non-immune populations. However, it does have the advantage of being given as a single dose.

Whole-cell vaccines are generally no longer used because they are frequently associated with adverse effects.

1. WHO. *The diagnosis, treatment and prevention of typhoid fever.* Geneva: WHO, 2003. Also available at: http://www.who.int/vaccine_research/documents/en/typhoid_diagnosis.pdf (accessed 20/02/06)

Preparations

Ph. Eur.: Freeze-dried Typhoid Vaccine; Typhoid Polysaccharide Vaccine; Typhoid Vaccine; Typhoid Vaccine (Live, Oral, Strain Ty 21a).

Proprietary Preparations (details are given in Part 3)
Arg.: Typhim Vi; Vivotif; ***Austral.:*** Typh-Vax; Typherix; Typhim Vi; Vivotif; ***Austria:*** Typherix; Typhim Vi; Vivotif; ***Belg.:*** Typherix; Typhim Vi; Vivotif; ***Canad.:*** Typherix; Typhim Vi; Vivotif; ***Chile:*** Typhim Vi; Vivotif; ***Cz.:*** Typherix; Typhim Vi; ***Denm.:*** Typhim Vi; Vivotif; ***Fin.:*** Typherix; Typhim Vi†; Vivotif; ***Fr.:*** Typherix; Typhim Vi; ***Ger.:*** Typherix; Typhim Vi; Typhoral L; Vivotif†; ***Gr.:*** Typherix; ***Hong Kong:*** Typhim Vi; Vivotif; ***Hung.:*** Typherix; Typhim Vi; ***India:*** Typhim Vi; Typhoral; Vactyph; ***Indon.:*** Typherix; Typhim Vi; Vivotif; ***Irl.:*** Typherix; Typhim Vi; Vivotif†; ***Israel:*** Typherix; Typhim Vi; ***Ital.:*** Typherix; Typhim Vi; Vivotif; ***Malaysia:*** Typherix; Typhim Vi; Typhovax†; Vivotif; ***Neth.:*** Typherix; Typhim Vi; Vivotif; ***Norw.:*** Typherix; Typhim Vi; Vivotif; ***NZ:*** Typh-Vax; Typherix; Typhim Vi; Vivotif; ***Philipp.:*** Typherix; Typhim Vi; Vivotif; ***Pol.:*** Typhim Vi; ***Port.:*** Vivotif†; ***S.Afr.:*** Typherix; Typhim Vi; Vivotif†; ***Singapore:*** Typherix; Typhim Vi; Vivotif; ***Spain:*** Typherix; Typhim Vi; Vivotif; ***Swed.:*** Typherix; Typhim Vi; Vivotif; ***Switz.:*** Vivotif; ***Thai.:*** Typhim Vi; Vivotif; ***Turk.:*** Typhim; ***UK:*** Typherix; Typhim Vi; Vivotif; ***USA:*** Typhim Vi; Vivotif; ***Venez.:*** Typhim Vi†.

Vaccinia Immunoglobulins

Inmunoglobulinas contra el virus de la vacuna.

ATC — J06BB07.

Pharmacopoeias. Many pharmacopoeias, including *US*, have monographs.

USP 31 (Vaccinia Immune Globulin). A sterile solution of globulins derived from the plasma of adult human donors who have been immunised with vaccinia virus (smallpox vaccine). It contains 15 to 18% of protein, of which not less than 90% is gamma globulin. It contains glycine as a stabilising agent, and a suitable antimicrobial agent. It should be stored at 2° to 8°.

Profile

Vaccinia immunoglobulins have been used intramuscularly for the treatment of clinical complications of smallpox vaccination. They are not effective for postviral encephalitis. A currently available intravenous vaccinia immunoglobulin is given in a usual dose of 100 mg/kg, increased to 200 to 500 mg/kg in the absence of a response.

◊ References.

1. Hopkins RJ, *et al.* Safety and pharmacokinetic evaluation of intravenous vaccinia immune globulin in healthy volunteers. *Clin Infect Dis* 2004; **39:** 759–66.
2. Hopkins RJ, Lane JM. Clinical efficacy of intramuscular vaccinia immune globulin: a literature review. *Clin Infect Dis* 2004; **39:** 819–26.

Preparations

USP 31: Vaccinia Immune Globulin.

Varicella-Zoster Immunoglobulins

Inmunoglobulinas contra el virus de la varicela zóster.

ATC — J06BB03.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii) and *US*, have monographs.

Ph. Eur. 6.2 (Human Varicella Immunoglobulin; Immunoglobulinum Humanum Varicellae). A liquid or freeze-dried preparation containing immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma from selected donors having specific antibodies against *Herpesvirus varicellae*. Normal immunoglobulin may be added. It contains not less than 100 international units/mL. The liquid and freeze-dried preparations should be stored, protected from light, in a colourless, glass container. The freeze-dried preparation should be stored under vacuum or under inert gas.

Ph. Eur. 6.2 (Human Varicella Immunoglobulin for Intravenous Administration; Immunoglobulinum Humanum Varicellae ad Usum Intravenosum). A liquid or freeze-dried preparation containing immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma from selected donors having antibodies against human herpesvirus 3 (varicella-zoster virus 1). Human normal immunoglobulin for intravenous administration may be added. It contains not less than 25 international units/mL. Storage requirements are similar to those for Human Varicella Immunoglobulin, except that the freeze-dried preparation is stored at a temperature not exceeding 25°.

USP 31 (Varicella-Zoster Immune Globulin). A sterile solution of globulins derived from the plasma of adult donors selected for high titres of varicella-zoster antibodies. It contains 15 to 18% of globulins, of which not less than 99% is immunoglobulin G with traces of immunoglobulin A and immunoglobulin M. It contains glycine as a stabilising agent and thiomersal as a preservative. It contains not less than 125 units of specific antibody in not more than 2.5 mL of solution. It should be stored at 2° to 8°.

Adverse Effects and Precautions

As for immunoglobulins in general, p.2201.

Interactions

As for immunoglobulins in general, p.2201.

Uses and Administration

Varicella-zoster immunoglobulins are used for passive immunisation against varicella (chickenpox) in susceptible persons considered to be at high risk of developing varicella-associated complications after exposure to varicella or herpes zoster (shingles).

In the UK, varicella-zoster immunoglobulins are recommended for individuals who are at high risk of severe varicella and who have no antibodies to varicella-zoster virus and who have significant exposure to chickenpox or herpes zoster. Those at increased risk include immunosuppressed patients, neonates including those whose mothers develop chickenpox (but not herpes zoster) in the period 7 days before to 7 days after delivery, and pregnant women. Varicella-zoster immunoglobulin does not prevent infection when given after exposure but may modify the course of disease. Treatment with antivirals may be necessary in severe disease (see p.855).

The doses, given by deep intramuscular injection, of the varicella-zoster immunoglobulin available in the UK are: 250 mg for children up to 5 years of age; 500 mg for those aged 6 to 10 years; 750 mg for those aged 11 to 14 years; and 1 g for all those 15 years of age or older. A further dose is required if a second exposure occurs more than 3 weeks later. Varicella-zoster immunoglobulin should be given as soon as possible and not later than 10 days after exposure. Preparations of normal immunoglobulin for intravenous use may be used to provide an immediate source of antibody.

Preparations

Ph. Eur.: Human Varicella Immunoglobulin; Human Varicella Immunoglobulin for Intravenous Administration;
USP 31: Varicella-Zoster Immune Globulin.

Proprietary Preparations (details are given in Part 3)
Arg.: Varitect; ***Austria:*** Varitect; ***Canad.:*** VariZIG; ***Cz.:*** Varitect†; ***Ger.:*** Varicellon; Varitect; ***Gr.:*** Varitect; ***Hong Kong:*** Varitect; ***Irl.:*** Varitect; ***Israel:*** Varitect; ***Ital.:*** Uman-Vzig†; Varitect; ***Neth.:*** VariQuin; ***Pol.:*** Varitect; ***Port.:*** Varitect; ***S.Afr.:*** Vazigam; ***Singapore:*** Varitect; ***Switz.:*** Varitect; ***Thai.:*** Varitect; ***Turk.:*** Immunozig; Varitect.

Varicella-Zoster Vaccines

Vacunas de la varicela zóster.

Ветряночные Вакцины

ATC — J07BK01.

Pharmacopoeias. Many pharmacopoeias have monographs including *Eur.* (see p.vii).

Ph. Eur. 6.2 (Varicella Vaccine (Live); Vaccinum Varicellae Vivum). A freeze-dried preparation of a suitable attenuated strain of *Herpesvirus varicellae* grown in cultures of human diploid cells. The culture medium may contain suitable antibiotics at the smallest effective concentration. It is prepared immediately before use by reconstitution from the dried vaccine; it may contain a stabiliser. The dried vaccine should be stored at 2° to 8°. Protect from light.

The BP 2008 states that Var(Live) may be used on the label.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Varicella vaccines are generally well tolerated. Rashes may occur at the injection site and generalised varicella-like rashes elsewhere have been reported. The vaccine strain of virus can become latent, which could result in late development of zoster infections, but the incidence of herpes zoster is lower after vaccination than in an unvaccinated population. Breakthrough cases of chickenpox have been reported after single- and 2-dose vaccination regimens, but were in most cases milder. The incidence of breakthrough varicella is markedly lower after the 2-dose regimen.

High potency varicella vaccines licensed for active immunisation against herpes zoster (shingles) should not be used for active immunisation against varicella (chickenpox). Persons with active untreated tuberculosis should not be vaccinated.

◊ General references.

1. Black S, *et al.* Postmarketing evaluation of the safety and effectiveness of varicella vaccine. *Pediatr Infect Dis J* 1999; **18:** 1041–6.

Pregnancy. Normally occurring varicella zoster infection may cause fetal harm, therefore as a precautionary measure, vaccination of pregnant women against varicella is generally contra-indicated; advice is also given to avoid pregnancy for 3 months after the last dose of vaccine. However, surveillance of women inadvertently vaccinated during pregnancy has not identified any increased risk, either in terms of congenital varicella or for congenital abnormalities.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Live attenuated varicella-zoster vaccines may be used for active immunisation against varicella (chickenpox) and herpes zoster (shingles).

In the UK, vaccination against varicella is recommended only for persons considered to be at high risk of contracting the infection or highly susceptible to any complications it might cause; such patients include susceptible healthcare workers, and healthy contacts of immunocompromised patients when continuing close contact is unavoidable. A single dose of 0.5 mL is given subcutaneously to children aged 12 months to 13 years. Those aged 13 years and older should receive two doses at an interval of 4 to 8 weeks.

In the USA, a 2-dose vaccination regimen is recommended as part of the primary immunisation schedule of infants and children (see under Vaccines, p.2202). The first dose of 0.5 mL is given subcutaneously to children aged 12 to 15 months and the second dose at 4 to 6 years of age. Routine vaccination is also recommended for persons over the age of 13 years without evidence of immunity; two doses are given at an interval of 4 to 8 weeks. Those who only received 1 dose should receive a second, catch-up dose.

In the USA, a high potency vaccine (containing a minimum of 19 400 plaque-forming units) against herpes zoster is recommended for persons 60 years of age and older. A single dose of 0.65 mL is given subcutaneously.

A combination vaccine of measles, mumps, rubella, and varicella (MMRV) is available in the USA for use in children aged 12 months to 12 years.

◊ Results of studies of varicella-zoster vaccines for active immunisation against chickenpox in healthy and leukaemic children have been largely favourable. Protective **efficacy** in healthy children appears to be over 90%. In healthy adolescents and adults, adding a second dose 4 or 8 weeks after the first increased seroconversion rates from about 70 to 80% to 97% or better.[1] A protective efficacy of about 85% has been reported in leukaemic children given one dose of varicella-zoster vaccine[2,3] and interruption of chemotherapy for vaccination does not appear necessary in terms of immunogenicity of the vaccine.[2,4]

The **duration of immunity** after a 1-dose regimen for active immunisation against chickenpox is also under debate; despite at least 70 to 90% effectiveness, some consider that a single dose does not provide sufficient herd immunity levels to prevent outbreaks, especially in school settings.[5,6] Initial studies show that the immunity induced by natural infection with wild type virus is superior to that induced by the vaccine. In one study,[3] antibodies were absent in about one-quarter of all vaccinees (both leukaemic children and healthy adults) 1 year after a second dose of vaccine, but were still present after up to 6 years in all those who had breakthrough varicella infection.

However, immunity to varicella-zoster is complex, depending not only on circulating antibody but also on cellular immunity and secretory antibody. Thus, although a person may become seronegative after vaccination, protection from varicella may remain, albeit partial.[2] Both humoral and cell mediated immunity have been shown to persist for up to 20 years after vaccination.[7] Leukaemic children observed up to 6 years after immunisation have continued to be well protected[2] and varicella in previously-vaccinated persons is usually mild.[5,6]

Surveillance data collected from 11 356 children in the USA between 1995 and 2004 found that annual rates of breakthrough varicella increased significantly with time. Children aged 8 to 12 years at the onset of disease who had been vaccinated 5 years or more previously were 2.6 times more likely to have moderate or severe breakthrough varicella than those vaccinated less than 5 years previously.[8] The efficacy of a 2-dose vaccination regimen (doses given 3 months apart) was assessed in 2216 children over a period of 9 to 10 years.[9] Children vaccinated with the 2-dose regimen were 3.3 times less likely to develop varicella more than 42 days after vaccination than those who had received a single dose. During the 10-year follow-up period most breakthrough cases occurred in years 2 to 5, for both treatment regimens. No breakthrough cases were reported in years 7 to 10 for those who received the 2-dose regimen, while 10 cases were reported for those who received the 1-dose regimen. Since June 2007 the US Advisory Committee on Immunization Practices (ACIP) has recommended that children between the ages of 4 and 6 years receive a second dose of varicella vaccine.[6]