NORMAL IMMUNOGLOBULIN (HUMAN): INDICATIONS AND SAFETY

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Human normal immunoglobulin (NIGH) refers to the antibodies in pooled plasma which, injected, can be used as a form of passive immunisation to boost the immunoglobulin G (IgG) of patients and therefore temporarily increase immunity against common infections.

Samples are not tested for the amount or type of IgG present. It is assumed that pooled plasma from blood donors contains high levels of antibodies specific to infections found in that population. If an infection is not common in Australia, the antibody level in pooled plasma is low or negligible, so an injection of NIGH would not prevent or modify the infection. If the infection is common, the antibody level is high. For example, measles and hepatitis A are common diseases, so antibody levels should be high and immunisation will be effective¹. Typhoid and cholera are uncommon, so the immunoglobulin from the Commonwealth Serum Laboratories Limited (CSL), which is taken from the Australian donor pool, would not be useful in prevention.

Human immunoglobulin does not appear to protect a recipient against hepatitis C. In any case, anti-hepatitis-C-positive blood is excluded from the pool.

Where an infection is common, protection is immediate¹. For immunisation given intramuscularly at the recommended dosage, antibodies usually remain at protective levels for four to six weeks, and longer for hepatitis A².

Two specific forms of immunoglobulin are prepared – one for intramuscular and the other for intravenous use. The intramuscular form is the more common.

INTRAMUSCULAR IMMUNOGLOBULIN

Intramuscular immunoglobulin may be used as prophylaxis for susceptible contacts if given early in the infection. The optimal timing depends on the disease.

The NSW Health Department recommends intramuscular immunoglobulin for the following non-immune contacts of people with hepatitis A as soon as possible, but within two weeks of exposure:

- household or sexual contacts;
- staff and children in an associated day-care centre; and
- food handlers in an associated catering establishment.

The department recommends intramuscular immunoglobulin for infants (children under one year of age) within six days of first exposure to measles.

Intramuscular immunoglobulin is also useful for:

- travellers to areas endemic for hepatitis A² for whom hepatitis A vaccine is not practicable;
- treatment of patients with abnormal antibody production^{1,2}; and
- prophylaxis for certain contacts of cases of poliomyelitis, varicella-zoster etc².

The following specific-use intramuscular immunoglobulins are available: tetanus, zoster, hepatitis B and Rh(D) immunoglobulins.

The intramuscular form must not be given intravenously, as it may cause severe adverse reactions¹.

Preparation of the intramuscular form

The Commonwealth Serum Laboratories prepare immunoglobulin from blood obtained from volunteer blood donors in Australia. Australian Red Cross blood transfusion services screen the blood for evidence of active infection with hepatitis B virus (HbsAg), hepatitis C virus (anti-HCV), human immunodeficiency virus 1 and 2 (anti-HIV1, anti-HIV2), human T cell lymphotropic virus type 1 (anti-HTLV-1) and syphilis⁴.

The plasma is extracted and treated with the Cohn cold-ethanol fractionation process. Thiomersal is added as an antimicrobial agent.

INTRAVENOUS IMMUNOGLOBULIN

Intravenous immunoglobulin is prepared differently from the intramuscular form. It may be used for:

- treatment of congenital or acquired primary hypogammaglobulinaemia^{2,3};
- prophylaxis for infection in patients with secondary immunodeficiency^{2,3}; and
- treatment of autoimmune disorders³.

Specific intravenous tetanus and cytomegalovirus immunoglobulins are available for use in certain cases².

SAFETY

There are no known reports of transmission of infectious diseases from NIGH manufactured by CSL in Australia^{1,2}.

Blood donors are screened in a process designed to select those who are unlikely to carry infection. First, volunteer donors are considered to offer a lower risk of infection than paid donors or donors from institutions such as prisons⁵. Donors complete and sign a questionnaire about their medical history and health risks. Any donor with declared risk factors or a history of hepatitis or HIV is not accepted. Only blood negative for syphilis, hepatitis B surface antigen, antibody to hepatitis C, antibody to HIV-1, antibody to HIV-2 and antibody to HTLV is used⁴. However, blood taken during the incubation periods of these infections, when the virus is multiplying but the antibodies have not reached detectable levels (window period), would be accepted unwittingly. Transmission of the virus during this stage should be reduced by following the inactivation procedure.

Cohn cold-ethanol fractionation has been shown to inactivate viruses – especially HIV, which is relatively fragile⁶. The addition of thiomersal prevents bacterial contamination after the procedure.

These measures reduce the risk of infections transmitted by the blood product, but the possible transmission of known or unknown blood-borne diseases cannot be ruled out.

Experiments have shown that the standard Cohn cold-ethanol fractionation procedure reduces hepatitis B virus and HIV indicators in the final product to negligible levels⁷, but not necessarily for hepatitis C virus⁸. However, the reduction in risk would depend on the viral load in the initial plasma⁷.

Any alteration in the Cohn cold-ethanol procedure could alter its effectiveness⁶. The inactivation of viruses by ethanol is dependent on the concentration of ethanol used and temperature at which the process is carried out.

Since the introduction of routine HBsAg screening of donated blood in the 1970s and anti-HIV screening in the mid-1980s, no cases of hepatitis B or HIV transmitted by immunoglobulin products have been reported in Australia³. In the United States and Europe there have been reports of transmission of non-A, non-B hepatitis or hepatitis C – all arising from intravenous preparations. In most cases the preparation method deviated from the Cohn cold-ethanol fractionation process – because the product was new to the market or experimental, or the procedure itself had been altered^{3,9-12}. One product was responsible for 200 cases of hepatitis C, despite screening for hepatitis C with EIA-2, and was withdrawn from the market¹³. No other viruses appear to have been transmitted by immunoglobulins³.

In the US the residual risk of developing viral infections from intravenous immunoglobulins has been estimated to be 1 in 420,000 for HIV, 1 in 250,000 for hepatitis B (less than in the general population) and 1 in 100,000 for hepatitis C³. In Australia there have been no recorded cases of transmission³.

CONCLUSION

The mortality rate for hepatitis A is 1 in 1,000 for the population in general, and 27 in 1,000 for people over 50 years of age. Measles has a mortality rate of 2-3 per 1,000¹⁴ and has serious sequelae. The use of NIGH as recommended can prevent the morbidity and mortality of these common infections.

It must be remembered that immunoglobulin is a human product and so the risk of the disease being prevented must be weighed against the risk of iatrogenic disease.

Health care workers should advise patients that human immunoglobulin is safe, but cannot be guaranteed to be 100 per cent safe. The patient (or the patient's guardian) should make an informed decision whether to receive this form of treatment.

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CHANGES TO THE NSW PUBLIC HEALTH ACT 1991 – REPORTING OF BIRTH DEFECTS

In NSW from January 1, 1998, birth defects detected during pregnancy or in a child under one year of age will be notifiable to the NSW Health Department under the Public Health Act 1991.

All births in NSW have been notifiable to the NSW Health Department since 1991. Information on these births, including information on defects detected at birth, is collated by the NSW Midwives Data Collection. The NSW Birth Defects Register was established in 1990 and collates information on birth defects from the Midwives Collection and information provided voluntarily from clinicians, hospitals and laboratories.

It is anticipated that the change in legislation will provide a uniform basis for Statewide reporting and result in more reliable information for service planning purposes and for the evaluation of real and apparent clusters of birth defects.

The changes to the law will also allow information on full name and address to be collected, so the confidentiality of such information is explicitly protected by law. These details allow information for one person to be matched when information comes from more than one hospital or doctor. Paper forms are shredded and personal information such as name and address are removed from the computer database after five years.

Birth defects include structural malformations such as cleft lip and neural tube defects, and four medical conditions: cystic fibrosis, thalassaemia major, phenylketonuria and hypothyroidism. Congenital infections, cysts and tumours are not defined as structural malformations. Isolated talipes and undescended testis not requiring surgical intervention are also not notifiable.

New notification kits will be distributed to hospitals, general practitioners, obstetricians, paediatricians and pathology laboratories in December 1997. In the case of children, it is recommended that a copy of the notification form is placed in the Personal Health Record (Blue Book) in order to avoid duplication of notifications.

Any inquiries about the changes may be made to Dr Lee Taylor, Epidemiology and Surveillance Branch, NSW Health Department, telephone (02) 9391 9223 or facsimile (02) 9391 9232. The Manager of the NSW Birth Defects Register is Ms Susan Travis, telephone (02) 9351 7747 or facsimile (02) 9351 7742.

SOUTH EASTERN SYDNEY PUBLIC HEALTH UNIT

The South Eastern Sydney Public Health Unit has been working from two sites – one at St George Hospital and the other at Zetland. It is now consolidating at one site at Zetland. The director is Dr Mark Ferson.

The new contact numbers are:
Telephone: (02) 9382 8333
Facsimile: (02) 9382 8334