सत्यमेव जयते

Ministry of Health and Family Welfare
Government of India

National Guidelines for Rabies Prophylaxis, 2019

National Rabies Control Programme



NATIONAL CENTRE FOR DISEASE CONTROL



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FOREWORD

Rabies, a disease as old as our civilization, has terrified man since antiquity. Although the exact magnitude of the disease is not reliably known, some studies estimate that 174 lakh persons are bitten and approximately 20,000 persons succumb to the disease annually.

In last two decades, India had made considerable strides in many aspects of preventing human deaths due to rabies. Reactogenic Nerve Tissue Vaccine has been phased out since December 2004. India has capability and infrastructure for producing modern Rabies cell culture vaccines and Rabies immunoglobulin indigenously. The country has also adopted the WHO recommended strategy of more cost effective Intradermal of Rabies Vaccine which helps to achieve wider coverage of victims in the available quality of vaccine as compared to Intramuscular Route of Rabies vaccine.

National Rabies Control Programme approved by Ministry of Health and Family Welfare, Govt. of India, is being implemented in the country since 2013 with an objective to prevent deaths due to Rabies in humans. One of the important strategies to prevent human death is to provide appropriate animal bite management to all animal bite victims which includes proper wound managements and institution of Rabies Vaccine and Rabies Serum to the victims as per guidelines.

The guidelines are revised from time to time as per the recent developments and scientific evidences endorsed by WHO. Based on the recent WHO expert consultation on Rabies, WHO TRS 1012, the present guidelines are revised after having detailed deliberations on newer WHO recommendations in an expert group meeting called by National Centre for Diseases Control.

I congratulate Dr S.K Singh Director, NCDC, Dr. Simmi Tiwari, Officer In-Charge National Rabies Control Programs and her team for bringing out these updated Technical guidelines for Rabies Prophylaxis. I am confident that medical professional all over India will find these guidelines useful for providing appropriate animal-bites management including effective administration of Anti-Rabies prophylaxis. This will ensure uniformity in provision of post-exposure prophylaxis to all those who are in need of it.

(Rajiv Garg)

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PREFACE

Rabies is one of the oldest recognized Zoonotic disease with almost 100% case fatality rate. The disease causes extremely painful deaths where patient suffers from painful spasms and dies of extreme thirst and hunger because of hydrophobia.

In India, the disease is reported throughout the year and from all parts of the country with the exception of water-locked islands of Lakshadweep and Andaman and Nicobar. The Integrated Diseases Surveillance Program of Govt. of India reports approximately 6-7 Million Animal Bites each year of which more than 95% are by dogs. The disease is completely preventable by timely and appropriate Post Exposure Prophylaxis (PEP) which includes proper wound toilet and administration of Anti Rabies Vaccine and Anti Rabies serum as per the national guidelines.

Globally many countries have achieved Rabies elimination and there is Global call for Rabies Elimination i.e. "Rabies: Zero by 2030". To address the issue of Human Rabies, National Rabies Control Program (NRCP) was launched by Ministry of Health and Family Welfare, Govt. of India during 12th five-year plan for implementation in all States and UTs. The objectives of the program is to prevent human deaths due to Rabies. The strategies of the program includes capacity building of health professionals on appropriate animal bite management, advocacy for scaling up implementation of cost effective Intradermal (ID) route for Rabies prophylaxis, strengthening surveillance of animal bites and Human Rabies cases, strengthening Rabies diagnostics, increasing awareness in general community and inter-sectoral coordination.

National Guidelines for Rabies Prophylaxis is revised by National Center for Disease Control, the nodal agency for implementation of National Rabies Control Program from time to time as per the recent developments and scientific evidences endorsed by the experts and WHO. The present National guidelines on Rabies prophylaxis have been revised after extensive expert consultations on newly endorsed WHO Recommendation for Rabies Prophylaxis in WHO TRS 1012.

I sincerely hope that this publication will serve as a useful technical guidance documents for all health care professionals for undertaking appropriate Animal Bite Management and will bring out uniformity in practicing post-exposure prophylaxis in the country.

(Dr Sujeet K Singh)

From the Desk of Programme officer

Rabies, an ancient disease, continues to be a major public health problem even in this era. About 130- 210 rabies deaths in hospital are reported every year under rabies control programme and approximately 6-7 Million animal bites are reported annually under IDSP. Reporting of animal bites under IDSP and suspected rabies cases admitted in hospitals has improved over the years due to improved surveillance while the rabies death cases in hospital have shown declining trend .

The disease is endemic throughout the country. To address the issue of Rabies in the country, National Rabies Control Programme (NRCP) is being implemented since 12th five year plan. The key activities envisaged under the program are training of health professional on appropriate animal bite management and ID route of inoculation for rabies PEP, IEC activities, monitoring and evaluation and strengthening surveillance of animal bites and rabies cases. National Guidelines for Rabies Prophylaxis has been revised (2019) in line with recent WHO TRS1012. To further strengthen the Animal bites and Rabies Surveillance, Standard case definition has been introduced under IDSP and new Integrated Health Information Platform portal of Ministry of Health and Family Welfare, GOI. Networking with Infectious Diseases hospitals of the States is continued to provide regular data on rabies deaths. Expansion of Laboratory Network for rabies diagnosis in the country is underway.

Timely availability of Rabies Vaccine and Rabies serum is the key to prevent deaths due to rabies hence continued advocacy to the State to use Intradermal Route for Rabies prophylaxis in all the health facilities. States are also requested to include Rabies Vaccine and Rabies serum in essential drug list and to utilize the funds available under National Free Drug Services Initiative of National Health Mission (NHM) to procure the same. For awareness generation in the community Standard IEC material is developed and disseminated to the States. World Rabies Day is observed (28th Sep) each year to take up rabies as priority public health problem.

Globally call has been given by all International organization working in field of Rabies to accelerate the actions towards the elimination of 'Dog-Mediated Rabies' by 2030 i.e **'Zero by Thirty'.** Accordingly to address Rabies in India "National Action Plan for Rabies Elimination' (NAPRE) in India with "One Health" approach is being prepared in consultation with Department of Animal Husbandry and Dairying and other Stakeholders such as Wild life and WHO, OIE, CDC, NITI Aayog, ICMR ICAR, National Human Right Commission, Animal Welfare Board of India, CDSCO, State health and veterinary representatives, Academicians and other relevant stakeholders. The proposed plan as a technical guidance document for the States to draw and implement their own Straetegic plan to address Rabies in a time bound manner.

NRCP programme urges the states/districts officials and concerned stakeholders to take up the programme activities at the forefront of their agenda so that collective efforts will ensure the rabies elimination from the country in near future.

I sincerely hope that this guidelines developed by Division of Zoonotic Diseases, NCDC with expert consultation will help healthcare professionals and programme mangers to follow standard guidelines for Rabies prophylaxis.

Dr. Simmi Tiwari
Deputy Director & Officer In-charge
National Rabies Control Program

ABBREVIATIONS

CCEEVs	Cell Culture and Embryonated Egg-Based Rabies Vaccine
CCVs	Cell Culture Vaccines
DCGI	Drug Controller General Of India
ERIG	Equine Rabies Immunoglobulin
HRIG	Human Rabies Immunoglobulin
IAP	Indian Academy of Pediatrics
ID	Intra Dermal
IM	Intra Muscular
NCDC	National Centre for Disease Control
NRCP	National Rabies Control Program
NTV	Nerve Tissue Vaccines
PCECV	Purified Chick Embryo Cell Vaccine
PEP	Post Exposure Prophylaxis
PFS	Pre Filled Syringe
PrEP	Pre-Exposure Prophylaxis
PVRV	Purified Vero Cell Rabies Vaccine
RABIES VACCINE	Anti-Rabies Vaccines
RABV	Rabies Virus
RIG	Rabies Immunoglobulins
WHO	World Health Organization

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1 INTRODUCTION

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 (following bites, scratches, licks on broken skin and mucous membrane). In India, dogs are responsible for about 95% human rabies, followed by cats (2%), jackals, mongoose and others (1%). Therefore, the disease is mainly transmitted by the bite of a rabid dog.

Rabies has terrified man since antiquity. The fear is by no means unfounded since the disease is invariably highly fatal and perhaps the most painful and dreadful of all communicable diseases in which the sick person is tormented at the same time with thirst and fear of water (hydrophobia). Fortunately, the development of Rabies can be prevented to a large extent if animal bites are managed appropriately and in time. In this regard, the post-exposure treatment of animal bite cases is of prime importance.

National Rabies Control Programme (NRCP) is being implemented in the country since the 12 Five Year Plan with an objective to prevent deaths due to rabies in humans. National Centre for Disease Control is the nodal centre for implementation of the programme. The key strategies of the programme are:

- Strengthening surveillance of animal bites and human rabies
- Capacity building of health care professionals for appropriate management of Animal Bite victims
- Strengthening laboratory diagnosis of Rabies
- Increase awareness about Rabies in the community
- Strengthening Inter-Sectoral Collaboration with other sectors particularly veterinary and animal husbandry

National Centre for Disease Control (formerly National Institute of Communicable Diseases), Delhi, WHO Collaborating Centre for Rabies Epidemiology, organized an expert consultation in 2002 to formulate National Guidelines for Rabies Prophylaxis to bring out uniformity in post-exposure prophylaxis practices. These guidelines were revised in expert consultations in 2007, 2013 and 2015. Recently, the WHO position paper on rabies vaccines and WHO expert consultation on rabies, third report (WHO Technical Report Series, No. 1012) published in 2018, has provided new recommendations for rabies PEP. Consequently, an expertgroup meeting was called by NCDC, NRCP programme, Division for Zoonotic Diseases Programmes on 8th January 2019, to review the new recommendations of WHO. Based on the recommendation of the expert group, the National Guidelines on Rabies Prophylaxis have been revised.

2 POST EXPOSURE PROPHYLAXIS

2.1. DECISION TO TREAT

In a rabies endemic country like India, where there is sustained dog-to-dog transmission, every animal bite is suspected as a potentially rabid animal bite, and treatment should be started immediately after exposure. Post-exposure prophylaxis needs to be considered in the following conditions:

- Bites by all warm-blooded animals.
- **Exposure to wild animals:** Exposures to all wild animals should be treated as Category III exposure.
- **Rodent Bites:** Exposure to domestic rodents, hare and rabbits do not ordinarily require PEP. However, rodent bites in forest areas necessitate institution of PEP.
- **Exposure to bats:** Bat rabies has not been conclusively proven in India and hence, at present, exposure to bats does not warrant PEP.
- **Human-to-human transmission:** The risk of human-to-human transmission is minimal and there are no well-documented cases, other than the few cases resulting from infected organ/tissue (cornea) transplant. However, people who have been exposed closely to the secretions of a patient with rabies may be offered PEP as a precautionary measure. Organ/ tissue (cornea) for transplantation should not be collected from suspected/confirmed rabies or Rabies-like encephalitis cases.

2.2. OBSERVATION OF BITING DOG/CAT:

The PEP should be started immediately after the exposure. The observation period of 10 days is valid for dogs and cats only. The natural history of rabies in mammals other than dogs and cats is not fully understood and therefore the 10 day observation period is not applicable in such animals.

The treatment may be modified if the suspected dog or cat involved in the incident is healthy after a 10 day observation period and PEP can be converted to pre-exposure prophylaxis (PrEP) by skipping the vaccine dose on day 14 and administering it on day 28 while using **IM regimen** (Essen Schedule).

While using **ID route** of administration complete course of vaccination should be given irrespective of the status of the animal.

2.3. VACCINATION STATUS OF BITING ANIMAL:

Animals vaccinated against rabies do not suffer and transmit the disease. However,

animal vaccine failures may occur because of improper administration, inadequate doses, poor quality of the vaccine or poor health status of the animal. Thus, the history of Rabies vaccination in an animal does not guarantee that the biting animal is not rabid.

Therefore, in the absence of laboratory documentation of immunization (antibody titre), it cannot be presumed that a vaccinated dog is actually protected, given the variable efficacy of various anti-rabies vaccines in animals or health status of animals. Hence, irrespective of the vaccination status of the biting animal, the PEP should be given.

2.4.PROVOKED VERSUS UNPROVOKED BITE:

A bite by a provoked animal does not mean that the animal is not rabid. Therefore, a provoked dog bite should also be managed as exposure and PEP should be started immediately.

2.5.CONTRAINDICATIONS AND PRECAUTIONS:

As rabies is a nearly 100% fatal disease, **there is no contraindication to PEP.** Pregnancy, lactation, infancy, old age and concurrent illness are not the contraindications for Rabies PEP in the event of an exposure. Moreover, rabies vaccine does not have any adverse effect on pregnant woman, course of pregnancy, foetus or lactating mother. Hence, complete PEP should be given depending on the category of exposure.

People taking Chloroquine for Malaria treatment or prophylaxis may have a reduced response to Intradermal (ID) Rabies vaccination. These patients should receive the rabies vaccine by **Intramuscular (IM)** route.

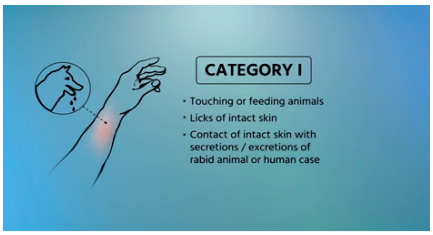
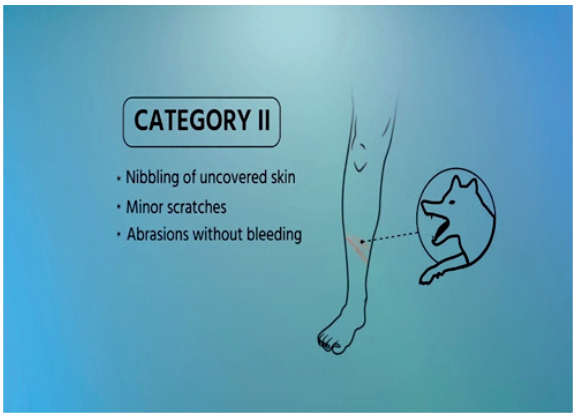
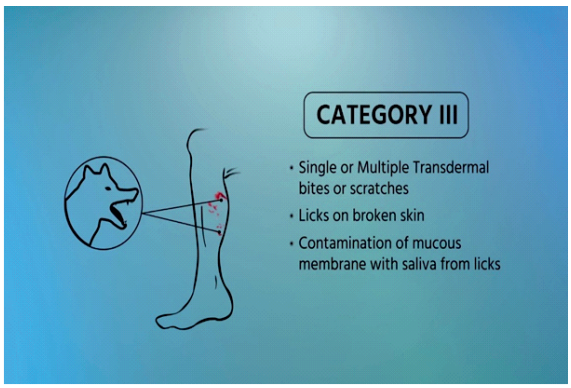
As with all other immunizations, vaccinated persons should be kept under medical supervision for at least **15-20 minutes** following vaccination. Previous reaction to any component of a vaccine is a contraindication to the use of the same vaccine for PEP or PrEP.

The long and variable incubation period, which is typical of most human rabies cases, provides a window of opportunity to initiate PEP and protect the individual. This must be started at the earliest to ensure that the individual is immunized or protected before the rabies virus reaches the nervous system. However, people who present for treatment even months or years after a possible rabies exposure should be evaluated and treated as if the event had occurred recently.

Risk assessment of potential rabies exposure can be complex and confusing. When in doubt PEP should be initiated and the attending physician should consult a specialist at Anti Rabies Clinics (ARC).

The categorization of animal bite wound depending on the type of exposure is as under:

Table No. 1: Type of contact, exposure and recommended post-exposure prophylaxis

Category of Exposure	Type of Exposure	Recommended Post-Exposure Prophylaxis
I		
II		
III	 	• Wound Management • Rabies Immunoglobulin • Rabies Vaccine

Note: Bites by **wild animals** and all bites in **forest areas** should be considered as **Category III** exposure and treated accordingly.

2.6. APPROACH TO POST-EXPOSURE PROPHYLAXIS (PEP)

PEP is a three-pronged approach as given below. All three carry equal importance and should be done simultaneously as per the category of exposure.

1 Management of animal bite wound(s)

2 Passive immunization with Rabies Immunoglobulin (RIG)

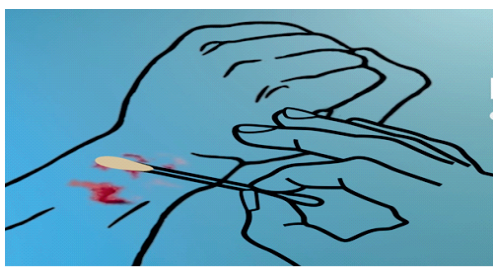
3 Active immunization with Anti-Rabies Vaccines (RABIES VACCINE)

2.6.1. Management of animal bite wounds

2.6.1.1. Wound(s) toilet:

Since RABV enters the human body through a bite or scratch, it is imperative to remove as much saliva as possible, and thereby the virus, from the wounds by efficient wound management without causing additional trauma. Prompt local treatment of all bite wounds and scratches is an important step in PEP. The recommended first-aid procedures include immediate, thorough flushing and washing of all wounds with **soap and water** and application of **Povidone Iodine or Antiseptic** having virucidal activity. Washing of wounds is desirable up to 15 minutes and should be carried out as soon as possible with soap and water. Since RABV can persist and even multiply at the site of the bite for a long time, wound management must be performed even if the patient reports late.

Table: 2 Wound(s) Management

Do's	Act	Effect
Physical	Wash **all wounds** with running water 	Mechanical removal of virus from the wound
Chemical	Wash all wounds with **soap and water,** apply **antiseptic** 	Inactivation of the virus 

Do's	Act	Effect
Biological	Infiltrate immunoglobulin into the **depth and around the wound(s)** in Category III exposures 	Neutralization of the virus
Don'ts		
• **Don't Touch the wound(s) with the bare hands** • **Don't Apply irritants like soil, chilies, oil, lime, herbs, chalk, betel leaves, etc.**		

If soap or a virucidal agent is not available, the wound(s) should be thoroughly and extensively washed with water. Eyes and mucosa, if exposed, should be thoroughly rinsed with water. The maximum benefit of wound washing is obtained when a fresh wound is cleaned immediately.

It should be noted that immediate washing of wounds is a priority. However, the victim should not be deprived of the benefits of wound management as long as there is an unhealed wound which can be washed (in case the victim reported late).

The application of irritants (like chilies, oil, turmeric, lime, salt, etc.) is unnecessary and damaging. In case irritants have been applied on the wounds, gentle washing with soap or detergent should be done to remove the external applicant/s followed by flushing with copious amount of water immediately.

Application of antiseptics:

After thorough washing and drying of the wounds, any available virucidal agents such as Povidone Iodine, alcohol, etc. should be applied.

A bleeding wound at any site indicates severe exposure and should be infiltrated with RIG. Severe bite wounds are best treated by daily dressing, followed by secondary suturing when necessary.

2.6.1.2. Suturing of wounds:

In case suturingcannot beavoided, cleanthe wound and the wound(s) should first be thoroughly infiltrated with ERIG or HRIG. The suturing should be delayed for several hours to allow diffusion of the RIG through the tissues before minimal suturingare

done. Secondary suturing is less likely to become infected and present better cosmetic results if done under optimal conditions. An infected bite wound is not a contraindication for injection of RIG. Bites on the tips of the fingers or toes, ear lobes, nasal area or external genitalia can be safely injected with RIG, provided excessive pressure is avoided, as this can cause compression syndromes.

2.6.1.3 Tetanus and antibiotic prophylaxis: Tetanus prophylaxis should be given as per national guidelines. To prevent sepsis in the wound(s), a suitable course of an antibiotic may be prescribed.

2.6.1.4 Counselling of Animal/Dog Bite Victim: The sudden attack by an animal/dog could be traumatic because of its unpredictability which overwhelms the person's capacity to act appropriately in a balanced manner. Hence, counselling services should be offered to all animal bite victims to minimize the physical and emotional stress of the event. The dog bite victim should be fully explained about the importance of timely completion of post-exposure prophylaxis.

2.7. RABIES IMMUNOGLOBULIN

The anti-rabies serum/RIG provides passive immunity in the form of ready-made antibodies before it is physiologically possible for the victim to produce his/her own antibodies following anti-rabies vaccination. RIG has the property of binding with the RABV, thereby resulting in neutralization and loss of infectivity of the virus. Therefore, RIG should be administered to all patients with category III exposure.

2.7.1. Indications:

1. All category III animal bite exposures cases
2. Exposures to all wild animals should be treated as category III exposure.

In immunocompromised individuals such as HIV/AIDS patients, patients on immunosuppressive therapy (steroids/cancer chemotherapy), congenital agammaglobulinemia etc., RIG should be administered in both Category II and III exposure.

2.7.2. Two types of RIGs are available:

- **Equine Rabies Immunoglobulin (ERIG):** ERIG is of heterologous origin produced by hyper-immunisation of horses. Currently manufactured ERIGs have highly purified Fab 2' fragments and the occurrence of adverse events have significantly reduced. These are produced in India in public and private sectors. (Annexure 2: Table 1, Currently available ERIG in India). Since ERIG is of heterologous origin, it carries a small risk of anaphylactic reaction (1/150,000).

  A skin test prior to administering ERIG is not required because testing does not accurately predict adverse reactions, and ERIG should be given irrespective of the result of the test. The treating physician should be prepared to manage anaphylaxis

which, although rare, could occur during any stage of administration, even when the skin test is negative. However, some manufacturers of ERIG still recommend performing a skin test.

- H**uman Rabies Immunoglobulin (HRIG):** HRIG is of homologous origin and is relatively free from the side effects encountered in serum of heterologous origin. (Annexure 2: Table 2, currently available HRIG in India). Because of longer half-life, HRIG is given at half the dose of ERIG.

2.8. DOSAGES OF RABIES IMMUNOGLOBULIN:

Generic Name	Dose
ERIG	40 IU per kg body weight
HRIG	20 IU per kg body weight

2.9. ADMINISTRATION OF RIG:

- The RIG should be brought to room temperature (25°C to 30°C) before administering to the patient.
- The role of RIG is to provide neutralizing antibodies at the site of exposure before patients starts producing their own antibodies as a result of vaccination. Therefore, RIG should be administered to all patients with category III exposure, except those who have previously received complete PrEP or PEP.
- RIG is administered only once, preferably at or as soon as possible after initiation of post-exposure vaccination. It is not indicated **beyond the seventh day** after the first dose of rabies vaccine, regardless of whether the doses were received on days 3 and 7, because an active antibody response to the rabies vaccine has already started, and this would represent a wastage of RIG.
- The maximum dose of HRIG is 20 IU/kg of body weight, while that of ERIG is 40 IU/kg of body weight.
- The entire immunoglobulin dose, or as much as **anatomically possible** (but avoiding possible compartment syndrome), should be infiltrated carefully into or as close as possible to the wound(s) or exposure sites. Evidence suggests that injecting the remaining RIG volume intramuscularly at a distance from the wound provides little or no additional protection against rabies as compared with infiltration of the wound(s) alone.
- If, however, there is a high likelihood that there are additional small wounds (e.g. if a child does not report all wounds), injection of the remaining RIG volume intramuscularly as close as possible to the presumed exposure site, to the degree that is anatomically feasible, is indicated. The same applies to mucosal exposure with no wound, and rinsing with RIG can be considered. In the case of suspected exposure to RABV via aerosols, an intramuscular injection of RIG is still recommended.

- Tip of the finger(s), toe(s), ear lobe(s) or bites on the nose or around the eye can be safely injected with RIG provided the injection is not done with excessive pressure, which can
- cause compression syndrome. RIG should never be administered in the same syringe or at the same anatomical site where the vaccine was administered.
- As for all immunizations, animal bite victim should be kept under observation for at least 15–20 min after administration of ERIG and there is no need to admit the patient.



Figure 7 : Infiltration of RIG into the wound



Figure 8 : Infiltration of RIG into the wound

2.10. TOLERANCE AND SIDE EFFECTS AFTER RIG INFILTRATIONS:

- There may be transient tenderness at the injection site and a brief rise in body temperature that does not require any treatment. Anaphylactic reactions are extremely rare. **RIG must never be given intravenously.**
- Serum sickness is rare and occurs usually 7 to 10 days after injection of ERIG, but it has not been reported after treatment with HRIG.
- A full course of Rabies vaccine should follow thorough wound cleansing and passive immunization.

3 RABIES VACCINE

Active immunization is achieved by administration of safe and potent cell culture vaccines (CCVs). Currently available CCVs could be administered by IM regimen and CCVs approved for ID use shall be administered by ID regimen.

Rabies vaccine is produced as one single IM dose with a potency of ≥ 2.5IU per IM dose for PEP and PrEP. It is absolutely essential that every batch of CCVs have minimum potency of 2.5IU per IM dose, irrespective of whether the vaccine is administered by IM or ID route.

3.1. INDICATIONS:

All animal bite victims of Category II and III exposures, irrespective of their age and body weight, require the same number of injections and dose per injection.

All Category III exposures and Category II exposures in immune-compromised individuals, in addition, require administration of RIG as discussed previously in section 2.2.

3.2. STORAGE AND TRANSPORTATION:

Though most CCVs are marketed in freeze-dried (lyophilized) form, it is recommended that these vaccines should be kept and transported at a temperature range of 2-8°C and protected from sunlight. Temperature monitoring devices should be used during storage or transportation of vaccine. Freezing does not damage the lyophilized vaccine but there are chances of breakage of ampoule containing the diluent.

3.3. RECONSTITUTION AND STORAGE

The lyophilized Rabies vaccine should be reconstituted with the diluent provided with the vaccine immediately prior to use. Some vaccines have 0.5ml diluents and while others have 1ml diluents as per the approval of the brand, which cannot be altered. It is imperative that the information booklet/sheetaccompanying the vaccine is carefully read and the instructions given are adhered to. While using ID administration, the vaccine vial should be stored at 2-8°C after reconstitution. The total content of the vial should be used as soon as possible, and not later than 6 hours after reconstitution.

While using IM administration, the vaccine should be used immediately after reconstitution. However, in case of an unforeseen delay, the vaccine should not be used after 6 hours of reconstitution.

After reconstitution with sterile diluent, the vaccines should be used immediately or within 6 h if kept at 2–8°C (2), as partially used vials of rabies vaccine may become contaminated.

Rabies vaccines for humans should meet WHO recommendations for characterization, production and control as set out by the WHO Expert Committee on Biological Standardization (3). The current WHO recommendations apply only to inactivated rabies vaccines produced in cell culture or embryonated eggs.

3.4. ADVERSE EVENTS FOLLOWING ANTI RABIES VACCINATION (AEFI)

The CCVs are widely accepted as the least reactogenic rabies vaccines available today. However, few studies have now shown that adverse effects can be either general in nature or allergic in origin. Mild systemic adverse events following immunization (AEFI)

include headache, malaise, nausea and fever. Symptomatic treatment may be needed. Minor and transient erythema, pain and/or swelling may occur at the site of injection, particularly following intradermal administration. Serious AEFIs, mainly of allergic or neurological nature, occur rarely.

3.5. SWITCH OVER FROM ONE BRAND/TYPE OF VACCINE TO THE OTHER

Shifting from one brand/type of CCV to another brand/type should not be encouraged in routine practice. However, under unavoidable circumstances, available brand/type may be used to complete PEP.

3.6. DURATION OF IMMUNITY

Modern Rabies Vaccines establish immunological memory that is assumed to persist for the life of the individual, even after titres of neutralizing antibodies decrease or are no longer measurable. Clinical data confirm that people vaccinated by modern Rabies Vaccine respond to booster immunization within 7 days, even if the initial course of PrEP or PEP was administered a decade back and regardless of the route of priming or booster immunization (IM or ID), and regardless of presence or absence of detectable titres of RABV-specific antibodies at the time of the booster.

In addition, published data indicate that periodic booster doses of vaccine are not required after primary rabies vaccination, except as an additional precaution in people whose occupation puts them at continual or frequent risk of exposure. Still, all vaccinated individuals subsequently exposed to rabies, as per the WHO definition of exposure, should receive an abbreviated course of PEP, as specified in section 6.

The ability to develop an anamnestic response to a booster vaccination is related neither to the route of administration of the initial series (intramuscular or intradermal) nor to whether the patient completed a pre-exposure or post-exposure series.

3.7. SEROCONVERSION FOLLOWING VACCINATION

Humoral antibodies play an important role in protection against rabies. Anti-rabies neutralizing antibody titre of 0.5 IU/ml or more in serum is considered as adequate

seroconversion post-vaccination. This level is achieved in most healthy individuals by day 14 of a PEP regimen, with or without simultaneous administration of Rabies immunoglobulin.

3.7.1. Mechanism of Immune Response:

Single-dose (0.5ml or 1ml) of Rabies Vaccine, when given by IM route, gets deposited in the muscle. Thereafter, the antigen is absorbed by the blood vessels and is presented to antigen-presenting cells which trigger the immune response. Whereas, while using ID route, a small amount (0.1ml) of Rabies Vaccine is deposited in the layers (dermis) of the skin at one or more than one site, the antigen is carried by antigen-presenting cells via the lymphatics to the regional lymph nodes and reticuloendothelial system eliciting a prompt and protective antibody response. Immunity is dependent mainly upon the CD 4 + T-cell dependent neutralizing antibody response to the G protein. Cell-mediated immunity is also 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 ID administration of Rabies Vaccine is comparable to Rabies IM route.

4 ROUTE OF ADMINISTRATION OF RABIES VACCINE

Rabies vaccine can be administered by intradermal or intramuscular route. In Feb 2006 as per WHO recommendations, results of clinical trial on safety, efficacy and feasibility DCGI approved the use of Safe efficacious and economical intradermal (ID) route of inoculation of Rabies vaccines.

4.1. INTRA-DERMAL (ID)ROUTE

National Rabies Control Program Strongly advocates use of intradermal route of Rabies vaccine. The use of the ID route leads to considerable saving in the total amount of vaccine needed to complete PrEP or PEP, thereby reducing the cost of active immunization.

However, Intradermal administration is not the preferred route of Rabies vaccine administration **for immune-compromised individuals or individuals receiving Chloroquine, Hydroxychloroquine or long-term corticosteroid or other immunosuppressive therapy.**

As the volume of an ID vaccine dose is lesser than that of an IM dose, the intradermal route is especially suitable for treating many patients at the same centre or where attendance of animal bite cases is more. However entire vial content should be utilized within 6 hours after reconstitution of the vaccine.

4.1.1. Vaccines and regimen approved for ID use in the country

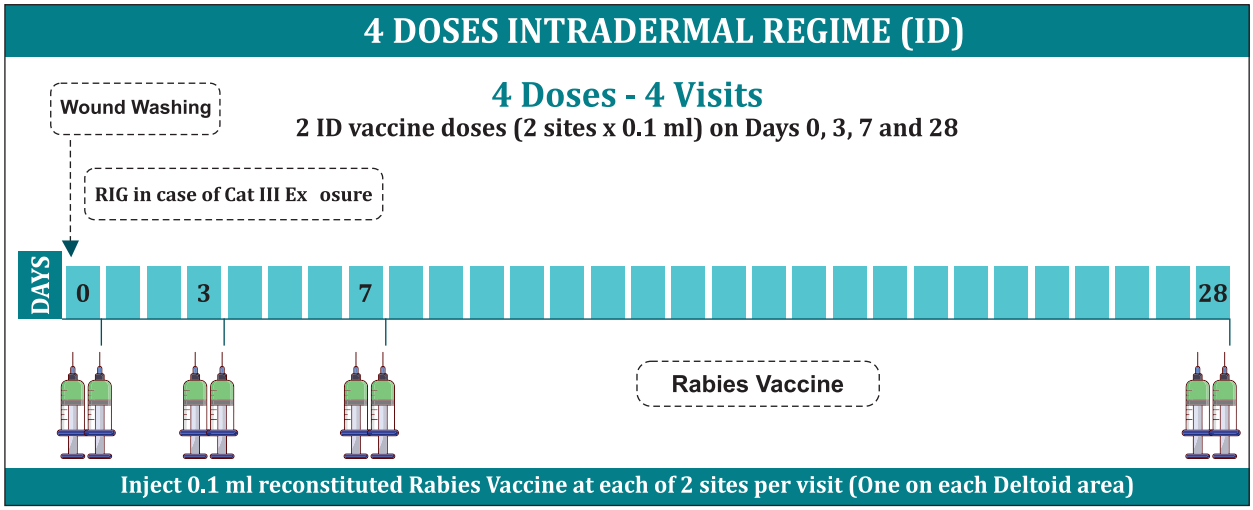
List of vaccines approved by DCGI for use by intradermal route is given in Annexure 1.

Only the Rabies Vaccine (lyophilized vaccine along with the diluent of specified volume) approved by DCGI for ID administration should be used for ID route. The vaccine package leaflet should include a statement indicating the potency as well as immunogenicity and route of administration for PEP and PrEP.

4.1.2. The potency of approved vaccines

The vaccines should have stated potency of ≥ 2.5 IU per IM dose, irrespective of reconstituted volume. (The volume of the diluent remains the same as that of the IM dose). The same vaccine is used for ID administration as per the stated schedule. A dose of 0.1ml of vaccine, irrespective of reconstituted volume for IM route (0.5ml or 1 ml) is administered per ID site as per the stated schedule.

4.1.3. Regimen for post exposure prophylaxis- Updated Thai Red Cross Schedule (2-2-2-0-2)



This involves the injection of 0.1ml of reconstituted vaccine per ID site and on two sites per visit (one on each deltoid area, an inch above the insertion of deltoid muscle) on days 0, 3, 7 and 28. Day 0 is the date of administration of the first dose of Rabies Vaccine.

4.1.3.1 Maintenance of vaccine vial in use

Use aseptic technique to withdraw the vaccine. Store in a refrigerator at 2°C to 8°C. Do not freeze the vaccine. Do not expose the vaccine to sunlight. Use reconstituted vaccine as soon as possible or within 6 hours if kept at 2°C to 8°C. Discard all unused reconstituted vaccine at the end of 6 hours.

4.1.3.2 Materials required



A vial of Rabies Vaccine, along with its diluent that is approved by the DCGI for ID administration, 2 ml disposable syringe with 24 G needle for reconstitution of the vaccine, disposable 1 ml insulin syringe (with gradations up to 100 or 40 units) with a fixed (self-mounted 28G or more) needle. Syringes with detachable needles are not preferred as they contribute to wastage of vaccine.

Disinfectant swabs (e.g. 70% ethanol, isopropyl alcohol) for cleaning the top of the vaccine vial and the patients' skin.

4.1.3.3 ID Injection Technique

Using aseptic technique, reconstitute the vial of lyophilized vaccine with the diluent

supplied by the manufacturer.



Figure 10: Insertion of needle for ID inoculation (Insulin syringe)



Figure 11: Bleb raised on ID inoculation (Insulin syringe)

With 1 ml syringe draw 0.2 ml (up to 8 units if the syringe is 40 units or 20 units in a 100-units syringe) of vaccine needed for one patient (i.e. 0.1 ml per ID site for 2 sites).

Expel the air bubbles carefully from the syringe thereby removing any dead space in the syringe.

Similar to the technique of BCG inoculation, for Rabies vaccine also stretch the surface of the skin and insert the tip of the needle bevel upwards, almost parallel to the skin surface and slowly inject half the volume of vaccine in the syringe (i.e.0.1ml; 4 units /10 units) into the uppermost dermal layer of skin, over the deltoid area an inch above the insertion of deltoid muscle. If the needle is correctly placed inside the dermis, resistance is felt while injecting the vaccine. A raised bleb (3-4 mm) should begin to appear immediately causing an orange peel (Peau d'orange) appearance.

Inject the remaining volume of vaccine (i.e. 0.1ml; 4 units /10 units) on the opposite deltoid area 1 inch above the deltoid insertion.

If the vaccine is injected too deeply into the skin (subcutaneous), bleb (Peau d'orange) is not seen. Then the needle should be withdrawn and reinserted at an adjacent site and ID vaccine given once more.

If for some reason the deltoid region cannot be used for injection, then the alternative sites are the suprascapular area or the anterolateral thigh.

4.1.3.4 Advise to the vaccinated person:

- Do not rub the injection site.
- Do not apply anything to the injection site
- Complete the course of vaccination

4.1.3.5 Adverse reactions following the ID administration of anti-rabies vaccine:

Adverse events may include mild itching, erythema; rarely body ache and fever that are usually self-limiting. Sometimes symptomatic management using analgesics and antihistamines may be needed.

4.1.3.6 Logistic requirements for giving Rabies Vaccine at health facility:

Each health facility practising ID Route for rabies prophylaxis should have adequately trained staff. There should be an adequate cold chain facility for vaccine storage and adequate supply of suitable self-mounted syringes for ID administration should be ensured. The health care staff should be well versed in the management of open vial and safe storage practices.

4.2. INTRA-MUSCULAR ROUTE

The currently available vaccines and regimen in India for IM administration are described in Annexure 1.

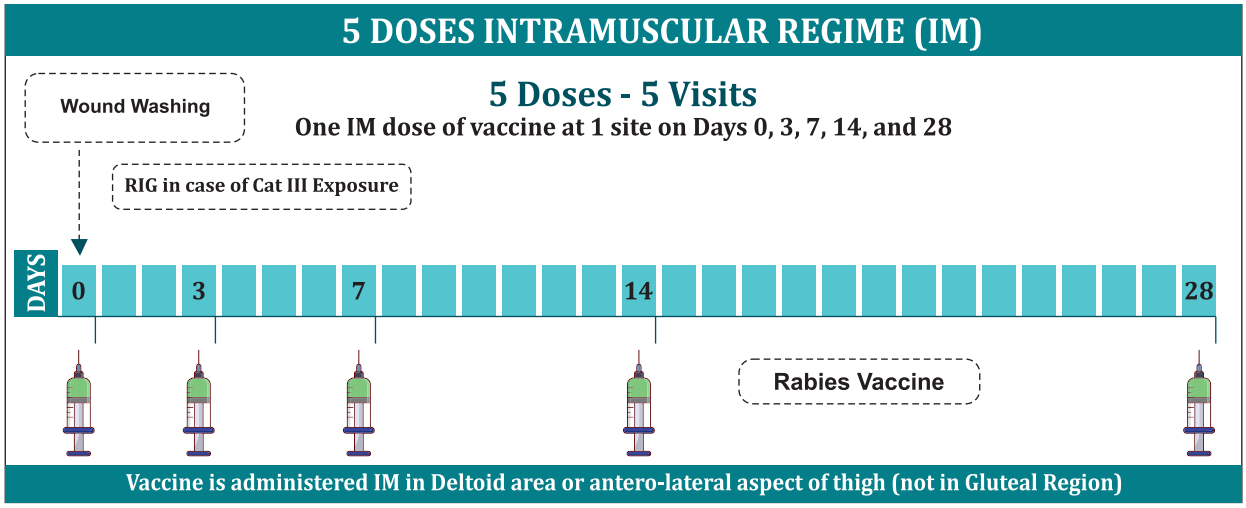
4.2.1 Intramuscular Regimen for Post exposure Prophylaxis - Essen regimen (1-1-1-1-1):

Five dose intramuscular schedule - the course for post-exposure prophylaxis consists of intramuscular administration of five injections, one dose each given on days 0, 3, 7, 14 and 28. Day 0 indicates the date of administration of the first dose of vaccine.

Switching the route of administration from IM to ID or vice versa and switch over from one type of modern Rabies Vaccines to the other during PEP is not recommended as a routine. However, whenever this is absolutely required, as per WHO recommendation, PEP need not be re-started and the regimen should be continued/ resumed as per the new vaccine/ route of administration.

4.2.2 Site of injection

The deltoid region is ideal for the administration of these vaccines. Gluteal region is not recommended because fat present in this region retards the absorption of antigen and hence impairs the generation of an optimal immune response. In case of infants and young children, anterolateral part of the thigh is the preferred site. Switching the route of administration from IM to ID or vice versa and switch over from one type of modern Rabies Vaccines to the other during PEP is not recommended as a routine. However,



whenever this is absolutely required, as per WHO recommendation, PEP need not be re-started and the regimen should be continued/resumed as per the new vaccine/route of administration.

As with all other immunizations, vaccinated persons should be kept under medical supervision for at least 15–20 minutes following vaccination. Previous reaction to any component of a vaccine is a contraindication to the use of the same vaccine preparation for PEP or (PrEP) Pre-exposure prophylaxis.



5 MANAGEMENT OF RE-EXPOSURE IN PREVIOUSLY VACCINATED INDIVIDUALS

For exposed or re-exposed patients who can document previous complete PrEP or PEP the following guidelines would be applicable:

- Proper wound management should be done.
- There is no need for administration of RIG.
- One-site Intradermal vaccine administration on days 0 and 3; Or
- One-site Intramuscular administration of an entire vaccine vial on days 0 and 3.

Only adequate wound washing would be required in case of re-exposure where animal bite victim has documented proof of complete **PEP or PrEP within last three months.**

People who have previously received full post-exposure treatment with neural tissue vaccines (NTV) or vaccine of unproven potency or CANNOT document complete previous PEP or PrEP treatment should be treated as fresh case and given full PEP.

6 RABIES PEP FOR IMMUNE-COMPROMISED INDIVIDUALS

People with documented immune-deficiency should be evaluated individually. Patients with immune-compromised conditions (HIV/AIDS, patients on chemotherapy, long term steroid therapy, cancer patients, etc.) may have a significantly lower or no detectable neutralizing antibody response to Rabies Vaccine. In most of the settings, it is not possible to determine the severity of immune suppression when patients consult for PEP. Therefore, in all Immune compromised individuals, in whom the presence of immunological memory is no longer assured, the following protocol should be followed: -

- Proper wound management followed by local infiltration of RIG in both Category II and III exposures.
- After this, a complete course of Rabies Vaccine by IM route in both the category II and III exposures should be undertaken.
- Preferably, if the facilities are available, anti-rabies antibody titre estimation should be done 14 days after the completion of the course of vaccination to assess the need for additional doses of vaccine.

7 PRE-EXPOSURE PROPHYLAXIS

7.1 HIGH RISK GROUPS FOR PRE EXPOSURE PROPHYLAXIS

Pre-exposure vaccination may be offered to High-Risk Groups such as:-

1. Laboratory staff handling the virus and infected material, clinicians and individuals attending to human rabies cases.
2. Veterinarians, animal handlers and dog catchers.
3. Wildlife wardens, quarantine officers etc.
4. Travelers from rabies-free areas to rabies endemic areas.

The Indian Association of Pediatrics (IAP) has recommended pre-exposure prophylaxis of children. This may be considered on a voluntary basis.

7.2 SCHEDULE OF VACCINATION:

Total three doses are recommended for pre-exposure prophylaxis.

In case of IM route 1 full vial to be given on days 0, 7 and booster on either day 21 or 28.

In case of ID route, 0.1 ml on one site to be given on days 0, 7 and booster on either day 21 or 28.

High-risk groups should have their neutralizing antibody titres checked every 6 months during the initial two years period after the primary vaccination. If it is less than 0.5 IU/ml, a booster dose of vaccine should be given. Subsequently, sero-monitoring is recommended every two years. Vaccine-induced immunological memory persists in most cases for years. A booster would be recommended only if rabies virus neutralizing antibody titres have dropped to less than 0.5IU/ml.

Vaccinated Individuals on being exposed to RABV after successful pre-exposure immunization would require only two booster injections of vaccine given on day 0 and day 3. There is no need for RIG.

8 DEVIATIONS IN PEP SCHEDULE

The PEP should be started as soon as patients report to the health facility, irrespective of time-lapse after the animal exposure. Health personnel are required to strictly follow the recommended PEP schedule to prevent PEP failure. The patient should be informed clearly about the schedule verbally and in a written prescription. The first three doses of the PEP i.e doses on day 0, day 3 and day 7 should be completed maximum within 10 days to achieve effective immunity against the rabies virus. One or two days deviation do not necessitate re-starting of the vaccination schedule. However, in instances when the patient fails to visit on the scheduled date of first three doses and misses one or more dose, the administration of additional doses should be considered to complete the vaccination to obtain effective immunity.

9 NEWER ADVANCEMENT IN POST EXPOSURE PROPHYLAXIS

WHO has recommended the use of Monoclonal Antibodies (mAb) as a "cocktail" containing at least two antibodies against RABV, as alternatives for RIGs in PEP. Few monoclonal antibody product are recently given license by DCGI in India. WHO recommends that a registry be maintained to monitor the clinical use and outcomes of mAb products for rabies PEP. Expert group recommends that the role of Monoclonal antibodies in case of category III bites as a replacement to Rabies Immunoglobulin needs to be studied with regard to its effectiveness and safety in multi-centric Indian settings before incorporation in National Guidelines.

10 SUMMARY OF VACCINATION SCHEDULE

The summary of vaccination schedule as per route is as under: -

Type of Prophylaxis	Route of Administration	Dose of Vaccine	Day of Dose	No. of injections	Total No. of Per Visit	Site of Injection Visits
Post Exposure Prophylaxis	Intra Dermal	0.1ml per dose	Day 0, 3, 7 and 28	2	4	**Adults:** Deltoid Muscle **Infants and Small Children:** Anterolateral Thigh
	Intra Muscular	1 entire vaccine vial	Day 0, 3, 7, 14 and 28	1	5	
Pre Exposure Prophylaxis	Intra Dermal	0.1ml 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	0.1ml per dose	Day 0 & 3	1	2	
	Intra Muscular	1 entire vaccine vial	Day 0 & 3	1	2	

ANNEXURES



ANNEXURE I

Details of Anti-Rabies Vaccine (Human)

Name of the firm	Doses & Route of Administration	Presentation (Vial/PFS/other)*
M/s Human Biological Limited, Hyderabad	0.5 ml/1 ml – 1 dose Intramuscular 0.1ml- 1 dose Intradermal	Vial
M/s Cadila Healthcare Limited, Ahmedabad	1 ml: 1 dose Intramuscular 0.1 ml: 1 dose Intradermal.	Vial
M/s Chiron Behring Vaccines Ltd., Gujarat	1 ml: 1 dose Intramuscular 0.1 ml: 1 dose Intradermal	Vial
M/s Serum Institute of India Pvt. Ltd., Pune	1 ml : 1 dose Intramuscular 0.1ml : 1 dose Intradermal	Vial
M/s Bharat Biotech International Ltd. Hyderabad	0.5 ml/1 ml: 1 dose Intramuscular 0.1 ml: 1 dose Intradermal	Vial

*Wherever the label mentions as multidose that may be considered as multidose, otherwise it may be treated as single dose. As there may be changes in the presentations from time to time, please refer to the current package insert provided by manufacture before use of Rabies Vaccine.

ANNEXURE II

Details of Equine Rabies Immunoglobulin

S. no	Name of firm	Strength	Route of Administration	Presentation of vaccine (Vial/PFS/other)	Shelf life and storage condition
1	M/s Haffkine Biopharmacuticals Corporation Ltd Pimpri, Pune- 411018	Each ml contains 300IU/ml	Intramuscular	5 ml/vials Pack of 10 Vials each box	24 Months Store between 2° C and 8° C
2	M/s Serum institute Pvt ltd., 212/2 Hadapsar, Pune-411028	1500 IU/ 5mL 1000 IU/ 5mL	Intramuscular	5 ml Vial	24 Months
3	M/s Bharat Serum and Vaccine Ltd Plot No: K-27/ Anand Nagar, Mumbai-400008	1000 IU/ 5mL	intramuscular	5ml Vial	24 months Store between 2° C and 8° C
		300 IU/ mL	intramuscular	5 ml Vial	24 months Store between 2° C and 8° C
4	M/s Central Research institute Distt- Solan (H.P.) 173205	1500 IU/ 5mL	intramuscular	5 ml vial	24 months
5	M/s Virchow Biotech Pvt ltd, Sy. No. 172 part, Gaglapur Village- Quthbullahpur mandal reddy distrct Telangana	1500 IU/ 5mL Liquid	intramuscular	5 ml vial	24 months
6	M/s Vins Bioroducts Ltd Sy. No.117 Thimapur Village Kothur Mandal mahbubnagar Dist- Telangana	1500 IU/ 5ML Liquid viel 1000 IU/ 5mL (For Export)	intramuscular	5ml vial	24 months
7	M/s Premium Serums and Vaccines pvt Ltd., S.No. 354-1 & 2A/1 Narayangaon, Tal. Junnar, dist. Pune-410504 Pune	1500 IU/ 5mL Vial 1000 IU/ 5mL Liquid	intramuscular	5 ml vial	24 months

ANNEXURE-III

Details of Human Rabies Immunoglobulin

Importer Name	Product
M/s Bharat Serum and Vaccine Limited, 17th Floor, Hoechst House, Nariman Point, Mumbai-400021	Human Rabies Immunoglobulin solution IP for IM 150IU/ml
M/s Plasmagen Biosciences Pvt. Ltd, KCI Chambers, 2nd Floor, 5th Main Road, Chamarajpet, Bangalore-560018, Karnataka, India	Anti Rabies Immunoglobulin IM E.P. 150IU/ml
M/s Prosper Channel Life science India Private Limited, B-244 (Ramphal Chowk), Sector-7, Dwarka, New Delhi-110077	Human Rabies Immunoglobulin 150IU/ml

Source : DCGI, 2020

ANNEXURE-IV

NATIONAL RABIES CONTROL PROGRAM
ANIMAL BITE EXPOSURE REGISTER*

Name of the Health Facility: Type of Health Facility:

Address & Contact Details

Health Facility Code: Reporting Month Year

Registration		Type of Patient (New/ OLD)	Patient Detail				Exposure History			Exposure details		Post Exposure Prophylaxis			Previous History of ARV Vaccination(Complete / partial/NA)	Biting Animal Status after 10 days (Dead / Alive/ Not traceable)	Remarks (Dose no/ PEP status complete/ incomplete)
S / N	Date		Name	Age	Sex (M/ F/ Other)	Residential Address	Date of Bite	Site of Bite on Body: (Extremities/ Trunk/ Head-Neck Face/ Back)	Biting Animal Species - dog/ cat/ monkey / others (specify)	Category of Bite (I/II/III)	Address where bite incidence took place	Adequate Washing of Bite wound Done(Y/ N)	Rabies Immunoglobin Given (Y/ N)	ARV Route ID/ IM			

Any Clustering of cases Observed: if yes write the details

Category I: Touching or feeding of animals; Licks on intact skin; Contact of intact skin with secretions / excretions of rabid animal / human case,

Category II: Nibbling of uncovered skin; Minor scratches or abrasions without bleeding,

Category III: Single or multiple transdermal bites or scratches, licks on broken skin; Contamination of mucous membrane with saliva (i.e. licks)

*To be maintained by Health facility providing treatment to animal bite cases

Summary

Indicator	Old	New		Total
Total Number of Patients attended				
	I	II	II	
Category wise Number of Patients				

VIndicator	IM	ID
Route of ARV Administration		
Total Number of Cat II patients receiving ARS		

ANNEXURE: V

Rabies Post Exposure Prophylaxis treatment Card

NATIONAL RABIES CONTROL PROGRAM
RABIES POST EXPOSURE TREATMENT CARD

Name and address of the health facility

Patient Reg. No

Name Age/ Sex	
Patient Residential Address & Contact No	
CATEGORY OF EXPOSURE	
I. Touching or feeding of animals Licks on intact skin Contact of intact skin with secretions /excretions of rabid animal/human case	[ ]
II. Nibbling of uncovered skin Minor scratches or abrasions without bleeding	[ ]
III. Single or multiple transdermal bites or scratches, licks on broken skin Contamination of mucous membrane with saliva (i.e. licks)	[ ]
Biting Site: Extremities/ Trunk/ Head-Neck Face/ Back	
Date of Exposure/bite (DD/MM/YYYY) Site of Bite/ Bites Type of animal — Biting animal status Dog [ ] — Monkey [ ] — Alive [ ] Cat [ ] — Other [ ] — Dead [ ] Unknown [ ] Date treatment started (DD/MM/YYYY)	Past h/o vaccination If Yes Specify whether Partial / complete
WOUND MANAGEMENT	
Washed immediately with water ( ) Yes ( ) No Antiseptic application ( ) Yes ( ) No	Wound washed at facility ( ) Yes ( ) No ARS Infiltration ( ) Yes ( ) No
Post exposure vaccination record Route of Administration ( ) ID ( ) IM	

Period	Date due	Date given	Signature
Day 0			
Day 3			
Day 7			
Day 14 (for IM only)			
Day 28			

Outcome: PEP Complete/ Incomplete

Signature

ANNEXURE: VI

GUIDANCE NOTE FOR STATES ON PREVENTING SHORTAGE OF RABIES VACCINE, HUMAN & ANTI RABIES SERUM

1. Manufacturing of Human Rabies Vaccineis a complex biological process and require a minimum of 3-4 months for manufacturing and testing. Accordingly, the statesor procurement agencies may be sensitized about the minimum lead time required for supply.
2. The annual requirement of Human Rabies Vaccine& Anti Rabies Serum must be calculated 4-6 months in advance. The requirement must include 10% Wastage factor and buffer stock for three months (lead time from order placement to the actual delivery of vaccines). Accordingly, the tender/ purchase order needs to be placed in advance.
3. As per the Drugs and Cosmetics Rules, 1945, the batch of Rabies Vaccine has to be released by the manufacturer after testing in manufacturer's laboratory and after ensuring that the vaccine complies with the specifications. It is also mandatory, as per procedures defined, to submit the samples of Human Rabies Vaccinealong with protocols to Central Drugs Laboratory (CDL), Kasauli for evaluation and lot release before it is supplied in the country. Normally, testing of Human Rabies Vaccinetakes approximately 3 to 4 weeks.
4. Tenders should be issued for fixed quantities rather than the rate contracts.
5. Human Rabies Vaccine & Anti Rabies Serum stock must be monitored on a regular basis. Monitor the district/institute-wise stock situation and accordingly, plan the supply based on consumption. If necessary, additional procurement order may be placed.
6. The States shall analyse average time required for completing the tender process to the actual placement of the order and accordingly, the procurement procedures to be started well in advance to avoid shortage of Human Rabies Vaccine& Anti Rabies Serum supply.
7. The State Authorities need to be sensitized to analyse their annual requirement and the lead time required for completing all procedures well in advance, in order to guard against shortages in the supply of Human Rabies Vaccine& Anti Rabies Serum.
8. Anti-rabies vaccine and Anti rabies serum is part of an essential drug list of National Health Mission (NHM). Budget for Human Rabies Vaccine& Anti Rabies Serum may be proposed under NHM PIP under National Free Drug Initiative.
9. As per national guidelines, the preferred route of administration for Human Rabies Vaccine is Intradermal. It is cost-effective and requires 0.2 ml/ Visit/patient for intradermal route vs. 1 ml/visit/patient for intramuscular route.
10. In case of shortage of Rabies vaccine (Human), please inform to National Pharmaceutical Pricing Authority (NPPA), Department of Pharmaceuticals (DoP) or Ministry of Health and Family Welfare (MoHFW) for addressing the issue. Non-supply of Human Rabies vaccinedue to the pendency of bills should not be referred to DoP/MoHFW/CDSCO.

ANNEXURE: VII

Case definition for Human Rabies for IDSP

1. Suspect Case : To be reported in S Form (by Health Worker)

Definition : Death of a human with history of dog bite few weeks/months preceding death

Wherever available, the details of such cases should be shared in a line list– Name, Age, Gender, Address

2. Probable Case : To be reported in P form (by Medical Officers/Doctors)

Definition: A suspected human case plus history of exposure# to a (suspect¥ / probable€) rabid animal

#Exposure is usually defined as a bite or scratch from a rabies-susceptible animal (usually dogs). It could also be lick exposure to open wound, abrasion, mucous membranes of the patient.

¥A suspect rabid animal is a rabies-susceptible animal (usually dogs) which presents with any of the following signs at time of exposure or within 10 days following exposure: unprovoked aggression (biting people or animals or inanimate objects), hypersalivation, paralysis, lethargy, abnormal vocalization, or diurnal activity of nocturnal species. Whenever the history of mentioned signs cannot be elicited, the history of exposure to rabies-susceptible animal would be considered adequate.

€A probable rabid animal is a suspect rabid animal (as defined above) with additional history of a bite by another suspect / probable rabid animal and/or is a suspect rabid animal that is killed, died, or disappeared within 4-5 days of observing illness signs.

Wherever available, the details of such cases should be shared in a line list as per line list design of IDSP.

3. Laboratory Confirmed case : to be reported in L-Form (by Laboratories having confirmatory test facilities for rabies)

Definition: A suspect or a probable human case that is laboratory-confirmed$.

$Laboratory confirmation by one or more of the following:

- Detection of rabies viral antigens by direct fluorescent antibody test (FAT) or by ELISA in clinical specimens, preferably brain tissue (collected post mortem).
- Detection by FAT on skin biopsy (ante mortem).
- FAT positive after inoculation of brain tissue, saliva or CSF in cell culture, or after intracerebral inoculation in mice or in suckling mice.
- Detectable rabies-neutralizing antibody titre in the serum or the CSF of an unvaccinated person.
- Detection of viral nucleic acids by PCR on tissue collected post mortem or intra vitam in a clinical specimen (brain tissue or skin, cornea, urine or saliva).



Question 1: Is there a single-dose human rabies vaccine that will provide life-long immunity?

Answer: At present, there is no single-dose rabies vaccine available anywhere in the world that can provide life-long immunity. Rabies vaccines are given as a series. Regardless of previous vaccination, if exposed to the virus, you will require another series of vaccines.

Question 2: Application of chilies, lime, salt and mustard oil to animal bite wound is common practice. Does it confer any advantage over washing with soap and water?

Answer: Application of any of these materials does not confer any advantage. On the contrary, irritation produced by any of these may provide more avenues to the virus to gain entry into nerves and spread to the brain. This also gives a false sense of security that some treatment has been administered.

Question 3: Are there any dietary restrictions for animal bite victims receiving anti-rabies vaccination?

Answer: No dietary restriction needs to be imposed aftervaccination. However, excessive intake of alcohol should be discouraged.

Question 4: Can a vaccinated dog transmit rabies?

Answer: A dog effectively vaccinated against rabies cannot suffer and transmit the disease. However, in the absence of laboratory documentation of protection, it cannot be presumed that a vaccinated dog is actually protected, given the variable efficacy of various anti-rabies vaccines in animals and health status of animals. Hence, irrespective of the vaccination status of the biting dog, the PEP should be given.

Question 5: Do we need to consider specific vaccine potency for ID vaccination?

Answer: There has been a concern as single IM doses are reconstituted in different volumes depending on manufacturers. The recommended minimum potency of all anti-rabies vaccine is ≥ 2.5 IU per IM dose. The recommended volume of a single dose of rabies vaccine administered per ID site is 0.1 ml. The DCG(I) approved vaccine (pack

containing i.e. lyophilized vaccine and the specified amount of diluent) with a potency of ≥ 2.5 IU/IM dose should be used for ID inoculation. The recommended dose is 0.1 ml at 2 sites on day 0, 3, 7 & 28.

Question 6: Is it necessary to perform an antibody test following anti-rabies vaccination in all animal bite victims?

Answer: No, it is not required in all cases. When human rabies vaccines are given according to the approved schedule in a healthy individual it is not necessary to do antibody titre estimation. It is recommended only under special circumstances such as for immune-compromised patients, patients receiving immunosuppressive therapy or patients who have not taken the vaccination as per recommended schedule.

Question 7: Is there any possibility of failure after PEP?

Answer: There are occasional human rabies cases reported despite PEP, due to various factors related to negligence and individual health status. Most cases have been reported due to delayed vaccination, or non-use of rabies immunoglobulin in category III exposure, or incomplete course of vaccination. Some cases are related to immune-compromised statuses such as HIV/AIDS, cirrhosis or use of chloroquine, long term steroids, or anti-cancer drugs. Unexplained failure in cases where everything was apparently done correctly have also been documented, but are very rare.

Question 8: DCG (I) approved vaccine is being used in the anti-rabies clinic which reconstitutes to 0.5ml volume. Is it advisable to add extra diluent to this and use it for ID inoculation using 0.1 ml per site at 2 sites on days 0, 3, 7 &28?

Answer: No, this should never be done.

Question 9: Is simply observing the biting animal for 10 days without starting PEP justified?

Answer: No. In countries where rabies is prevalent, it is necessary to start post-exposure prophylaxis for the exposed person promptly and keep the biting animal under observation for 10 days where possible. An animal infected with rabies will usually show clinical signs, or die, within 1-7 days, providing the basis of the 10-day observation period. This is applicable only to dogs & cats.

If the animal remains healthy during the observation period then post-exposure prophylaxis can be discontinued after 10 days or converted into a pre-exposure regimen, by omitting the day 14 dose, but taking the day 28 dose

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Question 10: Is it safe to give Rabies Vaccine to a pregnant woman?

Answer: Rabies is a potentially fatal disease and PEP is life-saving. Hence pregnancy is not considered a contraindication to post-exposure prophylaxis. Studies have indicated no increased incidence of abortion, premature births, or foetal abnormalities associated with rabies vaccination

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Question 11: Can the consumption of raw meat from a rabies-infected animal

transmit rabies?

Answer: Consuming the meat from a rabid animal is strongly discouraged. Although no human cases have been documented following the consumption of uncooked meat from a rabid animal, butchering or eating a rabid animal may potentially transmit rabies. If exposure occurs, PEP should be initiated. Cooked meat does not transmit rabies; however, it is not advisable to butcher or consume the meat of any kind from an infected animal. The carcass should be buried or burned if possible, with advice from a veterinary professional.

Question 12: How to protect the pet dog/cat from getting rabies?

Answer: First, visit the veterinarian with the pet on a regular basis and keep rabies vaccinations up-to-date for all pet animals. Secondly, pet animals should be kept under supervision during outdoor activities and not allowed to come in close contact with potentially rabid stray animals.

Question 13: Is PEP required following a rat/rodent bite?

Answer: Under normal circumstances, rabies is not transmitted by domestic rats. As a general rule, it is therefore not necessary to receive PEP if bitten by a rat but the wound should be cleaned and washed as in case of any other animal bite wound. Consult physician for other care, e.g. anti-tetanus prophylaxis, if required.

However, in many cases, the history given by the patient seems unreliable due to similarly looking species such as mole, mongoose etc, in such cases, to be on safer side the PEP should always be offered to the victim.

Question 14: Can rabies be transmitted through organ transplantation?

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

Question 15: Is it possible to develop rabies from the vaccination?

Answer: No. All Rabies Vaccines for human use are inactivated. Human rabies vaccines undergo a series of quality control tests such as potency, toxicity, safety and sterility. It is not possible for the rabies vaccination to cause the disease. Human rabies vaccines are safe and highly effective in preventing rabies.

Question 16: How should anti-rabies vaccines be stored to maintain their safety and potency before administration?

Answer: After growth in cell culture (or embryonic egg), rabies vaccines are concentrated, purified, inactivated and lyophilized to extend their shelf-life and stability. Human rabies vaccines are not supplied in multi-dose vials for intramuscular injection, and usually do not contain preservatives. The shelf-life of these vaccines is indicated by the manufacturer on the package insert, generally ≥ 3 years, provided they

are stored at 2–8 °C and protected from sunlight. After reconstitution with sterile diluent, the vaccines should be used immediately or within 6 h if kept at between 2 °C and 8 °C, as partially used vials of rabies vaccine may become contaminated.

Question 17: How does intradermal rabies vaccination work when the dose is so small? Does it fully protect against rabies exposure?

Answer: Intradermal vaccination is a multi-site (upper arms, lateral thighs, suprascapular) vaccination technique that elicits a prompt and highly protective immune response with a small dose. In the past, eight-site and four-site ID administration schedules were standard. However, clinical trials and immunological studies clearly demonstrate that two-site ID administration is efficacious, user-friendly and cost–effective. The immune responses induced by ID and IM regimens are comparable, although the immune response pathways are slightly different. In ID vaccination, rabies antigen is injected into the dermis of the skin to elicit a stronger immune response. It has been shown that the antigen-presenting cells in the skin are more effective than the ones in muscle. ID rabies vaccination has been used successfully over decades and has saved millions of lives.

Question 18: What are side/adverse effects after Rabies Vaccination?

Answer: Adverse reactions to rabies vaccine and immune globulin are uncommon. Newer vaccines in use today cause fewer adverse reactions than previously available vaccines. Mild, local reactions to the rabies vaccine, such as pain, redness, swelling, itching at the injection site have been reported. Rarely, symptoms such as headache, nausea, abdominal pain, muscle aches and dizziness have been reported. Local pain and low-grade fever may follow the injection of rabies immunoglobulin.

Question 19: How should the dead bodies of confirmed rabid patients be disposed of?

Answer: Humans who die of rabies generally present a small risk of transmission to others.

Blood does not contain the rabies virus. However, rabies virus may be present in many tissues, such as the central nervous system, salivary glands and muscle and in saliva and urine. Tissues and body fluids should be disposed of in the same manner as practised for other infectious diseases such as tuberculosis and hepatitis.

Disinfect the instruments used for any procedures on the patient by autoclave or boiling after use. Discourage embalming. Early disposal of the human remains by burial or cremation is highly recommended

If the conditions permit and death has occurred in a health facility/hospital where facilities for obtaining post-mortem brain sample are available then the efforts should be made to collect the sample as per the standard protocols with strict infection control measures using proper personal protective equipment (PPE), and laboratory result should be communicated to the concerned authority.

LIST OF EXPERTS

1. Dr. N.S. Dharamshaktu, Pr Advisor (PH) MoH&FW, Government of India,
2. Dr. Inder Prakash, Advisor (PH) MoH&FW, Government of India
3. Dr. Sujeet Kumar Singh, Director, National Centre for Disease Control, Delhi
4. Dr. Sunil Gupta, Addl. Director & Head, Department of Microbiology, National Centre for Disease Control, Delhi
5. Dr. Gyanendra Gongal, Food Safety & Zoonosis, WHO SEARO
6. Dr. Santosh Kutty, CMO (SAG), Central Research Institute, Kasauli
7. Dr. Jugal Kishore, Director Professor, Vardhaman Mahavir Medical College & Safdarjung Hospital, Delhi
8. Dr. Mala Chhabra, Sr. Consultant (Microbiology), Dr. Ram Manohar Lohia Hospital, New Delhi
9. Dr. Harmeet Rehan, HoD (Pharmacology) Lady Hardinge Medical College, Delhi
10. Dr. Vandana Roy, HoD (Pharmacology) Maulana Azad Medical College, Delhi
11. Dr. Naveen Gupta, Joint Director, Centre for Arboviral and Zoonotic Diseases, National Centre for Disease Control, Delhi
12. Dr. Pradeep Khasnobis, Joint Director, IDSP, National Centre for Disease Control, Delhi
13. Dr. D H Ashwath Narayana, President APCRI & HoD (Community Medicine) KIMS Bengaluru
14. Dr. Gowri Sengupta, ADG, MoHFW, India
15. Dr. Hemant Gohil, Medical Officer I/C, Maharishi Valmiki Infectious Diseases Hospital-Delhi
16. Dr. Anurag Agarwal, Associate Professor, Paediatrics, Maulana Azad Medical College -Delhi
17. Dr. Khan Amir Maroof, Associate Professor of Community Medicine, University College of Medical Sciences, Delhi
18. Dr. Ritu Singh Chauhan, NPO, IHR- WHO Country office,
19. Dr. Simmi Tiwari, Deputy Director & OIC, Division of Zoonotic Disease Program, National Centre for Disease Control, Delhi
20. Dr. Sampath Gade , Former Member, WHO-SAGE Group
21. Dr. Omesh Bharti, State Epidemiologist, Government of Himachal Pradesh
22. Dr. Monil Singhai, Deputy Director, Centre for Arboviral and Zoonotic Diseases, National Center For Disease Control, Delhi
23. Dr. Ajit Shewale, Assistant Director, Division of Zoonotic Disease Program, National Centre for Disease Control, Delhi
24. Dr. Tushar Nanasaheb Nale, Assistant Director, Division of Zoonotic Disease Program, National Centre for Disease Control, Delhi
25. Mr. Yogesh Shelar, Assistant Director, Drug Controller General of India, GOI

MINISTRY OF HEALTH AND FAMILY WELFARE
GOVERNMENT OF INDIA

RABIES POST EXPOSURE PROPHYLAXIS PROTOCOL AFTER ANIMAL BITE

DECISION TO TREAT



CATEGORY I • Touching or feeding of animals • Licks on intact skin		Gently wash all scratches or wounds with mild soap and running water for at least "15 minutes"	Vaccine and RIG not indicated
CATEGORY II • Nibbling of uncovered skin • Minor scratches or abrasions without bleeding		Gently wash all scratches or wounds with mild soap and running water for at least "15 minutes"	 ONLY RABIES VACCINATION
CATEGORY III • Single or multiple transdermal bites or scratches • Licks on broken skin • Contamination of mucous membrane with saliva		Gently wash all scratches or wounds with mild soap and running water for at least "15 minutes"	 RABIES VACCINATION + RIG INFILTRATION

*All categories of bite should be reported in NRCP monthly report.

POST EXPOSURE PROPHYLAXIS PROTOCOL

CATEGORY I

Vaccine and RIG not indicated

CATEGORY II

PREVIOUSLY NOT IMMUNISED

RIG IS NOT INDICATED

IMMUNE COMPETENT PERSON

Give 04 doses OF RABIES VACCINE via intradermal route - ID (0.1 ml 2 sites) on day 0 - 3 - 7 - 28

OR

Give 05 doses OF RABIES VACCINE via intramuscular route-IM (1 vial, 1 site) on day 0 - 3 - 7 - 14 - 28

PREVIOUSLY* IMMUNISED

RIG IS NOT INDICATED**

IMMUNE COMPETENT PERSON

Give 02 doses OF RABIES VACCINE via intradermal route - ID (0.1 ml 1 site) on day 0 - 3

OR

Give 02 doses OF RABIES VACCINE via intramuscular route-IM (1 vial, 1 site) on day 0 - 3

CATEGORY III

PREVIOUSLY NOT IMMUNISED

INFILTRATE WOUNDS WITH RIG AS SOON AS POSSIBLE

IMMUNE COMPETENT PERSON

Give 04 doses OF RABIES VACCINE via intradermal route - ID (0.1 ml 2 sites) on day 0 - 3 - 7 - 28

OR

Give 05 doses OF RABIES VACCINE via intramuscular route-IM (1 vial, 1 site) on day 0 - 3 - 7 - 14 - 28

Rabies vaccine should be administered in deltoid muscles for adult and children & in anterolateral thigh (IM) for infants and small children. Rabies vaccine should not be injected in the gluteal region

FOR IMMUNE COMPROMISED PERSON

- Proper wound management followed by local infiltration of RIG in both category II and III exposures
- After this, complete coures of Rabies vaccine via Intramuscular route in both category II and III exposures should be undertaken

*Previously Immunised Case: Animal bite patient who can document previous history of complete post exposure or pre exposure prophylaxis by modern vaccines.

FOR CATEGORY II & III, IF REPEAT EXPOSURES IN THE FUTURE, TREAT AS PREVIOUSLY IMMUNIZED AND FOLLOW THE ALGORITHM AS ABOVE

RABIES IMMUNOGLOBULIN - RIG DOSAGE



- The maximum dosage for HRIG i.e. Human Rabies Immunaglobulin is 20 IU/Kg of the body weight and that of ERIG i.e. Equine Rabies Immunoglobulin is 40 IU/Kg of body weight.
- The entire immunoglobulin dose or as much as anatomically feasible but possibly avoiding compartment syndrome, should be carefully infiltrated into or as close as possible to the wound(s) or exposure site.
- Do not give RIG beyond the 7th day after the 1st vaccine dose on day 0.
- **In previously vaccinated individual/s where direct nerve exposure is suspected treating physician may consider RIG infiltration

NRCP ADVOCATES INTRADERMAL ROUTE FOR RABIES VACCINE ADMINISTRATION

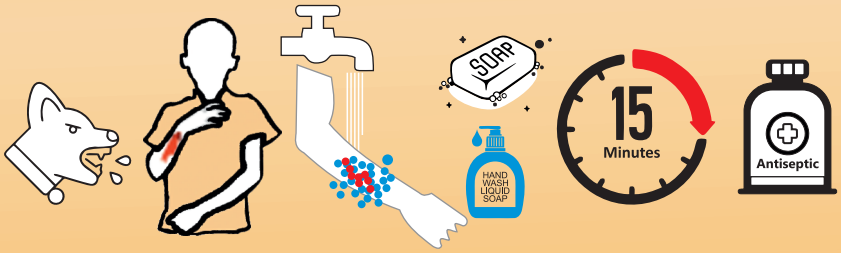
NATIONAL RABIES CONTROL PROGRAMME

ADOPT ONE HEALTH, STOP RABIES

Prevent Rabies, Vaccinate To Save Lives

After Dog Bite or Scratches or Licks

STEP 1 Wound Management for Category I, II & III Exposure

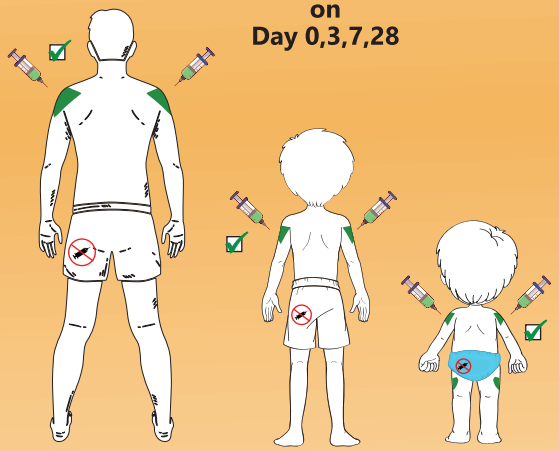


- **Wash all wounds** under running water with soap for upto 15 minutes.
- Apply Antiseptic

STEP 2 Vaccinate for Category II & III Exposure

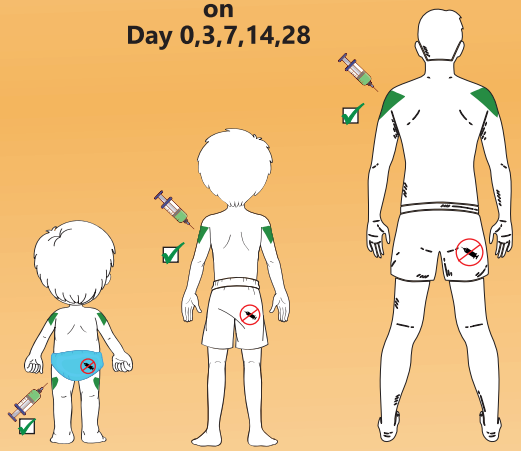
Intradermal Route

0.1 ml at 2 Sites on Day 0,3,7,28

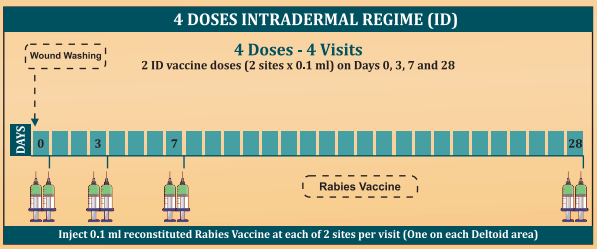


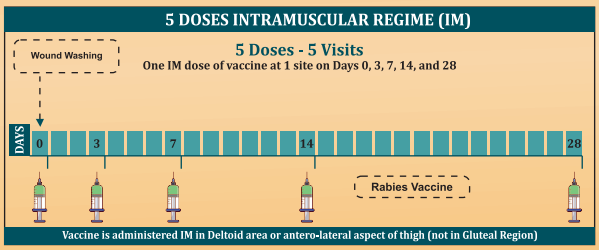
Intramuscular Route

1 vial at 1 Site on Day 0,3,7,14,28



Do not inject Rabies Vaccine in Gluteal Region





Step 3: Infiltrate (RIG) in Category III Exposure

Infiltrate Rabies Immunoglobulin in all wounds.

RABIES IS 100 PERCENT FATAL BUT PREVENTABLE

Rabies can be caused by bite or scratch of rabid animal such as dogs, cats etc

Do not apply chillies, mustard oil or any other irritant on the bite wounds

Wash the wound immediately with plenty of soap & water

Do not apply dressing & Do not get the wound stitched

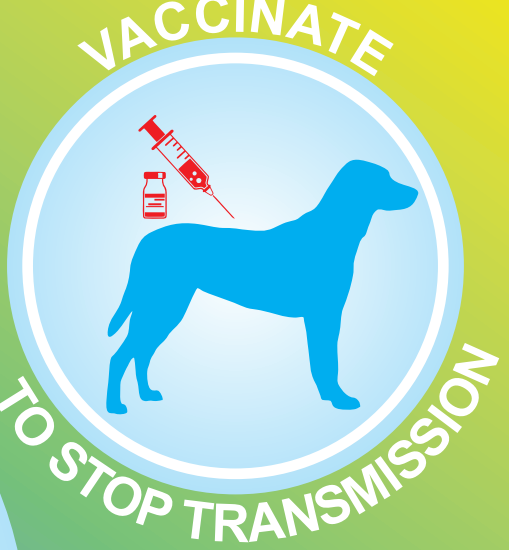
Consult your doctor immediately or rush to nearest antirabies clinic

Complete the course of antirabies vaccination, as advised by your doctor

In severe bites, combined antirabies serum and vaccine therapy is recommended

Vaccinate your pets against rabies every year





NATIONAL CENTRE FOR DISEASE CONTROL
(DIRECTORATE GENERAL OF HEALTH SERVICES)
22-SHAM NATH MARG, DELHI - 110 054
www.ncdc.gov.in

NATIONAL HEALTH MISSION
राष्ट्रीय स्वास्थ्य मिशन

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