National Guideline

Rabies Prophylaxis in Nepal (2019)

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Foreword

I am very pleased to know that the Epidemiology and Disease Control Division (EDCD) has developed the National Guideline for Rabies Prophylaxis and Management in Nepal with the technical support from the WHO Country Office, Nepal.

As we know that rabies is an infectious viral disease that is almost always fatal following the onset of clinical symptoms. However, with immediate post exposure prophylaxis of local wound washing, vaccination, and immunoglobulins, it is 100 % preventable.

I sincerely hope that this guideline will support the national, provincial and local government authorities to guide the health workers on prevention and management of rabies. Furthermore, its transmission, diagnosis and most importantly on the correct methods in the administration of rabies vaccine and immunoglobulins will provide insight for preventing death from human rabies. Therefore, I highly recommend our health workers to adhere to the recommended steps provided the guideline.

Lastly, I would like to express my sincere gratitude to EDCD, WHO Country Office, Nepal and all others who have contributed to developing this guideline.

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Foreword

Government of Nepal is conducting different interventions to achieve WHO's target of zero human death by rabies by 2030. For this, government has been implementing different strategies via animal health, local government bodies and public health sector. Yet, the approach of one health strategy in different sectors are in very rudimentary form in real practice. There is a large gap in coordination part of these sector. We know the basics for rabies control and prevention for elimination are impossible without collaborated one health approach. Even in such scenario, public health sector has been struggling for prevention of human death due to rabies. So, EDCD has been supplying anti-rabies vaccine to health facilities, providing orientation to health workers about rabies vaccination. We have been facing shortage of anti-rabies vaccine due to our dependency to another county. Large volume of money has been spent on huge volume of anti-rabies vaccine.

It is my immense pleasure to express that the "**NATIONAL GUIDELINES FOR RABIES PROPHYLAXIS AND MANAGEMENT IN NEPAL**" has been developed to guide proper use of anti-rabies vaccine. It also addresses different issues we have been facing in recording and reporting along with proper use in absence of national guideline. Moreover, the guideline has introduced three dose (0,3,7) intradermal vaccine use protocol which not only reduces cost and visit to health facilities but also increases compliance without compromising effectiveness of vaccination.

I hope the guideline assists health workers to practice properly and ensure uniformity in indications and use of rabies vaccine and rabies immunoglobulins. Finally, I would like to thank all the experts and my colleagues who have actively initiated and finalized the guideline. My sincere thanks to WHO team for providing thorough support in bringing the guideline to this shape.

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Abbreviations and Acronyms

RABV	Rabies Virus
PEP	Post Exposure Prophylaxis
PrEP	Pre Exposure Prophylaxis
WHO	World Health Organization
GARC	Global Alliance for Rabies Control
FAO	Food and Agriculture Organization
OIE	World Organization for Animal Health
CSF	Cerebrospinal Fluid
CCEEVs	Cell Culture and Embryonated Egg based Rabies Vaccines
ID	Intradermal
IM	Intramuscular
RIG	Rabies Immunoglobulin
IPC	Institut Pasteur du Cambodge
IDRV	Intradermal Rabies Vaccine
HIV	Human Immunodeficiency Virus
ART	Anti-Retroviral Therapy
RFFIT	Rapid Fluorescent Focus Inhibition Test
FAVN	Fluorescent antibody virus neutralization test
OP	Out Patient

1 Introduction

Rabies is a vaccine-preventable viral zoonotic disease responsible for an estimated 59,000 human deaths every year across the world. All warm-blooded mammals are susceptible to infection by the rabies virus (RABV). Transmission of RABV by dogs is responsible for up to 99% of human rabies cases in rabies-endemic regions, and more than 95 % of the patients seek Rabies PEP for dog bites. However, there is a small proportion of human rabies reported due to transmission via wildlife (such as foxes, wolves, jackals, mongoose, racoons, skunks and bats). The virus is present in the saliva of the infected animal and is transmitted to other animals and to humans through the saliva.

Rabies is a disease with the highest documented case-fatality rate, close to 100%. Rabies has terrified man since antiquity. Rural populations are disproportionately affected, experiencing the greatest burden with the least access to affordable preventive treatment.

Many European countries and North America have already eliminated rabies as a public health problem through mandatory vaccination of dogs and good access to post exposure prophylaxis for human beings. In Latin American countries, where poverty remains widespread, 90% reductions in the incidence of human and canine rabies have been seen. This is achieved by strong government commitment and support from international organizations for control of Rabies through one health approach, since the 1980s.

In Nepal, it is estimated that the annual incidence of human rabies is around one hundred. Many human rabies cases are not admitted, or patients leave against medical advice (LAMA).The number of animal bite cases has fluctuated over the past few years. It is estimated that around 50,000 people seek post-exposure prophylaxis in Nepal based on available medical records, vaccine distribution trend and services provided by private clinics.

In the fiscal year 2073/74 (2016-17),39744 animal bite cases were reported in the national annual report, out of which 37226 (94%) were dog bite cases. In the fiscal year 2074/75(2017/18), 28514 animal bite cases, including 26312 dog bite cases (92%), were reported

WHO MISSION OF "GLOBAL ERADICATION OF DOG MEDIATED RABIES BY 2030"

In 2015, World Health Organization (WHO) and World Organization for Animal Health (OIE), in collaboration with Food and Agriculture Organization (FAO) and the Global Alliance for Rabies Control (GARC), organized a global rabies conference in Geneva, bringing together partners and stakeholders in veterinary and human health, government and the private sectors, and launched the *Global framework for the elimination of dog-mediated human rabies*, outlining the commitment and actions required to achieve a common goal of zero human rabies deaths by **2030**, worldwide.

Since the launch of the Global framework, WHO has been working with partners to prepare a global strategic plan to end human deaths from dog-mediated rabies by 2030. This includes a country-centric approach, with international partners (WHO, FAO, OIE and GARC) to support, empower and catalyze national entities to control and eliminate rabies.

This national guideline on human rabies prophylaxis have been prepared in the light of new recommendations made by the WHO Expert Consultation on Rabies in 2017, which will improve patient compliance to PEP regimen and make rational use of rabies vaccine and immunoglobulin.

2 Rabies Virus

The Rabies Virus (RABV) belongs to the genus *Lyssavirus* in the family *Rhabdoviridae* and order *Mononegavirales*. All *Lyssavirus eselicit* an acute progressive encephalitis in human beings. There are at least 14 individual Lyssavirus species, subdivided into 2 phylogroups based on genetic distance and serological cross-reactivity.

RABV is an unsegmented, single-stranded, negative-sense, enveloped RNA virus and belongs to Phylogroup 1. The genome encodes five proteins; the most important of these from an immunization perspective is the G glycoprotein, which includes the antigenic sites targeted by rabies vaccines and passive immunization.

3 Transmission

Rabies is transmitted through direct contact between the virus (e.g. in contaminated saliva), and mucous membranes or wounds. Human infection most frequently occurs following a transdermal bite or scratch from an infected animal. Very rarely, rabies has been contracted by inhalation of virus-containing aerosol (e.g., in caves inhabited by bats). Human-human transmission has never been confirmed, with the exception of organ transplants from rabid patients.

Figure 1. ***A dog bite case reported from Sukraraj Tropical and Infectious Disease Hospital***

PC: Dr A Bastola/Mr. S Pandey

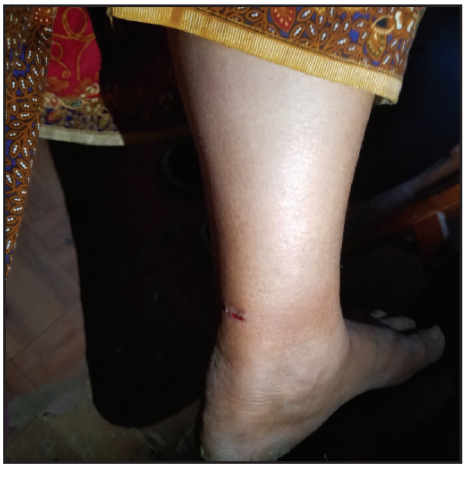


Figure 2. ***A dog bite case visiting Sukraraj Tropical and Infectious Disease Hospital for Rabies PEP***

PC: Dr A Bastola/Mr. S Pandey

4 Disease

Human rabies can manifest clinically as either:

- **Furious form** (classical)- widely recognized form OR
- **Paralytic form**

Neither form can be correlated with a specific anatomical localization of RABV in the central nervous system.

The consequence of an exposure to RABV depends on several factors, including

- the severity of the wound
- the location of the bite on the body
- the quantity of virus inoculated into the wound(s), and
- the timeliness of post-exposure prophylaxis (PEP)

Without PEP, the average probability of developing rabies following a bite by a rabid animal to the head is 55%, upper extremity 22%, the trunk 9% and a lower limb 12%.

Viral load in the saliva of RABV-infected dogs varies during the course of the disease and influences the risk of infection for bite victims.

Inoculated virus travels via the peripheral nerves to the central nervous system. Upon reaching the brain, it replicates and disseminates rapidly to the salivary glands, throat muscles and other tissues. The rabies virus is concealed from immune surveillance and neutralization by immunoglobulin by its location inside the neurons. Therefore, antibody responses in serum and cerebrospinal fluid (CSF) are rarely detected before the second week of illness. The virus does not enter the bloodstream, and human immunoglobulin prophylaxis is considered to be effective only when the rabies virus is present in the bite wounds.

The incubation period of most of cases is 1–3 months. This can vary from less than one week (in the case of direct nerve inoculation) to more than **one year**.
Clinical diagnosis of rabies is indicated by patient presentation, history of exposure to a suspect rabid animal, and whether PEP has been administered or not.

Signs and Symptoms of Rabies

Initial Symptoms	Later
• Pain or paraesthesia at the wound site • Fever	• Hyperactivity • Fluctuating consciousness • Hallucinations • Hydrophobia (furious rabies) • Paralysis and coma (paralytic rabies) • Followed by death

As the virus spreads through the central nervous system, a progressive fatal encephalomyelitis develops. In both furious and paralytic forms, death usually occurs by cardio respiratory arrest within 7-10 days of the first clinical sign.

Approximately 80% of the patients present with Classical (Furious) Rabies and 20% present with Paralytic Rabies.

The clinical presentation of the two types of rabies in human beings are given below

Furious Rabies (Classical)	Paralytic Rabies
• Hydrophobia • Aerophobia and Photophobia • Excitation and confusion • Excessive sweating and salivation • Dehydration • Death in 2-5 days	• Gradual ascending paralysis • Hydrophobia is not seen • Myoedema and piloerection • Stupor, Coma • May resemble Guillain–Barré syndrome • Death in 1-2 weeks

With the exception of hydrophobia, clinical signs of rabies can be unreliable, and contribute to under or misdiagnosis of rabies in humans. Additionally, rabies patients often die at home, or leave hospital when no treatment can be offered, and are therefore not included in clinical databases and mortality statistics.

5 Diagnosis

5.1. Standard Case Classification

The standard human case classifications for rabies are:

SUSPECTED CASE	A case that is compatible with a clinical case definition: *"A subject presenting with an acute neurological syndrome (i.e. encephalitis) dominated by forms of hyperactivity (i.e. furious rabies) or paralytic syndromes (i.e. paralytic rabies) progressing towards coma and death, usually by cardiac or respiratory failure, typically within 7–10 days after the first sign, if no intensive care is instituted. This may include any of the following signs: aerophobia, hydrophobia, paresthesia or localized pain, dysphagia, localized weakness, nausea or vomiting."*
PROBABLE CASE	a suspected case plus a reliable history of contact with a suspected, probable or confirmed rabid animal
CONFIRMED CASE	a suspected or probable case that is laboratory-confirmed (usually post-mortem)

A case would also be considered confirmed, even in the absence of clinical suspicion of encephalitis or a history of animal exposure, if confirmed by appropriate laboratory diagnostic testing. Access to rabies confirmatory testing in endemic countries is extremely limited.

RABV causes encephalitis, as do several other etiologies, therefore differential diagnosis and laboratory confirmation should be performed to exclude treatable conditions.

5.2. Differential Diagnosis

The clinical picture in rabies is often variable and may represent a continuum of signs and symptoms. Rabies can be confused clinically with

- Cerebral malaria
- Organophosphate poisoning
- Herpes simplex encephalitis
- Post-vaccinal encephalitis
- Scorpion and snake envenomation
- Illicit drug use
- Psychiatric disorders

Guillain–Barré syndrome is often clinically indistinguishable from the paralytic form of rabies.

5.3. Laboratory Diagnosis

A diagnosis of rabies is usually based on clinical features and dog bite history, as brain sample collection is difficult in view of sociocultural reasons.
Laboratory confirmation of Rabies must be done wherever feasible. Laboratory diagnosis is important to confirm or rule out rabies in suspected paralytic or encephalitis cases. It is useful in medico-legal cases.

Antemortem diagnosis

Postmortem diagnosis

Antemortem diagnosis will help physicians to plan critical care and palliative treatment. Reporting of laboratory confirmed cases is useful for estimation of disease burden and helps prioritize resources towards prevention of human rabies. Details of laboratory diagnosis is given in *Annex 1.*

6 Post Exposure Prophylaxis (PEP)

Rabies in humans can be prevented, after exposure, by PEP. Proper wound management combined with prompt post-exposure use of Cell Culture Vaccines and Embryonated Egg-based Vaccines (CCEEVs) and simultaneous administration of RIG in severe exposures, is close to 100% effective in preventing rabies.

6.1. Indication

The indication and procedure for PEP depend on the

- type of contact with the suspected rabid animal and
- immunization status of the patient

In a rabies endemic country like Nepal, every bite due to an animal which can transmit rabies, is suspected to be a potentially rabid animal bite, and treatment should be started as soon as possible, after an exposure. However, the decision on PEP should be made after taking a rational decision based on risk assessment.

6.2. WHO Classification of Exposures

WHO Classification of Exposures should be followed for deciding the treatment.

CATEGORY OF EXPOSURE	TYPE OF CONTACT
Category I	• Touching or feeding of animals • Animal licks on intact skin **(NO EXPOSURE)**
Category II	• Nibbling of uncovered skin • Minor scratches or abrasions without bleeding **(EXPOSURE)**
Category III	• Single or multiple trans dermal bites or scratches • Contamination of mucous membrane or broken skin with saliva from animal licks • (Exposures due to direct contact with bats*) **(SEVERE EXPOSURE)**

In Nepal bat transmitted rabies has not been reported

6.3. PEP by Category of Exposure

	Category I Exposure	Category II Exposure	Category III Exposure
Immunologically naive individuals of all age groups	**No PEP required**	**Wound washing and Immediate vaccination**	**Wound washing and Immediate vaccination and RIG administration**

People with WHO category II or III exposures should receive PEP without delay. The comparatively long incubation period of Rabies provides an opportunity for highly effective PEP.

6.4. PEP Components

PEP consists of the following three steps as per the category of exposure

- Local wound treatment
- Rabies Immunoglobulins (Passive Immunity)
- Rabies Vaccines

6.4.1. Local Wound Treatment

All bite wounds and scratches should be attended to as soon as possible after exposure. Since rabies virus can enter 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.

- Thorough washing and flushing of the wounds for approximately **15 minutes** with soap or detergent and plenty of water is required.
- If soap and detergent are not immediately available, wash with running water for **15 minutes**.

- 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.
- Wound toilet must be performed even if the patient reports late, as long as the wounds are not healed, since the rabies virus can persist and even multiply at the site of bite for a long time.
- Application of local remedies on the wounds should be strongly discouraged.
- If local irritants like herbs, oil, chilli or turmeric powder have been applied, these should be removed by thorough washing of the wounds.
- After wounds have been washed, **local antiseptics** (viricidal topical preparation) like Povidone Iodine should be applied on the wounds.

Thorough wound washing with soap or detergent and water and application of viricidal agents reduces the viral inoculum at the wound site.

***Suturing of wounds should be avoided**

If suturing is unavoidable (as in lacerated wounds), Rabies Immunoglobulins should be first infiltrated into the wounds and suturing should be delayed by a few hours to allow diffusion of the immunoglobulins into the tissues. Later, minimum number of sutures should be applied. For cosmetic purposes, secondary sutures can be done two weeks after initiating vaccination.

Whenever necessary, **Tetanus prophylaxis** should be instituted. Tetanus Toxoid (0.5ml IM) can be given. Antibiotics may be recommended, if needed.

6.4.2. Rabies Immunoglobulins

The role of RIG in passive immunization is to provide neutralizing antibodies at the site of exposure before patients start producing their own antibodies as a result of vaccination. RIG has the property of neutralization of the rabies virus, and hence it is appropriate to infiltrate RIG locally at the site of exposure.

RIG is administered only once, preferably at or as soon as possible after initiation of post-exposure vaccination. Rabies immunoglobulin should be given with the first dose of vaccine into and around the wound site. 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 or 7) because an active antibody response to the rabies vaccine would have already started, and administration of RIG at this stage can suppress the immune response of the patient to the Rabies Vaccine received. In Nepal, where the one-week Institut Pasteur Cambodge (IPC) vaccine schedule is being used, it is preferable to administer RIG on day 0 or at least by day 3 of the vaccine dose.

Where RIG is unavailable, scrupulous wound cleaning and deep irrigation, with application of a potent antiseptic agent, and timely administration of the first CCEEV dose should be performed immediately when the patient presents.

Two types of RIGs are available (both are considered to have similar clinical effectiveness):

Equine Rabies Immunoglobulin (eRIG)

eRIG is of heterologous origin produced by hyperimmunization of horses. Currently manufactured eRIGs are highly purified Fab 2' fragments.

Human Rabies Immunoglobulin (hRIG)

hRIG is of homologous origin and is relatively free from the side effects which may be seen after administration of eRIG. However, it is expensive.

Dose of RIGs

The maximum dose of

- Human RIG -20 IU/kg of body weight
- Equine immunoglobulin and F(ab')2 products- 40 IU/kg of body weight

Storage of RIGs

RIGs should be stored and transported at a temperature of +2 to 8°C and should not be frozen.

Method of infiltration of RIGs

Please refer to ***Annex 3***

Rabies Monoclonal Antibodies (RmAb)

WHO has recommended use of "cocktails" of monoclonal antibodies containing at least two antibodies against RABV.

A Rabies monoclonal antibody (single mAb) product was licensed in 2017 in India and is currently being used there in clinical settings as an alternative to hRIG. The dose is 3.33 IU/kg body weight. It is available in vials of 2.5ml volume. Each ml. contains 40IU of the RmAb. One vial can be used for persons weighing upto 30 kgs.

6.4.3. Rabies Vaccines

Cell culture and embryonated egg-based rabies vaccines (CCEEVs) have been shown to be safe, highly immunogenic and well tolerated and have proved to be effective in preventing rabies. CCEEVs are produced by propagating RABV in cell substrates such as human diploid cells, vero cells, primary chick or duck embryo cells or embryonated duck eggs. After growth in cell culture (or embryonic egg) the viral harvest is concentrated, purified, inactivated and lyophilized. The minimal acceptable potency of CCEEVs is **2.5 IU** per intramuscular dose.

Since 1984, WHO has strongly recommended discontinuation of production and use of nerve tissue vaccines and their replacement by modern, concentrated, purified CCEEVs.

Vaccines supplied through United Nations agencies should be prequalified by WHO. Prequalification ensures the quality, safety and efficacy of vaccines and their suitability for use in national immunization programs in low and middle-income countries. The producer must also meet international standards of quality and good manufacturing practice. After initial prequalification, products are reassessed at regular intervals to ensure continuing quality.

Indications

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

Storage and transportation

The shelf-life of these vaccines is ≥ 3 years, provided they are stored at **+2 to 8 °C** and protected from sunlight. As CCEEVs are available in lyophilized (freeze dried) form, they are more tolerant to variations of temperatures, but it is recommended that these vaccines should be stored and transported at a temperature range of **+2 to 8 °C**

Reconstitution

The sterile diluent supplied by the manufacturer should be used for reconstitution of the vaccine. After reconstitution, the vaccine should be used immediately or within 6 to 8 hours, if kept at + 2 to 8 °C.

Routes of vaccine administration

CCEEVs can be administered by intradermal (ID) route or intramuscular (IM) route.
One intradermal dose is 0.1 ml of vaccine, and one intramuscular dose is an entire vial of vaccine, irrespective of the vial size (0.5 ml. or 1 ml.).
Day 0 is the date of administration of the first dose.
As far as possible, vaccination schedules should be completed in the stipulated time.

Intradermal route

In rabies endemic countries with limited resources for ensuring PEP to all animal bite victims, intradermal administration of PEP is the preferred, most cost–effective route in clinics in which several new bite patients are seen per week. WHO recognizes the equivalent clinical effectiveness of the intradermal route.

The WHO approved regimen for intradermal route is the **1-week, 2- site regimen (2-2-2-0-0)**. This (IPC) regimen is evidence based, saves time and ensures compliance. **The Government of Nepal has recommended this schedule to be used in the country**. Many commercially available rabies vaccines are labeled for IM use and off label use by ID route can be applicable in Nepal after recommendation by the authorities.

Dose of IDRV and sites of administration

0.1ml of reconstituted vaccine is administered per ID site. 0.1ml. is injected into the upper layer of the skin over the deltoid area of one arm. Similarly, 0.1ml. is injected in the other arm.

The common site of injection is the **deltoid (upper arm)**. The other sites recommended for IDRV administration are the **supra scapular region** and **the lateral part of the thigh.**

Intradermal IPC vaccine regimen

Dose	Route	Duration	No of Injection Sites Per Clinic Visit	Sites
0.1ml Each site	Intradermal	1 week • Day 0 • Day 3 • Day 7	2-2-2-0-0	• Deltoid OR • Lateral thigh

Safety of Rabies Vaccines

CCEEVs have been shown to be safe and well tolerated. However, in 35–45% of vaccinees, minor and transient erythema, pain and/or swelling may occur at the site of injection, particularly following ID administration, in case of repeat vaccination. Mild systemic adverse events following immunization, such as transient fever, headache, dizziness and gastrointestinal symptoms, have been observed in 5–15% of vaccinees. Serious adverse events following immunization seldom occur and no causality has been established in cases of neurological symptoms.

Co-administration with other vaccines

Evidence supports safe co-administration of CCEEVs with other inactivated vaccines, such as diphtheria-tetanus-pertussis (DTP) and the inactivated Japanese encephalitis and poliomyelitis vaccines, and with live vaccines such as measles-mumps-rubella vaccine.

6.5. PEP for Re Exposure

Persons who have previously received complete pre- or post-exposure prophylaxis will elicit an anamnestic response to one or more booster doses of rabies vaccine even if the initial series of vaccination was administered several years previously.
This response will occur whether:

- the initial vaccine regimen was administered IM or ID
- the booster dose is given by IM or ID route
- the previously vaccinated person has detectable rabies virus neutralizing antibodies or not, at the time of re-exposure

PEP for re exposure cases based on category of exposure

	Category I Exposure	Category II Exposure	Category III Exposure
Previously immunized individuals of all age groups	**No PEP required**	**Wound washing and Immediate vaccination** RIG is not indicated	**Wound washing and Immediate vaccination** RIG is not indicated

Note:

If an individual has a repeat exposure less than 3 month after a previous exposure, and has already received a complete PEP, only wound treatment is required; neither vaccine nor RIG is needed.
Persons who cannot document previous pre- or post-exposure prophylaxis, should be treated as a fresh case and given complete PEP

Vaccine regimen for re-exposure

Dose	Route	Duration	No of Injection Sites Per Clinic Visit	Sites
0.1ml	Intradermal	Days • Day 0 • Day 3	1-1-0-0-0	• Deltoid OR • Lateral thigh

6.6. PEP in Special Groups

HIV-infected and other potentially immunocompromised individuals

HIV-infected individuals receiving ART, who are clinically well and immunologically stable (normal CD4 percent >25% for children aged <5 years or CD4 cell count ≥200 cells/mm³ if aged ≥5 years) can receive rabies vaccination.

For immunocompromised individuals (such as HIV-infected persons who are not receiving ART or who are receiving ART but do not meet minimum CD4 cell count criteria) with WHO Category II and III RABV exposure, the following is recommended:

- Thorough washing of the wound should be emphasized
- Administration of a full course of rabies vaccine
- RIG in both **Cat. II and III** exposures, even if previously immunized

If facilities are available, RVNA (rabies virus neutralizing antibodies) estimation should be done 14 days after the completion of course of vaccination to assess the need of additional doses of vaccine.

6.7. Points for Consideration

Bite by rodents

RABV infection in rodents is very uncommon. No human rabies cases due to bites by rodents have been reported. Exposure to domestic rodents, squirrel, hare and rabbits do not routinely require PEP.

Observation of biting animal

The observation period of 10 days is valid for dogs and cats only. A dog or cat suffering from Rabies will die within a period of 10 days after the clinical symptoms are seen in the dog/cat. 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 to other animals.

PEP should be started immediately after the exposure, even if it is due to a dog or cat. With the latest WHO protocol, treatment by ID route ends by day 7.

Vaccination status of the biting animal

A history of rabies vaccination in an animal is not always a guarantee that the biting animal is not rabid. Vaccine failures may occur because of improper administration or improper storage of the vaccine, poor health status of the animal, and the fact that one vaccine dose does not always provide long-lasting protection against rabies infection in dogs.

Provoked versus unprovoked bites

PEP should be immediately instituted irrespective of whether the bite was provoked or unprovoked.

Bite by wild animals

Bite by all wild animals should be treated as Category III exposure.

Consumption of raw meat or milk from a rabid animal

No case of human rabies resulting from consumption of raw meat or milk from a rabid animal has been documented. PEP is not required in persons consuming milk of a rabid animal.

Human-to-human transmission

The only documented cases of human-to-human transmission occurred via tissue and organ transplants from RABV-infected individuals, and a single case of likely perinatal RABV transmission via transplant was reported.

Caution should be exercised before transplanting organs from people who have died with neurological symptoms.

Individuals who had symptoms of encephalitis before death should be excluded from organ donation unless rabies can be excluded out as a cause of the encephalitis. People who have been exposed closely to the secretions of a patient with rabies may be offered PEP as a precautionary measure.

The risk of an infant contracting rabies from breast milk is similar to that of drinking milk from a rabid animal: it does not pose a risk to the infant.

Contraindications and Precautions

In view of the almost invariably fatal outcome of rabies, there is no contraindication to PEP vaccination.

There is no contraindication for individuals receiving treatment with chloroquine or hydroxychloroquine; both ID and IM route of vaccine administration can be used. However, in case of PrEP, if possible, it should be completed before chloroquine or hydroxychloroquine treatment is initiated.

Because of long and variable incubation period, people who present for treatment even months after a possible rabies exposure should be carefully evaluated and treated, as if the event had occurred recently. Both RIG and Rabies Vaccine can be given, if needed.

Pregnant and lactating women

Rabies vaccine and RIG can be administered safely to pregnant and lactating women. PEP should never be withheld from pregnant or lactating women.

7 Management of Patients with Rabies

There is no effective curative treatment for rabies once the clinical signs have appeared. Almost all patients with rabies will die.

Most patients with rabies remain conscious and are aware of the nature and outcome of their illness. Unfortunately, in some countries, many rabies patients are turned away from hospitals in view of the prognosis and receive terminal care only from their families.

Hospital care for patients with clinical rabies is advisable when possible, in order to reduce their suffering and ensure that they receive adequate, respectful palliative care. Although almost all patients will die, it is essential to provide prompt, effective, holistic, compassionate, culturally sensitive management. This can be done even with extremely limited equipment and drugs.

Patients with confirmed rabies should receive adequate hydration, sedation (benzodiazepines, barbiturates, morphine) and care in an appropriate medical facility, preferably in a calm, draft free, quiet room, with suitable emotional and physical support and avoidance of intubation or life-support measures. Excessive salivation can be treated with anti-cholinergic agents such as scopolamine.

1. Recommendations for health care personnel attending on patients suffering from Rabies

- Hospitals that are likely to receive rabies patients should consider PrEP for health care staff who may be involved in their management.
- Staff should be offered PrEP before they are posted to the units/wards where rabies patients are hospitalized. A full course of PrEP, should be administered. Periodic booster doses of vaccine should be administered to the staff who regularly attend to the hospitalized rabies patients.
- Staff should adhere to barrier nursing and wearing personal protective equipment (standard precautions, including wearing gloves, glasses and mask), as recommended for all infectious diseases.
- Patients should be hospitalized in a separate ward with individual cubicles. External stimuli like draughts of air and excessive lighting should be avoided in these rooms.

2. Recommendations for family members of patients with rabies

- PEP may sometimes be necessary for the partners of patients, as close contact and sexual intercourse in the early stages of the disease pose a hypothetical risk for transmission (infectious RABV is present in saliva).
- The spouse of the patient and the family members who are attending on the patient should be given PEP.

8 Pre-Exposure Prophylaxis (PrEP)

WHO recommends PrEP for individuals at high risk of RABV exposure

- Sub-populations in highly endemic settings with limited access to timely and adequate PEP
- Individuals at occupational risk
- Travelers who may be at risk of exposure

Sub-populations in highly endemic settings with limited access to timely and adequate PEP

- PrEP should be considered in sub-populations living in remote, rabies-endemic areas, where the dog bite incidence is >5% per year or vampire bat rabies is known to be present.

Individuals at occupational risk

- PrEP is indicated for individuals who are at risk of occupational exposures, particularly animal health-care workers. PrEP may be considered for medical professionals who regularly provide care to persons with rabies.

- Professionals who are at continual or frequent risk of exposure through their activities should have regular serological monitoring. If Virus Neutralizing Antibodies (VNA) levels fall to <0.5 IU/mL, a 1-site ID or a 1-site IM PrEP booster vaccination is recommended. If serological testing is not available for those at continual or frequent occupational risk, a periodic 1-dose (ID or IM) PrEP booster vaccination can be considered based on the assessment of relative risk.
- In case of suspected RABV exposure through aerosols, PEP including IM RIG injection can be provided, based on a risk assessment.

Travelers who may be at risk of exposure

- Individual assessment of the risk of RABV exposure for travelers is recommended. Considerations include: the remoteness of the destination in endemic areas, the prevailing rabies epidemiology and the cumulative duration of the stay in the endemic setting(s).

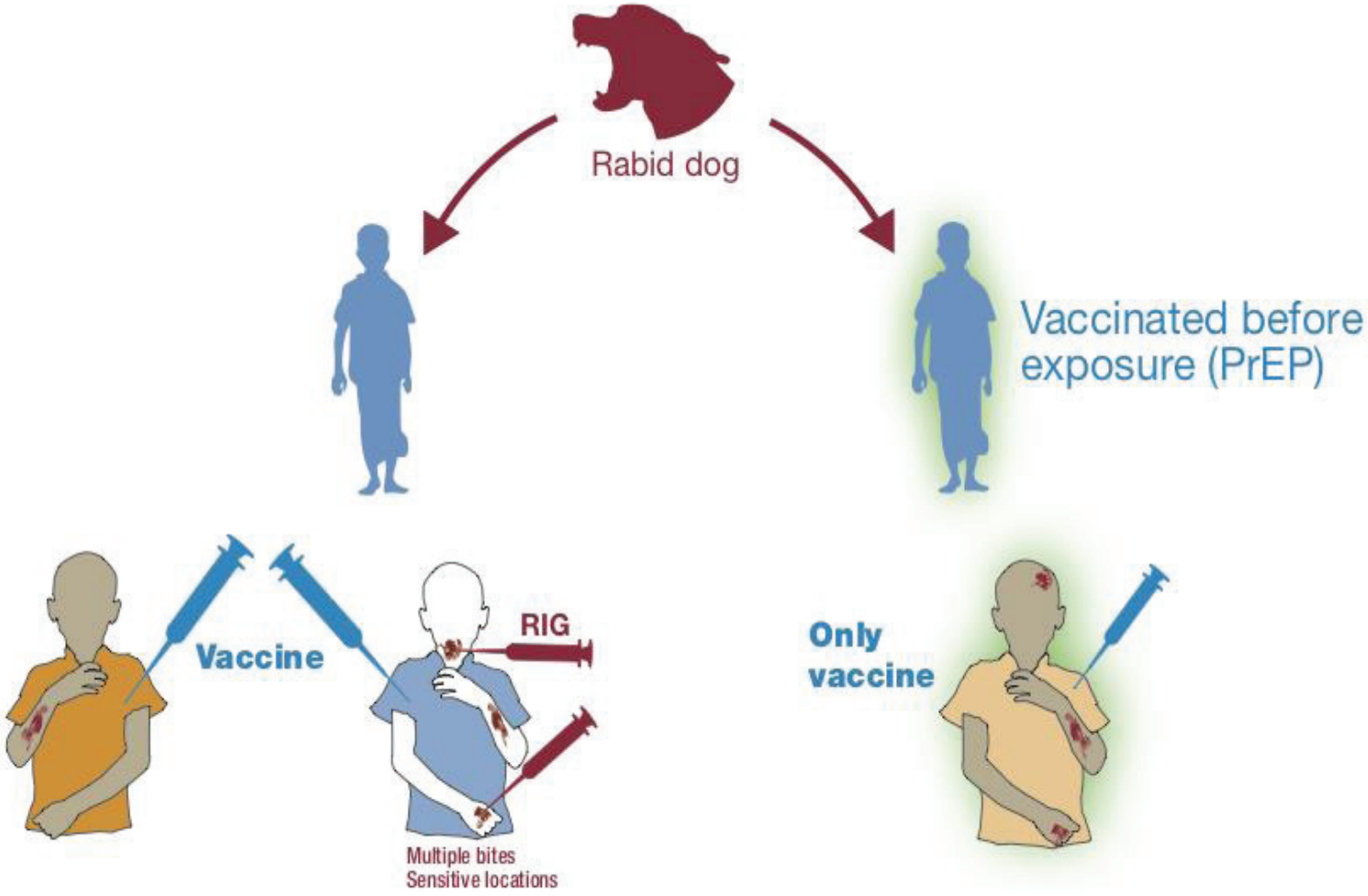
- PrEP should be considered for travelers who will have extensive outdoor activities in remote rural areas, including activities in caves that may lead to direct contact with bats, and where timely access to adequate PEP is not guaranteed.

Precautions

Individuals with a history of severe hypersensitivity to any of the components or to excipients listed by the vaccine manufacturer should receive an alternative rabies vaccine product for PrEP.

Recommended vaccine regimen for PrEP

Dose	Route	Duration	No of Injection Sites Per Clinic Visit	Sites
0.1ml Each site	Intradermal	2 visits (1 week) • Day 0 • Day 7	2 sites 2-0-2-0-0	• Deltoid OR • Lateral thigh



Post-exposure Prophylaxis (PEP)

Annexes

9 Annexes

Annex 1
Laboratory Diagnosis of Rabies

Antemortem diagnosis tests

The sensitivity of these tests depends on the

- Clinical presentation
- Stage of the disease
- Immunological status of the patient and
- Intermittent viral excretion

Detection of viral nucleic acid

Studies have demonstrated that testing at least 3 samples of saliva, taken at 3 to 6-hour intervals, together with a nuchal skin biopsy will help in almost 100% confirmation of an encephalitic case of Rabies. The tests done are for detection of viral nucleic acid, viz.,reverse transcriptase and polymerase chain reaction (RT-PCR) or nucleic acid amplification and detection methods (NASBA). However, a negative test result does not rule out a diagnosis of Rabies.

Detection of anti-rabies antibodies

Detection of anti-rabies antibodies in serum (in unvaccinated individuals) and CSF is also useful especially when the survival is prolonged beyond a week. RFFIT (Rapid fluorescent Focus Inhibition Test) and FAVN (Fluorescent antibody virus neutralization test) are used to detect the neutralizing antibodies and ELISA is used for detection of specific anti-rabies antibodies.

A combination of tests conducted on different samples in a serial order is helpful in antemortem diagnosis of Rabies.

Postmortem diagnosis tests

When brain tissue is available for testing, the commonly used test is FAT (Direct Fluorescent Antibody Test) which detects the rabies virus nucleoprotein antigens in the brain tissue.

Postmortem brain tissue can be obtained by craniotomy. However, brain biopsy is the preferred postmortem sampling technique. This can be done via the orbital or trans-nasal route (samples are obtained from orbitofrontal cortex) using biopsy needles or through the occipital route through the foramen magnum (samples from cerebellum and brain stem) using lumbar puncture needles.

The direct rapid immunochemistry test (DRIT) for detection of viral antigen in the brain tissue is useful for diagnosis of animal rabies and can be done in field conditions. There is no need of a fluorescent microscope for doing this test. Similarly, RDIT (Rapid Immunochromatographic diagnostic test) is available for diagnosis of animal rabies in field conditions. These tests are not adequately validated for diagnosis of human rabies.

When brain tissue is not available for post mortem testing, presence of viral RNA can be tested by nucleic acid amplification techniques from samples obtained by nuchal skin biopsy. However, the sensitivity is less when compared to samples obtained from brain tissue.

Annex 2
Correct Technique of Intradermal Route of Administration

- Intradermal Route of Administration of Tissue Culture Anti Rabies Vaccine was first developed in 1980s. Two regimens (Oxford and Thailand) were initially approved by World Health Organization.
- Thailand red cross (TRC –ID) regimen has been extensively used in countries like Thailand, Philippines, Sri Lanka and India and has proven to be safe and efficacious.
- The advantage of Thai regimen is that this regimen considerably lowers the cost of vaccination against Rabies, as the total volume required is much less than that required for intramuscular regimens.
- IDRV was started in Thailand in 1984. After it was successfully implemented there, WHO approved it for use, especially in developing countries, in 1992.

Situation in Nepal

Nerve Tissue Vaccine (Semple Vaccine)was phased out in Nepal from 2006 onwards. Consequently, only Cell Culture Vaccines are being used in the entire country.
IDRV is being used in Nepal from November 2017. The IPC Regimen (given above) has been approved and will be introduced in the entire country from 2019.

Preparation of a Patient for IDRV

The patient must be made to sit comfortably, and adequate privacy should be ensured especially for female patients. Both the sites of vaccination (deltoid) must be adequately exposed.

Equipment required

- A vial of freeze dried rabies vaccine and diluents
- 2 ml. disposable syringe with needle for reconstitution of vaccine
- Disposable 1 ml syringe. *Preferably an insulin syringe with a fixed needle (28 or more gauge) should be used*
- Disinfectant swabs (e.g.70% ethanol) for cleaning the top of the vial and the patient's skin

Procedure

STEP 1

- Reconstitute the vial of freeze-dried vaccine immediately before administration with the diluent supplied by the manufacturer, using aseptic technique
- With the 1 ml syringe, draw up the volume of vaccine needed to inject at two sites, i.e., 0.2 ml, allowing for any dead space in the syringe. Expel any air bubbles carefully
- If a 100-unit insulin syringe is used, draw up to 20 units
- If a 40-unit insulin syringe is used, draw up to 8 units
- Do not use a 1ml syringe with a detachable needle for administering IDRV, as a small volume of the vaccine remains in the nozzle of the syringe after injecting the vaccine

With the disinfectant swabs clean the patient's skin on both the sites. Allow the disinfectant to dry before administering the vaccine

STEP 2

- Stretch the surface of the skin and insert the tip of the needle, bevel upwards, almost parallel to the skin surface and slowly inject 0.1ml the vaccine into the uppermost layer of skin over the deltoid area (similar to the technique for BCG inoculations).
- If the needle is correctly placed, considerable resistance is felt while injecting the vaccine. A raised papule should begin to appear immediately resulting in a visible & palpable bleb in the skin. Blanching of the skin is also observed.
- Finally, a "peau d' orange" (orange peel) appearance is seen.
- In a similar way inject 0.1 ml of vaccine on the opposite deltoid area
- If the vaccine is injected too deeply into the skin, and a papule is not seen, the needle should be withdrawn and reinserted nearby.
- If there is complete failure to inject intradermally at one site, a single extra intradermal dose should be given in the adjacent area.

- Some difficulty may arise with elderly patients who have thin, inelastic skin, and with infants who are crying.

STEP 3

- Once all doses of vaccine have been injected into the patient discard the needle and the syringe in appropriate infectious disposal bins.

As per the WHO approved regimen, **0.1 ml** of reconstituted vaccine is given per ID site and on two such ID sites per visit on **days 0, 3 ,7**.

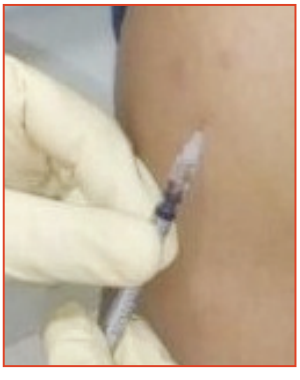


Figure 1 Insertion of needle for ID injection

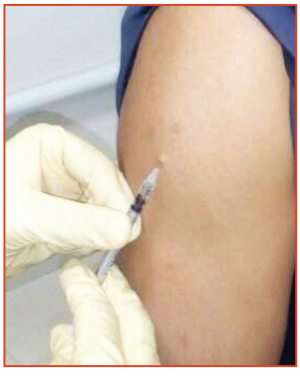


Figure 2 Formation of bleb (papule) after ID injection

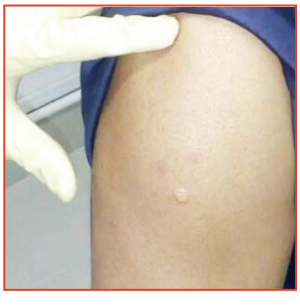


Figure 3 Blanching and 'Peau de Orange' appearance

Storage of reconstituted vaccines

If great care is taken with aseptic technique, an appropriate dose of vaccine may be withdrawn from a vial and the remainder used for another patient, provided that the vial is stored in a refrigerator at + 2° to 8°C. Reconstituted vaccines should be used as soon as possible but at least within 6 to 8 hours if kept at +2° to 8°C.
Discard all unused reconstituted vaccine at the end of 8 hours.

Precautions

A sterile needle and syringe must be used to draw up vaccine for each patient, to prevent cross-infection due to hepatitis, HIV and other infections. Intradermal injections must be administered by staff trained in this technique.

Advice to Patients

- Patients should be advised not to rub at the site of intradermal injection after administration of vaccine.
- They must be advised to complete the full course of vaccine as per the advised schedule.

Annex 3
Method of Infiltration of Rabies Immunoglobulins (RIGs)

- The entire immunoglobulin dose, or as much as anatomically possible, should be infiltrated carefully into or as close as possible to the wound(s) or exposure sites. Multiple needle injections into the wound/s should be avoided.
- The old practice of administering half of the immunoglobulin dose into the wounds and half intramuscularly, should not be followed. Importance must be given to local infiltration of the wounds with RIG.
- RIGs should be carefully infiltrated, without excessive pressure, in areas such as tip of fingers and toes, ear lobe, nose or around the eye, to avoid compartment syndrome.
- Injecting the remaining RIG volume intramuscularly at a distance from the wound provides no or little additional protection against rabies, as compared with infiltration of the wounds.
- If, however, there is a high likelihood that there are additional small wounds (e.g. *if a child does not report all wounds*) or exposure was other than through a bite, 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 for mucosal exposure with no wound and rinsing with RIG can be considered. In the case of suspected exposure to RABV in aerosols, an intramuscular injection of RIG is nevertheless recommended.
- Sometimes there may be multiple or severe wounds due to animal bites. In such cases, the calculated dose of the rabies immunoglobulin may not be sufficient to infiltrate all the wounds. In such situations, the calculated volume of **RIG** should be diluted in **sterile physiological saline** to a volume sufficient to infiltrate all the wounds.
- Infected bite wounds are not a contraindication to administration of rabies immunoglobulins.

Example for Calculation of dose of ERIG

A patient weighing 60 kg, with dog bite wounds on the right forearm and elbow came for treatment to the clinic.

Body Weight	**60 kg**	**60 kg**
Dose (maximum) of eRIG to be administered	**60 x 40 = 2400 IU**	**60 x 40 = 2400 IU**
Each ml. of eRIG contains	**200 IU**	**300 IU**
Volume of eRIG to be used for infiltration of wounds	**2400 ÷ 200 = 12ml**	**2400 ÷ 300 = 8ml**
As patient has multiple wounds the volume is sufficient to infiltrate all the wounds		

Precautions for RIG administration

- The total recommended dose of RIG must never be exceeded as it may suppress the antibody production stimulated by Rabies vaccine. Also, the maximum total dose of RIG to be used are:

  hRIG- 1500 IU

  OR

  eRIG- 3000 IU

- Rabies Immunoglobulin should never be administered in the same syringe or at the same anatomical site as rabies vaccine.
- Rabies Immunoglobulin must never be given intravenously.
- Rabies Immunoglobulin, which is stored in the refrigerator, should be brought to room temperature (25°C to 30°C), before administration to the patient.
- There is no scientific ground for performing a skin test prior to administration of eRIG, as such tests poorly predict severe adverse events and their results should not be the basis for not giving equine immunoglobulin, if it is needed

- If eRIG is being administered, carefully elicit history of any previous administration of horse sera viz. anti-tetanus, anti-diphtheria, anti-gas gangrene, anti-snake venom serum.
- Animal bite victim should be kept under observation for at least half–an–hour after administration of eRIG.

Adverse reactions to RIGs

- The common adverse events are pain, redness & swelling at the site of RIG administration. Sometimes brief rise in body temperature is seen. If RIGs are accidentally injected intravenously, circulatory reactions like shock may be seen.
- The incidence of anaphylactic reaction after administration of eRIG is low (1 in 150,000) and the reaction is generally treatable.
- Centers or clinics where eRIG is administered should always be ready to treat anaphylactic reactions. The dose of adrenaline is 0.5 ml of 0.1 percent solution (1 in 1000, 1mg/ml) for adults and 0.01ml/kg body weight for children, injected subcutaneously or IM. Other emergency drugs and supportive therapy (Oxygen, IV Fluids, anti-histamines) should also be available.
- Serum sickness like reaction may occur, in < 1–3% of recipients, usually 7 to 10 days after injection of eRIG. The clinical manifestations are fever, pruritis, rash, urticaria, erythema, arthralgia and lymphadenopathy. These are relieved by symptomatic treatment.

Annex 4
Switch Over of Vaccine Type or Route of Administration

Switch over from IM to ID route of administration or vice versa and switch over from one type of CCEEV to the other during PEP, is not recommended as a routine. However, in unavoidable circumstances, this can be allowed, to complete the PEP schedule. Schedule of the new route of administration should be adopted, in such a situation (for the remaining doses of the vaccine).

Annex 5
Recording and Reporting Tools

Basic recording and reporting for animal/ dog bites and human rabies prophylaxis is important for information, analysis, feedback including adverse events and informed policy decision making. Five forms will be used for collection of basic and important information:

1. OPD card
2. Animal bite reporting form
3. Human rabies treatment form
4. Monthly reporting form
5. Animal bite investigation form
6. Adverse event reporting form

OPD CARD

Name of the health facility_____
Registration number_____
Name _____
Age/Sex _____
Address _____
Contact number _____
Date of Exposure _____
WHO Category of Exposure: II/III

Intradermal Rabies Vaccine Schedule

Day	Date given	Signature of Staff
0		
3		
7		

Rabies Immunoglobulin: **Given/ Not Given**

Remaks_____

_____

Signature of Medical Officer_____

Instructions for dog bite patients

(to be printed on the reverse of the OPD Card)

1. Wash the wound thoroughly with soap and water for at least 15 minutes.
2. Take Tetanus Toxoid / antibiotics as per your doctor's advice.
3. Do not apply sutures on the wound.
4. There is no diet restriction.
5. Daily bath can be taken
6. Do not take vaccine on an empty stomach
7. Complete the course of vaccination.

ANIMAL BITE REPORTING FORM

Registration no	Victim's										Animal Bite Details														
	Name	Age in yrs	Gender		Address					Contact no	Date bitten			Type of animal 1. Dog 2. Cat 3. Monkey 4. Others (specify)	Was the animal 1. Owned 2. Wild 3. Stray 4. Unknown	Place of animal bite					No of people biten by same animal If yes how many	Has the animal been vaccinated for rabies 1. Yes 2. No 3. Unknown	Animal's sign of disease 1. Agression 2. Hypersalivation 3. Lethargy 4. Biting 5. Paralysed 6. Unknown	Animal's assessment for Rabies 1. Health 2. Sick 3. Dead 4. Unknown	Animal's status 1. Quarantined 2. Dead 3. Euthanized 4. Unknown	If quarantined results after 2 weeks 1. Healthy 2. Dead 3. Unknown
			M	F	Province	District	Palika	Ward	Village		DD	MM	YY			Province	District	Palika	Ward	Village						

HUMAN RABIES TREATMENT FORM

Registration no	Victim's											Details of Exposure										Details of Animal					Treatment History		Current Treatment Details		
	Name	Age in yrs	Gender		Address						Contact no	Place of animal bite					Nature of Exposue 1. Lick 2. Scratch 3. Bite 4. Saliva	Site of eXposure	Was the skin broken? 1. Yes 2. No	Did the wound bleed? 1. Yes 2. No	Number of wounds	Depth of bite	WHO category of exposure (Cat 1, 2 or 3)	Type of animal 1. Dog 2. Cat 3. Monkey 4. Others (specify)	Was the animal 1. Owned 2. Wild 3. Stray 4. Unknown	Was the bite 1. Provoked 2. Unprovoked	No of people biten by same animal If yes how many	Has the animal been vaccinated for rabies 1. Yes 2. No 3. Unknown	History of atleast 2 doses of previous vaccination with ARV (ID or IM for PEP/PrEP)	Has the pt previously received RIG? 1. Yes 2. No	Did the patient receive ID ARV? 1.Yes 2. No	If Yes, number of doses?	Did the patient receive RIG? 1.Yes 2. No
			M	F	Provinc	District	Palika	Ward	Village			Provinc	District	Palika	Ward	Village																

MONTHLY REPORTING FORM

Number of											
		Animal Blte	Dog Bite	Category of exposure				PEP		Human Rabies cases	Death due to Human Rabies
				Cat I	Cat II	Cat III	Unknown	Received Rabies Immunoglobulin	Received Rabies Vaccine		
Age	<15 years										
	≥15 years										
Sex	F										
	M										
TOTAL											

ANIMAL BITE INVESTIGATION FORM

NOTIFICATION

1. Reported on		_____
2. Reported by		_____
3. Contact no		_____
4. Institution	Name	_____
	Place	_____
5. Reason for report	Human exposure	_____
	Sick animal	_____
	Other	_____
6. Type of animal	Domestic	_____
	Stray	_____
	Unknown	_____
7. Location of animal exposure	Province	_____
	District	_____
	Palika	_____
	Village	_____

INVESTIGATION

1. Date of investigation		
2. Type of investigation	Over telephone	_____
	In person	_____
3. How many people were bitten by the animal?		_____
4. How many people started Rabies vaccine?		_____
5.How many people started RIG?		_____
5. How many people did you refer for medical treatment?		_____
6. What other animals were bitten by this animal?		_____
7. Was the animal located?	Yes, If yes	
	Alive	_____
	Dead, killed	_____
	Dead, natural causes	_____
	No	
8. Has the animal been vaccinated for rabies	Yes, year	_____
	If yes, documented?	_____
	No	_____
	Unknown	_____

ASSESSMENT		
1. Signs of disease	Aggression	_____
	Biting	_____
	Hypersalivation	_____
	Paralyzed	_____
	Lethargy	_____
	Others	_____
2. Rabies assessment	Healthy	_____
	Sick, signs of rabies	_____
	Sick, not rabies	_____
	Dead	_____
	Others	_____
3. Assessment decision	Quarantine	_____
	Euthanize	_____
	Dead	_____
	Other	_____
4. If quarantined, results	Healthy after 14 days?	_____
	Yes	_____
	No	_____
5. Was the animal submitted for testing?	Yes	_____
	No	_____

AEFI reporting ID Number: Y/M/00

REPORTING FORM FOR AEFI

Patient's:	**Reporter's:**
Name:	Name:
Age/Sex:	Institution/Designation:
Address:	Address:
Telephone Number:	Telephone Number:
	Date patient notified event:
	Reporting date:

Vaccination Details

Date/Time of vaccination:

Vaccine details:

Name of manufacturer	Dose given	Vaccination site	Route	Vaccine batch no	Vaccine expiry date	Diluent batch no	Diluent expiry date	Reconstitution date and time

Adverse Events

Date/Time AEFI started:

○ Severe Local reactions ▪ Pain ▪ Itching ▪ Redness ▪ Others ○ Fever ≥ 38° C ○ Seizures ○ Febrile ○ Afebrile ○ Others (specify)	Describe AEFI (signs/symptoms):

Serious AEFI: Yes/No, If yes

- ○ Death
- ○ Life threatening
- ○ Hospitalization
- ○ Persistent or significant disability
- ○ Congenital anomaly
- ○ Other medical event (specify)

Outcome ○ Recovering ○ Recovered ○ Recovered with sequelae ○ Not recovering	○ Unknown ○ Dead ○ If died, date of death _____ ○ Autopsy done: **YesNoUnknown**
Past medical history (including history of similar reaction or other allergies), concomitant medication and other relevant information Use additional sheets, if required:	
National level to complete:	
Date report received:	Received by Name: Designation: Institution: Signature:
Comments:	

Annex 6
Frequently Asked Questions (FAQs)

FAQs on RABIES

1. WHAT SHOULD BE DONE WHEN A PERSON REPORTS WITH AN ANIMAL BITE WOUND?

If a person is bitten by an animal:

- Wounds should be washed and flushed immediately with soap and water for 10–15 minutes. If soap is not available, flush with water alone. This is the most effective first-aid treatment against rabies.
- Wounds should be cleaned thoroughly at the health care facility with 70% alcohol or povidone iodine.
- Assess the vaccination status: e.g. whether diphtheria, pertussis, tetanus (DPT) or tetanus toxoid vaccination has been given in the past. Tetanus toxoid should be inoculated when necessary.
- Antimicrobials should be prescribed to prevent possible bacterial infection.

2. WHAT SHOULD NOT BE DONE WITH AN ANIMAL BITE WOUND?

Avoid:

- Covering the wound with dressings or bandages.
- Suturing which facilitates further inoculation of rabies virus.

1. If necessary for closing large wounds, suturing should be done after infiltration of wound with rabies immunoglobulin (RIG). Rabies immunoglobulin of human origin (HRIG) is expensive and only limited amounts are available. Rabies immunoglobulin of equine origin (ERIG) is available in many countries and is considerably cheaper than HRIG.

2. The sutures should be loose and not interfere with free bleeding and drainage. It is well established that secondary suture of bite wounds preferably two weeks after starting vaccination results in better cosmetic outcomes.

3. WHAT ARE THE CLINICAL FEATURES OF RABIES IN DOGS?

Rabies in dogs is characterized by changes to its normal behavior, such as:

- Biting without any provocation
- Running for no apparent reason and eating abnormal items such as sticks, nails, faeces, etc.
- Excessive salivation or foaming at the angles of the mouth – but not hydrophobia
- A change in sound e.g. hoarse barking and growling or inability to make a sound

4. IS SIMPLY OBSERVING THE BITING DOG OR CAT FOR 10 DAYS WITHOUT STARTING TREATMENT JUSTIFIED?

- No! In countries like Nepal, where rabies is prevalent in a large population of dogs and cats, it is compulsory to start treatment immediately after exposure to the dog/cat.
- The biting dog/cat can be kept under 10 days of observation, if possible.

5. WHAT SHOULD BE DONE IF A PERSON IS BITTEN BY A RAT?

- There is no reported case of human rabies due to a rat bite. Most of the times a person is bitten during night time by a rat, while she /he is sleeping on the floor.
- Rats are nocturnal animals and will be moving around during night time for food and it is a normal behavior of the rats to bite during night time. It is not necessary to take PEP in such a situation.

6. IS THERE A SINGLE DOSE RABIES VACCINE WHICH PROVIDES LIFELONG IMMUNITY?

- No! There is no single-dose rabies vaccine available anywhere in the world which can provide lifelong immunity.

7. HOW DOES ID RABIES VACCINATION WORK WHEN THE DOSE IS SO SMALL? DOES IT FULLY PROTECT AGAINST RABIES EXPOSURE?

- The immune response induced by ID rabies vaccination is the same as with the IM regimens. Rabies antigen is inoculated into the dermis of the skin which helps trigger a high immune response. It has been shown that the antigen presenting cells in the skin are more effective than the ones in muscle.

8. IS IT NECESSARY TO PERFORM A SKIN SENSITIVITY TEST WHILE USING ERIG?

- Most ERIG products currently being manufactured are highly purified and the occurrence of adverse events has been significantly reduced. There are no scientific grounds for performing a skin test prior to administering ERIG because testing does not predict reactions, and it should still be given whatever the result of the test.
- The treating physician should be prepared to manage anaphylaxis which, although rare, could occur during any stage of administration. However, some manufacturers of ERIG still recommend performing a skin test. It should be kept in mind that a negative skin test does not guarantee that anaphylaxis would not occur.

9. WHAT IS THE RABIES VACCINATION SCHEDULE FOR PET DOGS?

- Puppies are often obtained from reliable dog breeders where bitches are vaccinated against rabies. These puppies get maternal antibodies against rabies for 3 months. Therefore, it is recommended to vaccinate the puppies at 3 months of age, then at 4 months of age and revaccinate annually.
- If the puppies adopted are street dogs, the first vaccination can be given as early as 2 months, followed by another dose after one month and revaccinate annually.

10. WHAT SHOULD BE DONE IF A PERSON IS BITTEN BY A MONKEY?

- Monkeys are mammals, but rarely transmit rabies. However, based on the Category of Exposure, PEP can have given to a person who reports with a monkey bite.

11. A PERSON IS BITTEN ON THE LEFT SHOULDER BY A STRAY DOG IN A VILLAGE, ABOUT 2 MONTHS BACK. HE HAS TAKEN HERBAL TREATMENT FOR THE SAME AND HAS NOT TAKEN ANY PEP. HE REPORTS TO THE DISTRICT HOSPITAL WITH HYDROPHOBIA AND DIES AFTER 4 DAYS. ANOTHER PERSON/ HIS FRIEND WAS BITTEN BY THE SAME DOG ON HIS LEFT LEG AT THE SAME TIME AS THE ONE WHO DIED. HE REPORTS TO THE DISTRICT HOSPITAL AFTER HE KNEW THAT HIS FRIEND DIED. HE IS CLINICALLY FINE. HE DID NOT TAKE ANY PEP AFTER THE DOG BITE. HE REQUESTS THE DOCTOR TO GIVE SOME TREATMENT TO HIM. WHAT MUST BE DONE?

- The second person was bitten by the same dog, which is a suspected rabid dog. Though 2 months have lapsed, he has to be given PEP, in view of the fact that the dog is not available for observation and another person bitten by the same dog died with rabies.
- The incubation period of rabies is variable. Therefore, this patient has to be given PEP. RIG has to be given at the site of the bite, though the wound has healed. This has to be followed by a full course of vaccination.

12. A BUFFALO HAS DIED IN A VILLAGE A FEW WEEKS AFTER BEING BITTEN BY A STRAY DOG. THE VILLAGERS SUSPECT THAT THE BUFFALO DIED OF RABIES AND MANY OF THEM VISIT THE PHC AND ASK THE STAFF TO GIVE THEM VACCINE SHOTS. WHAT MUST BE DONE?

- There is no reported case of transmission of rabies by consumption of milk of a rabid buffalo or cow. These people do not require PEP. Moreover, the traditional practice of boiling milk before consumption kills many bacteria and viruses which may be present in the milk. These people have to be reassured and need not be given PEP.

13. WHAT SHOULD BE DONE IF A PERSON IS BITTEN BY A BAT IN NEPAL?

- There is no evidence-based information on human rabies cases due to bat exposure in Nepal. No PEP is required. The person can be asked to wash the wounds and has to be reassured.
- He/she must be advised not to play with or handle sick or dead bats.

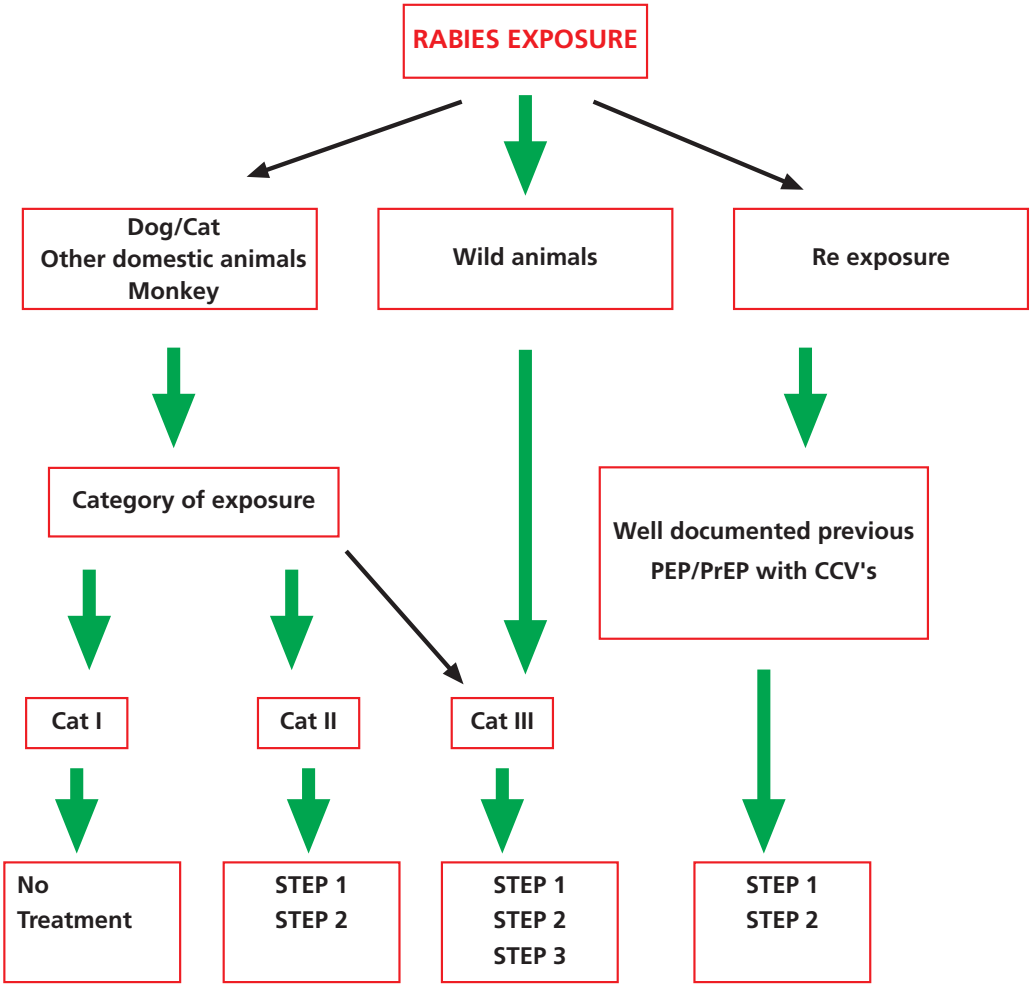
14. IF A RABID ANIMAL BITE VICTIM TAKES 1st DOSE OF IDRV ON DAY 0 AND MISSES ON DAY 3, BUT TURN UPS ON DAY 6 , SHOULD THE IDRV REGIMEN BE RESTARTED FROM 1st DOSE OR 2nd DOSE SHOULD BE GIVEN AT ANYTIME OF HIS VISIT? WHEN SHOULD THE 3rd DOSE BE GIVEN IN THE GIVEN SCENARIO?

- The 2nd dose should be given on day 6, (when the patient comes) and the 3rd dose to be given on day 10 (4 days after the 2nd dose). Be sure that the patient has been given RIG on day 6, if he has not received on day 0.

15. A PERSON IS BITTEN BY A STRAY DOG AND COMES FOR TREATMENT ON THE NEXT DAY.THE PATIENT TAKES THE 1ST DOSE OF VACCINE (IDRV) AFTER LOCAL WOUND TREATMENT. THE PATIENT DOES NOT REPORT ON DAY 3. THE PATIENT COMES ON DAY 9 AND INFORMS THAT THE DOG HAS DIED.WHAT IS TO BE DONE?

- Administer RIG immediately, even if the wounds are healing or healed. Start vaccination (IDRV) again. Complete the full course of vaccine, i.e., give 3 doses of vaccine starting from this date.

Annex 7
Decision tree guide to PEP



STEP 1	LOCAL WOUND TREATMENT
STEP 2	RABIES VACCINE
STEP 3	RABIES IMMUNOGLOBULIN

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