

Rabies vaccines and immunoglobulins: WHO position



SUMMARY OF 2017 UPDATES



The new WHO recommendations for rabies immunization supersede the 2010 WHO position on pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) for rabies. These updated recommendations are based on new evidence and directed by public health needs that are cost-, dose- and time-sparing, while assuring safety and clinical effectiveness. In addition, new guidance on prudent use of rabies immunoglobulins (RIG) is provided.

The following sections summarize the main points of the updated WHO position as endorsed by the Strategic Advisory Group of Experts on immunization (SAGE) at its meeting in October 2017¹. The full version of the WHO position on rabies vaccines and immunoglobulins will be published in the Weekly Epidemiological Record² in April 2018.

Rabies prevention involves two main strategies: (i) dog vaccination to interrupt virus transmission to humans; and (ii) human vaccination as a series of vaccine administrations before or after an exposure. Currently, rabies vaccines made from inactivated cell cultures are extremely well tolerated and have no contraindications.

POST-EXPOSURE PROPHYLAXIS (PEP)

Individuals with WHO category II or III exposures should receive PEP without delay.

The WHO rabies exposure categories are:

- Category I** Touching or feeding animals, licks on intact skin
- Category II** Nibbling of uncovered skin, minor scratches or abrasions without bleeding
- Category III** Single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposure due to direct contact with bats

PEP consists of the following steps:

1. All bite wounds and scratches should be attended to as soon as possible after the exposure; thorough washing and flushing of the wound for approximately 15 minutes, with soap or detergent and copious amounts of water, is required. Where available, an iodine-containing, or similarly viricidal, topical preparation should be applied to the wound.
2. RIG should be administered for severe category III exposures. Wounds that require suturing should be sutured loosely and only after RIG infiltration into the wound.
3. A series of rabies vaccine injections should be administered promptly after an exposure.

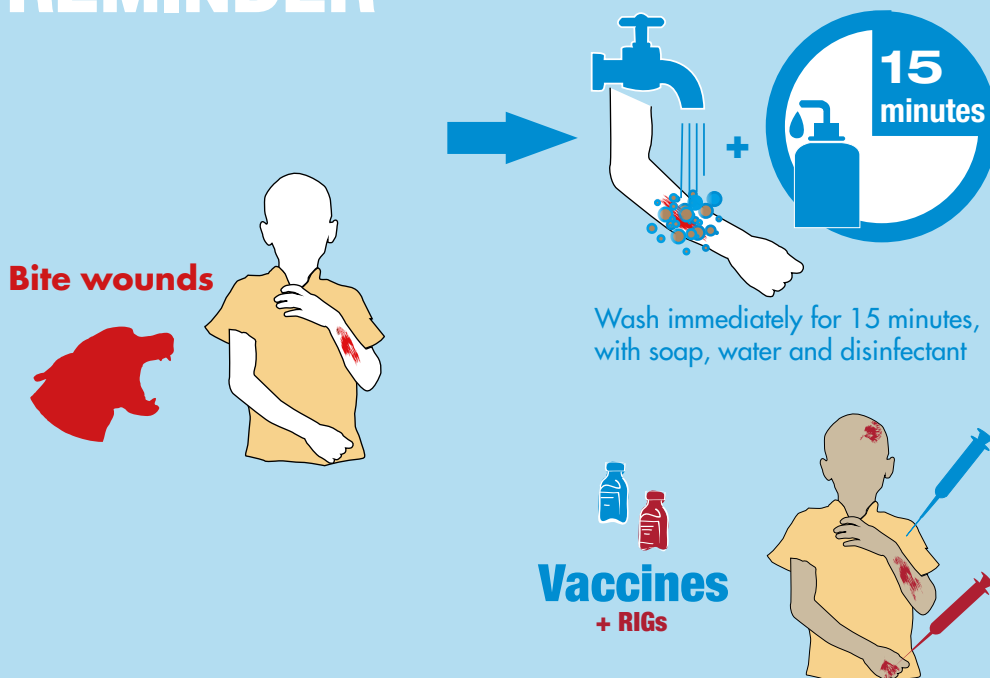
¹ <http://apps.who.int/iris/bitstream/10665/259533/1/WER9248.pdf>

² <http://www.who.int/wer/en/>

PEP for rabies-exposed individuals of all ages and who were not subject to previous PrEP or PEP

- Rabies vaccines can be administered by two different routes, intradermal (ID) or intramuscular (IM), and according to different schedules.
- For adults, the vaccine should always be administered in the deltoid area of the arm; for young children (aged < 2 years), the anterolateral area of the thigh is recommended.
- One ID dose is 0.1 ml of vaccine and one IM dose is an entire vial of vaccine, irrespective of the vial size.
- ID PEP regimens have cost- and dose-sparing effects, even in clinics with low patient throughput.
- The recommended WHO option is, therefore, the cost-, dose- and time-sparing ID PEP regimen:
 - 2-site ID vaccine administrations on days 0, 3 and 7
- The previously WHO-recommended IM PEP regimens below are still considered valid options, but may not be as cost-, dose- or time-sparing. The feasibility of either regimen is also dependent on the clinical setting and patient preferences.
 - 1-site IM vaccine administration on days 0, 3, 7 and the fourth dose between days 14 to 28;
 - 2-site IM vaccine administration on day 0 and 1-site IM on days 7 and 21.
- Changes in rabies vaccine product and/or the route of administration during the same PEP course are acceptable, if unavoidable, to ensure PEP course completion.
- Should a vaccine dose be delayed for any reason, the PEP regimen should be resumed (not restarted).
- Individuals with documented immunodeficiency should be evaluated on a case-by-case basis and receive a complete course of ID or IM PEP, including RIG.

REMINDER



Rabies post-exposure prophylaxis

by Neglected Tropical Diseases (NTD)

- All individuals who experience a V or III exposure **should receive PEP** as an emergency procedure
- Immediate, thorough **washing** of the wound for approximately 15 minutes
- Previously immunized individuals

For individuals with category III exposures and where RIG is indicated

- RIG provides passive immunization and is administered only once, as soon as possible after the initiation of PEP and not beyond day 7 after the first dose of vaccine.
- Vaccines should never be withheld, regardless of the availability of RIG.
- Correctly administered, RIG neutralizes the virus at the wound site within a few hours.
- Less costly than hRIG is eRIG, both of which have shown similar clinical outcomes in preventing rabies. As eRIG products are now highly purified, skin testing before administration is unnecessary and should be abandoned.
- To confer the maximum public health benefit, WHO recommends the following:
 - The maximum dose is 20 IU (hRIG) and 40 IU (eRIG) per kg body weight. There is no minimum dose.
 - Infiltrate as much as possible into the wound; the remainder of the calculated dose of RIG does not need to be injected IM at a distance from the wound but can be fractionated in smaller, individual syringes to be used for other patients, aseptic retention given.
- If RIG is not available, thorough, prompt wound washing, together with immediate administration of the first vaccine dose, followed by a complete course of rabies vaccine, is highly effective in preventing rabies.
- If a limited amount of RIG is available, RIG allocation should be prioritized for exposed patients based on the following criteria (highest priority descending):
 - multiple bites;
 - deep wounds;
 - bites to highly innervated parts of the body, such as head, neck and hands;
 - patients with severe immunodeficiency;
 - the biting animal is confirmed or probable rabies; and
 - bites, scratches or exposures of mucous membranes that are caused by a bat.

PEP for rabies-exposed individuals who can document previous PrEP or PEP

- No RIG is indicated
- Accelerated PEP regimens apply:
 - 1-site ID vaccine administration on days 0 and 3;
 - 4-site ID vaccine administration (equally distributed over the left and right deltoids, thigh or suprascapular areas) on day 0 only; or
 - 1-site IM vaccine administrations on days 0 and 3.
- If repeat exposure occurs (i.e. re-exposure within 3 months of completion of PEP), only wound treatment is required, neither vaccine nor RIG are needed.

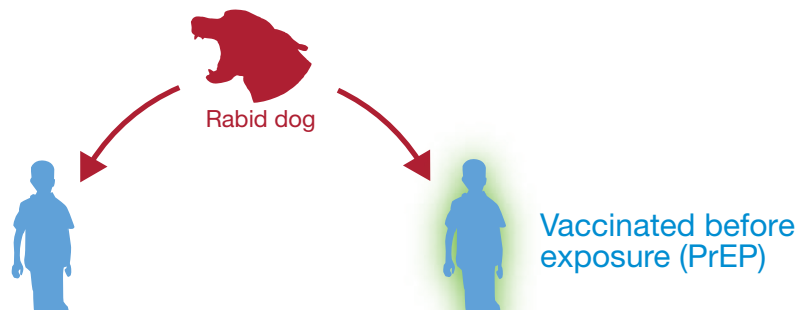


PRE-EXPOSURE PROPHYLAXIS (PrEP)

PrEP recommendations for individuals at higher risk due to occupation or for sub-populations in remote rabies-endemic settings were updated considering: (i) timely access to rabies biologicals; (ii) access to rabies serological testing; (iii) requirements for booster vaccination; and (iv) presence of rabies in wildlife reservoirs.

PrEP makes administration of RIG unnecessary after a bite. Rabies vaccination likely provides lifetime protection, with vaccine booster in case of an exposure. A routine PrEP booster or serology for neutralizing antibody titres would be recommended only if a continued, high risk of rabies exposure remains.

- Rabies vaccines can be administered by two different routes, intradermal (ID) or intramuscular (IM), and according to different schedules.
- For adults, the vaccine should be administered in the deltoid area of the arm; for young children (aged < 2 years), the anterolateral area of the thigh is recommended.
- One ID dose is 0.1 ml of vaccine and one IM dose is an entire vial of vaccine, irrespective of the vial size.
- PrEP should be considered as a large-scale intervention in remote settings which have limited access to PEP if annual dog bite incidence is > 5% or vampire bat exposures prevail.
- PrEP regimens for individuals of all ages are:
 - 2-site ID vaccine administrations on days 0 and 7
 - 1-site IM vaccine administrations on days 0 and 7
- Individuals with documented immunodeficiency should be evaluated on a case-by-case basis and best receive an ID or IM PrEP regimen as above, plus a third vaccine administration between days 21 to 28. Additionally, in the event of an exposure, a complete PEP course, including RIG, is recommended.



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