

ARV - Operational Protocol



Anti Rabies Vaccine administration Integrated Teaching

20 Dec 2017

By

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About Rabies

- Rabies – a 100% fatal vaccine preventable viral zoonotic disease of mammals occurring in 100 countries and territories, with ~3.3 billion people.
- causes an acute, progressive **encephalitis**.
- ~60 000 people die of rabies per year, 20,000 deaths (~2 /100 000 population at risk) in India alone, **~40% are children**.
- Human Rabies – In India: 97% from dogs, 2% from cats, 1% from Jackals / mongoose / others.
- In Africa it is 4 /100 000 population.
- Post-exposure prophylaxis (PEP) averts **~3,27,000** deaths per year in **2** regions: **Africa** and **Asia**.

Strategic Advisory Group of Experts (SAGE) Meeting 17-19 2017: Recommendations.

2 main strategies for prevention:

- (i) vaccination of **dogs** to interrupt virus transmission to humans;
- (ii) **human** vaccination,
 - a) pre-exposure prophylaxis (**PrEP**, using vaccine only)
 - b) post-exposure prophylaxis (**PEP**, using vaccine alone or together with rabies immunoglobulin [**RIG** – eRIG / hRIG]).

**APPROPRIATE VACCINATION ACHIEVES ~100%
IMMUNIZATION AND ~100% CURE.**

Barriers as per SAGE & +

- Long complicated PEP regimens,
- High cost, Low demand,
- Uncertain supply, availability,
- Variable quality & short shelf-life of RIG,
- **~1%** of needy patients receive RIG in endemic countries.
- Sub-optimal Community Participation **(CP)**.

Accelerated PrEP regimens for all age groups

For healthy individuals in the general population –
on days 0 & 7 **[2 visits]**

i) 2-site (0.1 mL per site) **ID** regimen

[2+2= 4 pricks i.e. **0.4mL** vaccine] or

ii) 1-site (**1 vial** per site) **IM** regimen **[2 visits]**

**Global goal is to achieve zero dog transmitted human
deaths by 2030 by vaccination of dogs and humans.**

NRCP of NCDC focuses on:

1. National Centre for Disease Control launched National Rabies Control Programme – insists
 - A) Creating **awareness** to seek PEP
 - B) **Training Doctors** in managing animal bites & **ID route inoculation of CCEEVs.** (Cell Culture / Embryonated Egg)
2. Rabies is 100% fatal; **animal bites are medical emergencies;** life saving **PEP** to be provided.
3. Human to **H**uman transmission is **uncommon.**

From WHO Position paper on ARV..1

- No rabies vaccines are supplied in **multi dose vials** for intramuscular **[IM]** injection **[MDVP Not applicable]**.
- Rabies vaccines **do not contain preservatives [WHO]**.
- The shelf-life of these vaccines is **≥3 years**, provided they are stored at **+2°C to +8°C and protected from sunlight**.
- Following reconstitution with the **accompanying sterile diluent**, the vaccines should be used immediately or within **6–8 hours** if kept at **+2°C to +8°C and protected from sunlight**.
- All CCEEVs should comply with the WHO recommended potency of **≥2.5 IU [antigen]** per single intramuscular dose (**0.5 ml or 1.0 ml** volume after reconstitution, depending on the type of vaccine).
- Anamnestic response is for **long duration**, not related to **IM / ID**.

From WHO Position paper on ARV..2

VACCINATE TO IMMUNIZE.

- Cell-Culture-based rabies vaccines are **safe** and **effective**.
- **≥2.5 I.U** per 0.5 / 1ml ARVs are for intramuscular **[IM]** & or intra-dermal **[ID]** use.
- On proper vaccination, **100%** of millions of healthy vaccinees attained neutralizing antibody concentrations of **≥0.5 I.U/mL, i.e. 100% seroconversion (Immunization)**.
- So far, no **“Immunized individual”** suffered from rabies.

About Vaccine

- **Reading manufactures notes is mandatory.**
- Abhay Rab – Freeze dried, containing purified inactivated Rabies Virus [L.Pasteur 2061 / Vero strain propagated in **Vero** Cells].
- 0.015% w/v **Thiomersal** is preservative.
- Potency: **≥2.5 I.U** per vial.
- Stabilizers: Maltose and Human Albumin.
- **Interchanging** the brand is not recommended.
- **Trained** staff to **administer / document** adequately.

FOR HUMAN USE
RABIES VACCINE, HUMAN I.P.
 (PURIFIED VERO CELL RABIES VACCINE)

Abhayrab[®]

FOR INTRAMUSCULAR/ INTRADERMAL USE



GOVERNMENT OF KARNATAKA
 HEALTH DEPARTMENT
 NOT FOR SALE
 ಕರ್ನಾಟಕ ಸರ್ಕಾರ
 ಆರೋಗ್ಯ ಇಲಾಖೆ



VVM
type:

Reading product specific information provided by the respective manufacturer is mandatory prior to vaccination including cold chain.



30
or
none

This Pack Contains
 20 Vials of Vaccine
 20 Diluents (1.0 mL each) for reconstitution

Abhayrab Details
 Mfg. Lic. No.: 15
 Batch No. : 16URAB102
 Mfg. Date : DEC16
 Exp. Date : NOV19

Diluent Details
 Mfg. Lic. No.: 00/449
 Batch No. : SCSV180416
 Mfg. Date : 12/16
 Exp. Date : 11/20

FOR HUMAN USE

Store at +2°C to +8°C

Reconstitution : Reconstitute the freeze dried vaccine with provided 1.0 mL diluent (0.9% w/v Sodium Chloride Inj. I.P.) for ID administration or reconstitute with 0.5 mL out of 1.0 mL diluent for IM administration.
 Use immediately after reconstitution.
 Refer Literature for Dosage, Administration & Further information.

FOR INTRAMUSCULAR/ INTRADERMAL USE

- *Pre-exposure prophylaxis is recommended for anyone who will be at continual, frequent or increased risk of exposure to rabies virus, either by nature of their residence, travel or occupation, Children living in or visiting rabies-affected areas are at particular risk.*
- The protection is long lasting (at least 10 years) and booster doses are only recommended for people whose occupation puts them at continual or frequent risk of exposure.
- **The Key Point: Development of clinical disease can be prevented through timely immunization even after exposure to the infecting agent.**

- Intra-dermal **[ID]** regimens have been successfully introduced for post-exposure prophylaxis in countries such as India, the Philippines, Sri Lanka and Thailand.
- However, in addition to using vaccines explicitly authorized for the **ID route**, proper delivery of the vaccine requires sufficient **staff training to ensure correct storage, reconstitution & administration.**

Recommendation of Vaccination

- For category I exposures, no prophylaxis is required;
- for category II, immediate vaccination is recommended;
- category III, immediate vaccination and administration of rabies **immunoglobulin** are recommended.

Indications:

1. Pre Exposure vaccination:

- a) All high risk groups – veterinarians, Municipal workers, Medical / Para Medical Personnel, Forest / zoo personnel, lab personnel
- b) Persons staying in or visiting endemic areas.

2. Post exposure Vaccination: For **IM** use; reconstitute

With only **0.5mL** 0.9% saline diluent provided, **discard 0.5mL diluent.**

Dosage & Administration

- IM – **0.5mL**, Antero lateral aspect of mid thigh / Deltoid.
- ID – **0.1mL**, at 2 different lymphatic drainage sites – right & left upper arms.

Schedule:

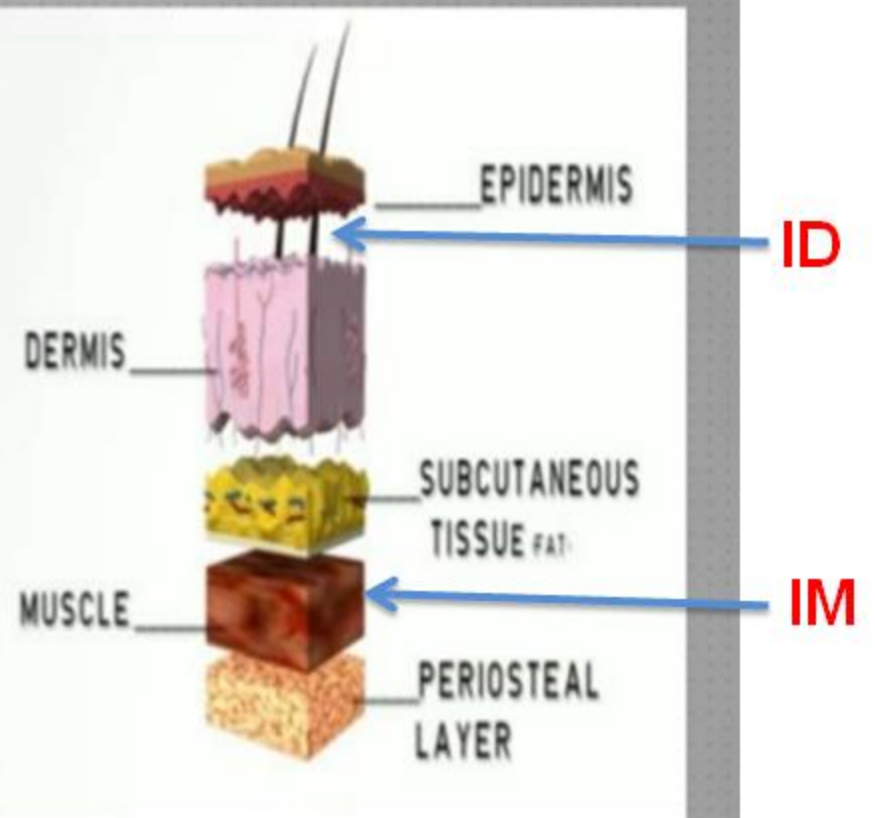
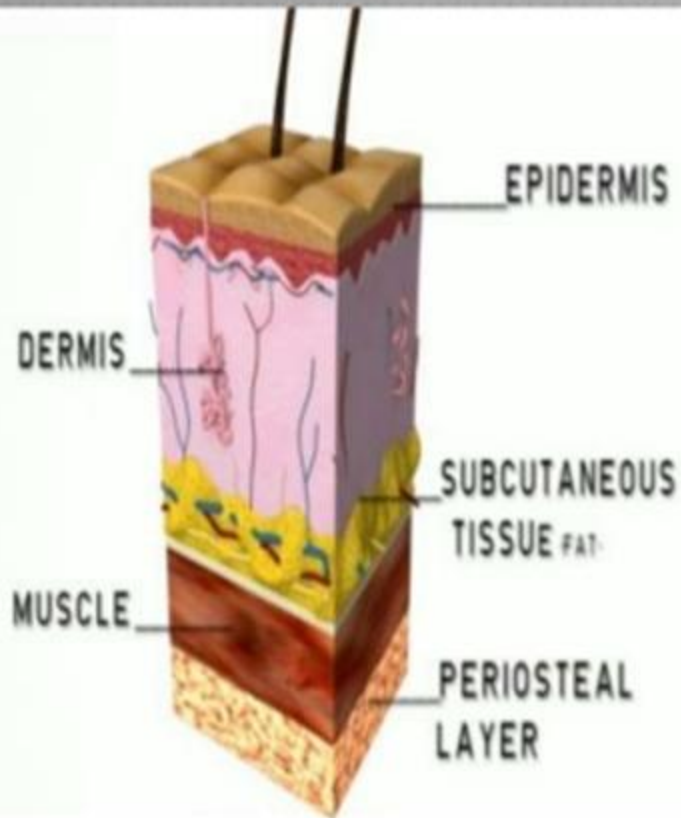
- **For IM route:**
- Pre exposure – 0.5mL, 3 doses: 0/7/21 or 28.
- Post exposure – 0.5mL, 5 doses: 0/3/7/14/28. **[+Immunoglobulin for Cat III].**
- Previously vaccinated – 2 booster doses: 0 & 3.
- Immunocompromised – **add Immunoglobulin.**

Administer at 2 different sites.

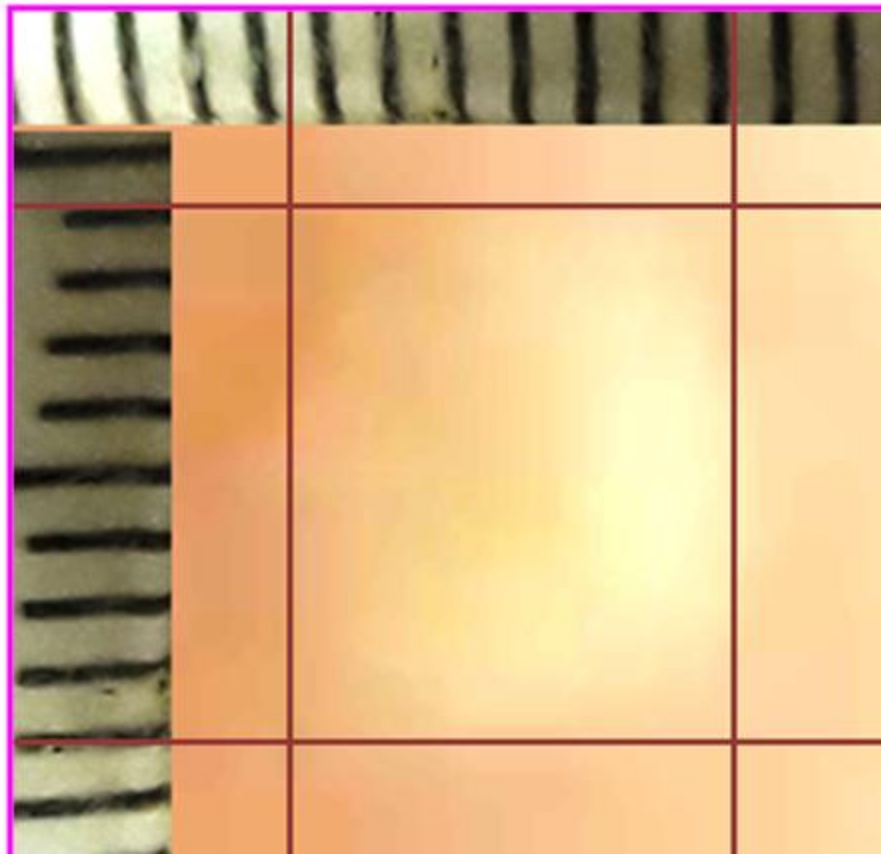
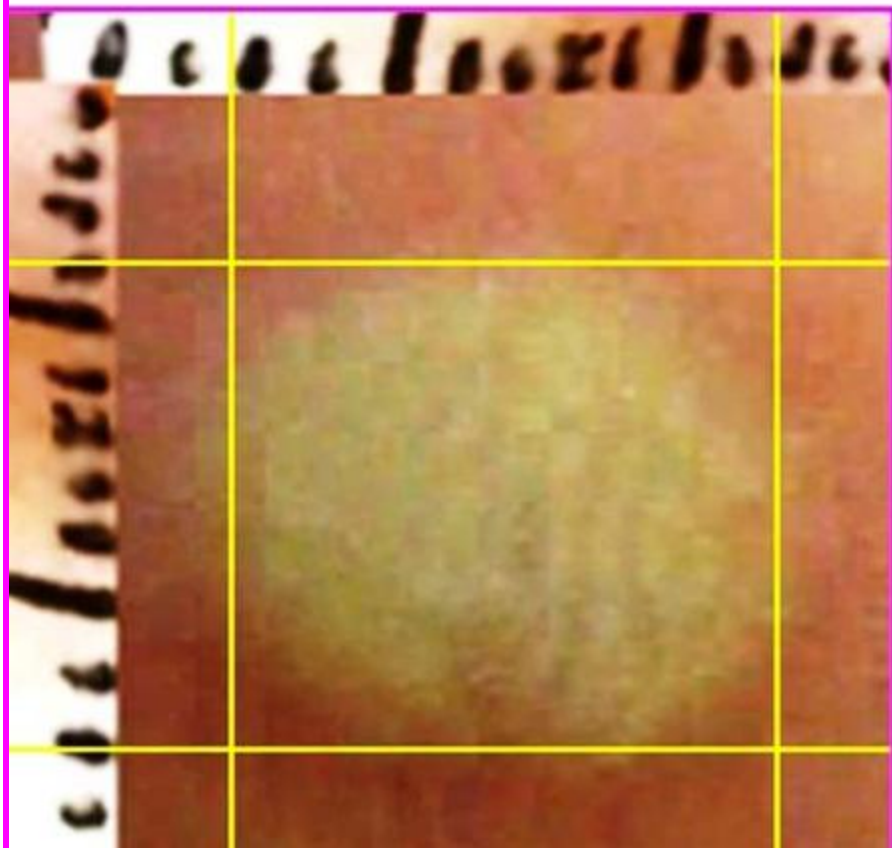
- **ID Route**
- Pre Exposure – 0.1mL, 2 doses, 0/7/21 or 28 [6 pricks]+ yearly booster.
- Post exposure – 2-2-2-0-2 **[8 pricks]**: 0/3/7/28 **[+ Immunoglobulin for Cat III]**.
- Previously vaccinated–2 boosters: 0 & 3 [4 pricks].
- Immunocompromised – **add Immunoglobulin.**

NO INTRAVASCULAR ROUTE.

SKIN



0.1mL ID administration produces ≥ 7 to 9mm diameter weal.



Contraindications

- For pre-exposure prophylaxis, previous severe reaction to any components of the vaccine is a contraindication to further use of the same vaccine.
- No contraindications for post-exposure prophylaxis; during infancy or pregnancy and for immunocompromised individuals, including children with HIV / AIDS.
- People taking **chloroquine** for malaria treatment or prophylaxis may have a reduced response to **ID** rabies vaccination. These patients should receive the vaccine **IM**.

Precautions

- Do not use immuno suppressive concurrently.
- In case of **severe or delayed Cat III** cases administer **IM**.
- **IM** route for those on **chloroquin** therapy.
- Do not administer in the **gluteal** region.
- Keep **AEFI kit** available.
- Clean injection site with spirit & allow it to dry.

AEFI

- **Minor** AEFIs, such as transient erythema, pain, induration, pruritus, rash and oedema may occur at the site of injection, particularly following **ID** administration of a booster **in 35–45%** of vaccinees.
- **Mild** systemic AEFIs, such as transient fever, headache, dizziness and gastrointestinal symptoms, observed in **5–15%** of vaccinees.
- **Serious** AEFIs mainly of allergic or neurological nature, rarely occur.

Categorization

- **Category I** – touching or feeding animals, licks on intact skin;
- **Category II** – nibbling of uncovered skin, minor scratches or abrasions without bleeding;
- **Category III** – single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks, licks on broken skin, and exposures to bats.

Rabies Immunoglobulins (RIG)

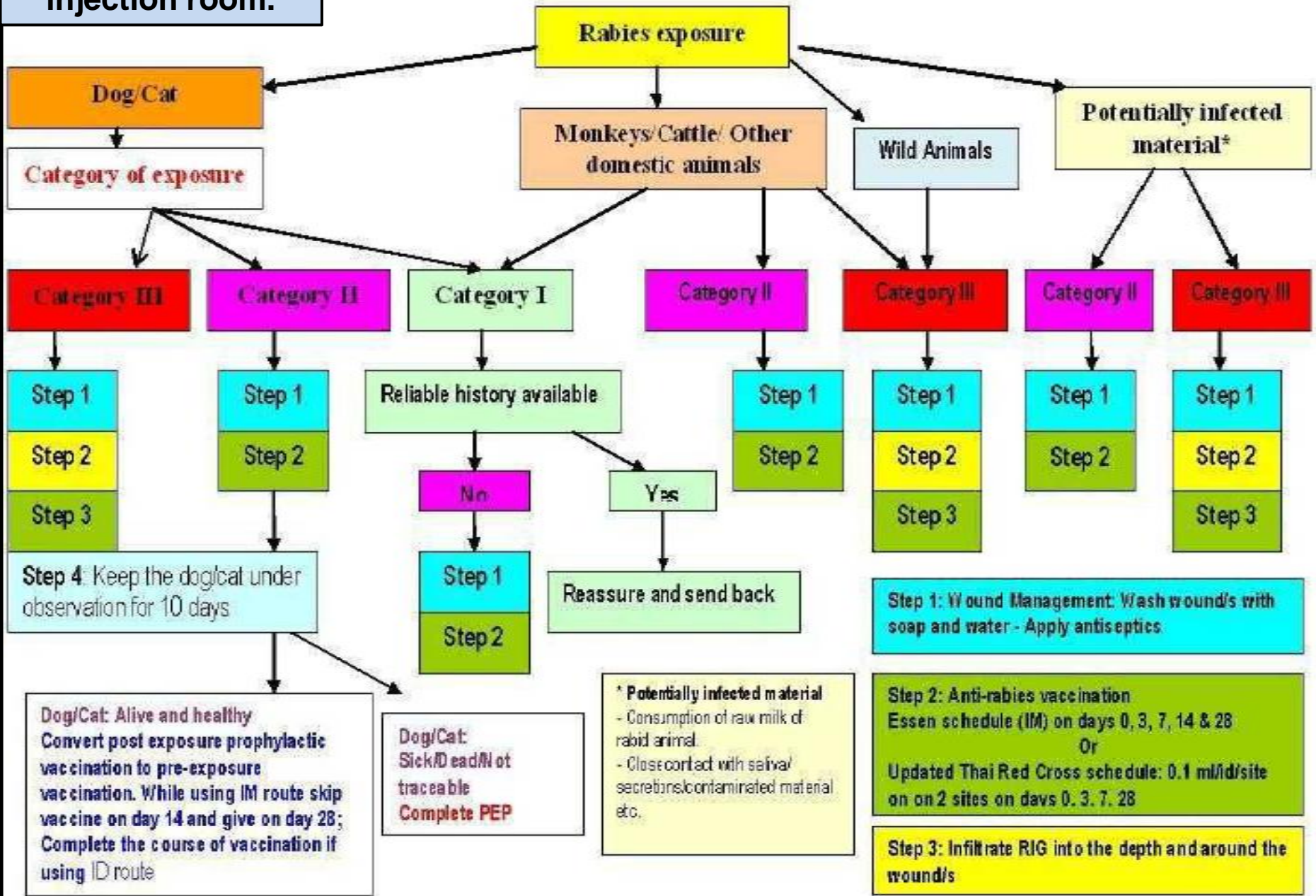
- eRIG: 40 IU per kg body wt; 300 IU/mL. **Heterologous**, small risk of anaphylaxis but no test dose recommended as it cannot predict reaction.
- hRIG: 20 IU per kg body wt; 150 IU/mL. **Homologous**, free from side effects, expensive.
- Both require cold-chain but it has to be administered at room temperature **[25-30°C]**.
- Avoid multiple punctures, common site / syringe to RIG & Vaccine.
- Administer with 1st dose of vaccine within 7 days of bite; delayed administration **suppresses** immune response to vaccine.
- **30 minutes** observation following administration.

Key messages

- Rabies is 100% fatal but preventable.
- Caused by bite or scratch of rabid animal.
- Do not apply chillies, mustard oil, irritants.
- Wash the wound immediately with plenty of soap & water.
- Do not apply dressing / stitch the wound.
- Visit nearest anti rabies clinic for consultation.
- Complete the course of ARV.
- Combined ARV & Immunoglobulin recommended in severe cases.
- Vaccinate the pets adequately.

Job-aid for display at casualty / OPD / injection room.

Decision Tree: Guide to Post Exposure Prophylaxis (PEP)



Annexure 2 : Proforma for management of animal bite case at an antirabies centre/clinic(ARC)

Name: Age : Gender :

Residential address :

Telephone/Mobile Nos.:

Occupation: Monthly Income (In Rupees)

Previous anti- rabies vaccination Status(with dates): Not vaccinated () Vaccinated () :

Record available () Not available/Not applicable () DD/MM/YY(doses)

Date of animal bite: Time of bite:

Address/ Place where bite took place:

Interval between bite and reporting to ARC (In hours/days) :

Site of bite/s: Number of wounds: SuperficialDeep Total

Biting Animal- species: Dog/Cat/Monkey/Mongoose/Others (specify)

Type: Pet/Stray/Wild

Vaccination Status of Animal: Vaccinated/Not vaccinated /Not known

If vaccinated: number of doses received: Vaccination card : not available ()available()(show it)

Bite: Provoked/unprovoked

Type of provocation:

Fate of animal: Alive/Killed/Died/Unknown/Untraceable:

No. of other persons bitten by same animal within one week of the bite: Not known ()

Outcome in other persons bitten: Not Applicable()

Type of exposure: WHO category – Category I () Category II () Category III ()

a) Licks on intact skin

b) Nibbling of uncovered skin

c) Minor scratches or abrasions without bleeding

d) Licks on broken skin

e) Single or multiple bites with bleeding

f) Contamination of mucus membrane with saliva

Remedy taken before coming to anti-rabies centre/ clinic:

- a) None ()
- b) Washed with water.....
- c) Washed with soap and water.....
- d) Antiseptic application.....
- e) Any other specify: application of oils/ointments/herbs/any other (specify).....

Duration between bite & Local treatment of wound:

Who advised you to come to anti-rabies clinic:

Treatment given at the anti-rabies clinic:

- a) Wound washed in the clinic.....
- b) RIG (Name) given..... Local (mL)..... Systemic (mL)..... Total (mL).....
- c) Wound suturing (if done, details).....
- d) Vaccine (Name): IM/ID: on days 0/3/7/14/28 (as applicable) (dates).....
- e) Injection TT.....
- f) Record/Report adverse events to vaccine or RIG:
- g) Antibiotics
- h) Analgesics/NSAID/Antihistamines.....
- i) Other drugs/treatment given (if any).....

Paradoxical situation & concern

All essential vaccines of National Immunization Schedule are dressed with VVM – indirectly depicting the potency of vaccine.

RI programme is blended with regular periodic training at all levels, monitoring, supportive supervision, review.

Rabies is the only 100% fatal VPD, ~40% among children.

Appropriate vaccination with ARV is 100% effective.

But, as of now, in India, ARV vaccination is discriminately deprived of this luxury and vaccines are denuded of VVM.

Recommendations

- **Regular training / reorientation of Doctors in managing animal bites.**
- **Skill based training in the storage, reconstitution, drawing required quantity using insulin syringe / 1mL syringe, proper Intra-Dermal administration of ARV.**
- **Proper documentation of individual case, line listing of cases for follow-up / research activity.**

References

Meeting of the Strategic Advisory Group of Experts on immunization, October 2017 – conclusions and recommendations.

1ST DECEMBER 2017, 92th YEAR, No 48, 2017, 92, 729–748

<http://www.who.int/wer>

NRCP, National Guidelines on Rabies Prophylaxis, accessed from <http://pbhealth.gov.in/guideline%20for%20rabies%20prophylaxis.pdf> dated 19-12-2017.

Rabies vaccines: WHO position paper accessed from <http://www.who.int/wer/2010/wer8532.pdf?ua=1> dated 19-12-2017.

Abhayrab Manufacturer notes.