Rabies; ***Mex.:*** BayRab†; Berirab-P; Kamrab; ***Philipp.:*** BayRab; Berirab-P; Favirab; ***S.Afr.:*** Rabigam; ***Singapore:*** BayRab†; ***Spain:*** Imogam Rabia; ***Switz.:*** Berirab; Rabuman; ***Thai.:*** Favirab; Imogam Rabies; Rabumun†; ***Turk.:*** Imogam; ***USA:*** HyperRab; Imogam Rabies; ***Venez.:*** Imogan Rabia†.

Rabies Vaccines

Vacunas de la rabia.

ATC — J07BG01.

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

Ph. Eur. 6.2 (Rabies Vaccine for Human Use Prepared in Cell Cultures; Vaccinum Rabiei ex Cellulis ad Usum Humanum; Rabies Vaccine BP 2008). A sterile freeze-dried suspension of inactivated rabies virus; a suitable strain is grown in an approved cell culture. The cell-culture medium may contain suitable antibacterials at the smallest effective concentration. The vaccine is prepared immediately before use by the addition of a suitable sterile liquid. The estimated potency is not less than 2.5 international units per dose. The dried vaccine should be stored at 2° to 8° and be protected from light.

The BP 2008 states that Rab may be used on the label.

USP 31 (Rabies Vaccine). A sterile preparation, in dried or liquid form, of inactivated rabies virus obtained from inoculated diploid cell cultures. It has a potency of not less than 2.5 international units per dose. It should be stored at 2° to 8°.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Patients receiving human diploid-cell or purified chick embryo-cell rabies vaccines may experience pain, erythema, and induration at the injection site. Systemic reactions including abdominal pain, diarrhoea, nausea and vomiting, headache, chills, dizziness, fever, malaise, convulsions, encephalitis, lymphadenopathy, arthralgia and myalgia, dyspnoea and wheezing, or rash may also occur. Reactions may become more severe with repeated doses. Hypersensitivity reactions including anaphylaxis occur more commonly with vaccines prepared from non-human sources than with human diploid-cell vaccine. However, these reactions have also been associated with the presence of β-propiolactone-altered human albumin in the human diploid-cell vaccine.

Neurological reactions (meningoencephalitis, meningoencephalomyelitis, mononeuritis multiplex, transverse myelitis, or ascending paralysis) have been associated with the use of animal nerve-tissue vaccines. WHO considers that nerve-tissue vaccines should no longer be used. There are only isolated reports of neurological reactions after use of human diploid-cell vaccines.

Patients known to be hypersensitive to a particular vaccine or its components should be given an alternative product if available, although there are no absolute contra-indications to postexposure treatment. Pre-exposure prophylaxis should be delayed in patients with febrile illness until fever has resolved.

Effects on the nervous system. Rabies vaccines were originally prepared from infected animal brain tissue. The incidence of neurological complications with these vaccines was about 1 in 1 600, with an overall mortality of 15%.[1] Neurological adverse effects were attributed to myelin basic proteins present in these vaccines.[1-4] Subsequently, a highly immunogenic rabies vaccine was produced from the relatively myelin-free nerve tissue of suckling mice. However, neuroparalytic complications were reported in about 1 in 8 000 persons treated.[1,5] Most of these complications were of a Guillain-Barré-type illness, and had a fatality rate of 20 to 50%.[1]

Neuroparalytic reactions occur less frequently (1 in 32 000 persons treated) with vaccines prepared from duck embryo tissue;[1,5] however, these vaccines are no longer manufactured.[5]

Cell-derived rabies vaccines have been developed with better safety profiles.[1,5,6]

Isolated cases of neuroparalytic reactions have been reported with human diploid-cell or chick embryo-cell vaccines, mostly manifesting as a Guillain-Barré-type illness.[1,7-10]

1. Bernard KW, *et al.* Neuroparalytic illness and human diploid cell rabies vaccine. *JAMA* 1982; **248:** 3136–8.
2. WHO. WHO expert committee on rabies: eighth report. *WHO Tech Rep Ser 824* 1992. Also available at: http://libdoc.who.int/trs/WHO_TRS_824.pdf (accessed 15/10/07)
3. Kulkarni V, *et al.* Biphasic demyelination of the nervous system following anti-rabies vaccination. *Neurol India* 2004; **52:** 106–8.
4. Siddiqui A, *et al.* Guillain-Barre syndrome occurring after rabies vaccination. *J Pakistan Med Assoc* 2005; **55:** 87–8.
5. Anonymous. Rabies vaccines. *Wkly Epidem Rec* 2002; **77:** 109–19.
6. WHO. WHO expert consultation on rabies: first report. *WHO Tech Rep Ser 931* 2004. Also available at: http://libdoc.who.int/trs/WHO_TRS_931_eng.pdf (accessed 15/10/07)
7. Knittel T, *et al.* Guillain-Barré syndrome and human diploid cell rabies vaccine. *Lancet* 1989; **i:** 1334–5.
8. Tornatore CS, Richert JR. CNS demyelination associated with diploid cell rabies vaccine. *Lancet* 1990; **335:** 1346–7.
9. Mortiere MD, Falcone AL. An acute neurologic syndrome temporally associated with postexposure treatment of rabies. *Pediatrics* 1997; **100:** 720–1.
10. Chakravarty A. Neurologic illness following post-exposure prophylaxis with purified chick embryo cell antirabies vaccine. *J Assoc Physicians India* 2001; **49:** 927–8.

Hypersensitivity. Systemic hypersensitivity reactions[1] have occurred in up to 6% of patients receiving booster immunisation with human diploid-cell rabies vaccine (HDCV), with onset after 2 to 21 days. Presenting features include generalised or pruritic rash or urticaria, angioedema, arthralgias, fever, nausea, and vomiting. These reactions have been linked to the presence of β-propiolactone-altered human albumin in HDCV. A lower risk of hypersensitivity reaction should exist with newer cell-derived vaccines that contain little or no human albumin, such as purified chick embryo cell rabies vaccines (PCECV) or purified Vero-cell rabies vaccines (PVRV). A review[2] noted that patients receiving booster immunisation with PCECV did not generally exhibit systemic hypersensitivity reactions. In a comparison study[3] involving 400 children, patients receiving a new chromatographically purified Vero-cell vaccine were found to have a lower incidence of systemic hypersensitivity (0.7%) than those in the HDCV group (1.2%) after booster immunisation.

1. Anonymous. Rabies vaccines. *Wkly Epidem Rec* 2002; **77:** 109–19.
2. Dreesen DW. A global review of rabies vaccines for human use. *Vaccine* 1997; **15** (suppl): S2–S6.
3. Sabchareon A, *et al.* A new Vero cell rabies vaccine: results of a comparative trial with human diploid cell rabies vaccine in children. *Clin Infect Dis* 1999; **29:** 141–9.

Spongiform encephalopathies. Possible transmission of Creutzfeldt-Jakob disease associated with sheep-brain rabies vaccine has been reported from India.[1] It was suggested that transmission of the abnormal prion protein from sheep with scrapie might be implicated.

1. Arya SC. Acquisition of spongiform encephalopathies in India through sheep-brain rabies vaccination. *Natl Med J India* 1992; **4:** 311–12.

Interactions

As for vaccines in general, p.2202.

Antimalarials. Studies have suggested that continuous antimalarial chemoprophylaxis with *chloroquine* during primary immunisation with human diploid-cell rabies vaccine, given intradermally for pre-exposure prophylaxis, may be associated with a poor antibody response.[1,2] WHO[3] recommends that people currently taking malaria prophylaxis or those unable to complete the 3-dose rabies pre-exposure regime before starting malaria prophylaxis should receive pre-exposure rabies vaccination by the intramuscular route instead.

1. Taylor DN, *et al.* Chloroquine prophylaxis associated with a poor antibody response to human diploid cell rabies vaccine. *Lancet* 1984; **i:** 1405.
2. Pappaioanou M, *et al.* Antibody response to preexposure human diploid-cell rabies vaccine given concurrently with chloroquine. *N Engl J Med* 1986; **314:** 280–4.
3. WHO. WHO expert consultation on rabies: first report. *WHO Tech Rep Ser 931* 2005. Also available at: http://libdoc.who.int/trs/WHO_TRS_931_eng.pdf (accessed 15/10/07)

Uses and Administration

Rabies vaccines are used for active immunisation against rabies. They are used as part of postexposure treatment to prevent rabies in patients who have been bitten by rabid animals or animals suspected of being rabid. Infection does not take place through unbroken skin but is possible through uninjured mucous membranes and has been reported after the inhalation of virus in the laboratory. Rabies vaccines are also used for pre-exposure prophylaxis against rabies in persons exposed to a high risk of being bitten by rabid or potentially rabid animals.

Schedules for prophylaxis and treatment of rabies are recommended by WHO (see Pre-exposure Immunisation, below) and many countries have immunisation schedules based on these.

In the UK, two types of rabies vaccine are available. The first type is prepared from inactivated Wistar rabies virus strain PM/WI38 1503-3M cultured on human diploid cells, and the second type is prepared from inactivated Flury LEP virus strain produced on purified chick embryo cells. Each contains not less than 2.5 international units/mL. The purified chick embryo-cell vaccine is given intramuscularly into the deltoid region in adults but into the anterolateral aspect of the thigh in children. The human diploid-cell vaccine is given intramuscularly into the deltoid region in both adults and children. Other cell culture-derived vaccines, such as Vero cell rabies vaccine, are available in other countries.

For **pre-exposure prophylaxis** against rabies, the recommended schedule in the UK is 3 doses, each of 1 mL, by intramuscular injection on days 0, 7, and 28; the third dose may in some instances be given on day 21 if there is insufficient time before travel. For persons at regular and continuous risk, a single reinforcing dose should be given 1 year after completion of the primary course with further doses at 3- to 5-year intervals. For those at intermittent risk, a booster dose should be given from 2 years after completion of the primary course.

For **postexposure treatment**, thorough cleansing of the wound with soap and water is imperative. The recommended schedule in the UK for unimmunised or incompletely immunised persons is 5 doses, each of 1 mL, by intramuscular injection on days 0, 3, 7, 14, and 30. In fully immunised persons two doses of vaccine should be given intramuscularly, one each on day 0 and day 3. Vaccination should be started as soon as possible after exposure, and may be stopped if it is proved that the patient was not at risk. In previously unimmunised patients at high risk, rabies immunoglobulin (see above) should also be given at the same time as the first dose of vaccine.

Rabies. Rabies is caused by infection with a rhabdovirus of the genus Lyssavirus. Rabies has a worldwide distribution, primarily in domesticated and wild dogs but also in bats and other warm-blooded animals, although some countries, including the UK, most of Australasia, and Antarctica are designated as rabies-free areas. Transmission of the rabies virus to humans is usually by the bite of an infected animal or contamination of broken skin by saliva. Infection is possible via intact mucous membranes and by aerosol transmission, but infection is unlikely after contamination of intact skin. Other body fluids such as urine and tears should be regarded as potentially infectious; rabies virus transmission has also been reported after organ transplantation from misdiagnosed donors.

Human rabies is almost always fatal once symptoms have appeared. The incubation period varies from 2 weeks to 6 years (average of 2 to 3 months) depending on the distance of the bite site from the brain and the amount of virus in the inoculum. There are 2 types of clinical presentations of rabies; encephalitic (furious) and paralytic (dumb). Encephalitic rabies presents with periods of hyperexcitability accompanied by severe agitation and bizarre behaviour alternating with periods of lucidity. Severe spasms of the larynx and pharynx may be provoked by attempts at swallowing (leading to hydrophobia) or by air blown at the face (aerophobia). Other symptoms include hypersalivation, fever, and convulsions. In the paralytic form, progressive flaccid paralysis develops in the bitten limb and ascends in a symmetrical or asymmetrical manner. Patients not dying through respiratory or cardiac arrest during the acute phase may develop any of a number of complications culminating in coma and death or (very rarely) recovery; only a few patients are documented as having survived after the onset of coma, and all had received either pre- or postexposure immunisation.

National control programmes involve epidemiological surveillance, mass canine immunisation campaigns, and dog population management. The development of oral animal vaccines delivered on baited food has met with considerable success in a number of areas and has become an essential tool for eliminating rabies in wild animals. Rigorously applied controls of international transfer of animals including certification of vaccination and quarantine for animals entering rabies-free areas are necessary to prevent re-introduction of rabies.

Although a number of treatments have been tried including antivirals, interferons, high doses of rabies immunoglobulin, and corticosteroids, none has shown evidence of effectiveness. Postexposure treatment after contact with a suspected or confirmed rabid animal may be effective in preventing death; it includes prompt and thorough cleansing of the contaminated site and the early use of rabies vaccine with or without rabies immunoglobulins. For a brief outline of postexposure treatment, see below.

Pre-exposure prophylaxis is recommended in persons at high risk of exposure, either due to their occupation or those travelling in enzootic areas. The main obstacle to mass pre-exposure vaccination appears to be the high cost of cell culture vaccines. See under Pre-exposure Immunisation (below) for outlines of recommended vaccination schedules.

Choice of vaccines. Many different rabies vaccines are available for human use. Some are derived from nerve tissue of animals, some from avian tissues (duck embryos), and some prepared in cell cultures. The first rabies vaccine was based on attenuated virus from desiccated nerve tissue. Later, inactivated nervous tissue-derived vaccines were prepared from rabid sheep, goat (Semple vaccines) or suckling mouse brains (Feunzalida Palacios vaccine). A complete postexposure treatment course of nerve-tissue vaccine consists of up to 23 injections and is associated with severe neurological reactions and a significant failure rate. WHO therefore strongly recommends that nerve-tissue vaccines should not be used, and that production should be stopped. Cell-derived rabies vaccines were subsequently developed; the human diploid cell rabies vaccine (HDCV) was introduced in 1967 and later less expensive purified chick embryo-cell vaccine (PCECV) and puri-

fied Vero-cell rabies vaccines (PVRV) entered use. There appears to be little difference in terms of safety and antigenicity between HDCV, PCECV, and PVRV in recommended regimens. The incidence of severe hypersensitivity reactions should, however, be lower with PVRV and PCECV than with HDCV since the purification process removes most human serum albumin in the cell-growth medium before virus inactivation (see Hypersensitivity, under Adverse Effects and Precautions, above). A purified duck-embryo vaccine (PDEV) provided similar efficacy and safety to vaccines produced from cell cultures, but is no longer manufactured.

There is little data concerning the efficacy of rabies vaccines. It appears that nerve-tissue vaccines afford limited protection after minor exposures to rabies virus, are less effective after head bites, and are of little use after very severe exposures. Failure rates for HDCV, PCECV, and PVRV (including cases with less than the recommended therapy) have been estimated as less than 1 in 80 000 treatments in the USA, Canada, and Europe, 1 in 12 000 to 20 000 in Thailand, and 1 in 30 000 in the remaining tropical countries. Reported failures of these vaccines are usually associated with severe lesions on or near the head and/or errors in treatment, such as deviation from recommendations, incorrect site of vaccine administration, or delay in treatment. WHO recommends a minimum potency of 2.5 international units per intramuscular dose for all cell-derived rabies vaccines.

The cost of cell-derived rabies vaccines is prohibitively high in the developing world. Although the adverse effects of nerve-tissue vaccines preclude their use for pre-exposure prophylaxis, they are still used in some countries for postexposure prophylaxis. WHO is anxious that nerve-tissue vaccines should be replaced with affordable cell-derived vaccines as soon as possible. In the meantime, cost-cutting regimens have been devised for use of cell-derived rabies vaccines by the intradermal route. Rapid immunisation is achieved by the use of several sites of injection; fewer injections are required than with traditional intramuscular regimens.

PRE-EXPOSURE IMMUNISATION. WHO[1,2] has developed guidelines as to who should receive pre-exposure vaccination with rabies vaccines. However, national policies may vary somewhat from that of WHO, depending on the local risk of contracting rabies and the vaccines available; it is generally recommended for use in persons at high risk of infection with rabies virus. Where available, the vaccines produced in cell culture or from purified embryonated eggs are preferred over the vaccines produced in animal tissues (see under Choice of Vaccine, above). WHO recommends[1,2] pre-exposure prophylaxis for persons regularly at high risk of exposure, such as certain laboratory workers, veterinarians, animal handlers, and wildlife officers, and those living in or travelling to areas where rabies is endemic (particularly in children under 15 years of age). The immunisation schedule should preferably consist of 3 injections of a rabies vaccine of potency at least 2.5 international units given on days 0, 7, and either day 21 or 28, but variation of a few days is unimportant. Vaccine should be given into the deltoid area of the arm or for young children into the anterolateral area of the thigh. Titres of virus-neutralising antibodies can be checked in serum samples collected 1 to 3 weeks after the last dose. Those who work with the live virus should have their antibody titres checked every 6 months and if the figure falls below 0.5 international units/mL they should receive a booster.[1,2] Other individuals at continuing risk should have their titres checked every 12 months and a booster given if the titre is below 0.5 international units/mL.[1]

WHO also suggests intradermal use of rabies vaccine in doses of 0.1 mL on days 0, 7, and either day 21 or 28 but intramuscular injection is preferable and is mandatory in those taking malaria prophylaxis.

In the UK,[3] the schedule for immunisation (see Uses and Administration, above) is similar to that recommended by WHO.

In the USA, immunisation with a human diploid cell vaccine, a vaccine adsorbed onto an aluminium salt, or a purified chick embryo cell vaccine is carried out similarly to the WHO schedule, with serum-antibody titres determined every 6 months to 2 years, depending upon the level of exposure, and booster doses given as necessary.[4]

1. WHO. WHO expert committee on rabies: eighth report. *WHO Tech Rep Ser 824* 1992. Also available at: http://libdoc.who.int/trs/WHO_TRS_824.pdf (accessed 15/10/07)
2. WHO. WHO expert consultation on rabies: first report. *WHO Tech Rep Ser 931* 2005. Also available at: http://libdoc.who.int/trs/WHO_TRS_931_eng.pdf (accessed 15/10/07)
3. Department of Health. *Immunisation Against Infectious Disease* 2006: "The Green Book". Available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079917?IdcService=GET_FILE&dID=115974&Rendition=Web (accessed 15/07/08)
4. CDC. Human rabies prevention—United States, 1999: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1999; **48** (RR-1): 1–21. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr4801.pdf (accessed 25/05/06)

POSTEXPOSURE TREATMENT. WHO guidelines[1,2] emphasise the importance of prompt local treatment for all bite wounds and scratches that may be contaminated with rabies virus and that, depending on the category of animal contact, rabies vaccine on its own or with rabies immunoglobulin should be given. The combination of these measures immediately after exposure is considered to guarantee almost complete protection. Pregnancy and infancy are not contra-indications to postexposure vaccination. These measures should be instituted even in patients who present months after having been bitten.

First aid or local treatment consists of immediate thorough flushing and washing of the wound with water, or soap and water, or detergent followed by the application of alcohol 70% or tincture or aqueous solution of iodine. Medical care may then consist of the instillation of rabies immunoglobulin into the depth of the wound and infiltration around the wound. Ideally the wound should not be sutured, but if suturing is necessary then it is essential that it be preceded by rabies immunoglobulin as above. Antimicrobials and tetanus vaccine may also be given as necessary.

The use of rabies vaccine and of rabies immunoglobulin depends on the category of animal contact. WHO classifies the type of contact with a suspect or rabid animal into 3 categories:

- category I covers touching or feeding of animals and licks on intact skin
- category II covers nibbling of uncovered skin, minor scratches or abrasions without bleeding, and licks on broken skin
- category III covers single or multiple transdermal bites or scratches and contamination of mucous membranes with the animal's saliva

Generally no treatment is required for category I contact. Patients who have had category II contact should be given rabies vaccine but the course may be stopped if the contact has been with a cat or dog that remains healthy throughout an observation period of 10 days or if postmortem study of the contact animal shows it to be negative for rabies. Patients with category III contact should be given rabies vaccine preceded by rabies immunoglobulin infiltrated around the wound and instilled into it as described above.

There are 2 types of immunoglobulin available; human rabies immunoglobulin (HRIG) and pepsin-digested or highly purified equine rabies immunoglobulin (ERIG). The recommended dose for HRIG is 20 international units/kg and for ERIG products is 40 international units/kg. As much as possible of the dose should be infiltrated into and around the wound, with the remainder being injected intramuscularly into a site remote from that where vaccine was given, such as the anterior thigh.

The potency of rabies vaccines should be at least 2.5 international units per single human dose. For intramuscular vaccination schedules one dose should be given on days 0, 3, 7, 14, and 28 into the deltoid region or, for small children, into the anterolateral area of the thigh. An abbreviated multisite intramuscular schedule (the 2-1-1 regimen) induces an early antibody response and may be particularly effective when postexposure treatment has not included a rabies immunoglobulin. This schedule consists of one dose given in the right arm and one in the left arm on day 0, and one dose intramuscularly into the deltoid region on days 7 and 21.

Intradermal vaccination reduces the volume of injection required and is therefore suited to situations where vaccine or money is in short supply. For intradermal vaccination one dose (0.1 mL) of purified chick embryo-cell or purified Vero-cell vaccine may be given at each of two sites, usually the left and right upper arm, on days 0, 3, 7, and 28. Alternatively, in emergency situations when no rabies immunoglobulin is available, either human diploid cell or purified chick embryo-cell rabies vaccine may be given intradermally in one dose at each of 8 sites on day 0, in one dose at 4 sites on day 7, and subsequently in one dose at one site on days 28 and 90.

For postexposure treatment of previously vaccinated patients, WHO recommends local treatment of wounds followed by rabies vaccine given on days 0 and 3, either as a standard intramuscular dose or as one intradermal dose per site. No rabies immunoglobulin should be given. Patients who previously received vaccines of unproven potency or who have failed to develop an acceptable rabies neutralising antibody titre should be given full treatment as for those previously unimmunised.

In the UK,[3] rabies immunoglobulin is given if the patient is previously unimmunised and at high risk. Vaccine is given on days 0, 3, 7, 14, and 30 (five doses) in unimmunised persons (although the UK licensed product information for human diploid cell vaccine also recommends a sixth dose on day 90); two doses, one each on day 0 and day 3 are given to previously fully immunised persons.

In the USA, a human diploid-cell vaccine, an adsorbed rabies vaccine, or a purified chick embryo cell vaccine may be used for postexposure treatment.[4] In previously unimmunised individuals, a 1-mL dose of vaccine is given intramuscularly on days 0, 3, 7, 14, and 28, with rabies immunoglobulin as in the WHO schedule. In previously immunised individuals, two doses of vaccine are given on days 0 and 3, and rabies immunoglobulin is not required.

1. WHO. WHO expert committee on rabies: eighth report. *WHO Tech Rep Ser 824* 1992. Also available at: http://libdoc.who.int/trs/WHO_TRS_824.pdf (accessed 15/10/07)
2. WHO. WHO expert consultation on rabies: first report. *WHO Tech Rep Ser 931* 2005. Also available at: http://libdoc.who.int/trs/WHO_TRS_931_eng.pdf (accessed 15/10/07)
3. Department of Health. *Immunisation Against Infectious Disease* 2006: "The Green Book". Available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079917?IdcService=GET_FILE&dID=115974&Rendition=Web (accessed 15/07/08)
4. CDC. Human rabies prevention—United States, 1999: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1999; **48** (RR-1): 1–21. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr4801.pdf (accessed 25/05/06)

Preparations

Ph. Eur.: Rabies Vaccine for Human Use Prepared in Cell Cultures; ***USP 31:*** Rabies Vaccine.

Proprietary Preparations (details are given in Part 3)
Arg.: Verorab; ***Austral.:*** Rabipur; ***Austria:*** Rabipur; ***Braz.:*** HDCV; Vacina Anti-Rabica Humana; Verorab†; ***Canad.:*** Imovax Rabies; RabAvert; ***Chile:*** Verorab; ***Cz.:*** Rabipur; Verorab; ***Denm.:*** Rabies-Imovax; ***Fin.:*** Rabies-Imovax; ***Fr.:*** Rabipur; ***Ger.:*** Rabipur; Rabivac†; Tollwut-Impfstoff (HDC); ***Hong Kong:*** Verorab; ***India:*** Rabipur; Rabivax; ***Indon.:*** Verorab; ***Israel:*** Rabipur; ***Ital.:*** Imovax Rabbia; Lyssavac N†; Rabipur; Rasilvax†; ***Malaysia:*** Verorab; ***Neth.:*** Rabipur; ***Norw.:*** Rabies-Imovax; ***Philipp.:*** Rabipur; Verorab; ***Pol.:*** Verorab; ***Port.:*** Rabipur; ***S.Afr.:*** Rabipor; Verorab; ***Spain:*** Vacuna Antirrabica; ***Swed.:*** Rabies-Imovax; ***Switz.:*** Lyssavac N†; ***Thai.:*** Lyssavac N; Rabipur; Verorab; ***Turk.:*** HDCV; Rabivac; ***UK:*** Rabipur; ***USA:*** Imovax Rabies; RabAvert; ***Venez.:*** Verorab.

Respiratory Syncytial Virus Immunoglobulins

Inmunoglobulinas contra el virus sincitial respiratorio.

Palivizumab *(BAN, rINN)*

Palivitsumabi; Palivizumabum. immunoglobulin G 1 (human-mouse monoclonal MEDI-493 γ1-chain antirespiratory syncytial virus protein F), disulfide with human-mouse monoclonal MEDI-493 κ-chain, dimer.

Паливизумаб
CAS — 188039-54-5.
ATC — J06BB16.

Adverse Effects and Precautions
As for immunoglobulins in general, p.2201.

Interactions
As for immunoglobulins in general, p.2201.

There is some evidence that antibody responses to diphtheria, tetanus, pertussis, and Haemophilus influenzae vaccines may be reduced in infants also receiving respiratory syncytial virus immunoglobulins.

Uses and Administration
Respiratory syncytial virus immunoglobulin is available in some countries for the passive immunisation of infants against lower respiratory-tract infections caused by RSV. It is prepared from the pooled plasma of adults selected for high titres of antibodies that neutralise the virus. Each mL of respiratory syncytial virus immunoglobulin contains about 50 mg of protein.

In the USA, children under 2 years of age with chronic lung disease (bronchopulmonary dysplasia) or a history of premature birth may receive a prophylactic intravenous infusion once a month during the RSV season (typically November to April or early May). The drug is given in a dose of up to 750 mg/kg at an initial rate of 75 mg/kg per hour for 15 minutes, followed by 180 mg/kg per hour until the end of the infusion.

Palivizumab, a human monoclonal antibody to RSV, is available in some countries and is used intramuscularly for similar purposes, in a dose of 15 mg/kg monthly. Palivizumab is also recommended in children under 2 years of age with haemodynamically significant congenital heart disease. Children undergoing cardiac bypass should be given an extra dose of palivizumab as soon as they are stable after surgery; doses are subsequently resumed monthly thereafter.

◊ The American Academy of Pediatrics has issued revised indications for the use of palivizumab and respiratory syncytial virus immunoglobulin.[1] Palivizumab or respiratory syncytial virus immunoglobulin prophylaxis should be considered for infants younger than 2 years of age with chronic lung disease (bronchopulmonary dysplasia) who have required medical therapy for their condition within 6 months of the anticipated start of the RSV season. Infants born at 32 weeks' gestation or earlier may benefit from prophylaxis even if they do not have chronic lung disease. Although prophylaxis has been shown to reduce hospitalisation for infants born between 32 and 35 weeks' gestation, the cost for this large group of infants should be considered carefully. Palivizumab, may in addition be given to children under 2 years of age with haemodynamically significant congenital heart disease.

Both palivizumab and respiratory syncytial virus immunoglobulin have been shown to decrease the risk of severe RSV infection in high-risk infants and children. Palivizumab is preferred over respiratory syncytial virus immunoglobulin for most high-risk children because of its comparative ease of administration, safety, and efficacy. Monthly use of palivizumab during the RSV season results in a 45 to 55% reduction in hospitalisation. Although palivizumab is usually preferred, respiratory syncytial virus immunoglobulin may also decrease the incidence of other respiratory-tract infections in addition to those caused by RSV, and this may be of benefit for infants younger than 6 months who are not eligible for influenza immunisation and those with severe pulmonary disease who may be more prone to other respiratory-tract infections. Palivizumab has not been shown to affect the rate of hospitalisation for non-RSV infections or the incidence of otitis media.

1. Committee on Infectious Diseases and Committee on Fetus and Newborn, American Academy of Pediatrics. Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus infections. *Pediatrics* 2003; **112:** 1442–6. Also available at: http://aappolicy.aappublications.org/cgi/reprint/pediatrics;112/6/1442.pdf (accessed 24/05/06)