Guidelines on Rabies Prophylaxis

National Rabies Control Programme

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DIRECTORATE OF HEALTH SERVICES

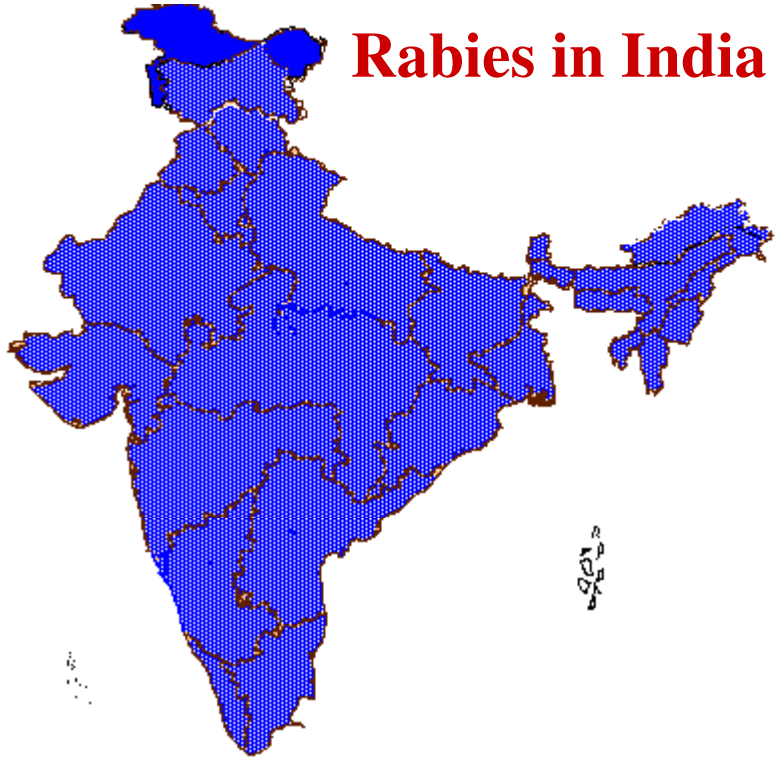
GOVT. OF WEST BENGAL

2019

Introduction

- 20,000 Deaths, 17.4 million animal bite cases annually. (APCRI 2004)
- India accounts for 36% of the Global and 65% of the Asian human rabies deaths.
- No age or sex predilections (higher incidence of animal bites and rabies deaths among children and adult males).
- 96% of human rabies cases are due to bites from Rabid dogs.

Rabies is reported from all states except Lakshadweep and the Andaman & Nicobar Islands.



1. POPULATION OVER 1 BILLION
2. LAND AREA 3.28 MILLION SQ. KM.
3. SHARES BORDER WITH CHINA, PAKISTAN, BHUTAN, NEPAL, MYANMAR AND BANGLADESH
4. 29 STATES AND 6 UTs
5. RABIES ENDEMIC

Decision to treat

- Disease is endemic in India
- Suspect all animal bites
- Treat as per merits of the bite

Observation of animals

- Valid only for dogs and cats
- Start treatment and observe
- Modify PEP

Vaccination Status of Animal

- Unvaccinated animals are more likely to transmit rabies
- Vaccinated animals can transmit if the vaccination ineffective for any reason.
  - improper administration
  - poor quality of the vaccine
  - poor health status of the animal
- One dose does not provide long-lasting immunity.
- Appropriate documentation
- Proper history

Animal Transmitting rabies in India

Domestic :-

- ❖Dogs & Cats

Wild :-

- ❖Foxes & Jackals
- ❖Monkeys
- ❖Mongoose
- ❖Bears

Peridomestic :-

- ❖Cows & Buffaloes
- ❖Sheep & Goats
- ❖Pigs
- ❖Donkeys
- ❖Horses
- ❖Camels

Courtesy of Dr. P. Kitching, England

Rabid Goat

Not reported :-

- ❖Bats*
- ❖Rodents*
- ❖Birds
- ❖Squirrel

All exposures in wild are considered as category III exposures.

*** Bite by Bats or Rodents do not ordinarily necessitate rabies vaccination. However, bites by Bats or rodents in unusual circumstances may be considered for vaccination in consultation with an expert in the field of rabies.**

PEP of immune-compromised patients

- Patients with low CD4 (<200 counts), chemotherapy, steroid therapy, cancer patients, etc mount a significantly lower or no response
- Proper and thorough wound management and antisepsis
- Local infiltration of RIG
- Complete course of ARV by IM route in category II and III exposures
- Anti-rabies antibody estimation 14 days after the completion of course to assess the need of additional doses of vaccine.

Mode of Transmission

Common Modes:-

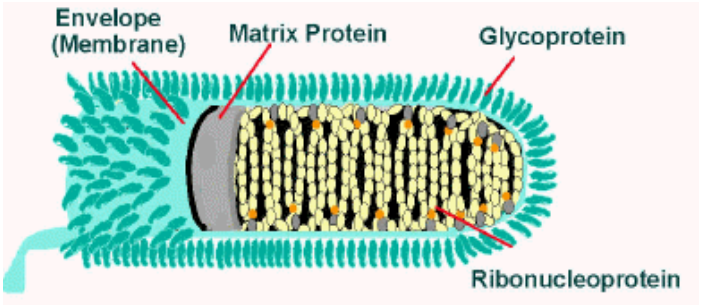
- ❖ Animal Bites
- ❖ Licks on abraded skin/mucosa
- ❖ Scratches

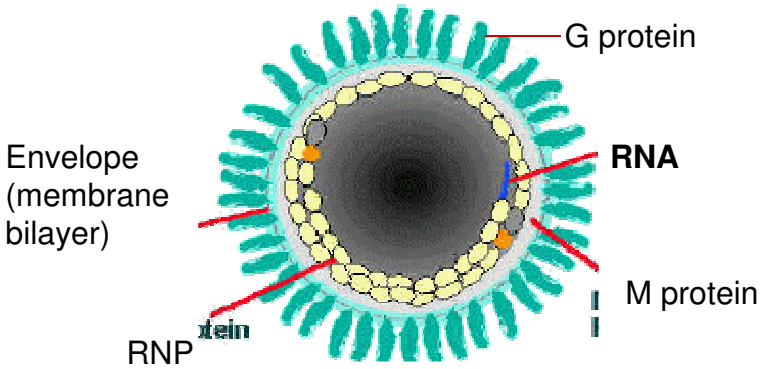
Uncommon Modes:-

- ❖ Aerosols (respiratory) transmission
- ❖ Organ Transplantation
- ❖ Ingestion
- ❖? Sexual

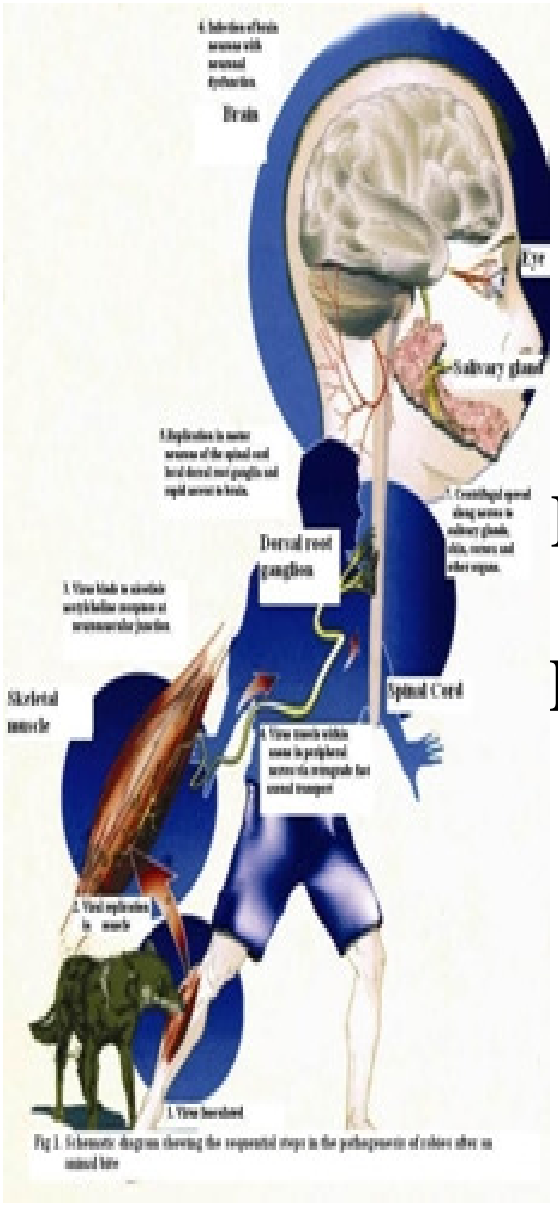
Structure of Rabies Virus

- **Bullet Shaped.**
- **Enveloped Virus.**
- **Measures 75 nm x 180 nm.**
- **Numerous spikes present on the envelope, these are made up of glycoprotein.**
- **Glycoprotein necessary for viral attachment & also induce protective antibodies.**





Pathogenesis



Brain

Salivary glands & Other organs

Spinal cord

Dorsal root ganglia

Peripheral nerves

Local treatment & RIG

Multiplication locally (in the muscle fibres)

Note: <u>The virus is neurotropic and there is no viremia in rabies.</u>

Incubation Period (in man)

- Incubation period highly variable
- Ranges between 6 days to 6 years
- Average : 30 – 90 days

commonly

- More than 6 months in less than 1%
- Bites on the head or face - upto 1 month.
- Bites on the extremities - upto 3 months.

Guide for Post-Exposure Prophylaxis

Category	Type of contact	Recommended Post exposure prophylaxis
I	Touching or feeding of animals Licks on intact skin	None, if reliable case history is available.
II	Nibbling of uncovered skin	Wound management Administer anti-rabies vaccine immediately
	Minor scratches or abrasions	Convert post exposure prophylaxis to pre exposure prophylaxis if dog/cat remains healthy throughout the observation period of 10 days or if it is euthanised and found to be negative for Rabies by appropriate laboratory techniques.

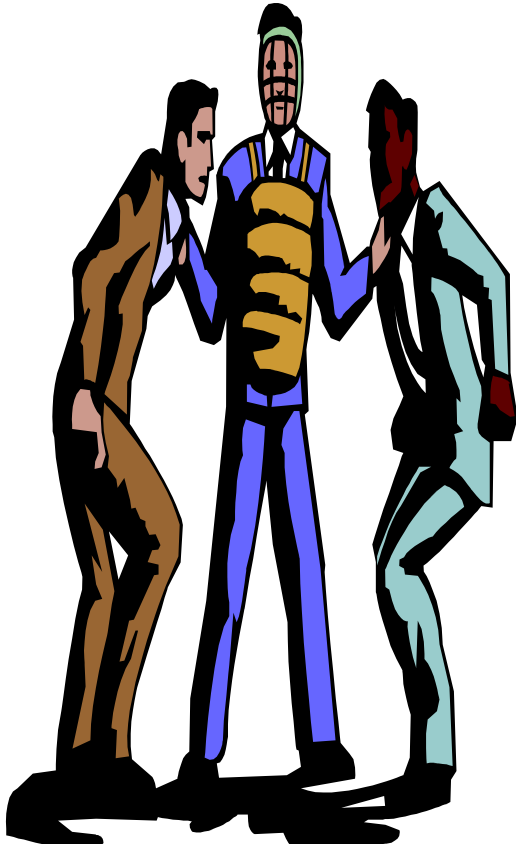
Guide for Post-Exposure Prophylaxis (Cont'd)

Category	Type of contact	Recommended Post-exposure prophylaxis
III	Single or multiple transdermal bites or scratches. Contamination of mucous membrane with saliva (i.e. licks) Licks on broken skin	Wound Management Administer rabies immunoglobulin and vaccine immediately. Stop treatment if dog/cat remains healthy throughout an observation period of 10 days or if it is killed humanely and found to be negative for rabies by appropriate laboratory techniques.

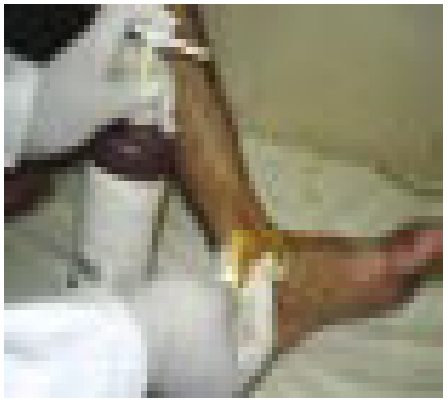
Category III Exposures

Principles of Treatment

- Wound treatment
- Vaccination
- Immunoglobulin/anti sera
- Advice to Patient



Wound Management



DO'S

MECHANICAL: Wash under Running tap water

CHEMICAL: Soap (Preferably detergent)

Disinfectants - Povidone Iodine, spirit, household antiseptics

BIOLOGICAL: Infiltrate immunoglobulins

Suturing only if required (1 - 2 loose sutures) and only after administration of RIGs.

DON'T'S

- Don't apply irritants viz. soil, chillies, oil etc.
- Don't cauterize
- Don't touch the wound with bare hands
- TT prophylaxis as per requirement

Passive Immunization

IMPORTANCE OF RIG INFILTRATION

- **The anti-rabies serum/Rabies Immunoglobulin (RIG) provides passive immunity in the form of ready-made anti-rabies antibodies, before it is physiologically possible for the victim to begin producing his/her own antibodies following anti-rabies vaccination.**

- **So RIG must be administered to all animal bite patients with Category III bite. [Incubation period of rabies is shorter here].**

Indication

- **All Category III exposures:** irrespective of the biting animal.
- **In immune compromised individuals:** RIG should be administered in both Category II and III exposures.
- RIG is administered only once, preferably within 24 hrs after exposure (on day 0 along with the first dose of ARV).
- **Administer even when treatment is delayed** but should not be given after 7 days of start of vaccination.
- In re-exposure cases (completed post exposure prophylaxis previously) RIGs are not indicated.
- Immunoglobulins (RIG) are life saving.

RIG Infiltration

Dose of RIG

Dose of Rabies Immunoglobulin:

- ERIG : 40 IU per kg body weight of patient.
  The ERIG produced in India contains 300 IU per ml.
- HRIG : 20 IU per kg body weight.

RIG provides passive immunity:

- Immediate acquisition of rabies virus-neutralizing antibodies (RVNA).
- Provides protection until active immunity begins (7-10 days since initiation of vaccination).

Administration of Rabies Immunoglobulin

- **RIG is most effective when administered locally and early.**
- **The RIG should be brought to room temperature (25°C to 30°C) before administration to the patient.**
- **Inject RIG into all wounds (anatomically feasible).**
- **Infiltrate as much as possible in the depth and around the wound(s). Remaining quantity, *if any,* to be given by deep intramuscular injection at a site distant from the vaccine injection site.**
- **RIG must never be given intravenously.**

Administration of Rabies Immunoglobulin (Cont'd)

- Multiple needle pricks into the wound(s) should be avoided. Use as few entry points as possible.
- Secondary infection of bite wound is no contra-indication to infiltration of immunoglobulin.
- Wounds on tip of finger/toe, ear lobe or nose or around the eye can be safely injected with RIG, provided the injection is not done with excessive pressure which can cause compression syndrome.
- After injecting a small quantity of RIG into the finger/ toe/ ear lobe, rest of the dose may be injected around proximal part of the finger/ toe/ external ear as far as practicable.

Administration of Rabies Immunoglobulin (Cont'd)

- For any mucosal exposure rinsing with diluted RIG can be done.
- Rabies Immunoglobulin should never be administered with the same syringe or at the same anatomical site as vaccine.
- Patient should be kept under observation for at least half-an-hour after administration of ERIG.

RIG Treatment in Children

Animal bite wounds 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.**
- **Dilute the calculated volume of RIG in sterile normal saline to a volume sufficient to infiltrate all the wounds.**
- **The total recommended dose of RIG may not preferably be exceeded as it may suppress the antibody production stimulated by the anti-rabies vaccine.**

Skin Test Not Required

- There is no rationale of performing a skin test before RIG administration.
- Skin Test does not reliably predict reaction.
- Presently available ERIGs are highly purified and the occurrence of adverse events has been significantly reduced. So anaphylactic reactions are extremely rare.

In Case of Any Side Effect by RIG Infiltration

Although anaphylactic reactions are extremely rare, still the Anti-Rabies Centre must take following measures as preparedness for any adverse condition:

- **Physicians administering ERIG should always be ready to treat anaphylactic reactions with adrenalin.**
- **The dose is 0.5 ml of 0.1 percent solution (1 in 1000, 1mg/ml) for adults and 0.01ml/kg body weight for children by SC or IM route.**
- **Other emergency drugs and supportive therapy should also be available.**

Shelf-life of inj adrenalin is short. Note the expiry date of inj adrenalin and replenish before expiry or stock-out

Table1: Currently available equine rabies immunoglobulin in India

	Brand	Product	Pharmaceutical
1.	Anti-Rabies Serum (ARS)	Purified equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency)	Central Research Institute, Kasauli, Himachal Pradesh
2.	Equirab	Purified Equine RIGs, 5ml vial (300 IU/ml, 1500 IU potency)	Bharat Serums and Vaccines Limited, Mumbai
3.	Vinrig	Purified Equine RIGs, 5ml vial (300 IU/ml, 1500 IU potency)	VINS Biopharma, Hyderabad.
4.	Abhayrig	Purified Equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency)	Human Biologicals Institute, Hyderabad

Table 2: Currently available human rabies immunoglobulin in India

	Brand	Product	Pharmaceuticals
1.	Berirab-P	Human Rabies Immunoglobulin, 150IU/ml; 2 ml (300 IU) ampoule and 5 ml (750 IU) ampoule	ZLB Behring AG,Marburg, Germany/Bharat Serums and Vaccines Ltd., Mumbai.
2.	Imogamrab	Human Rabies Immunoglobulin, 150IU/ml; 2 ml (300 IU) ampoule and 5 ml (750 IU) ampoule	Sanofi Pasteur, France
3.	Kamrab	Human Rabies Immunoglobulin, 150 IU/ml; 2 ml (300 IU) vial and 5 ml (750 IU) vial	Kamada Ltd.,Beit-Kama, Israel /Synergy Diagnostics Pvt. Ltd.,Thane,Maharashtra

Good Bye to Nervous Tissue Vaccine

- Annual production 35-40 million ml
- Utilized to immunize 450,000 people/annum
- Efficacy 90 – 95%
- Neuroparalytic accidents : 1:4000 – 1:11000
- Production stopped since December 2004

Currently available anti-rabies vaccines in India#

	Brand	Product	Pharmaceutical
1.	Abhayrab	Purified Vero cell Rabies Vaccines (PVRV)	Human Biologicals Institute, Hyderabad
2.	Indirab	Chromatographically purified (PVRV)	Bharat Biotech International Ltd, Hyderabad
3.	PVRV*	Purified Vero cell Rabies Vaccine (PVRV)	Pasteur Institute of India, Coonoor, Tamilnadu
4.	Rabipur	Purified Chick Embryo Cell Vaccine (PCECV)	Novartis Vaccines, Mumbai
5	Rabivax	Human Diploid Cell Culture Vaccine (HDCV) (Liquid)	Serum Institute of India, Pune
6	Vaxirab	Purified Duck Embryo Vaccine (PDEV)	Zydus Health Care ltd., Ahmedabad
7	Vaxirab-N	Purified Chick Embryo Cell Vaccine (PCECV)	Zydus Health Care Ltd, Ahmedabad
8.	Verorab	Purified Vero cell Rabies Vaccines (PVRV)	Sanofi Pasteur/ Zuventus Health Care, Mumbai
* Limited production, since July 2001.			

 # A few other vaccines are being used in the country in limited quantities

Routes of Administration of Anti-rabies Vaccines

- **Intramuscular**

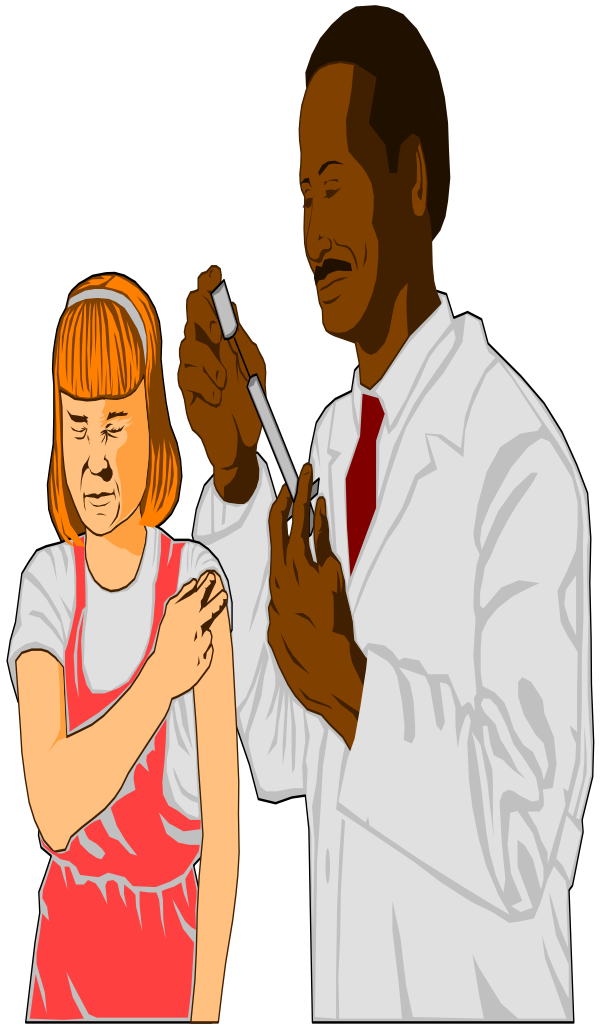
- **Intradermal**

Site of Inoculation

- **Deltoid muscle**

Or

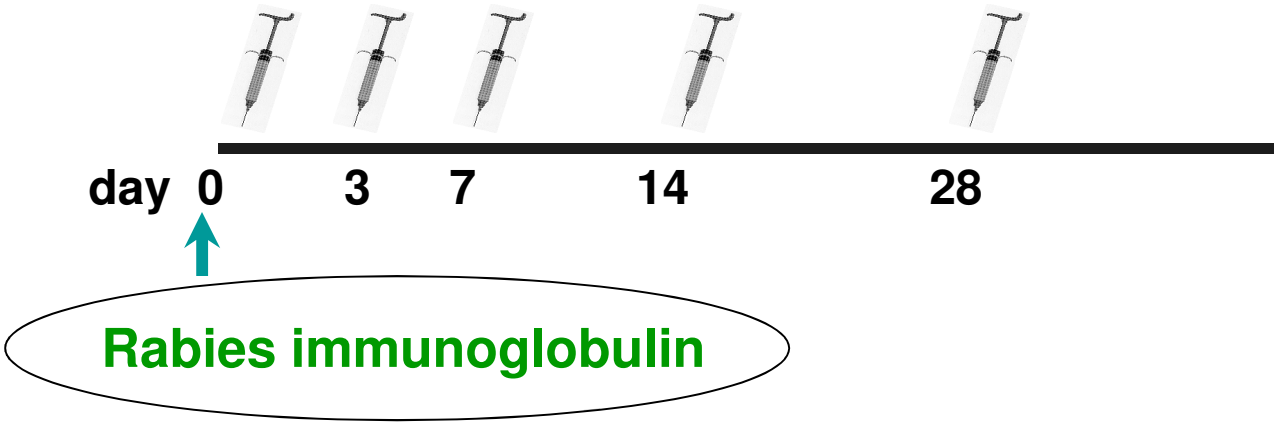
- **Anterolateral part of thigh**
- **Not recommended in gluteal region due to poor absorption**



Post Exposure Vaccination Schedule

Essen intramuscular Regimen

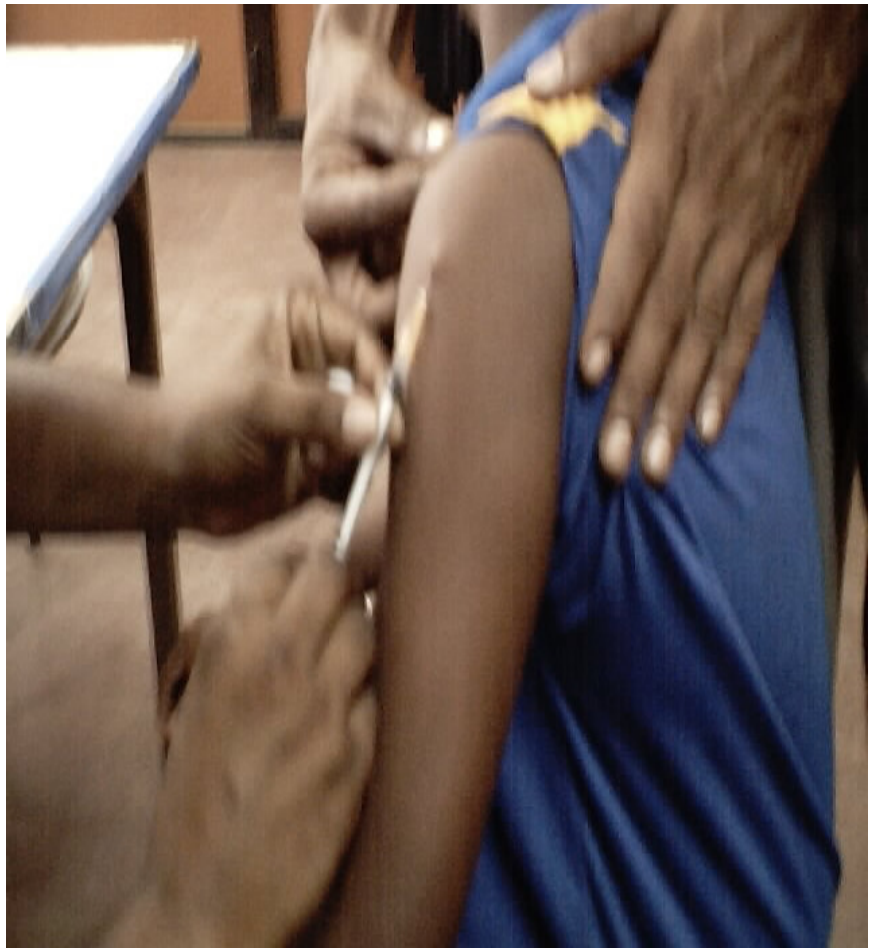
Standard intramuscular regimen. One dose into deltoid on each of days:



5 vials
5 visits

Intra Dermal Regimens for Post Exposure Prophylaxis

- Cost effective.
- Viable alternative to replace Nerve Tissue Vaccine in India.
- Studies in India confirm safety efficacy and feasibility.
- Notified by DCGI for use in India. (February 2006)



Intra Dermal Regimens

2 site regimen (Updated Thai regimen)

Dose : 0.1 ml (PVRV, HDCV, PCEC)

Site : Upper arm over each Deltoid

Schedule : 2- 2- 2- 0- 2

- Day 0 - 2 sites
- Day 3 - 2 sites
- Day 7 - 2 sites
- Day 14 - No Dose
- Day 28 2 sites

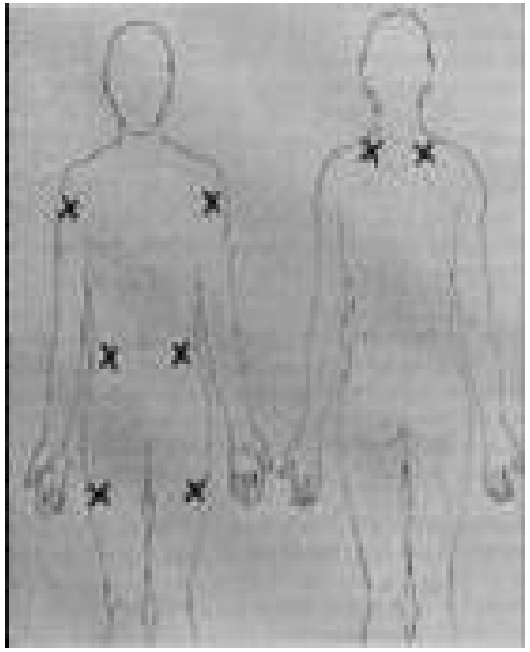
8 site regimen (Oxford Regimen)

(to be used only with PCEC or HDCV)

Dose : 0.1 ml

Schedule : 8-0-4-0-1-1

- Day 0 - 8 sites
- Day 3 - No Dose
- Day 7 - 4 sites
- Day 14 - No Dose
- Day 28 - 1 site
- Day 90 - 1 site



ID Regimen approved in India

2 site regimen (Updated Thai regimen)

Dose: 0.1 ml

Site : Upper arm over each Deltoid/ antero lateral aspect of thigh

Schedule :	**2- 2- 2- 0- 2**	
Day 0	**-**	**2 sites**
Day 3	**-**	**2 sites**
Day 7	**-**	**2 sites**
Day 14	**-**	**No Dose**
Day 28	**-**	**2 sites**

General guidelines for use of IDRV

Vaccines approved by DCG (I) should be used

Intradermal injections must be administered by staff trained in this technique

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) and immunosuppressed should be given ARV by intramuscular route.

Vaccines approved for ID use in India

- **PVRV – Verorab, Aventis Pasteur (Sanofi Pasteur) India**
- **PCECV – Rabipur, Chiron Behring Vaccines Pvt. Ltd.**
- **PCECV – Vaxirab N, Zydus Cadila**
- **PVRV – Pasteur Institute of India, Coonoor**
- **PVRV – Abhayrab, Human Biologicals Institute**
- **PVRV- Indirab, Bharat biotech**
- ***Only the anti-rabies vaccines approved by DCGI for ID administration should be used for ID route.***

Potency & Volume of approved vaccines

Stated potency of > 2.5 IU per IM dose, irrespective of the re-constituted volume.

The same vaccine is used for ID administration as per stated schedule

0.1 ml of vaccine, irrespective of reconstituted volume is administered per ID site.

Materials required

- Vial of approved rabies vaccine
- 2 ml disposable syringe with 24 G needle for reconstitution of vaccine
- Disposable 1 ml syringe with graduations with a fixed 28 G needle
- Disinfectant swabs for cleaning the top of the vial and the patient's skin

Maintenance of vaccine vial in use

Use aseptic technique to withdraw the dose

Store in a refrigerator at 2^0C to 8^0C

Reconstituted vaccines should be used as soon as possible or within 6 to 8 hours if kept at 2^0C to 8^0C.

All unused reconstituted vaccine at the end of 6-8 hours must be discarded.

Correct technique for ID injection

Anti-Rabies treatment Centres using ID route

- Trained staff to give anti-rabies vaccination by ID route.
- Cold chain facilities for vaccine storage and supply of syringes and needles.
- Are well versed in management of open vial and safe storage practices.

Post Exposure Prophylaxis

Points to remember

- Day 0 (D_0) - Day of 1st dose of vaccine given, not the day of bite.
- All modern Tissue Culture Vaccines (TCVs) are equally effective and safe.
- Never inject the vaccines into the gluteal region.
- Interchange of vaccines acceptable in special circumstances but not to be done routinely.
- Reconstituted vaccine to be used immediately.
- Vaccine dosage is same for all age groups.

Medical advice to Vaccinee

- No dietary restriction.
- No restriction of physical exercise.
- Avoid immune suppressants (Steroids, anti-malarials) if possible.
- Best to avoid consumption of alcohol during the course of treatment.
- Complete the course of vaccination.

Management of Re-exposure

Re exposure after a full course (Pre/Post-exposure) I/M or I/D irrespective of Category of exposure or Time since previous vaccination

2 boosters (Day 0 & Day 3) No RIG

All incomplete/partial vaccinations - Treat as fresh case

Re-exposure following PEP with NTV

- **As fresh case**
- **Treatment as per merits of the case**

Pre-Exposure Prophylaxis (PEP)

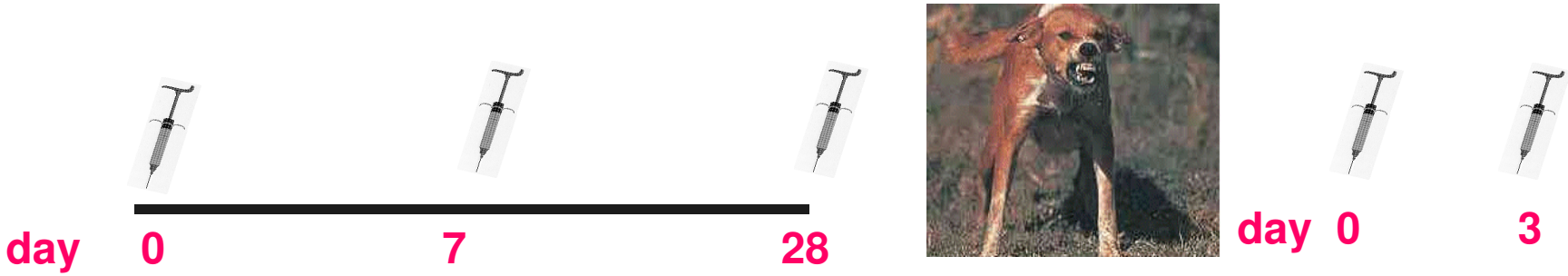
Recommended for risk groups like

- **Veterinarians, Laboratory personnel working with rabies virus, medical and Paramedical personnel treating Rabies patients.**
- **Dog catchers/Dog pound workers, Forest staff, Zoo keepers.**
- **Postmen, Policemen, Courier Boys, School Children in endemic countries.**

Pre-exposure Prophylaxis

Pre-exposure

3-dose series intramuscular (1ml/0.5ml)
or intradermal regimen(0.1ml)



Exposure: No Rabies immunoglobulin needed


Thank You