
Contraindications

Rabies vaccines (WHO position paper)

Because rabies is a lethal disease, no contraindications to post-exposure prophylaxis following high-risk exposure exist. This also pertains to post-exposure rabies prophylaxis in infancy and pregnancy.

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Rabies vaccines (WHO position paper)

For pre-exposure immunization, previous severe reaction to any of the vaccine components is a contraindication to further use of the same vaccine.

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Rabies vaccines (WHO position paper)

In immunocompromised individuals, including patients with HIV/AIDS, comprehensive wound management and local infiltration with RIG, in combination with a complete intramuscular CCV series, are of utmost importance for the successful prevention of rabies. In these situations, the VNA response should be determined 24 weeks following vaccination to assess the possible need for an additional dose of the vaccine.

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Rabies vaccines (WHO position paper)

People taking chloroquine for treatment or malaria prophylaxis can have a reduced response to ID rabies vaccination. These patients should receive the vaccine by the IM route.

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General

State of the art of new vaccines: research and development

This type of vaccine (inactivated rabies vaccine) is still unfortunately manufactured and used in South-East Asia, but the number of countries doing so has been decreasing during the past 10 years in accordance with the WHO recommendations to replace them by cell-cultured vaccines.

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State of the art of new vaccines: research and development

A number of cell-culture based rabies vaccines are being developed in China and India on Vero cells, human diploid cells (HDC), or duck embryo cells. These vaccines however have not yet been prequalified by WHO and may require further assessment in terms of safety and efficacy before they can be traded internationally.

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State of the art of new vaccines: research and development

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Of importance for the supply of rabies vaccine is the use of the intradermal route schedule which reduces the number of vaccine vials and thereby the cost of PEP by up to 80% (US\$ 5-10 for vaccine alone).

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It is well known that rabies PEP [post-exposure prophylaxis] with vaccine alone is not always sufficient, especially in cases of severe exposure (category 3) where concomittant passive immunization with rabies immunoglobulins (RIG) is strongly recommended.

Rabies vaccines (WHO position paper)

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Following exposure to a suspected rabid animal, prevention of human rabies consists of prompt wound cleansing and administration of a modern CCV and, in cases of severe (category III) exposure, of rabies immunoglobulin (RIG).

Rabies vaccines (WHO position paper)

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it is strongly recommended that the production and use of NTVs for humans be discontinued and replaced by modern CCVs as soon as possible.

Rabies vaccines (WHO position paper)

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Pre-exposure immunization is recommended for anyone at increased risk of exposure to rabies virus, either by nature of their residence or occupation, or when travelling.

Rabies vaccines (WHO position paper)

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Countries are encouraged to implement control programmes to ensure coordination between all public sectors involved in rabies control.

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Pre-exposure rabies vaccination requires IM doses of 1 ml or 0.5 ml, depending on the vaccine type, given on days 0, 7 and 28 (day 28 preferable, but administration may be advanced towards day 21 if time is limited).

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For adults, the vaccine should always be administered in the deltoid area of the arm; for children aged <2 years, the anterolateral area of the thigh is recommended. Rabies vaccine should not be administered in the gluteal area, where the induction of an adequate immune response may be less reliable.

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ID administration of 0.1 ml volumes on days 0, 7, and 28 (day 28 preferable, but administration may be advanced towards day 21 if time is limited) is an acceptable alternative to the standard IM route. However, ID administration is technically more demanding and requires appropriate staff training and qualified supervision.

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Rabies vaccines (WHO position paper)

Periodic booster injections are recommended only for people whose occupation puts them at continuous or frequent risk of rabies exposure. In such cases, a booster dose should be given at intervals ideally dictated by regular testing for antirabies antibodies. Potential laboratory exposures to high concentrations of rabies virus motivates testing as often as every 6 months; VNA titres of at least 0.5 IU/ml indicate protection. Where serological testing is unavailable, booster vaccination every 5 years may be an acceptable alternative.

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The indication for post-exposure prophylaxis with or without RIG depends on the type of contact with the suspected rabid animal:- Category I touching or feeding animals, licks on the skin (i.e. no exposure);
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- Category III single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks, exposures to bats.
For category I exposures, no prophylaxis is required; whereas for category II, immediate vaccination, and for category III, immediate vaccination and administration of RIG are recommended. For categories II and III, thorough (for ~15 minutes) washing and flushing with soap/detergent and copious amounts of water of all bite wounds and scratches should be done immediately, or as early as possible.

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Post-exposure prophylaxis can be discontinued if the suspect animal is proved by appropriate laboratory examination to be free of rabies, or, in the case of domestic dogs or cats, the animal remains healthy throughout a 10-day observation period.

Factors that should be taken into consideration when deciding whether or not to initiate post-exposure prophylaxis include the likelihood of the concerned animal being rabid, category of exposure (VIII), clinical features of the animal, as well as its availability for observation and laboratory testing. In most situations in developing countries, the vaccination status of the offending animal should not be taken into consideration to withhold prophylaxis.

Rabies vaccines (WHO position paper)

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Intramuscular administration

The post-exposure vaccination schedule is based on IM doses of 1 ml or 0.5 ml, depending on the manufacturer. The recommended regimen consists of either a 5-dose or a 4-dose schedule.

- (i) The 5-dose regimen prescribes 1 dose injected into the deltoid muscle (or anterolateral thigh in children aged <2years) on each of days 0, 3, 7, 14 and 28.
- (ii) The 4-dose regimen prescribes 2 doses on day 0 (1 in each of the 2 deltoid/thigh sites) followed by 1 dose on each of days 7 and 21.

Intradermal administration

Either the 8-site or the 2-site regimen should be used, as recommended by the respective vaccine manufacturer.

- (i) The 8-site ID regimen prescribes on day 0, injections of 0.1 ml given at 8 sites (1 in each upper arm, 1 in each lateral thigh, 1 on each side of the suprascapular region, and 1 on each side of the lower quadrant region of the abdomen); on day 7, 1 injection in each upper arm and each lateral thigh; and on each of days 30 and 90, 1 injection in one upper arm.8 The 1 dose on day 90 may be replaced by 2 ID injections on day 30.
- (ii) The 2-site ID regimen9 prescribes 1 injection of 0.1 ml at 2 sites on days 0, 3, 7 and 28.

For rabies-exposed patients who have previously undergone complete pre-exposure vaccination or postexposure prophylaxis with a CCV, 2 IM or ID doses of such a vaccine administered on days 0 and 3 are sufficient. RIG is not necessary in such cases. The same rules apply to people vaccinated against rabies who have demonstrated VNA titres of at least 0.5 IU/ml. Vaccination cards carefully recording previous immunizations are invaluable for correct decision-making.

Rabies vaccines (WHO position paper)

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Rabies immunoglobulin for passive immunization

RIG should be administered in all category III exposures and in category II exposures involving immunodeficient individuals. Given its relatively slow clearance, human rabies immunoglobulin (HRIG) is the preferred product, particularly in cases of multiple severe exposures.

However, HRIG is in short supply and available mainly in industrialized countries. Where HRIG is not available or affordable, purified equine immunoglobulin (ERIG) or F(ab)₂ products of ERIG should be used. Most of the new ERIG preparations are potent, highly purified, safe and considerably less expensive than HRIG. However, they are of heterologous origin and carry a small risk of hypersensitivity reactions.¹⁰ There are no scientific grounds for performing a skin test prior to administration of ERIG because testing does not predict reactions, and ERIG should be given whatever the result of the test.

RIG for passive immunization should not be injected later than 7 days after the initiation of post-exposure vaccination. The dose for HRIG is 20 IU/kg body weight, and for ERIG and F(ab)₂ products 40 IU/kg body weight. All of the RIG, or as much as anatomically possible (cave compartment syndrome), should be administered into or around the wound site(s). Any remaining RIG should be injected IM at a site distant from the site of vaccine administration.

Policy

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Program Management

State of the art of new vaccines: research and development

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Schedule

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Travellers

Rabies vaccines (WHO position paper)

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Vaccine Administration

State of the art of new vaccines: research and development

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