Preparations

Ph. Eur.: Tetanus Vaccine (Adsorbed);
USP 31: Tetanus Toxoid; Tetanus Toxoid Adsorbed.

Proprietary Preparations (details are given in Part 3)
Arg.: Tetanol; Tetavax; ***Austral.:*** Tet-Tox; ***Austria:*** Tetanol; ***Belg.:*** Tevax†; ***Braz.:*** Tetavax†; ***Chile:*** Tetavax; ***Cz.:*** Alteana; Tetavax; ***Ger.:*** Tetamun SSW†; Tetanol; ***Gr.:*** Anatoxal-TE-Berna†; ***Hong Kong:*** Te Anatoxal; Tetavax; ***Hung.:*** Tetanol; ***Ital.:*** Anatetall; Imovax Tetano; Tanrix†; Tetatox†; ***Malaysia:*** Te Anatoxal†; Tetavax†; TT Vaccine; ***Mex.:*** Tetamyn; Tetanol; Tetinox; ***Neth.:*** Tetavax†; ***Norw.:*** Tetavax; ***NZ:*** Te Anatoxal; Tet-Tox; ***Philipp.:*** Te Anatoxal; Tetavax; ***Port.:*** Anatoxal Te†; ***S.Afr.:*** Tetavax; ***Singapore:*** Te Anatoxal†; ***Spain:*** Anatoxal Te; ***Switz.:*** Anatoxal Te; ***Thai.:*** Anatetall†; Bio-TT; Te Anatoxal; Tetavax; TT Vaccine; ***Turk.:*** Anatetall; Tetavax; ***UK:*** Clostet†; ***USA:*** Te Anatoxal.

Tetanus and Influenza Vaccines

Vacunas del tétanos y la gripe.

Profile

Tetanus and influenza vaccines are available in some countries for active immunisation.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Tetagrip.

Tetanus and Poliomyelitis Vaccines

Vacunas del tétanos y la poliomielitis.

Profile

Tetanus and poliomyelitis (inactivated) vaccines have been used in some countries for active immunisation against tetanus and poliomyelitis.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: T. Polio†; Vaccin TP†.

Tick Venom Antisera

Antisuero contra el veneno de garrapata; Tick Antivenins; Tick Antivenoms.

Profile

An antiserum is available in Australia for treatment of the neurotoxic effects of envenomation by the tick *Ixodes holocyclus*. The antiserum is prepared from the serum of dogs that have been immunised with tick venom.

Tick venom antiserum is given by slow intravenous infusion.

Tick-borne Encephalitis Immunoglobulins

Inmunoglobulinas de la encefalitis transmitida por garrapatas.
ATC — J06BB12.

Profile

Preparations containing antibodies against tick-borne encephalitis are available in some countries for passive immunisation against the disease.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: FSME-Bulin†; ***Cz.:*** FSME-Bulin†; ***Ger.:*** FSME-Bulin†.

Tick-borne Encephalitis Vaccines

Vacunas de la encefalitis transmitida por garrapatas.
ATC — J07BA01.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.
Ph. Eur. 6.2 (Tick-borne Encephalitis Vaccine (Inactivated); Vaccinum Encephalitidis Ixodibus Advectae Inactivatum). A liquid preparation of a suitable strain of tick-borne encephalitis virus grown in cultures of chick-embryo cells or other suitable cell cultures and inactivated by a suitable method. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.
The BP 2008 states that Tic/enceph may be used on the label.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Effects on the nervous system. Severe progressive sensorimotor spastic paralysis occurred in a 54-year-old man after a second booster dose of tick-borne encephalitis vaccine.[1] Partial recovery was noted after about 6 months.

1. Bohus M, *et al.* Myelitis after immunisation against tick-borne encephalitis. *Lancet* 1993; **342:** 239–40.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

A vaccine is available in some countries for active immunisation against tick-borne viral encephalitis.

In the UK, vaccination against tick-borne encephalitis is recommended for those who anticipate prolonged exposure to the infective agent, for example persons visiting or working in the warm forested parts of Europe and Scandinavia. The vaccine is given by intramuscular injection in adult doses of 0.5 mL. The primary course consists of three doses, the second being given 4 to 12 weeks after the initial dose, and a third dose 5 to 12 months later. In children over 1 year of age and below 16 years of age, 3 doses of 0.25 mL of the junior formulation of the vaccine are given; the intervals between each dose are the same as for the adult schedule. To achieve rapid short-term protection in adults and children, the second dose may be given 2 weeks after the first dose. Booster doses for adults and children at continued risk should be given within 3 years of the last primary vaccination or booster dose.

Preparations

Ph. Eur.: Tick-borne Encephalitis Vaccine (Inactivated).

Proprietary Preparations (details are given in Part 3)
Austria: Encepur; FSME-Immun; ***Belg.:*** FSME-Immun; ***Canad.:*** FSME-Immun; ***Cz.:*** Encepur; FSME-Immun; ***Denm.:*** TicoVac; ***Fin.:*** Encepur; TicoVac; ***Fr.:*** TicoVac; ***Ger.:*** Encepur; FSME-Immun; ***Hung.:*** Encepur; FSME-Immun; ***Ital.:*** TicoVac; ***Norw.:*** TicoVac; ***Pol.:*** Encepur; FSME-Immun; ***Rus.:*** Encevir (Энцевир); ***Swed.:*** Encepur; FSME-Immun; ***Switz.:*** Encepur; FSME-Immun; ***UK:*** TicoVac.

Trichomoniasis Vaccines

Vacunas de la tricomoniasis.

Profile

A trichomoniasis vaccine containing inactivated *Lactobacillus* spp. is available in some countries for the prophylaxis of recurrent vaginal trichomoniasis. The vaccine is reported to stimulate production of antibodies against the aberrant coccoid forms of the lactobacilli associated with trichomoniasis and also, by cross-reaction, against the trichomonads themselves.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Gynatren.

Tularaemia Vaccines

Vacunas de la tularemia.

Profile

A tularaemia vaccine prepared from a live attenuated strain of *Francisella tularensis* has been used for active immunisation against tularaemia in persons at high risk of contracting the disease.

◊ References.

1. Titball R, Oyston P. A vaccine for tularaemia. *Expert Opin Biol Ther* 2003; **3:** 645–53.
2. Conlan JW. Vaccines against Francisella tularensis: past, present and future. *Expert Rev Vaccines* 2004; **3:** 307–14.

Typhoid Vaccines

Vacunas de la fiebre tifoidea.
ATC — J07AP01; J07AP02; J07AP03.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.
Ph. Eur. 6.2 (Typhoid Vaccine; Vaccinum Febris Typhoidi). A sterile suspension of inactivated *Salmonella typhi* containing not less than 500 million and not more than 1000 million bacteria per dose which does not exceed 1 mL. It is prepared from a suitable strain of *S. typhi* such as Ty 2. The bacteria are inactivated by heat, or by treatment with acetone, formaldehyde, or phenol, or by phenol and heat. The vaccine should be stored at 2° to 8°, and be protected from light.
The BP 2008 states that Typhoid may be used on the label.
Ph. Eur. 6.2 (Typhoid Vaccine, Freeze-dried; Vaccinum Febris Typhoidi Cryodesiccatum). A freeze-dried preparation of inactivated *Salmonella typhi* containing not less than 500 million and not more than 1000 million bacteria per dose which does not exceed 1 mL. It is prepared from a suitable strain of *S. typhi* such as Ty 2. The bacteria are inactivated by heat, or by treatment with acetone or formaldehyde. Phenol may not be used in the preparation. The vaccine should be stored at 2° to 8°, and be protected from light. It is reconstituted by the addition of suitable sterile liquid and should be used within 8 hours.
The BP 2008 states that Typhoid may be used on the label.
Ph. Eur. 6.2 (Typhoid Vaccine (Live, Oral, Strain Ty 21a); Vaccinum Febris Typhoidis Vivum Perorale (Stirpe Ty 21a)). A freeze-dried preparation of live *S. typhi* strain Ty 21a grown in a suitable medium. It contains not less than 2×10^9 bacteria per dose. It should be stored at 2° to 8°, and be protected from light.
The BP 2008 states that Typhoid(live,oral) may be used on the label.
Ph. Eur. 6.2 (Typhoid Polysaccharide Vaccine; Vaccinum Febris Typhoidis Polysaccharidicum). A preparation of purified Vi capsular polysaccharide obtained from *S. typhi* Ty2 strain or some other suitable strain that has the capacity to produce Vi polysaccharide. It contains 25 micrograms of polysaccharide per dose. It should be stored at 2° to 8° and be protected from light.
The BP 2008 states that Typhoid may be used on the label.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Oral live typhoid and parenteral polysaccharide vaccines have been associated with fewer adverse effects than parenteral killed typhoid vaccines and have replaced them in many countries.

Interactions

As for vaccines in general, p.2202.

Conflicting advice has been issued about the use of live oral typhoid vaccines with antibacterials or antimalarials (particularly mefloquine or proguanil). WHO has stated that all these drugs should be stopped from 3 days before until 3 days after receiving the Ty 21a live oral vaccine. The UK licensed product information advises a separation of 3 days for antibacterials, 12 hours for mefloquine, and 3 days for other antimalarials (but the fixed-dose combination of atovaquone and proguanil may be given with the vaccine). The US product information has indicated that mefloquine (and chloroquine) can be given with the vaccine but that proguanil should only be taken 10 days after the vaccine.

Uses and Administration

Typhoid vaccines are used for active immunisation against typhoid fever. As with many vaccines, the efficacy of typhoid vaccine is not complete and the importance of maintaining attention to hygiene should be emphasised to those travelling to endemic areas.

Typhoid vaccination is advised for laboratory workers handling specimens which may contain typhoid organisms and for persons travelling to areas where typhoid fever is endemic. In the UK, vaccination of contacts of a known typhoid carrier is not recommended; in the USA such persons are advised to receive the vaccine. Typhoid vaccine is not useful in controlling outbreaks of the disease in non-endemic areas.

In the UK, two vaccines are used: a capsular polysaccharide vaccine for parenteral use, and a live oral vaccine.

The capsular polysaccharide typhoid vaccine contains 25 micrograms of the Vi polysaccharide antigen per dose. A single dose of 0.5 mL is given by deep subcutaneous or intramuscular injection. Booster doses may be given every 3 years to those who remain at risk. The response in children under 18 months of age may be suboptimal, and the decision to vaccinate will be governed by the risk of exposure to infection.

The live oral typhoid vaccine contains an attenuated strain of *Salmonella typhi*, Ty 21a, and is given as enteric-coated capsules containing not less than 2×10^9 bacteria per dose. A primary immunisation schedule of one capsule every other day for 3 doses is given.

In the USA, the Vi capsular polysaccharide vaccine and the live oral Ty 21a vaccine are available. The capsular polysaccharide vaccine is given intramuscularly similarly to that in the UK, with a booster dose suggested every 2 years. For the oral vaccine, 4 doses on alternate days are recommended for both primary immunisation and boosters, which are given every 5 years if exposure continues.

In areas where typhoid is endemic WHO advises that immunisation should be considered as part of the routine schedules; either the Vi capsular polysaccharide vaccine or the Ty 21a live oral vaccine should be given to schoolchildren over the age of 2 years. Immunisation of the whole community should also be considered during an outbreak of typhoid; if this is not possible, persons aged 2 to 19 years should be the target group.

Immunisation for travellers. In most developed countries where typhoid is not endemic, the major use for typhoid vaccine is for non-immune travellers visiting endemic areas. The highest incidence of the disease is associated with travel to the Indian subcontinent and parts of tropical South America, although immunisation is also recommended for travellers to lower risk areas of Africa, Asia, and south-east Europe. By far the most important form of protection against gastrointestinal infection is strict attention to personal, food, and water hygiene, although in practice this advice is often difficult to follow.[1]

None of the vaccines used has been 100% effective in preventing disease. The effectiveness of the vaccines has generally been assessed in field trials in the populations of endemic areas. Such populations acquire a degree of natural immunity due to continued exposure and it may not be possible to equate protection rates in these populations to non-immune travellers. The live oral vaccine has been shown to confer a useful degree of immunity in field trials but the dose used may have been insufficient to protect non-immune individuals. The degree of immunity induced may be increased by the use of higher inocula or liquid preparations. In addition, compliance with dosing and storage requirements may further limit the effectiveness of this dosage form.

Large field studies have verified the effectiveness of the capsular polysaccharide vaccine but its efficacy has not been assessed in

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]