Preoperative Evaluation of Medication and Malignant Hyperthermia

Presented by :Dr.Nosiba A. Alsharafy
Supervised by : Dr.Abdullwahab ALhifi

Preoperative Evaluation of Medication

- Medications
- In addition to a thorough medical history, the surgeon must inquire about all prescribed, over-the-counter, and herbal medications that a patient is taking. Many common medications can profoundly affect the perioperative and postoperative outcomes. Three major areas in which certain medications may interfere with surgical outcomes include hemostasis, wound healing, and drug interactions.

Hemostasis

- *. Aspirinand other nonsteroidal anti-inflammatory drugs (NSAIDs) :*
- *inhibit platelet function* ⟹ *a major source of perioperative bleeding in surgery.*
- *Aspirin irreversibly inhibits cyclooxygenase, and its effect lasts the entire duration of the platelets' lifespan (7-11 d).*
- *Aspirin can be restarted 1 day after surgery if medically necessary. Otherwise, restarting the drug 5-7 days after surgery is probably best.*
- *During surgery, compression stockings are recommended, and altering the amount of calf compression is ideal.*

NSAIDs

- reversibly inhibit cyclooxygenase
- It takes approximately 4.5 half-lives for any drug to reach negligible levels from its effective dose.
- Similar to aspirin, NSAIDs can be restarted 1 day after surgery if absolutely necessary, but using nonaspirin, non-NSAID pain relievers postoperatively is most prudent.
- Discontinuation of aspirin 2 weeks prior to surgery and of NSAIDs at least 5 half-lives of that particular NSAID dose prior to surgery is recommended.

Heparin

- is a glycosaminoglycan with potent anticoagulant activity.
- Its anticoagulant activity is due to a portion of the molecule's high affinity binding to antithrombin III and subsequent acceleration of its already potent anticoagulant action. Heparin also inhibits platelet function and increases the permeability of vessel walls. Low-dose heparin (5000 U subcutaneously bid) has a negligible effect on measurable coagulation and does not require discontinuation or adjustment prior to surgery. Full-dose intravenous or subcutaneous heparin does have a significant effect and needs to be stopped prior to surgery. The half-life of standard heparin ranges from approximately 45-60 minutes. Therefore, it should be discontinued 5 half-lives, or at least 5 hours, prior to the surgery.

Low molecular weight heparin

- (eg, enoxaparin) is a relatively new heparin that is increasingly being used. It has a lower molecular weight and negligible effects on platelet function and vascular permeability. It inhibits activated factor Xa. The average half-life of low molecular weight heparin is approximately 3 hours. Therefore, discontinuation at least 15 hours prior to surgery is recommended.

Warfarin (Coumadin)

- is another commonly used anticoagulant that acts by inhibiting a hepatic microsomal reductase that converts vitamin K to its active form
- Anticoagulant effects are delayed in onset and persist for several days after discontinuation. Stopping warfarin at least 3 days prior to surgery is recommended. In situations in which anticoagulation is absolutely necessary, heparin can be started while warfarin is stopped. The heparin can then be stopped hours prior to surgery. Warfarin can be restarted at the presurgery dosage 1 day after surgery.
- Always carefully consider the underlying reason (eg, stroke, thrombosis) for anticoagulation before it is discontinued. For many patients, the risks of discontinuing their anticoagulant agents exceed the risk of perioperative bleeding, which may be as low as 1.6%. Thoughtful consideration of the risk-to-benefit ratio is needed. Consultation with the patient's primary care physician is warranted if any doubt exists with regard to managing the perioperative dose of warfarin or heparin

Wound healing

- Several medications have been shown to retard wound healing and should be discontinued before surgery if possible.
- · Absolute
- o Glucocorticoids
- o Antiplatelet agents
- o Anticoagulants
- o Nicotine
- · Relative
- o Antineoplastic agents
- o Immunosuppressive agents
- o Colchicine
- o Penicillamine
- o Isotretinoin
- o Phenytoin

Wound healing

- Antiplatelet agents and anticoagulants adverse effect on wound healing. Resultant hematoma formation has been shown to cause mechanical disruption, increase the risk of infection, and disturb the fibrin matrix needed for proper wound healing.
- Glucocorticoids Fibroblast proliferation is decreased, and the amount of granulation tissue is reduced. Inflammation is diminished. Protein and collagen production is decreased. Epidermal proliferation is reduced, and the host defense mechanisms are altered.
- A single dose of a corticosteroid and doses less than the equivalent of 10 mg/d of prednisolone are thought to have little effect on wound healing. In patients on large doses of corticosteroids, switching the corticosteroid to cortisone acetate and administering supplemental vitamin A are recommended. Vitamin A, in doses of 25,000 IU/d, has been shown to reverse many of the adverse effects of corticosteroids, except for restoration of wound contraction.
- Nicotine is a potent vasoconstrictor cause of flap necrosis, especially where extensive surgical undermining is needed. A history of cigarette smoking is important to elicit in elderly persons, in whom slow wound healing is already a risk. Patients should be urged to discontinue smoking before and after surgery at least 1 week preoperatively and 2 days postoperatively to minimize adverse reactions.
- Many antineoplastic and immunosuppressive agents have been thought to retard wound healing.

Drug interactions

- Diuretics → are hypokalemia and hypomagnesemiain combination with epinephrine → cardiac arrhythmias. In such patients, a baseline potassium and magnesium level prior to surgery may be indicated.
- Propranolol → malignant hypertension and reflex bradycardia when used together with epinephrine.
- intravenous hydralazine or chlorpromazine may be effective.

SKIN DISEASES

- epidermolysis bullosa (EB) and ectodermal dysplasia (ED).
- In EB, conventional methods of intubation such as direct laryngoscopy or use of airway adjuncts, such as laryngeal mask airways or oral airways may be associated with blister formation in the pharynx, tongue, or supraglottic area. This formation may be associated with discomfort or postoperative airway obstruction. Many of these patients (both EB and ED) have scarring on the skin of their hands and feet, which restricts their options for venous access. Involvement of the face, neck, and mouth may result in decreased mouth opening, neck mobility, supraglottic airway narrowing, or any combination. Because of these concerns, the anesthesia team should have advanced notice of these patients' scheduling to afford the opportunity for complete face-to-face preoperative evaluation that will allow for appropriate consultation with the patient's dermatologist and PCP, followed by discussion with the family of risks and methods for skin protection and airway management.

- Definition
  - Epidemiology
  - Cellular mechanism
- MH Crisis/Treatment
- Genetics of MH
- Testing for MH
- Common questions

WHAT IS MH ?

- Inherited disorder of skeletal muscle
- Triggered in susceptible humans or animals by volatile inhalation agents or succinylcholine
- Characterized by the following:
  - Hypermetabolism
  - Skeletal muscle damage
  - Hyperthermia
  - Death (if left untreated)

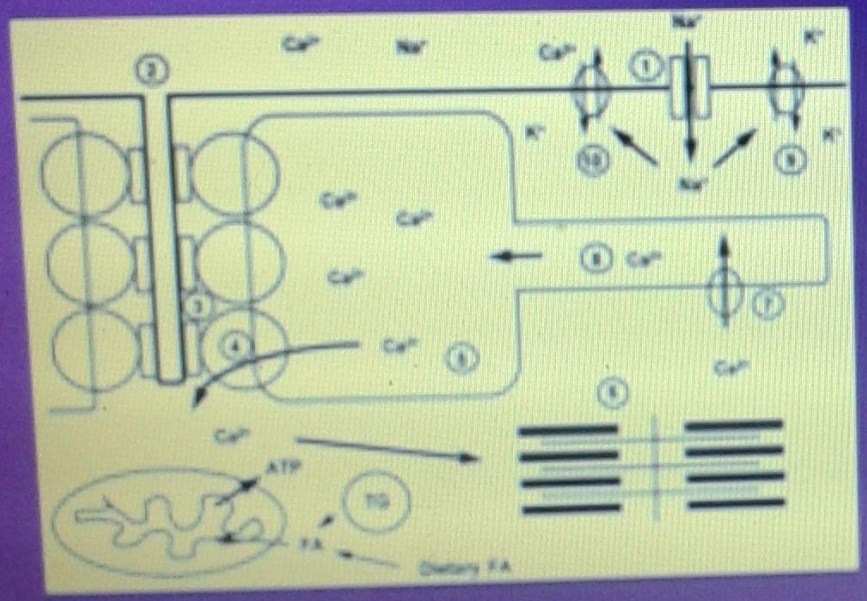
Incidence of MH

- Clinical incidence: 1 in 10,000 to 50,000 anesthetics
- Pediatric incidence: 1 in 15,000 anesthetics
- May depend on
  - Age
  - Sex
  - Concomitant drug administration
  - Comorbidities

Timing of MH

- Onset: intraoperatively or shortly afterwards (PACU)
- Rate of onset
  - Fulminant: onset of full blown syndrome within minutes of induction of GA
  - More indolent
- ??Environmental triggers

Increase in intracellular Ca



- Actin-myosin
- Glycogenolysis
- ↑ cell metabolism
- Activation of oxidative cycle

Contracture (rigidity) – Heat –
Excess lactate – O_2 consumption –
CO_2 production – Cell breakdown

MH Crisis: Clinical Signs

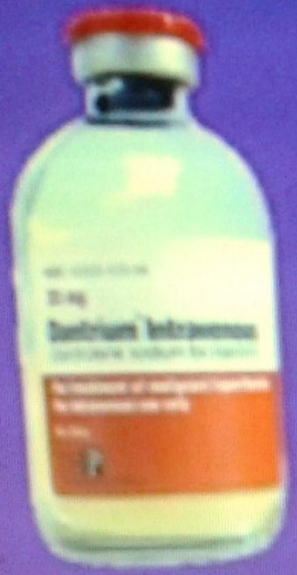
- Tachycardia (hypertension)
- Tachypnea/ inc MV
- Increase ETCO2
- Skin mottling
- Rigidity: MMR or generalized
- Ventricular dysrhythmias
- Hyperthermia
- Myoglobinuria (cola-colored urine)
- DIC

MH Crisis: Laboratory Find

- Respiratory acidosis
  - Increase a-v pCO_2 gradient
- Metabolic (lactic) acidosis
- Hyperkalemia (↑ K^+)
- HyperCKemia (↑ CK)
- Increase serum and urine myoglobin
- Abnormal coagulation tests

Treatment of MH Crisis

- Call for help
- Turn off triggering agents (volatile agents)
- Alert surgeon and nurses
- Hyperventilate with $FIO_2 = 1.0$
  - High gas flows
- Cool
- Assistant to mix dantrolene



Dantrolene

- Initial dose 2.5 mg/kg
- Each bottle has 20 mg dantrolene
- Mix with sterile WATER 60 mL
- Administer quickly through large bore IV
- Repeat dose until symptoms resolve

Treatment of MH Crisis

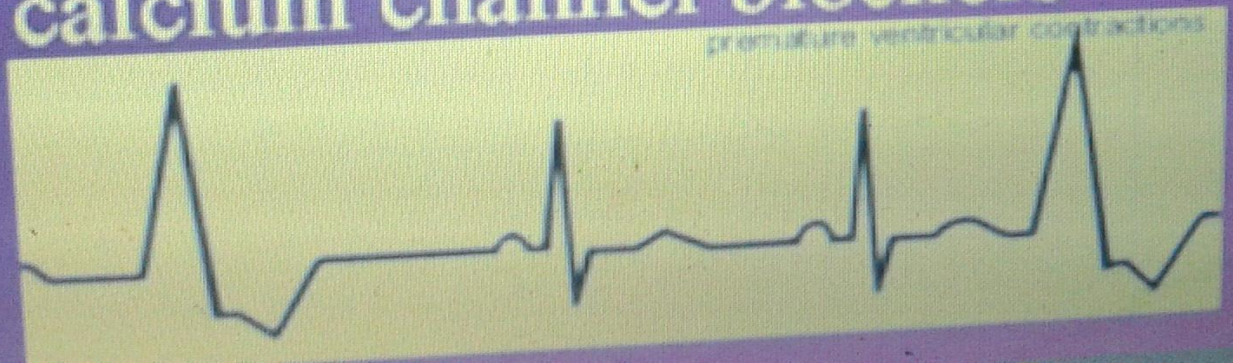
- Large bore IV access, ?A-line, CVP
- Draw labs
  - ABG
  - Electrolytes, BUN/Cr
  - CK, myoglobin
  - DIC panel
- Foley
- Cool IV fluids

Cooling

- Turn down room temperature
- Uncover patient
- Ice packs to neck, groin, axilla
- Cool IV fluids
- Gastric lavage
- ?Sterile ice in surgical field
- Don't overcool

Dysrhythmias

- Secondary to acidosis and hyperkalemia
- Acidosis: $NaHCO_3$
- Hyperkalemia: insulin and glucose
  - Insulin 0.1 U/kg
  - D25 2 mL/kg over 30 min
  - Calcium
- Avoid calcium channel blockers



After Immediate Crisis

- Sedation
- Monitor core temperature
- Maintain urine output
  - IV fluids
  - Diuretics

After Immediate Crisis

- Transfer to hospital
- ICU admission
- Central temperature monitoring
- Serial labs
  - CK
- Dantrolene 1 mg/kg q 6 h x 24–48 h
  - Recrudescent rate 25%
- Kidney protection: saline and $NaHCO_3$

After Immediate Crisis

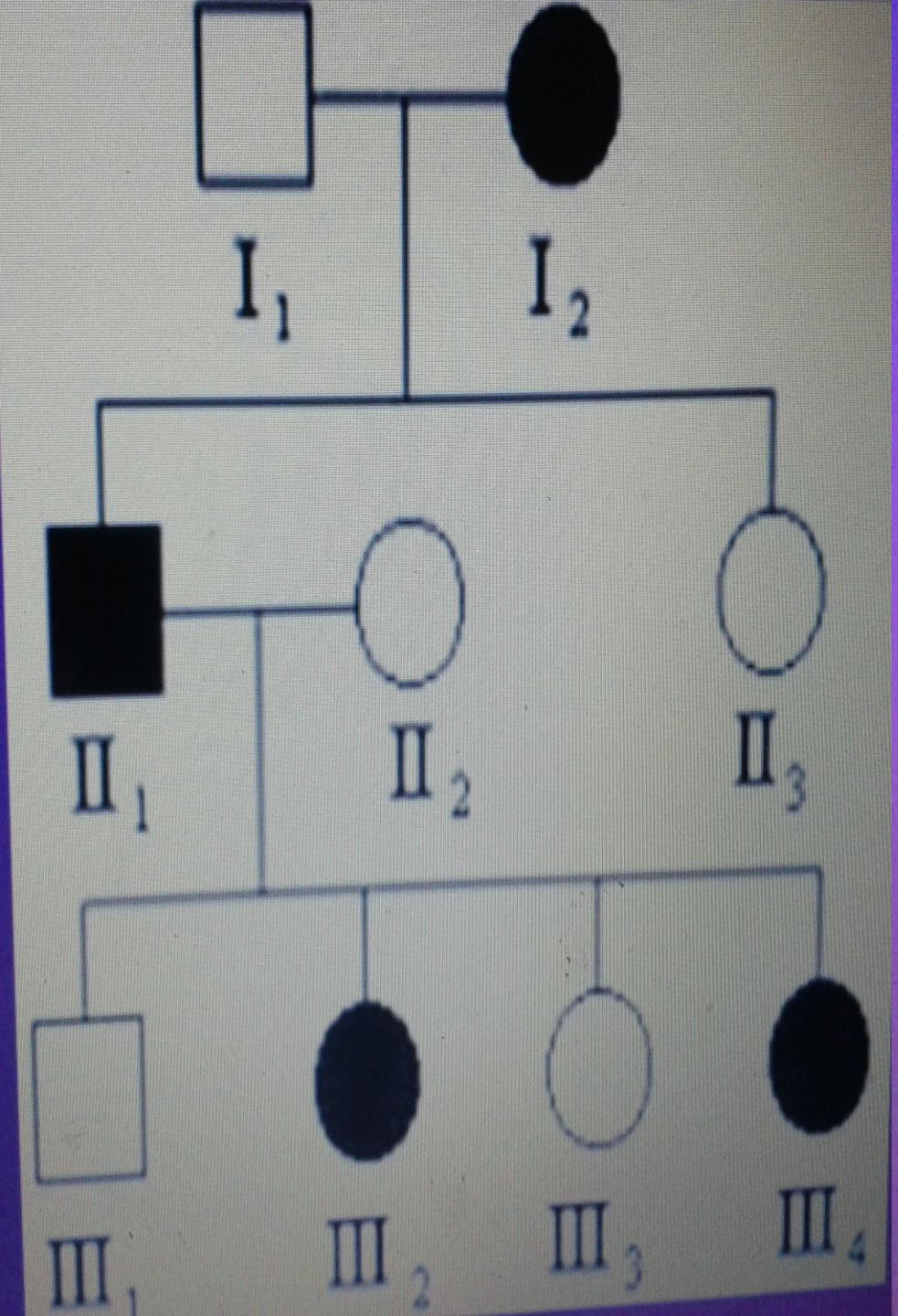
- Patients and family counseling
  - ID bracelet/necklace
- North American Malignant Hyperthermia Registry
- AMRA
- Testing
  - Refer to MH Testing Center

MH Crisis: Differential Diagnosi

- Light anesthesia
- Inadequate ventilation
  - Rebreathing
  - Fresh gas flow
- Infection/sepsis
- Iatrogenic overheating
- Serotonin syndrome
- Pheochromocytoma

MH Crisis: Differential Diagnosis

- Other muscle disease (dystrophinopathy)
- Neuroleptic malignant syndrome
- Myotonic syndromes
- Cerebral ischemia
- Ascending tonic-clonic syndrome
- Rhabdomyolysis
  - Statins
  - Hypoperfusion



Genetics of MH

- Autosomal dominant
- Variable penetrance

Triggering Agents

Volatile Anesthetics

- Isoflurane
- Desflurane
- Halothane
- Enflurane
- Sevoflurane

Depolarizing Muscle Relaxants

- Succinylcholine

Care of MHS Patient: Equipment

- Shut down and/or disable vaporizers
- Flow oxygen at 10 L/min for 20 minutes through machine and ventilator
- New anesthesia machines require longer flushing time
- Check MH Kit
- Dantrolene pretreatment not recommended

Care of MHS Patient

- Prepare anesthesia machine
- Non-triggering anesthetic
- Dantrolene is not necessary
- Core temperature monitoring
- Monitor in Phase I PACU: 1 h
- Phase II PACU: 1 h

Important Questions ???

Q: May surgery be done without a muscle biopsy test for MH?

Q: Should MHS patients be pretreated with dantrolene?

Q: Can local anesthetics be used for dental work?

Q: How long should MHS patients be monitored after uneventful anesthesia?

Q: How should I manage a patient with a family history of MH?

Q: Is MH linked to other serious medical problems?

Q: Can calcium gluconate or calcium chloride be used when treating hyperkalemia cardiac toxicity during an MH crisis?

MH Kit

Required Medications

- Dantrolene (36 vials)
- Sterile water for injection
- Sodium bicarbonate
- Dextrose
- Mannitol
- Furosemide
- Antidysrhythmics drugs

Necessary Equipment

- Temperature probes
- Nasogastric tubes
- Assorted catheters
- Blood collection tubes
- Syringes
- Needles
- Normal saline

MH Hotline
1-800-644-9737
Outside the US:
1-315-464-7079

EMERGENCY THERAPY FOR MALIGNANT HYPERTHERMIA

DIAGNOSIS

Signs of MH:

- Increased $ETCO_2$
- Trunk or total body rigidity
- Masseter spasm or trismus
- Tachycardia/tachypnea
- Acidosis
- Increased temperature (may be late sign)

Sudden/Unexpected Cardiac Arrest in Young Patients

- Presume hyperkalemia and initiate treatment (see #6)
- Measure CK, myoglobin, ABGs, until normalized
- Consider dantrolene
- Usually secondary to occult myopathy (e.g., muscular dystrophy)
- Resuscitation may be difficult and prolonged

Trismus or Masseter Spasm with Succinylcholine

- Early sign of MH in many patients
- If limb muscle rigidity, begin treatment with dantrolene
- For emergent procedures, continue with non-triggering agents; consider dantrolene
- Follow CK and urine myoglobin for 36 hours at least. Check CK immediately and at 6–hour intervals until returning to normal. Observe for cola colored urine. If present, test for myoglobin.
- Observe in PACU or ICU for at least 12 hours

ACUTE PHASE TREATMENT

1 GET HELP. GET DANTROLENE – Notify Surgeon.

- Discontinue volatile agents and succinylcholine.
- Hyperventilate with 100% oxygen at flows of 10 L/min. or more.
- Halt the procedure as soon as possible; if emergent, use non-triggers.

(The circle system and CO_2 absorbent need not be changed.)

2 Dantrolene 2.5mg/kg rapidly IV through large-bore IV, if possible

To convert kg to lbs for amount of dantrolene, give patients 1 mg/lb (2.5 mg/kg approximates 1 mg/lb).

- Repeat until there is control of the signs of MH.
- Sometimes more than 10 mg/kg (up to 30 mg/kg) is necessary.
- Dissolve the 20 mg in each vial with at least 60 ml **sterile preservative-free water** for injection. Prewarming (not to exceed 38°C) the sterile water will speed solubilization of dantrolene.
- The crystals also contain NaOH for a pH of 9; each 20 mg bottle has 3 gm mannitol for isotonicity.

3 Bicarbonate for metabolic acidosis.

- 1-2 mEq/kg if blood gas values are not yet available.

4 Cool the patient with core temperature >39°C. Lavage open body cavities, stomach, bladder, or rectum. Apply ice to surface. Infuse cold saline intravenously. Stop cooling if temp. <38°C and falling to prevent drift <36°C.

5 Dysrhythmias usually respond to treatment of acidosis and hyperkalemia.

- Use standard drug therapy <u>except calcium channel blockers, which may cause hyperkalemia or cardiac arrest in the presence of dantrolene.</u>

6 Hyperkalemia - Treat with hyperventilation, bicarbonate, glucose/insulin, calcium.

- Bicarbonate 1-2 mEq/kg IV.
- For **pediatric**, 0.1 units insulin/kg and 1 ml/kg 50% glucose **or** for **adult**, 10 units regular insulin IV and 50 ml 50% glucose.
- Calcium chloride 10 mg/kg or calcium gluconate 10-50 mg/kg for life-threatening hyperkalemia.
- Check glucose levels hourly.

7 Follow $ETCO_2$, electrolytes, blood gases, CK, core temperature, urine output and color, coagulation studies. If CK and/or K+ rise more than transiently or urine output falls to less than 0.5 ml/kg/hr, induce diuresis to >1 ml/kg/hr urine to avoid myoglobinuria-induced renal failure.

- Venous blood gas (e.g., femoral vein) values may document hypermetabolism better than arterial values.
- Central venous or PA monitoring as needed and record minute ventilation.
- Place Foley catheter and monitor urine output.

POST ACUTE PHASE

A Observe the patient in an ICU for at least 24 hours, due to the risk of recrudescence.

B Dantrolene 1 mg/kg q 4-6 hours or 0.25 mg/kg/hr by infusion for at least 24 hours. Further doses may be indicated.

C Follow vitals and labs as above (see #7)
- Frequent ABG
- CK every 6 hours

D Follow urine myoglobin and institute therapy to prevent myoglobin precipitation in renal tubules and the subsequent development of Acute Renal Failure. Follow standard intensive care therapy for acute rhabdomyolysis and myoglobinuria (urine output > 200 ml/h, alkalinization of urine with Na-bicarbonate infusion with careful attention to both urine and serum pH values, etc.).

E Counsel the patient and family regarding MH and further precautions; refer them to MHAUS. Fill out and send in the Adverse Metabolic Reaction to Anesthesia (AMRA) form (www.mhreg.org) and send a letter to the patient and her/his physician. Refer patient to the nearest Biopsy Center for follow-up.

Non-Emergency Information

MHAUS
11 East State Street
PO Box 1069
Sherburne, NY 13460-1069
Phone
1-800-986-4287
(607-674-7901)
Fax
607-674-7910
Email
info@mhaus.org
Website
www.mhaus.org

Since 1981
Dedicated to Patient Safety

CAUTION: This protocol may not apply to all patients; alter for specific needs.

Produced By the Malignant Hyperthermia Association of the United States

THANKS