

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



جمعية طب الأطفال اليمنية

YEMENI PEDIATRIC SOCIETY

السبت .. 21 / يونيو / 2014م

صنعاء- مستشفى الكويت الجامعي

All about immunoglobulins

الدكتور

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البيورد العربي- طب الأطفال



Case 1:

3 years old child has chronic liver disease is living with his 5 yrs old brother who had HAV infection before 5 days.



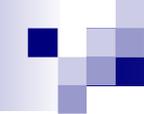
Case 2:

2 years old child with compromised immunity had come into contact with measles case yesterday.



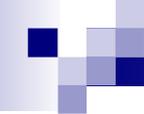
Case 3:

Family of 2 yrs girl with confirmed rubella infection visited a 17 years old pregnant girl in her 9th weak today.



Case 4:

10 years old child (HBV-DNA negative) had undergone liver transplantation for liver failure caused by HBV.



Case 5:

During trying to take a liver biopsy under ultrasound guidance from your HBsAg +ve patient, you were injured by the needle.

Case 6:

5 years old child has nephrotic syndrome on prednisolone 60mg/day for last 3 wks, was exposed to 3 years old child with vesicular skin rash diagnosed as chickenpox before 2 days.

Case 7:

1.5 years old patient had received IV immunoglobulin for ITP before 2 weeks, the patient came now for 2ed dose of measles vaccine.. Will you give the vaccine? And what you will tell his mother?

Case 8:

12 months old baby had undergone abdominal surgery before 1 month, during operation he had received 20ml/Kg fresh blood. Now the patient came for the 1st dose of MMR vaccine.. Will you give the vaccine? And what you will tell his mother?



What are the
?immunoglobulins

Immunoglobulins (IG):

Human immunoglobulin is a sterile preparation of concentrated antibodies (immune globulins) recovered from pooled human plasma or serum, tested and found non-reactive for hepatitis B surface antigen and for antibodies against hepatitis C virus and HIV (types 1 & 2). The antibody concentrations in IG reflect the infectious disease exposure and immunization experience of plasma donors.

Hyperimmune Animal Antisera:

Immunoglobulins of animal origin are called antisera.

Immunoglobulins of animal origin were frequently associated with hypersensitivity reactions and are no longer used.

Antisera preparations available for humans:

- **Diphtheria antitoxin**, which is used to treat diphtheria.
- **Botulinum antitoxin**, which is available for use in adults with botulism but is not used in infants for whom botulism IVIG (Baby-BIG), a human-derived antitoxin, is licensed.



Types of **immunoglobulins**



Two types of human immunoglobulin preparation are available:

- Normal immunoglobulin
- Disease-specific immunoglobulins.

Normal immunoglobulin

Human normal immunoglobulin (HNIG) is prepared from pools of donations of human plasma; it **contains** immunoglobulin G (**IgG**) and **antibodies to hepatitis A, measles, mumps, rubella, varicella**, and other viruses that are currently prevalent in the general population.

Disease-specific immunoglobulins:

Specific immunoglobulins are prepared by pooling the plasma of selected human donors with high levels of the specific antibody required:

- Tetanus immunoglobulin**
- Rabies immunoglobulin**
- Hepatitis B immunoglobulin**
- Varicella–zoster immunoglobulin (VZIG)**
- Cytomegalovirus IG (CMV-IG).**
- Botulism IVIG human**



There are **no** specific immunoglobulins for hepatitis A, measles, or rubella.
Normal immunoglobulin is used in certain circumstances.

There is **no** specific immunoglobulin for **mumps**; neither normal immunoglobulin nor MMR vaccine is effective as post-exposure prophylaxis.

<ul style="list-style-type: none">■ Normal immunoglobulin	<ol style="list-style-type: none">1. Intravenous (IV)2. Intramuscular (IM)3. Subcutaneous (S/C)
<ul style="list-style-type: none">■ Disease-specific immunoglobulins	<ol style="list-style-type: none">1. Tetanus IG.2. Rabies IG.3. Hepatitis B IG.4. Varicella–zoster IG (VZIG)5. Cytomegalovirus IG (CMV-IG).6. Botulism IVIG (human).



Indications of **immunoglobulins**

Indications of Normal immunoglobulin

Intravenous immunoglobulin (IVIG)

1. Replacement therapy for children with congenital agammaglobulinaemia, hypogammaglobulinaemia,
2. Short-term treatment of idiopathic thrombocytopenic purpura
3. Kawasaki disease
4. Prophylaxis of infection following bone-marrow transplantation
5. Pediatric HIV infection.
6. Hypogammaglobulinemia in chronic B-cell lymphocytic leukemia
7. Treatment of Guillain-Barre syndrome
8. Varicella post-exposure prophylaxis
9. Staph. or strept. toxic shock syndrome & necrotizing fasciitis
10. Refractory dermatomyositis & polymyositis, sever anaemia due to parvovirus B19 infection

Indications of Normal immunoglobulin

Intramuscular immunoglobulin (IM)	<ol style="list-style-type: none">1. For replacement therapy, but intravenous formulations are normally preferred.2. Protection of susceptible contacts against hepatitis A virus (infectious hepatitis), measles and, to a lesser extent, rubella. <p>Injection of immunoglobulin produces immediate protection lasting for several weeks.</p>
Subcutaneous (S/C)	<ol style="list-style-type: none">1. For replacement therapy, but intravenous formulations are normally preferred. <p>Preparations for subcutaneous use may be administered by intramuscular injection if subcutaneous route not possible.</p>

Monoclonal Antibodies:

- Monoclonal antibodies are antibody preparations produced against a single antigen.
- **Palivizumab:** the major monoclonal antibody used in infectious diseases, which can prevent severe disease from respiratory syncytial virus (RSV) among children ≤ 24 mo of age with chronic lung disease (bronchopulmonary dysplasia), with a history of premature birth or with congenital heart lesions or with neuromuscular diseases.

Anti-D (Rh₀) immunoglobulin:

Anti-D (Rh₀) immunoglobulin is available to prevent a rhesus-negative mother from forming antibodies to fetal rhesus-positive cells which may pass into the maternal circulation. The objective is to protect any subsequent child from the hazard of haemolytic disease of the newborn.



Doses of **immunoglobulins**

Intravenous Immune Globulin (IVIg)

Replacement therapy for antibody-deficient disorders:

- (1) 400–500 mg/kg IV every 4 weeks to start
- (2) Children with severe hypogammaglobulinemia (<100 mg/dL) may benefit from a total loading dose of 800 mg/kg given in two separate doses a few days apart, followed by 400 to 500 mg/kg every month
- (3) Adjust dosing based on clinical response and to maintain trough IgG level of at least 500 mg/dL

Immune thrombocytopenic purpura:

- (1) Initially 400–2000 mg/kg (up to 1000 mg/kg given on a single day or in divided doses over 2–5 consecutive days)
- (2) Maintenance dose: 400–1000 mg/kg/dose every 3–6 weeks based on clinical response and platelet count
- (3) May also use Rh (D) immunoglobulin (WinRho) in Rh-positive patients

Intravenous Immune Globulin (IVIg)

Kawasaki disease:

- (1) 2 g/kg × 1 dose over 8–12 hr
- (2) If signs and symptoms persist, consider second dose of 2 g/kg
- (3) Doses should be started within first 10 days of symptoms

Pediatric human immunodeficiency virus (HIV) infection with antibody deficiency (IgG concentration <400 mg/dL, failure to form antibodies to common antigens, recurrent serious bacterial infections, or measles prophylaxis):

dosing same as for antibody-deficient disorders mentioned previously

Bone marrow transplantation:

- (1) 400–500 mg/kg/dose to start, adjust dosing to maintain trough IgG level of at least 400 mg/dL
- (2) May decrease incidence of infection and death but not acute graft-versus-host disease

Intramuscular Immune Globulin (IMIG)

Hepatitis A postexposure prophylaxis:

0.02 mL/kg given within 14 days of exposure. IG is not needed if at least one dose of hepatitis A vaccine was given at ≥ 1 month before exposure

Measles prophylaxis:

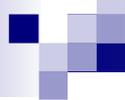
- 0.25 mL/kg/dose (maximum dose: 15 mL) given within 6 days of exposure in immunocompetent patient
- 0.5 mL/kg (maximum dose: 15 mL) immediately following exposure in immunocompromised patients

Rubella prophylaxis during pregnancy:

0.55 mL/kg/dose within 72 hours of exposure

Rabies:

20 international units/kg single dose administered as soon as possible after exposure with the first dose of rabies vaccine



Subcutaneous Immune Globulin

- 100–125 mg/kg weekly (maximum rate: 20 mL/hour; doses >15 mL usually should be divided between sites, but it depends on the amount of subcutaneous tissue)
- Larger doses can be given simultaneously in multiple sites or more frequently than once per week
- Using the same areas for injections improves tolerability



Precautions and adverse reactions

Intravenous Immune Globulin (IVIg)

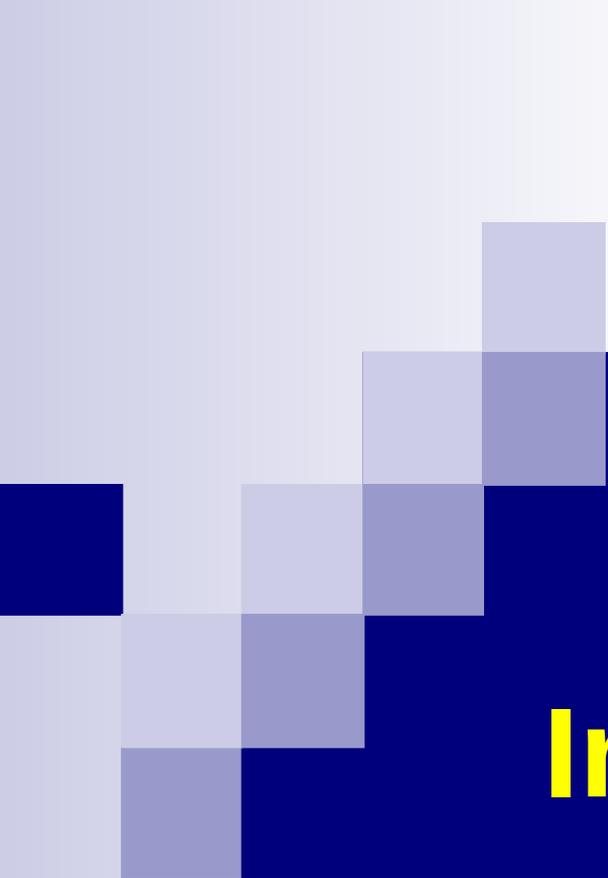
- **Severe systemic symptoms** (hemodynamic changes, respiratory difficulty, anaphylaxis)
- **Less severe systemic reactions** (headache, myalgia, fever, chills, nausea, vomiting) may be alleviated by decreasing infusion rate or premedication with IV corticosteroids, antihistamines, and/or antipyretics
- **Aseptic meningitis syndrome**
- **Acute renal failure** (increased risk with preexisting renal insufficiency and with sucrose-containing IVIG)
- **Acute venous thrombosis** (increased risk with sucrose-containing IVIG)
- **Use with caution in patients with undetectable IgA level** due to trace amounts of IgA in IVIG, although routine screening for IgA deficiency is not recommended in potential recipients

Intramuscular Immune Globulin (IMIG)

- **Severe systemic symptoms** (hemodynamic changes, anaphylaxis)
- **Local symptoms** at the site of injection increase with repeated use
- High risk for **anaphylactoid reactions** if given intravenously
- **Use with caution in patients with undetectable IgA levels** due to trace amounts of IgA in IMIG

Subcutaneous Immune Globulin

- Similar to IMIG and IVIG



IG and Immunization

Immunoglobulins and Immunization:

- Live-virus vaccines (MMR & varicella vaccine) may have diminished immunogenicity when given shortly before or during the several months after receipt of IG (both IM & IV preparations). So, there must be an interval between receiving IG and live-virus vaccines administration
- Administration of **IG** preparations **does not** interfere with antibody responses to **yellow fever, OPV, or oral rotavirus vaccines.**
- **IG doesn't** cause significant inhibition of the immune responses to **inactivated vaccines** and **toxoids.**
- **Palivizumab does not interfere** with response to inactivated or live vaccines.

Suggested interval between IG administration and MMR & varicella immunization:

Indications or Product	Route	Dose		Interval, mo ^a
		U or mL	mg IgG/kg	
Tetanus prophylaxis (as TIG)	IM	250 U	10	3
Hepatitis A prophylaxis (as IG)				
Contact prophylaxis	IM	0.02 mL/kg	3.3	3
International travel	IM	0.06 mL/kg	10	3
Hepatitis B prophylaxis (as HBIG)	IM	0.06 mL/kg	10	3
Rabies prophylaxis (as RIG)	IM	20 IU/kg	22	4
Varicella prophylaxis (as VariZIG)	IM	125 U/10 kg (maximum 625 U)	20–40	5
Measles prophylaxis (as IG)				
Standard	IM	0.25 mL/kg	40	5
Immunocompromised host	IM	0.50 mL/kg	80	6
RSV prophylaxis (palivizumab monoclonal antibody) ^b	IM	...	15 mg/kg (monoclonal)	None
Cytomegalovirus Immune Globulin	IV	3 mL/kg	150	6
Blood transfusion				
Washed RBCs	IV	10 mL/kg	Negligible	0
RBCs, adenine-saline added	IV	10 mL/kg	10	3
Packed RBCs	IV	10 mL/kg	20–60	5
Whole blood	IV	10 mL/kg	80–100	6
Plasma or platelet products	IV	10 mL/kg	160	7
Replacement (or therapy) of immune deficiencies (as IGIV)	IV	...	300–400	8
ITP (as IGIV)	IV	...	400	8
ITP	IV	...	1000	10
ITP for Kawasaki disease	IV	...	1600–2000	11

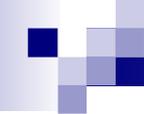
Source: Red Book



Case 1:

3 years old child has chronic liver disease is living with his 5 yrs old brother who had HAV infection before 5 days.

Intramuscular Immunoglobulin 0.02 ml/kg within 14 days of exposure.



Case 2:

2 years old child with compromised immunity had come into contact with measles case yesterday.

Intramuscular Immunoglobulin, 0.5 ml/kg, maximum dose 15 ml, within 6 days of exposure.

Case 3:

Family of 2 yrs girl with confirmed rubella infection visited a 17 years old pregnant girl in her 9th weak today.

Deep Intramuscular Immunoglobulin 750 mg within 72 hours of exposure and serological follow-up.

Case 4:

10 years old child (HBV-DNA negative) had undergone liver transplantation for liver failure caused by HBV.

Intravenous preparation of hepatitis B-specific immunoglobulin should be given.. (Hepatect CP 500 units/10 ml -Biotest UK)

Case 5:

During trying to take a liver biopsy under ultrasound guidance from your HBsAg +ve patient, you were injured by the needle.

Hepatect CP (500 units/10 ml) should be given as soon as possible after exposure; ideally within 48 hours, but not later than 72 hours after exposure.

Case 6:

5 years old child has nephrotic syndrome on prednisolone 60mg/day for the last 3 wks, was exposed to 3 years old child with vesicular skin rash diagnosed as chickenpox before 2 days.

Varicella–Zoster Immunoglobulin 250 mg, deep intramuscular injection (as soon as possible—not later than 10 days after exposure).

Case 7:

1.5 years old patient had received IV immunoglobulin for ITP before 2 weeks, the patient came now for 2ed dose of measles vaccine.. Will you give the vaccine? And what you will tell his mother?

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Case 8:

12 months old baby had undergone abdominal surgery before 1 month, during operation he had received 20ml/Kg fresh blood. Now the patient came for the 1st dose of MMR vaccine.. Will you give the vaccine? And what you will tell his mother?

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My message

(1) Don't forget that you have a powerful guard against (what may be fatal) diseases.

My message

(2) Don't forget that IG which is present in blood interferes with MMR& Varicella vaccines action..

POSTPONE THE DOSE.

لِلَّهِ مَا أَخْلَى الطُّفُولَةَ
أَنَّهَا حِلْمُ الْحَيَاةِ

مَا

تَرْنُو إِلَى الدُّنْيَا
بَيْنَ أَحْنَجَةِ السَّبَابِ
وَمَا فِيهَا

بَعِينٍ بِاسِيْمَهُ
وَتَسِيرُ فِي

عَدَوَاتٍ وَوَادِعِهَا

Thank You

أَنَّ الدُّفُولَةَ حَقِيْقَةٌ
بِنَفْسٍ خَالِئَةٍ
بِنَفْسٍ خَالِئَةٍ