

ANIMAL BITE MANAGEMENT AND POST EXPOSURE PROPHYLAXIS OF RABIES

Rabies is an acute viral disease that causes fatal encephalomyelitis in virtually all warm blooded animals including man. The virus is found in wild and some domestic animals and is transmitted to other animals and humans through their saliva. In India, dogs are responsible for about 95% human rabies followed by cats (2%).

It is vaccine preventable disease caused by rabies virus of the Lyssavirus genus, with in the family Rhabdoviridae.

Decision to treat:

- ✓ Rabies is endemic in India; so management of animal bites is essential.
- ✓ Suspect all warm blooded animal bites, even scratches.
- ✓ Treat as per merit of the bite.
- ✓ Post Exposure Prophylaxis (PEP) should be started as soon as possible after the bite.

Guide for Post-Exposure Prophylaxis (PEP)

Category	Type of contact	Recommended Post Exposure Prophylaxis
I	Touching or feeding animals Licks on intact skin	 None, if reliable case history is available. Wash exposed area with soap and water and apply antiseptic.
н	Nibbling of uncovered skin. Minor scratches or abrasions without bleeding	 Wound management. Administer anti-rabies vaccine immediately.
Ш	Single or multiple transdermal bites or scratches. Contamination of mucous membrane with saliva (i.e. licks). Licks on broken skin.	 Wound Management. Administer rabies immunoglobulin. Administer anti-rabies vaccine immediately.

NB: All animal bites in forest or all wild animal bite should be treated as Category III exposures.

Animals transmitting rabies in India

- A. Domestic: Dogs and cats
- **B.** Peri-domestic:
 - ✓ Large ruminants (cows and buffaloes)
 - ✓ Small ruminants (sheep and goat)
 - ✓ Mammals like pigs, donkeys, horses, camels etc.
- **C. Wild:** Any wild animal
 - ✓ Foxes and jackals, mongoose, leopard, bear etc. and even monkey.

Not reported:

✓ Bird, squirrel, bats*, rodents* (* See below.)

*Bites by **Bats** or **Rodents** do not ordinarily necessitate rabies vaccination. However, in unusual circumstances cases may be considered for vaccination in consultation with an expert in the field of rabies. (Example: exposure to domestic rodents does not require PEP but if the rodent is wild then the bite victim may be considered for PEP in consultation with the expert). A mouse is usually a domestic rodent, but for a large size rat it is difficult to determine whether it is domestic or wild. Vaccination may be necessary in case of bite by such rats).

Principles of treatment:

- A. Wound management
- B. Passive immunization i.e. inj. of immunoglobulin/anti-sera (RIG).
- C. Active immunization i.e. inj. of anti-rabies vaccine (ARV).

General Considerations in rabies PEP (Post-Exposure Prophylaxis)

- ✓ If rabies immunoglobulin (RIG) is not available on first visit, its use can be delayed by a maximum of 7 days from the date of first dose of vaccine.
- ✓ **Pregnancy** and **infancy** are never contraindications to PEP.
- ✓ If the patient comes even months after having been bitten, he/she should be dealt with in the same manner as if the bite has occurred recently.
- ✓ PEP is not required in case of consumption of milk of a rabid animal, no matter the milk is boiled or raw. According to WHO, "Infectious RABV has never been isolated from milk of rabid cows and documented human rabies case has been attributed to consumption of raw milk". (**Ref.** Rabies vaccines: WHO position paper- April 2018).
- ✓ Cooking of meat kills any rabies virus in it, but consumption/handling of raw meat of a rabid animal requires PEP.

A. Wound management:

- ✓ Wash the wound immediately (as early as possible) under running tap water for at least 15 minutes.
- ✓ Use soap or detergent to wash the wound (if soap is not available then use water only to wash the wound).
- ✓ After thorough washing and drying the wound apply antiseptic e.g. Povidone iodine, etc.
- ✓ Don't apply irritants viz. chillies, soil, oils, turmeric powder, lime, salt, plant juice etc.
- ✓ Don't touch the wound with bare hands.
- ✓ Wound washing must be performed even if the patient reports late.
- Postpone suturing if possible; if suturing is at all necessary, it should be performed after cleaning and infiltrating RIG at the depth of wound and only minimum number of loose suture should be applied.
- ✓ Don't cauterize.
- ✓ Administer systemic antimicrobial and tetanus toxoid if necessary (follow usual norm of wound management in this regard).

Following an animal bite, wound washing with running tap water is one of the most important and the first step of PEP to be done immediately, as wound washing removes the traces of saliva (containing the lethal rabies virus) from the wound. Moreover, use of soap inactivates the virus, if present. This simple process greatly eliminates the risk of rabies infection. B. Passive immunization (immunoglobulin/anti-sera):Human Rabies Immunoglobulin (HRIG): 20 IU/kg body wt, maximum 1500 IU
 Equine Rabies Immunoglobulin (ERIG): 40 IU/kg body wt, maximum 3000 IU

Either of the above is to be used where indicated – i.e. all Category III exposure and also **Category II exposure in case of immune-compromised persons.**

Local infiltration of rabies immunoglobulin:

- ✓ Infiltrate into all Category III wounds.
- RIG should be infiltrated in the depth and around each of the wounds to inactivate the locally present rabies viruses.
- ✓ Infiltrate the entire immunoglobulin dose, or as much as possible (avoiding compression syndrome), in the depth and around the wounds.
- ✓ As per the new recommendation/ guideline of WHO and GOI, injecting the remaining volume of RIG intramuscularly at a distance from the wound provides little or no additional protection against rabies as compared with infiltration of the wound(s) alone. Hence the remaining RIG can be given to other patients using separate syringe /needle.
- ✓ If RIG is insufficient (by volume) to infiltrate all the wounds, dilute it with sterile normal saline to a volume sufficient to infiltrate all wounds.
- ✓ Wounds on tip of finger/toe, ear lobe, nose, external genitalia or around the eye can be safely injected with RIG, provided the injection is not done with excessive pressure which can cause compression syndrome.
- ✓ Suspected exposure to aerosols of rabies virus (as example accidental exposure in labs) is to be treated as category III exposure. In such cases ARV is to be given as per normal schedule but RIG is to be given in IM route.
- ✓ RIG must never be given intravenously.

C. Active immunization (Anti Rabies Vaccination):

- Route of inoculation: Intramuscular or Intradermal.
- Site of inoculation: Deltoid muscle or anterolateral part of thigh. Not recommended in gluteal region, since there is chance of low absorption due to presence of fatty tissue.

Post exposure Vaccine schedule:

The vaccination schedule may be either of the following. However, in healthcare institutions, the latter (Intradermal Regimen) is more cost effective and is mandatory in State Government set-ups except in documented exceptional cases.

i. Essen Intramuscular Regimen: 1-1-1-1

- ✓ One dose comprises of the entire content of one vial (content may be 0.5ml or 1ml) into the deltoid /anterolateral aspect of thigh.
- ✓ One dose each on day 0, 3, 7, 14 and 28.
- ✓ Infiltrate anti-rabies immunoglobulin locally on day 0 as described under Passive Immunization.

ii. Intradermal Regimen (approved in India)

2 site regimen (Updated Thai Red Cross regimen)

Dose : 0.1 ml (2 doses per visit) Site : Upper arm over each deltoid/ antero- lateral aspect of thigh Schedule: 2-2-2-0-2 Day 0 -2 sites Day 3 2 sites -Day 7 2 sites -Day 14 -No Dose Day 28 -2 sites

So, 2 injections per visit x 4 visits in total i.e. on Days- 0, 3, 7 and 28.

The above ID regimen is as effective as IM regimen, if not more, and is very costeffective. Hence it is recommended in all Govt. Anti-Rabies Clinics where a multiple no. of cases attend on a single day.

General guideline for use of IDRV:

- ✓ Only the rabies vaccine (lyophilized vaccine along with the diluent of specified volume) approved by DCGI for ID/ IM administration should be used for ID route. The vaccine should have stated potency of ≥ 2.5 IU per IM dose. The same vaccine is used for ID administration as per the stated schedule. A dose of 0.1 ml of vaccine, irrespective of reconstituted volume for IM route (0.5 ml or 1 ml) is administered per ID site as per the stated schedule.
- ✓ Intradermal injections must be administered by staff trained in this technique.
- ✓ Vaccine when given intradermally should raise a visible and palpable "bleb" in the skin.
- ✓ If the ID dose is inadvertently given subcutaneously or intra-muscularly or in the event of spillage, a new dose should be given intradermally (maybe at a nearby site).
- ✓ Animal bite victims on chloroquine therapy (for cure or prophylaxis of malaria) and immune-suppressed persons should be given ARV by IM route, not by ID route.
- Points to remember for PEP:
 - \checkmark Day 0 is the day of 1st dose of vaccine given, not the day of bite.
 - ✓ Never inject the vaccine in gluteal region.
 - ✓ Reconstituted vaccine to be used immediately. However, in unforeseen delay the vaccine vial should be stored at 2-8°C after reconstitution and should be used within 6 hours of reconstitution.
 - ✓ Dose is same for all age groups.
 - ✓ Switching the route of administration from IM to ID or vice versa and switch over from one type of modern rabies vaccine to the other during PEP is not recommended as routine. However, whenever this is absolutely required, PEP need not be restarted and the regimen should be continued/ resumed as per the new vaccine / route of administration (ref.- WHO recommendation and GOI Guideline for rabies prophylaxis).
 - ✓ In case of IM regimen (Essen Schedule), if the bite is by a dog or cat and the animal is alive & healthy till 10 days after bite, the PEP may be discontinued after 10 days or PEP can be converted to Pre Exposure Prophylaxis (PrEP) by skipping the vaccine dose on day

14 but administering the dose of day 28. However, this provision is not applicable for any animal other than dogs or cats.

- ✓ Please note, while using ID route of administration, complete course of vaccination should be given irrespective of the status of the animal.
- ✓ As for all immunizations, animal bite victim should be kept under medical supervision for at least **15-20 minutes** after administration of ARV as well as ERIG.

Management in immune- compromised patients:

- ✓ Thorough wound washing and antisepsis as described above.
- ✓ Local infiltration of RIG in both Category II and Category III exposure.
- ✓ Complete course of ARV by IM route in Category II and III exposures.
- ✓ If facilities are available, anti-rabies antibody estimation should be done 14 days after the completion of course of vaccine to assess the need of additional doses of vaccine.

Guide for Pre-Exposure Prophylaxis (PrEP):

- 3-dose series intramuscular (entire vial x 1 site) or intradermal regimen (0.1ml x 2 sites) at day 0, 7 and 28.
- Persons at high risk of exposure should get serum antibody level measured every 6 months and take a booster dose if the level falls below 0.5 IU/ml. Routine booster doses are not recommended for general people.

Management of re-exposed cases after a full PEP or PrEP:

In case of re-exposure after a full course and documentation of (Pre/Post-exposure) IM or ID vaccination, irrespective of category of exposure or time since previous vaccination -

- ✓ Proper wound toileting should be done.
- ✓ Doses only on day 0 and 3 (these actually serve as booster doses).
- ✓ Either intramuscular (entire vaccine vial) or intra-dermal injection (0.1ml) at 1 site.
- ✓ No RIG needed.
- ✓ If previous course of vaccination was partial/ irregular, treat it as a fresh case and give full course as usual.

Re-exposure following PEP with a nerve tissue vaccine (NTV) or if previous PEP or PrEP is not clearly documented - Treat as a fresh unvaccinated case.

If the animal bite victim has documented proof of complete PEP or PrEP within last 3 months, then adequate wound washing would be required in case of re-exposure, but no vaccine or RIG is needed in such cases.

Deviation from recommended PEP/PrEP vaccination schedule:

- Every effort should made to adhere to the recommended PEP/PrEP schedule, especially for the first 2 days of treatment.
- Deviation of a few days will not necessitate fresh vaccination from the beginning of the course.
- For most minor delay or interruptions, the vaccination schedule can be shifted and resumed as though the patient were on schedule. [See FAQ for example].

SUMMARY OF ANTI- RABIES VACCINATION SCHEDULE AS PER ROUTE OF ADMINISTRATION

Type of Prophylaxis	Route of Administration	Dose of Vaccine	Day of Dose	No. of Injections	Total no. of visit	Site of Injection visit
Post Exposure Prophylaxis	Intra Dermal	0.1 ml per dose	Day 0, 3, 7 & 28	2	4	Adult: Deltoid Muscle Infants and small children: Anterolate ral thigh
	Intra Muscular	1 entire vaccine vial	Day 0, 3, 7, 14 & 28	1	5	
Pre Exposure Prophylaxis	Intra Dermal	0.1 ml per dose	Day 0, 7 and booster on either day 21 or 28	1	3	
	Intra Muscular	1 entire vaccine vial	Day 0, 7 and booster on either day 21 or 28	1	3	
Re -exposure	Intra Dermal	0.1 ml per dose	Day 0 & 3	1	2	
	Intra Muscular	1 entire vaccine vial	Day 0 & 3	1	2	

NB: For exceptions and details please refer to the guideline for animal bite management.

FREQUENTLY ASKED QUESTIONS ABOUT ANIMAL BITE & RABIES



Q 1: Is it permissible to change the vaccine type during the course of vaccination with ARV?

Answer: It is desirable that the same type of modern rabies vaccine is used through the full course of vaccination with ARV. However, when completion of PEP with the same vaccine is not possible, switching may be done. It does not necessitate fresh starting of the course. [Note that only the cell culture vaccines that are approved by Govt. of India are recommended for ID route vaccination].

Please also note that a course of vaccine should be either ID or IM. Switching from IM to ID or reverse, in the middle of the course, is not advisable but may be done if absolutely required.

Q 2. A monkey bite patient received the first two doses of ARV on time (on days 0 and 3) and also RIG on day 0. Then he defaulted for the third dose of ARV (day 7). However, the patient comes back on day 9. What should be done?

Answer: In this case, day 0 and 3 inj. were given and inj. due on day 7 could not be given as the patient did not turn up. When he comes back on day 9, the two remaining doses of vaccine must be given as close to the original dates of the schedule as possible i.e. the pending 3rd dose on day 9 itself and the fourth dose on day 28 as usual.

The first two doses of ARV are the most important. For the 3rd or 4th doses two or three days deviation may be accepted (although not recommended). So the running schedule can be resumed if a patient comes back a few days late.

Q 3. A boy bitten by a cat received the first three doses of ARV in time (Day-0, Day-3 and day 7). In between 3rd and 4th shot of vaccine the boy got scratched again by a monkey drawing blood. What should be done?

Answer: No need to repeat the vaccine schedule. Just complete the usual vaccination up to 4th dose as per schedule. As first 3 doses of vaccination would be enough to produce antibodies, immunoglobulin is not needed for the latter incident.

Q 4. If for some reason, IDRV (intradermal rabies vaccine) cannot be given in deltoid region, what are the alternative sites?

Answer: The two doses of ID injection have to be given at two sites that do not share the same lymphatic drainage. So, deltoid region of the two arms are all right. However, if deltoid region cannot be used for some reason, ID inj. can be given in suprascapular region or anterolateral aspect of thigh.

Q 5. Where is IM regimen of ARV particularly recommended i.e. ID regimen is contraindicated?

Answer: In immune-compromised persons, ID route is not recommended for PEP. IM regimen is to be used in such persons. The same is true for persons who are on chloroquine for treatment or prophylaxis of malaria.

Q 6. Why is RIG considered as life-saving?

Answer: Administration of Anti-Rabies Vaccine stimulates production of neutralizing antibodies by the patient's immune system. Protective levels of antibodies (of more than 0.5 IU/ml of serum) appear as late as 7 to 14 days after the initial doses of vaccine (window period). Therefore, in case of shorter incubation period the patients are vulnerable to develop rabies during this window period of 7 to 14 days. RIGs are readymade anti-rabies antibodies and provide immediate passive immunity to rabies.

Q 7. A boy bitten by a dog, has come to a PHC-OPD 3 days after the bite. Is wound washing necessary at this stage?

Answer: Yes. Since the rabies virus can persist and even multiply at the site of bite for a long time, wound washing must be performed even if the patient reports late.

Q 8. A man, complaining of scratches by a monkey drawing blood, comes to the OPD 4 days after the incident. The M.O. examines the wound and decides to give anti-rabies vaccine. Should he also be given RIG although it is 4 days late?

Answer: Yes. RIG should be given at the first opportunity (but not beyond 7 days of initiation of ARV).

Q 9. An animal bite patient presented at BPHC on the day of bite itself and has been given ARV inj on the day of bite. The second dose of ARV has also been given on Day-3. But RIG was not available at that time and would become available after Day-5. Can it be administered on Day-6 to that patient?

Answer: Yes. it can be administered up to the seventh day after the administration of the first dose of ARV, but not beyond that. Although it is recommended that RIG be administered on day 0 itself (i.e. the day of first dose of ARV), it is not essentially required that RIG and first ARV are given on the same day.

Q 10. Why RIG should not be administered after seventh day of first vaccination?

Answer: Beyond the seventh day (after 3 doses of ARV have been administered), RIG is not indicated since an antibody response to ARV would have occurred by that time and administration of RIG at this stage can suppress the immune response of the patient to the ARV received.

Q 11. Can RIG alone be administered if inj. ARV is not available at that time?

Answer: If the category of bite deserves administration of RIG (as per treatment protocol), the same should be given as early as possible even if inj. ARV is not available at that time. However, inj. ARV should follow at the earliest opportunity.

Q 12. Splash of animal saliva in eye or on lips: What to do?

Answer:

- Contact of cornea or conjunctiva with animal saliva constitutes Category III exposure.
- Thorough rinsing with water is to be done immediately.
- Thereafter RIG is to be instilled as drops in the eye in normal dilution (as is used for injection).
- If animal saliva falls on lips, the saliva is to be washed away thoroughly with water and mouth is to be rinsed well.
- Then the lips may be rinsed with RIG in normal dilution.

Q 13. Why is observation of 10 days recommended in dog or cat, but not in bite by any other animal?

Answer: The observation period of 10 days is valid only for dogs and cats due to the fact that the incubation period of rabies is known and quite specific in dogs & cats, unlike in other animals. If the biting dog or cat had rabies virus in its saliva when it did the biting, research shows that it would die or show clinical signs of rabies within 10 days of bite.

However, this observation period does not come to any help if ID route is used for ARV administration, since the course of ID vaccination does not vary with the status of the animal.

Q 14. Can rabies be transmitted from human- to- human?

Answer: Human-to-human transmission has never been confirmed other than organ transplantation. Organ transplanted from rabies –infected donors can transmit the infection to the organ recipient. Individuals with symptoms of unexplained encephalitis before death should, therefore be excluded as organ donors.

Also, people who have been exposed closely to the secretions of a patient with rabies should be offered PEP as a precautionary measure.

Q 15. What is the purpose of Pre Exposure Prophylaxis (PrEP)? Who should take PrEP?

Answer: Purpose of PrEP is to pre-immunize the persons who are at high risk of getting infection so that they can get protection against rabies exposure.

High risk group includes:

- Veterinarians
- Laboratory staff handling the virus and infected materials
- Clinicians and persons attending to human rabies cases
- Animal handlers and catchers, wildlife workers
- Quarantine officers and
- Travelers from rabies free areas to rabies endemic areas.