30%, but levels do not correlate well with neurological outcome
- CO displaces O_2 from haemoglobin and inhibits mitochondrial respiration. There may also be a direct toxic effect on brain tissue.

Management
- Give 100% oxygen (reduces elimination half-life) and support airway and ventilation as needed. (Note: pulse oximetry readings will be inaccurate.)

- If any neurological signs, treat for cerebral oedema/raised ICP
- There is insufficient evidence to support use of hyperbaric oxygen, especially if transport over long distances would be required.

Corrosives

- Cause immediate symptoms of burning in the mouth and throat, retrosternal and abdominal pain, difficulty swallowing and drooling. Airway obstruction may result from laryngeal oedema, haematemesis and shock may occur from oesophageal or gastric injury
- Strong alkalis cause deeper burns and affect the oesophagus more than the stomach
- Strong acids cause more gastric damage.

Management

- Use of milk as a diluent is controversial—avoid large volumes of fluid
- Activated charcoal is contraindicated
- Treatment is supportive
- Urgent airway assessment. Supra/epiglottic erythema is an indication for urgent intubation for airway protection (lack of oral lesions does not exclude oesophageal/gastric injury)
- Perform CXR (preferably erect) for signs of perforation (requires surgery and antibiotics)
- Opiate analgesia for pain
- Treat shock with fluids and blood as appropriate
- Proton pump inhibitors may prevent later strictures (treated with bougienage)
- Early endoscopic evaluation may help define extent of injury.
- Corticosteroids are not recommended.

Hydrocarbons

(E.g. petrol, mineral oil, lamp oil, paint thinners.)

Main problem is aspiration pneumonitis and non-cardiogenic pulmonary oedema.

- Treat is supportive—gastric lavage and charcoal are not indicated
- Inhalation may cause ventricular fibrillation. Initially heart may be sensitized to catecholamines

Lead

Usually causes chronic symptoms, but can cause an acute encephalopathy (whole blood lead >70mcg/dL or >3.4micromol/L)

- Airway support may be necessary due to ↓level of consciousness
- If ingestion of chips is suspected, they may be seen on plain AXR, and polyethylene glycol electrolyte solution may hasten gut transit and reduce absorption.
- Chelating drugs (dimercaprol 4mg/kg IM q4h, followed at least 4h later by $CaNa_2EDTA$ 1000mg/m^2 IV infusion daily) should be used after toxicology advice.

Organophsophates

- Organophosphates come from some insecticides, certain drugs (e.g. malathion) and are a constituent of some nerve gases (e.g. sarin)

- Organophosphate insecticides may come as powders or dissolved in organic solvents. Absorbed through the respiratory and GI tract, as well as through the skin
- Main effect is inhibition of acetylcholinesterase, leading to muscarinic, nicotinic, and CNS symptoms.

Muscarinic

Bradycardia and hypotension, bronchospasm, cough, severe respiratory distress and ↑secretions, hypersalivation, nausea, vomiting, and diarrhoea, abdominal pain, incontinence, blurred vision.

Nicotinic: muscle fasciculation cramp and weakness. Hypertension, tachycardia, mydriasis, and pallor.

CNS: anxiety, confusion, ataxia, seizures and coma.

Management

- Protect healthcare staff from contamination. Remove patient's clothes and wash skin (irrigate eyes with saline if ocular exposure)
- Control airway and ventilation/oxygenation
- 12-lead ECG—magnesium may help ventricular arrhythmias
- Measure RBC (more accurate) and plasma cholinesterase levels
- Repeated high doses of atropine (0.05mg/kg) used to treat tachycardia
- Pralidoxime 30mg/kg IV within first 48h aids reactivation of phosphorylated acetylcholinesterase (not effective once binding is irreversible)
- Repeat dose if needed in 1–2h, then q12h prn if ongoing symptoms.

Paraquat

Selling and use of paraquat was banned in Europe in Sept 2007:

- Ingestion of large quantities causes myocardial depression and pulmonary oedema, with ARF
- Smaller quantities produce vomiting and diarrhoea with painful ulceration of the oropharynx and oesophagus.

Management

- Repeated doses of activated charcoal
- Haemoperfusion, cyclophosphamide and steroids may be of benefit
- Pulmonary fibrosis (develops over days to weeks) is universally fatal.

Plant poisoning

Most are not serious other than certain mushrooms, digitalis containing plants and hemlock.

Mushrooms

- Early GI symptoms usually indicate mild disease
- Muscarinic symptoms (see 📖 p.751) after 6h indicate more serious poisoning.

Management

- Activated charcoal if recent ingestion
- Atropine to treat muscarinic symptoms (bradycardia and bronchospasm)
- Monitor for hypoglycaemia
- NB late hepatotoxicity may rarely occur from certain species.

Digitalis compounds

Oleander, foxglove, lily of the valley:

- Cause nausea, vomiting, diarrhoea, prolonged PR and QRS intervals causing bradycardia. AV block with dissociation and ventricular escape rhythms may occur

Management

- Activated charcoal if <1h of ingestion, or very large ingestion
- 12-lead ECG
- Measure digoxin levels and U&Es (especially potassium)
- Hyperkalaemia may only respond to haemodialysis (dextrose and insulin may be tried. Correct metabolic acidosis; avoid calcium)
- Digoxin-specific Fab antibodies may prevent ventricular arrhythmias (indicated if haemodynamically unstable arrhythmias)
- Arrhythmias—correct electrolytes (especially potassium and magnesium). Atropine (20mcg/kg) may help bradycardia and AV block (repeated doses may be needed)
- Consider magnesium, even with normal serum levels
- Pacing may be needed if these manoeuvres fail.

Hemlock

- Symptoms are acute and nicotinic, followed rhabdomyolysis and bradycardia.

Management

- Activated charcoal/gastric aspiration if recent ingestion
- Otherwise supportive care with ventilation, inotropes and benzodiazepines for seizure management as needed.

Further information

Database of dialysable drugs. Available at http://www.nephrologypharmacy.com/downloads/us_dod_2004.pdf

Environmental toxins and poisons: http://toxnet.nlm.nih.gov

Erickson T, Ahrens W, Aks S, *et al.* (2004). *Pediatric Toxicology: Diagnosis and Management of the Poisoned Child*. McGraw-Hill Medical.

Identification of tablets—TICTAC for Healthcare (CD-Rom). Virtual Health Network: http://tictac.vhn.net/Healthcare/

Klaassen CD (2001). *Toxicology: The Basic Science of Poisons.* McGraw-Hill Medical, New York.

Klaassen CD, Watkins JB (eds) (2003). *Casarett & Doull's Essentials of Toxicology*. McGraw-Hill Medical, New York.

National Poisons Information Service (UK): 0844 892 0111.

Toxbase—clinical information database of the UK poisons information service: www.spib.axl.co.uk

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Chapter 37

Technology-dependent children

Background

- Advances in medicine and technology mean that increasing numbers of children are living with chronic medical conditions and are dependent on technology for long-term survival and quality of life
- In PIC increasing numbers of children are admitted who either end up receiving or are already receiving long-term ventilation
- The principles involved in managing children on long-term ventilation can be applied to other technology-dependent children
- Technology-dependent children have better opportunities and quality of life if they are looked after in a home environment, rather than an acute hospital setting. Once it becomes clear that a child will require continued technological support, the aim should be to get them home with appropriate help for the family as soon as possible.

Long-term technological dependencies

- Ventilation, both invasive and non invasive
- Gastrostomy tubes/feeding pumps
- Suction machines
- Nebulizers
- Dialysis
- IV therapies/feeding
- Oxygen.

Definition of long-term ventilation

'Any child who, when medically stable, continues to require a mechanical aid for breathing, after an acknowledged failure to wean, or a slow wean, three months after the institution of ventilation.[1]

Medical stability is defined by:

- Clinically-based assessment
- Stable airway
- Stable oxygen requirement (generally <40%)
- Acceptable CO_2 levels on ventilation
- Adequate nutritional input
- Other medical conditions are well controlled.

Diagnoses of children that require long-term ventilation

- Spinal injury
- Neuromuscular disease (e.g. spinal muscular atrophy, congenital myopathies, Duchenne muscular dystrophy)
- Infection (e.g. encephalitis or myelitis)
- Congenital brain malformations (e.g. Arnold Chiari, vascular malformations)

- Acquired brain injury.
- Chronic lung disease (e.g. bronchopulmonary dysplasia, cystic fibrosis)
- Airway obstruction (e.g. congenital malformations, craniofacial syndromes, morbid obesity)
- Congenital central hypoventilation syndrome.

Identifying the child who needs long-term support

Children who require invasive long-term ventilation almost always present with an acute problem requiring intensive care and then fail to wean from ventilation. In all cases there should be proper consideration and explicit discussion with the family about whether it is appropriate and in the child's best interest to embark upon or to continue with long-term ventilation. The parents must understand the long-term prognosis and be willing and capable of providing care of the child at home. Once it is decided that a child will receive long-term ventilation, there must be a shift in thinking for both family and staff, from the acute management of a critically ill child, to planning long-term support and maximizing opportunities and quality of life.

Discharge planning and setting up a care package

- Discharge planning is a complex process requiring a multidisciplinary approach. It is best coordinated by a 'case manager' responsible for liaison with all involved disciplines
- A social and healthcare needs assessment should be carried out to help define the level of support that will be required. Setting up a care package can take many months, and if possible the child should be transferred to a transitional care unit during this time
- A care package should provide the family with the support they need to safely look after the child at home. It is likely that the family will need a team of trained carers to help them look after their child. The carers do not necessarily need to have nursing qualifications, but each team should be headed by a qualified paediatric nurse
- Discharge planning should start as soon as it is recognized that a child will require long-term ventilation. The child has to be changed onto a ventilator which can be used long term in a non-hospital environment
- Parents should start the training they require to look after the child's medical needs. Once stable enough, the child can start going out of the unit for short trips. The parents and carers will need to be trained to give them the knowledge and practical skills required to safely look after the child
- The amount of support required varies considerably, and depends on the level of dependency of the child, interventions that they require, parental confidence, and social circumstances. The Barnardo's document 'From Hospital to Home'[2] and the NHS 'UK Children on

Long-term Ventilation' website[3] give detailed information and advice about discharge planning and ongoing support for children receiving long-term ventilation.

Essential skills/training required for carers

(For tracheostomy details, see 📖 p.141 and p.869.)

- Change of tracheostomy tube
- Dealing with decannulation: train for bag and mask ventilation if airway patent above tracheostomy. This can prevent repeated panicked attempts at reinsertion and subsequent damage to tract or formation of false tracts
- Suctioning tracheostomy
- Physiotherapy
- Ventilator settings and troubleshooting problems, battery packs etc.
- NG or gastrostomy tube skills and feeding.
- Resuscitation training.

Equipment

All the equipment needed to safely look after the child at home needs to be obtained. Adequate arrangements must be made for routine servicing and emergency replacement of equipment. For a ventilated child equipment required will include:

- Ventilator(s)
- Oxygen supply (oxygen concentrator)
- Suction machine
- Tracheostomy tubes
- Humidifier
- Batteries
- Pulse oximeter
- Disposables, e.g. ventilator circuits, suction catheters, syringes, gauze etc.
- Travel kit.

Ideal characteristics of a ventilator/other equipment for use at home:

- Robust
- Simple to use
- Quiet
- Reliable
- Mains and battery operated
- Portable (small and light)
- Simple, lightweight circuit
- Requires infrequent servicing.

Managing risk

- Families and professionals have to recognize and accept that there are significant risks involved in looking after a child on long-term ventilation in the community. The risks must be balanced against the benefit to the child of being at home rather than in hospital long term. Risks should be made explicit and managed appropriately
- A full assessment of all risks of relevance to the child, their family, and any carers should be carried out. Whilst risks should be minimized, a balanced approach is necessary to maximize quality of life, educational, social, and developmental opportunities
- A risk assessment of the home should be carried out early in the process of discharge planning. If any home adaptation or re-housing is required this can take a very long time to be arranged.

Financial issues

Care packages can be very expensive, particularly if a number of trained carers are needed to support the family. Relevant funding agencies should be approached at an early stage in order to identify funding. Social, educational, and mobility needs must be addressed in addition to any healthcare needs.

Other needs

The child on long-term ventilation invariably has needs extending beyond their respiratory problems. There should be a multidisciplinary approach to assess all the child's needs and provide support as necessary:

- Nutritional support (nutritionist)
- Posture management (physiotherapy and occupational therapy)
- Communication aids
- Mobility and transport requirements
- Psychological, educational, and social support should all be considered.

Continuing support

Once a child on long-term ventilation has been discharged home, there should be regular medical review, including assessment of the ongoing ventilation requirements. There should be regular, multidisciplinary assessment to make sure that all the child's needs continue to be met. Arrangements should be made for respite care as appropriate, either in the home or an alternative setting. There should be clear plans for the management of any acute deterioration, including open access to hospital admission if necessary. It may be appropriate to set limits to further escalation of therapy, and to develop an explicit 'end of life plan' for those children with life limiting or progressive illnesses.

References

1. Jardine E, Wallis C (1998). Core guidelines for the discharge home of the child on long-term assisted ventilation in the United Kingdom. Thorax **53:** 726–67.
2. Noyes J, Lewis M (2005). From Hospital to Home. Guidance on discharge management and community support for children using long-term ventilation. Barnardos, Barkingside.
3. NHS 'UK Children on Long Term Ventilation' website: http://www.longtermventilation.nhs.uk

Chapter 38

Genetic syndromes

Quick reference to syndromes

Introduction

Table 38.1 includes selected genetic/dysmorphic syndromes that have issues specifically of interest and importance to the paediatric intensivist. All regions of the United Kingdom are covered by Regional Genetics Services. A Clinical Geneticist would be available to provide a clinical opinion on request. If there are any doubts about which blood samples to send for diagnostic tests, please contact your regional genetics laboratory. The British Society of Human Genetics website (www.bshg.org.uk) has a comprehensive list of all the regional genetics services.

Key to abbreviations

ACEI = angiotensin converting enzyme inhibitor
AD = autosomal dominant
AI = aortic incompetence
AoV = aortic valve
AR = autosomal recessive
AS = aortic stenosis
ASD = atrial septal defect
AV = atrioventricular
CDH = congenital diaphragmatic hernia
CMV = cytomegalovirus
CNS = central nervous system
CPVND = congenital polyvalvar nodular dysplasia
CRF = chronic renal failure
DCM = dilated cardiomyopathy
DD = developmental delay
DORV = double outlet right ventricle
FISH = fluorescent *in situ* hybridization
FTT = failure to thrive
HCM = hypertrophic cardiomyopathy
ITP = idiopathic thrombocytopenia
ICP = intracranial pressure
IUGR = intrauterine growth retardation
LD = learning difficulties
MS = mitral stenosis
NIV = non-invasive ventilation
NMBDs = neuromuscular blocking drugs
OA = oesophageal atresia
PS = valvular pulmonary stenosis
PAS = pulmonary artery stenosis
PDA = patent ductus arteriosus
pPS = peripheral pulmonary stenosis
PV = pulmonary valve
PVS = pulmonary vein stenosis
RAS = renal artery stenosis
RDS = respiratory distress syndrome
SIDS = sudden infant death syndrome
TBM = tracheobronchomalacia

TOeF = tracheo-oesophageal fistula
TOF = tetralogy of Fallot
VSD = ventriculoseptal defect
XR = X-linked recessive.

Diagnosis

α = 2–5mL blood in lithium heparin bottle to cytogenetics laboratory
β = 2–5mL blood in EDTA bottle to molecular genetics laboratory

Table 38.1 Genetic syndromes

Syndrome	Clinical components	Dysmorphology	Chromosome or single gene abnormality and testing	Prognosis	PICU specific points
Achondroplasic dwarfism	Small foramen magnum, narrow and flat vertebral bodies, wide intervertebral distances, lumbar lordosis, short ribs, short and bowed long bones.	Short stature, macrocephaly, broad nasal bridge, mid-face hypoplasia, frontal bossing.	AD mutation, mutation in fibroblast growth factor receptor 3 gene. Diagnosis = β. 80% new mutations. Incidence 1:33,000.	Homozygous achondroplasia often lethal in neonatal period. Delayed motor development, normal cognitive development.	Narrow spinal canal, C1/C2 instability can cause spinal injury; care with intubation. Restrictive thoracic cage and narrow upper airways can cause respiratory failure. Hydrocephalus. SIDS more frequent than normal population.
Alagille syndrome (arteriohepatic dysplasia)	Chronic cholestasis. Intrahepatic bile duct paucity (may not be present in infancy). Cardiac anomalies (95%)—TOF, pPS. Renal anomalies. Vertebral arch defects. Eyes—posterior embryotoxon. Small bowel stenosis/atresia.	Prominent forehead, deep-set eyes, straight nose, flattened tip, prominent chin.	AD mutations or JAG1 microdeletions. Diagnosis = β (If negative for mutation can request FISH 20p12). Incidence 1/70,000.	Approximately 10% early mortality caused by cardiac disease or severe liver disease, late mortality by vascular accidents. End stage liver failure (15%).	High risk for bleeding spontaneously and post-surgery. Intracranial haemorrhage reported with and without vascular anomalies. Tracheal and bronchial stenosis may cause ventilation difficulties.

Apert syndrome (acrocephalosyndactyly)	Congenital synostosis of coronal and sagittal sutures causes acrocephaly, mid-face hypoplasia, shallow orbits. Associated cardiovascular (10%) and genitourinary malformations (10%).	Tower-shaped skull, prominent eyes and forehead, high, narrow palate (+/- cleft), syndactyly of fingers and toes.	AD but mostly new mutations in *FGFR2* gene. Diagnosis = β. Incidence 1:65,000.	50% have developmental delay even in absence of raised ICP. < 10% develop hydrocephalus. Optic atrophy and deafness also occur.	May need tracheostomy secondary to midface hypoplasia and choanal stenosis. C5–6 fused in 70% Solid cartilaginous trachea and common origin of carotid arteries are associations. Seizures can cause raised intracranial pressure.
Becker muscular dystrophy	DCM from teenage years. Loss of ambulation in 40s or 50s.		XR mutation in dystrophin gene. Diagnosis = β. Incidence 1/60,000.	Survival to middle age and beyond.	Cardiac and respiratory evaluation prior to surgery (see guidelines[1]). Suxamethonium contraindicated (hyperkalaemia and risk of fatal arrhythmias). Sensitive to non-depolarizing NMBDs (longer time to recovery of motor function).

(*Continued*)

Table 38.1 Genetic syndromes (*Continued*)

Syndrome	Clinical components	Dysmorphology	Chromosome or single gene abnormality and testing	Prognosis	PICU specific points
Beckwith–Wiedemann syndrome	Neonatal hypoglycaemia (pancreatic hyperplasia), polycythemia, poor feeding, large for gestational age, organomegaly, macroglossia, Wilms tumour (7%), hepatoblastoma (10%), hemihypertrophy, omphalocele, umbilical hernia.	Growth parameters above 97th centile, macroglossia, facial naevus flammeus (capillary haemangioma on forehead), face and limb hemi-hypertrophy.	Dominant mutations in an imprinted gene cluster at 11p15. Diagnosis = α & β. Parental β samples. Incidence 1/14000, higher after assisted conception.	96% of tumours present by 8 years. Developmentally normal unless prolonged neonatal hypoglycaemia.	Difficult intubation—macroglossia. Cardiomegaly of infancy usually resolves. Cardiomyopathy very rare but can be severe.
CHARGE syndrome	**C**oloboma (80-90%), **H**eart defects (75%)—TOF, DORV, VSD, ASD, PDA, truncus arteriosus, aortic arch abnormalities, **A**tresia choanae, **R**etardation of growth and/or development, **G**enital defect,	Square face, broad prominent forehead, prominent nasal bridge and columella, flat midface, simple, protruding ears.	AD mutation of *CHD7* gene. Diagnosis α & β. Incidence 1/10,000.	Depends on severity of malformations.	Airway compromise — choanal atresia, TOeF, aspiration pneumonias, TBM, or vascular ring. 60% need tracheostomy. Incoordinate swallow and epiglottic closure cause aspiration pneumonia.

	Ear anomalies and/or deafness, Mondini defect of cochlea or semicircular canals (90%). Cranial nerve dysfunction, TOeF (15%), orofacial cleft, feeding problems, developmental delay ± LD.				
Crouzon syndrome (craniofacial dysostosis)	Premature fusion of coronal, sagittal and lambdoidal sutures, high arched short palate.	Tall, prominent forehead, brachycephaly, hypertelorism, exophthalmos, mid-face hypoplasia.	AD mutation in *FGFR2* gene. Diagnosis = β. Incidence 1/60,000.	High risk of raised ICP with tonsillar herniation. Usually normal development. Corrective cosmetic and neuro-surgery available.	Raised intracranial pressure may occur. May be difficult intubation. Solid cartilaginous trachea and bifid epiglottis are associations.
Cystinosis (3 types: infantile nephropathic, juvenile nephropathic, adult non-nephropathic)	Cystine accumulation in lysosomes. Infantile form—Fanconi syndrome, CRF by 10 years, photophobia, hypothyroidism, diabetes, short stature. Adolescent form: less severe renal disease.	Blond hair, fair skin compared to siblings, corneal crystals.	AR mutations in the gene *CTNS* Diagnosis = β. Fibroblast or leukocyte cystine concentration↑. Incidence 1/100,000.	Untreated infantile form leads to end-stage renal failure by 10 years.	Electrolytes and acid-base problems during intercurrent illness or post-operatively due to Fanconi syndrome. Long term neurological problems, myopathy, inco-ordinate swallow and pancreatic exocrine and endocrine dysfunction.

(*Continued*)

Table 38.1 Genetic syndromes (*Continued*)

Syndrome	Clinical components	Dysmorphology	Chromosome or single gene abnormality and testing	Prognosis	PICU specific points
Down syndrome	Hypotonia, LD, DD, atlanto-axial subluxation, cardiac defects (40–50%)– AV canal defects, Primum ASD, VSD, PDA, TOF. Duodenal atresia, thyroid dysfunction, coeliac disease, leukaemia.	Upslanting palpebral fissures, flat facial profile, epicanthic folds, short nose with depressed nasal bridge, brachycephaly, patent posterior fontanelle.	Trisomy 21 47, +21. Diagnosis = α. Incidence 1/650.	Median survival 49 years. Significant difference in survival between those with and without cardiac defects.	20% have atlanto-axial subluxation—do not hyperextend neck during intubation. Post-extubation stridor common—consider prophylactic dexamethasone prior to extubation. Difficult to sedate.
Duchenne muscular dystrophy	Proximal limb weakness, loss of ambulation between 7–13 years, respiratory failure, cardiomyopathy, deep Q waves and tall R waves on ECG, may have tachycardia, scoliosis, cognitive impairment.	Calf hypertrophy	XR mutation in dystrophin gene. Diagnosis = β. Incidence 1/3000 males.	Without treatment for nocturnal hypoventilation, death can occur within months. Mean life expectancy 25 years with specialist care.	Comprehensive cardiac and respiratory evaluation prior to surgery, high risk of perioperative arrhythmia. Nocturnal NIV commonly used in teenage years. Suxamethonium contraindicated (hyperkalaemia and risk of fatal arrhythmias). Sensitive to non-depolarizing NMBDs (prolonged time to motor recovery).

Edwards syndrome	IUGR, severe DD, cardiac defects (90%)—VSD, ASD, PDA, bicuspid AoV & PV, TOF, DORV, CPVND with regurgitation (95%). Right lung malsegmentation or agenesis, renal anomalies, omphalocoele, spina bifida, facial clefts.	Prominent occiput, simple ears, overriding fingers, nail hypoplasia, rocker-bottom feet.	Trisomy 18 47, +18 Diagnosis = α. Incidence 1/7000. Female:male 3:1.	Median survival 4 days, survival to 1 week 45%, to 6 months 9%, to 1 year 5%.	High index of suspicion if combination of severe IUGR and cardiac defects 70% deaths due to cardiopulmonary arrest. Prone to aspiration and central apnoea.
Ehlers–Danlos syndrome (classical, hypermobile, and kyphoscoliotic types)	Cardiac defects—mitral & tricuspid valve prolapse, aortic root dilatation. Joint hypermobility, kyphoscoliosis, soft skin, easy bruising		Classical type—AD mutations in *COL5A1* and *COL5A2* genes. Kyphoscoliotic type—AR mutations in *PLOD1* gene. Diagnosis made on clinical grounds.		Aortic rupture uncommon but reported in classical and hypermobile types. Poor wound healing. Spontaneous rupture of large arteries, intracranial aneurysms and arteriovenous fistulae may occur rarely with severe classical form.
Ehlers–Danlos syndrome, vascular type	Risk of arterial rupture, dissection or aneurysm. Risk of rupture of bowel, bladder and uterus. Thin, translucent skin, visible veins, easy bruising.	Prominent eyes, thin, pinched nose, thin lips, hollow cheeks.	AD mutations in the gene *COL3A1*.	Average life expectancy 48 years ¼ patients experience severe medical problems by 20 years.	Arteriograms not recommended—risk of vascular injury. Spontaneous pneumothorax in childhood. Arteriovenous carotid-cavernous sinus fistula.

(*Continued*)

Table 38.1 Genetic syndromes (*Continued*)

Syndrome	Clinical components	Dysmorphology	Chromosome or single gene abnormality and testing	Prognosis	PICU specific points
Fanconi anaemia	Aplastic anaemia (median age onset 7yrs), AML, other malignant tumours, FTT, cardiac defects—ASD, VSD. Renal abnormalities (25%), radial abnormalities, LD.	Ragged café-au-lait patches, generalized hyperpigmentation. Microcephaly, thumb anomalies.	6 genes known. AR. Store DNA (β). Incidence 1/100,000.	Average life expectancy 20 years.	Bleeding diathesis, intracranial tumours, ↑risk of infection.
Fetal alcohol syndrome	Microcephaly, IUGR, cleft lip and palate, DD, LD, cardiac defects, renal anomalies, behavioural and cognitive deficits.	Flat midface, short palpebral fissures, long, flattened philtrum, thin vermillion of upper lip.	Not genetic, caused by excessive alcohol intake in pregnancy.	Dependent on severity of cardiac defects.	Features of ethanol withdrawal are abdominal distention, opisthotonos, ↑muscle tonicity, tremors and convulsions
Holt–Oram syndrome	Upper limb skeletal defects—abnormal carpal bone (100%), phocomelia, radial ray anomalies, congenital heart disease (95%)—ASD, VSD, mitral valve prolapse, cardiac conduction defects.		AD mutations in the gene *TBX5*. Diagnosis = β. Incidence 1/100,000.	Depends on severity of heart defect and/or cardiac conduction defects.	Neonatal sinus bradycardia or 1st degree AV block. Can progress to 3rd degree block +/- atrial fibrillation. Risk of congestive heart failure, pulmonary hypertension and infective endocarditis.

Homocystinuria	Long limbs, thin habitus, lens dislocation/severe myopia, pectus excavatum, LD, scoliosis, thromboses—cerebral, lung and kidney.	Marfanoid appearance, blue eyes, fair hair/skin.	AR mutations in the gene *CBS*. Diagnosis = β. Incidence varies worldwide, average 1/100,000.	↑mortality due to thrombotic events.	Avoid surgery if possible (increase in plasma homocystine increases risk of thromboembolism). If surgery required hyperhydrate with extra 50% iv fluids until taking oral fluids.
Hunter syndrome 2 forms: IIA (severe) and IIB (mild)	Cardiac defects—AS, MS, cardiomegaly. Hepatosplenomegaly, scoliosis, short stature, progressive neurological degeneration, hydrocephalus, characteristic radiological changes of skull, ribs, vertebrae, clavicles.	Progressive coarse facial features. Macroglossia.	XR mutation in the gene *IDS2*. Diagnosis = β.	Onset 2-4 years of age in IIA. Death before age 15 in IIA. Survival to 20s-60s in IIB.	Potential difficult intubation—macroglossia. Cervical cord compression, hydrocephalus, TBM, obstructive sleep apnoea—may need NIV.
Hurler syndrome MPS I (severe type)	LD, umbilical & inguinal hernias, hepatosplenomegaly, cardiac defects due to infiltrates in valves and myocardium, cardiomyopathy, recurrent respiratory infections, DD.	Macrocephaly, frontal bossing, coarse facies, corneal clouding, macroglossia, prominent sternum, cloudy cornea.	AR mutations in the gene *IDUA*. Diagnosis = β. Incidence 1/100,000.	Onset 1–2 years. Death between 6–10 years from cardiorespiratory failure.	Difficult intubation due to laryngeal infiltrates and macrocephaly. Do not hyperextend neck risk of atlanto-occipital instability. Sleep apnoea requires tracheostomy or CPAP. Progressive spinal cord compression & hydrocephalus, congestive heart failure, arrhythmias.

(*Continued*)

Table 38.1 Genetic syndromes (*Continued*)

Syndrome	Clinical components	Dysmorphology	Chromosome or single gene abnormality and testing	Prognosis	PICU specific points
Jeune syndrome (asphyxiating thoracic dystrophy)	Long, narrow thorax, short ribs, short limbs, short stature, cystic kidneys, hepatic & pancreatic fibrosis, post-axial polydactyly.	Long, narrow thorax, short ribs, short limbs, short stature.	Genetically heterogeneous. AR.	Fatal in 70% of cases in infancy due to respiratory insufficiency. Chronic renal failure may develop in childhood.	Pulmonary hypoplasia often compounded by intercurrent infection, e.g. bronchiolitis.
Marfan syndrome	Cardiovascular defects—mitral valve prolapse, AI, aortic root dilatation, aortic dissection. Pectus deformity, scoliosis, upward lens subluxation, retinal detachment, myopia, joint hypermobility.	Downslanting palpebral fissures, narrow face, dental overcrowding, high arched palate, arachnodactyly.	AD mutation of *Fibrillin 1* gene. Diagnosis = β. Incidence 1/3000–1/5000.	Untreated Marfan syndrome, life expectancy reduced by 30–40%. Severe neonatal form prognosis extremely poor.	Cardiac complications are the commonest cause of death, specifically dissection of the aorta. Prone to spontaneous pneumothorax.
Myotonic dystrophy	Abnormal swallowing, CDH, neonatal RDS ± prolonged ventilation, LD, diabetes mellitus, cardiac conduction defects.	Myopathic facies, 'tented' mouth, ptosis.	AD expansion in the gene myotonin. Infants often more severely affected than mothers. Diagnosis = β. Incidence 1/8000.	Congenital myotonic dystrophy—neonatal mortality rate 20%, survival to mid 30s 50%. Adult-onset myotonic dystrophy—mean life expectancy 60 years.	Suxamethonium contraindicated (hyperkalaemia and risk of fatal arrhythmias). Suxamethonium and neostigmine also cause myotonia. Local anaesthetics and regional blocks cause prolonged weakness.

Neurofibromatosis type 1 (Von Recklinghausen's disease)	Cardiac anomalies including PS. Vasculopathy causing aortic coarctation, RAS, cerebrovascular stenoses/ occlusion. Scoliosis, CNS and malignant tumours, mild to moderate LD, short stature.	Coarse facial features, café-au-lait spots, neurofibromata, axillary/inguinal freckling, relative macrocephaly.	AD mutations in the gene *neurofibromin*. Usually clinical diagnosis. Diagnosis = β. Incidence 1/2500.	Average life expectancy reduced by 15 years. Malignancy, especially malignant peripheral nerve sheath tumors, and vasculopathy are causes of early death.	Aqueduct stenosis is rare but well recognized in infancy. Hypertension secondary to phaeochromocytoma or RAS (caution with ACEI). Difficult intubation—severe plexiform neurofibromata of head/neck.
Noonan syndrome	Cardiac defects (50-80%)—PVS, pPS, ASD, VSD, TOF, coarctation aorta, HCM (20%). Bleeding diathesis, lymphatic anomalies, pectus excavatum/ carinatum, short stature, male cryptorchidism, risk of leukaemia and myeloproliferative disorders.	Tall forehead, hypertelorism, low-set ears, short upturned nose, heavy eyelids or ptosis, epicanthic folds, short neck.	Heterogenous—4 genes known. AD mutations in the gene *PTPN11* (50%). Diagnosis = α & β. Incidence 1/2000.	↑risk of death from HCM and malignancy.	Clotting factor deficiencies common—coagulation screen prior to surgery. Prone to chylothorax.
Osteogenesis imperfecta	4 types. Defective production of collagen and pro-collagen. Poor fetal ossification, multiple fractures. Hypotonia, hypermobile joints, atrophic skin, sclera may be white or blue, deafness. Skull vault—poorly ossified with wormian bones and wide sutures. Ground glass appearance of bones on X-ray.	Stunted and deformed growth due to fractures.	AD mutation of *COL1A1* or *COL1A2* gene. Type II usually new mutation.	Type II usually lethal in neonatal period. Premature death from pneumonia secondary to chest wall deformity common. Usually normal intelligence.	Extreme care with handling and care when intubating. Ensure adequate analgesia. CNS haemorrhage may occur. May be confused with non-accidental injury (fractures and bleeding).

(*Continued*)

Table 38.1 Genetic syndromes (*Continued*)

Syndrome	Clinical components	Dysmorphology	Chromosome or single gene abnormality and testing	Prognosis	PICU specific points
Patau syndrome	IUGR, severe DD. Holoprosencephaly, seizures, cleft lip/ palate, cardiac defects (80%)—VSD, ASD, PDA, bicuspid AoV & PV. Encephalocoele, omphalocoele.	Facial cleft, microphthalmos, postaxial polydactyly.	Trisomy 13 47, +13. Diagnosis = α. Incidence 1/6000.	Median survival 7–10 days. 5–10% survive to 1 year.	High index of suspicion if a combination of IUGR, dysmorphology and cardiac defects. Prone to aspiration and central apnoea.
Pierre Robin sequence	Micrognathia, cleft palate, upper airway obstruction.	Micrognathia, other dysmorphic features depend on underlying diagnosis/cause.	Pierre Robin sequence is not a diagnosis; consider Stickler or 22q11.2 deletion syndromes Incidence 1/8500.	Depends on severity of malformations and underlying diagnosis, plus other associated malformations.	Difficult intubation—micrognathia. Respiratory obstruction—glossoptosis (prone positioning ± nasopharyngeal airway may help, if severe may need tracheostomy).
Pompe disease (severe infantile glycogen storage disease type II)	HCM, congestive cardiac failure, DD, hypotonia, respiratory distress.	Macroglossia.	AR mutations in the gene GAA. Diagnosis = β. Incidence varies with ethnicity.	In severe infantile form, life expectancy up to 1 year without enzyme replacement therapy. Death from cardiorespiratory failure.	Difficult intubation—macroglossia. Risk for tachyarrhythmia and sudden death high. Caution with positive inotropes (digoxin and adrenaline) as they may worsen HCM.

					Respiratory support using CPAP, BiPAP ± tracheostomy.
Spinal muscular atrophy type 0	Arthrogryposis multiplex congenital, diaphragmatic paralysis in first months of life, absent reflexes, progressive swallowing and respiratory failure.		AR mutations in the genes *SMN1* or *IGHMBP2*. Diagnosis = β.	Life expectancy few months.	Close liaison with families for palliative care. May have autonomic nervous system involvement.
Spinal muscular atrophy type I	Proximal muscle weakness, progressive hypotonia, absent reflexes, progressive swallowing and respiratory failure.		AR mutations in the gene *SMN1*. Diagnosis = β. Incidence 1/25,000.	Fatal respiratory failure before 2 years, often before 6 months.	Close liaison with families for palliative care. Increasing use of NIV & invasive ventilation for palliative symptom relief.
Tuberous sclerosis	Hamartomas in brain and skin, renal cysts, renal angiomyolipomata, seizures, LD (50%), cardiac rhabdomyoma.	Facial angiofibromata, forehead plaque, ≥3 hypomelanotic macules, shagreen patch.	AD mutations in the genes *TSC1* or *TSC2*. Diagnosis = β. Incidence 1/10,000.	Usually normal life expectancy.	Seizures can be intractable Raised ICP secondary to giant cell astrocytomas. Cardiac rhabdomyomas may cause outflow tract obstruction or arrhythmia in neonates. Retroperitoneal haemorrhage, intrarenal haemorrhage from renal angiomyolipomata. Pulmonary lymphangiomyomatosis, causing emphysema and pneumothorax (rare).

(*Continued*)

Table 38.1 Genetic syndromes (*Continued*)

Syndrome	Clinical components	Dysmorphology	Chromosome or single gene abnormality and testing	Prognosis	PICU specific points
Turner syndrome	Short stature, congenital lymphoedema, cardiac defects—bicuspid AoV 30%, co-arctation aorta 10%, AS, mitral valve prolapse, VSD, PDA, aortic dilatation. Renal anomalies 60%, ovarian dysgenesis, hypothyroidism.	Short, broad, webbed neck. Low hairline, ptosis, lymphoedema of hands and feet.	Monosomy X 45, XO. Diagnosis = α. Incidence 1/2500.	Reduced life expectancy due to obesity and cardiac disease.	Aortic dissection secondary to co-arctation. Blood loss from bowel telangiectasiae.
VACTERL association	**V**ertebral defects **A**nal atresia **C**ardiac anomalies (80%)—VSD, TOF **T**oeF O**E**sophageal atresia **R**enal anomalies (80%) **L**imb defects	Radial ray defects in upper limbs only, facial asymmetry.	No known chromosomal or single gene cause. Check chromosomes and store DNA (α & β). Incidence 0.16/1000	Depends on severity of malformations.	Difficult intubation—short neck due to vertebral anomalies. Respiratory compromise secondary to recurrent aspiration, TBM, TOeF and ectopic bronchus.

Williams syndrome	Cardiac defects (80%); supravalvular & valvar AS (75%); supravalvular PS (25%); pPS RAS, renal anomalies, hypercalcaemia (15%). Hypothyroidism, DD, mild to severe MR, feeding difficulties, FTT, hypotonia.	Full cheeks, periorbital fullness Bulbous nasal tip, long philtrum, wide mouth, small widely spaced teeth, malocclusion.	Hemizygous deletion of chromosome 7q11.23. 46, del 7q11.23. Diagnosis = α. State 'for FISH 7q11.23' on request form. Incidence 1/7500.		Hypercalcaemia. Caution with ACEI (RAS). Any artery may be narrowed. Biventricular cardiac hypertrophy may lead to arrhythmias and sudden death. Hypersensitivity to sound.
22q11.2 deletion syndrome (includes velocardiofacial syndrome, DiGeorge syndrome, Shprintzen syndrome)	Cardiac defects (75%)—truncus arteriosus, aortic arch abnormalities, VSD, TOF (20%). Thymic hypoplasia with T cell lymphopenia and immunocompromise, cleft palate /velopharyngeal insufficiency, chronic serous otitis media (75%), hypocalcaemia (60%). Hypothyroidism, OA, TOeF, renal anomalies.	Subtle dysmorphic features. Small mouth, prominent nasal bridge and root, short palpebral fissures.	Hemizygous deletion of chromosome 22q11. 46, del 22q11.2 Diagnosis = α, request FISH 22q11.2. Incidence 1/4000.	92% survival to 6 months. Severe congenital heart defects account for majority of deaths.	All blood products must be CMV negative and irradiated. Hypocalcaemia can lead to neonatal seizures. Anomalies of the internal carotid arteries and other major neck arteries are frequent. Mild thrombocytopenia is common, autoimmune haemolytic anaemia and ITP occasional.

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Further information

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Free, National Institutes of Health funded medical genetics information resource developed for physicians and other healthcare providers. Regularly updated reviews of single gene disorders authored by experts in the field, including management of syndromes. www.geneclinics.org

Chapter 39

Paediatric intensive care medicine in the developing world

Introduction

- PICM is still in its infancy in much of the developing world
- Childhood undernutrition (estimated as an underlying cause in 35% of all deaths among children <5 years) and the global HIV pandemic are some of the particular challenges faced in PICM
- The United Nations' Millennium Development Goal 4 is to reduce the global under-5 mortality rate by 2/3 by 2015. Achieving this goal requires substantial strengthening of health systems in low-income countries. Emergency and critical care services are often one of the weakest aspects of the health system and improving such care has the potential to significantly reduce mortality.

Available data for the profile of patients managed in the PICUs of the developing and developed countries highlight significant differences—developed world PICUs have a significantly higher population of postoperative children compared to those in developing countries (Table 39.1).

Some of the major differences between developing and developed world PICUs are as follows:

- Limited availability of technology: monitoring, equipment, therapy, laboratory support
- Inadequate number and/or inadequately trained staff: nursing, medical, and support staff.
- Limited availability of medications and support services:
  - Many drugs are not available or are simply too expensive
  - IV fluids and oxygen availability can be limited
  - Often blood transfusion is limited
- Inadequate transport facilities: availability of transport with mobile intensive care services has been shown to improve survival of critically ill children. This is often not available especially from a rural health care facility to a city hospital with an ICU
- Delay in care-seeking: this is an important issue in most settings and often leads to greater severity of illness and poor outcomes
- Cost issues: lack of governmental support and limited availability of health insurance schemes means that a substantial part of healthcare cost must be met by the family of the patients. This obviously limits access to more sophisticated intensive care.

Table 39.1 Common diseases/conditions prevalent among patients admitted to PICUs in developing countries

	Asia	Africa	Americas
Infectious diseases	• Malaria • Dengue • Respiratory infections • Diarrhoeal diseases • Sepsis/ shock • HIV • Fulminant hepatic failure	• Malaria • HIV • Respiratory infections • Diarrhoeal diseases • Sepsis/ shock • Fulminant hepatic failure	• Respiratory infections • Sepsis/ shock • Fulminant hepatic failure
Toxin/ evenomation	• Environmental toxins • Snake bites • Scorpion stings	• Environmental toxins • Snake bites • Scorpion stings	• Environmental toxins • Snake bites • Scorpion stings
Other illnesses	• Metabolic disorders • Trauma	• Trauma	• Metabolic disorders • Trauma

Dengue fever, dengue haemorrhagic fever, and dengue shock syndrome

- Dengue fever (DF) is an acute febrile illness caused by viruses belonging to the Flaviridae family and is characterized by biphasic fever, myalgia, arthralgia, and rash
- Dengue haemorrhagic fever (DHF) is characterized by abnormalities in haemostasis and by marked leakage of plasma from the capillaries; the later may lead to shock—dengue shock syndrome (DSS).

Epidemiology

- The disease is now endemic in >100 countries in Africa, the Americas, the Eastern Mediterranean, South-east Asia, and the Western Pacific. South-east Asia and the Western Pacific are most seriously affected
- Nearly 2.5 billion people are at risk from dengue. WHO currently estimates there may be 50 million cases of dengue infection worldwide every year. An estimated 500,000 cases of DHF require hospitalization each year, of whom a very large proportion are children.

Aetiology

- DF and DHF are caused by infection due to any of the 4 serotypes of dengue viruses: DENV-1, DENV-2, DENV-3, and DENV-4, respectively
- Dengue viruses are transmitted to humans through the bites of infective female *Aedes* mosquitoes

- DF can occur in all groups including children. Severity of infection depends on:
  - Virus strain-DENV 2 >3 >4 >1 for DHF
  - Age-the condition is more severe in younger children
  - Endemicity-2 or more virus serotypes may be circulating at high level.

Pathophysiology

- The major pathophysiologic changes that determine the severity of disease in DHF and differentiate it from DF are:
  - Plasma leakage from capillary leak
  - Abnormal haemostasis leading to rising haematocrit values, moderate to marked thrombocytopenia and varying degrees of bleeding manifestations
- Endothelial cell dysfunction in dengue virus infection manifests as diffuse increase in capillary permeability
- There is activation of blood clotting and fibrinolytic pathways. Mild disseminated intravascular coagulation, liver injury, and thrombocytopenia together contribute to haemorrhagic tendency.

Clinical manifestations

The clinical manifestations of dengue virus infection vary from asymptomatic to severe life threatening illness—DHF/DSS.

- Some patients with dengue infection have varying degrees of mucosal and cutaneous bleeds with some degree of thrombocytopenia in absence of haemoconcentration or objective evidence of fluid leak. These patients are classified as *DF with unusual bleeding*.
- Typically, after an incubation period of 4–6 days the patients develop abrupt onset of high-grade fever, facial flushing, and headache. Vomiting, abdominal pain, and tender hepatomegaly are seen
- All patients have some haemorrhagic phenomena ranging from petechial spots and bruising to major haemorrhagic symptoms
- Fever may subside after 2–7 days. Prior to the child becoming afebrile, thrombocytopenia and a rise in haematocrit occurs; these features are characteristic of the DHF. At this stage the child may show varying degrees of peripheral circulatory failure, characterized by excessive sweating, restlessness, and cold extremities.
- Patients with shock and bleeding manifestations usually show increasing haematocrit and thrombocytopenia
- Unusual manifestations of DHF/DSS include encephalopathy (hyponatraemia hypoglycaemia), hepatitis, myocardial dysfunction, and glomerulonephritis has been reported.

Grading of DHF

The presence of thrombocytopenia with concurrent haemoconcentration differentiates DHF from DF. On the basis of clinical features, DHF is classified into 4 grades of severity. Grades III and IV define DSS. Table 39.2 shows the classification.

Table 39.2 Grading of DHF

	Clinical features	Bleeding manifestations	Haemodynamic status
Grade I	Fever accompanied by non-specific constitutional symptoms	A positive tourniquet test* and or easy bruising	Tachycardia ± normal BP, pulse pressure
Grade II	Fever accompanied by non-specific constitutional symptoms	Spontaneous bleeding, usually in the form of skin or other haemorrhages	Tachycardia ± normal BP, pulse pressure
Grade III (DSS)	Same as Grade I/II May present with cold peripheries	Spontaneous bleeding may be present	Circulatory failure manifested by a rapid weak pulse, narrowing of pulse pressure, or hypotension, with cold clammy skin and restlessness
Grade IV (DSS)	Same as Grade I/II; may present with cold peripheries May have features suggestive of organ hypoperfusion	Spontaneous bleeding may be present	Profound shock with undetectable blood pressure or peripheral pulse

*An appropriate size BP cuff is applied to the arm and inflated to a point between the systolic and diastolic BP for 5min. The test is positive if there are >20 petechiae per square inch.

Diagnosis

- Diseases which mimic DHF/DSS include meningococcemia, typhoid, leptospirosis, rickettsial infections, other viral haemorrhagic fevers, and, rarely, plague. Occasionally falciparum malaria may manifest with fever and bleeding but is distinguished by the presence of splenomegaly and significant pallor
- During febrile phase the clinical presentation of both DF and DHF are almost the same. Once afebrile, DF patients will recover rapidly but DHF patients continue with illness may rapidly progress to shock.

The following features are useful for making a provisional diagnosis of DHF/DSS:

Clinical criteria

Acute onset high fever, haemorrhagic manifestations (at least a positive tourniquet test), hepatomegaly and shock.

Laboratory criteria

- Thrombocytopenia (platelets count below 100,000/mm^3), haemoconcentration (haematocrit elevated at least 20% above the standard for age, sex, and population baseline or baseline haematocrit)

- 2 clinical observations plus 1 laboratory findings (or at least a rising haematocrit) are sufficient to establish a provisional diagnosis of DHF
- A rise in haematocrit can be documented if the haematocrit is monitored regularly from the early stages of illness. Since patients are likely to present with symptoms suggestive of DHF, a drop in haemoglobin or haematocrit of >20% following volume replacement therapy can be taken as an indication of previous haemoconcentration. In monitoring haematocrit one should bear in mind the possible effects of pre-existing anaemia, severe haemorrhage, or early volume replacement therapy
- Presence of pleural effusion on X-ray film of chest or hypoalbuminaemia provide supportive evidence of capillary leak, the distinguishing feature of DHF. In a patient with suspected DHF, the presence of signs of shock suggests the diagnosis of DSS.

Laboratory investigations

- A patient who has positive viral identification and/or has HI antibody ≥1280 or a positive IgM/ IgG ELISA test in convalescence serum could be labelled as a confirmed case (Table 39.3).

Table 39.3 Diagnostic tests for dengue

Period	Tests
Within first 5 days of onset of fever	Viral isolation from blood (inoculated either in suckling mice or in various tissue cultures)
After defervescence/in convalescent phase	• Serologic tests: • IgM: MAC ELISA; strip test • IgG: Haemagglutination inhibition test; strip test

Treatment (Box 39.1)

The treatment of DF is symptomatic:

- Fever is treated with paracetamol, avoid salicylates and NSAIDs
- For severe vomiting, domperidone 1mg/kg/day in 3 divided doses for 1–2 days may be adequate
- H2-blockers for GI bleed.

In an epidemic setting all patients with DF need regular monitoring by a primary care physician for early detection of DHF:

- Any patient developing cold extremities, restlessness, acute abdominal pain, ↓urine output, bleeding, and haemoconcentration should be admitted in a hospital
- Children with rising haematocrit and thrombocytopenia without clinical symptoms should also be admitted
- Children should be encouraged to improve the oral fluid intake. Electrolyte solutions such as WHO oral rehydration salt solutions may be preferred over plain water.

Box 39.1 Treatment for DHF/DSS

The management discussed here is based on guidelines issued by the WHO:

As there are no specific antiviral medications for dengue infections, oxygen via face mask/nasal cannula, aggressive fluid therapy, and supportive care are the cornerstone of management of DHF and DSS. Early recognition of these conditions is crucial for decreasing the case fatality rates.

Without hypotension

- In the hospital, all children without hypotension (DHF grades I and II) should be given Ringer's lactate or Hartmann's solution infusion at the rate of 7mL/kg over 1h
- After 1h if haematocrit decreases and vital parameters improve, fluid infusion rate should be ↓ to 5mL/kg over next hour and to 3mL/kg/hour for 24–48h
- When the patient is stable as indicated by normal BP, satisfactory oral intake and urine output, the child can be discharged
- If, at 1h the haematocrit is rising and vital parameters do not show improvement, fluid infusion rate is ↑ to 10mL/kg over next hour
- In case of no improvement fluid infusion rate is further ↑ to 15mL/kg over the 3rd hour
- If no improvement is observed in vital parameters and haematocrit at end of 3h, colloids or plasma infusion (10mL/kg) is administered
- Once the haematocrit and vital parameters are stable the infusion rate is gradually reduced and discontinued over 24–48h.

With hypotension

- In children with hypotension Ringer's lactate solution, 10–20mL/kg is infused over 1h
- If BP is unrecordable (DSS grade IV) Ringer's lactate solution is given as a bolus over 5–15min. The bolus may be repeated twice if there is no improvement
- If there is no improvement in vital parameters and haematocrit is rising, colloids 10mL/kg are rapidly infused
- If the haematocrit is falling without improvement in vital parameters, blood is transfused (fresh whole blood 10mL/kg/dose or pack red cell 5mL/kg/dose), presuming that lack of improvement is due to occult blood loss
- Also consider and correct hypoglycaemia, hyponatraemia, hypocalcaemia, acidosis
- Once improvement starts then fluid infusion rate is gradually ↓. In addition to fluids, oxygen should be administered to all patients in shock.

For uncontrolled bleeding in DHF or DSS, the role of plasma or platelet infusion remains unclear. Infusion of fresh frozen plasma and platelet concentrates may be beneficial in patients with disseminated intravascular coagulation.

Monitoring

Close monitoring of the patient is crucial in the first few hours of illness as the DHF may deteriorate rapidly.

- HR, respiratory rate, BP, and pulse pressure should be measured every 30min till the patient is stable and thereafter every 2–4h
- Central venous pressure monitoring is desirable in children who develop hypotension. Difficulties are often encountered in insertion of central lines in critically ill small children
- Laboratory monitoring includes haematocrit measurement every 2h for the first 6h or till stable. Platelet counts may be carried out once a day till it shows a rising trend. Platelet counts are repeated and coagulation studies performed if there is uncontrolled bleeding
- It must be emphasized that infusion rates decrease rapidly in the first 6h following intervention in most uncomplicated cases of DSS and DHF.
- ***Patient can be sent home*** after a minimum of 3 days after recovery from shock if:
  - Afebrile for at least 24h without the use of anti-fever therapy
  - Has return of appetite, good urine output, no respiratory distress, and no ascites, and platelet count is >50,000/mm^3.

Prognosis

- If left untreated, the mortality in patients with DHF or DSS may be as high as 40–50%
- Early recognition of illness and shock with careful monitoring and appropriate fluid therapy alone has resulted in reduction in mortality to 1–5%.

Viral haemorrhagic fevers

Viral haemorrhagic fevers (VHFs) are a group of clinical syndromes characterized by haemorrhagic manifestations. Disseminated intravascular coagulopathy appears to be the common pathogenetic feature of these illnesses. The illnesses can range from mild to life-threatening multisystem disease such as VHF with renal syndrome (HFRS)

- The pathogenic viruses are (see Table 39.4):
  - Flaviviridae family (Kyasanur forest disease, Omsk, dengue, and yellow fever viruses)
  - Bunyaviridae family (Congo, Hantaan, and Rift Valley fever viruses)
  - Arenaviridae family (Junin, Machupo, Guanarito, and Lassa viruses)
  - Filoviridae family (Ebola and Marburg viruses)
- See Box 39.2 for VHF transmission.

Box 39.2 Transmission of haemorrhagic fevers

The dengue viruses, Rift Valley fever virus, and yellow fever virus are transmitted by mosquitoes. Ticks are responsible for transmission of Omsk, Kysanur forest disease and Congo viruses. Human infection may occur from infected animals or materials in case of Junin, Lassa, Marburg, Ebola, and Hanta viruses. Some viruses that cause haemorrhagic fever—Ebola, Marburg, Lassa, and Crimean-Congo haemorrhagic fever viruses—can spread from one person to another. This type of secondary transmission of the virus can occur directly, through close contact with infected people or their body fluids. It can also occur indirectly, through contact with objects contaminated with infected body fluids.

These conditions may be seen in patients with recent travel to the endemic areas.

Clinical features

Table 39.4 summarizes the clinical features of different types of VHFs.

Diagnosis

- There is a need for a high index of suspicion in endemic areas
- In non-endemic areas, histories of recent travel, recent laboratory exposure, or exposure to an earlier case should evoke suspicion of a VHF
- In all VHFs, the virus can be recovered during the early febrile stage; the inoculation being in tissue cultures or animals/insects. The viruses are readily identified by electron microscopy
- Specific complement-fixing and immunofluorescent antibodies appear during convalescence
- Viral RNA may also be detected in blood or tissues using PCRs.

Box 39.3 Precautions with VHF

- Handling blood and other biologic specimens is hazardous and must be performed by specially trained personnel
- For those haemorrhagic fever viruses that can be transmitted from one person to another (Ebola, Marburg, Lassa, and Crimean-Congo haemorrhagic fever viruses), avoiding close physical contact with infected people and their body fluids is the most important way of controlling the spread of disease
- Barrier nursing or infection control techniques include isolating infected individuals and wearing protective clothing. Other infection control recommendations include proper use, disinfection, and disposal of instruments and equipment used in treating or caring for patients with VHF, such as needles and thermometers.

VHF isolation precautions include:

- Isolation of the patient (universal, contact, droplet)
- Wearing protective clothing in the isolation area, in the cleaning and laundry areas and in the laboratory. Wearing a scrub suit, gown, apron, 2 pairs of gloves, mask, headcover, eyewear, and rubber boots

(*Continued*)

Box 39.3 Precautions with VHF (*Continued*)

- Cleaning and disinfecting spills, waste, and reusable equipment safely
- Cleaning and disinfecting soiled linens and laundry safely
- Using safe disposal methods for non-reusable supplies and infectious waste
- Providing information about the risk of VHF transmission to health facility staff. Reinforce use of VHF isolation precautions with all health facility staff.

Differential diagnosis

Mild cases of haemorrhagic fever are similar to many self-limited systemic bacterial or viral infections. In severe cases, the differential diagnoses include typhoid fever, typhus, leptospirosis, or a rickettsial spotted fever.

Management

Box 39.4 Management of VHF

- Attend to ***airway, breathing,*** and ***circulation*** (ABCs) as appropriate
- Ribavirin administered intravenously is effective in reducing mortality in Lassa fever and HFRS
- The principle involved in management of all these diseases, especially haemorrhagic fever with renal syndrome, is meticulous attention to fluid balance:
  - Dehydration should be treated with IV fluids. Haemoconcentration and oliguria should be looked for. If renal failure ensues then it should be treated appropriately. PD may be necessary
- Protein loss and electrolyte abnormalities can occur
- The management of haemorrhage should be individualized. Transfusions of fresh blood and platelets are frequently given. Good results have been reported in a few patients after the administration of clotting factor concentrates
- The efficacy of other modalities like corticosteroids, ε-aminocaproic acid, pressor agents has not been established
- Sedatives should be selected with regard to the possibility of kidney or liver damage.

Prognostic factors

The presence of significant volume depletion, coupled with haemodynamic instability is a poor prognostic sign in patients with VHF infection.

Table 39.4 Viral haemorrhagic fevers

Disease	Virus	Vector	Geographic areas	Incubation period	Clinical features	Case fatality
Crimean-Congo haemorrhagic fever	Congo virus	Ixodid Ticks (*Hyalomma*)	Bulgaria, western Crimea, Rostov-on-Don and Astrakhan regions, Pakistan, Afghanistan, Arabian Peninsula, South Africa, Oman, and southern Russia	3–12 days	Fever, severe headache, myalgia, abdominal pain, anorexia, nausea, and vomiting; erythematous facial or truncal flush and injected conjunctivae; haemorrhagic enanthem on the soft palate and a fine petechial rash on the chest and abdomen Large areas of purpura and bleeding from gums, nose, intestine, lungs, or uterus may be seen. Hepatomegaly in absence of icterus In severe illnesses, CNS symptoms and signs may be seen	2–50%
Kyasanur forest disease	Kysanur forest disease virus	Ticks	Mysore State, India	3–8 days	Severe myalgia, prostration, and bronchiolar involvement; it often presents without haemorrhage but occasionally with severe GI bleeding, bronchopneumonia, acute renal failure and focal liver damage, meningoencephalitis	3–10%

(*Continued*)

Table 39.4 Viral haemorrhagic fevers (*Continued*)

Disease	Virus	Vector	Geographic areas	Incubation period	Clinical features	Case fatality
Omsk haemorrhagic fever	Omsk virus	Ticks	South central Russia and northern Romania	3–8 days	Moderate epistaxis, haematemesis, and a haemorrhagic enanthem but no profuse haemorrhage, bronchopneumonia	1–10%
Rift Valley fever	Rift Valley fever virus	Mosquitoes	North, Central, East, and South Africa, Saudi Arabia, and Yemen	3–6 days	Fever, headache, prostration, myalgia, anorexia, nausea, vomiting, conjunctivitis, and lymphadenopathy, purpura, epistaxis, haematemesis, and melena	~1%
Argentine haemorrhagic fever	Junin virus	Rodent	Argentina	Approx. 7–14 days	Fever, headache, diffuse myalgia, and anorexia, sore throat, dysphagia, cough, oropharyngeal ulcers, nausea, vomiting, diarrhoea, and pains in chest, abdomen, pleuritic chest pain; tourniquet test may be positive Hypovolaemic shock may be accompanied by pleural effusion and renal failure. Respiratory distress (airway obstruction, pleural effusion, or congestive heart failure) Neurologic symptoms, seizures	10–40%
Bolivian haemorrhagic fever	Machupo virus	Rodent	Amazonian Bolivia			
Lassa fever	Lassa virus	Rodent (*Mastomys*)	Nigeria, Sierra Leone, and Liberia			

Marburg disease	Marburg virus	Unknown	Congo Republic, Germany, Yugoslavia Zimbabwe, Kenya, South Africa	4–7 days	Headache, malaise, drowsiness, lumbar myalgia, vomiting, nausea, and diarrhoea. Maculopapular eruption, often haemorrhagic, dark red enanthem on the hard palate, conjunctivitis, and scrotal or labial oedema GI haemorrhage in severe illness Hypotension and coma in severe cases. Disseminated intravascular coagulation and thrombocytopenia are seen in most patients	Marburg disease: 25% Ebola haemorrhagic fever: 50–90%.
Ebola haemorrhagic fever	Ebola virus	Unknown	Northern Zaire and southern Sudan, Uganda and Central and West Africa			
Haemorrhagic fever with renal syndrome	Hanta virus	Rodents (*Apodemus agrarius, Clethrionomys glareolus, Apodemus flavicollis)*	Japan, Korea, Far Eastern Siberia, north and central China, European and Asian Russia, Scandinavia, Czechoslovakia, Romania, Bulgaria, Yugoslavia, and Greece	9–35 days	Fever, petechiae, mild haemorrhagic phenomena, and mild proteinuria Thrombocytopenia, petechiae, and proteinuria Hypotension may follow defervescence Haemoconcentration, ecchymoses, oliguria. Confusion, extreme restlessness. Fatal cases may manifest retroperitoneal oedema and marked haemorrhagic necrosis of the renal medulla	5–10%.

(*Continued*)

Table 39.4 Viral haemorrhagic fevers (*Continued*)

Disease	Virus	Vector	Geographic areas	Incubation period	Clinical features	Case fatality
Yellow fever	Yellow fever virus	Mosquitoes (*Aedes* and *Haemogogus*)	Tropical areas of Africa and the Americas	3–6 days	Abrupt onset. Fever, headache, severe myalgias, diarrhoea, vomiting, severe prostration, conjunctival suffusion, photophobia, cervical and axillary adenopathy, and more rarely splenomegaly or hepatosplenomegaly Papulovesicular lesions involving the soft palate and pulmonary manifestations are frequent during the first stage of the illness. The second stage of the illness is associated with neurological involvement. Haemorrhagic manifestations are similar to those observed with other viral haemorrhagic fevers	<10%

Malaria

- Malaria is caused by protozoan parasites of the genus ***Plasmodium***. 4 species of *Plasmodium* can produce the disease in its various forms: *P. falciparum, P. vivax, P. ovale,* and *P. malaria*
- *P. falciparum* is by far the most serious type of malaria infection
- The disease is due to the parasites' development within the red blood cells (RBCs) (merozoite, trophozoite, schizont). Other stages are important for transmission but they do not contribute to pathogenesis.

Epidemiology:

Malaria is a public health problem in >90 countries. In 2006, there were an estimated 247 million malaria cases among 3.3 billion people at risk causing nearly a million deaths, 85% of these in children >5 years. More than 90% of all malaria cases are in sub-Saharan Africa.

Box 39.5 Pathogenesis of severe falciparum malaria

- Majority of cases of severe complicated malaria are caused by *P. falciparum*. Cytoadherence, rosetting (adhesion of infected RBCs to other RBCs) and clumping (adhesion between infected cells) are the major pathogenetic mechanisms
- Infected RBCs adhere to the endothelium as well as to each other and cause clogging of blood vessels and haemorrhaging
- High cytokine levels induce expression of endothelial adhesins and inflammation makes the endothelia 'stickier'. Adherence and inflammation reinforce each other in an unholy circle causing pathology.

Clinical features

- Complicated malaria is the major cause of mortality in malaria. It includes cerebral malaria, and malaria complicated by shock, acute renal failure (ARF), severe anaemia, acute respiratory distress, hypoglycaemia, and disseminated intravascular coagulation.
- According to the WHO guidelines in a patient with *P. falciparum* asexual parasitaemia and no other obvious cause of their symptoms, the presence of 1 or more of the following clinical or laboratory features indicates severe malaria:

Clinical manifestation: prostration, impaired consciousness, respiratory distress (acidotic breathing), multiple convulsions, circulatory collapse, pulmonary oedema (radiological), abnormal bleeding, jaundice, haemoglobinuria.

Laboratory test: severe anaemia, hypoglycaemia, acidosis, renal impairment, hyperlactataemia, and hyperparasitaemia

All patients with cerebral malaria have fever and impaired sensorium. Generalized seizure, decerebration and other signs of raised ICP are seen in half of the patients. Focal seizure is uncommon. Splenomegaly and anaemia are common.

Diagnosis

Blood smears: thick smear is considered gold standard for diagnosis; it can detect 5–10 parasites/μL of blood, provided at least 100 oil immersion fields are examined. Thin smears are needed for species diagnosis and defining intensity of infection (estimation of parasite count), parasite maturity and monitoring the effect of treatment. Although it is cost-effective, smear examination has disadvantage in being observer dependent and time consuming.

Immunochromatographic tests—rapid diagnostic tests: the tests use a dipstick or cassette format and provide results in 2–10min, and have sensitivity and specificity exceeding 90%. Two of the commercially available tests are *parasite lactate dehydrogenase* (pLDH)—*OptiMal*®, and *Histidine-rich protein 2 of P. falciparum* (PfHRP2)—*Parasight- F*®.

Molecular methods: Parasite nucleic acids can be detected using PCR.

In all suspected cases of severe malaria, a parasitological confirmation of the diagnosis of malaria is recommended. In the absence of or a delay in obtaining parasitological diagnosis, patients should be treated for severe malaria on clinical grounds.

Other investigations: complete blood count, serum chemistry, ABGs, glucose and lactate, and coagulation parameters and D-dimers, are needed to fully characterize complicated malaria. CSF studies and blood cultures may be needed to rule out other infection.

Management of severe malaria

Management of severe malaria comprises 3 main areas:

- Stabilization
- Specific antimalarial drug therapy
- Adjunctive therapy and supportive care.

Stabilization

- Stabilization should begin with ***airway***, ***breathing***, and ***circulation*** particularly in the patient with depressed level of consciousness
- Venous access should be achieved and immediate measurements of blood glucose, haematocrit/haemoglobin, parasitaemia and renal function should be taken.

Drug treatment (Box 39.6)

- Therapy has to be parenteral. IV chloroquine is not recommended due to widespread resistance. Artesunate is the recommended choice in low transmission areas or outside malaria endemic areas
- For children in high transmission areas IV quinine, artesunate, or artemether are recommended as there is insufficient evidence to recommend any of these antimalarial medicines over another for severe malaria (Table 39.5).
- The dosage of artemisinin derivatives does not need adjustment in vital organ dysfunction. With quinine if there is no clinical improvement or the patient remains in ARF the dose should be reduced by 1/3 after 48 h. Dosage adjustment by 1/3 is necessary in patients with hepatic dysfunction.

Box 39.6 Artemesinin vs. quinine

A meta-analysis of 16 RCTs found artemesinin to be only marginally better than quinine. No difference was found in areas where quinine was very sensitive. Parasite clearance was better with artemesinin, but fever clearance was same. No significant difference in adverse effect profile was noted including hypoglycaemia. In cerebral malaria, artemesinin was found to be marginally better, but no significant difference was noted in their coma recovery time. No significant advantage with combined artemesinin and quinine has been found.

Monitoring for response: response to drugs is monitored by examining blood smears daily, until clearance of all trophozoites is obtained. A paradoxical increase in parasite count can be noticed in first 24 hrs. The count should fall after 24 hrs, consider treatment failure if it does not.

Table 39.5 Drugs for management of severe malaria

Drug	Administration
Quinine	20mg salt/kg (loading dose) diluted in 10mL of isotonic fluid/kg by infusion over 4h. Then 12h after the start of loading dose give a maintenance dose of 10mg salt/kg over 2h. This maintenance dose should be repeated every 8h, calculated from beginning of previous infusion, until the patient can swallow; then quinine tablets, 10mg salt/kg 8-hourly to complete a 7-day course of treatment (including both parenteral and oral)*
	If controlled IV infusion cannot be administered then quinine salt can be given in the same dosages by IM injection in the anterior thigh (not in buttock). The dose of quinine should be divided between 2 sites, half the dose in each anterior thigh. If possible, IM quinine should be diluted in normal saline to a concentration of 60–100mg salt/mL*
Artesunate	2.4mg/kg IV, then at 12 and 24h, then 1.2mg/kg daily once a day for total 7 days. If the patient is able to swallow, then the daily dose can be given orally*
Artemether	3.2mg/kg (loading dose) IM, followed by 1.6mg/kg daily for 6 days. If the patient is able to swallow, then the daily dose can be given orally*

*Tetracycline or doxycycline or clindamycin is added to quinine as soon as the patient is able to swallow and should be continued for 7 days.

Supportive care

- Supportive care is critical in determining the outcome. Patients with severe malaria require intensive nursing, in an ICU if possible
- General management includes haemodynamic, respiratory, and neurological monitoring (recording of vital signs, respiratory rate and pattern, coma score)

- Urinary catheter, NG tube, eye care, mouth care. Meticulous attention is paid to fluid balance and hydration and volume status. This includes intake and output chart (to avoid positive fluid balance), urinary catheter and NG tube and monitoring of electrolytes and blood glucose (using rapid stick tests every 4h if possible).

Fluid therapy: fluid therapy is problematic in malaria (Box 39.7). On the one hand it is imperative to resuscitate the patient and keep the circulating volume intact. On the other overhydration may cause or worsen cerebral oedema and pulmonary oedema.

- Hypovolaemia is common in children with severe malaria and metabolic acidosis and there is good evidence to suggest that they respond well to fluid resuscitation
- In hypotension, consider early use of inotropes; avoid overhydration. Fluid requirements should be assessed individually. Always bear in mind that over-aggressive fluid therapy can be harmful
- The volume of antimalarial drugs must be included in the fluid regimen
- Careful and frequent evaluations of signs of hydration, the jugular venous pressure, peripheral perfusion, and urine output should be made. If CVP is elevated (usually because of excessive fluid administration) use IV furosemide.

Box 39.7 IV fluids and malaria

Until relatively recently there was a school of thought that suggested holding back IV fluid resuscitation in emergency rooms and wards in the fear that it may worsen cerebral oedema. Now it is generally accepted that in severe malaria (with metabolic acidosis) IV resuscitation is mandatory. However there is some controversy about which fluid to use. There is some evidence that initial resuscitation with colloids significantly reduces mortality when compared to crystalloids, in children. In fact one study shows a significant mortality reduction with the use of human albumin compared to a gelatine-based solution (gelofusine). The reduction in mortality is thought to be due to the large molecular size of albumin—it is postulated following the capillary leak of malaria albumin is less likely to leak from the circulation to the interstitium and thus does not aggravate cerebral oedema and intracranial pressure. Unfortunately human albumin solution is expensive and is not freely available in many places in the developing world. So far studies are small and further research is necessary in this important area before a major change of practice can be recommended.

Antibiotics: consider early use of antibiotics; Gram-negative sepsis, meningitis, UTI, pneumonia are important complications. The threshold for administering antibiotic treatment should be low in severe malaria. Severe sepsis and severe malaria may coexist and there is diagnostic overlap, particularly in children.

Box 39.8 Cerebral malaria

Coma in cerebral malaria is usually attributed to sequestration of parasites in cerebral circulation and release of inflammatory mediators. However, in a postmortem study performed on Malawian children, 23% did not show sequestration. Some of these children had Reye syndrome, meningitis, liver failure, and cerebral haemorrhage. Raised ICP has been documented in children with cerebral malaria, (unlike in adults). The most likely cause is large biomass of sequestered red blood cells. Mannitol has a limited role and only in severe intracranial hypertension. Supportive management is crucial. Convulsions should be aggressively managed with a benzpdiazepine such as diazepam, midazolam, or lorazepam. Prophylactic anticonvulsants are not recommended. Phenobarbitone should be prescribed with care and avoided without the availability of respiratory support. 5–10% of patients with cerebral malaria have long-term sequel such as ataxia, paresis, hearing/speech/visual defects, developmental delay or behavioural problems.

Respiratory care: metabolic acidosis, severe anaemia, secondary or aspiration pneumonia, and fluid overload are common causes of respiratory distress in malaria. Less frequent, but more difficult to manage is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).

- Patients with acute pulmonary oedema should be nursed in an upright position and given oxygen. Right-sided filling pressures should be reduced according to available treatments; loop diuretics, opiates, venodilators, haemofiltration, or dialysis can all be used if necessary
- Positive pressure ventilation should be started early, if available, in hypoxemic patients. Ventilatory support is also needed for patients for severe shock, deep coma, or brainstem involvement
- Treat secondary pneumonia as indicated (cephalosporins, clindamycin).

Glucose control:

- Hypoglycemia occurs in 10– 20% children and should be suspected in any patient who deteriorates suddenly. Treat with 0.3–0.5g/kg bodyweight of glucose followed with an infusion of 6mg/kg/min using 10% glucose.

Metabolic acidosis:

- Severe metabolic acidosis is common. It has a strong association with outcome. It is a marker of ineffective aerobic respiration.
- It is caused by ↑production of lactate because of sequestration of parasitized RBCs in brain and muscle and associated intracellular hypoxia
- Apart from correction of hypovolaemia and anaemia, no specific treatment is of proven value. For severe metabolic acidosis unresponsive to rehydration, haemofiltration should be started early, if available
- Serial lactate levels are helpful in monitoring response to treatment and prediction of recovery time from coma.

Anemia:
- Anaemia occurs because of erythrocyte destruction, splenic sequestration of non-parasitized erythrocytes, and bone marrow dysfunction (bone marrow suppression, and ineffective erythropoiesis and dyserythropoiesis)
- Role of blood transfusion is controversial, except in patients with very severe anaemia causing circulatory compromise. In children in high transmission settings, blood transfusion is recommended at a haemoglobin level 5g/dL or less (haematocrit <15%). However, the thresholds for blood transfusion are uncertain.

Other complications that need ICU care
- *ARF*: early dialysis is beneficial. In ARF, haemofiltration is associated with a lower mortality, and more rapid correction of biochemical abnormalities compared with PD. There have been no comparative trials of haemodialysis and haemofiltration
- *Bleeding*: secondary to thrombocytopenia and disseminated intravascular coagulation. Treat with fresh blood transfusions (cryoprecipitate, fresh frozen plasma, and platelets if available) and vitamin K
- *Hyponatraemia and hypocalcaemia*
- *Acute haemolysis.*

Other adjunctive therapies

Exchange transfusion, pentoxyphyline, heparin, prostacyclin, low-molecular-weight dextran, iron chelators, anti-TNF antibodies, dichloroacetate, n-acetyl cysteine have been tried with varying success. None of these have an established role.

Outcome
- With adequate treatment, on average it takes about 2.5 days for defervescence of fever, 3.2 days (up to 6 days) to recovery from coma, and 24–72h to get negative smears
- Death occurs in 10–30% cases in spite of adequate drug therapy.
- Poor prognostic signs are: age <3 years., deep coma (GCS ≤5), early onset seizures, signs of decerebration, PCV <20% (Hb <7. 1g/dL), hyperparasitemia >5%, leucocytosis >12,000/cu mm, renal failure, hepatic dysfunction and hypoglycaemia (random blood sugar <2mmol/L).

HIV and the critically ill child in the developing world

(See 🕮 p.544.)
- HIV infection has become an important contributor to childhood morbidity and mortality, especially in many developing countries. The pandemic has undone many of the significant gains in child health
- Increasing numbers of infants and children with HIV infection/AIDS are being admitted to PICUs, a significant proportion of whom will be first diagnosed with HIV infection/ AIDS during their PICU stay

- Most patients are admitted because of respiratory infections and respiratory failure, septic shock, and CNS disorders. As the number of children receiving antiretroviral therapy increases, severe complications of therapy may also become indications for admission into the PICU
- The WHO estimated that >33.2 million persons worldwide were living with HIV infection at the end of 2007; 2.1 million of these were children <15 years of age
- Sub-Saharan Africa accounts for nearly 90% of the world's total population of HIV-infected children. India and Thailand dominate the epidemic in Southeast Asia, with more recent expansion into Vietnam, China, and Cambodia
- Without access to antiretroviral therapy, 20% of vertically infected children will progress to AIDS or death in their 1st year of life and more than half of HIV-infected children will die before their 5th birthday.

Transmission

- Transmission of HIV-1 occurs via sexual contact, parenteral exposure to blood, or vertical transmission from mother to child. The primary route of infection in the paediatric population is vertical transmission, accounting for virtually all new cases in the developed countries
- In many developing countries, where screening of blood donors is not uniform, the risk of transmitting HIV infection via transfusion is still significant.

Respiratory diseases complicating HIV infection

- Acute respiratory failure secondary to *Pneumocystis jiroveci* or bacterial infections is the most important cause of PICU admission. *Pneumocystis* pneumonia is common in HIV infected children with severe immunodeficiency and untreated is universally fatal
- Other causes of respiratory failure are infectious pneumonitis: bacterial, fungal, mycobacterial, and viral infections.

Pneumocystis jiroveci pneumonia

- *Pneumocystis jiroveci* (previously *P. carinii*) pneumonia (PCP) is one of the commonest AIDS-defining illnesses in children in the US and Europe. However, data regarding the incidence of PCP in children in other parts of the world are scarce. The majority of the cases occur between 3rd and 6th months of life
- Untreated, PCP is universally fatal. With the use of appropriate therapy, the mortality decreases to <10%.

Recurrent bacterial infections

- The common pathogens for community-acquired pneumonia in these children are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*. However, in children with severe immunosuppression and in hospital-acquired infections, Gram-negative organisms, such as *Pseudomonas aeruginosa* occur
- Since *Pneumocystis jiroveci* pneumonia cannot be excluded at the outset in most HIV-infected children with severe respiratory infections, co-trimoxazole should be added to broad spectrum antibiotics unless another diagnosis has been definitively made

- The principles of supportive care of HIV-infected children admitted to PICU with severe pneumonia are similar to those in non-HIV-infected children.

Tuberculosis

- HIV infected children are more likely to have extra-pulmonary and disseminated TB
- All HIV-infected children with active TB should receive longer duration of antitubercular therapy. 6–12 months' therapy is preferred.

Gastrointestinal diseases

- A variety of bacterial (*Salmonella, Campylobacter, Mycobacterium avium intracellulare* complex), protozoal (*Giardia, Cryptosporidium, Isospora*, microsporidia), viral (CMV, HSV, rotavirus), and fungal (*Candida*) GI infections can occur leading to severe diarrhoea
- AIDS enteropathy, a syndrome of malabsorption and failure to thrive both occur
- Chronic liver inflammation is relatively common in HIV-infected children although it is important to recognize that several of the antiretroviral drugs such as didanosine, and protease inhibitors may also cause reversible elevation of transaminases
- The principles of management of these conditions are similar to those in non-HIV infected children.

Neurological impairment (more common in the developing world than the developed world), cardiac failure, and nephritic syndrome all occur; whilst the management of these conditions is similar to that in non HIV-infected children; the response rates and outcomes may be poorer.

Diagnosis

Several specific viral diagnostic assays exist: HIV DNA PCR, HIV culture, and HIV p24. All can be used for diagnosis of young infants born to HIV infected mothers. HIV DNA PCR is the preferred virologic assay in developed countries. HIV culture has similar sensitivity to HIV DNA PCR; however, it is more technically complex and expensive, and results are often not available for 2–4 week compared to 2–3 days with PCR. The p24 antigen assay is less sensitive than the other virologic tests.

Box 39.9 Prevention of transmission in the PICU

- The staff in the PICU should always adhere to universal precautions, regardless of the presence or absence of known or suspected HIV infection in their patients. There is greater likelihood of exposure to HIV-contaminated body fluids in the PICU due to the ↑number of invasive procedures
- In case of exposure, the staff should follow the standard guidelines for post-exposure prophylaxis (PEP)
- The majority of HIV exposures will warrant a 2-drug regimen, using 2 nucleoside reverse transcriptase inhibitors (zidovudine and lamivudine or emtricitabine) or one nucleotide reverse transcriptase inhibitor and one nucleoside reverse transcriptase inhibitor (tenofovir and lamivudine or emtricitabine).

Box 39.9 Prevention of transmission in the PICU (*Continued*)

- The US Public Health Service now recommends that expanded PEP regimens be protease inhibitor (PI) based, e.g. using lopinavir/ritonavir (LPV/RTV) or other PIs. Efavirenz may be considered when viral resistance is suspected. (Caution is advised when efavirenz is used in women of childbearing age because of the risk of teratogenicity.)
- PEP should be initiated as soon as possible, preferably within hours rather than days of exposure. If a question exists concerning which antiretroviral drugs to use, or whether to use a basic or expanded regimen, the basic regimen should be started immediately rather than delay PEP administration. PEP should be administered for 4 weeks, if tolerated.

Box 39.10 Antiretroviral therapy and outcome in the developing world

- Decisions about antiretroviral therapy for paediatric HIV-infected patients are based on the magnitude of viral replication (i.e. viral load), CD4 lymphocyte count or percentage, and clinical condition. The WHO has issued guidelines for management of HIV infection in resource limited settings[1]
- In the developed world, the decision to initiate treatment is based on clinical, immunologic, and virologic parameters. In contrast, in resource-limited settings, where access to laboratory tests is limited, the decision to treat may be based only on clinical symptoms
- Availability of antiretroviral therapy has transformed HIV infection from a uniformly fatal condition to a chronic infection, where children can lead a near normal life. The currently available therapy does not eradicate the virus and cure the child; it rather suppresses the virus replication for extended periods of time.
- The 3 main groups of drugs are nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), and PIs. Highly active antiretroviral therapy (HAART) is a combination of 2 NRTIs with a PI or a NNRTI
- Some complications of antiretroviral therapy such as lactic acidosis, severe pancreatitis, and Stevens–Johnson syndrome may require care in PICU. The therapy for these conditions includes discontinuing the offending drug, when possible, and supportive care similar to the care provided for these problems in non-HIV-infected children.

(*Continued*)

Box 39.10 Antiretroviral therapy and outcome in the developing world (*Continued*)

Outcome

There is little published literature on the outcomes after initiation of antiretroviral treatment in critically ill HIV-infected children. In a recently published report from South Africa, it was observed that the majority of HIV-infected children survived to discharge from the PICU, but only half survived to hospital discharge. Limitation of intervention decisions, usually made in PICU, directly influenced short-term survival and the opportunity to commence HAART. Although few critically ill HIV-infected children in developing countries survived to become established on HAART, the long-term outcome of children on HAART remains encouraging.

Reference

1. WHO (2006). Antiretroviral Therapy of HIV Infection in Infants and Children: Towards Universal Access: Recommendations For A Public Health Approach. Available at : http://www.who.int/hiv/pub/guidelines/paediatric020907.pdf

Lyme disease

- Lyme disease is a multisysystem disease caused by *Borrelia burgdorferi (spirochaete)*
- It is a tick-borne infection—*Ixodes scapularis.*

Clinical features

- These can be divided into 3 stages.
  - 1st stage: (3–30 days after a tick bite) skin rash with low grade fever, malaise, fatigue, headache, vomiting, stiff neck and myalgias
  - 2nd stage: (appear within 2–11 weeks of a tick bite) fever, neurological (meningitis, ataxia, cranial neuritis, myelitis) and cardiac (AV block, myopericarditis and left ventricular failure) symptoms predominate
  - 3rd stage: arthritis is the most common finding
- It is in the 2nd stage that a child may need acute care in ICU
- It is important to differentiate Lyme disease from acute rheumatic fever. The neurologic manifestations may be confused with enteroviral or leptospiral meningitis.

Diagnosis

The diagnosis is made on clinical grounds particularly early in the course of illness from appearance of erythaema migrans. Serology and PCR may be useful.

Treatment

- For early, localized Lyme disease, doxycycline, 100mg twice daily for 2–3 weeks is recommended for children >8 years. For younger children, amoxicillin (30–50mg/kg/ day in 3 divided doses) is used. Erthromycin (30–50mg/kg/day in 4 divided doses) is an alternative for penicillin-allergic children. Neurologic complications are best treated with ceftriaxone (75– 100mg/kg/day) for 2 weeks

- Patients with cardiac complications such as 1st- or 2nd-degree AV block are treated with oral antibiotic while those with 3rd-degree block receive ceftriaxone. Temporary pacing may be required.

Prognosis

Excellent particularly, if treated promptly. Small percentage of patients may have chronic musculoskeletal symptoms.

Leptospirosis

- Leptospirosis is an acute systemic infection caused by *Leptospira interrogans*
- The transmission of leptospires occurs after contact with body fluids (often urine) or tissues of infected animals (rodents, dogs) or an exposure to an environment contaminated by leptospires
- Leptospirosis is characterized by the development of vasculitis, endothelial damage, and inflammatory infiltrates composed of monocytic cells, plasma cells, histiocytes, and neutrophils. In addition there is haemolysis, the cause for which is uncertain. Immune-mediated disease has been proposed as one factor influencing the severity of the symptoms.

Clinical features

Anicteric leptospirosis

The great majority of infections caused by leptospires are either subclinical or of mild severity. The differential diagnosis must include common viral infections, such as influenza, dengue, in addition to the bacterial causes of fever of unknown origin, such as typhoid.

Icteric leptospirosis (Weil's syndrome)

- Icteric leptospirosis is a much more severe disease with a rapidly progressive course requiring intensive care. Severe cases often present late in the course of the disease contributing to the high mortality rate (5–15%). Between 5–10% of all patients with leptospirosis may have the icteric form of the disease
- The jaundice occurring in leptospirosis is not associated with hepatocellular necrosis, and liver function returns to normal after recovery. Serum bilirubin levels may be high, and many weeks may be required for normalization. There are moderate rises in transaminase levels, and minor elevation of the alkaline phosphatase level usually occurs
- The complications of severe leptospirosis originate from the multisystemic nature of the disease:
  - ARF occurs in 20–40% of cases. Thrombocytopenia occurs in more than half of cases and is a significant predictor for the development of ARF
  - The severity of respiratory disease is unrelated to the presence of jaundice; the symptoms range from cough, dyspnoea, and haemoptysis to ARDS. Intra-alveolar haemorrhage is common even in the absence of overt pulmonary symptoms and may be severe

enough to cause death. Both alveolar infiltrates and dyspnoea are poor prognostic indicators in severe leptospirosis
- Cardiac involvement in leptospirosis is common but may be underestimated. ECG changes are non specific. Fatal myocarditis has been observed
- Conjunctival suffusion in the presence of scleral icterus is said to be pathognomonic of Weil's disease. Anterior uveitis, either unilateral or bilateral, occurs after recovery from the acute illness in a minority of cases
- Hyponatraemia is commonly observed in severe leptospirosis
- Rare complications include cerebrovascular accidents, rhabdomyolysis, TTP, acute acalculous cholecystitis, Guillain–Barré syndrome, and reactive arthritis.

Diagnosis
- Microscopy of blood is of value only during the first few days of the acute illness, while leptospiremia occurs. Dark-field microscopic examination of body fluids is both insensitive and lacks specificity
- Detection of leptospiral antigens by radioimmunoassay (RIA) could detect 10^4–10^5 leptospires/mL and an enzyme-linked immunosorbent assay (ELISA) method could detect 10^5 leptospires/mL. Leptospira can also be isolated from various body fluids in culture (blood, urine, CSF)
- Most cases of leptospirosis are diagnosed by serology. The reference method is the microscopic agglutination test (MAT), in which patient sera are reacted with live antigen suspensions of leptospiral serovars. Complement fixation tests have generally been replaced by ELISA methods. IgM antibodies become detectable during the first week of illness. PCR has also been developed.

Treatment
- The management of icteric leptospirosis requires PICU admission if available. ECG and BP monitoring are desirable
- Children with prerenal failure can be rehydrated initially while their renal function is observed. Patients with established ARF (with acute tubular necrosis) need some form of renal replacement. Peritoneal dialysis is suitable
- Meticulous attention to fluid and electrolyte balance
- Parenteral aqueous penicillin G, 6–8 million U/ m^2/day in 6 divided doses should be started early in the course of disease. IV tetracycline (10–20mg/kg/day) may be used in older penicillin-allergic children.

Rickettsial infections

The rickettsial diseases comprise of infections caused by micro-organisms of the genera *Rickettsia*. These include endemic and epidemic typhus, Rocky Mountain spotted fever (RMSF), Mediterranean spotted fever, and rickettsial pox, *Orienta* (scrub typhus), *Coxiella* (Q fever), and *Anaplasma* (Ehrlichosis).
- The spotted fever diseases are the most severe, RMSF being the most common in the USA. Less severe forms of tick typhuses occur in Asia, Africa, Europe and Australia

- Vascular injury is pathognomonic of the spotted fevers. Endothelial proliferation and perivascular mononuclear cell infiltration may lead to thrombosis leading to multiorgan injury.

Clinical features

- Rickettsial infections have many common features. Fever, rash (especially in spotted fever and typhus groups rickettsiae), myalgias, headache, and respiratory tract symptoms are most prominent symptoms. Local primary eschars may be seen in spotted fevers
- Rickettsial diseases may become life threatening rapidly:
  - Cardiac involvement: congestive failure and arrhythmias—occur frequently
  - Pulmonary involvement, manifested as auscultatory crackles, abnormal CXR. Impaired gas exchange (altered ABGs) occurs in a 25% of patients
  - Ocular manifestations may be severe in some: retinal oedema, haemorrhage, and retinal artery occlusion
- In RMSF:
  - High grade fever occurs early after a bite of an infected tick
  - Rash appears by 2–3 days; initial lesions are erythematosus macules that blanch on pressure, appear first on wrists and ankles and spreads rapidly
  - Rarely, they progress to extensive skin necrosis. Headache and toxicity are salient features of the illness. Signs of meningoencephalitis are common and children may often be comatose. A few may develop seizures
- Long-term neurologic sequelae occur in severe disease
- The manifestations in epidemic typhus can be severe similar to RMSF, while endemic typhus is less severe.

Diagnosis

- Group-specific antibodies are detectable in serum in patients 7–14 days after the onset of illness. Indirect immunofluorescent antibody assay is recommended in most circumstances. PCR tests are also available. Immunochemical staining and PCR testing of skin biopsy specimen can also help in diagnosis
- Early in the course, the white cell count is normal or low (uncommon in severe bacterial infections). Thrombocytopenia of varying degree occurs in most patients
- Measles and meningococcemia are important differential diagnoses. Other differential diagnoses include leptospirosis, typhoid fever, rubella, infectious mononucleosis, ITP, and TTP.

Treatment and outcome

- As rickettsial diseases, particularly RMSF, can be fulminant, initiation of prompt and specific treatment is essential. Doxycycline is the drug of choice, even in children <8 years old—for children weighing <45kg, the dose is 2mg/kg orally twice daily (oral or IV) for 7–10 days; for older children, 100mg twice daily is recommended
- Thrombocytopenia and coagulopathies are common and may need blood component therapy

- Supportive therapy for extensive endothelial injury and resultant multi-organ dysfunction
- Meticulous attention to fluid and electrolyte balance—hyponatraemia is common
- In severe diseases, the mortality may be up to 10%. Vascular collapse, severe thrombocytopenia, cardiac and renal failure usually precede death. Secondary bacterial infections may also worsen the prognosis.

Aluminum phosphide poisonings

Aluminum phosphide is a solid fumigant pesticide, commonly used for grain preservation. Due to its low cost, free availability and highly toxic nature, it has emerged as a commonly used, self-poisoning agent. Children can ingest the compound accidentally, but often they are the innocent victims.

- On exposure to moisture, aluminum phosphide liberates highly toxic phosphine gas (PH_3). After ingestion of aluminum phosphide tablets, phosphine gas is absorbed throughout the GI tract
- Like cyanide, phosphine produces hypoxia by non-competitive inhibition of cytochrome oxidase at mitochondrial level. Within 24h of ingestion, there are features of severe metabolic acidosis, peripheral capillary leakage, ECG changes and enzymatic evidence of global myocardial injury, depressed left ventricular ejection fraction, and a development of ARDS.

Clinical features

The onset of the symptoms is almost instantaneous:

- ***Mild toxicity***: patient usually has nausea, vomiting, pain abdomen, thirst, headache; these patients usually recover
- ***Moderate to severe poisoning***: this is usually associated with marked symptoms and systemic manifestations which are progressive and invariably fatal: *GI* symptoms; epigastric burning, persistent vomiting usually appear first and are followed by *cardiovascular* symptoms—hypotension, shock, bradycardia or tachycardia, acute congestive heart failure, toxic myocarditis presenting with electrocardiographic abnormalities like ST-T changes, conduction and rhythm disturbances. *Respiratory* symptoms and signs appear later. Headache and dizziness and restlessness without alteration in consciousness are other important features. Oliguric or non-oliguric renal failure may be seen. Few patients may have diarrhoea, jaundice, convulsions, ataxia, paraesthesias, coma and pericarditis
- Death usually occurs within 24h due to acute cardiotoxicity. Other causes of death include ARDS, GI bleeding, metabolic derangements, and hepatic failure.

Diagnosis

- From history or from characteristic blackening of silver nitate, $AgNO_3$ (0.1N) impregnated filter paper by the patient's breath supports the diagnosis.

Management

Box 39.11 Management of aluminum phosphide poisonings

- Since there is no specific antidote, treatment is basically symptomatic and supportive and aimed to maintain organ function until phosphine is excreted from body through lungs and the kidneys
- Measures may be taken to decrease phosphine absorption from the GI tract:
  - Repeated gastric lavage with mild oxidizing agents (e.g., 1:10,000 potassium permanganate) followed by sodium bicarbonate lavage
  - Activated charcoal administered orally followed by a cathartic to increase phosphine excretion
  - H_2 receptor antagonist (IV ranitidine)
  - Liquid paraffin may be administered to increase the excretion of aluminum phosphide and phosphine from the gut. However, ***gastric lavage is contraindicated as more phosphine is released upon contact with water in the stomach.***
- Adequate hydration to maintain a satisfactory urinary output is recommended. IV diuretics may be used if BP is normal
- Other supportive measures include oxygen, treatment of shock with fluids, low dose inotropes (dopamine), IV hydrocortisone, and correction of acidosis. Mechanical ventilation early in the course may be beneficial. IV magnesium sulfate has been used in adults with some benefit; however, paediatric data are not available.

Outcome

- The reported mortality from aluminum phosphide poisoning varies from 37–100%
- The outcome depends on the number and freshness of tablets, presence of shock and presence other prognostic factors—shock not responsive to standard therapy, severe metabolic acidosis, hypoxia, electrolyte imbalance, arrhythmias, aspiration pneumonia and anaemia due to GI bleeding.

Pyrethroid poisoning

- These are commonly used as insecticides, particularly for mosquitoes. Common agents are: allethrin, D-allethrin, pyrethrum, deltamethrin, decamethrin, and permethrin (used for scabies)
- Pyrethrin and pyrethroid act directly on the sodium channels of nerve cell axons, leading to hyperexcitation. Allergic reactions occur.

Clinical features

- ***Dermal exposure:*** tingling and burning sensation, numbness of skin, intense pruritis, allergic dermatitis
- ***Inhalation:*** stuffy nose, nasal discharge, sneezing, throat irritation, wheezing, cough, dyspnoea, chest pain, pulmonary oedema

- ***Eye exposure:*** burning, itching, rarely corneal damage.
- ***Ingestion***: nausea, vomiting, diarrhoea, anorexia, abdominal cramps, dizziness, headache, muscle weakness. Fasciculations, facial dysthesias may occur. Ingestion of large quantity of concentrated formulations may cause hypotension, tachycardia, seizures and coma.

Management

Box 39.12 Management of pyrethroid poisoning

- Attend to ***ABCs***
- As there is no specific antidote, and often the illness is mild, supportive care suffices. In case of skin or eye exposure, water should be used to decontaminate. In case of ingestion, *do not induce vomiting*. Activated charcoal may be used in ingestions
- In children requiring intensive care: give humidified oxygen. Seizures need a prompt control with benzodiazepines. Diphenhydramine may be used for allergic reactions. Inhaled bronchodilators (salbutamol) should be used for bronchospasm.

Kerosene poisoning

- Kerosene is widely used in developing countries for cooking, heating, and lighting
- Data from the developing countries suggest poisonings represent up to 2% of all paediatric hospital admissions and half of all poison admissions in the group <5 years of age
- As kerosene has a low viscosity, most of the manifestations are due to aspiration. Small amounts cause significant pulmonary symptoms
- Respiratory symptoms, as a result of chemical pneumonitis, restlessness, fever, and abdominal distension are common. Convulsions and coma may occur. Radiological changes, which might occur within 1h, include basilar infiltrates, emphysema, pleural effusion, and pneumatocoeles
- In developed countries admission decisions following hydrocarbon exposure have predominantly been based on a 6-h observation period and radiography at 6h. In developing countries, the presence of wheezing, any alteration in consciousness (lethargy or any restlessness), or a rapid respiratory rate for age (RR ≥50/min if age <12 months, ≥40/min if age ≥12 months) at presentation may be used to identify children needing observation and intensive care.

Management

- Symptomatic with ***ABCs*** in unconscious patients. Gastric emptying is contraindicated
- Supportive care is the mainstay of management. Mechanical ventilation may be required. Corticosteroids have no role in treatment
- Mortality ranges from 2–10% and is higher in malnourished children. Prior lavage, hypoxemia at admission, need for ventilation, secondary sepsis and ventilator related complications are associated with poor outcome.

Snake bites

- Out of >3000 species of snakes worldwide only 1/10 are venomous. These belong to 3 major families:
  - Elapidae (cobra, krait, coral snakes)
  - Viperidae (Russel's viper, saw scaled viper, rattle snakes, pit viper)
  - Hydrophiladae (sea snakes)
- Worldwide it is estimated that there are 20,000–90,000 deaths per year from snakebite (11,000 in India alone) mainly in rural areas.

Toxin and pathogenesis

- Snake venom is a complex chemical poison. It contains ~5–15 enzymes and 3–12 non-enzyme proteins and peptides, which exert toxic and lethal effects on various systems
- Viper venom is primarily vasculotoxic. It causes ischaemic local necrosis as thrombosis blocks blood vessels. Systemic absorption of venom occurs via lymphatics and causes consumption coagulopathy (DIC) and bleeding due to direct endothelial damage (Box 39.13)
- Elapid venom is primarily neurotoxic. It acts at peripheral neuromuscular junction causing selective neuromuscular blockade of the muscles of eye, tongue, throat, and chest. Cobra venom causes an antidepolarizing, neuromuscular block of the motor end plate similar to d-tubocurarine. Krait and Sea snake venom producing pre-synaptic neuromuscular block by decreasing the acetylcholine output from the motor nerve endings
- Sea snake venom has a potent myotoxin that leads to muscle necrosis, myoglobinuria, and hyperkalaemia.

Clinical features

Clinical features depends on size and species of snake, number and location of bites, and quantity of venom injected, age and health of victims. About 50% of elapid bites and 30% of viper bites are 'dry bites' with no sequele.

- Snake bite should be considered in any severe pain or swelling of a limb or in any unexplained illness that presents with bleeding or neurological signs
- Pain and swelling are most intense with viper bites and least with krait, so much so that the bite may go unnoticed till neurological signs appear
- It may be difficult to determine the type of snake based on the bite marks. Many venomous species are in possession of >1 set of fangs and non-venomous species can leave just 2 punctures from enlarged teeth, which can appear to be fang-like
- The general signs include vomiting and headache
- Examine for local swelling, and necrosis, ecchymoses. Bleeding may be external from nose, gums, wounds or sores or internal particularly intracranial
- Signs of neurotoxicity: weakness, paresthesia and numbness at bite. Ptosis, diplopia, dysphagia, hyporeflexia, respiratory muscle weakness and paralysis, bulbar palsy, and signs of muscle injury and myalgia

- Cardiac signs are tachycardia and hypotension. Myocardial depression, cardiogenic and/or vasogenic shock and cardiac arrest may be seen in *cobra* bites
- Respiratory symptoms include stridor and signs of respiratory distress from muscle weakness and developing pulmonary oedema/ARDS
- Oliguria and haematuria may be seen. Renal failure can occur from haemolysis and myoglobinuria.

Box 39.13 Coagulopathy

The 20-min whole blood clotting test (20 WBCT) has been adopted as a test for coagulopathy. It is simple to carry out but crucially requires a clean, new and dry test tube. A few mL of fresh venous blood is left undisturbed for 20min, and then gently tilted. If the blood is still liquid this is evidence of coagulopathy and confirms that the biting species is viperine. Cobras or kraits do not cause antihaemostatic symptoms.

Management

Box 39.14 Management of snake bites

The first aid recommended is based around the mnemonic: 'Do it RIGHT.' It consists of:

- ***R*** = Reassure the patient. 70% of all snakebites are from non-venomous species. Only 50% of bites by venomous species actually envenomate the patient
- ***I*** = Immobilize in the same way as a fractured limb. Children can be carried. Use bandages or cloth to hold the splints, not to block the blood supply or apply pressure. Do not apply any compression in the form of tight ligatures
- ***GH*** = Get to Hospital immediately
- ***T*** = Tell the doctor of any systemic symptoms such as ptosis, stridor etc. that manifest on the way to hospital.
- Attend to ***ABCs***
- Give antivenom. (consider giving antihistamines, IV hydrocortisone as pretreatment) as directed
- Supportive ICU care as necessary.

Antisnake venom (ASV) administration criteria

- ASVs and their doses and timings of treatment vary between countries
- ASV should not be used without evidence of systemic envenomation or severe local swelling
- Essentially systemic envenomation will be evident from the 20 WBCT, signs of spontaneous bleeding or by visual recognition of neurological impairment such as ptosis
- Purely local swelling is not grounds for administering ASV.

ASV

In India a polyvalent antivenin, active against the 4 common poisonous snakes in India—cobra, *krait, Russel's viper* and *saw scaled viper (Echis)*, is available in a lyophilized form. Each vial is reconstitution with 10mL of distilled water. On average potency 1mL antiserum neutralizes 0.6mg cobra, 0.45mg krait, 0.6mg Russel's viper, and 0.45mg saw scaled viper venom.

Doses and administration

- Symptomatology is no help as a means of determining severity of envenomation as it is too dynamic and constantly evolving. The initial dose—8–10 vials for both adults and children—is calculated to neutralize the average dose of venom injected. This ensures that the majority of victims should be covered by the initial dose and keeps the cost of ASV to acceptable levels. A maximum ASV dose of around 25 vials may be used. There is no good evidence to suggest children should receive either more ASV because of body mass or less in order to avoid adverse reactions. ASV should be administered over 1h
- Adverse reactions, either anaphylactoid or pyrogenic, have often been identified as reasons not to administer ASV in smaller local hospitals. The fear of these potentially life-threatening reactions has caused reluctance amongst some doctors to treat snakebite. However, if handled early with the primary drug of choice, these reactions are easily surmountable and should not restrict doctors from treating snakebite
- At the first sign of ***any*** of the following: urticaria, itching, fever, shaking chills, nausea, vomiting, diarrhoea, abdominal cramps, tachycardia, hypotension, bronchospasm and angio-oedema *ASV should be discontinued and 0.01mg/kg body weight of 1:1000 adrenaline should be given IM*
- In addition, to provide longer-term protection against anaphylactoid reactions, 100mg of hydrocortisone and 10mg of H1 antihistamine will be administered intravenously. The dose for children is 0.2mg/kg of antihistamine and 2mg/kg of hydrocortisone IV. If after 10–15min the patient's condition has not improved or is worsening, a 2nd dose of adrenaline 1:1000 IM is given. This can be repeated for a 3rd and final occasion but in the vast majority of reactions, 2 doses of adrenaline will be sufficient. Once the patient has recovered, the ASV can be restarted slowly for 10–15min, keeping the patient under close observation. Then the normal drip rate should be resumed
- Pretreatment with antihistamines, IV hydrocortisone, and subcutaneous adrenaline before administering ASV is recommended in some countries (e.g. Australia)
- ASV test doses have been abandoned
- In coagulopathic bites, once the initial dose has been administered over 1h, no further ASV is given for 6h. Perform 20 WBCT test every 6h will determine if additional ASV is required
- In the case of neurotoxic bites, once the 1st dose has been administered, and a neostigmine (anticholinesterase) test given, the victim is closely monitored. If after 1–2h the victim has not improved or has worsened then a 2nd and final dose should be given

- Anticholinesterases may reverse neurological signs in bites due to cobra bites. Neostigmine may be started immediately at the first evidence of neuroparalysis. 5 × IV doses of 0.05mg/ kg are administered every 30min initially. The interval between doses is then gradually increased till neurological recovery occurs. Each dose of neostigmine is preceded by IV dose of atropine (0.02mg/kg).

Supportive care

- Supportive care includes ***analgesics*** for pain, ***antibiotics*** for infection (cover for anaerobic infection), and ***antitetanus*** prophylaxis
- Children with severe envenomation bites need intensive care to manage:
  - Shock- haemodynamic support with fluids and vasoactive drugs may be required.
  - Children with respiratory muscle weakness may require airway protection (intubation) and mechanical ventilation
  - DIC—blood and blood components may be required in children with bleeding manifestations.
  - Neuroparalysis
  - Haemoglobinuria, myoglobinuria, and renal failure.

Other bites and stings

Spiders

- Generally not medically significant
- Rare cytotoxic spider venom may cause local necrosis and occasionally intravascular haemolysis, DIC, and renal failure.
- Rare neurotoxic spider venom may cause autonomic storm with tachycardia, hypertension, salivation, twitching, and psychosis. This may be followed by neurotransmitter depletion and hypotension, muscle weakness, and respiratory failure—management should be similar to scorpion sting and generally supportive.

Ants, bees and wasps

- These may cause anaphylaxis
- See management of anaphylaxis for details (📖 p.32). This should include ***ABCs*** (intubation and ventilation if necessary); IM adrenaline, steroids, antihistamines, and volume expansion if indicated.

Box jellyfish

- Box jellyfish are found in shallow waters of the Indian and Pacific oceans
- Venom is cardio- and neurotoxic and can cause severe tissue necrosis
- Treat as for snakebite: use antivenom (if available) and repeat as necessary
- Supportive care may include cardiac and respiratory support.

Scorpion stings

- Scorpion stings are a major public health problem in many tropical countries. Worldwide, there are about 100,000 cases of scorpion envenomation. Babies and children are at particular risk and have a significant mortality rate from scorpion stings
- Almost all of the 50 lethal scorpions, except the *Hemiscorpius* species, belong to the scorpion family called the *Buthidae* and live in warm, dry regions. The lethal members of the *Buthidae* family include the genera of *Buthus, Parabuthus, Mesobuthus, Tityus, Leiurus, Androctonus,* and *Centruroides*
- Accidental stings are more common during summer months and occurs when scorpions are touched while in their hiding places. Most of the stings occur on the hands and feet.

Pathophysiology

- The venom glands of the scorpion are located on the tail lateral to the tip of the stinger. The potency of the venom varies with the species. Venom deposited via the IV route can cause symptoms within 5min after the injection
- The venom is composed of varying concentrations of neurotoxin, cardiotoxin, nephrotoxin, haemolytic toxin, phosphodiesterases, phospholipases, hyaluronidases, histamine, serotonin, tryptophan, and cytokine releasers. The most potent toxin is the neurotoxin which results in autonomic and neuromuscular overexcitation symptoms, and prevents normal nerve impulse transmissions
- Venom alters voltage-dependent ion channels, opens presynaptic sodium channels, and inhibits calcium dependent potassium channels. This has a direct effect on the gating mechanisms of excitable membranes. It results in release of excessive neurotransmitters such as epinephrine, norepinephrine, acetylcholine, glutamate, and aspartate from sympathetic nerve endings and adrenal medulla, causing initially ***cholinergic storm*** followed by ***adrenergic storm***
- Release of catecholamines results in variety of metabolic changes including glycogenolysis, lipolysis resulting in elevation of serum glucose and free fatty acids depleting cardiac muscle of substrate
- The resulting intense vasoconstriction and ↑myocardial oxygen demand results in myocardial ischaemia
- In Indian scorpion stings cardiac toxicity is much more pronounced, while neurotoxicity is more common in South Africa and USA. Polypeptides of yellow scorpion (*Buthus cosmobuthus* and *Hemiscorpus*) also cause direct local inflammation, skin necrosis, lymphangitis at the site of sting
- Initiation of systemic inflammatory response (SIRS), ↑levels of various cytokines—interleukin-6, IL-1a and NO, α1-antitrypsin—may cause direct tissue injury, acute DIC, blood clotting abnormalities, ALI, and ↑capillary permeability
- While adults are stung more often than children, children are more likely to develop a more rapid progression and ↑severity of symptoms because of their lower body weight.

Clinical features

- For children presenting with scorpion stings, it is important to ascertain the time of envenomation, nature of the incident, description of the scorpion, local and systemic symptoms
- Symptoms may start within 5min and evolve over 30min–6h
- Severe sharp burning pain (without progression) at the sting site, followed by pruritus, erythema, local tissue swelling, and ascending hyperesthesia, is characteristically seen in the Indian subcontinent. The local evidence of a sting may be minimal or absent in as many as 50% of cases of neurotoxic scorpion stings
- Closer proximity of the sting to the head and torso results in a quicker onset of systemic manifestations. They may display disproportionate restlessness, inconsolable crying; uncontrollable jerking of the extremities; and chaotic thrashing, flailing, and writhing combined with contorted facial grimaces
- There are prominent autonomic nervous system signs: sympathetic, parasympathetic signs, or a combination of signs:
  - Symptoms of cholinergic storm, sweating, salivation, vomiting, priapism, fever, shivering, are evident early; between 0–4h after sting (and can last for 6–13h)
  - Manifestations of adrenergic storm, tachycardia, hypertension, myocardial dysfunction, arrhythmias, pulmonary edema, non–cardiogenic pulmonary oedema, appear between 4–48h
  - Common signs include mydriasis, nystagmus, hypersalivation, dysphagia, and restlessness
  - Hypertension is secondary to catecholamine and renin stimulation and can be observed as early as within 5min after the sting; this lasts a few hours. It may be severe enough to cause ventricular failure or hypertensive encephalopathy
  - Initial hypotension is less common. Hypotension and shock occur because of severe LV dysfunction, or because of exhausted catecholamine stores, or profuse loss of fluids from sweating, vomiting, diarrhoea
- The grading of the scorpion envenomations depends on whether the presence and severity of cardiac and neurological signs predominate
- The neurologic signs range from local pain or paresthesia at the sting site to cranial nerve and somatic neuromuscular dysfunction. The sensorium initially is normal. Classic rotary eye movement may result in ptosis and blurred vision. Some patients have mydriasis, tongue fasciculations, dysphagia, dysarthria, and stridor occur secondary to pharyngeal reflex loss or muscle spasm. Convulsions, cerebral infarcts, aphasia, hemiplegic, cerebral haemorrhage can occur as complications of clotting alterations and DIC
- The mode of death is usually via respiratory failure secondary to anaphylaxis, bronchoconstriction, bronchorrhoea, pharyngeal secretions, and/or diaphragmatic paralysis.

Differential diagnoses include botulism, organophosphate toxicity, myasthenia gravis diphtheria, Guillain–Barré syndrome, neuroleptic overdose, sympathomimetic overdose.

Laboratory investigations may show evidence of multiple organ dysfunction.
- Echocardiography may show diffuse global biventricular dysfunction.
- ECG changes are observed in approximately 2/3 of children in the form of sinus tachycardia, QTc prolongation, ST changes, T-wave inversion, ventricular repolarization abnormalities, bundle-branch block, and first-degree block.

Treatment

- Stabilize patients. Attend to ***ABCs***. Use oxygen, ventilation, and IV fluid therapy as necessary
- Monitor closely for respiratory and cardiovascular deterioration
- Give antivenin
- Institution of symptomatic and local treatment.

Local treatment includes use of a negative-pressure extraction device, use of ice bags, analgesics and, if needed, local infiltration of local anaesthetic to reduce pain and to slow the absorption of venom via vasoconstriction, immobilization of the affected part below the level of the heart, calming the child. Sedation may be required in some cases to restrain an agitated child. Diazepam is recommended (antagonizes toxin's ability to stimulate specific ion channel). Long-acting sedatives should be avoided.
- For ***hyperdynamic*** cardiovascular changes, administration of a combination of β-blockers with α-blockers is most effective in reversing this venom-induced effect:
  - Use of prazosin (30mcg/kg/dose) early in children with evidence of autonomic storm has been proven to be beneficial; it suppresses sympathetic outflow and activates venom-inhibited potassium channels. It should not be given as prophylaxis in children when pain is the only symptom
  - Avoid using β-blockers alone because this leads to an unopposed α-adrenergic effect
  - Nitrates can also be used for hypertension and myocardial ischaemia.
  - In children with bradycardia atropine may be useful
- For ***hypodynamic*** cardiovascular changes, a titrated monitored fluid infusion with afterload reduction helps reduce mortality:
  - Prazosin, nifedipine, nitroprusside, hydralazine, or ACE inhibitors all reduce afterload adequately
  - Furosemide can be used for pulmonary oedema in the absence of hypovolaemia
  - Dobutamine is preferable dopamine for the inotropic effect
  - Finally, a pressor such as norepinephrine can be used as a last resort to correct hypotension refractory to fluid therapy
- Role of specific antivenin is not fully established. As the venom reaches its target very rapidly, antivenom is most useful if administered within 30min of sting. However, routine administration has not offered better outcome, irrespective of clinical severity
- Corticosteroids are contraindicated; has been shown to enhance the necrotizing effects of excessive catecholamines on myocardium.

Prognosis

- Mortality rate in children due to scorpion sting has declined from 13% to 3% after prazosin was introduced as the first line of management
- Poor prognostic factors include age <6 years, delay in initiating prazosin therapy, encephalopathy, pulmonary oedema, and arrhythmia
- Dilated cardiomyopathy has been reported among survivors.

Severe malnutrition

- Childhood undernutrition is an underlying cause in an estimated 35% of all deaths among children under 5 and 11% of total global disability adjusted life years (DALYs) lost
- A severely malnourished child (weight for height SD-score <−3 or visible severe wasting) can have many complications which may need intensive care. These include: hypoglycaemia, hypokalaemia, severe infections, dehydration/ shock, and hypothermia.

Hypoglycaemia

- All severely malnourished children are at risk of hypoglycaemia (blood glucose level <54mg/dL or 3mmol/L), hence blood glucose should be measured immediately at admission. If blood glucose cannot be measured, one must assume hypoglycaemia and treat
- For correction of ***symptomatic*** hypoglycaemia, 5mL/kg of 10% glucose (dextrose) should be given intravenously. This should be followed with 50mL of 10% dextrose or sucrose solution by NG tube
- For correction of ***asymptomatic*** hypoglycaemia, 50mL of 10% glucose or sucrose solution (1 rounded teaspoon of sugar in 3½ tablespoons of water) should be given orally or by NG tube followed by the first feed
- Blood glucose levels must be estimated every 30min till the glucose level becomes normal and stabilizes. Once stable, the 2-hourly feeding regimens should be started. Most episodes of symptomatic hypoglycaemia can be prevented by frequent, regular feeds and one must ensure that the child is fed regularly throughout the night
- Hypoglycaemia, hypothermia, and infection generally occur as a triad.

Hypokalaemia

- All severely malnourished children have deficiencies of potassium which may take 2 weeks or more to correct. Severely malnourished children may develop severe hypokalaemia and clinically manifest with weakness of abdominal, skeletal, and even respiratory muscles. This may mimic flaccid paralysis. Electrocardiography may show ST depression, T-wave inversion, and presence of U waves
- If serum potassium is <2mmol/L or <3.5mmol/L with ECG changes, correction should be started at 0.3–0.5mmol/kg/h infusion of potassium chloride in IV fluids, preferably with continuous monitoring of the ECG
- Once severe hypokalaemia is corrected, all severely malnourished children need supplemental potassium orally at 3–4mEq/Kg/day for at least 2 weeks.

Severe infections

- Infection may not produce the classical signs of fever and tachycardia in severely malnourished children. Often instead, severe infection may be associated with hypothermia
- Localizing signs of infection are often absent. The most common sites for infection to occur are the skin, the alimentary tract, the respiratory tract (including the ears, nose, and throat), and the urinary tract
- The majority of the infections and septicaemia are caused by Gram-negative organisms. Therefore, all severely malnourished children should be assumed to have a serious infection on their arrival in hospital.

Dehydration

- Dehydration tends to be over-diagnosed and its severity overestimated in severely malnourished children
- It is also important to recognize the fact that hypovolaemia can coexist with oedema
- Dehydration should be corrected slowly over a period of 12h. Some dehydration can be corrected with oral rehydration solution (ORS)
- IV therapy should be given only for severe dehydration and shock or if the enteral route cannot be used
- Malnourished children with severe dehydration and shock should be treated with IV fluids. Ideally, Ringer's lactate with 5% dextrose should be used as rehydrating fluid
- If not available, Ringer's lactate alone or half normal saline (N/2) with 5% dextrose or can be used. One should ***never*** use 5% dextrose alone
- After providing supplemental oxygen, the rehydrating fluid should be given at a slow infusion rate of 15mL/kg over the first hour with continuous monitoring of pulse rate, volume, respiratory rate, capillary refill time, and urine output.

Septic shock

Management of septic shock in severely malnourished children poses unique challenges. Rapid fluid infusions may cause myocardial failure and pulmonary oedema. This may necessitate slower fluid infusions.

Hypothermia

- All severely malnourished children are at risk of hypothermia due to impairment of thermoregulatory control, lowered metabolic rate, and ↓thermal insulation from body fat
- Children with marasmus, concurrent infections, denuded skin, and infants are at a greater risk
- Hypothermia is diagnosed if the rectal temperature is <35.5°C or 95.9°F or axillary temperature is <35°C or 95°F
- The child should be rewarmed providing heat using radiation (overhead warmer) or conduction (skin contact) or convection (heat convector)
- Rapid rewarming may lead to disequilibrium and should be avoided.

Malnourished children need early nutritional rehabilitation to achieve catch up growth. This is started soon after admission, even as the child is being stabilized.

Conclusion

- Wide prevalence of malnutrition and particular diseases that are specific or commoner in tropical and developing countries such as malaria, dengue, HIV, diarrhoeal diseases, envenomations, and exposure to various toxins contribute significantly to severity of illnesses and poor outcome of childhood illnesses
- This is compounded by limited availability of trained personnel, quality infrastructure for delivery of critical care, and delay in patient arrivals
- All these factors need consideration while planning intensive care services in developing countries.

Further information

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Section 4

Compassionate and family-orientated care

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The child and family in PICU

Play

Play is an essential part of every child's existence. Through it they learn about the world around them, and develop social skills and the confidence to experiment. The majority of children in PICU are sedated to such an extent that they cannot interact with the outside world. However, in those who are awake, play may be utilized to support their development and provide them with the tools to understand what is happening to them. Where available the guidance of play therapists is invaluable. However, basic play and interaction may be facilitated by any staff available.

Preparation for procedures

Many medical procedures are frightening to children because they do not know what to expect and do not understand what is happening to them. Prior to undertaking such interventions a play therapist may provide them with this information and understanding. Common problems such as needle phobia may be overcome.

Normal development

A small number of children spend long periods in PICU. Not surprisingly these children often have complex conditions which make the pursuit of a normal spectrum of childhood activities difficult even when they are at their best. It is therefore vital that the facilitation and encouragement of play forms a key part of their management.

Siblings/other children

The effects of a child being admitted to PICU on family dynamics can be profound, especially where the admission is prolonged. A sick child's sibling may feel sidelined because of the focus on the ill child. The incorporation of activities that involve the whole family can have a positive effect on relationships within the family.

Children in special circumstances

Regular attendees

Children with complex and chronic conditions may be admitted to PICU on repeated occasions, often requiring respiratory support:

- Chronic lung disease
- Congenital airway abnormalities
- Congenital heart disease
- Neuromuscular disease.

Relationships and conflict

The staff on the unit inevitably develop a strong rapport with these patients and their families. In the majority of instances this is harmonious, but can lead to difficulties when the boundaries between friendship and staff–patient relationships become blurred.

In general, a willingness by staff to listen to parental concerns and to modify clinically irrelevant practices will always be appreciated. However, if demands are made for excessive attention or for clinical interventions

to be modified to an unacceptable extent (through act or omission), then positive action must be undertaken. A senior clinician, usually the consultant in charge, must meet with the family, discuss the situation, and agree a set of 'ground rules'. The clarity of such intervention will often resolve a difficult situation. It is important that all such conversations be accurately and contemporaneously recorded in the clinical notes. These records often prove invaluable should later conflict occur.

Clinical issues

This group of children may be advantaged by the medical team's knowledge of their previous medical history, however, it can also generate complacency. Familiarity should not preclude or over hasten the processes of careful history taking and examination that are necessary for assessment.

Adolescents

One must always be mindful that these young people are in transition from childhood to adulthood. The physical and emotional changes they are undergoing often create difficulties in communication and make them acutely prone to embarrassment.

The adolescent's capacity to be regarded as a fully autonomous individual is approaching or has already reached that of an adult. Observation of this autonomy is often complex given that they are still dependent on the support of their parents. Consideration must be given to the fact that fear that can result in a degree of emotional regression.

The 'adult' child

A number of young people over 16 years of age are admitted to PICU because they have conditions that reduce their life expectancy to that of early adulthood or the knowledge of their condition is limited in adult ICU. In either case staff should be aware of the psychological age of the child and act appropriately. Staff should also be aware of the law regarding consent in this age group (this varies between countries).

Ethics in PICU

The resolution of complex moral dilemmas presents some of the greatest challenges in PICU practice. Each particular scenario merits individual examination. However, there are a number of basic principles and underlying themes that will assist in examining difficult cases.

Areas of issue include

- Consent
- Limitation of treatment
- Disagreement in management
- Rationing
- Research.

It is important to note that the following discussions are focused on the ethical rather than the legal issues (see 🕮 Chapter 41). And that any reference to a child's parents should be taken to refer to any individual that has parental responsibility for the child.

Consent

The principle of obtaining informed consent is fundamental to the observation of respect for an individual's autonomy. It is important to appreciate that it is not just secured through the signature of a child or their parent on a consent form, but through a. process where full disclosure occurs. Options in management should be discussed and an agreement to proceed in a particular way should be achieved between the clinical team, the parents, and/or the child. Any documentation simply serves as a record that a consent process has been followed.

Where a child has the capacity to consider the options and make an informed decision they should generally be afforded this opportunity. That is not to say that their family, and, in particular, their parents, should not also be involved. 'Life or death decisions' are thankfully rare and in general children will either be incapacitated by virtue of their condition or too young.

Elective procedures

Consultation must not be rushed. It is vital that those involved in the consent process are given sufficient support and time to fully understand and evaluate the various treatment options.

Emergency procedures

In cases where a child will die if immediate action is not taken it is reasonable to undertake any procedures directed at preventing their demise. Pursuing this course would be considered good medical practice and would be supported should a legal review follow. Once out of the life-threatening situation consent procedures should be followed in the usual way.

Limiting treatment

Perhaps the greatest challenge in modern medicine is the recognition of when to stop? When should the goal change from cure to palliation? In adults this process may be relatively straightforward when it is possible to discuss the situation directly with the patient. Paediatric practice is often more complex, usually fraught with emotion and requires the involvement of the family and the entire clinical team. Children that have always had to live with a disability may not perceive a further limitation in the same light as one who has known no such restrictions.

Futility, No Chance, and No Hope

The concept of futility underpins much practice in this area. 'A futile intervention' is one where the long-term outcome will not be changed in any significant way by that intervention. It may also, inaccurately, be used to describe situations where success is unlikely.

The challenge is that there are no absolute right answers in this area. Every individual's own life experience will lead them to attach certain value to various physical and mental states. Sometimes these values will be attributable to recognized religious or secular beliefs but not always. The challenge to the clinical team is to communicate all of the key information and facilitate a process that allows a decision that is acceptable to

all to be reached. Ethicists often structure their discussions around key principles (Box 40.1).

Box 40.1 Some key principles

- Respect for autonomy (a norm of respecting the decision making capacity of autonomous persons)
- Nonmaleficence (a norm of avoiding the causation of harm)
- Beneficence (a group of norms for providing benefits and balancing benefits against risks and costs)
- Justice (a group of norms for distributing benefits, risks and costs fairly).

These principles provide a good basis for academic discussion. However, a more pragmatic approach for clinical practice considers

- Why?
- When?
- Who?
- How?

Why?

Why should we ever consider withholding or withdrawing certain treatments? On the face of it this is relatively straightforward—if treatment is futile, or so burdensome as to make it unacceptable, or so likely to result in very severe disability, then it may not be in the patient's best interests. Additionally the spectre of limited resources will always cast a shadow over deliberations.

The RCPCH clarifies the situation in its exemplary document on 'Withholding or Withdrawing life sustaining treatment in Children'. It describes 5 scenarios where treatment may become primarily palliative.

Box 40.2 5 scenarios for withholding or withdrawing life sustaining care

- The 'Brain Dead Child'
- The 'Permanent Vegetative State'
- The 'No Chance Situation'; the child has such severe disease that life-sustaining treatment simply delays death without significant alleviation of suffering
- The 'No Purpose Situation'; the child may be able to survive, with treatment, but the degree of physical or mental impairment will be so great that it is unreasonable to expect them to bear it
- The 'Unbearable Situation'; the child/family believe that in the face of progressive and irreversible illness further treatment is more than can be borne.

Scenario 1, brain death, is the most straightforward. It is also the only situation that must be dealt with close to the final fatal event. In Western society the concept of brain death is well established. With explanation, it is understood and accepted by the majority of families. However, the presence of their child, pink, warm and breathing (on the ventilator) can

make acceptance of the facts difficult. In those who either do not grasp, or do not accept, the concept of brain death, ongoing discussion and time will usually resolve the situation.

The child in a *permanent vegetative state* is thankfully rare. Its management falls between that if those in scenario 1 and those in all the others.

Scenarios 3, 4, and 5 are similar. Each requires careful consideration of the child's current condition and a consideration of the options for further treatment. The clinical team and family must work together to decide on what is the best course for the child. In all cases the family must be fully informed. That is to say all of the key facts should be shared with them together with the various options for moving forward, and the expected outcomes associated with those options. The family should be given time to ask any questions they have. Any differences in opinion and understanding of the situation between the clinical team and the family must be explored in order to reach consensus but despite this occasionally fundamental differences in philosophical approach may provide apparently insurmountable barriers. These are often based in religious beliefs. On these occasions the inclusion of an appropriate spiritual adviser may be helpful.

When?

Ideally discussion about limitation of care should take place when the child is not under immediate threat of death. This should allow careful exploration of all the options in a less emotive environment without the fear of rapid enactment which precludes the opportunity of time for reflection. Unfortunately this rarely occurs and discussions often occur when the child is admitted to PICU at a time of crisis. Sadly, this means that these decisions are faced in discussion with an unfamiliar medical team when the emotional status of the family is unlikely to afford optimal objectivity to their deliberations.

With regular attendees, the PICU team may have an opportunity to raise this issue, if appropriate, after the admitting crisis is resolved, but before discharge.

Who?

The process that leads to a decision to limit the clinical intervention offered to a child is not dissimilar to that of consent for a clinical procedure. Nevertheless it must be made clear from the onset that the family are not solely responsible for the decision. Rather, that it is a decision made on the basis of medical advice. This can make the decision easier for the family to live with subsequently.

Given that the expected endpoint of the child's death is both final and irreversible it is vitally important that all interested parties are given an opportunity to contribute to the debate. Discussions will always include the child's parents and their lead consultant. Other consultants, GPs, nurses or Allied Heath Professionals (AHPs) that have worked closely with the child should also be involved. The immediate family may also involve extended family and spiritual advisors. Clearly this could extend to very large numbers of people; however, in practice it does not usually become unmanageable. The goal of the whole process is that all appropriate

views have been aired and considered and that no answerable questions are left unanswered.

How?

Having agreed the best interests of the child would be served by withholding or withdrawing therapy how should one proceed? The clinical goal is now of palliation and of facilitating a 'good death'. Although the focus must be centred upon the child, consideration must also be extended to their family.

The events leading up to a child's death will live with the family for a long time. It is important to revisit the goals of the child and their family. For example, do they want certain relatives to visit before the child dies, or do they want to get home with their child? Clearly it will not be possible in all cases to achieve the stated desires but those that can be achieved in a reasonable time frame should be pursued with vigour.

With these factors in mind the clinical team must agree the mechanism of limitation. Although it may be argued that there is no moral difference between withholding a treatment compared with withdrawing a treatment that has already been started, there can be little doubt that it feels different to those present. The course that is usually the most palatable for all parties is to clearly state that particular therapies would be considered inappropriate and should not be started. Then at a later time when that therapy might be indicated because of the natural progression of their disease, or the advent of an intercurrent clinical event, it is not started. Thus the focus of treatment is wholly upon palliation.

Disagreement

There is a huge variation in the time needed by families to come to terms with the idea that limitation of treatment is appropriate. For a small number an agreement cannot be reached even after repeated discussions. When this occurs it will become necessary to refer to the courts for an appropriate decision. This is a very stressful process for both the family and the medical teams. It is vital that before such proceedings are started that all of the following avenues have been explored:

- Any difference of opinion within the medical team should be explored and if possible resolved
- All avenues of communication between the medical team and the family are exhausted, particularly the involvement of an appropriate spiritual advisor
- The involvement of an ethicist or ethical team
- A second opinion from another hospital should be sought
- An informal discussion with hospital lawyers.

Rationing

In day-to-day practice it is neither practical nor appropriate that the bedside clinician takes a direct role in the rationing of healthcare. Such decisions are more appropriately made at a strategic level.

End of life care

The dying child

You matter because you are you. You matter to the last moment of your life and we will do all we can not only to help you die peacefully but to live until you die.

Dame Cicely Saunders (founder of the hospice movement)

Current practice means that the majority of children that die in tertiary paediatric hospitals do so in PICU (average 5% of admissions). Consequently intensive care staff see more childhood deaths than most other staff. It is the duty of all staff, despite all the difficulties and emotion surrounding the death of a child, to do our utmost to give the dying child and their family as much dignity, compassion, and understanding as we can. Clearly every child and their family are different but some patterns emerge:

Acute presentation in a previously well child

The families of these children will exhibit the behaviour and emotions associated with the loss of a child. Disbelief and anger can be the most difficult of these to deal with. The turmoil of emotion may also significantly depress the individual's ability to absorb and process information. Wherever possible the key is to give these families time to absorb and understand the issues. This is especially important where decisions regarding limitation of treatment need to be addressed.

The child with a pre-existing life limiting condition

Given the central role that such children often have within their families, the death of a child with a chronic illness can have a devastating impact on the family. Consequently their loss may lead to greater changes for the family than those that occur following the sudden death of a previously well child.

Planned The children and families in this group are likely to be known to the unit already. However, it is important to review the wishes of the child and their family in the context of the child's current condition. The child and family will require the support of all the staff involved in care.

Unplanned These can be very difficult cases—especially where clinical opinion suggests that a limitation should be placed on the child's treatment (see 📖 p.824). Essentially the situation may not be dissimilar to that described for the previously well child. Although there is not a legal imperative for the clinical staff to provide treatment that is not considered in the child's best interests, it is best to ensure the family are given an opportunity to come to terms with the situation before a limitation is put on therapies. On occasions this may mean that the child survives the current ICU admission following interventions that are felt inappropriate by the clinical team. It is vital in these circumstances that the issues of appropriate limitation are raised with the family in anticipation of the next admission.

Clinical care

- The focus of care should be to ensure that the child is comfortable and pain free at all times. Where possible they should be moved to a cubical to provide a private environment for the family. Whilst life must continue on the unit it is important that staff try to ensure quiet in surrounding areas
- Hospital/PICU counsellors and chaplaincy staff should be contacted as appropriate to offer advice and support to the family. It is very important that any religious practices that the family wish to be undertaken before death are facilitated.

Withdrawal of advanced support

- Where treatment, such as oxygen, ventilation, or inotropes, are to be withdrawn the family must be adequately prepared. Wherever possible the child should be moved to a private room. If they wish to cuddle their child ask them whether they wish the therapy to be stopped prior to moving the child to their lap or afterward
- If the child is intubated the ventilator should be switched off and the child extubated by the intensivist. Do not maintain some futile therapies whilst withdrawing others. However, analgesic and sedative therapies are not futile and provide palliation and as such should be maintained or adjusted as necessary particularly due to the uncertainty of the duration of the dying process
- Some or all monitoring should be stopped or at least the alarms disabled as they distract and take the focus away from the child. ***It should be explained that it is difficult to predict quite how long it will take for their child to die***
- It is important to note that active euthanasia is illegal. Therefore infusions of paralysing agents must not continue beyond the point of extubation nor should analgesic or sedative agents be ↑ beyond that which is required to maintain the child's comfort (Doctrine of double effect)
- Once the therapy has been stopped and child is settled the staff should seek to provide privacy for the family. This will often mean stepping out of the cubicle or outside the curtains. However the family must not be abandoned and a member of staff should be close at hand at all times should they be required. See Box 40.3.

Box 40.3 Withdrawal of intensive care

- Explain process in detail, especially timeframe
- Provide contact with spiritual/religious advisor
- Provide for privacy
- Allow for prayers and other religious/spiritual practice
- Consider moving child to parent's lap
- Intensivist should withdraw support and turn off machines (extubate)
- Reduce monitoring and disable alarms
- Adjust analgesia and sedation for palliation/comfort
- Staff available at close hand.

Organ donation

(See 🕮 Chapter 35.)

It is important to consider the possibility of organ and tissue donation for all children that die on the ICU. Until recently it was only possible to consider this option for those who had been certified as brain dead. However, many centres now also offer the option of non-heartbeating donation programmes. This may be considered where it is expected that a child will die shortly after ceasing advanced support.

The possibility of donation should not be raised until deliberations are complete and a course is set where the child is expected to die. If the child is eligible to become a donor it is very important that appropriate consideration is given to approaching the family. There is no evidence to suggest that asking a family for their consent for donation is detrimental and it is not possible to predict which families will wish to give their consent. However, there are reports of families who feel they have missed a positive opportunity where they have not been approached (see 🕮 Chapter 35).

Your local transplant coordinator will be able to offer both advice and practical support in this regard.

Premortem considerations

When a child without a definitive diagnosis is expected to die it is vital that all appropriate specialist teams are consulted promptly to establish whether any further investigations may be indicated in order to establish the aetiology. Any tests that may be performed postmortem should be considered and discussed with the family premortem. This is particularly important in young children with conditions that might be genetic in origin, as a positive result will not only provide a form of closure for the family but may also be vital for their future family planning.

Postmortem considerations

Referrals to the Coroner are dealt with elsewhere (🕮 p.839).

It is important to note that the Coroner's role is to estazblish if the death is attributable to natural causes or otherwise. It is not to classify the actual pathophysiological cause of death.

Children who die from explicable pathology, but who have other, possibly associated, medical issues which remain unexplained might be considered for a hospital postmortem. Where the clinical team feel this is appropriate it should be discussed with the child's parents and may only be undertaken with their consent.

Spiritual issues

Some religious groups have strict rules regarding the management of a person's body after death. Where a Coroner's postmortem is required it is not always possible to fully observe this rule. However the Coroner will usually make every effort to minimize disruption of the normal process. It is helpful if the clinical team advises the Coroner of such issues at their earliest opportunity.

After death

When a child dies on the PICU it is important that that all the professionals with responsibilities to the family are promptly notified so that they can appropriately manage their own response. It is also vital that administrative records are appropriately updated in order to ensure that inappropriate letters or appointments are not sent out to the family. Most units will have a check list for this that should include certain individuals (see Box 40.4).

Box 40.4 Checklist

- Coroner (if necessary)
- Child's lead (non-PICU) consultant
- Child's DGH consultant
- Child's GP
- Pathologist (if PM required)
- Police (in case of trauma/suspicious death)
- Child's health visitor
- Family/bereavement counsellor
- Macmillan or specialist nurse.

Guidance for the family

The majority of families will not have dealt with a death before. They will need practical advice with respect to registering the death and making funeral arrangements. Where the coroner is involved the Coroner's office will usually maintain close contact with the family.

Most PICUs will have a booklet available that summarizes the necessary actions on the part of the family and provides a list of useful contact numbers. This may be accompanied by the following (Box 40.5):

Box 40.5 Items and information for family

- Hand/foot prints
- Lock of hair
- Photograph
- Details of Registrar's office
- Hospital/ward telephone numbers
- Death certificate (if available)
- Cremation form (if required)
- Literature from support groups (Brake etc).

Follow-up

Family

- The events surrounding the death of a child will often seem quite a blur to the family. As they begin the process of coming to terms with the loss of their child they will often have a number of questions about the condition, the events surrounding the death, and the decisions that were made at the time; particularly when therapy is withheld or withdrawn

- Parents should be offered support by hospital counselling staff, where available, and offered an opportunity to meet with the lead PICU clinician 6–8 weeks after their child's death to discuss any issues. It is important that the clinicians attending this meeting have reviewed the notes and gathered any outstanding results that may not have been previously available. This meeting will usually be led by the PICU consultant that was responsible for the child's care but it is important that other clinicians involved in care of the child are also involved
- All families whose children die secondary to conditions that may have genetic origins should be referred to the genetics team for advice and counseling regarding further expanding their family.

Staff

The PICU team are often the forgotten ones following the death of a child in their care. In theory, a staff debrief should be undertaken after every death on the unit. In practice this will not always occur and may not be useful in cases such as a short stay after a major trauma. However, where children have been on the unit for some time before their death, or there has been exceptional staff input to try and save their lives it is important to hold a debriefing meeting. This should give all those involved an opportunity to explore their own questions and concerns in an open non-judgemental environment.

Good practice and audit

- All deaths that occur on PICU should be formally reviewed at a mortality meeting. The purpose of this is to promote good practice and reflective learning. Meetings should occur in an objective, neutral, multidisciplinary environment. They should review the process of care without a focus on the actions individual clinicians. They should also be scheduled to enable the maximum number of PICU team members to attend
- Any questions that arise regarding the competency of an individual or a critical failing of the hospital system should not be addressed at these meetings. However, it is vital that these concerns are referred to the appropriate governance structures within the hospital for further examination and action.

Further reading

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Fortune, P-M (2006). Limiting and rationing treatment in paediatric and neonatal intensive care. *Best Pract Res Clin Anaesthesiol* **20:** 577–88.

General Medical Council Guidance: http://www.gmc-uk.org/guidance/current/library/witholding_lifeprolonging_guidance.asp

Royal College of Paediatrics and Child Health (1997). *Withholding or withdrawing life saving treatment in children. A framework for practice.* RCPCH, London.

Aspects of the law in paediatric intensive care

Introduction

Despite the wide range of beliefs, ethics, and opinions that we all hold, everybody involved in the care of children has the same duty of care. This compels us to promote the best interests of the child and to maximize the child's ability to achieve optimal physical, mental, and social health.

Medical decisions or recommendations must be consistent with contemporary ethical reasoning and must be legal. It is absolutely necessary to listen to the child and to take their views into account, even if their wishes cannot always be followed (see 📖 p.837). When their views cannot be ascertained (as is common in PICU with sedated and ventilated children), then the parents are accorded the power to make decisions on their behalf as long as they appear to be acting in the best interests of their child.

This chapter will concentrate mainly on the key areas of the law and how they affect PIC practice law in the United Kingdom (although there will be some differences between England and Wales, and Scotland).

Box 41.1 Key issues in PIC

Human rights
- Rights of the child
- Parental rights.

Consent
- Parental consent
- Treatment refusal/insistence
- Age and Gillick/Fraser competence.

Best interests
- Parental responsibility
- Duty of care of the health professional
- Dispute between clinical team and parents
- Cultural and religious factors.

End of life decisions
- Resuscitation
- Withholding and withdrawing intensive care support.

Confidentiality and disclosure

Child protection

Research

Rights and responsibilities

Rights of the child

- Doctors should act in partnership with the child whenever possible
- The child's view should be heard (Children Act 1989)
- Clinicians should give due weight to the views of the child according to age and maturity (United Nations Convention on the Rights of the Child).

Parental rights

- A parent or legal guardian has the right to make decisions about a procedure on behalf of their child (Children Act 1989). Pragmatically, this is the person who is able to consent for investigation and treatment of a child
- Parental rights do not equate with ownership. Thus parents do not have the right to insist on a doctor doing something that the doctor does not consider to be in the child's best interest. Occasionally a doctor may be forced to act against the parents in the interests of the child.

The Children Act 1989

- The welfare of the child is paramount
- This is usually best achieved by supporting the family
- Social services have a duty to investigate when they believe (with reasonable grounds) that a child is suffering or is at risk of suffering 'significant hardship'.

The Human Rights Act 1998

- Article 2. The right to life
- Article 8. The right to respect private and family life.

Parental responsibility

- This is defined as 'all the rights, duties, powers, responsibilities and authority which by law a parent of a child has in relation to the child and his property'
- The Adoption and Children Act 2002 modified those who are considered to have parental responsibility, with the legal definition varying between different countries in the UK:
  - The mother automatically has parental responsibility
  - For children born after December 2003, both the biological parents named on the birth certificate have parental responsibility
  - Adoptive parents gain parental responsibility through the formal adopting procedure (as the child's biological parents lose it)
  - For children born before the 1 December 2003, both parents have parental responsibility if they were married at the time of conception or afterwards
  - The father can gain parental responsibility by agreement with the mother or through a court order.

Consent

In the UK, consent must be sufficiently informed and requires competence. Children are one group where competence may not be deemed to be present. Those generally recognized to be competent include:

- A person aged >16 years
- An *adolescent* aged <16 years (a *child* <16 years in Scotland) and judged to be competent (Gillick or Fraser competent, see Box 41.2)
- Parents
- Individuals or local authority with parental responsibility
- A court.

Competence

The law does not and cannot set out precise criteria for determining competence in a child aged <16 years. Whether a child has the capacity to consent or not depends on the maturity of the individual and the complexity of the issues to be faced. A comparatively young child may be deemed able to consent to minor procedures such as simple surgery or antibiotic treatment for infection but may not be deemed to have the capacity to consent to risky procedures.

Capacity for competence ultimately depends on the individual's understanding, intelligence, and experience. Criteria may include:

- The individual demonstrates understanding of the nature, purpose, and necessity of the proposed procedure
- Demonstrates understanding of benefits, risks, and potential consequences of not having the treatment
- Understands information applies to him or her and uses this to make a decision
- Decision is made free from pressure.

Assessment of competence is the legal responsibility of the patient's doctor (or other designated healthcare professional).

Once an *adolescent* is deemed competent it is not necessary to have parental consent as well. The adolescent should be encouraged to involve their parents but this choice belongs to them.

Refusal of consent

Although it is accepted that children deemed competent can refuse consent to procedures it is also accepted in UK law that there is a difference between consent to treatment and its refusal; the latter requires greater maturity and understanding than the former. Therefore:

- Children <18 years old cannot refuse treatment (that their parent has consented to) if that treatment is intended to prevent their serious harm or death (adolescents with anorexia nervosa or heart failure who have refused life-saving treatment have been overruled by the courts)
- Parental refusal cannot override the consent of a competent adolescent.

Note:

- If a child refuses to cooperate with competence assessment this does not automatically demonstrate incompetence for that individual

- Because a child makes a decision that goes against medical opinion this does not mean that they have made a wrong decision, nor that the child is incompetent.

Box 41.2 Gillick competence

This is named after a House of Lords ruling (Gillick versus W Norfolk Area Health Authority 1985) and concerns Mrs Victoria Gillick. Mrs Gillick sought a legal order to stop the local health authority prescribing contraception, even if requested, to her daughters whilst they were under the age of 16. The finding, eventually in the court of appeal, was that it was lawful to give contraceptive advice to children under the age of 16 if a child had 'sufficient understanding and intelligence to enable him or her to understand fully what is proposed'. Thus the notion of Gillick competence was born; precisely what Mrs Gillick had wanted to stop. Having said that, a degree of clarity was achieved which was previously absent. The House Of Lords also emphasized that every attempt should be made to persuade the child to involve their parents. The term Fraser competence has somewhat superseded Gillick and takes into account the complexity of the medical needs of a child and allows for parents to overrule a child's refusal of consent in some circumstances.

Assent

In the USA the term 'assent' is used in children rather than 'consent' which is used for adults. The American Academy of Pediatrics suggests that clinicians seek the assent of school-age patients as well as informed permission of the parent for a variety of procedures.

The law and best interests

- It is the duty of all healthcare workers involved with child health to safeguard the best interests of the child
- Children who are in the process of developing competency as decision-makers do not enjoy the same degree of autonomy as adults. Until they become competent others have the rights and responsibilities to decide on their best interests for them
- A child's best interests are not always easy to define but nevertheless when they are judged by a proxy decision-maker such as a parent, it is important to separate the interests of the child from those of the decision-maker.

Withholding or withdrawing life sustaining treatment

There are situations where instituting or continuing intensive care support may not be in the child's best interests. In these situations withholding or withdrawing life-sustaining treatment may be appropriate.

It is important to remember that there are two overriding principles in this situation:

- The law requires that all we all act lawfully. Euthanasia, i.e. any action with the primary intention of causing death is illegal in the UK.
  - If discontinuation of mechanical ventilation does not lead to death then the treatment goal must be palliation of symptoms (distress and suffering)
- Health professionals have a duty of care to the child. It is our duty in PICU to provide comfort and to avoid distress and pain in terminally ill children. We do this in partnership with the child's parents or carers (see Box 41.3).
  - The *Doctrine of Double Effect* refers to situations where doses of drugs (generally analgesics and anxiolytics) which are used to alleviate symptoms of pain and suffering can also shorten a child's life
  - These doses may be large due to severity of pain and tolerance to the drugs.

The process of decision-making and recommendations for situations in which withholding or withdrawing of life-sustaining treatment are appropriate are discussed in 📖 p.828.

Box 41.3 Dispute between the clinical team and the parents

The care of the child is directed to achieving what is in the best interests of the child. It is easy to appeal to best interests, but it is less clear what they are in practice. What happens when the treating clinical team and family are unable to agree on appropriate management? In PIC this is not a rare occurrence and is usually distressing for the family, the staff, and occasionally the patient. This is most often manifest when staff and family have differing views on whether to continue or whether to stop intensive care support of a child. Three scenarios that we seen with critically ill children are:

- When the clinical team wishes to withhold or withdraw life-sustaining intensive care support in the belief that this treatment is futile and is prolonging unnecessary suffering for the child in question but the family disagrees and wishes to continue with all medical management that may keep the child alive
- When the clinical team advises a course of medical intervention but the family disagrees and wishes to stop further medical intervention
- When parents disagree with each other about further management.

Box 41.3 Dispute between the clinical team and the parents (*Continued*)

These difficult situations are coloured by the experiences, beliefs, opinion, and ethics of all those concerned and can be emotive and stressful for all involved. In these circumstances honesty, patience, understanding, empathy, sympathy, and humility are some of the requisite virtues demanded of the staff of the PICU. Good communication is vital and relationships must be based on mutual trust. It is important to remember that despite the best intentions and will, disagreements between the team and the family will still occasionally occur.

- *Compromise.* In the first instance an attempt should be made to secure a compromise, acceptable to parents and clinicians
- *Second opinion.* If, despite attempted compromises, the parents and clinical team are still unable to agree a management plan, then referral for a second opinion, perhaps from a different hospital, is appropriate
- There may also be a clinical ethics committee or a practising ethicist in the hospital whose advice may be helpful
- Involvement of a religious or spiritual leader may be helpful. It can be very useful to foster relations between PICU and a spiritual leader when there is no pending matter of controversy. Subsequent difficult situations can be dealt with in a more proactive manner
- *The last resort.* If none of these approaches are successful, then the courts may be asked (as a last resort) to decide appropriate management for the child. The court may make a specific issue order under the Children Act 1989, or an order that the proposed course of treatment would not be illegal.

Administrative aspects of death

- The doctor who cares for a child who dies has a responsibility to issue a death certificate if able to give a cause of death
- Specific death certificates are used to certify the cause of death of children aged <28 days.

In the UK a Coroner is a public official whose duty it is to make enquiry into deaths of a particular nature (Box 41.4). The Coroner assigns cause and manner of death and lists them on the certificate of death. The coroner is usually a lawyer or a doctor.

Box 41.4 The following cases must be referred to the UK Coroner for consideration:

- The cause of death is unknown
- The deceased was not seen by the certifying doctor either after death or within 14 days of death
- The death was violent, unnatural, or suspicious
- The death may be due to an accident (whenever it occurred)
- The death may be due to self-neglect or neglect by others.

- In addition it is advisable to discuss any cases with the coroner where the family may be questioning the quality of the care during the child's final illness.

The Coroner will then make a decision as to whether a postmortem and an inquest are required. He/she will follow due legal process in making their decision which is legally binding. ***It is important that the family is aware that they will not be able to ensure or prevent a Coroner's post-mortem proceeding.***

The law relating to human tissue (Box 41.5)

Box 41.5 The Human Tissue Act 2004

The Human Tissue Act 2004 was introduced in response to concern over the widespread retention of tissues following postmortem. It demands informed consent for a postmortem examination and specific consent for the storage of material from the postmortem for future review. The Human Tissue Authority was set up to monitor and implement the Act. Storage of tissues without consent may be a criminal offence. There is helpful advice available from the British Medical Association (BMA).[1]

Reference

1. http://www.bma.org.uk/ap.nsf/Content/Humantissue

Confidentiality and disclosure

Adolescent

Issues such as substance abuse, sexual activity, or mental health problems may present the intensive care doctor with dilemmas related to confidentiality and disclosure:

- The doctor has a duty of confidentiality to the adolescent (and must respect the patient's objections to disclosure of information—see Gillick competence, Box 41.2)
- This duty is not absolute and can be breached when there is a risk to the health or welfare of the adolescent, e.g. episodes of self-harm or parasuicide
- Disclosure should only take place after consulting the adolescent. Obviously this cannot be done when they are on a ventilator. Generally it is not appropriate to withhold information from parents unless there is good reason to do so
- The doctor's (or nurse's) personal beliefs should have no influence on disclosure or the care the adolescent receives.

Box 41.6 'Telling the truth, the whole truth…'

Generally as doctors we have a duty to tell our patients the whole truth at all times. This is straightforward when dealing with parents but problems can arise when the child directly asks you 'what is wrong with me?', 'what is going to happen to me?' or 'may I die?'. Conveying information to a child requires much thought and sensitivity. Unfortunately one is often caught unawares by an unexpected direct question. Whilst it is essential always to tell the truth, how much to tell is a difficult call. A child's right to know certain information depends upon various factors:

- Their ability to understand what they are being told, i.e. their age, maturity, cognitive ability
- The personal, cultural, and religious context of the child's knowledge and experience
- The General Medical Council UK provides some guidance in such matters. But judgement needs to be exercised and on most occasions the medical and nursing staff must work with parents to convey information to the child in an appropriate way.

Disclosure to other agencies

Various agencies involved in child welfare need to share relevant information about children (e.g. social workers, police, and other health workers). If information is to be conveyed then it is appropriate to ask for the parent's consent (or adolescent's).

Child protection

(See 🕮 Chapter 43.)

Some children will be admitted to the ICU with child protection concerns. The primary concern is the safety of the child and also of other children within the family who may be at risk.

- History and examination should be documented clearly. Bear in mind that these notes may be used in subsequent court proceedings. Write clearly and legibly. Use diagrams when appropriate, e.g. for examination
- Social services should be involved and must consult the *Child protection Register* for children who have been already identified to be at risk of harm
- The named doctor for child protection should be involved with further management of the child This is likely to involve multidisciplinary meeting meetings with other professionals
- Care orders may need to be instituted if the welfare of the child and others is believed to be threatened
- The UK government recently updated the guidelines, entitled *Working Together To Safeguard Children.*[1]

Reference

1. 🖱 http://www.everychildmatters.gov.uk/resources-and-practice/IG00060/

Research

- Research may benefit children as a group but may be of little benefit to the child as an individual. There is widespread agreement that it is ethical to use children in medical research provided that the research in question involves negligible risk to the child
- 6 ethical principles have been outlined by the UK Royal College of Paediatrics and Child Health (2000):
  - Research is important for the benefit of all children and should supported, encouraged, and conducted in an ethical manner
  - Children are not small adults and have an additional, unique set of interests
  - Research should only be done on children if comparable research on adults cannot answer the same question
  - A research procedure which is not intended to directly benefit the child subject is not necessarily either unethical or illegal
  - All proposals involving research on children should be submitted to the hospital/trust research ethics committee
  - Legally valid consent should be obtained from the child, parent or guardian as appropriate
- The laws governing research have changed significantly over the last few years. The European Clinical trials directive 2001/20/EC sought to harmonize the laws regarding clinical trials of medicines within the EU, ensuring good clinical practice in trials
- Each hospital is responsible for research governance through its own R & D committee
- The Medical and Healthcare products Regulatory Agency (MHRA) is responsible for national implementation and supervision of adherence to the EU directive for studies which involve a drug or device
- The Human Tissue Act 2004 and the Mental Capacity Act 2005 have had an effect on the conduct of some aspects of research.

Further information and reading

BMA guidance on Parental responsibility and the Human Tissue Act 2004. Available at: http://www.bma.org.uk

Cartlidge P (ed) (2007). *Ethical Legal and Social Aspects of Child Healthcare.* Elsevier, Oxford.

GMC guidance. 0–18 years: guidance for all doctors: Available at: http://www.gmc-uk.org

Medical and Healthcare products Regulatory Agency: http://www.mhra.gov.uk

Montgomery J (2003). *Health Care Law*, 2nd edn. Oxford University Press, Oxford.

Clinical governance, audit, and risk management

Clinical governance

- Clinical governance is the framework through which healthcare organizations (an ICU, a hospital, or a PCT) are accountable
- Organizations have a responsibility to monitor the way they work to ensure the quality of the care they deliver
- Audit and risk management are elements of clinical governance.

Components of good clinical governance

- Management structure:
  - A clearly delineated management structure is necessary in any organization
  - This enables staff to understand who they are accountable to, the limits of their responsibilities, and aids in the dissemination of information up and down the management tree
  - Multiple tiers of management can lead to unwieldy bureaucracy, inefficiency, anonymity ('the faceless decision-maker'), and may contribute to poor morale
- Quality control, improvement, and assurance:
  - Standards are monitored and quality improved through the process of clinical audit and service evaluation (see 🕮 p.846)
  - If standards fall below what is expected (by performance indicators) then measures must be taken to ensure that performance improves
- Clinical effectiveness needs to be measured:
  - Evidence-based practice is essential where good quality evidence exists
  - Protocols and guidelines help to standardize care and prevent 'rogue practice', but do not replace clinical judgement
- Risk assessment and management (see 🕮 p.847)
- Staff appraisal:
  - Re-validation by professional bodies such as the General Medical Council and the Royal Colleges in the UK
  - Regular in-hospital appraisal is now standard for all medical consultants in UK hospitals
  - Patient-centred care and a sense of responsibility are encouraged, whereupon staff may report concerns about a colleague's quality of practice without fear of reprisal or cover up
- Professional development:
  - Study leave and course attendance
  - Teaching and research
- Complaints procedures:
  - Patient liaison groups
  - Hospital medico-legal departments
  - There must be a quick and efficient system to deal with and investigate complaints. Prompt and honest assessments can avert upset and costly legal proceedings and awards.
- Feedback:
  - Patient and relative questionnaires and surveys may help to improve the service

- Clear managerial responsibility for clinical governance:
  - Within an organization, this rests with the hospital board
  - Clinical lead for children's services
  - An individual is still responsible for their clinical practice and should aim to learn and improve care at all times
- Communication:
  - Separate individuals, teams, or organizations should cooperate to deliver effective integrated care
  - Integration of different services can significantly improve the overall quality of care.

The past 10 years have witnessed a sea-change in the way many healthcare professionals in the UK are expected to practise. Gone are the days when 'Sir Lancelot Spratt' struck fear into the heart of his forelock tugging patients. In the past, the doctor knew best and the unpalatable truth was often withheld from the patient if the doctor so decided. We now strive for patient-centred care where the doctor is accountable and the patient has the right to good quality medicine. This is the age of team work, good communication, informed consent, and 'fitness to practise'. Many of these changes have reflected the change in society as a whole and had been instituted by the medical profession. Unfortunately many came in response to a number of reports that were critical of the medical profession. In the words of one report 'the public have been badly let down' by the medical profession.

Recent issues have been diverse in topic but have all been characterized by a failure to apply the tenets of good clinical governance. Major incidents range from failure of social services intervention (Climbié Inquiry), to excess deaths following heart surgery in children (Bristol Inquiry), and include hospital acquired infection (*C. difficil*e, MRSA), organ retention following postmortem in children, and a single doctor (Harold Shipman) committing multiple murder.

The report of the Bristol Inquiry (2001) into excess death following cardiac surgery highlighted issues of consent, openness, and fitness to practise. It commented that although the majority of clinicians involved were 'dedicated and well motivated', problems arose from poor team work, communication, and leadership.

Healthcare professionals have always been responsible and accountable for the care they deliver. The major change is that the hospital board is also accountable and by continually monitoring and improving quality they must ensure that the standard of care delivered meets national standards.

Clinical governance should not be seen as a separate structure from clinical care. Its core principles of evidence-based medicine, audit, patient consultation, openness, continuing professional development, and revalidation underpin what should be embedded in our clinical practice.

Clinical audit

Audit describes the systematic evaluation of the outcome of healthcare against specific standards. In other words, comparing practice in your hospital or unit with best practice or guidelines. It is one of the key components of clinical governance. In situations in which clear standards do not exist, the term *service evaluation* may be used to describe a similar process of evaluation. The intention is to monitor (and so assure) the quality of the care delivered. Audit may involve a review of activity, performance against predetermined indicators, or cost-effectiveness (see Box 42.1). If problems are found at audit then changes can be implemented and the process reaudited. The process is called the audit cycle (Fig. 42.1).

Defining a standard can be difficult. One may audit postoperative complications or mortality but what is the standard? In the UK all PICUs record data in the national database (PICANet, see 🕮 Chapter 2). Performance is measured and a standardized mortality rate calculated. This is published and allows for comparison between units and against other units but that is a national audit (PICANet, see 🕮 Chapter 2).

Many hospitals have an audit department that can help with advice, and support in data collection and analysis. Further information can be gleaned from the National Research and Ethics Service (NRES) website (see 🕮 p.848).

Box 42.1 How to perform an audit

- Ask a question (e.g. is the infection rate too high? Are we ordering too many X-rays?)
- Define criteria to be measured (infection rate or X-ray requests)
- Define the population to be studied (patients in PICU)
- Define the standard that is expected (there may be established expert or national standards)
- Collect data
- Analyse data and compare with predefined standard
- After consultation institute intervention/change in practice (new handwashing guidelines, X-ray requests are signed by consultants)
- Re-audit.

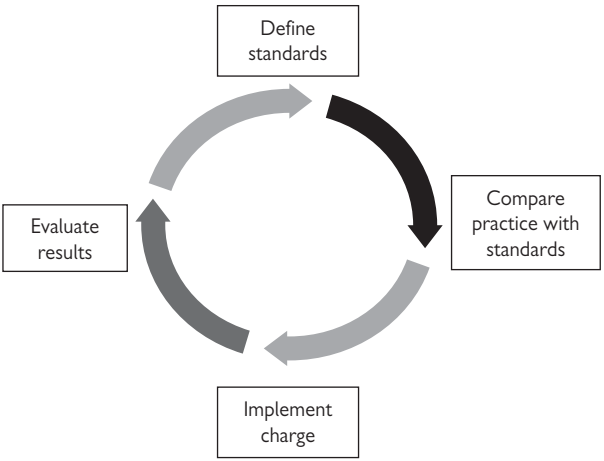

Fig. 42.1 The audit cycle.

Risk management

Risk management is another major component of clinical governance:

- It is the requirement that potentially harmful activity should be identified
- Following recognition, attempt should be made to reduce the risk of that harm occurring or possibly to eliminate the risk entirely.

For example, if 2 drugs have similar names or appearance and are easily confused, the hospital or department may choose to provide neither of them. Alternatively, if both drugs are essential then other measures are taken such as additional labelling or alternative packaging. In the first case the risk is eliminated, in the other scenarios the risk is reduced. There are certain risks which are always present (e.g. operating on the wrong side of a patient) despite risk reduction measures (marking the patient and checking the patient). Even where the risk is retained, awareness of the risk and familiarity with the problems it causes can reduce the likelihood of harm.

- Critical incident reporting systems have been introduced nationally as one of the bedrocks of risk management. They allow identification of problem areas in clinical practice
- Adverse incidents (including those that do not result in patient harm but which could have resulted in harm) are reported and graded as to their level of seriousness
- Changes can be made to minimize the risk, the urgency of which will depend on the seriousness (in terms of patient safety) of the incident.

It is important to recognize that addressing a perceived risk may create other risks. For example, removal of dangerous drugs from the clinical setting (e.g. potassium or suxamethonium) may lead to harm when they are required urgently (e.g. severe hypokalaemia or accidental extubation).

There are several national agencies that are directly involved in risk management: NICE (the National Institute for Health and Clinical Excellence), Healthcare Quality improvement Partnership (HQIP), and NPSA (the National Patient Safety Agency) regularly publishes recommendations.

Aspects of risk management in PICU

- Drug labelling (syringes should be labelled with drug they contain immediately)
- Typed prescriptions (reduces handwriting errors)
- Standardization in writing units (e.g. nanograms and micrograms)
- Prescription protocols (e.g. IV fluid guidelines)
- Management protocols (e.g. head injury, DKA, post surgery etc.)
- Locking away or removal of drugs or fluids (e.g. potassium and hypotonic glucose 4% and saline 0.18%)
- Critical incident reporting.

Further information and reading

http://www.icservices.nhs.uk/clinicalgovernance
National Research Ethics Service: http://www.nres.npsa.nhs.uk/
NICE: www.nice.org.uk/
Paediatric Intensive Care Audit Network: http://www.picanet.org.uk/
The Bristol Inquiry: http://www.bristol-inquiry.org.uk/final_report/index.htm#
The Victoria Climbé Inquiry: http://www.victoria-climbie-inquiry.org.uk/
HQIP: http://www.hqip.org.uk/
National Patient Safety Agency: http://www.npsa.nhs.uk/

Chapter 43

Child protection

Introduction

Safeguarding children is defined as protecting children from maltreatment, preventing the impairment of children's health or development, and ensuring that children are growing up in circumstances consistent with the provision of safe and effective care. The United Nations Convention on the Rights of the Child is very relevant to the field of child protection, including the best interests of the child, the right to life, protection from abuse and neglect, and the right to the highest attainable level of health among its standards.

Staff working in critical care have a responsibility to protect their patients and should recognize that children may also be harmed by inappropriate treatment, treatment errors and poor staff expertise. Clinicians' first duty is to the child. Clinicians should not be distracted by a parallel duty to anyone else, including parents.

All staff should undergo training in Child Protection, should know of the relevant agencies working together, and should be up to date with local policies and procedures.

In the critical care setting, physical abuse is the most likely form of abuse to present (Box 43.1).

Presentation

Box 43.1 Presentations where physical abuse should be considered

• Head injury	Accidental or non-accidental?
• Loss of consciousness	Consider head injury, poisoning, suffocation
• Acute life-threatening event	Consider suffocation or head injury
• Shock	Consider head injury, abdominal injury
• Scalding and burns	Accidental or non-accidental?
• Drowning	Accidental or non-accidental?
• Severe abdominal pain	Consider abdominal injury
• Sudden and unexplained death in infancy	

Practice point

Consider possibility of abuse in all emergency admissions—otherwise cases will be missed.

History: concerning features

- Vague
- Unwitnessed
- Injuries inconsistent with the child's developmental age
- Injuries inconsistent with history given

- Inappropriate parent/carer response (e.g. time delay without appropriate explanation, unconcerned or aggressive carers)
- Inappropriate child response (e.g. didn't cry, felt no pain)
- Presence of other injuries
- Child/family known to social services
- Age of child—infants who are immobile rarely have accidental injuries and are at high risk of severe head injury
- Previous history of unusual injury
- Repeated hospital attendance may be due to abuse or neglect.

Examination—see Box 43.2

Box 43.2 Physical examination: concerning features

- Failure to thrive
- Signs of neglect or maltreatment
- Affect in an older child—withdrawn, frightened, uncommunicative
- Bruising—distribution, varied ages, imprints
- Bleeding from nose or mouth—may occur in imposed upper airway obstruction
- If there is a history of resuscitation, take careful details
- Burns and their distribution—deliberately inflicted burns occur in ~10% of physically abused children.

Bruising

NAI should be considered if the following are present:

- Bruising in unusual sites
- Imprints from objects or fingers
- Bite marks
- Petechiae on face.

Assessment

(Also see Box 43.3.)

- History:
  - Of injury
  - Family history of coagulation disorders
  - Drug history
- Documentation of bruises:
  - Number
  - Type
  - Where
  - Pattern
  - Measurements
- Formal photography
- If child less <2 years consider skeletal survey
- First-line blood investigations:
  - FBC and film
  - Coagulation screen

- Second-line blood investigations (after discussion with haematologist):
  - Von Willebrand screen
  - Factor assays
  - Platelet aggregation studies
  - Bleeding time.
- Both inflicted injury and bleeding disorder may coexist.
- The absence of bruising does not exclude a fracture, particularly rib fractures—80% will have no associated bruising.

Practice point

Good note keeping implies good practice. Every set of notes should be kept as if it might need to be viewed in court. Failure to keep adequate notes can mean that a child's life may be put at risk. It can also mean that clinical competence may be open to question. Every page should have an addressograph, be written legibly, with date and time documented. Be meticulous in documenting any wounds and bruises. All documentation must be signed and the name of the doctor printed clearly.

Box 43.3 If you suspect that a child has been harmed

- Don't assume that someone else will raise the concerns or deal with them
- Promoting children's wellbeing and safeguarding them from harm is the responsibility of all staff working with children
- Don't conduct your own investigation or keep the problem to yourself
- Always share concerns with senior colleagues
- Consult and communicate widely both within the health service and with other agencies outside the health service
- Remember the child's welfare is always the paramount concern
- Don't let other concerns get in the way of your responsibility to the child
- Do remember other children in the family may be at risk of harm
- Do not confront or accuse parents of abusing their child, but calmly explain your concerns and reasoning to them
- Don't conduct interviews and examinations without having another professional person present
- There is no need to make a firm diagnosis of child abuse prior to referral to social services—consult them early.

Consent

(See 🕮 Chapter 41.)

- A child can be examined without consent only if the child is in need of urgent medical treatment. If the child is subject to a child protection investigation, consent for any examination will usually be from the parent or carer. Where such a child is subject to an Interim or Full Care Order, parents retain responsibility, although the local authority becomes the senior partner, and it is then essential that permission for examination is given by social services and the courts (social services are responsible for gaining the court's permission)
- If consent is refused for essential investigations legal advice must be sought. The welfare of the child takes priority. If consent is refused for non-essential investigations (e.g photography), this needs to be clearly documented and discussed with other authorities. Legal advice may need to be sought
- Where there are any concerns in undertaking specific examinations including parental refusal, or the person with parental responsibility is unavailable, then the team should consult the hospital's legal advisors and child protection specialists
- If the child requires urgent attention, or is at risk of harm, it may be necessary to consider emergency legal action, initiated by social services or the police.

Confidentiality

(See 🕮 Chapter 41.)

- Doctors must share information with other agencies on a need to know basis. Confidentiality must not be allowed to stand in the way of child protection
- With respect to confidentiality the doctor must disclose information about the child if they feel that it is in the child's best interest. In the General Medical Council document 'Confidentiality: Protecting and providing information' it is stated 'If you believe a patient to be a victim of neglect or physical, sexual or emotional abuse and that the patient cannot give or withhold consent to disclosure, you must give information promptly to an appropriate responsible person or statutory agency, where you believe that the disclosure is in the patient's best interests'
- More guidance may be obtained from the Royal College of Paediatrics and Child Health (RCPCH) documents relating to child protection.

Common forms of physical abuse presenting to critical care

Non-accidental head injury (NAHI); also known as inflicted traumatic brain injury (iTBI)

Epidemiology

NAHI has features that include shaking injury, cerebral lesions as a result of direct impact, compression, and penetrating injuries. In the UK the annual incidence of shaking injury is ~25 per 100,000 children <1 year.

Head injury is the commonest cause of death in physical child abuse. 95% of severe head injury in the first year of life is inflicted.

Infants with NAHI present to hospital with a variety of symptoms ranging from poor feeding, lethargy, seizures, and respiratory difficulty to sudden death. In some cases the absence of either a history or external signs of injury may delay diagnosis.

The diagnosis of NAHI must be considered in any infant or young child who inexplicably collapses.

Important features of NAHI

Such injury arises from impact to the head or as a result of severe repetitive rotational injury with or without additional impact.

Consequences may include:

- Bruising/abrasions or lacerations to the head including scalp or face
- Skull fracture
- Intracranial bleeding
- Subdural collections
- Brain injury-hypoxic-ischaemic and direct traumatic injury of the brain
- Retinal haemorrhages
- Neck and cervical spinal cord injury
- Bruising to body or limbs
- Think of associated abdominal injury.

Radiological investigations

- Neuroimaging
- CT head scan as soon as stabilized
- MRI where available on day 3 or 4
- Skeletal survey.

Laboratory investigations

- Serial full blood counts: may demonstrate low or falling Hb
- Coagulation studies
- Septic screen
- Urine for toxicology and metabolic screen.

Other investigations

- Eye examination for retinal haemorrhages by an experienced ophthalmologist

Box 43.4 Differential diagnosis

- Birth trauma—subdural haemorrhage and retinal haemorrhages may occur in the perinatal period
- Severe accidental head injury, e.g. following a road accident
- Bleeding disorders, e.g. haemophilia, haemorrhagic disease of the newborn-vitamin K deficiency
- Cranial malformations
- Glutaric aciduria type 1
- Postoperative complication of open-heart surgery or neurosurgery
- Hypernatraemic dehydration

Team approach and multi-agency working

- Follow local procedural guidelines
- Where NAHI is considered possible a strategy discussion involving police and social services should be initiated to decide whether to initiate a criminal investigation

Secondary problems needing neurocritical care

The main problems needing attention are:

- Seizure control
- Cerebral oedema with brain swelling, raised ICP, and tissue herniation and infarction. Some PICUs undertake ICP monitoring in infants with NAHI
- Intracranial haemorrhage.

Outcome

The mortality from NAHI is up to 30%. Half of the survivors have residual neurodisability of variable type and severity:

- Cranial nerves lesions: sensorineural deafness
- Speech and language problems
- Epilepsy
- Vision: cortical or optic radiation injury is the major cause
- Neuroromotor: hemiparesis, ataxia, tetraplegia

Intra-abdominal injury

Inflicted intra-abdominal injury is very uncommon. It typically occurs in young children aged <3 years and has a high mortality rate. Diagnosis can be difficult with delay in presentation and no history of trauma provided by the parent/carer. Hollow viscous injury, particularly of the small bowel, may occur. The liver is the commonest solid organ injured.

Features

- A child may present with unexplained collapse/severe abdominal pain/sepsis
- Clinical signs may be difficult to elicit particularly when retro-peritoneal structures are injured
- There may be no signs of external injury or development of bruising may be delayed
- Free gas may be found on X-ray.

Laboratory investigations
- Serial FBC/haematocrit for blood loss
- Serum amylase (pancreatic or splenic injury)
- Liver enzymes
- Urinalysis for haematuria.

Radiology
- CT scan—with oral and intravenous contrast
- US scan if too unstable
- AXRs and CXRs to look for free air and fluid levels—may appear normal despite significant injury.

Management
- Resuscitation
- Discussions with radiology and paediatric surgical colleagues
- Follow local child protection guidelines.

Fabricated or induced illness

Fabricated and induced illness is a broad term to describe a group of behaviours most often by parents or carers which cause harm to children. It is more common in children <2 years of age. Organic illness may coexist with fabricated or induced illness. In the past the term 'Munchausen by proxy' was used to describe fabricated or induced illness in a child by another, usually an adult.

Any symptoms can be verbally fabricated

Induction of illness

Direct induction of illness may take place through several methods which are more or less acute in their effects:
- Suffocation, which may present as an acute life threatening event
- Administration of noxious substances or poisons
- Excessive or unnecessary administration of ordinary substances (e.g. excess salt)
- Excess or unnecessary use of medication (prescribed for the child or others)
- The use of medically provided portals of entry (e.g. gastrostomy, central lines) give opportunity for infected or toxic material to be administered.

Recognition of acute presentations (direct inductions)
- Are difficult and associated with patterns of presentation in the child which are not consistent with any known disease and are incongruent
- The occurrence of unobserved parental access with crises or deterioration in the child's health, suggesting suffocation, tampering, or ingestion.

Differential diagnosis
- Acute medical problem, e.g. arrhythmias or apnoea, i.e. organically explained life-threatening events
- Only close monitoring is likely to tease out the cause in these cases.

Recognition of fabricated and induced illness is more difficult

- When there is coexisting organic physical illness
- Where fabrication has already lead to unnecessary treatment/surgery
- Where the child is already handicapped with complex needs.

If you are concerned that a child may be suffering from a fabricated and induced illness

- As with any child protection issues it is vital to alert the appropriate authorities and follow local and national guidance with all agencies working together.

Salt poisoning

Hypernatraemia caused by salt poisoning must be distinguished from hypernatraemia caused by dehydration, as the 2 situations need different medical and legal approaches. Other medical causes of hypernatraemia are persistent and easy to exclude.

Distinguishing features

- Child's clinical history
- Acute changes in weight: ↑ with salt poisoning, ↓ with dehydration
- Fractional excretions of sodium and water calculated from serial paired 'spot' blood and urine samples (see 📖 p.650)
- Estimates of net sodium and water balances using fractional excretion and GFRs.

Practice point

As with any forensic samples, there should be a documented chain of evidence of the processing of each sample from the person taking it, to the porter, to the taxi driver, to the laboratory technician, and any other personnel involved.

Burns

- Severe burns requiring paediatric critical care are rare
- Evidence of non accidental injury should always be considered at admission of a burned child
- Specific patterns of injury suggesting inflicted injury are:
  - Isolated burns of the buttocks
  - Symmetrical scalded hands or feet of full thickness depths
- Children will require the involvement of professionals from paediatric critical care and paediatric burns care, as well as the involvement of the child protection team.

Further reading

HM Government (2006). *Working Together to Safeguard Children*. The Stationery Office, Norwich.
Royal College of Paediatrics and Child Health (2006). Safeguarding Children and Young People: Roles and Competences for Health Care Staff. Intercollegiate Document. Available at: www.rcpch.ac.uk
Royal College of Paediatrics and Child Health (2006). *Child Protection Companion*. RCPCH, London.
United Nations (1992). *The UN Convention on the Rights of the Child*. HMSO Welsh Office.

Appendix

Normal values and physiological data

Weights and surface area

Table A.1 Weights and surface area

Age		Weight (kg)	Surface area (m^2)	Length (cm)	Head circumference (cm)
Newborn	♂	3.3(2.5–4.3)	0.21	50(46–53)	34.5(32.1–36.9)
	♀	3.2(2.4–4.2)	0.21	49(46–53)	33.9(31.7–36.1)
3 month	♂	6.4(5.1–7.9)	0.33	61(58–65)	40.5(38.3–42.7)
	♀	5.8(4.6–7.4)	0.31	60(56–64)	39.5(37.2–41.9)
6 month	♂	7.9(6.4–9.7)	0.39	68(64–72)	43.3(41–45.6)
	♀	7.3(5.8–9.2)	0.37	66(62–70)	42.2(39.7–44.6)
1 year	♂	9.6(7.8–11.8)	0.45	76(71–80)	46.1(43.6–48.5)
	♀	8.9(7.1–11.3)	0.43	74(69–79)	44.9(42.3–47.5)
3 years	♂	14.3(11.4–18)	0.62	96(89–103)	49.5(46.8–52.1)
	♀	13.9(11–17.8)	0.61	95(88–102)	48.5(45.9–51.2)
5 years	♂	18.3(14.3–24)	0.75	110(101–119)	50.7(47.9–53.5)
	♀	18.2(14–24.4)	0.74	109(101–118)	49.9(47.2–52.6)
7 years	♂	23(18–33)	0.88	122(112–132)	
	♀	23(18–33)	0.88	122(112–133)	
10 years	♂	32(24–49)	1.11	139(127–152)	
	♀	33(24–51)	1.12	138(126–151)	
12 years	♂	41(29–63)	1.30	149(136–164)	
	♀	42(30–66)	1.33	151(137–165)	
14 years	♂	51(37–77)	1.52	164(149–179)	
	♀	49(37–78)	1.48	160(148–173)	
16 years	♂	61(46–89)	1.72	174(159–187)	55.0
	♀	54(42–84)	1.56	163(150–175)	54.2
Adult	♂	71(54–101)	1.87	177(163–190)	55.9
	♀	58(45–89)	1.62	163(151–175)	54.6

For weight, length and head circumference, the first value is the median; the range in brackets gives the 3rd to 97th centile. For length, values are rounded to the nearest integer. Data ages 0–5 from WHO Multicentre Growth Reference Study (http://www.who.int/childgrowth/mgrs/en/); ages 7+ from National Center for Health Statistics (http://www.cdc.gov/nchs/)

- Weight (kg) (age <10) = (2 × Age) + 8
- Weight (kg) (age 10–14) = 3 × Age
- SA (m^2) = $\sqrt{((ht\ in\ cm \times wt\ in\ kg))/3600}$
- BMI = weight (kg)/height^2 (m)

Growth prediction

- Mid parental height = ((mother's height + father's height) /2) + 7cm
- Boys target centile range = mid parental height ± 10cm
- Girls target centile range = mid parental height ± 8.5cm.

Cardiovascular formulae

Table A.2 Cardiovascular parameters

Age	Pulse	Blood pressure		
		Systolic	Mean	Diastolic
Newborn	95–145		40–60	
3 month	110–175		45–75	
6 month	110–175		50–90	
1 year	105–170	67–103	50–100	20–56
3 year	80–140	73–109	50–100	27–65
5 year	70–140	78–112	50–100	34–72
7 year	70–120	79–115	60–90	38–76
10 year	60–110	85–119	60–90	42–80
12 year	60–100	89–123	65–95	43–81
14 year	60–100	94–128	65–95	44–82
16 year	60–100	98–134	65–95	46–84

Values represent the 5th and 95th centiles at each age. Data from National Heart, Lung and Blood Institute (http://www.nhlbi.nih.gov/guidelines/hypertension/child_tbl.htm.)

- Systolic BP = (Age × 2) + 80
- Mean BP = (SBP + 2DBP)/3 ***or***
- Mean BP = DBP + (SBP–DBP)/3

- Cardiac output (CO): SV * HR
- Cardiac index (CI): CO / BSA (3.5–5.5L/min/m^2)
- Ejection fraction (EF): [(EDV–ESV)/EDV] × 100
  Normal 55–75% (LV); 50–60% (RV)
  (The fraction of end-diastolic volume ejected during ventricular systole) (ESV = end systolic volume; EDV = end diastolic volume)
- Fractional shortening (FS): 28–45% (LV)
- Stroke volume (SV): CO/HR (Normal 60–100mL/beat)
- Stroke volume index (SVI): SV/BSA = 33 – 47mL/m^2/beat
- Pressure measured by echo (from Bernoulli equation): 4 × $Vmax^2$ (m/sec^2)
- RV pressure (from echo): 4 × (TR Vmax)^2 + RAP (use CVP)

Pulmonary to systemic flow ratio (Qp/Qs):

$(SaO_2 – SmvO_2)/(SpvO_2 – SpaO_2)$. Normal 1.0.

Systemic vascular resistance index (SVRI):

$80 \times (MAP – CVP)/CI = 800–1600 dyne\ s/cm^5/m^2$

Pulmonary vascular resistance index (PVRI):

$80 \times (MPAP – LAP)/CI = 80–240 dyne\ s/cm^5/m^2$

Oxygen consumption (VO_2):

$CI \times [Hb] \times 1.36 \times [(SaO_2 – SmvO_2)/100]$

- Normal ($mL/min/m^2$): 160–180 (infant); 100–130 (child); 120–150 (adult)
- Oxygen content = $(1.34 \times [Hb] \times SaO_2) + (0.003 \times PaO_2)$

ECG

Table A.3 Normal ECG values*

	Normal ECG values (2^{nd}–98^{th} centile):			
	3–30d	1–6m	6–12m	1–3y
PR interval (ms)	70–140	80–130	80–140	80–150
QRS duration (ms)	50–80	50–80	50–85	55–85
QRS axis	65–155	10–140	10–120	0–120
QTc Interval (ms)*	380–450	380–450	380–450	380–450
	3–5y	5–8y	8–12y	12–16y
PR interval (ms)	100–150	100–160	100–170	100–180
QRS Duration (ms)	60–90	60–95	70–100	70–110
QRS axis	10–110	10–110	0–120	0–110
QTc Interval (ms)*	380–450	380–450	380–450	380–450

Based on Rijnbeek PR, Witsenburg M, Schrama E, Hess J, Kors JA. New normal limits for the paediatric electrocardiogram. *Eur Heart J* 2001: **22**:702–711 and Davignon A, Rautaharju P, Boisselle E, *et al*. Normal ECG standards for infants and children. *Pediatr Cardiol* 1979;**1**: 123–31.

*Corrected QT intervals (Bazett's formula – $QTc=QT^* \sqrt{(\text{heart rate}/60)}$)

To determine the atrial ECG: connect the atrial pacing wires to the arm leads on the ECG: lead 1 is an atrial trace.

Respiratory formulae

Alveolar gas equation: Alveolar PO_2 (PAO_2) = $PiO_2 – (PaCO_2/R)$
where $PiO_2 = FiO_2 \times$ (Patmosphere – Pwv).
Pwv for fully saturated air at 37°C is 6.3kPa or 47mmHg.
wv = water vapour.
R = respiratory exchange ratio.

R is normally 0.8 even in very sick children.
Alveolar-arterial oxygen difference (AaDO2) = $P_AO_2 - P_aO_2$
(normal <1KPa)

PaO_2/FiO_2 ratio: normal 300–500mmHg. Values <300 mmHg indicate abnormal gas exchange. Values < 200mmHg indicate severe hypoxia.

Oxygenation Index (OI):

$[(MAP \times FiO_2)/PaO_2] \times 100$ (where PaO_2 units are mmHg)

Mean airway pressure: ((PIP x Ti)+[PEEP x (60/RR)–Ti])/(60/RR)

Ventilation index (VI): $(PaCO_2 \times RR \times PIP)/1000$

Shunt equation:

$Q_s/Q_t=(CcO_2 - CaO_2)/(CcO_2 - CvO_2)$

Q_s = shunt flow; Q_t= total flow; CcO_2= Pulmonary capillary oxygen content; CaO_2 = arterial oxygen content; CvO_2=mixed venous oxygen content.

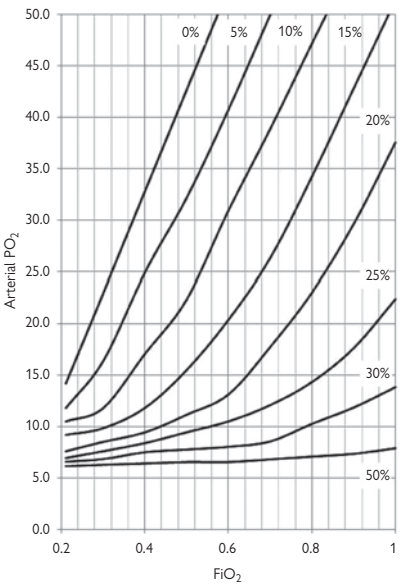

Fig. A.1 Iso-shunt diagram.

The lines show the relationship between arterial PO_2 (kPa) and FiO_2 for different levels of shunt. Normal levels for barometric pressure, Hb, PCO_2, pH, and arterial-mixed venous oxygen concentration are assumed. The graph may be used to *estimate* the optimal FiO_2 for a patient if the PaO_2 is known—plot the known PaO_2 against the FiO_2 when the gas was taken, and follow the nearest shunt line to the point of the desired PaO_2 and read off the required FiO_2.

Table A.4 Normal haematology values

Age	Hb (g/dL)	Haematocrit	MCV (fL)	WCC ($x10^9$/L)	Neutrophils	Lymphocytes	Eosinophils	Basophils	Platelets	Reticulocytes
Birth	15–23	0.45–0.75	100–125	10–26	2.5–14	2–7	0–0.9	0–0.1	150–450	110–450
2 weeks	13–20	0.4–0.65	88–110	6–21	1.5–5.5	3–9	0–0.9	0–0.1	170–500	10–80
6 months	10–13	0.3–0.4	73–84	6–17	1–6	3–11	0.5–0.9	< 0.2	210–560	15–110
12 months	10–13	0.3–0.4	70–80	6–16	1–8	3–10	<0.9	< 0.13	200–550	20–150
2–5 years	11–13	0.3–0.4	72–87	6–17	1.5–9	2–8	<1.1	<0.12	210–490	50–130
5–12 years	11–15	0.3–0.4	76–90	4–14	1.5–8	1.5–5	<1	<0.12	170–450	50–130
>12 years										
Female	12–15	0.35–0.45	77–95	4–13	1.5–6	1.5–4.5	<0.8	>0.12	180–430	50–130
Male	12–16	0.35–0.5	77–92	4–13	1.5–6	1.5–4.5	<0.8	>0.12	180–430	50–130

Reproduced from Crisp S and Rainbow J (2007). *Emergencies in Paediatrics and Neonatology*. Oxford University Press.

Activated partial thromboplastin time (aPTT)	18–41s
Prothrombin time (PT)	9–14s
International normalized ratio (INR)	0.9–1.2
Thrombin clotting time (TCT)	11–18s
Activated clotting time	100–140s
Bleeding time	2–9min
Fibrinogen	1.9–5g/L
Plasma free Hb	0.16–0.62micromol/L
Antithrombin III	0.8–1.2 U/mL
Carboxyhaemoglobin	<5%
Methaemoglobin	<2%

Biochemical values

Alanine aminotransferase (ALT)	0–35IU/L
Albumin	33–47g/dL
Alkaline phosphatase (<2 years)	100–350IU
Ammonia	<50micromol/L
Amylase	8–85IU
Aspartate transaminase (AST)	15–60IU
Base Excess	–2 to +3mmol/L
Bicarbonate	18–25mmol/L
Bilirubin (>1 month)	<10micromol/L
Caeruloplasmin	200–430mg/L
Calcium (ionized)	1.2–1.3mmol/L
Calcium (total)	2.0–2.7mmol/L
Chloride	98–110mmol/L
Chloride (sweat)	<50mmol/L
Cholesterol (>1 year)	3.1–5.4mmol/L
Cholinesterase	600–1500IU
Copper (1–9 years)	14–28micromol/L
Coproporphyrin	<0.3micromol/L
Cortisol	150–600nmol/L
Creatine kinase (CK)	40–240IU
Creatinine	10–60micromol/L
Cyanide	<8micromol/mL
Ferritin	18–300mcg/L
Free fatty acids	0.1–0.6mmol/L
Globulins	17–38g/L
Glucose	3.6–5.4mmol/L
Gamma-glutaryl transferase (GGT: >3m)	<40IU
Iron	9–27micromol/L
Lactate	1–1.8mmol/L
Lactate dehydrogenase	210–420IU
Lead	0.2–1.2micromol/L
Lipase	0–160IU/L
Magnesium	0.7–1.0mmol/L
Osmolality	270–296mmol/L
$PaCO_2$	3.5–5kPa
pH	7.36–7.44
Phosphate (>2 years)	1.1–1.8mmol/L
PaO_2	9.5–13.0kPa

Potassium	3.5–5mmol/L
Protein	57–80g/L
Protein C	0.7–1.4U/mL
Protein S	0.55–1.4U/mL
Protoporphyrin	0.3–1.0micromol/L
Pyruvate	<0.1mmol/L
Renin activity	1–4ng/mL/h
Sodium	135–145mmol/L
Thyroid stimulating hormone (TSH: >14d))	<5nmol/L
Free thyroxine	9–26pmol/L
Total thyroxine	70–155nmol/L
Triglycerides	0.9–2.0mmol/L
Triiodothyronine (T3)	1.0–2.7nmol/L
Troponin I	<0.29mcg/L
Urea	2.1–6.5mmol/L
Uric acid	0.13–0.4mmol/L
Zinc	11–22micromol/L

Urine

Amylase	50–500IU
Calcium	<0.12mmol/kg/d
Calcium:creatinine ratio	<0.7mmol/mmol
Copper	<0.3micromol/d
Coproporphyrin	<0.3micromol/L
Creatinine clearance	1.4–2.4mL/s/1.73m^2
Oxalate	<0.6mmol/d
Porphobilinogen	<9micromol/L
Protein	<4mg/h/m^2
Uroporphyrin	<0.05micromol/L

Fractional excretion of substance X = (Ux/Px) × (Pcr/Ucr) × 100

Pleural fluid

- Protein >30g/L suggests exudate
- Protein <30g/L suggests transudate
- Triglyceride >1.1mmol/L; leucocytes >1000/μL (>80% lymphocytes) suggests chylothorax
- High glucose in a patient on PD suggests PD fluid in the chest.

CSF

Glucose	>2.5mmol/L >60% blood glucose
Protein	0.5–4g/dL (preterm) 0.4–1.7g/dL(neonate) 0.05–0.4g/dL (>2 months)
Lymphocytes	$<20 \times 10^6$ (<1 week) $<6 \times 10^6$ (>1 week)
Neutrophils	$<10 \times 10^6$ (<1 week) $<0 \times 10^6$ (>1 week)
White cell: red cell ratio	<1:200
Carnitine	3.6–4.8micromol/L
Ammonia	<25micromol/L

Lactate	0.6–2.2mmol/L
Pyruvate	60–210micromol/L

Reference

1. Shann F, Henning R (2005). *Paediatric intensive care guidelines*, 3rd edn. Collective Pty Ltd, Melbourne, Australia.

Useful equations

Conversion factors

pH to [H+]

Table A.5 Relationship between pH and [H+] (nmol/L)

pH	6.8	6.9	7.0	7.1	7.2	7.3	7.4	7.5	7.6
H^+	158	125	100	79	63	50	40	31	25

$$pH = -\log_{10} aH^+$$

$$aH^+ = 10^{(-pH)}$$

where aH^+ is activity of H^+
pH 7.36 is 44 nM; pH 7.44 is 36 nmol;
Changes in the $[H^+]$ by a factor of 2 cause a pH change of 0.3

kPa to mmHg

- 1kPa = 7.52mmHg
- 1mmHg = 0.133kPa.

SI to US units

- Creatinine: 1mmol/L = 11.3mg/dL
- Calcium: 1mmol/L = 4.008mg/dL
- Glucose: 1mmol/L = 18.02mg/dL
- Phosphate: 1mmol/L =3.098mg/dL.

Centigrade to Fahrenheit

- To convert from Fahrenheit to Celsius, use this equation:

$$C = (F - 32) \times 5/9$$

- To convert from Celsius to Fahrenheit, use this equation:

$$F = (9/5 \times C) + 32$$

Yorkshire pudding

100g plain flour; 1 hen's egg; pinch of salt; 280mL of milk: 50g lard/fat. Mix the flour and salt in a basin and then stir in the egg. Add the milk gradually, stirring all of the time until the flour is worked in. Add rest of milk and beat well.

Melt the fat in cooking tin until spitting hot. Pour in the batter. Cook at 450°F, 230°C or gas mark 8. Large tins for about 30min, small tins 15–20min.

Line and catheter sizes

Table A.6 ET tube sizes and lengths

Age	Weight (kg)	Endotracheal tube				Suction catheter
		Diameter (mm)		Length (cm)		Size (FG)
		Internal	External	At lips	At nose	
Newborn	2.0	3.0	4.3	7	9	7
Newborn	3.0	3.0	4.3	8.5	10.5	7
Newborn	3.3	3.5	4.9	9	11	8
3 month	6.4	3.5	4.9	10	12	8
6 month	7.9	3.5–4.0	4.9–5.6	10.5	13	8
1 year	9.6	4.0	5.6	11	14	8
3 years	14.3	4.5	6.2	13	16	8
5 years	18.3	5.5	7.5	14.5	18	10
7 years	23	6.0	8.2	16	19.5	10
10 years	32	6.5	8.9	17	21	12
12 years	41	7.0	9.5	18	22	12
14 years	51	7.5	10.2	19	23	12
16 years	61	8.0	10.8	20	24	12

ETT size (mm) = (Age/4) + 4
Oral ETT length (cm) = (Age/2) + 12
Nasal ETT length (cm) = (Age/2) + 15

Table A.7 LMA sizes

Weight (kg)	LMA size	Cuff volume (mL)
<5	1	2–5
5–10	1 ½	5–7
10–20	2	7–10
20–30	2 ½	12–14
30+	3	15–20

Tracheostomy sizes

Table A.8 Details of Shiley® neonatal and paediatric tracheostomy tubes

Size	ID (mm)	OD (mm)	Length (mm)
3.0 NEO	3.0	4.5	30
3.5 NEO	3.5	5.2	32
4.0 NEO	4.0	5.9	34
4.5 NEO	4.5	6.5	36
3.0 PED	3.0	4.5	39
3.5 PED	3.5	5.2	40
4.0 PED	4.0	5.9	41
4.5 PED	4.5	6.5	42
5.0 PED	5.0	7.1	44
5.5 PED	5.5	7.7	46
5.0 PDL	5.0	7.1	50
5.5 PDL	5.5	7.7	52
4.0 PDC *	4.0	5.9	41
4.5 PDC	4.5	6.5	42
5.0 PDC	5.0	7.1	44
5.5 PDC	5.5	7.7	46
5.0 PLC *	5.0	7.1	50
5.5 PLC	5.5	7.7	52

ID = internal diameter, OD = outside diameter, * PDC and PLC tubes are cuffed.

Bronchoscope sizes

Table A.9 Bronchoscope sizes

Age	ETT size (ID mm)	Bronchoscope size (OD mm): ETT	Bronchoscope size (OD mm): LMA
Prem	2.5–3.0	2.2	2.4
Term	3.0–3.5	2.2	3.0
6 months	3.5–4.0	2.4	3.0
1 year	4.0–4.5	3.0	3.4

Table A.9 Bronchoscope sizes (*Continued*)

Age	ETT size (ID mm)	Bronchoscope size (OD mm): ETT	Bronchoscope size (OD mm): LMA
2 years	4.5–5.0	3.0	3.4
3 years	5.0–5.5	3.6	4.0
5 years	5.5–6.0	4.0	5.0
10 years	6.5–7.0 cuffed	4.4	6.0
14 years	7.0–7.5 cuffed	5.0	6.0

How to do a non-bronchoscopic BAL

Non-bronchoscopic BAL may be performed on intubated children as part of a septic screen or infectious diseases work up. NBBAL reduces the contamination with upper airway organisms seen in routine endotracheal suctioning, and provides a better guide to the presence and treatment of respiratory infections including ventilator associated pneumonia. As NBBAL is a relatively blind technique, it is most appropriate for patients with diffuse lung disease.

Equipment

- Wall suction.
- Sputum trap
- Connector
- Male:male luer adaptor
- 3-way tap
- Syringe ×2
- Sterile normal saline 0.9%
- Suction catheter (end hole or Penine FT 1605.40)
- Sterile gloves.

► Ensure that the sputum trap is upright when sampling, or you may lose all your sample.

Technique	Rational
• Explain the procedure	• To obtain cooperation and reduce anxiety in the patient/carer
• Warn microbiology and other laboratories as appropriate	• Urgent microscopy is needed. Other tests may be required, especially if looking for PCP
• Gather appropriate equipment	• See equipment list
• Ensure sterile technique	• To reduce risk of contamination and false positive result

(*Continued*)

Technique	Rational
• Position the child supine with the head turned to the left	• >90% chance of the catheter passing into the right lower lobe • Positioning the head to the right gives approx 80% chance of the catheter passing into the left lower lobe
• Preoxygenate for >1min	• Helps to reduce hypoxia during procedure
• Disconnect ETT from ventilator and advance the NBBAL catheter until resistance is felt	• If the ETT connector has a port that allows access to the ETT, use this. When the catheter meets resistance, or buckles in the ETT, it is probably wedged in a bronchus
• Instill 1 aliquot of 1mL/kg normal saline (max. 10mL) over 5 seconds	• Slow instillation reduces the risk of desaturation
• Turn the 3-way tap to apply suction to the catheter • Twist and withdraw the catheter a fraction to increase the yield, then withdraw the catheter rapidly	• Expect to get back around 50% of the volume instilled. Rapid withdrawal of the catheter after the first cm reduces the risk of contamination with secretions from the large airways
• Reconnect the patient to the ventilator. Oxygenate and hand bag as necessary until the child is stable • Repeat the process with the second aliquot.	• Most children tolerate the procedure well, but some desaturate. Ensure that the child is stable before leaving.

Tests

- Aspirate should be sent for urgent microscopy, culture and sensitivity, and for virology (immunoflourescence/viral culture). Microbiology will split the sample if warned in advance and 2 forms (micro and virology) sent
- If TB, non-tuberculous mycobacterium, fungi, or PCP suspected, specifically request these tests and discuss with Microbiology
- If alveolar proteinosis is suspected, discuss with Histology first
- If cellular type important (i.e. pulmonary Hodgkin's) discuss with Haematology first re performing cytospin.

Suction catheter sizes

Table A.10 Calculating suction catheter sizes for ETTs

Patient age	ETT size (ID mm)	Suction catheter size (FG)
Preterm	2.5	5
Preterm/Term	3.0	5–6
Term–6 months	3.5	6–7
6 months–18 months	4.0	6–8
18 months–3 years	4.5	7–8
3–5 years	5.0	8–10
5–8 years	5.5	8–10
8–10 years	6.0	10–12
10–12 years	6.5	10–12
12–14 years	7.0	12–14
14–16 years	7.5	12–14
>16 years female	8.0	12–14
>16 years male/female	8.5	14
>16 years male	9.0	14

- Ideally, OD of catheter should be 30–50% less than ID of ETT:
  - Catheter size (FG) = ID ETT (mm) × 1.5 (50% less)
  - Or catheter size (FG) = ID ETT (mm) × 2 (30% less).

Needle and catheter sizes

Table A.11 Needle and catheter sizes

Standard wire gauge	French or Charriere (Ch) scale	Diameter (mm)
10	10.20	3.25
12	8.29	2.64
14	6.38	2.02
16	5.12	1.63
18	3.83	1.22
20	2.87	0.91

Table A.11 Needle and catheter sizes (*Continued*)

Standard wire gauge	French or Charriere (Ch) scale	Diameter (mm)
22	2.23	0.71
24	1.75	0.56
26	1.43	0.46
28	1.18	0.38
30	0.99	0.31

IV catheter sizes

UAC/UVC: <1500g 3.5F
>1500g 5F

Use a double lumen UVC if likely to need inotropes or multiple infusions.

IV catheter insertion lengths

- UAC:
  - High position: T6–T9: above the coeliac axis (T12), the superior mesenteric artery (T12–L1), and the renal arteries (L1)
  - Low position L3–L4: below the structures listed above, and above the aortic bifurcation (L4–L5)
  - Insertion (high position) = measured distance from shoulder to umbilicus +2cm
- UVC:
  - Insertion = (1.5 × birthweight (kg))+ 5.5cm
  - Or half UAC insertion length (high position) + 1cm
  - Or (0.75 × distance from shoulder to umbilicus) – 1.5cm
- X-ray catheters after insertion to check placement.
- Internal jugular; subclavian:
  - Correct length of insertion (cm) for right internal jugular catheter

    = (height in cm/10) –1 for patients <100cm in height

    = (height in cm/10) –2 for patients >100cm in height
  - See Figs. A2 and A3
  - **Always** X-ray after insertion to check catheter position and to look for pneumothorax or bleeding. X-ray again after 4h in ventilated patients
  - Do not allow the catheter tip to lie within the heart.

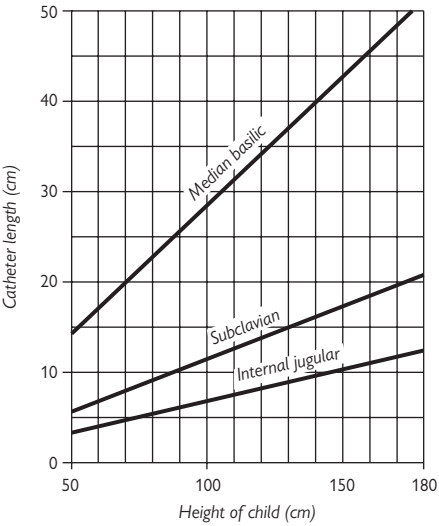

Fig. A.2 Predicted catheter length from height. Reproduced from Latto IP, Ng WS, Jones PL, *et al.* (1992). *Percutaneous Central Venous and Arterial Catheterization*, 2nd edn. WB Saunders, London, copyright © Elsevier (1992)

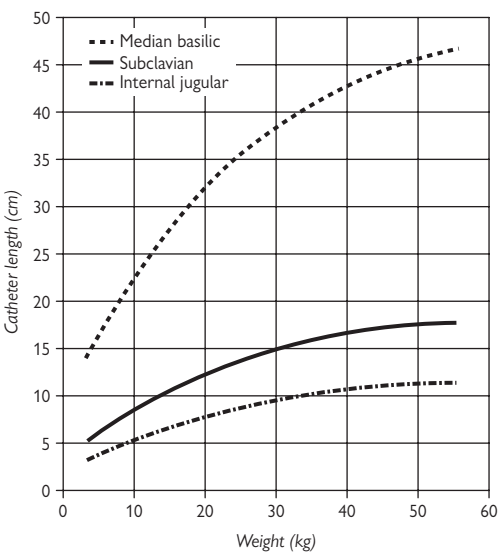

Fig. A3 Predicted catheter length from weight. Reproduced from Latto IP, Ng WS, Jones PL, *et al.* (1992). *Percutaneous Central Venous and Arterial Catheterization*, 2nd edn. WB Saunders, London, copyright © Elsevier (1992)

Haemofiltration catheter sizes

Table A.12 Haemofiltration catheter sizes

Weight (kg)	Size (FG)	Catheter length (cm)
<3	5	8–10
3 to 10	6.5	10–12.5
10 to 20	8	12.5–15
20 to 50	11	12.5–15
>50	12	15

Drug doses and information

We have not included a detailed pharmacopoeia. The editors all rely on a combination of Shann[1], the British National Formulary for Children[2], and the sound advice of a good paediatric pharmacist. We recommend that you do the same.

Resuscitation drugs

The table gives the mL of drug needed for different weights of patient.
⚠ Amiodarone, bicarbonate and adenosine may need further dilution, or to be given in a specific way—please check!

Table A.13 Resuscitation drugs per weight of patient

Age	**3/12**	**1**	**6**	**10**	**12**	**15**
Weight (kg)	**5**	**10**	**20**	**30**	**40**	**50**
Epinephrine (1:10,000)	0.5	1.0	2.0	3.0	4.0	5.0
Amiodarone (30mg/mL) over at least 3 min	0.9	1.7	3.4	5	6.7	8.4
Atropine (100mcg/mL)	1	2	4	6	6	6
Atropine (600mcg/mL)	–	0.3	0.7	1	1	1
Bicarbonate (8.4%)	5	10	20	30	40	50
Calcium chloride (10%)	0.5	1	2	3	4	5
Glucose (10%)	25	50	100	150	200	250
Adenosine (3mg/mL)* (initial dose 50mcgm/kg)	0.08	0.16	0.33	0.5	0.66	0.83
Naloxone (20mcg/mL)	2.5	5				
Naloxone (400mcg/mL)		0.25	0.5	0.75	1	1.25

Table A.13 Resuscitation drugs per weight of patient (*Continued*)

Age	3/12	1	6	10	12	15
Weight (kg)	**5**	**10**	**20**	**30**	**40**	**50**
Initial fluid bolus (mL)	100	200	400	600	800	1000
Defibrillation energy (J)	20	40	80	120	160	200

*Further dilution required.

Emergency treatment of seizures

- A prolonged convulsive seizure is one that has persisted for more than 5–10min, or where there is no awakening between shorter repetitive seizures for the same period of time.
  - Establish airway and administer high flow oxygen
  - Check blood sugar (BM)
  - Commence emergency treatment if convulsive epileptic seizures have persisted >5min
  - Diazepam (rectal) 0.5mg/kg ***or*** midazolam (buccal) 0.5mg/kg ***or*** lorazepam 0.1mg/kg IV
  - Commence monitoring; get IV access if not already obtained, check blood gas and electrolytes
  - If still convulsing, give lorezepam 0.1mg/kg IV or paraldehyde (rectal) 0.4mL/kg (0.8mL/kg of prepared solution; max 12mL)
  - If still convulsing after 10min, give phenytoin 20mg/kg IV/IO over 30min (ensure cardiac monitoring in place)
  - NB if already on phenytoin give phenobarbitone 20mg/kg IV/IO over 20min
  - Alert anaesthetist and PICU
  - If still convulsing 10min after phenytoin/phenobarbitone infusion completed, RSI with thiopentone 4mg/kg IV/IO or high dose IV Midazolam bolus then infusion.

Buccal midazolam		Rectal diazepam	
• 0–6 months:	1.25mg	• 0 –1 month:	1.25mg
• 6 months–1 year:	2.5mg	• 1 month–1 year:	2.5mg
• 1– 5years:	5mg	• 1–5 years:	5mg
• 5–10years:	7.5mg	• 5–10 years:	7.5mg
• >10 years:	10mg	• > 10 years:	10mg

References

1. Shann F (2008) Drug doses 2008, 14th edn, Collective Pty Ltd., Melbourne, Australia
2. *British National Formulary for Children* (2009) 5th edn, BMJ Publishing Group, London, UK

Emergency treatment of anaphylaxis (See 🕮 p.32)

Miscellaneous

Immunizations

Table A.14 UK immunization schedule

Age	Immunization
2 months	• Diptheria/tetanus/pertussis • Polio • *Haemophilus influenza* B • Pneumococcal
3 months	• Diptheria/tetanus/pertussis • Polio • *Haemophilus influenza* B • Meningococcus Gp C
4 months	• Diptheria/tetanus/pertussis • Polio • *Haemophilus influenza* B • Meningococcus Gp C • Pneumococcal
12 months	• *Haemophilus influenza* B • Meningococcus Gp C
13 months	• Measles, mumps, and rubella • Pneumococcal
3 years, 4 months to 5 years	• Diptheria/tetanus/pertussis • Polio • Measles, mumps, and rubella
13 to 18 years (before leaving school)	• Diptheria/tetanus/polio

'Non-routine' immunizations

- BCG. Give at birth to at-risk groups (e.g. ethnic minorities living in, or parents/ grandparents from high-risk area/country)
- Hepatitis B. Give at birth, 1 month, 2 months etc. for sero positive mothers (some countries give it to all babies).

Current UK neonatal screening

Inborn errors of metabolism

The UK National Screening Committee recommend that all babies in the UK are offered screening for phenylketonuria, congenital hypothyroidism, sickle cell disease, cystic fibrosis, and medium-chain acyl-CoA dehydrogenase deficiency. Some UK-wide programme variation exists.

- Blood-spot sample posted to reference laboratory

- Performed on a heel-prick blood sample taken from all neonates by midwife/HV at age 5–8 days
- If the child is on PICU, this needs to be organized by the PICU staff
- Samples taken on day 5, where possible
- Samples taken irrespective of medical condition, prematurity, or feeding status
- Repeated at 36 weeks' gestation for premature babies
- Sample should be taken prior to planned transfusion—post-transfusion repeats at 72h (for PKU, CHT, and CF) and 3 months (SCD)
- Send blood spots to reference laboratory in pre-paid 'screening envelopes' within 24h by first class post or locally identified alternatives.
- Avoid the use of internal mail.

Routine neonatal examination

- Undertaken in the first 3 days of life and at 6 weeks of age. Used to screen for:
- Congenital heart disease
- Congenital cataracts
- Other congenital malformations including congenital dislocation of the hip, cryptorchidism and undescended testes.

Newborn hearing screening

- Offered to all babies in the UK by 4–5 weeks of age
- For babies that have spent more than 48h in NICU or SCBU the hearing test should be offered by 44 weeks gestational age
- A combination of automated otoacoustic emissions and automated auditory brainstem response is used.

List of reasons that mean deaths must be reported to the Coroner (England and Wales)

- Where doctor has not treated the patient within 14 days of the death
- When the death has occurred during or following a medical procedure in hospital or, in any event, within 24h of admission to hospital.
- When the death has occurred as a result of homicide, suicide, accident, industrial disease, or any other unnatural cause
- When there are real grounds for believing that neglect contributed to the death
- When the death has occurred in prison, in police custody or whilst the deceased was detained in hospital under the Mental Health Act
- Where the cause of death is not known or there are any other circumstances which justify an investigation by the Coroner.

List of reasons that mean deaths must be reported to the Procurator Fiscal (Scotland)

- Sudden deaths, including deaths where there is evidence or suspicion of homicide, suicide, accident, industrial disease or any other unnatural cause
- Any death of a person subject to legal custody
- Any death occurring in health premises in the community

- Deaths related to neglect or complaint, or where the circumstances seem to indicate fault or neglect on the part of another person or organisation, including a Health Board or NHS Trust
- Certain deaths of children
- Deaths caused by an industrial disease or industrial poisoning
- Deaths due to a disease, infectious disease or syndrome which poses an acute, serious public health risk
- Deaths associated with medical or dental care, including:
  - Any unexpected or clinically unexplained death;
  - Any death which is apparently associated with lack of medical care;
  - Any death which occurs during the administration of a general or local anaesthetic or which may be associated with the administration of an anaesthetic
- Deaths caused by the withdrawal of life-sustaining treatment to a patient in a persistent vegetative state.

See http://www.copfs.gov.uk/Resource/Doc/13546/0000506.pdf.

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