Post exposure prophylaxis (Rabies)

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What is Post exposure prophylaxis (PEP)?

➢ PEP is the emergency response to a rabies exposure.

➢ This prevents the virus from entering the central nervous system, which would invariably result in death.

➢ PEP consists of:

- Extensive washing with water and soap for at least 15 minutes and local treatment of the wound as soon as possible after a suspected exposure;
- A course of potent and effective rabies vaccine (for category II & III) that meets WHO standards; and
- Administration of rabies immunoglobulin or monoclonal antibodies into the wound (for category III)

Exposure risk and indication for PEP (WHO)

Categories of contact with suspect rabid animal	Post-exposure prophylaxis measures
Category I - touching or feeding animals, animal licks on intact skin (no exposure)	Washing of exposed skin surfaces, no PEP
Category II - nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure)	Wound washing and immediate vaccination
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)	Wound washing, immediate vaccination and administration of rabies immunoglobulin/monoclonal antibodies

Local treatment of wound

- All animal bites should be washed for 10–15 minutes with copious amount of water and soap (detergent soap preferable).
- After allowing the wounds to dry for few minutes, antiseptics like povidone iodine and surgical spirit should be applied on all wounds to chemically inactivate or kill the rabies virus at the site of bite.
- Rabies risk is reduced to almost 50% by early and proper local treatment of wounds.
- Routine suturing of wounds and surgical dressing is not recommended. Few stay sutures can be applied to stop bleeding only after infiltration of RIGs/RMAbs into wounds

Passive immunization

- Administration of RIGs/RMAbs (passive immunization): For individuals with category III (severe) exposures, vaccine alone is not enough and additionally RIG/RMAbs is indicated as vaccine induced antibodies appear only after 7–14 days.
- During this window period of 7–14 days, patient is unprotected, hence, RIG/RMAbs need to be administered.
- RIG/RMAbs is administered only once, as soon as possible after the animal bite and not beyond day 7 after the first dose of vaccine.
- RIG/RMAbs are also indicated in category II in immunocompromised patients

Passive immunization cont..

There are two classes of rabies passive immunizing agents:

1. Rabies immunoglobulins:

i. Equine rabies immunoglobulin (ERIG): Dosage—40 IU/kg body weight. It is indigenously manufactured; to be used only after skin sensitivity test as per product insert.

ii. Human rabies immunoglobulin (HRIG): Dosage—20 IU/kg body weight. It is imported and expensive; no skin sensitivity test required. It is available in prefilled syringe.

Rabies monoclonal antibody:

i. Human RMAb (single MAB—RabishieldTM): Dosage—3.33 IU/kg body weight. Potency: 40 IU/mL

ii. Cocktail of RMAbs (Docaravimab and Miromavimab-TwinrabTM): Dosage—40 IU/kg body weight. Potency: 600 IU/mL No skin sensitivity test required before administration of RMABs.

The WHO (2018) recommends that if available, the use of RMAbs instead of RIG is encouraged.

Passive immunization cont..

Procedure of RIG/RMAb administration:

- As much of the calculated dose of RIG/RMAb, as is anatomically feasible, should be infiltrated into and around all the wounds.
- The RIG/RMAb shall be injected into the edges and base of the wound(s) till traces of RIG/RMAb oozes out.
- RIGs/RMAbs are always to be used along with rabies vaccine as early as possible. A full course of vaccination should follow thorough cleansing of wounds and passive immunization, otherwise treatment failures can occur.

Active immunization

The available anti rabies vaccines in India can be grouped on the basis of the substrate used to grow the vaccine virus strain.

Name of the vaccine	Fixed virus strain	Substrate	Availability
Neural tissue vaccine BPL inactivated sheep brain vaccine (Semple type)	PV 11	Sheep brain	Production stopped since December 2004
Cell culture vaccines i) Human Diploid Cell Vaccine (HDCV) ii) Purified Chick Embryo Cell Vaccine (PCEC) iii) Purified Vero Cell Rabies Vaccine (PVRV)	 Pitman Moore (PM) LEP-Flury Pitman Moore (PM)	 MRC-5 Primary SPF chick embryo cells Vero Cells	 imported Produced locally in pvt. Sector Imported + produced locally in public sector
Purified Duck Embryo Vaccine	Pitman Moore (PM)	Duck embryo	imported

Route of administration & Doses

WHO recommends administering rabies vaccines intradermally, as this reduces the amount of necessary vaccine and therefore the cost by 60–80% without compromising any safety or efficacy.

Administration of anti-rabies vaccine:

Currently available rabies vaccine recommended in India are of two types:

1. Purified chick embryo cell rabies vaccine (PCECV) and

2. Purified Vero cell rabies vaccine (PVRV) Rabies vaccine for PEP can be administered either by

- Intramuscular route: One dose of vaccine administered on days 0–3–7–14–28 (1–1–1–1–1)
- Intradermal route: 0.1 mL × 2 sites on days 0–3–7–28 (2–2–2–0–2)

Site: Anterolateral thigh or deltoid No condition including pregnancy is a contraindication for PEP. It is safe in all age groups.

Supportive therapy: Tetanus containing vaccine if indicated as per previous immunization status; anti-inflammatory, and antibiotics depending on the type of wound/s can be given

Route of administration & doses cont..

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

- Only two doses of vaccines on days 0 and 3 either by IM/ID.
- No RIG/RMAbs is indicated: ; 1-site IM vaccine administration on days 0 and 3 or ; 1-site ID vaccine (0.1 mL) administration on days 0 and 3
- If repeat exposure occurs (i.e., reexposure within 3 months of completion of PEP), only wound treatment is required, neither vaccine nor RIG are needed.

References

1. National Centre of Disease Control. National Guidelines for Rabies Prophylaxis, 2019 National RabiesControl Programme. New Delhi: National Centre of Disease Control; 2019.
2. World Health Organization. Rabies Vaccines: WHO position paper–April 2018. Geneva: World HealthOrganization; 2018. pp. 201-20.
3. World Health Organization. WHO Expert Consultation on Rabies: Third Report. Geneva: WorldHealth Organization; 2018.