RABIES POST EXPOSURE PROPHYLAXIS

Narendra Kumar*[1], Alok Mishra[2], Mayank Dubey[1], Vipin Maurya[3], Shailendra Chaurasia[4]

[1]Assistant Prof. Department of Livestock Production Management, College of Veterinary and Animal Sciences, Banda University of Agriculture & Technology, Banda, U.P. 210001, [2] Assistant Prof. Department of Animal Husbandry and Dairying BRD PG College, Deoria , UP, [3]Assistant Prof. Department of Livestock Production Management, Faculty of Veterinary and Animal Sciences, Institute of Agricultural Sciences, RGSC- B.H.U.,[4] Associate Professor Department of Veterinary Anatomy, College of Veterinary and Animal Sciences, BUAT, Banda, U.P. 210001.

Corresponding author's email: *narendrakumarvet@gmail.com*

DOI: https://doi.org/10.5281/zenodo.17328467

ABSTRACT

Animals are the source of 60% of known infectious diseases in humans and more than 75% of newly emerging infectious diseases. Among these zoonoses, rabies is of paramount public health concern because to its lethality. More than 99% of rabies-related deaths in India are caused by dog bites, making the disease a major cause of death in the nation, which requires Rabies Post Exposure Prophylaxis. Rabies post-exposure prophylaxis (PEP) prevents almost invariably fatal rabies infection after a bite, consisting of immediate wound care (soap and water, antiseptics), rabies vaccine, and, for severe exposures, rabies immunoglobulin (RIG) or monoclonal antibodies. While effective, access and adherence to PEP are major global challenges, highlighting the need for community education, improved access to affordable, and the importance of sustained canine rabies vaccination programs as the primary prevention strategy. Strict adherence to recommended schedules and protocols ensures maximum protection, reduces the risk of fatal infection, and supports the broader goal of rabies elimination in both humans and animals.

INTRODUCTION

Rabies is a fatal, acute, progressive encephalomyelitis caused by neurotropic viruses belonging to the family Rhabdoviridae, genus Lyssavirus. Rabies is a viral zoonotic disease that affects the central nervous system and is almost always fatal once symptoms appear. Rabies is practically 100% fatal, yet practically 100% preventable provided timely and correct management of animal bite is done in the victim.In India, Rabies is transmitted commonly by dogs and cats (~97%), followed by wild animals (2%) such as mongoose, foxes, jackals, and wild dogs, and occasionally by horses, donkeys, monkeys, cows, goats, sheep, and pigs. Rodents, rats and bandicoots, squirrels, rabbits, birds, and bats are generally not known to transmit Rabies. The presence of unvaccinated free-roaming dogs (FRD) or street dogs, amidst human settlements is a major contributor to the high incidence of Rabies in India, which is endemic. Rabies is endemic throughout the country and human cases of Rabies are reported from all over throughout the year except for Andaman & Nicobar and Lakshadweep Islands. In India, about 96% of the mortality and morbidity due to Rabies is associated with dog bites. Although Rabies affects people of all age groups, children are the most vulnerable which constitutes 40% of people exposed to dog bites in Rabies-endemic areas. Different studies quote different figures of Animal Bites incidence and deaths due to Rabies in humans. As per WHO estimates, India accounts for 36% of the global and 65% of the human

Rabies deaths in the South East Asia region. The number of Animal Bites reported under the Integrated Disease Surveillance Project, has increased from 42 lakhs in 2012 to 72 lakhs in 2020. These bites include bites from animals such as due to dog, cat, monkeys. which requires Rabies Post Exposure Prophylaxis.

POST EXPOSURE PROPHYLAXIS

Post Exposure Prophylaxis The post-exposure prophylaxis is a three-pronged approach. All three carry equal importance and should be done simultaneously.

1. Management of wound
2. Passive immunization
3. Active immunization

Management of wound

Wound management is an important component of post exposure prophylaxis (PEP), but often ignored by the bite victims. Hence, establishing a dedicated wound washing area in health facilities is essential to support these efforts. To bring out uniformity globally, the classification of animal bite for post-exposure treatment has been based as per WHO recommendations (Table 1).

Table1: Type of contact, exposure and recommended post-exposure prophylaxis

Category	Type of contact	Type of exposure	Recommended post-exposure prophylaxis
I	Touching or feeding of animals Licks on intact skin	None	None, if reliable case history is available
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding	Minor	Wound management Antirabies vaccine
III	Single or multiple transdermal bites or scratches, licks on broken skin Contamination of mucous membrane with saliva	Severe	Wound management Rabies immunoglobulin Antirabies vaccine

Since the rabies virus enters the human body through a bite or scratch, it is imperative to remove as much saliva, and thereby the virus, from the wound as is possible by an efficient wound toilet that should not involve additional trauma. Since the rabies virus can persist and even multiply at the site of bite for a long time, wound toilet must be performed even if the patient reports late. It should be noted that the immediate washing of the wound is a priority. The maximum benefit of the wound washing is obtained when fresh wound is cleaned immediately.

Application of antiseptic

After thorough washing and drying the wound, any one of the available chemical agents should be applied: Savlon (in appropriate recommended dilution), Dettol (in appropriate recommended dilution), Povidone iodine, alcohol etc.

Local infiltration of rabies immunoglobulin

In category III bites rabies immunoglobulins should be infiltrated in the depth and around the wound to inactivate the locally present virus.

Suturing of wound should be avoided as far as possible. If unavoidable, minimum loose sutures should be applied after adequate local treatment along with proper infiltration of anti-rabies serum. Cauterization of wound is no longer recommended as it leaves very bad scar, and does not confer any additional advantage over washing the wound with water and soap. Injection tetanus toxoid should be given to the un-immunized individual. To prevent sepsis in the wound, a suitable course of an antibiotic may be recommended.

Importance of wound washing for animal bite cases

Reducing the risk of rabies infection: Rabies is a deadly viral disease, transmitted through the saliva of infected animals, primarily following bites.

- Washing wounds with copious amounts of water is a vital step in the post-exposure prophylaxis for rabies. It helps in removing saliva containing the rabies virus from the wound site. The removal of the virus eliminates the risk of infection. Also the use of soap by its lipolytic action inactivates the rabies virus.
- Wound washing also cleanses the dirt, reduces bacterial load and thus minimizing the chances of secondary infection.
- The National Rabies Control Programme (NRCP) recommends immediate wound washing with soap and water upto15 minutes and applying disinfectant to the wound/s to minimize the risk of rabies infection.

Guidance on establishing wound washing area Requirements

To establish an effective wound washing area, the following aspects need to be considered:

- *Location*

  Identify an appropriate location within the healthcare facility, preferably near the emergency department, casualty, dressing room, or dedicated animal bite treatment area/ anti-rabies clinic (ARC). Avoid locating it adjacent to or in the toilets.
- *Spacious room*

  The area should have sufficient space (minimum 6X6 ft) to accommodate patients (often mother and child) and necessary fixtures, etc. It should be designed to promote infection control practices, including providing hand hygiene facilities and personal protective equipment (PPE).
- *Water supply*

  Continuous clean running tap water supply should be available for wound washing procedures. Adequate plumbing, drainage, and access to clean water are essential.
- *Medical supplies*

  Ensure there is a plinth or bench for proper wound management and attending medical procedures.
- *Ventilation*

  Ensure the area is well-ventilated (exhaust fan fitted), well lit, and easily accessible for patients and staff.
- *Waste management*

  Proper high-rise drainage (no stagnation) of water, and biomedical waste management should be followed as per standard protocol /guidelines.

Step-by-step instructions for wound washing procedure

i. Wash/flush all the wound/s immediately (or as soon as possible) under running water for up to 15 minutes.
ii. Use soap to wash the wound/s.
iii. After thorough washing and drying the wound with sterile gauze, apply a disinfectant such as povidone iodine or chlorhexidine.
iv. Do not touch the wound with bare hands.
v. Wound washing procedure must be performed even if the patient reports late.
vi. Application of irritants such as chili, soil, oils, turmeric, lime, salt, ash, plant juice, etc. by the patient is strictly prohibited
vii. For further rabies prophylaxis like vaccine administration, rabies immunoglobulin infiltration, wound management, etc. refer to a medical officer/ nearest health facility.

Passive Immunization by Rabies Immunoglobulin (RIG)

The anti-rabies serum provides passive immunity in the form of ready-made antirabies antibody to tide over the initial phase of the infection. Antirabies serum or RIG has the property of binding with the rabies virus, thereby resulting in the loss of infectivity of the virus.

Equine Rabies Immuno-globulin (ERIG)

ERIG is serum of heterologous origin raised by hyper-immunisation of horses. Hence these should be administered after sensitivity test. However, currently manufactured ERIG are highly purified and the occurrence of adverse events has been significantly reduced.

Human Rabies immunoglobulins (HRIG)

HRIG are free from the side effects encountered in a serum of heterologus origin, and because of their longer half-life, are given in half the dose of equine antirabies serum. The antirabies sera should always be brought to room temperature (20 – 25^{0}C) before use.

Dose of rabies immunoglobulin

The dose of equine anti rabies serum is 40 I.U. per kg body weight of patient and is given after testing of sensitivity, up to a maximum of 3000 I.U. The ERIG produced in India contains 300 I.U. per ml. The dose of the human rabies immunoglobulins (HRIG) is 20 I.U. per kg body weight (maximum 1500 I.U.). HRIG does not require any prior sensitivity testing. HRIG preparation is available in concentration of 150 I.U. per ml.

Administration of immunoglobulin

As much of the calculated dose of RIG as is anatomically feasible should be infiltrated into and around the wounds (Fig). Multiple needle injections into the wound should be avoided. Remaining, if any, after all wounds have been infiltrated, should be administered by deep intramuscular injection at an injection site distant from the vaccine injection site. Animal bite wounds inflicted can be severe and multiple, especially in small children. In such cases, the calculated dose of the rabies immunoglobulin may not be sufficient to infiltrate all wounds. In these circumstances, it is advisable to dilute the immunoglobulins in sterile normal saline 2 to 3-fold to be able to permit infiltration of all wounds. The total recommended dose of immunoglobulin must not be exceeded as it may reduce the efficacy of the vaccine. If immunoglobulin was not administered when vaccination was begun, it can be administered up to the seventh day after the administration of the first dose of vaccine. Beyond the seventh day, Rabies Immunoglobulin (RIG) is not indicated since an antibody response to anti rabies vaccine is presumed to have occurred. Immunoglobulin should never be administered in the same syringe or at the same anatomical site as vaccine.

Tolerance and side effects

With RIG, there may be transient tenderness at the injection site and a brief rise in body temperature which do not require any treatment. Skin reactions are extremely rare. RIG must never be given intravenously since this could produce symptoms of shock, especially in patients with antibody deficiency syndromes. Serum sickness occurs in 1% to 6% of patients usually 7 to 10 days after injection of ERIG, but it has not been reported after treatment with HRIG.

Active Immunization:

Active immunization is achieved by administration of safe and potent TCVs. In India, NTV was used for post exposure treatment in public sector which was being given free of cost. However, as this vaccine was reactogenic, the production was stopped in December, 2004.

Intra-muscular Regimen (IM) The currently available vaccines in India for IM administration are described in Table 2.

Schedule

Essen Schedule

Five dose intramuscular regimen - The course for post exposure prophylaxis should consist of intramuscular administration of five injections on days O, 3, 7, 14 and 28. The sixth injection (D90) should be considered as optional and should be given to those individuals who are immunologically deficient, are at the extremes of age and on steroid therapy. Day 0 indicates date of first injection. This schedule is followed in India.

Zagreb schedule

Abbreviated multisite intramuscular regimen (2-1-1) – One dose of vaccine administered intramuscularly in the left and one into right deltoid region on day 0 followed by one dose on days 7 and 21 in deltoid region.

This schedule saves 2 clinic visits and one vaccine dose.

Table 2: Anti Rabies Vaccines Currently available in India

Name of the vaccine	Fixed virus strain	Substrate	Available
Cell Culture vaccines			
Human Diploid Cell Vaccine (HDCV)	Pitman Moore (PM), LEP-Flury, Pitman Moore (PM)	MRC-5, Primary SPF, chick embryo cells,Vero Cells	Produced locally in private. Sector
Purified Chick Embryo Cell Vaccine (PCEC)			Produced locally in private sector
Purified Vero Cell Rabies Vaccine (PVRV)			Imported + produced locally in public & private sector
Purified Duck Embryo Vaccine	Pitman Moore (PM)	Duck Embryo	Produced locally in private Sector

Indications

All age groups of animal bite victims of Category II and III require the same number of injections and dose per injection. The Category III exposures, in addition require administration of rabies immunoglobulins as discussed earlier.

Site of inoculation

The deltoid region is ideal for the inoculation of these vaccines. Gluteal region is not recommended because the fat present in this region retards the absorption of antigen and hence impairs the generation of optimal immune response.

Storage and transportation

Though most tissue culture vaccines are marketed in freeze dried (lyophilized) form which is more tolerant of vagaries of temperature, yet it is recommended that these vaccines should be kept and transported at a temperature range of 2-8^{o}C. Freezing does not damage the lyophilized vaccine but there are chances of breakage of ampoule containing the diluent. Liquid vaccines should never be frozen.

Reconstitution and storage

The lyophilized vaccine should be reconstituted with the diluent provided with the vaccine immediately prior to use. However, in case of unforeseen delay it should not be used after 6-8 hours of reconstitution.

Intra-dermal (ID) Regimens

Intra-dermal regimens consist of the intra-dermal administration of a fraction of intramuscular dose of certain rabies vaccine on multiple sites. The vaccines used are same; however, route, dose and site of administration differ. The use of intra dermal route leads to considerable savings in terms of total amount of vaccine needed for full pre- or post- exposure vaccination, thereby reducing the cost of active immunization.

Intra-muscular route (IM)

Single bolus dose (1ml) of Rabies vaccines/antigen when given by IM route gets deposited in the muscles. There after the antigen is absorbed by the blood vessels and is presented to antigen presenting cells which triggers immune response.

Intra-dermal route (ID)

Small amount (0.1ml) of Rabies vaccines/antigen is deposited in the layers of the skin at multiple sites. The antigen is directly presented to the antigen presenting cells (without circulation/dilution in blood) at multiple sites triggering a stronger immune response.

Mechanism of Action of IDRV

Intra-dermal inoculation is deposition of approved rabies vaccine (or antigen) in the layers of dermis of skin. Subsequently the antigen is carried by antigen presenting cells via the lymphatic drainage to the regional lymph nodes and later to the reticulo-endothelial system eliciting a prompt and

highly protective antibody response. Immunity is believed to depend mainly upon the CD 4 + T- cell dependent neutralizing antibody response to the G protein. In addition, cell-mediated immunity has long been reported as an important part of the defense against rabies. Cells presenting the fragments of G protein are the targets of cytotoxic T- cells and the N protein induced T helper cells. The immune response induced by IDRV is adequate and protective against rabies.

Schedules approved by WHO for ID route

Updated Thai Red Cross Schedule (2-2-2-0-2)

Regimen: 2-2-2-0-2 i.e. one dose of vaccine, in a volume of 0.1ml is given intra dermally at two different lymphatic drainage sites, usually the left and right upper arm, on days 0,3,7 and 28.

Eight site intradermal regimen (8-0-4-0-1-1)

Regimen: 8-0-4-0-1-1 i.e. one dose of 0.1 ml is administered intra dermally at eight different sites (Fig.1) (upper arms, lateral thighs, suprascapular region and lower quadrant of abdomen) on day 0. On day 7, four 0.1ml injections are administered intra-dermally into each upper arm (deltoid region) and each lateral thigh. Following these injections one additional 0.1ml dose is administered on 28 and 90.

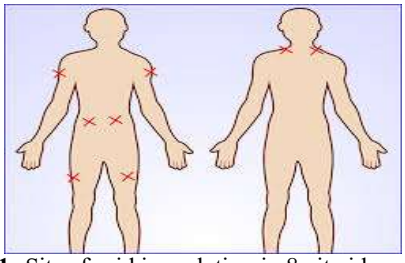

Fig. 1: Sites for id inoculation in 8-site id regimen

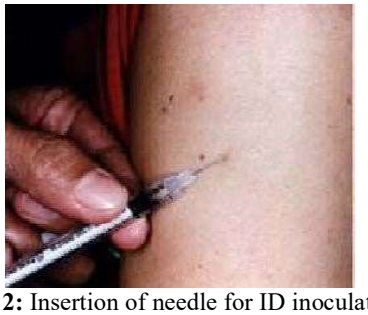

Fig. 2: Insertion of needle for ID inoculation

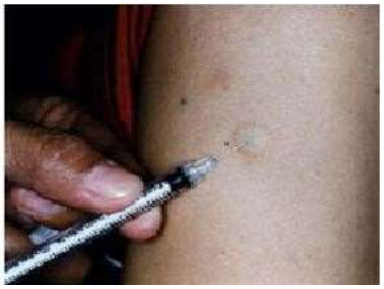

Fig. 3: Bleb raised on ID inoculation

ID injection technique

- Using aseptic technique, reconstitute the vial of freeze-dried vaccine with the diluent supplied by the manufacturer.
- With 1 ml syringe draw 0.2 ml (up to 20 units if a 100 units syringe is used or up to 8 units if a 40 units syringe is used) of vaccine needed for one patient (i.e. 0.1 ml per ID site X 2 sites 0.2 ml)
- Expel the air bubbles carefully from the syringe thereby removing any dead space in the syringe.
- Using the technique of BCG inoculation, stretch the surface of the skin and insert the tip of the needle with bevel upwards, almost parallel to the skin surface (Fig 2) and slowly inject half the volume of vaccine in the syringe (i.e. 0.1mL; either 10 or 4 units) into the uppermost dermal layer of skin, over the deltoid area, preferably an inch above the insertion of deltoid muscle.
- If the needle is correctly placed inside the dermis, considerable resistance is felt while injecting the vaccine.
- A raised papule should begin to appear immediately causing a peau d' orange (orange peel) appearance (Fig 3). Inject the remaining half the volume of vaccine (i.e. 0.1ml; either 10 or 4 units) on the opposite deltoid area.
- If the vaccine is injected too deeply into the skin (subcutaneous), papule is not seen.

- Then the needle should be withdrawn and reinserted at an adjacent site and the ID vaccine given once more.

Precautions while using ID regimen

When the intradermal route is used, precautions include staff training, conditions and duration of vaccine storage after reconstitution, use of appropriate 1 ml syringe and short hypodermic needles. Vaccines to be applied by intradermal route of administration should meet WHO requirements for production and control related to vaccines for intramuscular use, including an NIH test potency of at least 2.5 IU per single (intramuscular) dose. In addition, immunogenicity and safety of the vaccine in question should be demonstrated in appropriate human trials using WHO/national post-exposure prophylaxis regimens. The vaccine package leaflet should include a statement indicating that the potency as well as immunogenicity and safety allow safe use of the vaccine for intradermal post-exposure prophylaxis, in addition to other relevant information as described in the WHO requirements for vaccine production and control.

Post exposure therapy for previously vaccinated persons

Managing re-exposure following post-exposure treatment with TCV: If re-exposed, persons who have previously received full post-exposure treatment (either by IM or ID route) with a potent cell-culture vaccine should be given only two booster doses, intramuscularly/intra-dermally (0.1 ml at 2 sites) on days 0 and 3, but no rabies immunoglobulin.

Managing exposure following pre-exposure prophylaxis with TCV

If after recommended pre-exposure prophylaxis, a vaccinated person is exposed to rabies, a proper wound toileting should be done and two IM/ID (0.1 ml at 2 sites) doses of Tissue Culture Vaccine be given on days 0 and 3. Treatment with RIG is not necessary

Managing re-exposure following post exposure treatment with NTV

Persons who have previously received full post-exposure treatment with NTV should be treated as fresh case and may be given treatment as per merits of the case.

Protective level of anti-rabies antibody

Human antibodies are believed to play important role in protection against rabies and a titer of 0.5 I.U. /ml or more in serum is considered as protective.

Role of laboratory facilities in management of animal bite cases

In countries like India where rabies is endemic, the animal bite management should not depend on laboratory results. The treatment should be started immediately as per recommended guidelines.

CONCLUSION

Post-rabies prophylaxis is a life-saving intervention that must be initiated promptly after exposure to a suspected or confirmed rabid animal. Immediate wound washing, timely reporting, administration of anti-rabies vaccine, where indicated rabies immunoglobulin along with public awareness are critical steps in halting viral transmission. Strict adherence to recommended schedules and protocols ensures maximum protection, reduces the risk of fatal infection, and supports the broader goal of rabies elimination in both humans and animals.

Cite this article:
Narendra Kumar, Alok Mishra, Mayank Dubey, Vipin Maurya, Shailendra Chaurasia. (2025). Rabies post exposure prophylaxis. Vet Farm Frontier, 02(09), 46–52. https://doi.org/10.5281/zenodo.17328467