Therapeutic immunoglobulins

What are immunoglobulins?

Human immunoglobulins can be given to confer passive (temporary) immunity. They provide immediate protection and the effects last for weeks.

They are derived from plasma of non-UK blood donors and are safe from hepatitis B and C, HIV and syphilis. They can be tested for cytomegalovirus (CMV) and malaria if necessary.

There are two types of immunoglobulins

- Normal (nonspecific) - from unselected donors.
- Hyperimmune (specific) - from selected donors.

Human normal immunoglobulin

Human normal immunoglobulin (HNIg) is made from the plasma of about 1,000 donors. This provides antibodies against hepatitis A, rubella, measles and other viruses prevalent in the general population.[1]

It is most effective within three days of contact (but has some effect up to six days); protection is immediate and lasts several weeks.

It blocks the immune response to live vaccines (except yellow fever) for three months, and live vaccines should ideally be given at least three weeks before or three months after an injection of HNIg. This can, however, be ignored if there is insufficient time - eg, for travellers. It is contra-indicated in those with class-specific antibody to IgA.

HNIg is used for:

- **Hepatitis A contacts** should be given normal immunoglobulin (in addition to hepatitis A vaccine) if they are over 60 years, have chronic liver disease, or HIV infection, or who are immunosuppressed; normal immunoglobulin should be given as soon as possible, preferably within 14 days of exposure to the primary case (or 28 days if they have chronic liver disease).
- **Rubella contact in non-immune pregnant women where termination is unacceptable** - it does not prevent infection but reduces symptoms and the risks to the fetus. Risk is greatest in the first 11 weeks of gestation. Give as soon as possible after exposure only when termination is not acceptable. Measles, mumps and rubella (MMR) and anti-D may be given in the postpartum period (separate syringes and into different limbs). Measure rubella antibodies after eight weeks and vaccinate if necessary. However, rubella vaccine is not effective for post-exposure prophylaxis.
- **Measles contact, greatest effect if given within 72 hours of exposure (but some effect if given within six days)** in:
    - The immunocompromised.
    - Non-immune pregnant women (but there is no evidence it prevents fetal loss).
    - An infant aged under 9 months - if the mother is not immune
    - An infant aged 6-8 months - if the mother is immune (because under 6 months the child is protected by maternal antibodies and after 9 months MMR can be given for prophylaxis following exposure to measles).
- Poliomyelitis - there is some evidence that intravenous immunoglobulin Ig may have a role in the management of post-polio syndrome.

IV HNIg is also used to give broad-spectrum passive protection to premature babies, patients with congenital hypogammaglobulinaemia, immunoglobulin deficiencies, autoimmune disorders - eg, thrombocytopenic purpura (where temporary, rapid rise in platelets is needed, such as pregnancy, or pre-operatively), Kawasaki disease, following bone-marrow transplantation, children with HIV, Guillain-Barré syndrome, and myasthenia gravis (unlicensed use) when it can induce remission in severe relapse.

Immunoglobulin therapy has been used in critical care settings to manage severe COVID-19 infection.[2]

NB: for mumps contacts, neither HNIg nor MMR offers protection.

Human specific immunoglobulins

- Hepatitis B **immunoglobulin**:[3] this is used after needlestick or sexual exposure and in infants born to infected mothers (persistent carrier with detectable hepatitis e antigen or its antibody or in recent infection). It should also be given in hepatitis B mothers when the birth weight of the baby is <1500 g. The sexual contacts of acute hepatitis B sufferers and chronic hepatitis B sufferers (newly diagnosed) should also receive specific immunoglobulin if unprotected sexual contact occurred in the previous seven days. It should be given preferably within 12 hours and not later than one week after exposure. Hepatitis B vaccine should also be given. See the separate Hepatitis B Vaccination and Prevention article.

- **Human varicella-zoster immunoglobulin**:[4] this is only given to neonates (within seven days of birth) of exposed women, or to the non-immune exposed to chickenpox or shingles if at risk of severe infection **when they are unable to take the recommended antivirals** (aciclovir or valaciclovir).[5] This will include:

    - Immunocompromised individuals.
    - High-dose steroidal therapy (an adult who has received 40 mg daily for more than a week in the previous three months, or a child who has received a daily dose of 2 mg/kg for more than a week, or 1 mg/kg for more than a month, in the previous three months).
    - Non-immune pregnant women (to protect the fetus).
    - People with significant exposure to the virus.
- **Rabies immune globulin**:[6] this is indicated for an unimmunised person exposed to a bite from an animal from a high-risk country. As much as possible is injected into or around the cleansed wound (after washing with soapy water). Rabies vaccine should also be given.
- Tetanus **immunoglobulin**:[7] together with metronidazole and wound cleansing, this is given for tetanus-prone wounds, in the non-immune or those not up-to-date with boosters. Tetanus vaccine should also be given. IV immunoglobulins are also given for treatment of tetanus.
- Cytomegalovirus **immune globulin**: on a named-patient basis, this is for patients receiving immunosuppressive treatment.

Side-effects of both types

- Malaise, chills, fever.
- Headache, nausea, facial flushing.
- Anaphylaxis (rarely).

Rarer uses of immunoglobulins

- Aplastic anaemia - IV antilymphocytic globulin (50% respond).
- Diphtheria antitoxin - (from horses) for suspected diphtheria, adverse reactions are common. Diphtheria antitoxin does not provide any benefit when used prophylactically.
- Botulism antitoxin for suspected botulism; again, adverse reactions are common.

Further reading

- Subgam, Human normal immunoglobulin solution; Summary of product characteristics, EMC, Oct 2018
- Rajabally YA; Immunoglobulin and Monoclonal Antibody Therapies in Guillain-Barre Syndrome. Neurotherapeutics. 2022 Apr;19(3):885-896. doi: 10.1007/s13311-022-01253-4. Epub 2022 Jun 1.
- von Achenbach C, Hevia Hernandez G, von Gunten S; The Choice between Intravenous and Subcutaneous Immunoglobulins: Aspects for Consideration. Pharmacology. 2022;107(11-12):556-563. doi: 10.1159/000527655. Epub 2022 Nov 8.

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