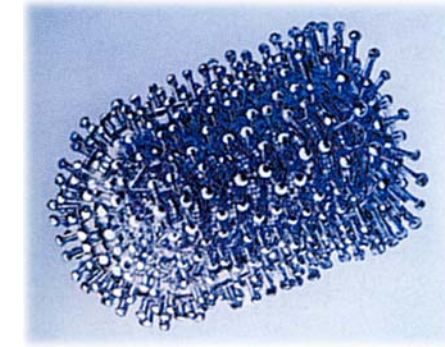


RABIES PREVENTION



A MEDICAL GUIDEBOOK (Includes frequently asked questions)

Prof. M.K. Sudarshan

Issued in public interest by
SERUM INSTITUTE OF INDIA LTD., PUNE

Layout and design : Vijay Kolhatkar

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Protection from Birth Onwards

4. ASSESSMENT OF EXPOSURE

The most common modes of exposure are:

- Bite
- Scratches
- Lick
- Drinking raw milk from rabid animal viz., cow, buffalo, etc.



According to new WHO categorization (2005),

Wounds or exposures can be classified into:

Category I(No risk)

Touching or feeding of animals
licks on intact skin



Category II(Moderate risk)

Minor scratches or abrasions without bleeding.
Licks on broken skin*.

*Application of spirit or alcohol to the affected spot of skin causes burning sensation.

Category III(High risk)

Wounds with bleeding.
Licks on mucus membrane.
Drinking raw milk of a rabid animal.



FOREWORD

PREFACE

ACKNOWLEDGEMENT

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विश्व स्वास्थ्य संगठन के अर्बोवायरस
तथा रक्तस्रावी बुखार संदर्भ और अनुसंधान सहयोगी केंद्र
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FOREWORD

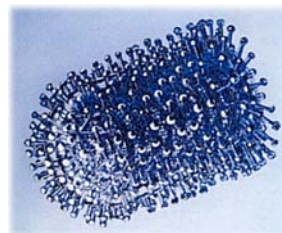
Rabies, a practically 100% fatal disease is endemic in India and continues to be a public health problem except in the Islands of Andaman & Nicobar and Lakshadweep which are rabies free. The incidence of rabies has reportedly declined from 30,000 annually to 20,000 following a recent assessment by a WHO sponsored national multicentric survey in 2003-04. This decline is due to increased usage of modern rabies vaccines and various other factors.

In this background it is heartening to note that Dr. M. K. Sudarshan, MD (BHU), DIH, DHM, Principal and Professor of Community Medicine, KIMS, Bangalore and Chief Investigator of WHO-APCRI Indian Rabies Survey, 2003-04 has written this guidebook to medical doctors mainly to ensure correct rabies prophylaxis by them in this country. It is hoped that the doctors benefit from this book and I congratulate Serum Institute of India Research Foundation, Pune, for publishing and distributing this to medical professionals.

A.C. Mishra
Director

31st January 2007

3. MODES OF TRANSMISSION

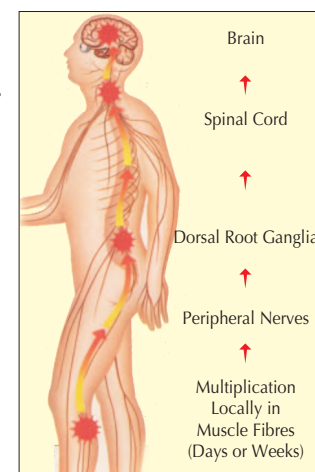


The rabies virus, bullet shaped is very minute (120 x 80 nanometer; 1 nanometer = One millionth of a millimeter) and seen only through an electron microscope.

The virus is present in the saliva of rabid animals; in the saliva of hydrophobia patients and also in the urine (low titres).

Following bite, scratch, lick on broken skin (cuts/abrasions) and on intact mucus membrane the virus enters the body, multiplies locally in the tissues, muscles and enters a nerve (neurotropic) and travels to brain (@ 3 mm per hour) and affects the brainstem function; causes hydrophobia (fear of water), aerophobia (fear of breeze) and photophobia (fear of light) and finally leads to death.

The time interval between bite/exposure and onset of hydrophobia (incubation period) is usually between 3 weeks to 3 months; rarely 4 days to 2 years.



Points to Remember

- The saliva and urine are the main source of virus / infection.
- The bites, even scratches and licks are dangerous.
- The virus multiplies locally and travels inside nerves (not in blood and hence, no viremia).

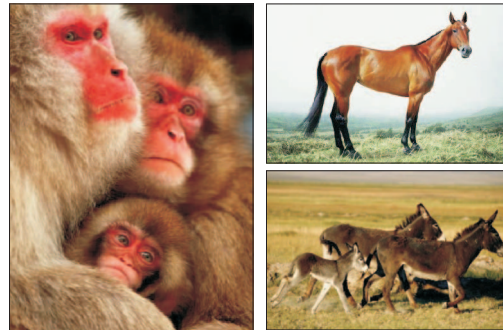
2. ANIMAL RESERVOIRS IN INDIA

The animals responsible for transmission of rabies in India are:

Most commonly (≈ 98%)
Dogs and Cats



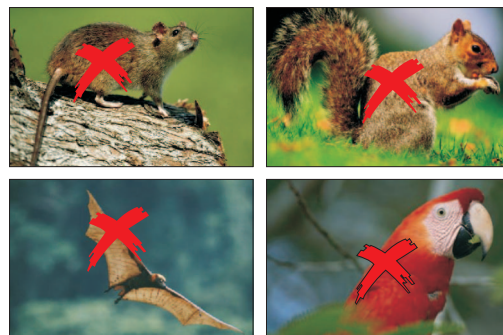
Sometimes (≈ 1%)
Monkeys, Donkeys, Horses
Cows, Buffaloes, Goats,
sheep and Pigs



Occasionally (≈ 1%)
Wild Animals
Mongoose, Foxes, Jackals,
Camels and Elephants



Not Reported
Rodents, Rats and
Bandicoots, Squirrel, birds
and Bats



Points to Remember

- Dogs, cats, monkeys, horses; mongoose, jackals and foxes mostly transmit rabies.
- Rodents, squirrels, birds and bats do not transmit rabies.

PREFACE

Rabies, a disease of antiquity, is practically 100% fatal even today with no cure anywhere in the world. However, it is preventable with currently available modern rabies vaccines and immunoglobulins. Consequently, more responsibility rests with the physician to advice and provide the patient the correct post-exposure prophylaxis. With the advent of consumer protection act in the country and the mass media providing rabies information to lay people, the role of physician in rabies prevention assumes significance.

Following the Supreme Court order the production of sheep brain vaccine was discontinued in December 2004. This has led to shortage of rabies vaccines in government hospitals. The modern vaccines are expensive by the intramuscular route and the poor animal bite victims are now hardly receiving one or two doses of vaccine. Hence, in February 2006 the drugs controller general of India (DCGI) approved the use of intradermal rabies vaccination (IDRV) in government hospitals. However, the producers of these approved vaccines are awaiting the DCGI clearance to incorporate the ID provision in their vaccine package insert. Once this is done the IDRV will be introduced in government hospitals. This shall ensure safe and ethical antirabies immunization of animal bite victims.

In this context this revised and updated guidebook provides the otherwise busy medical practitioner the necessary basic information on medical and veterinary aspects of rabies. It is also expected to guide the physician in the correct usage of modern rabies vaccines and immunoglobulins. It is hoped that this manual benefits the doctor and his/her patients. Lastly, I thank M/S Serum Institute of India, Pune/Mumbai for publishing and distributing this book for the benefit of medical and veterinary professions.

January, 2007
Second Edition
© Author

PROF. M. K. SUDARSHAN
(E-mail: mksudarshan@vsnl.com)

PLEASE NOTE: Though utmost care is taken to provide an updated information and expert opinion through this guidebook, ultimately the prerogative and decision to treat the patient lies solely with the physician.

ACKNOWLEDGMENT

M/S Serum Institute of India, Pune immensely values the expertise and experience of Dr.M.K.Sudarshan, Principal and Professor of Community Medicine and Head of Rabies Epidemiology Unit, Kempegowda Institute of Medical Sciences, Bangalore for his contribution to the field of rabies in India. He is the founder president of Association for Prevention and Control of Rabies in India (APCRI) and Rabies in Asia (RIA) Foundation. We thank him for writing this book on rabies in a simple and easy to understand way for the medical and veterinary professionals in India. This book, which was first published in October 2004 during the launch of Rabivax in India, is now revised and updated. This should enable the doctors to understand the problem of rabies more comprehensively and ensure better management of animal bite victims in the country. The book explains with simple diagrams and illustrations, the theoretical foundations on which sound anti-rabies treatment practices are advocated. A new chapter on intradermal rabies vaccination (IDRV) has been added and the chapter on frequently asked questions (FAQs) is revised and updated in the light of current scientific information. This should give to the practicing physicians a correct and clear perspective of rabies prophylaxis and clarify the common problems/issues faced in day-to-day practice. However, if there are still any doubts in this specialized area of medical practice the readers are encouraged to consult him or any other infectious diseases expert in rabies prophylaxis.

This book is intentionally kept concise to facilitate its easy reading by an otherwise busy medical practitioner. Readers are welcome to give their comments, suggestions and feedback in improving on this effort and add to the present knowledge of rabies prevention.

Serum Institute of India, Pune
January, 2007

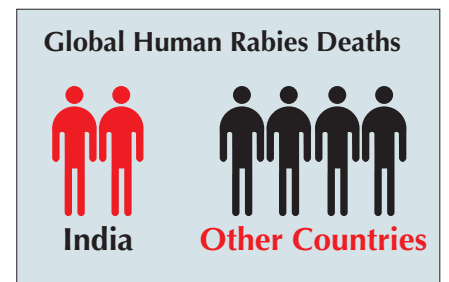
Dr. S. Bhardwaj
Medical Director

1. RABIES: A FATAL, BUT PREVENTABLE DISEASE

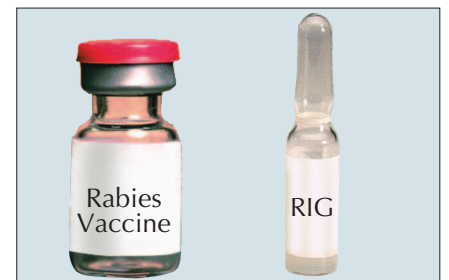
Rabies is practically a 100% fatal disease. There are only 4 recorded survivors till date who recovered following intensive life support and excellent nursing care.



According to World Health Organization (2005) globally each year about 55,000 (24,000 - 90,000) die of rabies of which 20,000 (36% or 2 out of 5 to 6 deaths) are from India alone.



However, rabies is preventable with modern vaccines and sera (immunoglobulins). So the physician must provide correct rabies prophylaxis following exposure failing which he/she may be sued for compensation under Consumer Protection Act.

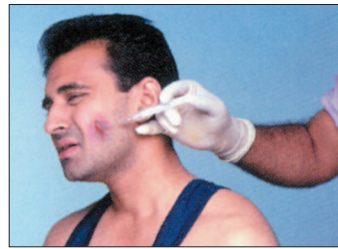


Points to Remember

- Rabies is 100% fatal.
- Rabies is preventable through wound care, correct use of vaccines and sera.
- Incorrect/wrong treatment to animal bite victims may lead to rabies death and litigation under Consumer Protection Act.

animals (as vaccine alone is not protective) and failure to advice/provide RIGs / ARS attracts litigation/compensation under Consumer Protection Act for deficient/faulty medical service. However, it is advisable to administer ERIG or ARS in an institutional (Nursing Home) facility and not in the practicing chambers/clinics of the doctor.

Failure to use RIG/ARS has been one of the reasons for rabies deaths despite the use of modern rabies vaccines.



Points to Remember

- Carefully instill [infiltrate all wounds (category III) with RIGs as per dosage (after skin testing in ERIG/ARS) particularly following exposure to high-risk animals.
- All category III exposures resulting from high-risk category of animals need life saving RIGs (in addition to vaccine).
- RIGs are life saving in rabid animal bites.

6.4. COUNSELLING OF PATIENTS AND ATTENDANTS

Animal bites, rabies exposures are very painful, stressful and due to conflicting messages the patients are very anxious and worried. It is more so in children, pregnant women and hence for every case atleast 5 to 10 minutes must be spent by the doctors to reassure them, alleviate anxiety and fears.

Other advices during vaccination period include:

- To avoid excessive alcoholic drinks; to restrict smoking.
- To avoid strenuous physical and mental work.
- No specific dietary restrictions; however, avoidance of meat and fish may be suggested to some (selectively for too young

It is very important also to elicit information about the biting animal (dog/cat).

- Healthy, pet and regularly vaccinated dog / cat (**low risk category**).
- Healthy, pet and vaccination doubtful or not done (**moderate risk category**).
- Rabid, Sick, died, stray (dog/cat) or other animals or wild animals (**high risk category**).

Points to Remember

- A wound with bleeding is a high risk.
- Even pet vaccinated animals carry low risk.
- A category II (moderate risk) or category III (high risk) exposure/wound from a category II (moderate risk) or category III (high risk) animal needs immediate anti-rabies treatment.

5. OBSERVATION OF ANIMALS FOR RABIES

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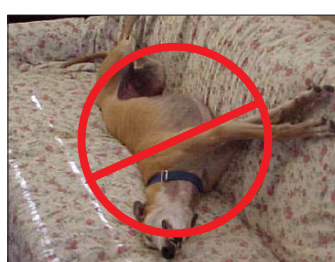
Observation of an animal for 10 days (from the day of biting the person) for signs of rabies is applicable only to dogs and cats and not to other domestic or wild animals. The rationale for observation is that if the dog or cat is incubating rabies it will show signs of disease in the next 3-5 days and die subsequently in another 3-5 days.

The signs of rabies in the dog/cat are:

- Any change in its normal behaviour suggesting either undue aggression or depression.
- Running aimlessly and attacking others without any provocation.
- Becomes too drowsy and withdraws itself to a corner.
- Excessive salivation.
- Change in its voice/bark.
- Refusal to feed or eating unusual objects like stone, paper, wood, metal pieces, etc.
- Death of the animal.

Wherever possible the bite victim must be educated about this and advised to watch the animal for 10 days minimum. (And not to kill or abandon the dog or cat).

During this period, however the vaccine/sera treatment must be



Two types of RIGs/ARS are available:

ARS or Equine Rabies Immunoglobulin (ERIG). (300 IU/mL)

ARS. Currently available from Central Research Institute (CRI), Kasauli, Himachal Pradesh-173205.

Equirab. Produced by Bharat Serums and Vaccines, Mumbai and **Zyrig** marketed by Zydus Alidac, Ahmedabad.

Abhayrig. marketed by Human Biologicals Institute, Hyderabad.

Carig. Produced and marketed by Cadila Pharma, Ahmedabad.

Human Rabies Immunoglobulin (HRIG). (150 IU/mL)

Berirab, Berirab-P, Imogamrab, Rabglob and Kamrab are imported and expensive and available only in metros and big cities.

Steps of Use

A skin test (as per product insert guidelines) must be performed prior to administration of ERIG/ARS only [not for HRIG].

As much as possible of the recommended dose (20 IU/kg of body weight for HRIG or 40 IU/kg of body weight of ERIG) should be carefully instilled (using 26G needle) into the depth of all wounds and also infiltrated around all wounds if anatomically feasible. All wounds should be carefully treated without fail with least traumatization. Any remainder RIG/ARS should be injected intramuscularly into thigh region (or away from vaccine site) in a single dose.

If the volume of RIGs is not sufficient to infiltrate all wounds, it may be diluted using sterile normal saline to a volume sufficient to infiltrate all wounds.

The accompanying modern rabies vaccine dosage shall be given as per schedule.

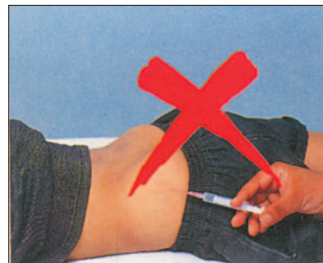
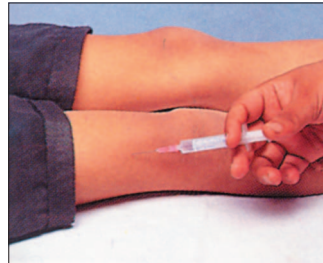
In conclusion, ARS/HRIG is known to have local viricidal effect and prevents the virus from entering the susceptible nerve cells.

Thus, RIG/ARS is life saving in category III wounds from high-risk

- Inject the vaccine deep intramuscularly (IM) into the deltoid or antero-lateral thigh in young children.
- Never inject the vaccine into the gluteal region as vaccine may be deposited in the fat and not get absorbed resulting in vaccine failure.

Points to Remember

- All category II and III wounds/ exposures need immediate starting of anti-rabies vaccination.
- Always inject the vaccine intramuscularly in deltoid or antero-lateral thigh (in young children).
- **Never inject** the vaccine into the gluteal region.

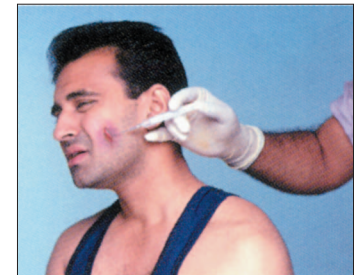


6.3 ADMINISTRATION OF RABIES IMMUNOGLOBULINS /ANTI-RABIES SERUM

The RIGs or ARS are readymade anti-rabies antibodies, which provide passive immunity and offer immediate protection. Even the best of modern vaccines take 10 to 14 days (or 3 injections minimum on days 0, 3 and 7) to elicit the protective antibody titre (of over 0.5 IU/ml of serum) and thus RIGs/ARS cover this vulnerable short incubation (or window) periods in category III exposures/severe wounds from high-risk category of animal. However, RIGs/ARS alone (without vaccine) should never be used.

started as per category of exposure suspecting that the animal is rabid (not to take chances with this 100% fatal disease.) and after Day 5 (from day of bite) in category II exposures and after Day 7 (from day of bite) in category III exposures the treatment may be stopped if the biting animal is alive after 10 days of observation.

However, 2 or 3 doses of modern vaccine (including s e r a) already given in these patients will result in partial immunization(wasted / incomplete protection). Hence, it is advisable to give an additional dose of vaccine on Day 21 or 28 and provide a modified pre-exposure regimen benefit in rabies endemic India.



Points to Remember

- Observation of dog or cat for signs of rabies for 10 days is valid and important.
- Modify the treatment regimen (from post-exposure to pre-exposure) if the dog/cat survives 10 days of observation.

6. ANTI-RABIES TREATMENT

As rabies is 100% fatal, anti-rabies treatment following animal bite is life saving and provides great relief to bite victims and apprehensive attendants. The Physician must view this seriously and it has 4 components, all of which need almost equal importance.

1. Wound care and treatment.
2. Administration of modern vaccine.
3. Administration of Rabies Immunoglobulins (RIGs)/Anti-Rabies Serum.
4. Counselling of patients and attendants.



6.1. WOUND CARE AND TREATMENT

This is often neglected and when done properly greatly reduces the risk of rabies (infection/death) to the extent of 50 to 70%.

Do

- Wash all wounds under running water (or flushing) for atleast 10-15 minutes.
- Gently clean all wounds with a detergent or any soap available (soaps are viricidal).
- Apply any household antiseptic like Dettol, Savlon, and Povidone iodine (preferred).
- In extraneous circumstances other alcoholic (>40%) preparations like Rum, Whisky, after-shave lotion may be applied on the wound (s).

Do not

- Bandage or dress the wound (wherever practicable or as far as possible).
- Use tincture iodine.
- Suture the wound.



Discourage

- Not to apply any local applicants like turmeric, neem, red chilli, lime, plant juices, coffee powder, coin, etc. as these will act as irritants and propel the virus in the wound deeper to cause nerve infection and resultant rabies encephalitis and death.



Points to Remember

- Proper wound care removes or reduces the virus load and improves the efficacy of rabies immunization.
- Discourage local wound applicants and avoid dressings.

6.2. ADMINISTRATION OF MODERN VACCINES

An early and correct administration of vaccine is life saving. The World Health Organization recommends administration of only the modern vaccines.

Post-Exposure (bite) regimen

- Administer the vaccine on days 0 (day of first dose of vaccine and not day of bite), 3, 7, 14 and 28.



Rabies Prevention

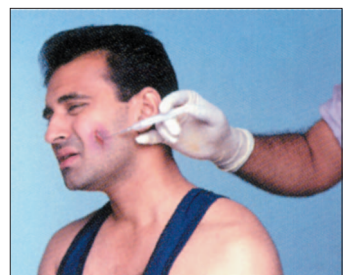
- Pre-exposure vaccination of "at risk" individuals should be encouraged.
- Pet owners should be strongly advised to get their dog/cat vaccinated regularly and obtain a license from local municipal authorities.

Rabies Prevention

and old; although it has no rationale, it may ensure better treatment compliance by some!

- To take bath regularly (except not to wet the wound).
- To take the prescribed tetanus toxoid, analgesic /anti-inflammatory and antibiotic as per advice.
- Not to apply any other applicants to wound or any dressing or bandage.
- To continue other prolonged medications viz. for diabetes, hypertension, asthma, etc.
- To observe the dog/cat on a daily basis (wherever relevant) for 10 days and on suspicion get a veterinary examination done (wherever feasible) and to inform the doctor.
- To emphasize the life saving value of anti-rabies treatment and need for compliance for the same.

A proper counseling and dialogue with the patient and attendants greatly builds the trust and confidence and eliminates possible conflicts.



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Points to Remember

- Animal bite is painful and stressful and counselling is soothing and reassuring.
- Counsel the patient for anti-rabies treatment compliance, habits, diet, drugs and work/activity.

9. KEY POINTS TO REMEMBER

- Rabies (in man and animals) is 100% fatal even today and there is no cure anywhere in the world.
- Rabies is enzootic (widely prevalent in animals) in India & hence, all animal bites/licks are dangerous.
- Carrier state of rabies in dogs (and cats) is not yet conclusively proven and established. Hence, both World Health Organization and Government of India recommend observation of animal during post-exposure treatment.
- In view of Consumer Protection Act (COPRA) the animal bites should be considered as “medical priority” and treated with due care and concern by the physicians.
- Immediate and early wound treatment to remove traces of saliva is very important.
- The physician should carefully go through the product information literature (of both vaccine & serum) and use the immunobiological accordingly.
- There is no contraindication for Post-exposure immunization including pregnancy, lactation, HIV, AIDS, other infectious diseases and conditions.
- When in doubt of degree of exposure to rabies risk it is safer to over treat than under treat.
- Correct post exposure immunization, more so use of serum in category III exposure is life saving.
- Modern Rabies vaccines viz., Rabivax, Rabipur, Verorab, Abhayrab, Vaxirab and Rabirix are superior and safer and shall always be PREFERRED and injected intramuscularly into deltoid/thigh in young children and NEVER in gluteal region.
- There is no single dose vaccine or a vaccine, which gives lifelong immunity.

- Train your dog not to bite. Train your dog to obey simple commands (sit, stay, come, no).
- Don't play aggressive games like wrestling or tug-of-war with your dog. Do not stare at dogs or provoke any animal.
- Don't leave children unattended with dogs. More bites involve children under 12.
- Talk to your children about avoiding strange dogs and growling dogs.
- Teach children not to take food and toys away from dogs.
- Don't run past a dog. They naturally love to chase and catch things. More attacks are seen with joggers and people out walking.
- Some people carry a stick when walking to protect themselves from dogs.
- If dogs are fighting don't try to break up by hand. Spray with water, yell at or make loud noises.
- Senior citizens are also at increased risk of dog bites. It is more difficult for them to move away due to arthritis, weak muscles and poor eyesight.
- Obey leash laws. Dogs on a public street, park or other property must be restrained by a leash.
- Neuter your dog, as neutered dogs are less likely to bite.

Points to remember

- Keep away from animals and their fomites.
- Encourage pre-exposure vaccination.
- Practice use of disposables.
- Recommend incineration for the rabies dead.
- Learn to avoid dog bites.

7. PRE-EXPOSURE VACCINATION

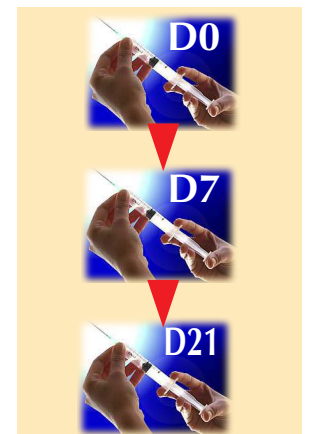
Only modern rabies vaccines (and not Semple vaccine) are recommended for pre-exposure (or pre-bite) vaccination. It is recommended primarily to those "at risk" individuals who are constantly exposed to animals by virtue of their job/habits, etc.

They mostly include:

- Veterinarians.
- Animal handlers and Taxidermists.
- Laboratory staff handling rabies virus.
- Pet owners.
- Postal and courier (door delivery) personnel.
- School Children, Joggers etc.
- People who complain of stray dog menace in their area.

The schedule consists of 3 primary series of injections (IM, deltoid) on days 0, 7 and 21 (or 28) followed by a booster after one year and subsequent boosters every three to five years.

After the initial primary 3 injections any (rabid) animal bite/exposure needs only 2 doses of any modern rabies vaccine on day 0 and 3 and there is no need for RIG/ARS at all (WHO, 2005). However, this may not be rigidly followed in confirmed rabies exposures, which is discussed in detail in FAQs, Chapter No. 11.



In view of scarcity of RIG/ARS in the country, it is beneficial to recommend pre-exposure vaccination to all those who can afford them and particularly to the school children.

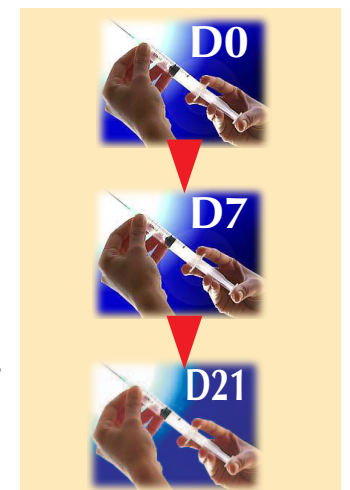
However, although rabies vaccines are known to be safe in pregnancy and lactation, unless strongly indicated it is recommended to avoid pre exposure vaccination in pregnancy and lactation.

Points to Remember

- Always advocate pre-exposure vaccination to all at risk individuals.
- Pre-exposure vaccination obviates the necessity of scarce RIGs in (some) category III high-risk exposures / bites later.

8. PERSONAL SAFETY AGAINST RABIES

- Do not touch animal bite wounds with bare hands.
- Do not touch the fomites viz. chain, food plate, etc. of an animal suspected or proven of rabies.
- Do not touch stray or sick animal.
- Take pre-exposure vaccination if you are in constant touch with animals.
- Avoid contact with saliva, urine, tears, semen and vaginal secretions of a hydrophobia (rabies) patient.
- Provide pre-exposure prophylaxis to those medical, nursing and ancillary staff who regularly attend to hydrophobia patients and to public health personnel removing rabid and stray animals.
- Veterinarians shall always be on pre-exposure prophylaxis, wear gloves, glasses, masks and long sleeved overall while examining rabid animals. Besides all instruments used shall be sterilized either by boiling or by placing them in a strong antiseptic solution.



The most important thing is to learn how to avoid dog bites.

How to avoid dog bites

- Typical warning signs of unfriendly dogs are snarling or a stiff stance ears laid back and fur/hair on back standing up.

122. Can a vaccinated dog succumb to rabies following bite by a rabid animal?

A dog effectively vaccinated against rabies ordinarily do not suffer and transmit the disease. But it is very difficult to say with certainty that a particular dog immunized with a specific vaccine is immune against rabies. If a tissue culture vaccine is regularly given to a healthy dog, it should develop sufficient protection. However, following severe and extensive bites (challenge dose of virulent virus infection) by a rabid dog, it may still succumb to rabies.

123. If the pet is immunized, whether the family members need pre exposure vaccination ?

A dog effectively vaccinated against rabies ordinarily will not suffer and transmit rabies. But it is very difficult to say with certainty that a particular dog immunized with specific vaccine is immune against rabies, more so in a rabies endemic area.

Animal lovers and Pet owners are always at the “high-risk” of rabies and therefore pre-exposure vaccination is recommended for all the family members.

124. What is the vaccination course of pet dogs ?

For dogs and cats, the primary schedule of 2 injections at 2 months age and 1 month later and a booster every year is recommended. Minimum 2 injections are considered immunologically efficacious.

The excitative phase follows the prodromal phase in some animals. This is also referred to as “furious form” of rabies. This is the categorical “mad-dog syndrome”, although it occurs in all species. The animal becomes irrational and, with the slightest provocation, may viciously and aggressively use its teeth, claws, horns or hooves. The posture and expression is one of alertness and anxiety with dilated pupils. Noise invites attack. Carnivores with this form of rabies frequently roam extensively and attack other animals, including humans and any moving object. Rabid cats attack suddenly, biting and scratching viciously. As the disease progresses, muscular incoordination and seizures are common. Death is the result of progressive paralysis.

119. Is there any species variation in the exhibition of signs of rabies?

Cattle with furious rabies are dangerous, attacking and pursuing man and other animals. Instead of placid expression, there is one of alertness. A common clinical sign is a characteristic abnormal bellowing, which may continue intermittently until shortly before death. Horses and mules frequently show evidence of distress and extreme agitation. They may roll on the ground, bite or strike viciously.

120. What is “paralytic form” of rabies in animals?

Dumb or paralytic rabies refers to animals in which the behavioural changes are minimal or absent and the disease is manifest mainly by paralysis. This is first manifested by paralysis of the throat and masseter muscles, often with profuse salivation and inability to swallow. Drooping of the lower jaw is common in dogs. The animals are not vicious and rarely attempt to bite. The paralysis progresses rapidly to all parts of the body leading to coma and death follows in a few hours.

121. Can rabies be transmitted to a dog, which has eaten the flesh of a dead rabid cow or buffalo?

Yes. The rabies virus after multiplying in the brain spreads to other organs of the body centrifugally like the heart, muscle, skin, etc. So the dog can definitely get infected because the virus can spread through oral mucus membrane.

important in transmission of rabies.

115. How should the animal causing the bite be handled ?

It is important to be able to establish if the animal causing the bite is healthy or diseased, bearing in mind that a rabid animal excretes the virus in its saliva not just throughout the illness, but also several days before the appearance of the first symptoms.

An unknown animal or one, which has disappeared, must be automatically considered as rabid, and curative treatment must be instituted immediately and carried out in full.

Cats and dogs, which can be identified, must be placed under observation and it is advisable to check if they have been effectively vaccinated against rabies. If the animal shows no sign of the disease after 5 days, the risk of infection can be considered as slight, and non-existent if the animal is still healthy on the 10th day (The European Standards recommend an observation period of 15 days). All wild animals, and those domestic animals suspected of having rabies, must be put down and the rabies diagnosis carried out in the laboratory.

If it is proven that the animal is not rabid – and only then – the anti-rabies treatment may be halted.

116. What is the clinical course of rabies in animals ?

The clinical course of rabies is divided into three phases viz. prodromal, excitative and paralytic. However, this division is of limited practical value because of the variability of signs and their irregular lengths of the phases.

117. What are the signs of rabies during the prodromal phase in animals ?

Prodromal phase may last for 1 to 3 days. The animal may show only vague CNS signs, which intensify rapidly. The disease progresses rapidly after the onset of paralysis and death is virtually certain within 10 days after the initial onset of signs. Some animals die rapidly without marked clinical signs.

118. What is “furious form” of rabies in animals ?

Caution is needed if injecting into a tissue compartment e.g. finger pulp. Excess fluid can result in increased compartmental pressure and lead to necrosis. Care is needed to avoid RIG seeping out of wounds during infiltration. If such a loss does occur, the volume should be estimated and replaced.

- The use of intradermal skin tests before ERIG treatment

However, the ID skin test detects IgE mediated type-I hypersensitivity, a reactogenic response to previous exposure to the antigen. Many opine that this has very little practical value but in India it must be done as it is mandatory under the drug laws.

85. What should be time gap between RIG and vaccination ?

Approximately within one hour after administering RIG, the vaccine should be given.

86. Is there any dietary restriction during PEP?

It is generally advisable to abstain from alcohol during the ARV administration as it may affect the immune response.

11.5 IntraDermal Rabies Vaccination(IDRV)

87. The IM dose of Verorab (PVRV) and Abhayrab (PVRV) is 0.5mL; that of Rabipur (PCEC) and PVRV (Coonoor) (where available) is 1mL. Still is the ID dosage of all vaccines uniformly 0.1mL?

The ID dosage of all approved vaccines is uniformly 0.1 mL per ID site irrespective of their IM dosage.

88. Can the type of vaccine be interchanged during the course of IDRV?

As far as possible, the same vaccine should be used throughout a course of IDRV.

89. Can the routes of vaccination viz., IM and ID be used interchangeably?

The route of vaccination, whether ID or IM should ideally remain the same throughout the course of vaccination in a patient.

dog is suspected to be rabid then the pet dog should ideally be put to sleep. But if the owner is not ready or the rabid status of stray dog is not known then post-exposure vaccination of the pet with cell culture vaccine and simultaneous careful observation of the dog is recommended for upto 2 months (upto 6 months desirable) for possible signs of rabies in it. During this period for any sickness in dog, the owner should take the dog to the veterinarian to get rabies ruled out at the first instance.

Simultaneously pre-exposure vaccination of all household members is necessary.

111. Can unvaccinated Pet dog / cat pose danger to the family?

As rabies is enzootic (prevalent in stray dogs) if pet unvaccinated dog is bitten by a stray rabid dog it will develop rabies and later pose threat at home to all family members.

112. If PEP is required for a bite by a vaccinated dog then why vaccinate the dog at all ?

Vaccination of the dog is to protect it against rabies following bite by a (stray) rabid dog. If potent CCV (veterinary) vaccine is given correctly as per schedule (pre-exposure) it will mostly prevent rabies in the vaccinated dog. But in enzootic (rabies prevalence in animals) India, where protection status of vaccinated dog by antibody estimation (RFFIT/MNT Test) is not possible due to scarce facilities & till such time rabies is eliminated from the stray dog population in our country, the need for PEP in exposed persons continues.

113. A vaccinated PEP dog is bitten by a rabid animal. What should the owner do ?

Ideally such dog should be humanely killed (put to sleep) by a veterinarian since post-exposure prophylaxis is not very successful. Such dogs pose risks (source of infection) to others and if the owner [much against professional advice] goes for post-exposure immunization of the dog, he should be informed of this risk.

114. Is age of biting dog important in rabies transmission ?

No. Neither the age nor the breed or sex of the dog is

10. INTRA DERMAL RABIES VACCINATION (IDRV)

The IDRV was first started in Thailand, in 1984 and found successful. In 1992, World Health Organization approved it for use in developing countries which face shortage of rabies vaccine due to paucity of funds. Consequently, Philippines in 1993 and Sri Lanka in 1996 have successfully implemented it. However, in India, as Semple (sheep brain) vaccine was widely used in Government hospitals till 2004 (till mid 2005 precisely) the shortage of rabies vaccine was not felt. But, now with the stoppage of Semple vaccine and the shortage of modern vaccines (due to budgeting constraints) is being increasingly felt. Consequently, it is now imperative to introduce IDRV as a safer, ethical and cost effective replacement of Semple vaccine in Government hospitals. As this is new to India, judicious planning and proper implementation are needed for its success as it largely benefits the poor and needy who visit Government hospitals.

10.1 MECHANISM OF ACTION OF IDRV

It is deposition of approved modern 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 neutralizing 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.

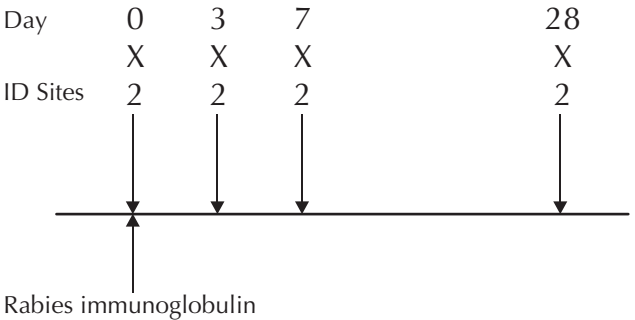
10.2 IDRV VACCINES

The following vaccines are currently approved for IDRV usage by Drugs Controller General of India (DCGI) These are Rabipur (PCEC), Verorab (PVRV), Abhayrab (PVRV) and PVRV of Pasteur Institute of India, Coonoor (PVRV). The Rabivax (lyophilized) from Serum Institute of India is in the final stages of ICMR trial and its approval is awaited. The anti-rabies vaccines Rabipur (PCEC) and Pasteur

Institute of India, Coonoor (PVRV), Rabivax, (HDCV), (lyophilized) are 1mL vaccines whereas Verorab (PVRV) and Abhayrab (PVRV) are 0.5mL by intramuscular route.

10.3 REGIMEN

As per Drugs Controller General of India (DCGI), the schedule recommended for IDRV is the updated Thai Red Cross (TRC) Schedule, which is 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.



For pre-exposure vaccination, 0.1ml of ID approved vaccine is to be given intradermally over one deltoid on days 0, 7 and 21 or 28. One booster is recommended after one year and subsequent boosters every three to five years.

10.4 PREREQUISITES

The IDRV is recommended for use in dog bite/anti rabies clinics, mostly in government, where there is a minimum of ten animal bite cases reporting everyday. This ensures proper use of the vaccine and minimizes its wastage. Though it is not a difficult technique, it must still be given by trained personnel namely Nurses, Pharmacists, Medical Officers under supervision. It is not recommended/advisable for use in private clinics and by general



Insulin syringe used for IDRV



Injecting IDRV



Bleb after correct IDRV

vaccination is required. But the dog must be further observed till 10 days from day of bite (wherever possible up to 15 days) and if it is healthy & alive no further vaccination is required. However, 2 doses of modern vaccine [day 0 and 3] received are not immunogenically protective and will go waste. Hence, in those who are in constant touch with animals, the person may be advised to take the 3rd injection on day 21 or 28 (3rd dose), which will offer the same benefit of pre-exposure prophylaxis with slightly modified schedule in this case (day 0, 3 and 21 or 28).

107. A Pet vaccinated dog died of sudden unexplained death. What should be done?

If facilities are available post-mortem of the dog for confirmation of rabies is required. If not possible, (or if the post mortem proves rabies) all those who came in contact with the saliva of the animal (directly or through its fomites) should be given PEP.

108. Whether treatment of provoked bites differ from unprovoked bites ?

Provocation is subjective & relative and specific to each dog/cat. However, obvious gross provocation viz., stamping, hitting, chasing, etc possibly suggest that the animal may not be rabid. However, the wound treatment of animal bites is the same.

109. Can Human ARVs viz. NTV or modern vaccines (HDCV, PCEC, PVRV and PDEV) be given to animals ?

Though human ARVs may not be harmful to animals, there is no dose-weight correlation of immune response nor their efficacy known in animals. Besides the incubation period of rabies in animals is long. Hence, it is advisable to reserve human vaccines for human use and use the veterinary vaccines for animals.

110. An unvaccinated or partially vaccinated Pet dog/cat is bitten by a dog. What should be done?

The wound should be immediately washed with a detergent soap and cold water and any household antiseptic like dettol/savlon/povidone iodine should be applied. If the stray

individual cases and on merit.

103. What should be done to a pet dog, which is bitten by a stray dog?

Thoroughly wash the wound with a detergent soap. Apply a household antiseptic viz. Dettol, Savlon, etc., and consult a veterinarian immediately.

104. Are there reports where the patient died of rabies but the biting dog is alive ?

Occasional such reports are seen which base their diagnosis of rabies in man on clinico-epidemiological basis and not on laboratory diagnosis. The most important is the laboratory confirmation of rabies virus secretion in the saliva of the biting dog. Hence, the so-called carrier state of rabies (otherwise healthy) is yet to be conclusively established; and till such time the current practice of simultaneous starting of vaccination and observation of dog shall continue.

105. A person has handled (or eaten) the raw meat of a rabid animal; what should be done ?

He should receive full course of 5 doses of rabies vaccine. In extremely rare cases if a person has eaten raw meat of a provenly (laboratory Diagnosis) rabid animal and if he has oral lesions or ulcers or is apprehensive, he may even be given ARS/HRIG [full dose in thigh IM on day 0 along with first dose of vaccine].

106. Can a vaccinated dog transmit rabies? How effective is dog vaccine ?

Modern veterinary vaccines (tissue culture) are efficacious. If in the last 2 years a dog has received 2 doses it is generally considered protected. Ideally its blood should be tested for protective antibody titre level but this is rarely practicable/feasible due to scarce facilities in our country. Consequently a bite by even a vaccinated dog in rabies endemic areas like India is suspected to be rabid and the bitten person is given 2 doses of post exposure immunization [day 0 and 3, injections] and after 5 days [day 7 in case of modern vaccines] if the dog is healthy no further

practitioners. The reconstituted vaccine, if any is left over at the end of the day, must be discarded and should never be used the next day. Lastly, proper refrigeration and storage of vaccine is essential to the success of IDRV.

WEB SITES ON RABIES

www.who.int/rabies
www.cdc.gov.in
www.apcri.org
www.rabiesinasia.org
www.kimscommunitymedicine.org

11. Frequently Asked Questions (FAQs:)

11.1 General Issues



1. Why does a person not acquire immunity against rabies natural infection, as it occurs in other viral infections?

From the site of bite the virus enters a nerve and via axoplasm reaches the central nervous system (CNS). Thus, there is no viremia and the virus is not accessible to the normal immune mechanism of the body. Only after travelling efferently from CNS via mostly autonomic nerves to different (target) organs the antibody production starts. But by that time the patient's brain stem neuronal cells are destroyed and he dies in a day or two either due to respiratory paralysis or due to cardiac arrest.

2. Can rabies be transmitted from man to man?

Theoretically, the saliva of a hydrophobia patient is infectious and occasionally such transmission is reported. But the well-documented transmission is through corneal transplantation. Hence, confirmation of cause of death, particularly in neurological cases is very important before corneal transplantation. Besides it is also important to avoid contact with saliva and secretions of a rabies patient. Recently in 2004 three cases of human rabies deaths were reported in USA following liver and kidney transplantations.

3. Are there any survivors of Rabies/hydrophobia?

There are 3 recorded survivors of rabies, 2 from USA (1970 & 1977) and 1 from Argentina (1972). All had received some immunoprophylaxis and they recovered following intensive care. No specific drug/therapy is responsible for their recovery (Kaplan, et. al.). In India, 2 survivors are reported from AIIMS, Delhi (1988) but they are not well acclaimed due to lack of laboratory evidence in their diagnosis.

4. Does kissing of a hydrophobia patient call for anti-rabies vaccination?

The saliva of a hydrophobia patient contains the rabies virus and is infective. If there is suspicion about contact with saliva of hydrophobia patient during kissing the contact person

There is no need to alter the dose or schedule of any concomitant medication during IDRV. All prescribed medications should be taken as per instructions.

11.6 Veterinary aspects

98. Is Bat Rabies Present in India?

No. Hence bat bites do not require post-exposure Immunization.

99. Is hydrophobia (fear of water) a sign in rabid dogs?

No. Rabid dogs can drink water and even swim in water.

100. What should be done to persons who have consumed milk of a rabid cow / buffalo / goat?

If they have heated/boiled the milk the virus is killed at 60°C in 30 seconds. They do not require any vaccination. However, if they are still very apprehensive and unconvinced or unsure about raw milk consumption, they may be advised PEP viz. 3 doses in doubtful exposure or 5 doses in possible exposure, at the exposure, at the discretion of physician viz. day 0, 7, and 21 (or 28) or day 0, 3, 7, 14 and 28.

However, if they have consumed raw milk, full course of PEP (5 doses) and if ulcers or injuries are found in the month then even ARS/HRIG is advisable (full dose IM, thigh, away from vaccine site in children).

101. What is the truth about carrier state of rabies in dogs?

Carrier state in dogs is very rare and are considered freaks of nature. Besides these dogs (mostly studied in experimental laboratories) excrete the virus intermittently & sometimes in low titre. Consequently the observation of dog for 10 days and appropriate simultaneous immunization of bitten person is considered valid even by WHO (1996).

102. Is 10 days duration of observation of dog (and cat) adequate and valid?

It is valid and adequate as per WHO. However, in Europe (rabies free areas) it is for 15 days and in India too wherever permissible/feasible this may be considered, only in

90. What should be done if the ID vaccine administration fails? (Spills out or goes subcutaneous).

Even if the IDRV fails in any one of the deltoids, then the vaccine must be given by IM route and the remaining doses given by IM route only.

91. If for some reason, IDRV cannot be given in deltoid region, what are the alternative sites?

The alternative IDRV sites are suprascapular, anterior abdominal wall and the upper part of the thigh (where socially acceptable).

92. Are there any contraindications to IDRV?

The only contraindications to IDRV are – the patient is on chloroquine or immunocompromised or any immunosuppressant therapy viz., anticancer drugs, radiation therapy, long-term steroid usage etc. In such cases the rabies vaccines should be given by IM route.

93. Are there any dietary restrictions during IDRV?

There are no dietary restrictions during IDRV.

94. If the IDRV patients miss some days of vaccination, how should they be managed?

The first three doses of IDRV given on days 0, 3 and 7 are very crucial and should be given as close to the original dates and preferably completed by day 7. About 1-2 days of variation for the fourth dose on day 28 is acceptable.

95. Is sera testing of IDRV patients necessary for checking the efficacy?

The IDRV is well tested and WHO approved and hence routine sera testing for rabies anti-bodies to know its efficacy is not required

96. Whether pregnancy and lactation are contraindications for IDRV?

Pregnancy and lactation are not contraindications for IDRV.

97. Is there a need to alter the dose or schedule of any concomitant medication during IDRV?

requires 5 doses of modern vaccine. If there are ulcers in the mouth of the contact then even serum or HRIG must be given by IM route.

5. Can rabies be transmitted through sexual intercourse?

Rabies virus is present in the semen and to some extent in vaginal secretions. In some patients, priapism, increased sexual libido and indulgence is seen (both in men & women patients). Hence, in the contact (exposed) person 5 doses of modern vaccine should be given. If there is doubt of category III exposure viz. abrasion on penis or in vagina then even serum or HRIG must be given by intramuscular route.

6. A pregnant woman develops hydrophobia. What should be done?

In humans, rabies virus is not known to cross the placental barrier and consequently the foetus is safe. Hence, the hydrophobia pregnant woman should be clinically managed and if induction of pregnancy / caesarean section is possible the obstetrician shall do it with due "personal precautions" and immunoprophylaxis (3 doses of modern vaccine usually or if any accidental negligible exposure/doubt 5 doses of any modern vaccine). The newborn has to be given 5 doses of any modern vaccine as PEP.

7. Can rabies be transmitted following bite by a hydrophobia patient?

It is possible and hence 5 doses of modern rabies vaccine (and RIGS, if category III) should be given to the bitten person.

8. What are the myths and wrong notions about rabies in India?

- Some herbal extracts and concoctions will cure rabies.
- In rural areas, people also resort to witchcraft, magico-religious practices, and other methods to cure rabies.
- Washing of the wound can cause hydrophobia.
- Dietary changes can cure viz. shift from vegetarianism to

non-vegetarianism and vice versa; stopping consumption of white things, etc.

- A single dose vaccine will prevent rabies. This is the most dangerous belief and is prevalent in all sections of society.
- Vaccines are more effective if taken on empty stomach.
- One should not take bath; eat meat and eggs during vaccination.

9. What is the problem of rabies and dog bites in India ?

According to a recent WHO-APCRI Indian Rabies Survey (2003) an estimated 20,000 human rabies deaths occur in India annually. Besides there are an estimated 17 million animal bites (> 90% due to dogs) annually.

10. What are the countries, which are free of rabies ?

There are about 59 countries, which do not report rabies. Two continents viz. Australia and Antarctica are free of rabies. Others include Guyana, Jamaica and Uruguay in America, Bahrain, Qatar and Japan in Asia; Great Britain, Scandinavian countries, Spain and Portugal in Europe, Australia, New Zealand, Fiji and Papua New Guinea in Oceania.

11. What are the areas in India, which are free of rabies?

The islands of Andaman and Nicobar and Lakshadweep are free of rabies. Besides the islands of Lakshadweep are free from dogs also!(WHO-APCRI, 2004).

12. Can rabies infection be transmitted through environment ?

The aerial (by aerosol) route of transmission of rabies virus is suspected in bat rabies (in Latin Americas) where men while passing through caves containing carcasses of bats reportedly acquired bat rabies infection and died later. It can also occur accidentally in rabies vaccine and research laboratories.

13. What are the determinants of (factors responsible for) rabies transmission in man from proven rabid animals ?

neutralize the virus. However, as it is a skilled procedure it requires some training and for expertise it needs some practice and practical experience to become competent and confident.

84. What are the important considerations while administering Rabies Immunoglobulin (RIG) ?

Human or Equine rabies immunoglobulin (HRIG or ERIG) is administered on day 0. If possible, RIG should be administered on the day of bite at the same time as the first dose of the vaccine. If such simultaneous prophylaxis was not given, i.e. if only the vaccine was given initially, then it is meaningful to administer RIG up to the 8th day after the first injection of the vaccine. The prescribed dosage of RIG must not be exceeded.

• Dosage

Human Rabies Immunoglobulin (HRIG) is given as 20 IU/kg. The maximum dosage is 1500 IU or 10mL

Equine Rabies Immunoglobulin (ERIG) is given as 40 IU/kg. The maximum dosage is 3000 IU or 10mL

Both are injected as much as possible into and around the wounds and any surplus / leftover is given by deep IM injection at a site away from the vaccine site. If the calculated volume is inadequate to inject all wounds, then dilute it in normal saline to a sufficient volume to infiltrate all wounds.

Disregard the old recommendation that half of the calculated volume of RIG should be injected into the wounds and half IM elsewhere.

• Site of injection

Wound infiltration is the most important part of RIG administration. If any of the dose remains after infiltration, it can be given IM into the antero lateral thigh, or at a site away from vaccine site and if necessary divided between the two thighs. Injection should not be given into the gluteal region.

• Method of wound infiltration

80. Can ARS/HRIG be given after starting vaccination ?

The combined use of ARS/HRIG (passive immunity) and vaccine (active immunity) must be carefully adjusted if the effects of one are not to cancel out the effects of the other. Hence, ideally the serum must be given within 72 hours of starting of vaccine. However, where serum is inevitably to be given beyond 72 hours of starting vaccine an additional extra dose of vaccine is recommended by IM deltoid/thigh administration.

81. If HRIG is not available can human normal immunoglobulin (polyvalent) be given ?

Human normal immunoglobulin (polyvalent) cannot substitute for HRIG.

82. How is ARS (Equine) or HRIG life saving ?

The local infiltration of wounds with ARS/HRIG is of paramount importance as it neutralizes any residual virus still present in wound (after wound treatment) & thus prevents entry of virus into a nerve ending at bite site. Besides ARS/HRIG also provides ready-made rabies antibody before an active response to vaccine takes place. The earliest protective level of antibody ≥ 0.5 IU/mL response to modern vaccines is by day 14. However, in severe bites/bites close to brain the incubation may be as short as 4-10 days. In these cases HRIG/ARS is lifesaving. After ARS/HRIG administration the rabies antibody can be detected within 24 hours, with HRIG it reaches a level of 0.1 IU/mL at 3 days & declines with half-life of about 21 days, whereas in ARS (Equine) this is still of a shorter duration. Hence, ARS/HRIG provides immediate passive protection before active protection to vaccine is induced by day 14.

83. How to inject RIGs locally?

The RIGs shall be warmed to room temperature (after removing it from refrigerator) before injecting. By using sterile hypodermic syringes (Mantoux/Insulin) with 26 G needles the RIGs are infiltrated carefully with minimal traumatization into and around all wounds to locally

- Quantum of saliva and dose of virus and strain.
- The site and severity of bites.
- The extent of trauma viz. wounds.
- Nature of wound care particularly application of irritants like red chilli, plant juices, copper coin, etc.
- Delay or incorrect vaccine treatment and gluteal injection of modern vaccines.
- Nonuse of RIGS.

14. What is the “reservoir” and “source of infection” in rabies ?

The reservoir is where the rabies virus normally thrives. In India, it is mostly the dogs, cats, mongoose, foxes, jackals, and other animals. The source is the medium through which the virus is spread/transmitted. It is the saliva of rabid animals.

15. Can rabies be transmitted to doctor/assistants conducting postmortem of a person died of rabies ?

No. There is no risk of postmortem transmission in rabies.

16. What are the symptoms of rabies in human beings ?

In humans the disease has two distinct clinical forms. The categorical is the aggressive form of “hydrophobia” and the less common is the “paralytic rabies”. The disease starts with prodromal symptoms characterized by headache, restlessness, fever, and itching at the site of bite, even if it is healed. In the categorical hydrophobia, which occurs in majority of the cases, there is fear of water, fear of draught of air/breeze (Aerophobia), fear of light (Photophobia), tremors, spasms, and convulsions. In the terminal stages there is respiratory paralysis, cardiac arrest and death in 1 to 5 days. In the less common paralytic rabies the clinical features are a gradual ascending paralysis, constipation and urinary retention, stupor, coma and death in 1 to 14 days. Hydrophobia is usually absent in these cases.

17. What should be done if there is a human rabies case ?

The patient should be admitted in a quiet isolation room.

The patient must be sedated along with administration of antipyretics, analgesics, antihistamines and anticonvulsant. Intravenous rehydration is a must. The cerebral degeneration has to be managed with mannitol. Mechanical ventilation of lungs, cardiac pacemaker and intensive nursing care (where facilities are available) are indicated.

18. What is a street virus ?

Street virus is virulent, has long and variable incubation period of about 3 weeks to 3 months.

19. What is fixed virus ?

Fixed virus is an attenuated street virus, least virulent and has a fixed short incubation period of 5 to 9 days. It is used as seed virus needed for manufacturing vaccines.

20. Can a “major surgery” be conducted after the dog bite?

Generally, there is no contraindication for any surgery along with anti-rabies treatment and a full course of anti-rabies immunization should be given, irrespective of the surgery or other procedures.

11.2 Wound care

21. What are the most dangerous sites of bites/exposure in man?

Theoretically the richly innervated areas like head, neck, face, hands and genitals are very dangerous. But in reality it is often the wounds on legs, which are ignored/neglected, which have caused rabies and death of patient.

22. Can the animal bite wounds be cauterized ?

In this era of modern rabies immunization, the use of carbolic acid or caustic agents amounts to medieval practice and are strictly prohibited. In fact it amounts to medical malpractice and the doctor can be sued for compensation following pain and scars.

23. Whether washing of animal bite wound (s) is essential? What is its role ?

Wound treatment is very valuable and by itself, can prevent rabies by eliminating or inactivating the inoculated virus.

cannot afford HRIG and the situation is life threatening, under signed informed consent ERIGs may still be administered following a premedication/ pretreatment with injecting avil (antihistamine), rantac (H2 blocker) and injection wysolone (hydrocortisone) half an hour before full dose administration of ERIGs. Such patients shall be given ERIGs in a hospital/nursing home facility and not in a clinic setup. Following the treatment they are kept under observation for about three hours and then sent home.

If this is also not possible then the wounds must at least be thoroughly flushed with povidone iodine or surgical spirit (to neutralize the virus) and the patient should preferably be given two doses of vaccine on day 0 in both deltoids.

76. If ERIG/ARS is inadequate to infiltrate extensive wounds and what should be done ?

Dilute it with normal saline upto a volume sufficient to infiltrate all wounds and any left over quantity be given in thigh (away from vaccine site) by IM route.

77. What if HRIG is inadequate?

Dilute it with normal saline upto a volume sufficient to infiltrate all wounds and any left over quantity be given in thigh (away from vaccine site) by IM route.

78. How to calculate the total dose of ARS/HRIG ?

ARS (CRI), Equirab, Zyrig and Abhayrig are 5 ml vials (300 IU/ml) or 1500 IU per vial

$1/300 \times 40 \text{ IU} \times \text{Body wt (Kgs)} = \text{Dose in mL}$

HRIG [Berirab, Berirab-P, Imogamrab and Kamrab] 2 mL and 5 mL ampoules (150 IU per mL)

$1/150 \times 20 \text{ IU} \times \text{Body wt (Kgs)} = \text{Dose in mL}$

79. Can ARS/HRIG be given locally to a healed wound ?

If a wound is healing viz. scab is formed, then without disturbing the scab the RIGs are infiltrated around it. If it is completely healed without any signs left, then the total dose of RIGs is given in thigh by IM route (at a site away from vaccine administration).

A person receiving/completed anti-rabies immunization (vaccine/ sera) can donate blood. However, the recipient does not benefit from the transfer of rabies neutralizing antibodies due to haemodilution.

11.4 Rabies immunoglobulins

73. How safe is ARS (Equine)? Can adverse reactions occur after negative skin test ?

Generally, the currently available ARS (Equine) are purified (enzyme refined and pepsin digested) and safe and the reported anaphylaxis is 1:40,000 patients. However, in 1-6% of patients, even after a negative skin test there may be adverse reactions ranging from serum sickness like reaction to anaphylaxis. Hence, it is always safer to keep emergency drugs (like adrenaline, Wysolone, antihistaminics, oxygen, etc.) on hand and ARS preferably be given in an hospital facility.

74. How adverse effects to ARS are managed? Does it influence subsequent vaccine therapy ?

The immediate reactions are anaphylactoid type viz. hypotension, dyspnoea, syncope, urticaria. Serious type of reactions like Quincke's edema or anaphylactic shock is rare (<1%). This is treated with adrenaline, oxygen, artificial respiration, hydrocortisone and antihistamines.

Serum sickness like reactions (1% subjects) may occur after 6 days. They consist of an inflammatory reaction due to compliment activation and formation of immune complexes (type III hypersensitivity reaction). Clinical symptoms are fever, pruritis, rash, urticaria, adenopathy, and arthralgia. This is treated with non-steroidal anti-inflammatory agents and anti-histamines.

The use of a small dose of Hydrocortisone is not known to suppress the immune response.

75. If a skin test is positive (to ERIG) in a category III rabid animal bite, what should be done ?

Ideally the patient should be persuaded to buy HRIG, which is practically safe, and no skin test is required. If the patient

Hence, wound treatment must be done immediately or as soon as possible.

Wound treatment

- Gentle washing of the wound using a detergent soap preferably under running tap water for atleast 10 - 15 minutes.
- Application of viricidal agents like povidone iodine, or other antiseptics like dettol or savlon.
- In some extensive deep wounds thorough exploration, debridement, removal of dirt, dead tissue and foreign bodies may be required in an institution and sometimes under anaesthesia.
- Suturing must be generally avoided as a rule, as it may risk inoculation of the virus deeply into the wound. However, if the wound has to be sutured, it should be done as late as possible from several hours to 3 days. The suture should be loose and not interfere with free bleeding and drainage.
- Generally animal bite wounds should not be dressed or bandaged and if unavoidable it should be loose and not occlusive.
- Proper tetanus prophylaxis viz. tetanus toxoid (and ATS or tetanus immunoglobulin in deserving cases) should be given.
- Systemic antibiotics like amoxycillin, cotrimoxazole are recommended to prevent wound sepsis. Application of irritants like plant juices, coffee powder, chilli powder, metals, coins, acids, and alkalies are strongly discouraged. With the advent of efficacious vaccines and sera, the age-old practice of chemical cauterization of the wound with strong acids and alkalies is discontinued.

24. Whether the dog bite wound should be allowed to bleed, or bandaged or stitched?

- Suturing must be generally avoided as a rule, as it may risk inoculation of the virus deeply into the wound.

However, if the wound has to be sutured, it should be done as late as possible from several hours to 3 days. The suture should be loose and not interfere with free bleeding and drainage.

- If suturing is done it should be done under local infiltration of anti-rabies serum (or HRIG). If ARS is not available, as a last resort the wound must be thoroughly flushed with atleast povidone iodine or any other antiseptic before suturing.
- Generally animal bite wounds should not be dressed or bandaged and if unavoidable it should be loose and not occlusive.

25. Can the wound be deepened for cleaning purpose ?

Never try to deepen the wound by cutting it further to bleed and then clean the wound. However, in some cases of extensive damage debridement and removal of tissue debris may be attempted.

26. Can we apply local antibiotics or anti-microbial agents on the site of bite ?

Local antibiotics or anti-microbial agents can be applied on the site of bite after cleaning the wound.

27. What should be done with severe animal bite wounds that would, with most other types of injury, be closed by primary suture ?

If possible, suturing of wounds should be avoided; however, if suturing is necessary, Rabies Immunoglobulin should be infiltrated into and around the wound. Any surgical manipulation of possibly rabies-infected animal bite wounds increase the risk of death. Three of the five children who died of rabies, according to the 1996 report from Thailand, India, and Sri Lanka, had primary suture before infiltration of the wounds with RIG.

It has also been the experience of Thailand's senior traumatologist that human and animal bite wounds are best closed by secondary suture after proper cleansing and daily

The first anti-rabies vaccines, prepared from animal brains, were capable of causing considerable side effects, notably serious post-vaccinal encephalitis, since they could contain neurological elements such as myelin.

Moreover, vaccination required a large number of injections, accompanied by considerable local reactions. That is why the anti-rabies vaccination acquired the reputation of being a "dangerous" vaccination, which should only be applied in cases of absolute necessity. This type of vaccine is still used in some countries.

These fears are no longer justified with modern rabies vaccines.

70. Whether modern rabies immunization is always protective? How can it be made more effective ?

There have been failures in anti-rabies treatment, even when carried out with modern vaccines, which are of course very immunogenic. The analysis of cases has been the subject of several meetings of WHO experts. It appeared that these failures did not call into question the immunogenicity of the vaccines, but were due mostly either to late vaccination or to the absence of immunotherapy, or to the immune deficiency of the patients linked to a disease or a treatment: malaria, chronic illness such as cirrhosis, congenital or acquired immune deficiency, immunosuppressant treatment.

That is why WHO experts recommend increasing the initial dose of the vaccine in treating such patients, and resorting increasingly to the injection of rabies immunoglobulins (RIGs).

71. How to approach in case of irregularities in treatment schedule, i.e. if patients missed the doses as per the due dates? (i.e. if the schedule is broken).

First three doses of modern vaccine should be very regular and for the fourth and fifth dose, one or two day variation would not affect the schedule.

72. Can a person receiving/completed anti-rabies immunization (pre or post) donate blood ?

(whatever schedule is used) in the following situations:

- In patients who seek treatment after a delay of 48 hours or more;
- In patients with very high-risk exposures or extensive wounds viz. on head, neck, face, hands and genitals, etc following bites by suspect or proven rabid animals or by wild animals viz. mongoose, jackal and fox.
- In patients who are congenitally immunodeficient or suffering from Acquired Immuno-Deficiency Syndrome;
- In patients taking immunosuppressive drugs including corticosteroids, anti-malarials and anti cancer drugs.
- In the severely malnourished patients;
- In patients with underlying chronic disease (e.g. liver cirrhosis);
- In patients where RIG is indicated but unavailable.

68. What should be done to patients who have been severely exposed to rabies and previously started on a vaccine series without RIG ?

This is a common situation in rabies endemic countries where Rabies Immunoglobulin (RIG) is often not available, although the vaccine may be on hand. Giving RIG after the vaccine results in suppression of the endogenous systemic antibody response, but it is not known to what extent this is clinically significant. It has been suggested that RIG should not be given after day 7 (upto day 8) when a potent modern rabies vaccine can be expected to have produced detectable circulating antibodies. However, this recommendation has never been confirmed by a prospective study in humans who have been severely exposed. Medico-legal considerations may make it prudent in some such cases to inject the wound sites even after day 7 (upto day 8) following the first dose of the vaccine, and give an extra dose of vaccine along with RIGs and complete the full course of vaccine (including day 90).

69. Why do some people fear the vaccine ?

wound care. Infection is much less of a problem when this is practised, and cosmetic end-results are better. Therefore, good daily wound care and secondary closure after 1 week is recommended. When primary surgical intervention is unavoidable, only the most urgent surgical manipulation should be carried out and only after thoroughly cleansing and careful infiltration of the wounds with RIG.

11.3 Modern rabies vaccines

The obituary to sheep brain (Semple Vaccine) was made in December 2004 following stoppage of its production after a Supreme Court order. Consequently all Rabies vaccines available in India now are cell culture or purified embryonated egg(PDEV) rabies vaccines.

28. What are the important considerations while administering a modern rabies vaccine ?

The combination of local treatment of the wound, passive immunization with Rabies Immunoglobulin (RIG) and vaccination is recommended for all severe (category III) exposures to rabies. Prompt and thorough cleansing of the wound, and administration of purified Equine or Human Rabies Immunoglobulin (ERIG or HRIG) and modern rabies vaccine immediately after exposure virtually guarantee complete protection.

All intramuscular injections must be given into the deltoid region or, in small children, into the anteriolateral area of the thigh muscle. The vaccine should never be administered in the gluteal region.

The most widely used WHO Essen scheme calls for a single vaccine dose IM, administered in the upper deltoid (anteriolateral area of thigh for children) on day 0, 3, 7, 14, and 28 or 30 with an optional further dose on day 90.

Often the day 90 dose is omitted except in those given passive immunization with RIG (usually category III bite).

The gluteal region is not recommended on account of high fat content in this region, which retards the absorption of the vaccine.

- 29. Continuous cell lines (like Vero cells) originate from malignant cells. Then the PVRV (Verorab, Abhayrab and Rabirix) is produced from Verocells (African green monkey kidney cell line). Can it cause malignancy?**

The verocell lines are thoroughly tested for their capability of inducing malignancy in most susceptible animals even in that passage (subculture) which is beyond the passage used for production of vaccine. Verocell lines have been shown not to produce any malignancy in both invivo and invitro systems. The verocell line used for production of PVRV has been approved by WHO and is a part of American Type Culture Collection [ATCC], which is, accepted Worldwide. The same cell line is now used for production of even polio vaccine.

- 30. SV40 (Simian Virus 40) is known to be a common contaminant of monkey derived cell lines, which can produce cancer in some lower animals. Is it a contaminant of Verocell also?**

Verocell line used for PVRV (Verorab, Abhayrab and Rabirix) is free of any SV40 virus.

- 31. What is abbreviated Multisite intramuscular schedule?**

In the abbreviated Multisite intramuscular schedule, (also known as Zagreb Schedule), the 2-1-1 regimen, one dose [of HDCV or PCEC or PVRV or PDEV] is given in the right arm and one dose in the left arm (IM) on Day 0 and one dose applied intramuscularly in the deltoid region on days 7 and 21. Though this is WHO approved it is not approved by Drugs Controller General of India and hence should not be used by medical practitioners in India.

- 32. Can modern vaccines be diluted with tetanus toxoid or water for injection or any other diluent and administered?**

Since mixing of biological products can lead to physical or chemical interactions and in the absence of specific studies the modern vaccines, which are costly should not be diluted with any other diluent other than that provided with the vaccine.

- 33. Accidentally the rabies vaccine was kept in the Freezer. Can**

not the case in India where there is rabies among a large stray dog population, where 50% of the dogs that had bitten man and were taken for laboratory examination proved to be positive for rabies.

Hence, it is mandatory to start treatment and discontinue it after the dog remains healthy, or has been found negative by laboratory examination.

For example: If the dog is available for observation we say that the risk can be reassessed, but start the immunization and observe the dog for 10 days. If the dog is well on day 7 (by which time the third vaccine dose is due), the day 7 vaccine is postponed to day 8; if the dog is well on day 8, it is postponed to day 9 and so on; if the dog is well on day 10 no further vaccine is given and post-exposure schedule is converted into a pre-exposure vaccine schedule.

If the dog is not available for observation, vaccine has to be given because risk cannot be reassessed later.

- 66. What should be done with a patient who has had exposure, but only goes for treatment after considerable delay (weeks to months)?**

Since prolonged incubation periods have been reported, persons who present themselves for evaluation and treatment even months after having been bitten should be dealt in the same manner, as if the exposure occurred recently. No one knows what happens to the rabies virus during prolonged ion periods. Does the virus reside at the bite site before suddenly replicating and migrating centrally, or is it already in nervous system? There is no way to determine whether such a patient is infected and whether he or she is now silently incubating the disease.

Consequently, ethical and medico-legal considerations mandate that such a patient be given full post-exposure vaccination, including injection of wound sites with RIG.

- 67. What are the indications for doubling the first dose of rabies vaccines?**

It may be appropriate to double the first dose of the vaccine

victims and more so in children. This is in conformity to the popular adage that “in rabies prevention when in doubt it is safer to over treat than under treat”. The rationale for this argument is the poor cold chain for vaccines, unsatisfactory wound treatment, late reporting, wrong vaccine injection practices, limited RFFIT testing facilities, doubtful immunity status of the patient, etc. in the country.

62. Whether egg (chick or duck) allergic subjects can be safely injected with chick or duck embryo derived vaccine ?

Despite the high degree of purity of PCEC and PDEV vaccines, there is a theoretical and remote risk of inducing anaphylactic reaction in person sensitized to avian proteins. HDCV (Human diploid cell culture vaccine) or Purified verocell rabies vaccine (PVRV) should be used in these persons with known sensitivity to avian proteins.

63. If a healthy dog is bitten by a rabid dog and the next day, that healthy dog bites a person, should he/she receive rabies vaccine?

In dogs the minimum incubation period of rabies is 3 days; still if the person can afford rabies vaccine he /she should be given the vaccine to alleviate anxiety and apprehension.

64. What drugs are contraindicated during rabies immunization ?

All immunosuppressive drugs are generally contraindicated viz. steroids, antimalarials drugs, anti-cancer drugs, etc. However, if they cannot be avoided then these patients may be given double dose of rabies vaccine on day 0 and may be even on all remaining days and tested for antibody titres where ever possible.

65. Is observing the dog for 10 days, without initiating treatment risky or justifiable ?

As rabies is practically 100% fatal, prevention of rabies infection after exposure is of utmost importance.

The practice of first observing a dog that has bitten man before starting treatment is encouraged in America, Australia and Europe which are rabies free. This is however

it be used ?

As freezing and thawing (liquefying frozen substance) is known to affect the potency of the vaccine, it should not be used.

34. Is it essential to perform an antibody test on the patient following ARV?

Antibody tests viz., Rapid Fluorescent Focus Inhibition Test (RFFIT), Mouse Neutralization Test (MNT), etc., are sophisticated tests and are done only at select few reference centres in the country. Besides antibodies test are not required on a routine basis when rabies vaccines are stored under proper cold chain and given according to the approved schedule.

35. A person started with PVRV wants to change over to HDCV or PCEC or PDEV. What should be done?

All modern vaccines viz., HDCV, PCEC, PVRV, and PDEV are freely interchangeable. This is done occasionally either for cost reason, or due to sudden non-availability of one brand or due to allergy to one of the CCVs or PDEV.

But it should not be encouraged as a practice as it will then be difficult to attribute any adverse effects or treatment failures to any one vaccine.

36. A dog/cat became unavailable or disappeared for observation from day 4 and the patient was given modern vaccine on day 7 (3rd dose). Subsequently from day 8 it became reavailable (reappeared).What should be done ?

The dog or cat should be observed till day 10 or wherever possible upto day 15 and if it is healthy and alive then the 4th injection due on day 14 is not required. But the earlier 3 injections (on days 0, 3, & 7) may provide protective antibody titres for about/upto 3 months.

37. A patient received two doses of modern vaccines (Day 0, 3) and the dog was well on day 5 & 7 (3rd injection due, but not given). However, the dog dies on day 8 to 15 (any day). What should be done ?

If rabies in the dog cannot be confirmed by post-mortem

then it is taken as “suspect” and the remaining (not to restart afresh) 3 doses of day 7, 14 & 28 shall be given as close to the original dates of schedule and all the 5 injections completed by day 28. In category III bites even RIGs should be administered.

38. Of the currently available modern vaccines viz., Rabivax, Rabipur, Verorab, Abhayrab, VaxiRab, and Rabirix which is the best vaccine?

For all practical purposes from safety and sero-efficacy point of view all are good and approved by Government of India. But each vaccine has its own merit, which the doctor should consider, while using it in a given situation/case.

- a. Rabivax (HDCV): This is of homologous [human] origin, considered by many as the "purest" antigen; the popular vaccine in the developed world and is often considered as "Gold Standard" in modern rabies vaccines. It was the most expensive vaccine and till 2002 was imported from France. It is now indigenously manufactured by Serum Institute of India, Pune and available from 2004 in liquid (adsorbed) form.

The lyophilized form is now under testing by ICMR for ID use and shall soon be available for both IM and ID usage.

- b. Rabipur [PCEC vaccine]: It is indigenously produced in India by Novartis Vaccines and Sanofi Aventis at Ankleshwar, Gujarat. Besides, it is exported from India to Nepal, Bangladesh, Philippines & Sri Lanka, thus signifying its quality. It is also approved by the Food and Drugs Administration (FDA) of USA and sold as “Rabavert” in USA.
- c. Verorab [PVRV]: It is a thermostable vaccine, has a dose of 0.5 ml unlike Rabivax /Rabipur/VaxiRab, which are 1ml. It is imported from France to India by Sanofi Pasteur and marketed by Ranbaxy Pharmaceuticals.
- d. Abhayrab (PVRV): It is a thermostable vaccine and has a dose of 0.5 ml. It is produced by Government of India, through Human Biologicals Institute, at Ootacamund, Tamilnadu, a unit of National Dairy Development Board

when exposed to poor cold chain conditions/higher temperatures.

59. Can Rabivax be stored at room temperature?

All rabies vaccines including Rabivax shall be stored between 2 to 8°C in a refrigerator. They shall not be kept at room temperature or frozen (kept in freezers). Besides the vaccines should not be exposed to sunlight, heat, dust and dirt.

60. Are there any failures in anti-rabies treatment ?

There are occasional reported failures despite the use of modern rabies vaccines. This has been discussed at several WHO and other international meetings of rabies experts. It appears that these failures did not call into question the immunogenicity of the modern vaccines, but were mostly due to either delayed vaccination or to the non-use of RIGs or to the immune deficiency of the patients linked to a disease or a treatment viz. malaria, cirrhosis of liver, chronic illness, use of steroids, antimalarials, anti-cancer drugs, etc.

61. A previously immunized person is bitten again. What is the re-exposure immunization schedule?

In persons who have received previously (anytime in the past) either pre-exposure (3 doses) or post-exposure (5/6 doses) vaccination now need only two doses of modern rabies vaccine as revaccination on day 0 and 3. This is because the previously vaccinated persons have the advantage that these two booster doses of vaccine will rapidly induce a large increase in antibody production (a secondary/anamnestic response) and this treatment is still needed urgently. However, no RIG treatment is necessary in them (WHO, 1997).

However, the author is of the personal opinion (much against the WHO guidelines) that in rabies endemic India it would be worthwhile to give full course post-exposure immunization (5 doses of vaccine + RIGs) in suspect (veterinary opinion) or confirmed (laboratory) rabies exposures or exposures to wild animals (category III) irrespective of the past rabies immunization status of the bite

In view of the above facts and practical difficulties, rabies being 100% fatal, we take no chances and start PEP (Immunization) in the bitten person & suspect the vaccinated dog to be incubating rabies (and infective) and simultaneously observe the dog.

However, in extremely rare situation, exceptions to the above thumb rule can be made at the professional discretion of the treating physician (which is beyond the scope of this manual).

55. As there are different strains of rabies viruses in different parts of the world, whether Rabivax is effective against all these (strains of) viruses ?

Molecular epidemiology studies have demonstrated that there are no considerable variations between vaccinal and wild strains. Hence, all modern rabies vaccines including Rabivax are considered as protective throughout the world.

56. If after two to three injections of Rabivax the seroprotective level is obtained, then why give further injections?

It is because – (a) To cover a longer incubation period of disease as it can be more than 3 weeks to 3 months. (b) To increase the cellular immunity and interferon production which are also to play a role in the mechanism of protection. This applies not only to Rabivax but for all rabies vaccines .

57. WHO recommends that potency of modern rabies vaccines to be atleast 2.5 IU per dose. Is it always guaranteed ?

The Central Drug Research Laboratory, at Central Research Institute, Kasauli, Himachal Pradesh tests every batch of all rabies vaccines in use in India. Only after its certification not only for its potency, but also for its sterility, stability, etc the vaccines are released into the market.

58. What are the consequences of a vaccine with a high potency?

There are absolutely no risks with vaccines of higher potency as sometimes upto 14 IU per dose are reported. A higher potency is generally (but not always) known to induce a higher antibody response and also may be of some help

(NDDB), Indian Immunologicals, Hyderabad. It is the most economical vaccine currently available in India.

- e. Vaxirab (PDEV): It is a modern embryonated egg rabies vaccine and not a cell culture vaccine. It is indigenously manufactured in India by Cadila Health Care Ltd at Ahmedabad, Gujarat. It has a 1 ml dose, highly purified from whole virion and free from any avian proteins. It is marketed by Zydus Alidac.
- f. Rabirix (PVRV) It is a 0.5ml vaccine by IM route. It is a chromatographically purified vaccine manufactured by Bharat Biotech, Hyderabad and launched in December, 2006.

39. What are the contraindications to PEP ?

Rabies is 100% fatal & hence there is no contraindication to PEP at all.

40. Can a rabies vaccine be given to a pregnant woman ?

All rabies vaccines are known to be safe during pregnancy. Besides pregnant women with history of animal bite are susceptible to rabies and should be given PEP. Hence, following ARV administration, MTP should be not done as a routine clinical practice.

41. Can a pregnant woman be given pre-exposure vaccination?

Modern rabies vaccines are considered generally safe during pregnancy (as of reports available till now) and no teratogenicity or other adverse effects are reported during pregnancy. However, pregnant women wherever possible should avoid both animal bites and pre-exposure vaccination.

42. Can a lactating mother be given anti-rabic vaccine ?

All anti-rabic vaccines are inactivated vaccines and can safely be given to lactating mothers and it has no effect on the breastfed baby.

43. What is the criteria for "protection" after immunization ?

Rabies Virus Neutralizing Antibody(RVNA) titre of ≥ 0.5 IU/ml. of serum in the vaccinee is considered protective. The

facilities for this test are available at select centres like CRI, Kasauli, Himachal Pradesh; Pasteur Institute, Coonoor, Tamilnadu; NICD, Delhi; NIV, Pune; and NIMHANS, Bangalore.

44. Is it essential to perform an antibody test on the patient following ARV?

Antibody tests viz., Rapid Fluorescent Focus Inhibition Test (RFFIT), Mouse Neutralization Test (MNT), etc., are some sophisticated tests and are done only at select few reference centres in the country. Besides ARVs, with proper cold chain maintenance and when given according to the approved schedule, do not require testing of antibody on a routine basis.

45. Is there a one shot ARV? Is there a ARV to protect life long?

There is no single shot/dose ARV anywhere in the world nor is there a ARV, which gives lifelong immunity.

46. Do the newborn or neonates or infants require lesser dosage of ARV?

In case of CCVs(HDCV/PCEC/PVRV) and PDEV the dosage is same for all age groups.

47. Can ARV be given along with other vaccines?

ARV can be given with other EPI vaccines. However, vaccines should be given at the recommended site (deltoid or thigh, IM) and at a site different from EPI vaccine.

48. Can ARV be given to a child with chicken pox or measles?

It can be given and it is protective.

49. Can ARV be given to HIV or AIDS patient?

The vaccines on Day 0 (1st injection) should preferably be doubled and given at two sites viz. deltoids/thigh IM in young children). It is desirable to administer the RIGs even in category II exposures. However, if facilities for antibody titres estimation are available it should be done (on day 14 or later).

50. If a person is on antimalarials or steroids or taking immunosuppressant drug, what is the schedule?

The vaccines on Day 0 (1st injection) should preferably be doubled and given at two sites (deltoids or thigh IM in young children). It is desirable to administer even the RIGs in category II exposures. However, if facilities for antibody titres estimation are available it should be done.

51. What is "potency" of ARV?

The "potency" is the capacity of the vaccine to induce immune response. It is ≥ 2.5 IU/dose.

52. Can ARV be given to a patient with jaundice?

If post exposure vaccination is required it should be given. If facilities permit antibody titre estimation is recommended. Serum or RIG (Equine or Human) if required (category III) should be used.

53. Beta Propiolactone (BPL) used for inactivation of vaccine is a known carcinogen. How is it safe to inject with vaccine?

BPL loses its carcinogenicity because of its hydrolysis during the process of inactivation of rabies virus where it is used in final concentration of 1:4000. Hence, it safe and any apprehensions are misplaced.

54. If PEP is required for a person bitten by a vaccinated dog, then why vaccinate the dog at all?

Vaccinating the Pet dog is primarily to protect it against contracting rabies following bites by stray rabid dogs/animals. Besides,

- No veterinary vaccine offers 100% protection against rabies.
- Rabies is enzootic in our stray animal/dog population.
- The facility of protective antibody titre test (in vaccinated dog) is available only at few centres in the country.
- The facility to quarantine the vaccinated dog is limited and difficult.
- The immunization record of the dog may not be available.

ABOUT THE AUTHOR

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Rabies, being a fatal disease, often panicks victims of animal bite and the absence of clear and precise information many a times leads to doubts in treating physician. For writing this simple guidebook the author has used his expertise of over two decades incorporating his regional, national and international experience in this specialized area. It is hoped that this book provides the necessary information and guidance to an otherwise busy doctor enabling him to provide better rabies prophylaxis to his/her patient.

12. RABIES IMMUNOBIOLOGICALS IN INDIA

I. MODERN RABIES VACCINES IN INDIA (MEDICAL)

	BRAND	PRODUCT	PHARMACEUTICAL
1.	Abhayrab	Purified Verocell Rabies Vaccine (PVRV) (0.5 ml)	Human Biologicals Institute, Hyderabad.
2.	Rabipur	Purified Chick Embryo Cell Vaccine (PCEC) (1 ml)	Novartis Vaccines/ Sanofi Aventis
3.	Rabivax	Human Diploid Cell Culture Vaccine (HDCV) (Liquid) (1 ml)	Serum Institute of India, Pune
4.	Vaxirab	Purified Duck Embryo Vaccine (PDEV) (1 ml)	Zydus Alidac Ahmedabad
5.	Verorab	Purified Verocell Rabies Vaccine (PVRV) (0.5 ml)	Sanofi Pasteur / Ranbaxy Pharma
6.	PVRV*	Purified Verocell Rabies Vaccine (PVRV) (1 ml)	Pasteur Institute of India, Coonoor, Tamilnadu.
7.	Rabirix	Chromatographically purified PVRV (0.5ml)	Bharat Biotech, Hyderabad

* Limited production, since July 2001.

II. RABIES IMMUNOGLOBULINS (RIGs) IN INDIA (MEDICAL)

A. EQUINE (ERIGs)

	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.	CARIG	Purified Equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency)	Cadila Pharmaceuticals, Ahmedabad.
3.	EQUIRAB	Purified Equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency)	Bharat Serums and Vaccines Limited, Mumbai.
4.	ZYRIG	Purified Equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency)	Zydus Alidac, Ahmedabad
5.	ABHAYRIG	Purified Equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency)	Human Biologicals Institute, Hyderabad

B. HUMAN (HRIGs)

	BRAND	PRODUCT	PHARMACEUTICAL
1.	Berirab – P	Human Rabies Immunoglobulins, 150 IU/ml; 2ml (300 IU) ampoule and 5 ml (750 IU) ampoule.	Aventis Behring, Cadila Health Care
2.	Imogamrab	Human Rabies Immunoglobulins, 150 IU/ml; 2ml (300 IU) ampoule and 5 ml (750 IU) ampoule.	Aventis Pasteur, France. Ranbaxy Pharma
3.	Rabglob	Human Rabies Immunoglobulins, 150 IU/ml; 2ml (300 IU) ampoule and 5 ml (750 IU) ampoule.	Bharat Serums and Vaccines Limited, Mumbai.
4.	Kamrab	Human Rabies Immunoglobulins, 150 IU/ml; 2ml (300 IU) ampoule and 5 ml (750 IU) ampoule.	Medlife, Thane.

III. MODERN RABIES (VETERINARY) VACCINES IN INDIA (FOR USE IN ANIMALS)

	BRAND	PRODUCT	PHARMACEUTICAL
1.	Raksharab	BHK - 21 Cell line inactivated (1 ml)	Indian Immunologicals, Hyderabad.
2.	Rabisin	NIL Cells, inactivated (1 ml)	Serum Institute of India, Pune.
3.	Rabigen	Hamster cell line, inactivated (1 ml)	Virbac / Vestas, France.
4.	Candur-R	Chick fibroblast cell, inactivated (1 ml)	Hoechst India (Veterinary), Mumbai.
5.	Nobivac-R	BHK cell line, inactivated (1 ml)	Intercare, Calcutta.
6.	Durarab	Inactivated vaccine (1 ml)	Vestas (Paris), France.
7.	Rabdomum	BHK cell line, inactivated (1 ml)	Cadila Health Care (Veterinary), Ahmedabad.

13. ACRONYMS & ABBREVIATIONS

- ARV - ANTI-RABIES VACCINE
- ARS - ANTI-RABIES SERUM
- ATS - ANTI-TETANUS SERUM
- BPL - BETA PROPIO LACTONE
- CCV - CELL CULTURE VACCINE
- CRI - CENTRAL RESEARCH INSTITUTE. KASAULI, H. P.
- EPI - EXPANDED PROGRAMME OF IMMUNISATION
- ERIG - EQUINE RABIES IMMUNOGLOBULIN
- FAT - FLUORESCENT ANTIBODY TEST
- HDCV - HUMAN DIPLOID CELL VACCINE (RABIVAX)
- HRIG - HUMAN RABIES IMMUNOGLOBULIN
- ID - INTRADERMAL
- IDRV - INTRADERMAL RABIES VACCINATION
- IM - INTRAMUSCULAR
- IU - INTERNATIONAL UNITS
- MNT - MOUSE NEUTRALISATION TEST
- MTP - MEDICAL TERMINATION OF PREGNANCY
- NICD - NATIONAL INSTITUTE OF COMMUNICABLE DISEASES, DELHI.
- NIMHANS - NATIONAL INSTITUTE OF MENTAL HEALTH AND NEUROSCIENCES, BANGALORE.
- NIV - NATIONAL INSTITUTE OF VIROLOGY, PUNE.
- PCEC - PURIFIED CHICK EMBRYO CELL VACCINE (RABIPUR).
- PDEV - PURIFIED DUCK EMBRYO VACCINE (VAXIRAB)
- PEP - POST EXPOSURE PROPHYLAXIS
- PIIC - PASTEUR INSTITUTE OF INDIA, COONOR, TAMILNADU.
- PVRV - PURIFIED VEROCELL RABIES VACCINE (VERORAB, ABHAYRAB & RABIRIX)
- RFFIT - RAPID FLUORESCENT FOCUS INHIBITION TEST
- RIG - RABIES IMMUNOGLOBULIN
- TIG - TETANUS IMMUNOGLOBULIN
- WHO - WORLD HEALTH ORGANISATION, GENEVA, SWITZERLAND.