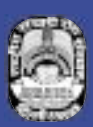
National Guidelines for Rabies Prophylaxis and Intra-dermal Administration of Cell Culture Rabies Vaccines

2007



National Institute of Communicable Diseases
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India
New Delhi

सत्यमेव जयते

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MESSAGE

Rabies continues to be a public health problem in India. The exact magnitude of animal bites in the country is not reliably known though some studies have estimated it to be as high as 17 million per annum. Government of India has banned the production and use of Nervous Tissue Vaccine (NTV) in December, 2004 which was the vaccine widely used in the public sector. With the stoppage of NIV, the availability and affordability of modern Cell Culture Vaccine became a major issue with many States. With the recommendations of WHO, National experts and ICMR study on the use of intradermal vaccines, National Regulatory Authority has permitted the use of this economical and efficacious route in India also. To operationalise the implementation of id route there was an urgent need to develop national guidelines for ID implementation, NICD convened expert group meeting and framed these guidelines.

I congratulate Director, NICD and his team for bringing out these guidelines. I am very optimistic that these guidelines will be extremely useful to the States to address the issue of use of Anti-Rabies Vaccine.

(Dr. R.K. Srivastava)

Preface

Rabies continues to be a major public health problem killing an estimated 20,000 people in India annually. This virtually cent percent fatal disease is nearly hundred percent preventable by timely and appropriate post-exposure treatment.

Based on vaccine utilisation approximately 3 million people receive post-exposure treatment in the country. Production and use of reactogenic Nervous Tissue Vaccine has been stopped since December 2004. Modern, safe and effective anti-rabies Cell Culture Vaccines (CCVs) are being used for post-exposure prophylaxis. Higher cost and limited availability are limiting factors for its wider use. To overcome these problems, WHO recommended the use of intra-dermal (ID) route of administration of CCVs which not only reduces the cost of post-exposure prophylaxis but also allows wider coverage in available quantity of vaccines.

Considering the recommendations of experts, results of clinical trials and international experience Drug Controller General of India approved the use of ID route of administration of CCVs in February 2006. However, need was felt to have revised guidelines for animal bite management including correct technique of intra-dermal inoculation of CCVs for its easier and wider implementation. An expert group meeting was held at NICD, Delhi to formulate the guidelines. The participants in the meeting included practitioners managing anti-rabies clinics, laboratory medicine practitioners, policy makers, public health experts and vaccine producers from both public and private sector. The guidelines, which emerged out of consensus deliberations of the expert group, have been brought out in this publication.

It is sincerely hoped that the publication will be of immense use for managing the animal bites and using ID route of inoculation of CCVs. The financial help received from WHO for this publication is thankfully acknowledged.

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Introduction

Rabies is an acute viral disease which causes fatal encephalomyelitis in virtually all the warm blooded animals including man. The virus is found in wild and some domestic animals, and is transmitted to other animals and to humans through their saliva (i.e. bites, scratches, licks on broken skin and mucous membrane). In urban areas, the disease is mainly transmitted by dogs, being responsible for about 96% of animal bite cases.

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

An expert group meeting for reviewing and finalising the guidelines for management of animal bite cases was held at National Institute of Communicable Diseases, Delhi. Following this, the national guidelines for management of animal bites were formulated in 2002 to bring out uniformity in post-exposure prophylaxis practices. Until recently the Nervous Tissue Vaccine (NTV) was the mainstay for post-exposure prophylaxis. As per WHO recommendations, the production and use of this reactogenic vaccine has been stopped since December 2004 in our country. Modern Cell Culture Vaccines (CCV) are now being used for post-exposure prophylaxis. Higher cost of intra-muscular administration of CCV is a limiting factor for its wider use. To overcome this problem, WHO has recommended use of efficacious, safe and feasible intra-dermal (ID) route of inoculation of CCVs. Sri Lanka, Thailand and Philippines have successfully adopted ID route of administration of CCV against rabies as part of their policy. Clinical trials conducted in India have proved intra-dermal route to be safe, efficacious and feasible for use in the country. National authorities after expert consultation have approved the use of ID route for administration of CCVs in the country in phased manner. Hence, the guidelines of animal bite management have been reviewed and revised with inclusion of correct technique of ID inoculation of anti-rabies CCVs.

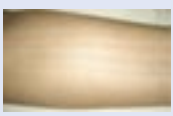
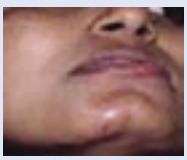
Post-Exposure Prophylaxis (PEP)

2.1 Decision to treat

In rabies endemic country like India, where every animal bite is potentially suspected as a rabid animal bite the treatment should be started immediately. Because of long incubation period, which is typical of most cases of human rabies, it is possible to institute prophylactic post-exposure treatment. This must be started at the earliest to ensure that the individual will be immunised before the rabies virus reaches the nervous system. However, people who present for treatment even months after a possible rabies exposure should be evaluated and treated as if the event had occurred recently.

To bring out uniformity globally, the classification of animal bite for post-exposure prophylaxis has been based on WHO recommendations (Table 1).

Table 1: Type of contact, exposure and recommended post-exposure prophylaxis

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

Vaccination status of the biting animal: Although unvaccinated animals are more likely to transmit rabies, vaccinated animals can also do so if the vaccination of the biting animal was ineffective for any reason. A history of rabies vaccination in an animal is not always a guarantee that the biting animal is not rabid. Animal vaccine failures may occur because of improper administration or poor quality of the vaccine, poor health status of the animal, and the fact that one vaccine dose does not always provide long-lasting protection against infection in dogs.
Provoked versus unprovoked bites: Whether a dog bite was provoked rather than unprovoked should not be considered a guarantee that the animal is not rabid as it can be difficult to understand what an attacking dog considers provocation for an attack.

Observation of biting animal: The treatment should be started immediately after the bite. The treatment may be modified if animal involved (dog or cat) remains healthy throughout the observation period of 10 days by converting post-exposure prophylaxis to pre-exposure vaccination by skipping the vaccine dose on day 14 and administering it on day 28 while using Essen Schedule. The observation period is valid for dogs and cats only. The natural history of rabies in mammals other than dogs or cats is not fully understood and therefore the 10-day observation period may not be applicable.

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

Bite by rodents: It should be noted that bites by domestic rats, mice, squirrel, hare and rabbits seldom require treatment.

Bat rabies: Bat rabies has not been conclusively proved in India and hence exposure to bats does not warrant treatment.

Special circumstances: Pregnancy, lactation, infancy, old age and concurrent illness are no contra indications for rabies post-exposure prophylaxis in the event of an exposure. Post-exposure prophylaxis against rabies takes preference over any other consideration since it is a life saving procedure. Moreover, rabies vaccine does not have any adverse effect on fetus, mother-to-be and the course of pregnancy. Hence complete post-exposure treatment should be given depending on the category of the exposure.

Post-exposure prophylaxis of immuno compromised patients: Several studies of patients with HIV/AIDS have reported that those with low CD4 (<200 counts) will mount a significantly lower or no detectable neutralising antibody response to rabies. In such patients and those in whom the presence of immunological memory is no longer assured as a result of other causes, proper and thorough wound management and antisepsis accompanied by

local infiltration of rabies immunoglobulins followed by anti-rabies vaccination are of utmost importance. Even immuno compromised patients with category II exposures should receive rabies immunoglobulin in addition to a full post-exposure vaccination. Preferably, if the facilities are available, anti-rabies antibody estimation should be done 10 days after the completion of course of vaccination.

Human-to-human transmission: The risk of rabies transmission to other humans from a human rabies case is very minimal and there has never been a well documented case of human-to-human transmission, other than the few cases resulting from organ transplant. However, people who have been exposed closely to the secretions of a patient with rabies may be offered PEP as a precautionary measure.

It is reemphasised that treatment should be started as early as possible after exposure. However, it should not be denied to person reporting late for treatment as explained previously.

2.2 Approach to Post-Exposure Prophylaxis (PEP)

The post-exposure prophylaxis is a three pronged approach. All three carry equal importance and should be done simultaneously as per the category of the bite (4. Decision tree: Guide to Post-Exposure Prophylaxis).

- Management of animal bite wound
- Passive immunisation: Rabies Immunoglobulins (RIG)
- Active immunisation: Anti-Rabies Vaccines (ARV)

2.2.1 Management of animal bite wound

Wound toilet: Since the rabies virus enters the human body through a bite or scratch, it is imperative to remove as much saliva, and thereby the virus, from the wound as is possible by an efficient wound toilet that should not involve additional trauma. Since the rabies virus can persist and even multiply at the site of bite for a long time, wound toilet must be performed even if the patient reports late. (Table 2)

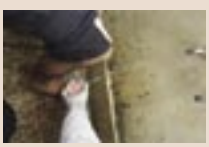
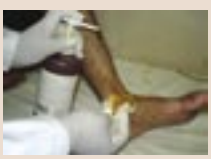
This can be done by prompt and gentle thorough washing with soap or detergent and flushing the wound with running water for 10 minutes. If soap and detergent are not immediately available wash with running water for at least 10 minutes. Avoid direct touching of wounds with bare hands. Considering the importance of this step the anti-rabies clinics should have wound washing facilities.

The application of irritants (like chilies, oil, turmeric, lime, salt, etc) is unnecessary and damaging. In case irritants have been applied on the wound, enough gentle washing with soap or detergent to remove the extraneous material especially oil should be done followed by flushing with copious amount of water for 10 minutes immediately.

It should be noted that the immediate washing of the wound is a priority. However, the victim should not be deprived of the benefit of wound toilet as long as there is an unhealed wound which can be washed even if the patient reports late. The maximum benefit of the wound washing is obtained when fresh wound is cleaned immediately.

Application of antiseptics: After thorough washing and drying the wound, any one of the available chemical agents should be applied viz Povidone iodine (Betadine), Alcohol, Chloroxylenol (Dettol), Chlorhexidine Gluconate and Cetrimide solution (Savlon - in appropriate recommended dilution), etc.

Table 2: Wound Management

Do's		
Physical	Wash with running tap water 	Mechanical removal of virus from the wound
Chemical	Wash the wound with soap and water  Apply disinfectant 	Inactivation of the virus
Biological	Infiltrate immunoglobulins in the depth and around the wound in Category III exposures 	Neutralisation of the virus
Don'ts		
• Touch the wound with bare hand • Apply irritants like soil, chilies, oil, herbs, chalk, betel leaves etc.		

Local infiltration of rabies immunoglobulins: In category III bites rabies immunoglobulins should be infiltrated in the depth and around the wound to inactivate the locally present virus as described below.

Suturing of wound should be avoided as far as possible. If surgically unavoidable, minimum loose sutures should be applied after adequate local treatment along with proper infiltration of rabies immunoglobulins.

Cauterisation of wound is no longer recommended as it leaves very bad scar, and does not confer any additional advantage over washing the wound with water and soap.

Injection tetanus toxoid should be given to the un-immunised individual. To prevent sepsis in the wound, a suitable course of an **antibiotic** may be recommended.

2.2.2 Rabies Immunoglobulins (RIG)

The anti-rabies serum/rabies immunoglobulin provides passive immunity in the form of ready-made anti-rabies antibody to tide over the initial phase of the infection. Anti-rabies serum or RIG has the property of binding with the rabies virus, thereby resulting in the loss of infectivity of the virus.
Two types of RIGs are available:

Equine Rabies Immunoglobulins (ERIG): ERIG is of heterologous origin raised by hyper-immunisation of horses. However, currently manufactured ERIGs are highly purified and the occurrence of adverse events has been significantly reduced. Still these should be administered after sensitivity test.

Human Rabies Immunoglobulins (HRIG): HRIG are free from the side effects encountered in a serum of heterologous origin, and because of their longer half life, are given in half the dose of equine anti-rabies serum.

The anti-rabies sera should always be brought to room temperature (20 – 25°C) before use.

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

Administration of immunoglobulins: As much of the calculated dose of RIG as is anatomically feasible should be infiltrated into and around the wounds.

Multiple needle injections into the wound should be avoided. Remaining, if any, after all wounds have been infiltrated, should be administered by deep intramuscular injection at an injection site distant from the vaccine injection site. Animal bite wounds inflicted can be severe and multiple, especially in small children. In such cases, the calculated dose of the rabies immunoglobulin may not be sufficient to infiltrate all wounds. In these circumstances, it is advisable to dilute the immunoglobulins in sterile normal saline 2 to 3 fold to be able to permit infiltration of all wounds. The total recommended dose of immunoglobulin must not be exceeded as it may suppress the antibody production by the vaccine.

If immunoglobulin was not administered when vaccination was begun, it can be administered upto the seventh day after the administration of the first dose of vaccine. Beyond the seventh day, Rabies Immunoglobulin (RIG) is not indicated since an antibody response to anti-rabies vaccine is presumed to have occurred.

Immunoglobulin should never be administered in the same syringe or at the same anatomical site as vaccine.

Sensitivity test before administration of ERIG: With antisera of equine origin, anaphylactic shock may occur and thus sensitivity testing is mandatory before giving ERIG. Skin test may be performed as per the manufacturers instructions given in the product insert. Otherwise general guidelines are described in Table 3.

Table 3: Skin testing prior to administration of ARS/ERIG

- Inject 0.1 ml ERIG diluted 1:10 in physiological saline intra-dermally into the flexor surface of the forearm to raise a bleb of about 3-4 mm diametre.
- Inject an equal amount of normal saline as a negative control on the flexor surface of the other forearm
- After 15 minutes an increase in diametre to > 10 mm of induration surrounded by flare is taken as positive skin test, provided the reaction on the saline test was negative.
- An increase or abrupt fall in blood pressure, syncope, hurried breathing, palpitations and any other systemic manifestations should be taken as positive test

A negative skin test must never reassure the physician that no anaphylactic reaction will occur. Those administering ERIG should always be ready to treat early anaphylactic reactions with adrenalin. The dose is 0.5 ml of 0.1 percent solution (1 in 1000, 1mg/ml) for adults and 0.01 ml/kg body weight for children, injected subcutaneously or IM. If patient is sensitive to ERIG, HRIG should be used.

Approach to a patient requiring rabies immunoglobulin when none is available: In circumstances where no immunoglobulin are available greater emphasis should be given to proper wound toileting followed by Essen Schedule of

Cell Culture Vaccine with double dose on day 0 at 2 different sites intramuscularly (0 day – 2 doses on left and right deltoid, 3, 7, 14 and 28 days). It is emphasised that doubling the first dose of CCV is not a replacement to RIG. A full course of vaccine should follow thorough wound cleansing and passive immunisation.

Tolerance and side effects: With RIG, there may be transient tenderness at the injection site and a brief rise in body temperature which do not require any treatment. Skin reactions are extremely rare. RIG must never be given intravenously since this could produce symptoms of shock, especially in patients with antibody deficiency syndromes.

Serum sickness occurs in 1% to 6% of patients usually 7 to 10 days after injection of ERIG, but it has not been reported after treatment with HRIG.

2.2.3 Anti-Rabies Vaccines

Active immunisation is achieved by administration of safe and potent CCVs. In India, NTV was used for post-exposure treatment in public sector. However, as this vaccine was reactogenic, the production was stopped in December, 2004. CCVs are now used for active immunisation.

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

Storage and transportation: Though most Cell Culture Vaccines are marketed in freeze dried (lyophilised) form which is more tolerant of vagaries of temperature, yet it is recommended that these vaccines should be kept and transported at a temperature range of 2-8°C. Freezing does not damage the lyophilised vaccine but there are chances of breakage of ampoule containing the diluent. Liquid vaccines should never be frozen.

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

Adverse effects with Cell Culture Vaccines: The Cell Culture Vaccines 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. The general adverse reactions include sore arm, headache, malaise, nausea, fever and localised oedema at the site of injection. Symptomatic treatment may be needed.

Switch over from one brand/type of vaccine to the other: Shifting from one brand/type of CCV to other brand/type should not be encouraged as literature supports that good immunity is best achieved with same brand. However under unavoidable circumstances, available brand/type may be used to complete PEP.

Protective level of anti-rabies antibody: Humoral antibodies play important role in protection against rabies and a titre of 0.5 IU/ml or more in serum as tested by Rapid Fluorescent Focus Inhibition Test (RFFIT) is considered as protective.

Currently available CCVs could be administered by IM regimen or approved CCVs could be administered by ID regimen.

2.2.3.1 Intra-muscular (IM) Regimen

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

Vaccines

1. Cell Culture Vaccines
   - Human Diploid Cell Vaccine (HDCV): Produced locally in private sector
   - Purified Chick Embryo Cell Vaccine (PCEC): Produced locally in private sector
   - Purified Vero Cell Rabies Vaccine (PVRV): Imported and produced locally in public & private sector
2. Purified Duck Embryo Vaccine: Produced locally in private sector

Regimen

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

Site of inoculation: The deltoid region is ideal for the inoculation of these vaccines. Gluteal region is not recommended because the fat present in this region retards the absorption of antigen and hence impairs the generation of optimal immune response. In case of infants and young children antero-lateral part of the thigh is the preferred site.

2.2.3.2 Intra-dermal (ID) Regimens

Concept of intra-dermal inoculation of anti-rabies vaccines (IDRV): Intra-dermal regimens consist of administration of a fraction of intramuscular dose of certain rabies vaccine on multiple sites in the layers of dermis of skin. The vaccines used are same; however route, dose and site of administration differ. The use of intra-dermal route leads to considerable savings in terms of total amount of vaccine needed for full pre- or post- exposure vaccination, thereby reducing the cost of active immunisation. Single dose (0.5ml/1ml) of rabies vaccine/antigen when given by IM route gets deposited in the muscles. There after the antigen is absorbed by the blood vessels and is presented to antigen presenting cells which triggers immune response. Whereas, while using ID route, small amount (0.1ml) of rabies vaccines/antigen is deposited in the layers of the skin at multiple sites. The antigen is directly presented to the antigen presenting cells (with out circulation/dilution in blood) at multiple sites triggering a stronger immune response.

Mechanism of action of IDRV: Intra-dermal inoculation is deposition of approved rabies vaccine (or antigen) in the layers of dermis of skin. Subsequently the antigen is carried by antigen presenting cells via the lymphatic drainage to the regional lymph nodes and later to the reticulo-endothelial system eliciting a prompt and highly protective antibody response. Immunity is believed to depend mainly upon the CD 4 + T-cell dependent neutralising antibody response to the G protein. In addition, cell-mediated immunity has long been reported as an important part of the defense against rabies. Cells presenting the fragments of G protein are the targets of cytotoxic T- cells and the N protein induced T helper cells. The immune response induced by IDRV is adequate and protective against rabies.

General guidelines for use of IDRV

- Vaccines to be applied by intra-dermal route of administration should be approved by DCGI.
- The vaccine package leaflet should include a statement indicating that the potency as well as immunogenicity and safety allow safe use of vaccine by ID pre- and post-exposure.
- Post Marketing Surveillance (PMS) data should be maintained for minimum of two years by vaccine manufacturers on a pre-designed and approved protocol.
- Intra-dermal injections must be administered by staff trained in this technique.
- Vaccine vials must be stored at 2° to 8°C after reconstitution.
- The total content of reconstitute vial should be used as soon as possible, but at least with in 8 hours.
- All the reconstituted vaccines should be discarded after 8 hours of reconstitution and at the end of the day

- Rabies vaccines formulated with an adjuvant should not be administered intra-dermally.
- Vaccine when given intra-dermally should raise a visible and palpable bleb in the skin.
- In the event that the dose is inadvertently given subcutaneously or intra-muscularly or in the event of spillage, a new dose should be given intradermally in near by site.
- Animal bite victims on chloroquine therapy (anti-malarial therapy) should be given ARV by intramuscular route.

Vaccines and regimen approved for ID use in the country

Considering the recommendations on intra-dermal application of rabies by WHO and results of safety, efficacy and feasibility trials conducted in India, Drug Controller General of India (DCGI) approved the use of reduced dosage intra-dermal vaccination regimen for rabies post-exposure prophylaxis. The use of this route leads to considerable savings in terms of the total amount of vaccine needed for a full post-exposure vaccination, thereby reducing the cost of active immunisation.

The following have been approved by DCGI currently for use by intra-dermal route. Vaccines

PVRV – Verorab, Aventis Pasteur (Sanofi Pasteur) India Pvt. Ltd.
PCECV – Rabipur, Chiron Behring Vaccines Pvt. Ltd.
PVRV – Pasteur Institute of India, Coonoor
PVRV – Abhayrab, Human Biologicals Institute.

Potency of approved vaccines: The vaccines should have stated potency of > 2.5 IU per IM dose, irrespective of reconstituted volume. The same vaccine is used for ID administration as per stated schedule. 0.1ml of vaccine, irrespective of reconstituted volume, is administered per ID site as per schedule below.

Regimen

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

This involves injection of 0.1ml of reconstituted vaccine per ID site and on two such ID sites per visit (one on each deltoid area, an inch above the insertion of deltoid muscle) on days 0, 3, 7 and 28. The day 0 is the day of first dose administration of IDRV and may not be the day of rabies exposure/animal bite.

Maintenance of vaccine vial in use

- Use aseptic technique to with draw the dose
- Store in a refrigerator at 2°C to 8°C
- Reconstituted vaccines should be used as soon as possible or within 6 to 8 hours if kept at 2°C to 8°C. All unused reconstituted vaccine at the end of 6-8 hours must be discarded.

Materials required

- A vial of rabies vaccine approved for IDRV and its diluent.
- 2 ml disposable syringe with 24 G needle for reconstitution of vaccine.
- Disposable 1 ml (insulin) syringe (with graduations upto 100 or 40 units) with a fixed (28 G) needle (Fig.1)
- Disinfectant swabs (e.g. 70% ethanol, isopropyl alcohol) for cleaning the top of the vial and the patients' skin.

Fig.1: 1ml syringe with hypodermic needle (Insulin syringe)

ID injection technique

Using aseptic technique, reconstitute the vial of freeze-dried vaccine with the diluent supplied by the manufacturer. With 1 ml syringe draw 0.2 ml (up to 20 units if a 100 units syringe is used or upto 8 units if a 40 units syringe is used) of vaccine needed for one patient (i.e. 0.1 ml per ID site X 2 sites) and expel the air bubbles carefully from the syringe thereby removing any dead space in the syringe.

Using the technique of BCG inoculation, stretch the surface of the skin and insert the tip of the needle with bevel upwards, almost parallel to the skin surface (Fig.2) and slowly inject half the volume of vaccine in the syringe (i.e. 0.1ml; either 10 or 4 units) into the uppermost dermal layer of skin, over the deltoid area, preferably an inch above the insertion of deltoid muscle. If the needle is correctly placed inside the dermis, considerable resistance is felt while injecting the vaccine. A raised papule should begin to appear immediately causing a peau d' orange (orange peel) appearance (Fig.3). Inject the remaining half the volume of vaccine (i.e. 0.1ml; either 10 or 4 units) on the opposite deltoid area.

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

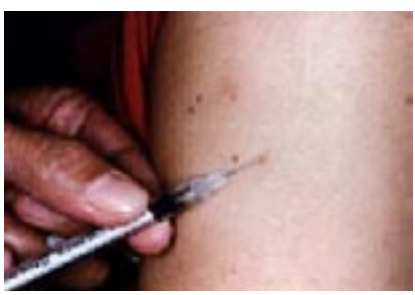


Fig.2: Insertion of needle for ID inoculation

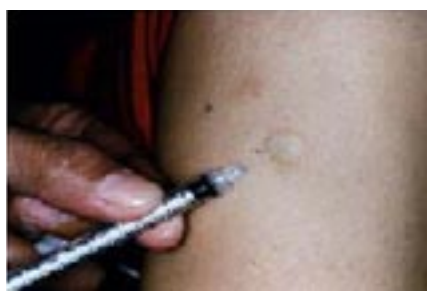


Fig. 3: Bleb raised on ID inoculation

Anti-rabies treatment centres which meet the following criteria may use ID administration :

- Have adequately trained staff to give ID inoculation of anti-rabies vaccine
- Can maintain cold chain for vaccine storage
- Ensure adequate supply of suitable syringes and needles for ID administration
- Are adequately well versed in management of open vial and safe storage practices.

2.3 Post-Exposure Prophylaxis for previously vaccinated persons

Managing re-exposure following post-exposure treatment with TCV: If re-exposed, persons who have previously received full post-exposure prophylaxis (either by IM or ID route) with a potent cell-culture vaccine should now be given only two booster doses, intramuscularly (0.5ml/1ml)/intra-dermally (0.1 ml at 1 site) on days 0 and 3. Proper wound toilet should be done. Treatment with RIG is not necessary.

Managing exposure following pre-exposure prophylaxis with TCV: If after recommended pre-exposure prophylaxis, a vaccinated person is exposed to rabies, a proper wound toileting should be done and two IM/ID (0.1 ml at 1 site) doses of Cell Culture Vaccine be given on days 0 and 3. Treatment with RIG is not necessary

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

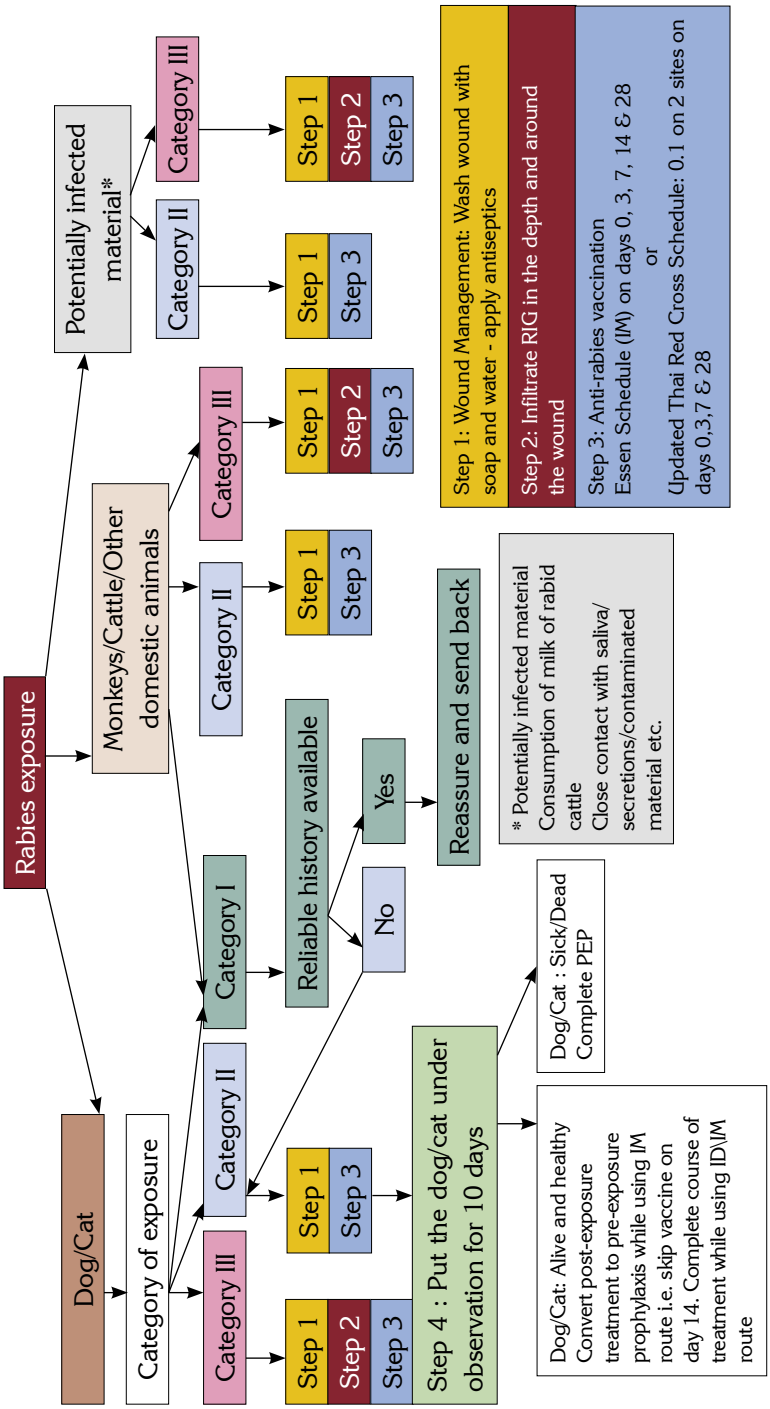
3

Pre-exposure Vaccination

Pre-exposure vaccination may be offered to high risk groups like laboratory staff handling the virus and infected material, clinicians and persons attending to human rabies cases, veterinarians, animal handlers and catchers, wildlife wardens, quarantine officers and travelers from rabies free areas to rabies endemic areas. Pre-exposure vaccination is administered as one full dose of vaccine intramuscularly or 0.1 ml intra-dermally on days 0, 7 and either day 21 or 28.

Laboratory staff and others at high continuing risk of exposure should have their neutralising antibody titres checked every 6 months. If it is less than 0.5 IU/ml a booster dose of vaccine should be given. Such individuals on getting exposed to rabies virus after successful pre-exposure immunisation require only two booster injections of vaccine given on days 0 and 3 without any anti-rabies serum/RIGs.

Decision Tree: Guide to Post-Exposure Prophylaxis (PEP)



Formulation of National Guidelines for Intra-Dermal Inoculation of Anti-Rabies Cell Culture Vaccines

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Finalisation of Draft of National Guidelines on Animal Bite Management and Intra-Dermal Inoculation of Anti-Rabies Cell Culture Vaccines

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