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]

Varicella-zoster vaccine may prevent or modify varicella if given within 3 days of exposure to the infection. It may be useful as an **adjunct** to varicella-zoster immunoglobulin. The treatment of varicella-zoster infections with antivirals is discussed on p.855.

One concern of varicella-zoster vaccination has been the possibility of an **increased risk of herpes zoster** (shingles) in immunised children. Although herpes zoster has been reported in vaccinated persons, a study involving 346 leukaemic children and 84 matched controls concluded that the incidence of herpes zoster following varicella-zoster vaccine was no greater than that following natural varicella infection.[10] The study did suggest that the risk of herpes zoster may be lowered by vaccination but this must be confirmed by long-term follow-up. Postmarketing surveys[11] of almost 90 000 vaccine recipients also showed a low incidence of herpes zoster. The vaccine strain of varicella-zoster virus is transmissible, particularly from vaccinees who develop a rash (see also Pregnancy under Adverse Effects, above). There is no evidence of reversion to virulence of the vaccine strain with secondary transmission.

Another concern is that vaccination of children could result in more severe infections in later life after immunity has waned. However, studies have shown that in general varicella is less severe in previously immunised than in non-immunised patients.[12,13]

The risk of zoster increases with age reflecting the waning of the specific cell-mediated immunity to the virus. Thus, the use of a high-potency varicella-zoster vaccine has been investigated in elderly subjects. In a randomised, double-blind, placebo-controlled study in over 38 000 subjects aged 60 or more the vaccine reduced the burden of illness due to herpes zoster by 61.1% and the incidence of herpes zoster and of postherpetic neuralgia by 51.3% and 66.5% respectively.[14] In the USA, high-potency varicella-zoster vaccine is recommended by the ACIP for all people 60 years of age and older, including those who have already had an episode of shingles.[15]

1. Kuter BJ, *et al.* Safety, tolerability, and immunogenicity of two regimens of Oka/Merck varicella vaccine (Varivax) in healthy adolescents and adults. *Vaccine* 1995; **13:** 967 72.
2. Gershon AA, *et al.* Persistence of immunity to varicella in children with leukemia immunized with live attenuated varicella vaccine. *N Engl J Med* 1989; **320:** 892–7.
3. Gershon AA, *et al.* Live attenuated varicella vaccine: protection in healthy adults compared with leukemic children. *J Infect Dis* 1990; **161:** 661–6.
4. Arbeter AM, *et al.* Immunization of children with acute lymphoblastic leukemia with live attenuated varicella vaccine without complete suspension of chemotherapy. *Pediatrics* 1990; **85:** 338–44.
5. Lopez AS, *et al.* One dose of varicella vaccine does not prevent school outbreaks: is it time for a second dose? *Pediatrics* 2006; **117:** 2253–4. Full version: http://pediatrics.aappublications.org/cgi/reprint/117/6/e1070 (accessed 06/07/07)
6. CDC. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2007; **56** (RR-4): 1–40. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5604.pdf (accessed 06/07/07)
7. Asano Y, *et al.* Experience and reason: twenty-year follow-up of protective immunity of the Oka strain live varicella vaccine. *Pediatrics* 1994; **94:** 524–6.
8. Chaves SS, *et al.* Loss of vaccine-induced immunity to varicella over time. *N Engl J Med* 2007; **356:** 1121–9.
9. Kuter B, *et al.* Ten year follow-up of healthy children who received one or two injections of varicella vaccine. *Pediatr Infect Dis J* 2004; **23:** 132–7.
10. Lawrence R, *et al.* The risk of zoster after varicella vaccination in children with leukemia. *N Engl J Med* 1988; **318:** 543–8.
11. Black S, *et al.* Postmarketing evaluation of the safety and effectiveness of varicella vaccine. *Pediatr Infect Dis J* 1999; **18:** 1041–6.
12. Watson BM, *et al.* Modified chickenpox in children immunized with the Oka/Merck varicella vaccine. *Pediatrics* 1993; **91:** 17–22.
13. Bernstein HH, *et al.* Clinical survey of natural varicella compared with breakthrough varicella after immunization with live attenuated Oka/Merck varicella vaccine. *Pediatrics* 1993; **92:** 833–7.
14. Oxman MN, *et al.* A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med* 2005; **352:** 2271–84.
15. CDC. CDC's Advisory Committee recommends "shingles" vaccination. Press release from the Advisory Committee on Immunization Practices (ACIP) (issued 26 October 2006). Available at: http://www.cdc.gov/od/oc/media/pressrel/r061026.htm (accessed 06/07/07)

Preparations

Ph. Eur.: Varicella Vaccine (Live).

Proprietary Preparations (details are given in Part 3)

Arg.: Varicela Biken; Varilrix; ***Austral.:*** Varilrix; Varivax; ***Austria:*** Varilrix; ***Belg.:*** Provarivax; Varilrix; ***Braz.:*** Vacina Contra A Varicela (Virus Atenuado); Vacina Contra Varicela; Varilrix†; Varivax†; ***Canad.:*** Varilrix; Varivax; ***Chile:*** Varicela Biken; Varilrix; ***Cz.:*** Varilrix; Zostavax; ***Denm.:*** Varilrix; ***Fin.:*** Varilrix; ***Fr.:*** Varilrix; Varivax; ***Ger.:*** Varilrix; Varivax; ***Gr.:*** Varilrix; Varivax; ***Hong Kong:*** Okavax; Varilrix; Varivax; ***Hung.:*** Varilrix; ***India:*** Varilrix; Varipox; ***Indon.:*** Okavax; Varilrix; ***Irl.:*** Varivax; ***Israel:*** Varilrix; ***Ital.:*** Varilrix; Varivax; ***Malaysia:*** Okavax; Varilrix; Varivax†; ***Mex.:*** Okavax; Varilrix; Varivax; ***Neth.:*** Provarivax; ***Norw.:*** Varilrix; ***NZ:*** Varilrix; Varivax; ***Philipp.:*** Okavax; V-Z Vax; Varilrix; ***Pol.:*** Varilrix; ***Port.:*** Varilrix; Varivax; Zostavax; ***S.Afr.:*** Varilrix; ***Singapore:*** Okavax; Varilrix; Varivax†; ***Spain:*** Varilrix; Varivax; ***Swed.:*** Varilrix; ***Switz.:*** Varilrix; Varivax; ***Thai.:*** Okavax; Varilrix; ***Turk.:*** Okavax; Varilrix; ***UK:*** Varilrix; Varivax; ***USA:*** Varivax; Zostavax; ***Venez.:*** Varilrix.

Yellow Fever Vaccines

Vacunas de la fiebre amarilla.

ATC — J07BL01.

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

Ph. Eur. 6.2 (Yellow Fever Vaccine (Live); Vaccinum Febris Flavae Vivum). A freeze-dried preparation of the 17D strain of yellow fever virus grown in fertilised hen eggs. It is reconstituted immediately before use. It should be stored at 2° to 8° and be protected from light.

The BP 2008 states that Yel(live) may be used on the label.

USP 31 (Yellow Fever Vaccine). A freeze-dried preparation of a selected attenuated strain of live yellow fever virus cultured in chick embryos. It is reconstituted, just prior to use, by the addition of sodium chloride containing no antimicrobial agent. It should be stored under nitrogen preferably below 0° but not above 5°.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Local and general reactions are not common after vaccination for yellow fever. Very rarely encephalitis has occurred, generally in infants under 9 months of age. Therefore, yellow fever vaccine is not usually given to infants under 9 months (but see Vaccine-associated Neurotropic Disease, below).

There is as yet limited data on the safety of yellow fever vaccine in HIV-positive individuals. In the UK, it is recommended that specialist advice should be sought regarding the use of yellow fever vaccine in such individuals. WHO advises that the vaccine should be given to HIV-positive individuals who are asymptomatic if the risk of infection is high.

Pregnancy. Although yellow fever vaccine has been given to women during pregnancy without producing adverse effects in the infants,[1] fetal infection has been reported.[2] US recommendations[3] therefore advise that the safety of yellow fever vaccination during pregnancy has not been established and the vaccine should only be given to pregnant women if travel to an endemic area is unavoidable and if an increased risk of exposure exists. Infants born to these women should be monitored closely for evidence of congenital infection or other adverse effects.

1. Nasidi A, *et al.* Yellow fever vaccination and pregnancy: a four-year prospective study. *Trans R Soc Trop Med Hyg* 1993; **87:** 337–9.
2. Tsai TF, *et al.* Congenital yellow fever virus infection after immunization in pregnancy. *J Infect Dis* 1993; **168:** 1520–3.
3. CDC. Yellow fever vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2002. *MMWR* 2002; **51** (RR-17): 1–11. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5117.pdf (accessed 25/05/06)

Vaccine-associated neurotropic disease. Yellow fever vaccine has been associated with rare reports of encephalitis, now termed vaccine-associated neurotropic disease (YEL-AND). WHO has stated[1] that, since 1945, there have been at least 26 cases of proven or probable YEL-AND of which 16 occurred in infants aged less than 6 months. Of the 26 cases, 24 recovered without further complications and there were 2 fatalities.[1] Vaccine virus recovered from one of the fatalities, a 3-year-old child, revealed that mutation had occurred in the envelope gene of the virus, but it is not known whether similar mutations occurred in the other cases. The other fatality occurred in an immunocompromised adult with HIV infection. As a precaution against possible encephalitis, infants less than 9 months of age are not generally immunised, although it may be advisable to immunise at 6 to 8 months of age during epidemics.

1. WHO. Yellow fever vaccine: WHO position paper. *Wkly Epidem Rec* 2003; **78:** 349–59.

Vaccine-associated viscerotropic disease. Yellow fever vaccine has been associated with rare reports of multiple organ failure, now termed yellow fever vaccine-associated viscerotropic disease (YEL-AVD). WHO has stated[1] that, between 1996 and 2001, there were 7 recorded cases of YEL-AVD of which 2 occurred in Brazil,[2] 4 in the USA,[3] and one in Australia.[4] Six of these 7 cases were fatal. A further case, also leading to fatality, was reported to have occurred in Spain in 2004.[5] It has been suggested that the most likely explanation is an idiosyncratic host susceptibility to the 17D vaccine strain rather than a reversion of the vaccine strain to a wild-type strain.[5] There is also some evidence to suggest that the risk of YEL-AVD is greater in patients aged over 60 years.[6]

1. WHO. Yellow fever vaccine: WHO position paper. *Wkly Epidem Rec* 2003; **78:** 349–59.
2. Vasconcelos PFC, *et al.* Serious adverse events associated with yellow fever 17DD vaccine in Brazil: a report of two cases. *Lancet* 2001; **358:** 91–7. Corrections. *ibid.*; 336. *ibid.*; 1018.
3. Chan RC, *et al.* Hepatitis and death following vaccination with 17D-204 yellow fever vaccine. *Lancet* 2001; **358:** 121–2.
4. Martin M, *et al.* Fever and multisystem organ failure associated with 17D-204 yellow fever vaccination: a report of four cases. *Lancet* 2001; **358:** 98–104.
5. Agencia Española del Medicamentos y Productos Sanitarios. A death associated with yellow fever vaccination reported in Spain. Available at: http://www.eurosurveillance.org/ew/2004/041104.asp (accessed 25/08/05)
6. Khromava AY, *et al.* Yellow fever vaccine: an updated assessment of advanced age as a risk factor for serious adverse events. *Vaccine* 2005; **23:** 3265–63.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Yellow fever vaccines are used for active immunisation against yellow fever. Immunity is usually established within about 10 days of administration and persists for many years. Only one dose is required for immunisation and is given by deep subcutaneous injection; the dose (0.5 mL) is the volume containing at least 1000 mouse LD_{50} units.

In the UK, immunisation against yellow fever is recommended for laboratory workers handling infected material, for persons travelling through or living in areas of infection, and for travellers entering countries which require an International Certificate of Vaccination. The immunity produced may last for life although officially an International Certificate of Vaccination against yellow fever is valid only for 10 years starting 10 days after the primary immunisation and only if the vaccine used has been approved by WHO and given at a designated centre.

Vaccination under 9 months of age is not generally recommended (see Adverse Effects and Precautions, above).

◊ General references.

1. Barrett ADT. Yellow fever vaccines. *Biologicals* 1997; **25:** 17–25.

◊ Recommendations of the Advisory Committee on Immunization Practices for the prevention of yellow fever in the USA.[1]

1. CDC. Yellow fever vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2002. *MMWR* 2002; **51** (RR-17): 1–11. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5117.pdf (accessed 25/05/06)

Immunisation schedules. The 17D (Rockefeller) yellow fever vaccine is now the only yellow fever vaccine produced.[1,2] The quantity available in the world has been limited and its relatively short half-life does not permit the accumulation of large stocks. The demand for the vaccine is also somewhat irregular, being suddenly high during epidemics and low during inter-epidemic periods.

In Africa and in South America two different strategies for yellow fever immunisation have been followed.[1,2] Firstly, an emergency immunisation programme takes place once an outbreak has begun, in an attempt to limit the spread of infection by immunising all persons in the focus, regardless of their former immune status. One disadvantage is that immunity does not appear until 7 days after immunisation and deaths may be expected to occur in the interim period. Secondly, a routine mass immunisation programme for yellow fever is aimed at immunising in advance all populations considered to be at risk. Yellow fever vaccine is included in the WHO Expanded Programme on Immunization; there are obvious logistic advantages in giving it at the age of 9 months at the same time as measles vaccine. In rural areas of the endemic zone that are considered at high risk, the minimum age for routine immunisation may be lowered to 6 months (see Vaccine-associated Neurotropic Disease, above).

1. WHO. *Prevention and control of yellow fever in Africa*. Geneva: WHO, 1986.
2. WHO. Yellow fever vaccine: WHO position paper. *Wkly Epidem Rec* 2003; **78:** 349–60.

Immunisation for travellers. A guide entitled *International Travel and Health* is published annually by WHO. Information is provided concerning the countries in Africa and South America where yellow fever is endemic and also countries requiring a traveller to hold a valid vaccination certificate. For some further details, see p.2203.

Preparations

Ph. Eur.: Yellow Fever Vaccine (Live);
USP 31: Yellow Fever Vaccine.

Proprietary Preparations (details are given in Part 3)

Arg.: Stamaril; ***Austral.:*** Stamaril; ***Belg.:*** Stamaril; ***Canad.:*** YF-Vax; ***Chile:*** Stamaril; ***Cz.:*** Stamaril; ***Denm.:*** Stamaril; ***Fin.:*** Arilvax†; Stamaril; ***Fr.:*** Stamaril; ***Ger.:*** Stamaril; ***Irl.:*** Arilvax†; Stamaril; ***Israel:*** Arilvax; ***Ital.:*** Stamaril; ***Malaysia:*** Stamaril†; ***Neth.:*** Arilvax; Stamaril; ***Norw.:*** Stamaril; ***NZ:*** Stamaril; ***Pol.:*** Stamaril; ***Port.:*** Stamaril; ***S.Afr.:*** Arilvax; Stamaril; ***Singapore:*** Arilvax†; Stamaril; ***Swed.:*** Arilvax†; Stamaril; ***Switz.:*** Arilvax†; Stamaril; ***Turk.:*** Stamaril; ***UK:*** Arilvax; Stamaril; ***USA:*** YF-Vax; ***Venez.:*** Stamaril†.