Indian Academy of Pediatrics (IAP)

STANDARD TREATMENT GUIDELINES 2022

Rabies Prophylaxis in Children

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Introduction

- ☑ Rabies is a zoonotic disease caused by *Lyssavirus* transmitted to human beings by bites from rabid animals. It is almost always fatal but can be prevented by timely initiation of post-exposure prophylaxis (PEP), viz., *local treatment of wounds, administration of rabies immunoglobulins (RIGs)/rabies monoclonal antibodies (RMAbs), and anti-rabies vaccines.*
- ☑ Globally, an estimated 59,000 human rabies deaths occur every year. India alone reports an estimated 20,000 (36%) (2004) of human rabies deaths and 17.4 million animal bites every year. A global burden of disease study estimates approximately 5,000 deaths/year. In December 2015, the World Health Organization (WHO) has set a goal of "elimination of dog-mediated human rabies by 2030".

Animals Transmitting Rabies in India

Rabies is transmitted to humans largely by dogs and cats (>97%). *Wild animals (2%) such as mongoose, foxes, jackals, wild dogs, wild rodents, and occasionally by monkeys, horses, donkeys, and others. Domestic rats, rabbits, and birds are ordinarily not known to transmit rabies.*

- ☑ Rabies virus is neurotropic; virus enters the peripheral nerves or cranial nerves from the damaged nerve endings from the site of bite **(Fig. 1)**, ascend up through dorsal route ganglion, spinal cord, and finally reaches brain where it multiply enormously.
- ☑ The rabies virus subsequently descends down to all secretory glands, viz., salivary glands, mammary glands, sweat glands, and urine via sympathetic nervous system.
- ☑ Hence, although all secretions of rabid patients are infectious, no human-to-human transmission has been reported. Since, there is *no viremia; rabies virus cannot be detected in blood*.

After an average incubation period of 30–90 days, a clinical symptom of hydrophobia occurs. There are two forms of rabies in man:

1. *Classic hydrophobia*: Hydrophobia, aerophobia, and photophobia—clinical course about 1 week to 10 days. More remarkable abnormalities (agitation, photophobia, priapism, increased libido, insomnia, nightmares, and depression) may also occur, suggesting encephalitis, psychiatric disturbances, or brain conditions.
2. *Paralytic rabies*: Ascending paralysis—clinical course about 3 weeks; death invariably occurs due to cardiorespiratory failure.

Around 20–30% patients present as encephalitis.

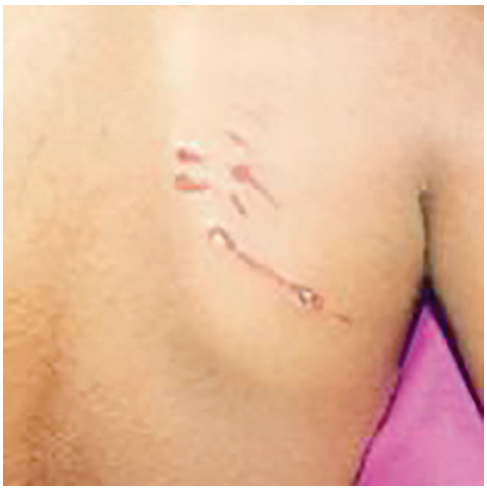

Fig. 1: Class III bite.

Human rabies is almost always fatal after an animal bites, it can be prevented either by *(1) pre-exposure prophylaxis (PrEP) or by (2) post-exposure prophylaxis (PEP).*

Pre-exposure Prophylaxis

Pre-exposure prophylaxis is recommended for individuals at higher risk due to occupation and for the children in endemic countries like India. Rabies vaccines can be administered by two different routes: intradermal (ID) or intramuscular (IM), and according to different schedules.

For young children (aged <2 years), the anterolateral area of the thigh is recommended.

- ☑ *IM regimen: One dose of vaccine on days 0, 7, and 21/28 into anterolateral aspect of thigh/deltoid region.*
- ☑ *ID: 0.1 mL of vaccine on days 0–7–21 or 28 in deltoid region/anterolateral thigh.*
- ☑ *Two-site ID administration of rabies vaccine has also been recommended on day 0 and 7.*

Pre-exposure prophylaxis makes administration of RIG unnecessary after a bite. A routine PrEP booster or serology for neutralizing antibody titers would be recommended only if a continued high risk of rabies exposure remains like in those handling rabies viruses in laboratories.

Post-exposure Prophylaxis

In Patients Previously not Taken any Rabies Vaccine

☑ *Assessment of risk by categorization of wounds*:

Category	*Type of contact*	*Type of exposure*	*Recommended PEP*
I	☑ Touching/feeding of animals ☑ Licks on intact skin	None	None, if reliable case history is available
II	☑ Nibbling of uncovered skin ☑ Minor scratches/abrasions without bleeding	Minor	☑ Local treatment of wounds ☑ Administer anti-rabies vaccine
III	☑ Single/multiple transdermal bites/scratches ☑ Licks on broken skin ☑ Contamination of mucous membrane with saliva (licks)	Severe	☑ Local treatment of wounds ☑ Administer RIG/RMAb ☑ Anti-rabies vaccine

☑ *Local treatment of wound(s)*: All animal bites should be washed for 10–15 minutes with copious amount of water and soap (detergent soap preferable) **(Fig. 2)**. 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.

Fig. 2: Local wound washing—15 minutes.

☑ *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.

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.

2. *Rabies monoclonal antibody*:
   i. *Human RMAb (single MAB—Rabishield™):* Dosage—*3.33 IU/kg body weight. Potency: 40 IU/mL*
   ii. *Cocktail of RMAbs (Docaravimab and Miromavimab-Twinrab™):* 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.

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. 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 following aseptic precautions.

For multiple bites, the calculated dose of RIG/RMAb may not be sufficient to infiltrate all wounds. In these circumstances, it is advisable to dilute the RIG/RMAb in sterile normal saline to a volume sufficient to inject all wounds. 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.

☑ *Administration of anti-rabies vaccine*: Currently available rabies vaccine recommended for children 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 **(Figs. 3 and 4)**:

- *Intramuscular route*: One dose of vaccine administered on days 0–3–7–14–28 (1–1–1–1–1)

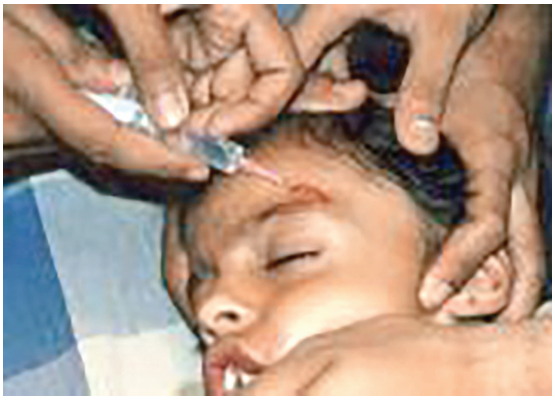

Fig. 3: Local rabies immunoglobulin (RIG) administration.

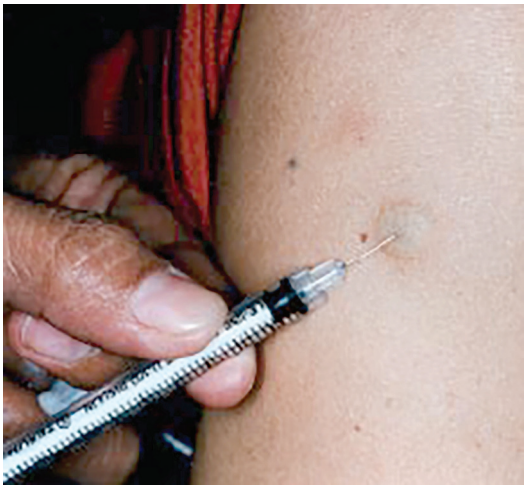

Fig. 4: Intradermal (ID) administration.

- 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.

PEP for rabies-exposed individuals who can document previous PrEP or PEP (IM/ID)

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.

☑ *Coronavirus disease (COVID) vaccine and rabies vaccine*: Both can be given together at different sites or at any interval as both are killed vaccines.
Should be administered irrespective of previous routine vaccination status.

Note:

☑ 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/continued (not restarted).

Key Points

- ☑ Rabies is a zoonotic disease with 100% mortality
- ☑ Wound washing should be done immediately with soap and water for 10–15 minutes
- ☑ RIG/RMAb must only be infiltrated locally in all category III bites
- ☑ Do not inject RIG/RMAb intramuscularly
- ☑ Completion of vaccination course as per schedule is paramount
- ☑ PrEP should be offered to all children.

Further Reading

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