Background

- Rabies is a viral zoonotic disease responsible for an estimated 59 000 human deaths and over 3.7 million disability-adjusted life years (DALYs) lost every year.
- Rabies is almost invariably fatal once clinical signs occur, as a result of acute progressive encephalitis.
- Up to 99% of human cases of rabies result from the bite of an infected dog.
- Mass vaccination of dogs is the principal strategy for interrupting RABV transmission between dogs and reducing transmission to humans and other mammals

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Background
Exposure to infection

The following categories describe the risk of a RABV exposure according to the type of contact with the animal suspected of having rabies.

- **Category I** touching or feeding animals, animal licks on intact skin (**no exposure**);
- **Category II** nibbling of uncovered skin, minor scratches or abrasions without bleeding (**exposure**);
- **Category III** single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (**severe exposure**).

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Background
Exposure to infection

- Human-to-human transmission of RABV is extremely rare. The only documented cases of human-to-human transmission occurred via tissue and organ transplants from RABV-infected individuals, and a single case of likely perinatal RABV transmission.
- No case of human rabies resulting from consumption of raw meat or milk from a rabid animal has been documented.
- RABV infection in rodents is very uncommon. No human rabies cases due to bites by rodents have been reported.

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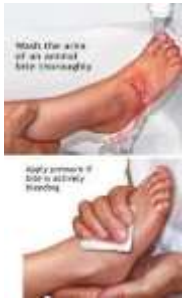
Postexposure Prophylaxis (PEP)

- PEP **always** includes:
  - Wound washing and wound care
  - A series of rabies vaccine injections should be administered **immediately** after an exposure
- PEP sometimes includes:
  - Administration of rabies immunoglobulins (RIG)
    - in severe category III exposures
    - in category II exposures to bats



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Pre Exposure Prophylaxis (PrEP)

- PrEP is vaccination in preparation for potential risk of exposure to RABV
- PrEP is recommended for individuals at higher risks due to occupation or for sub-populations in remote rabies-endemic settings.
- PrEP makes administration of RIG unnecessary after a bite wound
- Previously immunized individuals benefit from abridged PEP in case of exposure to RABV

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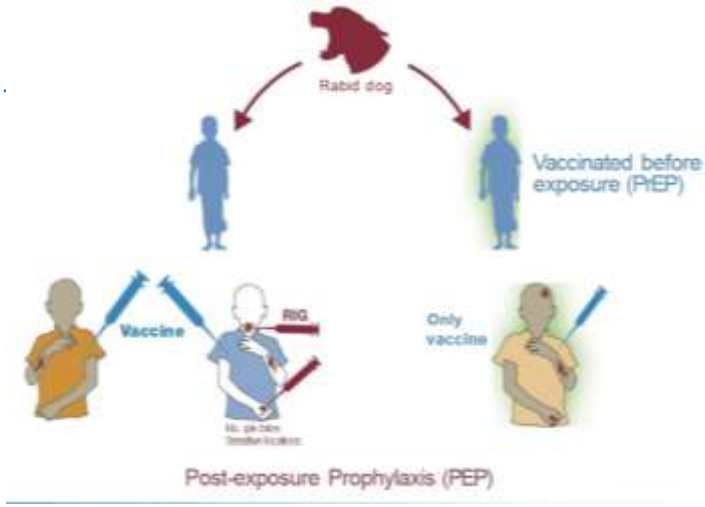

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Vaccines

- Cell culture and embryonated egg-based rabies vaccines (CCEEVs) are intended for use in both pre-exposure prophylaxis (PrEP) and for post-exposure prophylaxis (PEP).
- Since 1984, WHO has strongly recommended discontinuation of production and use of nerve tissue vaccines and their replacement by modern, concentrated, purified CCEEVs.
- CCEEVs have been shown to be safe, highly immunogenic and well tolerated.

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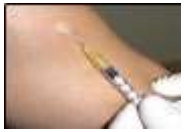
Vaccine administration

- Evidence supports administration of CCEEVs by intradermal (ID) injection.
- ID administration of rabies vaccines provides a cost-saving and dose-sparing alternative.



- A systematic review of vaccine potency has shown that current vaccines (> 2.5 IU/IM dose), when administered by the ID route for either PEP or PrEP, have efficacy equivalent to or higher than that of the same vaccine administered by the IM route.

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Rabies immunoglobulins (RIG)

- After exposure to RABV, RIG provides passive immunization by neutralizing the virus at the wound site before the immune system can respond to the vaccine by producing VNAs.
- RIG is derived from human blood (hRIG) or equine blood (eRIG). They are considered to have similar clinical effectiveness.
- A single monoclonal antibody (mAb) product against rabies, licensed in India in 2017, has been demonstrated to be safe and effective in clinical trials.

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WHO Position

WHO recommends two main immunization strategies for the prevention of human rabies:

- Post-exposure prophylaxis (PEP) which includes extensive and thorough wound washing at the RABV-exposure site, together with RIG administration if indicated, and the administration of a course of several doses of rabies vaccine;
- Pre-exposure prophylaxis (PrEP) which is the administration of several doses of rabies vaccine before an exposure to RABV.

WHO retains its recommendation that the production and use of nerve-tissue vaccines should be discontinued and replaced by vaccines based on RABV grown in cell culture or embryonated eggs (CCEEVs).

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WHO Position: Administration of rabies vaccines

- For both PEP and PrEP, vaccines can be administered the ID route.
  - One ID dose is 0.1 mL of vaccine;

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WHO Position: Administration of rabies vaccines

- If any doses are delayed, vaccination should be resumed, not restarted.
- A change in the route of administration or in vaccine product during a PEP or PrEP course is acceptable if such a change is unavoidable.

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WHO Position: Recommended Schedules

	Category I exposure	Category II exposure	Category III exposure
Immuno-logically naive individuals of all age groups	Wash exposed skin surfaces. No PEP required.	Wound washing and immediate vaccination: - 2-sites ID on days 0, 3 and 7 - - RIG is not indicated.	Wound washing and immediate vaccination - 2-sites ID on days 0, 3 and 7 RIG administration is recommended.
Previously immunized individuals of all age groups	Wash exposed skin surfaces No PEP required.	Wound washing and immediate vaccination*: - 1-site ID on days 0 and 3; - RIG is not indicated.	Wound washing and immediate vaccination*: - 1-site ID on days 0 and 3; RIG is not indicated.

** except if complete PEP already received within <3 months*

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WHO Position: Post-exposure prophylaxis (PEP)

- The indication and procedure for PEP depend on the type of contact with the suspected rabid animal and immunization status of the patient.
  - For category I exposures, no PEP is required;
  - for category II, immediate vaccination is recommended;
  - for category III, immediate vaccination is recommended, and administration of RIG, if indicated.
- For categories II and III, thorough washing and flushing with soap or detergent and copious amounts of water of all bite wounds and scratches should be done immediately, or as early as possible. Depending on the characteristic of the wound, antibiotics, analgesics and a tetanus vaccine booster might be indicated.

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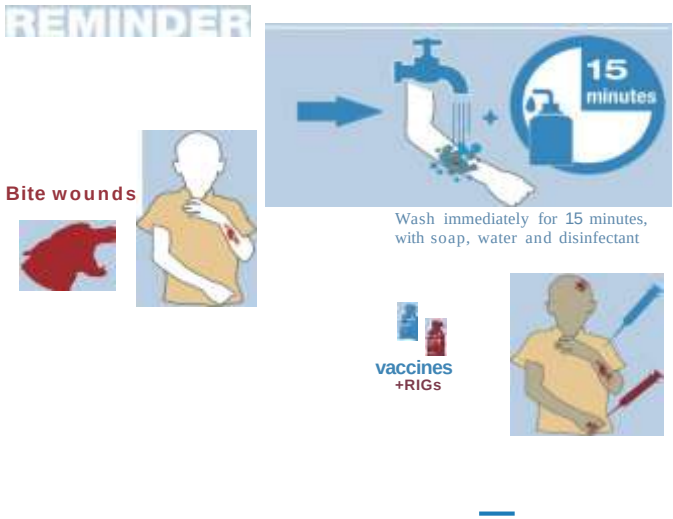

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WHO Position: *Administration of rabies immunoglobulins (RIG)*

- RIG should be administered only once, preferably at, or
- as soon as possible after, the initiation of PEP.
- RIG is infiltrated into and around the wound
- For optimal effectiveness, the maximum dose calculation for RIG is 40 IU/kg body weight for equine derived RIG (eRIG) products, and 20 IU/kg body weight for human derived RIG (hRIG). Skin testing before eRIG administration should not be done because of unreliable prediction of adverse effects.

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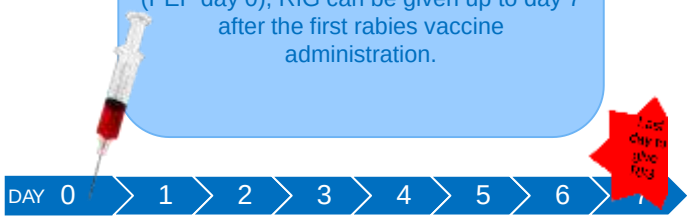
Did you know:

Even if RIG is not available at the first visit (PEP day 0), RIG can be given up to day 7 after the first rabies vaccine administration.



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WHO Position: Pre-exposure prophylaxis (PrEP)

- WHO recommends PrEP for individuals at high risk of RABV exposure:
  - These include sub-populations in highly endemic settings with limited access to timely and adequate PEP
  - Individuals at occupational risk
  - Travellers who may be at risk of exposure
- PrEP should be considered in sub-populations living in remote, rabies-endemic areas, where the dog bite incidence is >5% per year or vampire bat rabies is known to be present.
- WHO recommends the following PrEP schedule:
  - 2-site ID vaccine administered on days 0 and 7.

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