

Frequently Asked Questions On Rabies

By

Dr. A. K. Gupta

From Association for Prevention and Control of Rabies in India

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This book is dedicated to Louis Pasteur who developed rabies vaccine in 1885.

Preface

Rabies is one of the oldest and most feared zoonotic diseases. It is a neglected and severely under-reported disease. Rabies is practically **100% fatal** even today ***but easily preventable***.

Rabies is transmitted by infected secretions. Most commonly, transmission to humans takes place through exposure to saliva during a bite by an infected animal.

About half of the world's population lives in areas in which rabies is enzootic. Few countries are free of rabies. In India the islands of Andaman and Nicobar and Lakshadweep are free of rabies.

In most of the CMEs on rabies, I have to answer so many different types of queries which inspired me to write "frequently asked questions on Rabies" in a booklet form. The main purpose of this book is to spread awareness about rabies amongst medical professionals.

There is **no specific** treatment for clinical rabies. Key to survival after exposure to rabies virus is administration of post-exposure prophylaxis (PEP) as soon as possible. **Death** is virtually **inevitable** once clinical signs develop. Medical management is supportive and palliative.

Let us work together to make rabies history.

17th March, 2013

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Frequently Asked Questions

On

Rabies

A. General Considerations

1. What is Rabies?

Rabies is acute viral encephalitis **caused by** a RNA **virus** (Genus: Lyssavirus, Family: Rhabdoviridae). The genus name derives from lyssa, the Greek goddess of frenzy. The virus is **bullet** shaped and can be seen through an electron microscope only. Rabies is a **zoonotic disease** (i.e., transmitted by animals) that affects all mammals and is **endemic** in India.

2. Why is Rabies an important disease?

Rabies is one of the oldest and most feared zoonotic diseases, and has been a threat to human health for more than 4000 years. Rabies is a neglected and severely under-reported disease **killing each year** worldwide (WHO 2007) an estimated 55,000 people (24,000 to 90,000 deaths). All mammals, but mainly carnivores and bats, are susceptible and can transmit rabies virus. Human exposures are most frequently associated with bites by rabid dogs and transmission of virus from dogs' saliva. The Association for the Prevention and Control of Rabies in India (**APCRI**) estimated in 2004 that in India, there were **20,565** reported human **deaths** every year. Rabies is practically **100% fatal** even today ***but easily preventable***.

About half of the world's population lives in areas in which rabies is enzootic.

3. What are the important features of Rabies Virus?

The virus is **bullet** shaped and can be seen through an electron microscope only. These viruses have a phospholipids envelope with glycoprotein surface spikes and a negative polarity strand; single chain RNA. The rabies virus **genome** encodes **five proteins**: the nucleoprotein, the matrix protein, the glycoprotein, the phosphorylated protein and a large polymerase protein.

The existence of lyssaviruses that are closely related to rabies virus and that can also cause clinical disease (Duvenhage virus, Lagos bat virus, Mokola virus, Shimoni bat virus, and Ikoma virus) has been known for several decades.

4. What is a street virus?

Street virus is a type of rabies virus which is virulent, having a long and variable incubation period of about 3 weeks to 3 months.

When first isolated from natural human or animal hosts, rabies virus preserves its natural properties and is referred to as street virus. Most of the street virus isolates generally cause a lethal CNS infection.

5. What is a fixed virus?

It is a rabies virus that has been passaged in tissue culture or animals. The term fixed indicates only that the incubation period and virulence has been stabilized. It is least virulent, and has a fixed short incubation period of 5-9 days. It is used as *seed virus* for manufacturing rabies vaccines.

6. How can rabies virus be inactivated?

Rabies virus is inactivated:-

- (1) By heat (1 hour at 50°C),
- (2) On exposure to ultraviolet radiation,
- (3) By exposure to 70% ethanol, phenol, formalin, trypsin, β -propiolactone,
- (4) Detergents
- (5) By lipid solvents.
- (6) At pH below 3 or above 11.
- (7) Rabies virus is inactivated rapidly in sunlight and does not survive for long periods out of the host (in dried blood and secretions) as it is susceptible to sunlight and desiccation
- (8) X-rays,

7. Is rabies virus resistant to anything?

Rabies virus is resistant to cold and freeze drying.

8. Are there any survivors of human rabies?

Till date only seven survivors have been recorded. These patients survived not due to any specific anti-rabies therapy but following intensive life support and excellent nursing care. These patients survived for variable periods with residual neurological deficits. All the survivors had paralytic

form of rabies and majority had history of some anti-rabies vaccination in the past.

9. Name rabies-free countries.

There are about 59 countries that do not report rabies. Few countries are free of rabies as a result of their privileged geographical situation & strict application of stringent legislation.

According to Centers for Disease Control and Prevention, Countries and political units that reported no indigenous cases of rabies during 2009 are:-

REGION	COUNTRIES
Africa	Cape Verde, Libya, Mauritius, Réunion, São Tomé and Príncipe, and Seychelles
Americas	North: Bermuda, St. Pierre and Miquelon Caribbean: Antigua and Barbuda, Aruba, The Bahamas, Barbados, Cayman Islands, Dominica, Guadeloupe, Jamaica, Martinique, Montserrat, Netherlands Antilles, Saint Kitts (Saint Christopher) and Nevis, Saint Lucia, Saint Martin, Saint Vincent and Grenadines, Turks and Caicos, and Virgin Islands (UK and US)
Asia and the Middle East	Hong Kong, Japan, Kuwait, Lebanon, Malaysia (Sabah), Qatar, Singapore, United Arab Emirates
Europe	Austria, Belgium, Cyprus, Czech Republic, ² Denmark, ² Finland, Gibraltar, Greece, Iceland, Ireland, Isle of Man, Luxemburg, Netherlands, ² Norway, Portugal, Spain ² (except Ceuta and Melilla), Sweden, Switzerland.
Oceania³	Cook Islands, Fiji, French Polynesia, Guam, Hawaii, Kiribati, Micronesia, New Caledonia, New Zealand, Northern Mariana Islands, Palau, Papua New Guinea, Samoa, and Vanuatu

¹Bat rabies may exist in some areas that are reportedly free of rabies in other mammals.

²Bat lyssaviruses are known to exist in these areas that are reportedly free of rabies in other mammals.

³Most of Pacific Oceania is reportedly "rabies-free."

In India the islands of Andaman and Nicobar and Lakshadweep are free of rabies.

10.How is rabies transmitted?

Rabies is transmitted by infected secretions. Most commonly, transmission to humans takes place through exposure to saliva following a bite by an infected animal. Rabies virus can be excreted in saliva, urine, nasal discharge and respiratory secretions.

11.What are the factors responsible for rabies transmission in man from rabid animals?

- Rabies is most commonly transmitted to humans via the bite of a rabies-infected animal.
- Humans usually contract rabies through bite wounds from rabid animals (bite exposure) because the rabies virus is highly concentrated in the saliva of infected animals.
- The amount of virus reaching the lesion is also a factor in transmission; for example, when a bite has to penetrate clothing, the saliva may be retained in the fabric and be prevented from entering the wound.
- It can also be transmitted through non-bite exposure, although this rarely occurs. Airborne infections, such as inhaling an aerosol of infected animal brain tissue in virus laboratories, or of contaminated air in bat-inhabited caves, have been reported.
- Iatrogenic rabies cases have occurred in patients who received cornea, kidney, liver, or blood vessel graft transplantation from donors who had undiagnosed rabies.

- To date, the only medically verified cases of human-to-human rabies transmission are the cases infected through organ transplantation from undiagnosed rabies patients

Potential non-bite modes of transmission include contamination of a pre-existing wound, contact of mucous membrane or respiratory tract with the saliva of an infected animal, exposure to aerosolized rabies virus in the laboratory (or from bats), or via organ transplantation from an infected donor

12.How common are animal bites?

Animal bites are very common in India.

The annual incidence of animal bites is high, 1.7% and it was more in rural areas (1.8%), children (2.6%) and poor/low income group (75%). The main biting animal was dog (91.5%), mostly stray (63%), followed by cat (4.7%).

13.Can rabies infection be transmitted through environment?

Rabies infection can be transmitted through aerial (by aerosol) route. Airborne infections, such as inhaling an aerosol of infected animal brain tissue in virus laboratories, or of contaminated air in bat-inhabited caves, have been reported.

Bats that are the easiest to approach and capture (unable to fly, etc.) are the most likely to have rabies.

Bat Rabies is not present in India.

14.Can rabies be transmitted from man to man?

Man-to-man transmission of rabies is possible. Rabies can be transmitted following bite by a rabies patient.

In 2004, three cases of human rabies were reported in U.S. following liver and kidney transplantation from rabies patients.

Transplantation of rabies infected cornea can cause rabies in recipient.

Therefore a careful neurological history of donor must be taken before cornea transplantation.

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

As per Centre for Disease Control and Prevention (CDC) Morbidity and Mortality Weekly Report (MMWR), no confirmed case of rabies has ever been reported in persons who performed a postmortem examination of people or animals, although contact with decedents with confirmed or suspected rabies can cause anxiety. Even from living patients with rabies, human-to-human transmission has been documented only rarely, (in cases of organ or tissue transplantation).

Both CDC and the World Health Organization (WHO) have stated that the infection risk to health-care personnel from human rabies patients is no greater than from patients with other viral or bacterial infections. In addition, rabies post-exposure prophylaxis (PEP) is available for exposed personnel. Nevertheless, because of the nearly universal fatal outcome from rabies, both CDC and WHO recommend that all personnel working with rabies patients or decedents adhere to recommended precautions. Even the minimal risk for rabies virus transmission at autopsy can be reduced by using careful dissection techniques and appropriate personal protective equipment, including an N95 or higher respirator, full face shield, goggles, gloves, complete body coverage by protective wear, and heavy or chain mail gloves to help prevent cuts or sticks from sharp instruments or bone fragments.

Participation in the autopsy should be limited to persons directly involved in the procedure and collection of specimens. Previous vaccination against rabies is not required for persons performing such autopsies. PEP of autopsy personnel is recommended only if contamination of a wound or

mucous membrane with patient saliva or other potentially infectious material (e.g., neural tissue) occurs during the procedure.

16. What are the common animal reservoirs of Rabies?

Rabies exists in **two forms**:-

- (1) **Urban Rabies**, propagated chiefly by unimmunized dogs.
- (2) **Sylvatic rabies**, propagated by skunks, foxes, raccoons, mongooses, wolves, bats etc.

Worldwide the most common cause by far of human rabies infections is **dog** bites. The host animals of the rabies virus differ among regions, even though almost every mammal is capable of contracting rabies. The main vectors are foxes in Europe and Canada, raccoons, skunks, and fruit-eating and insectivorous bats in the United States, dogs in Asia, mongooses, jackals, and dogs in Africa, and dogs and vampire bats in Latin America.

In India, the animals commonly responsible for **transmission** of rabies are **dogs and cats** (97%) followed by wild animals like mongoose, foxes & jackals (2%) and occasionally by horses, donkeys, monkeys, cows, goats, sheep and pigs.

17. What is the dog population of India?

India has approximately 25 million dogs, with an estimated dog: man ratio of 1:36.2. The dogs fall into 4 broad categories: pets (restricted and supervised); family dogs (partially restricted, wholly dependent); community dogs (unrestricted, partially dependent); and undomesticated stray dogs (unrestricted, independent). Most dogs in India, perhaps 80%, would fall into the last 3 categories. The majority of the stray dog population is found in rural areas.

18. Do rat bite cases require rabies vaccination?

In India most rodents, rats, squirrel, rabbits, birds and bats have been found to be free of rabies. However, following exposure to mongoose, PEP is recommended.

Rat bite cases do not require rabies vaccination but this is a right opportunity to start pre-exposure vaccination.

19. What are the most common modes of exposures of rabies virus?

Human exposures to rabies can generally be categorized as bite, open wound, mucous membrane, or other types of exposure:

Bite exposure: Any penetration of the skin of a person by the teeth of a rabid or potentially rabid animal.

Open wound exposure: Introduction of saliva or other potentially infectious material (cerebrospinal fluid, spinal cord, or brain tissue) from a rabid or potentially rabid animal into an open wound (e.g., broken skin that bled within the past 24 hours).

Mucous membrane exposure: Introduction of saliva or other potentially infectious material (cerebrospinal fluid, spinal cord, or brain tissue) from a rabid or potentially rabid animal onto any mucous membrane (eyes, nose, mouth).

Other exposure: Any interaction with a rabid or potentially rabid animal where a bite, open wound, or mucous membrane exposure cannot be definitively ruled out.

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

A person does not acquire immunity against natural rabies infection, as it occurs in other viral infections because there is no viremia in rabies and the virus is not accessible to the normal immune mechanism of the body. The antibody

production starts only after travelling efferently from CNS via mostly autonomic nerves to different target organs. But by that time, the neuronal cells of patient's brain stem are affected.

B. Clinical Features

21. What is the best known clinical feature of rabies?

Hydrophobia and aerophobia are pathognomonic for rabies and occur in 50% of patients. Attempting to drink or having air blown in the face produces severe laryngeal or diaphragmatic spasms and a sensation of asphyxia. This may be related to a violent response of the airway irritant mechanisms. Even the suggestion of drinking may induce hydrophobic spasm. **Hydrophobia** is typically unique to human beings.

22. What is the incubation period of rabies in humans?

The **incubation period** of rabies that is the time interval between the exposure to virus and the onset of symptoms, is usually from 03 weeks to 03 months (rarely 04 days to 02 years). An incubation period as long as 19 years has been reported. **Children** are at an increased risk of a shorter incubation period because of their short stature and bites are often closer to CNS. Multiple bites to the head and neck are associated with very short incubation periods less than 1 month.

The incubation period varies with the amount of virus transmitted, virus strain, site of inoculation (bites closer to the head have a shorter incubation period), host immunity and nature of the wound.

During most of the long incubation period of rabies, the virus likely remains close to the site of viral entry. Centripetal spread to the central nervous system and spread within the central nervous system occur by fast axonal transport

People who are immuno-compromised will most likely be more susceptible to rabies. Rabies is usually undetectable during the incubation period, and infections can also be difficult to diagnose when the clinical signs first appear.

23. What are the initial (prodromal) symptoms of Rabies?

- Pain or paraesthesiae at the site of the bite is well known as a diagnostically useful prodromal symptom occurring in one-third to two-thirds of cases.
- In Thailand, however, a specific type of paraesthesiae-itching-was the earliest symptom in >40% of cases. Itching occurred at the site of the healed bite wound or involved the whole bitten limb and was sometimes so intense as to provoke frenzied scratching and excoriation of the skin. The explanation for local paraesthesiae may be the multiplication of virus in the dorsal root ganglion of the sensory nerve supplying the area of the bite.
- Pain behind the grafted eye was an early symptom in three of the four patients who developed rabies following corneal transplants.
- Priapism with frequent spontaneous orgasms was the first symptom in one Thai patient.
- Fever, malaise, nausea and vomiting.
- The skin becomes sensitive to changes of temperature, especially air currents.

24. What are the types of Rabies?

There are mainly **two types** of rabies:-

- a) Two-third of rabies patients suffer from typical ***furious (encephalitic) type of rabies***. The virus replicates in portions of the brain including the hippocampus, amygdala, anterior thalamic nuclei and limbic cortex.

Furious rabies has **three cardinal signs**:-

- Fluctuating consciousness, episodes of excitement and hallucinations.
- Phobic spasms – Aerophobia, Hydrophobia and Photophobia.
- Autonomic dysfunctions like increased salivation, excessive sweating, priapism & pupillary abnormalities.

It is typically believed that salivation and vomiting are linked, and contribute to the apparent hydrophobia (fear of water) in patients. These symptoms can last for few days, after which the patient may suffer from the second type of rabies, or may slip into a coma and die. It is when suffering from furious rabies that a person or animal is likely to attack those near them, and spread the disease.

- b) **Dumb** (paralytic) type which is characterized by flaccid muscle weakness, constipation, urinary retention, stupor, coma. Hydrophobia is usually **absent** in these cases. This is a condition resembling Guillain Barre Syndrome. Dumb Rabies occurs as the result of the virus replicating in the brain's neocortex. It is much harder for a doctor to diagnose rabies in its "dumb" form than it is in its "furious" form, because the symptoms are less indicative of a specific medical issue.

Both forms are progressive and will lead to death, usually within 7 days in patients with encephalitic rabies and 3 weeks in those with paralytic rabies.

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

A study on management of human rabies concluded that the dismal outcome of patients with rabies provides little optimism for heroic efforts. Palliative therapy is of paramount importance in this fatal disease.

26.Is there any seasonal variation in dog bite cases?

Maximum dog bites were observed in the autumn months. It is observed that there is an increase during warm-weather months (May through August) and a corresponding decrease during colder months (November through March).

C. Myths about Rabies

27.What are the myths about rabies in India?

Following myths about rabies are very much prevalent in India:-

- In India, there are many myths and wrong practices concerning the management of an animal bite. People apply turmeric, salt and sometimes ghee over the wound area. Chilies, hydrogen- peroxide and cow dung are some other wrong practices followed mainly in the rural parts of India.
- Some herbal extracts will cure rabies.
- In rural areas, people also resort to witchcraft and religious practices.
- Washing of wound(s) can cause hydrophobia.
- Dietary changes can cure, that is, shift from vegetarianism to non-vegetarianism or vice versa; stopping consumption of white things etc.
- A single dose vaccine will prevent rabies.
- Vaccines are more effective if taken on empty stomach.
- One should not take bath; eat meat and eggs during vaccination.
- Gems and stones have magical properties against rabies.

D. Post-Exposure Prophylaxis

28. Is there any specific treatment for clinical rabies?

There is **no specific** treatment for clinical rabies. Key to survival after exposure to rabies virus is administration of post-exposure prophylaxis (PEP) as soon as

possible. **Death** is virtually **inevitable** once clinical signs develop. Medical management is supportive and palliative.

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

Theoretically, the richly innervated areas like head, neck, face, hands and genitals are the most dangerous sites of bite in man. But practically, it is often the wounds on legs, which are ignored/neglected, that cause rabies.

30. What does post-exposure prophylaxis (PEP) include?

It includes:-

- (1) Local treatment of wound(s)
- (2) Categorization of animal bite wound(s)
- (3) Anti Rabies Vaccination. (ARV)
- (4) Administration of Rabies Immunoglobulin (RIG)
- (5) **In addition**, Tetanus prophylaxis, analgesics & systemic antibiotics may be given.

31.What are the contraindications to post exposure prophylaxis?

As rabies is 100% fatal, there are no contraindications to post exposure prophylaxis.

32.Whether washing of animal bite wound(s) is essential?

By mere washing of wounds and application of antiseptics, the risk of rabies will reduce by about 50%.

The maximum benefit of the wound washing is obtained when fresh wound is cleaned immediately. It is important to remove saliva containing rabies virus at the site of bite by physical or chemical means. This can be done by prompt and gentle thorough washing with ordinary soap or detergent and flushing the wound with running tap water for at least 15 minutes.

Washing of the wound must be done as long as the wound is raw; irrespective of the time elapsed since the exposure. Care must be taken not to disturb the scab, if formed.

After washing with water & soap, disinfectants like Povidone Iodine or Surgical Spirit must be applied.

In extraneous circumstances, other alcoholic (>40%) preparations like Rum, Whisky or after-shave lotion may be applied on the wound. If soap or antiviral agent is not available, the wound should be thoroughly washed with water.

33. Can we apply local antibiotics or antimicrobial agents on the site of bite?

After cleansing of the bite wounds, local antimicrobial agents can be applied. Discourage local wound applicants like turmeric, neem, red chili, lime, plant juices, coffee powder etc.

34.Can the animal bite wounds be cauterized?

Cauterizing the wound is not advisable as it leaves a very bad scar and also does not confer any additional advantage over washing the wound with water and soap. It amounts to malpractice and the doctor can be sued for compensation under COPRA.

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

Do not bandage the wound as far as possible and if unavoidable, apply non-adherent, absorbent dressings (paraffin gauze or Melolin) to absorb the discharge from the wound. Tincture iodine should not be used.

Avoid Suturing of the bite wound as a rule since 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 after infiltration of RIGs. If RIGs is not available, as a last resort, the wound must be flushed with povidone

iodine before suturing. The suture should be loose and not interfere with free bleeding and drainage.

Human and animal bite wounds are best closed by **secondary sutures** after one week and after proper cleansing and daily wound care. Primary surgical intervention must be avoided if possible.

36.Can the wound be deepened for cleaning purpose?

We should never try to deepen the bite wound. Deepening of wound for cleaning depends on area of injury, extent of injury and the aim should be to preserve as much tissue as possible and to excise dead tissue only.

37. How common are animal bites and infections?

Only 15 to 20 percent of dog bite wounds become infected. Puncture wounds and hand wounds are more likely to become infected than scratches.

38.Is there any role of systemic antibiotic treatment for animal bites infections?

Using antibiotics may be helpful, particularly in high-risk wounds such as those of the hand.

Antimicrobials effective in the empiric treatment of patients with animal bite and human bite wounds		
	Animal bite	Human bite
Amoxicillin-clavulanate (PO)	+	+
Ampicillin-sulbactam (IV)	+	+
Moxifloxacin (PO, IV)	+	+
Gatifloxacin (PO, IV)	+	+
Doxycycline (PO, IV)	+	+

Most mammalian bites are caused by dogs, cats or humans. Cat and human bites often become infected, so antibiotic prophylaxis should be considered in addition

to wound management. Amoxycillin with clavulanate is suitable for prophylaxis in most cases. Prophylaxis is usually continued for 5–7 days.

E. Categorization of Animal Bite Wound

39. How is animal bite wound categorized and what is the importance of categorization?

WHO Guide for treatment against rabies post-exposure:-

Category (Type of contact with a suspect or confirmed rabid domestic or wild animal, or animal unavailable for observation)	Recommended treatment.
I. Touching or feeding of animals, Licks on intact skin	None, if reliable case history is available
II. Nibbling of uncovered skin, Minor scratches or abrasions without bleeding,	Administer vaccine immediately. Stop treatment if animal remains healthy throughout an observation period of 10 days or if animal is killed humanely and found to be negative for rabies by appropriate laboratory techniques.
III. Single or multiple transdermal bites or scratches, Contamination of mucous membrane with saliva (i.e. licks), Licks on broken skin	Administer rabies immunoglobulin and vaccine immediately. Stop treatment if animal remains healthy throughout an observation period' of 10 days or if animal is killed humanely and found to be negative for rabies by appropriate laboratory

	techniques.
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When in doubt of degree of exposure to rabies risk, it is safer to over treat than under treat.

40. Is it important to elicit information about biting animal?

It is very important to elicit information about biting animal.

Low risk category includes healthy pets and regularly vaccinated dogs/cats.

Moderate risk category includes healthy pets but vaccination status doubtful or not done.

High risk category includes rabid, sick, died, stray dogs/cats, or wild animals.

F. Modern Rabies Vaccines

41. What are the various types of modern anti-rabies vaccines?

These are:-

- (1) Purified vero cell rabies vaccine (PVRV)
- (2) Purified chick embryo cell vaccine (PCECV)
- (3) Human diploid cell vaccine (HDCV)
- (4) Purified duck embryo vaccine (PDEV)

42. Does strain of virus used in rabies vaccine play a role in eliciting the required response?

Response to rabies vaccination is a unique mix of specificities to rabies virus antigens. Antibodies develop out of intrinsic host responses and in response to extrinsic factors such as the amount of antigen given, type of antigen, and

route of exposure or vaccination. There may be substantial variation in the neutralizing activity and quantity of rabies virus neutralizing antibodies (RVNA) produced. Therefore, the strain of virus used in antirabies vaccine plays a role in eliciting the required response.

43. Is there any advantage of PCEC vaccine with Pitman-Moore (PM) strain?

Compared to other continuous cell lines based rabies vaccines, PCEC vaccine with Pitman-Moore (PM) strain has several advantages, these includes:

- This method provides vaccine with high yield, greater potency and immunogenicity which makes the vaccine comparatively cost effective and unique.
- It is more readily scalable to large scale commercial vaccine production.

44. Why do some people fear for vaccine?

In the past, rabies vaccine was a sheep brain derived Nerve Tissue Vaccine (NTV) and used to have considerable side effects. Large volumes and number of injection were required. So, rabies vaccine acquired the bad reputation of a dangerous vaccination. However, these fears are no longer justified with modern rabies vaccines that are very safe.

G. Rabies Vaccine in Special Situations

45. A person started with PVRV wants to change over to HDCV or PCECV or PDEV or vice versa. What should be done?

Of the currently available TCVs such as HDCV, PCECV, PVRV, and PDEV, all are equally good and approved by WHO. All are interchangeable following non availability of one brand or due to allergy to one of the CCVs or PDEV.

All are considered protective throughout the world against different strains of rabies viruses in different parts of the world.

46.Can modern vaccines be diluted with tetanus toxoid or water or any other diluents and injected?

The modern anti-rabies vaccines should not be diluted with tetanus toxoid or any other diluents other than that provided with the vaccine.

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

Following animal bite, rabies vaccine can be given to a pregnant woman. Medical termination of pregnancy should not be done as a routine clinical practice.

48.Can a lactating mother be given antirabies vaccination?

Modern Anti-rabies vaccines being used now are Tissue Culture Vaccines (TCV) inactivated by beta-propiolactone (BPL) and can safely be given to a lactating mother.

49.Is there a one-shot ARV? Is there any ARV that offers lifelong protection?

There is no single dose vaccine or a vaccine that gives lifelong immunity.

50.Whether newborn or neonates or infants require smaller volume/lesser dosage of rabies vaccine?

All modern rabies vaccines have a uniform dosage for all age groups.

51.Can rabies vaccine be given to a child with chicken pox or measles?

As rabies is 100% fatal, there is no contraindication for anti-rabies vaccination. Rabies vaccine can be given to a child with chicken pox or measles and it is effective. If possible administration of measles vaccine should be postponed by a fortnight after the completion of antirabies immunization.

52.Can rabies vaccine be given to HIV or AIDS patient?

Rabies vaccine can be given to HIV or AIDS patient. It is recommended to administer RIGs even in category II exposures in such patients and double dose of anti-rabies vaccine must be given on day 0 of vaccination.

53.Can rabies vaccine be given to a patient with jaundice?

Rabies vaccine can be given to a patient with jaundice.

54.Can a person receiving/completed antirabies immunization, either pre-exposure or post-exposure donate blood?

A person receiving/completed antirabies immunization can donate blood. However, the recipient does not benefit from the transfer of rabies-neutralizing antibodies due to hemodilution.

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

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

56. What is “window period”?

It is the **time taken** by Anti-Rabies vaccine **to produce protective levels of antibodies** in the patient. The window period is of 7-14 days.

57.What is the criterion for “protection” after immunization?

The criterion for protection after immunization is that the rabies virus neutralizing antibody (RVNA) titer of $> \text{ or } = 0.5 \text{ IU/ml}$ of serum in the vaccinated person is considered protective.

The facility for this test is available at NCDC, Delhi, CRI, Kasauli, Pasteur institute, Coonnor, NIV, Pune and NIMHANS, Bangalore.

58.What is the “potency’ of rabies vaccine?

WHO recommends that the vaccine potency should be at least 2.5 IU per dose. The potency is the capacity of the vaccine to induce immune response.

59. Can modern rabies vaccines be stored at room temperature?

Vaccine must be stored at $+2^{\circ}\text{C}$ to $+8^{\circ}\text{C}$. It should not be stored at room temperature. Besides, the vaccine should not be exposed to sunlight and heat.

60. What are the consequences of a vaccine with a higher potency?

There are no risks with vaccine with a higher potency.

61. What is the post-exposure (WHO ESSEN-IM) Schedule?

The post-exposure (WHO ESSEN-IM) Schedule is I.M. vaccination on days 0 (day of first dose of vaccine and not the day of bite), 03, 07, 14 and 28. Vaccine should be injected deep into deltoid muscle (in Adults) or antero-lateral aspect of thigh (in Children).

62. Can the vaccine be injected in gluteal region?

Rabies vaccine **must not** be administered in **gluteal** region as the gluteal fat may retard vaccine absorption resulting in delayed and lower seroconversion.

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

The vaccine on day 0 (first injection) must be doubled and given at two sites (deltoids or thigh in young children). In category II exposures, it is recommended to administer even RIGs along with vaccine. Rest of the schedule is same as for any other patient.

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

Only two doses of vaccine at days 0 & 3 are required. RIGs are not required (WHO 2007). However, in laboratory confirmed rabies exposures, irrespective of past

rabies immunization, full course of PEP and RIGs is recommended. In rabies, it is safer to over treat than under treat.

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

An early and correct administration of modern anti-rabies vaccine is life saving. The vaccination must be started immediately irrespective of the status of the biting animal. Patients who seek treatment after a delay of 48 hours or even months after having been bitten should be dealt in the same manner as if the exposure occurred recently.

66. A pregnant woman develops rabies. What should be done?

In case the mother develops rabies, the rabies virus is not known to cross placental barrier, and as a result, the fetus is safe. Hence, the pregnant woman with rabies should be clinically managed and if induction of pregnancy or caesarean section is possible, the obstetrician should do it with some “personal precautions” and immuno-prophylaxis (usually three doses of modern vaccine or if any accidental exposure is there, then full course of post-exposure vaccination either by IM or ID route should be given to the obstetrician.) Later the new born may be given full course of rabies PEP vaccination.

67.Is it essential to perform an antibody test on the patient following antirabies vaccination?

Antibody tests, that is, rapid fluorescent focus inhibition test (RFFIT), mouse neutralization test (MNT) are done only at selected few reference centers in India. Antibody tests are not required on a routine basis following antirabies vaccination if vaccination is correct and reliable.

68.Whether observing the dog for 10 days without initiating treatment is risky or justifiable?

Observing the dog for 10 days without initiating treatment is risky and not at all justifiable. It is mandatory to start treatment soon after exposure. The vaccination must be started immediately irrespective of the status of the biting animal. Improper treatment to animal bite victims may lead to rabies death and litigation under Consumer Protection Act (COPRA). According to Consumer Protection Act, the animal bite should be considered as “medical urgency” and treated with due care.

69. Is there carrier state of rabies in dogs?

Carrier state of rabies in dogs/cats is not yet conclusively proven and established.

70. A patient received two doses of modern vaccine (on days 0 and 3) and the dog was well on days 5 and 7 (third injection due, but not given). However, the dog dies on any day between 8 and 15. What should be done?

In case, day 0 and 3 inj. were given and inj. due on day 7 was postponed because the dog was kept under observation but the dog dies between 8 and 15 days, three doses of vaccine must be given as close to the original dates of the schedule and all five inj. must be completed by day 28.

71. How to approach a case of irregularities in treatment schedule, e.g., if patients missed the doses as per the due dates, which means if the schedule is broken?

First three doses of modern rabies vaccine must be very timely and for the fourth and fifth, one or two days of variation is permissible.

72. As there are different strains of rabies viruses in different parts of the world, whether all antirabies vaccines are effective against all these strains of viruses?

All anti-rabies vaccines are considered protective against different strains of rabies viruses in different parts of the world.

73. Is there any dietary restriction during PEP?

It is advisable to abstain from alcoholic drinks during the course of rabies vaccination as it may affect the immune response.

H. Pre-Exposure Vaccination

74.What is Pre-exposure vaccination?

Pre-exposure (Prebite) vaccination means immunization before the bite.

75. What is I.M. pre-exposure vaccination schedule?

The regimen is three IM injections on days 0, 7 & 28.

76.What is the importance of pre-exposure vaccination?

Pre-exposure vaccination **simplifies** post-exposure vaccination because after bite, those who have received full Pre-exposure vaccination, only **two** doses of vaccine at days 0 & 3 are required. **RIG is not required** (WHO 2007).

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

Although no teratogenicity or other adverse effects are reported with modern rabies vaccines, pre-exposure vaccination should be avoided in pregnant woman.

78.What drugs are contraindicated during rabies immunizations?

Immunosuppressive drugs, such as steroids, antimalarials, anticancer drugs are generally contraindicated during rabies immunizations. However if these drugs cannot be avoided, then day 0 dose of vaccine should be doubled.

I. Intra-Dermal Rabies Vaccination

79.What is the dose and schedule of IDRV?

For PEP, the modified “TRC ID” schedule (2-2-2-0-2) is the only schedule approved by the DCGI at present. ID vaccine is given on days 0, 03, 07, and 28.

The dose of each ID shot has been specified to be of 0.1 ml. of the permitted vaccines.

For pre-exposure vaccination, 0.1 ml of ID-approved vaccine is to be given ID over one deltoid on days 0, 7 and 21 or 28 days.

80.What is eight-site intradermal regimen (“8–0–4–0–1–1” regimen)?

One dose of 0.1 ml is administered intradermally at eight different sites (Either upper arms, lateral thighs, supra-scapular region, and lower quadrant of abdomen) on day 0. On day 7, four 0.1 ml injections are administered intradermally into each upper arm (deltoid region) and each lateral thigh. Following these injections, one additional 0.1 ml dose is administered on days 28 and 90. This regimen lowers the cost of vaccine administered by intramuscular regimens and generally produces a higher antibody response than the other recommended schedules by day 14. It does not result in a significantly earlier antibody response and in order to ensure optimal treatment, a passive immune product must be administered to patients presenting with severe exposures.

However, it is not approved for use in India by DCGI.

81.The IM dose of Verorab (PVRV) and Abhayrab (PVRV) is 0.5mL; that of Rabipur (PCEC) and PVRV (Coonoor) 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.

82.What is the mode of action of IDRV?

It is deposition of approved modern rabies vaccine (or antigen) in the layers of dermis of skin by which the immuno-receptive Langerhan cells present within the dermis are stimulated. 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.

83.Can all available anti-rabies vaccines be used by intra-dermal route?

Not all vaccines produced in India are at present fit for Intra-dermal usage.

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

- (1) Purified chick embryo cell vaccine (PCEC) - Rabipur and Vaxirab-N.
- (2) PVRV (Purified verocell rabies vaccine) – Verorab-vial of 0.5 ml,
- (3) PVRV – Abhayrab – vial of 0.5 ml., Human Biological Institute
- (4) PVRV – Indirab, vial of 0.5 ml/1.0 ml. Bharath Biotech, Hyderabad.

PDEV (Vaxirab) and HDCV (Rabivax) are approved for IM use only and *not* for IDRV.

Rabies vaccines formulated with an adjuvant should not be administered intradermally.

84.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. However, in exigencies, the permitted vaccines are interchangeable.

85.Can the routes of vaccination IM and ID be used interchangeable?

It is recommended by many internationally reputed experts that the phenomenon of mixing of IM and ID schedules is not to be practiced and must be avoided as far as possible.

86.What should be done if the ID injection fails, that is, spills out or goes subcutaneous?

WHO recommends that in cases where the wheal over the skin is not formed then the patient should receive another dose of vaccine at a site nearby. If the IDRV fails in any one of the sites after two attempts, then the vaccine must be given by IM route and the remaining doses of the schedule given by IM route only.

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

IDRV can be given in deltoid region, supra-scapular, anterior abdominal wall and the upper part of thigh.

88.What are the common side effects of intra-dermal rabies vaccination?

Cell culture vaccines have proved remarkably safe and free of significant adverse events. However, mild symptoms of pain, erythema, irritation or swelling at the intradermal injection sites occur in 3% to 92% of patients. The most frequent symptom is local irritation in 7% to 64% of vaccines. Generalized symptoms reported by 3% to 14% of recipients include headache, fever and influenza-like illness. Transient macula papular and urticarial rashes are occasionally seen.

All these adverse effects are mild, transient and self limiting and rarely call for the use of anti-histamines (tablet or syrup Avil) and analgesics.

89.What precautions should be taken while vaccinating by IDRV route?

1. The ID injections must be administered by staff trained in this technique.
2. The Vaccine vials must be stored at +2⁰ C to + 8⁰ C after reconstitution and
3. The total content should be used as soon as possible, but at least within 8 hours.
4. The 0.1 ml. ID administration of cell-culture vaccine should create a wheal of at least 5 mm diameter with “peau de orange” appearance.
5. If ID dose is given sub-cutaneously then there is a possibility of poor immune response due to low antigen load. This may be life threatening.

90.Are there any dietary restrictions during IDRV?

There are no dietary restrictions during IDRV. However, alcohol may be avoided as it may affect the immune response.

91.Is sera testing of IDRV patients for antirabies antibodies necessary as a measure of knowing its efficacy?

Routine sera testing for rabies antibodies to know its efficacy is not required.

92.Whether pregnancy and lactation are contraindications for IDRV?

Pregnancy and lactation are not contraindications for IDRV.

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

There is no need to alter the dose or schedule of any concomitant medication during IDRV.

94.Can IDRV be given in private hospital?

The ID route has been permitted to be used in **selected anti-rabies clinics (ARCs)** having an adequate number of patients (at least 5/day) seeking

post-exposure prophylaxis against rabies every day to make IDRV viable and cost-effective.

95. A previously immunized person is bitten again. What is the re-exposure IDRV schedule?

Following re-exposure the bitten person needs only two doses of 0.1 ml. of ID dose at one site only on

Day 0 and day 3 and RIGs are not needed. Proper wound treatment is very important.

96. Can IDRV be given to infants whose skin is thin?

For children below 5 years of age, it is advisable to adopt IM vaccination.

97. What is the potency requirement of IDRV?

Only three countries are practicing IDRV in regular patients attending regular anti-rabies clinics (ARCs) for more than ten years. These countries are Thailand, Philippines and Sri Lanka.

In Thailand and Sri Lanka, the potency requirement is 0.7 IU/ID dose and in Philippines it is 0.5 IU/ID dose.

j. Rabies Immunoglobulin

98. How is RIG life saving?

Administration of Anti-Rabies vaccine stimulates production of neutralizing antibodies by the patient's immune system. Protective levels of antibodies (of more than 0.5 IU/ml of serum) are seen 7 to 14 days after the initial dose of vaccine (window period). Moreover when the bites are on the head, neck, face & hands, the incubation period will be shorter.

Thus the patients are vulnerable to develop rabies during this window period of 7 to 14 days. RIGs are readymade anti-rabies antibodies and provide passive immunity to rabies.

99. What are the situations where RIG is indicated?

Following situations need RIG:-

- All Category III exposures.
- Bites by all wild animals viz. by mongoose, jackal, fox etc.
- Even Category II exposures in immuno-compromised/immunosuppressed individuals including HIV infected people & AIDS patients.
- RIGs should also be administered in Category III exposures even by vaccinated pet animals.
- RIGs can be used in pregnant women and lactating mothers.

100. What are the limitations of Polyclonal Serum (RIG)?

Difficulties associated with the use of Polyclonal Serum (RIG) samples might consist of:-

- Batch-to-batch variation.
- Risk related to the use of human blood products. Because HRIG preparations are of human origin, they need to be treated to minimize the risk of transmission of infectious agents.
- Difficulties in finding immune donors during sudden mass exposures might lead to a low availability of RIG.
- Because of discontinued ERIG production by international manufacturers, supply of ERIG relies on regional production.
- The use of ERIG has raised ethical issues and has been condemned by animal protection groups.

101. What are the types of RIGs?

There are two types of RIGs:-

- (1) Human RIG (HRIG): Available as 2 ml. vial with a potency of 150 IU/ml.
- (2) Equine RIG (ERIG): Available as 5 ml. vial with a potency of 300 IU/ml.

102. How to calculate the total dose of HRIG/ERIG?

Dosage of RIGs:

Dosage for administration is decided on the basis of body weight.

For HRIGs: Dosage is 20 IU per kg body weight subject to a maximum of 1500 IU. HRIG has a longer half-life (about 21 days).

For ERIGs: Dosage is 40 IU per kg body weight subject to a maximum of 3000 IU.

103. What are the various brands of RIG available in India?

Availability of different RIGs in India:-

HRIG Brands

1. BERIRAB-P- manufactured by CSL Behring GmbH, Germany and marketed by Bharat Serum & Vaccines Ltd.
2. KAMRAB - manufactured by Kamada Ltd., Israel and marketed by Synergy.

ERIG Brands

1. Anti Rabies Serum - manufactured by CRI – Kasauli.
2. EQUIRAB - manufactured and marketed by Bharat Serum & Vaccines Ltd.
3. ABHAYRIG - manufactured by VINS Bioproducts and marketed by Human Biologicals Ltd.
4. VINIRIG - manufactured and marketed by VINS Bioproducts.

104. When should RIG be administered? What should be the time gap between RIG and vaccination?

RIG is more effective if infiltrated immediately or within 24 hours of animal bite along with first dose of vaccine. If vaccine alone was started, then RIG can be given up to 7 days after starting first dose of vaccine. *Ideally*, rabies vaccine should precede RIG. However, in exceptional situations, approximately within 1 hour after administering RIG, the vaccine must be given.

105. What are the precautions to be taken while administering RIGs?

- (1) Patient should not be on an empty stomach.
- (2) RIGs vial taken out from the refrigerator should be kept outside for a few minutes to warm it to room/body temperature.
- (3) While infiltrating RIGs into the bite wound, care must be taken to avoid injecting into blood vessels and nerves.
- (4) While injecting into finger tips, care must be taken to avoid compartment syndrome.
- (5) All emergency drugs and facilities for managing any adverse reactions must be available.
- (6) For ERIG, keep the patient under observation for at least one hour after ERIG administration and then send home.
- (7) RIGs can be infiltrated even to already sutured wounds without disturbing the sutures.

106. Can RIG and rabies vaccine be administered in the same syringe?

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

107. Can RIGs be safely injected into already infected animal bite wounds?

RIGs can be safely injected into already infected animal bite wounds following proper wound cleansing and administration of appropriate antibiotics.

108. Is it essential to perform skin sensitivity test prior to the administration of ERIG?

Majority of reactions to ERIG result from complement activation and **are not IgE mediated** and will not be predicted by skin testing.

The **recent WHO recommendation** states that there are no scientific grounds for performing a skin test prior to the administration of ERIG, because testing does not predict reactions and ERIG should be given whatever the result of the test.

However skin test is **mandatory** to avoid any possible litigation under consumer protection Act (COPRA) in India.

109. How skin sensitivity test is performed?

Inject 0.1 ml ERIG diluted 1:10 in physiological saline intra-dermally into the flexor surface of the forearm to raise a bleb of about 3-4 mm diameter.

Inject an equal amount of normal saline as a negative control on the flexor surface of the other forearm

After 15 minutes an increase in diameter to > 10 mm of indurations surrounded by flare is taken as positive skin test, provided the reaction on the saline test was negative.

An increase or abrupt fall in blood pressure, syncope, hurried breathing, palpitations and any other systemic manifestations should be taken as positive test.

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

Most ERIGs that are manufactured presently are highly purified and the occurrence of adverse events has been significantly reduced. Unlike the original unpurified rabies antisera which resulted in adverse reactions in as

many as 40% of recipients, the adverse-reaction rate of patients receiving highly purified ERIGs has been reduced to <1–2%. However adverse event like anaphylaxis cannot be completely ruled out.

110. What are the common adverse reactions to HRIG?

In rare cases the following adverse reactions may occur:

- Allergic reactions including fall in blood pressure, dyspnoea, cutaneous reactions, in isolated cases reaching as far as anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration of Immunoglobulins.
- Generalized reactions such as chills, fever, headache, malaise, nausea, vomiting, arthralgia and moderate back pain
- Cardiovascular reactions particularly if HRIG is inadvertently injected intravascularly.

Local reactions:

At the injection site local pain, tenderness or swelling can be observed in rare cases.

111. If the skin test is positive to ERIG, what should be done?

If skin test is positive, it is better to switch over to HRIG.

112. How adverse reactions to ERIGs are managed?

Anti-sera of equine origin may cause anaphylactic shock. A negative skin test must never reassure the physician that no anaphylactic reaction will occur.

Management if anaphylactic reaction occurs:

1. Adrenaline: The dose is 0.5 ml of 0.1 percent solution (1 in 1000, 1mg/ml) for adults and 0.01ml/kg body weight for children, injected intramuscularly (IM).
2. Inj Hydrocortisone: 100 mg stat and 6 hourly I/V.
3. Inj Chlorpheniramine I/V.
4. Inj Ranitidine I/V.

If patient is sensitive to ERIG, HRIG should be used. Patient who had prior exposure of anti-sera (e.g.-Anti-tetanus serum, anti-diphtheria serum) should receive subcutaneous dose of Inj adrenaline (the requirement will be half dose of that required for treatment for anaphylaxis).

ERIG should preferably be given in a hospital setting.

113. How to inject RIGs locally? What is the mode of administration of full dose of RIGs?

It is important to infiltrate all wounds with RIGs. Intra-muscular (IM) administration of RIGs is of very little value. The previous recommendation was to give anti rabies serum half into wounds and half IM, which is no longer recommended and may lead to treatment failure. As much of the calculated dose of RIG, as is anatomically feasible, should be infiltrated into & around all the wounds. In the event that some volume of RIGs is left over after all wounds have been infiltrated, it should be administered by deep IM at a site distant from the vaccine injection site.

If the calculated dose of RIG is insufficient to infiltrate all wounds, sterile saline can be used to dilute it 2 or 3 fold to permit thorough infiltration.

114. Can RIG be given locally to a healed wound?

Yes. If anti-rabies vaccination is not started, without disturbing the scab, RIG can be given locally.

115. If RIG is inadequate to infiltrate extensive wounds, what should be done?

If RIG is inadequate to infiltrate extensive wounds, the RIG should be diluted with normal saline. This is a particular issue in children, whose body weight may be small in relation to the size and number of wounds.

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

Human normal immunoglobulin cannot be a substitute for HRIG.

117. What should be done to a person who has consumed milk of a rabid animal?

If a person has consumed milk of a rabid animal, counseling should be done. If counseling is not effective, then PrEP by IM or ID route or as a last resort a course of PEP (only vaccine) should be given.

If the milk is boiled or heated then only counseling or at the most a course of PrEP should be given only due to compulsions in medical practice in Indian setting.

118. Can rabies be transmitted through sexual intercourse?

Rabies virus is present in the semen and to some extent in vaginal secretions.

Priapism, increased sexual libido and indulgence are seen both in male and female rabies cases.

Hence, in the exposed person, a full course of rabies post-exposure vaccination either by Intramuscular (IM) or Intradermal (ID) route should be given.

If there is any doubt of category III exposures, that is, abrasion on penis or in vagina, then even RIG must also be given by IM route.

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

Kissing a rabies patient may transmit disease because there may be contact with rabies patient's saliva. Full post-exposure immunization must be given either by Intramuscular (IM) or Intradermal (ID) route.

If there are ulcers in the mouth of the exposed person, then RIGs must be given by IM route.

120. A person has handled or eaten the raw meat of a rabid animal. What should be done?

If a person has handled or eaten the raw meat of a rabid animal, he should receive full course of rabies vaccine. If the person has eaten raw meat of a rabid animal and has oral ulcers/lesions, he may be given RIGs in thigh IM on day 0 along with first dose of vaccine.

121. If the rabid animal's saliva falls into the eyes, what should be done?

If the rabid animal's saliva falls into the eyes, the eyes should be washed with water/saline and then RIGs can be instilled as eye drops, after dilution (1:1) with sterile normal saline along with full course of anti-rabies vaccination.

122. How should you approach a patient requiring RIGs, when none is available?

- (1) Thorough wound cleansing.
- (2) ESSEN IM vaccination with **double dose** on day 0 and refer the patient to RIG center.

123. Do antibodies from rabies vaccination cross an intact blood-brain barrier?

No. Antibodies from vaccination do not cross an intact blood-brain barrier.

K. Rabies in Animals

124. What should be done to a pet dog that is bitten by a stray dog?

If a pet dog is bitten by a stray dog, wounds should be thoroughly washed and povidone iodine should be applied. Consult veterinarian for anti-rabies vaccination.

125. We often hear that the patient died of rabies but the biting dog was still alive. Is it possible?

It is not possible.

126. What is the incubation period in animals?

In dogs and cats, the incubation period is 10 days to 6 months; most cases become apparent between 2 weeks and 3 months. In cattle, an incubation period from 25 days to more than 5 months has been reported (in vampire bat-transmitted rabies).

127. What are the signs of rabies in dogs/cats?

1. Any change in normal behavior suggesting either undue aggression or depression.
2. Running aimlessly and attacking others without provocation.
3. Becomes too drowsy and withdraws to a corner.
4. Change in voice/bark.
5. Excessive salivation.
6. Refusal to feed or eating objects like stone, paper, wood, metal pieces etc.

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

The clinical course of rabies in animals is divided into three phases:-

- Prodromal,

- Excitative
- Paralytic.

However, the signs are variable and the lengths of phases may be irregular.

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

Prodromal phase may last for 1-3 days and the animal may show only vague CNS signs, which intensify rapidly and death is virtually certain within 10 days after the initial onset of signs.

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

The excitative phase follows the prodromal phase in some animals. The animal becomes irrational and may aggressively use its teeth, claws, horns, or hooves. The expression is one of anxiety with dilated pupils. Noise invites attack. Rabid animal roam extensively and attack other animals, including humans and any moving object. Cats usually manifest furious type of rabies.

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

Paralytic or dumb rabies refers to animals in which the behavioral changes are minimal or absent and the disease is manifested mainly by paralysis. This is first manifested by paralysis of the throat and masseter muscles, often with profuse salivation and inability to swallow. Dropping of 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.

132. What is the cause of death in a rabid animal?

Death in rabid animal is due to progressive paralysis.

133. Is hydrophobia a sign of rabies in dogs?

Hydrophobia is not a sign of rabies in dogs. Rabid dogs can drink water and even swim in water. If a rabid dog is not able to drink water, it is because of paralysis of jaw muscles and not due to hydrophobia.

134. Are there any variations in signs of rabies between different species of animals?

There are few variations in signs of rabies between different species of animals. Cattle with furious rabies attack man and other animals. A common clinical sign is a characteristic abnormal bellowing.

Head butting is a characteristic sign in case of rabies in cattle, sheep and goats.

135. Should modern rabies vaccines meant for use in man be given to animals?

It is advisable to use human vaccines for human use and use the veterinary vaccines for animals.

136. IF vaccination 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. 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 a few centers in the country. The facility to quarantine the bitten vaccinated pet is limited and difficult. In view of the above facts and practical realities, rabies being 100% fatal, we take no chances and start PEP (immunization) in the bitten person and presume the vaccinated dog to be incubating rabies (and infective) and simultaneously observe the dog.

However, in extremely rare situations exception to the above thumb rule can be made at the professional discretion of the treating physician.

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

If a potent veterinary vaccine is given correctly as per pre-exposure schedule, it will mostly prevent rabies in the vaccinated dog, unless the exposure is severe. *Ideally*, its sera should be tested for protective antibody titre level but this is rarely practicable due to scarce facilities in our country. Consequently, PEP vaccination is recommended following bites even by vaccinated dogs. It has been noted that:-

- (1) 6% of dogs found rabid have a reliable pre-exposure rabies vaccine history and that
- (2) 40% of dogs' vaccinated only one time lost most of their immunity 4-6 months later.
- (3) Post Exposure Prophylaxis (PEP) vaccination is not very successful in dogs.

138. What is important for the success of Animal Birth Control (ABC) program?

The success of this program hinges on the sterilization of 70% of the strays in a given geographic area within 6 months, before the next reproductive cycle begins; otherwise the entire effort is negated.

139. A pet 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.

140. Does 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.

141. An unvaccinated or partially vaccinated pet dog or cat is bitten by a stray dog. What should be done?

If an unvaccinated or partially vaccinated pet dog or cat is bitten by a stray dog, wounds should be thoroughly washed with water and povidone iodine should be applied. If the stray dog is suspected to be rabid, then the pet dog should be put to sleep (Euthanasia). But if the owner is not ready or the rabid status of the stray dog is not known, post-exposure vaccination of the pet with cell culture vaccine and simultaneous careful observation of the pet are recommended for up to 2 months (up to six months is desirable) for possible signs of rabies in the pet. 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. It should be noted that post-exposure vaccination is not very successful in dogs. Simultaneously, pre-exposure vaccination of all household members is necessary.

142. Can unvaccinated pet dog/cat pose danger to the family?

As rabies is enzootic, that is, widely prevalent in stray dogs in India, if unvaccinated pet dog/cat is bitten by a stray dog, the pet may develop rabies and later pose threat at home to all family members.

Dogs 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.

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

Ideally, the pet dog should be put to sleep (Euthanasia). The usual method of euthanasia for dogs is by IV injection of either concentrated Magnesium Sulphate solution or concentrated pentobarbitone.

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

No. Neither the age nor the breed or sex of the dog is important in transmission of rabies.

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

It is important to establish if the biting animal 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 signs. An unknown animal, which has disappeared, must be considered as rabid and full course of PEP must be given. Cats and dogs, which can be identified, must be kept under observation. The risk of rabies can be considered as slight if the animal shows no sign of disease after 5 days, 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 must be 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.

146. Can rabies be transmitted to a dog that 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 like the heart, muscles, skin, etc. So the dog can definitely get infected because the virus can spread through oral mucous membrane.

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

Following severe and extensive bites which mean injection of very high challenge dose of virulent virus by a rabid dog, a vaccinated dog can still succumb to rabies.

148. If the pet is immunized, do 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 high risk of rabies, and therefore, pre-exposure vaccination is recommended for all the family members.

L. World Rabies Day

149. When is World Rabies Day observed?

“World Rabies Day” is on 28th September.

150. What humanizing your dog means?

1. Talking to your dog like he/she is a person.
2. Treating your dog like he/she is a person.
3. Allowing dogs to do what they want because it will hurt their “feelings.”
4. Dressing them up in little doggie clothes.

Remember, humanizing your dog is fulfilling your own human needs, not your dogs. Humanizing dogs does **more harm** than good.

151. What are the rules every dog owner should follow?

(1) The number one way to communicate to a dog that you are his pack leader is to take him or her for a Pack walk daily, where the dog is made to heel beside or behind the human who is holding the lead. This is most important for all dogs, as in a dog's mind, the leader always leads the way.

- A dog must not be allowed to sniff or eliminate anywhere he wishes, but where you allow him.
- The dog should be concentrating on following the human.

(2) All humans must eat *before* the dogs.

(3) No table scraps should be fed to the dogs during a meal.

(4) Feedings must be at a scheduled time.

(5) Humans must not let the dog go through any doorways first.

(6) When you have left the house or the room, even for a minute and come back, ignore the dog for a few minutes.

(7) A simple obedience command should be given before any pleasurable interaction with the dog. A child in the house should give the dogs command at least once a day and reward with a treat when the command is followed.

(8) You should not lie on the floor to watch TV when the dog is around, as a human should never put himself in an equal or lesser height position than the dog.

(9) You are the first one who greets new comers; the dog is the last that gets attention.

(10) If a dog is lying in your path, do not walk around the dog, either make the dog move or step over the dog.

(11) If you establish eye contact with the dog, the dog must avert his gaze first. Tell the children not to have staring contest with the dog.

(12) Dogs must not sleep in your bed.

(13) Games of fetch or play with toys must be *Started* and *Ended* by the *Human*.

(14) Dog should not be allowed to lie on your furniture.

(15) No tug-of-war, as this is a game of power and you may lose the game giving the dog reinforcement (in the dog's mind) of top dog.

(16) Dogs need to be taught a drop it or release command.

(17) Dogs should not be allowed to pull on the leash.

(18) When you put his food dish down, he must wait until you give the "OK" to eat it.

(19) Small dogs or puppies who demand to be picked up or put down

should not get what they want until they sit or do another acceptable quiet behavior.

(20) Dogs should never be left unsupervised with children or *anyone* who cannot maintain leadership over the dog.

(21) Last but certainly not least... when you are around your dog avoid emotions. Your dog can sense these emotions and will see you as weak.

152. Why dogs always keep their mouth open with tongue protruding out?

Dogs do not sweat through the skin. They exchange most of their heat through the mouth, and extend the tongue to increase the surface exposed to the air.

153. What is the latest news about Rabies disease?

- (1) Study of passive immunity in the prevention of rabies discusses the advances in passive immunoprophylaxis, most notably the shift from the recommended polyclonal human or equine immunoglobulin to monoclonal antibody therapies. The first rabies-specific monoclonal antibodies are undergoing clinical trials, so passive immunization might finally become an accessible, affordable, and routinely used part of global health practices for rabies.
- (2) A report on use of a reduced (4-dose) vaccine schedule for post exposure prophylaxis to prevent human rabies summarized new recommendation and updates previous recommendations of the Advisory Committee on Immunization Practices (ACIP) for post exposure prophylaxis (PEP) to prevent human rabies.
- (3) Human rabies can be very effectively prevented, and animal control is an important component in reducing the public health risk to humans. Dog rabies can be eliminated by well established control methods and routine dog rabies vaccination programs.

154. Can a Rabies patient make a valid will?

A rabies patient can make a valid will.

According to Section 59 in the Indian Succession Act, 1925

Person capable of making will:-

1. Every person of sound mind not being a minor may dispose of his property by will.
2. A married woman may dispose by will of any property which she could alienate by her own act during her life.
3. Persons who are deaf or dumb or blind are not thereby incapacitated for making a will if they are able to know what they do by it.
4. A person who is ordinarily insane may make a will during interval in which he is of sound mind.
5. No person can make a will while he is in such a state of mind, whether arising from intoxication or from illness or from any other cause that he does not know what he is doing.

M. Monoclonal Antibodies and Rabies

155. What are monoclonal antibodies?

Monoclonal antibodies (mAb) are important reagents used in biomedical research, in diagnosis of diseases, and in treatment of such diseases as infections and cancer. These antibodies are produced by cell lines or clones obtained from animals that have been immunized with the substance that is the subject of study. The cell lines are produced by fusing B cells from the immunized animal with myeloma cells.

156. What is the role of monoclonal antibodies in Rabies?

Monoclonal antibodies against rabies virus have been widely used in the diagnosis and immunological analysis of rabies. Human monoclonal antibodies to rabies virus G protein are also expected to be used as a replacement for rabies

immunoglobulin (RIG) in the post-exposure treatment of rabies. In 1978, Wiktor reported the preparation of rabies virus monoclonal antibodies. Since then, rabies virus monoclonal antibody (mAb) technology has been more and more widely used in basic research and diagnosis of rabies.

N. Rabies Survivors

157. What is Milwaukee protocol?

The Milwaukee protocol is an experimental course of treatment of an acute infection of rabies in a human being. The treatment involves putting the patient into a chemically induced coma and administering antiviral drugs. It was developed and named by Dr. Rodney Willoughby, following the successful treatment of Jeanna Giese, a teenager from Wisconsin who became the first of only six patients known to have survived symptomatic rabies without receiving the rabies vaccine.

Medical history has shown most rabies deaths are caused by temporary brain dysfunction with little to no damage occurring to the brain itself. Using this information, Willoughby's team devised an experimental treatment for rabies. Giese's parents agreed to the experimental treatment. Dr. Willoughby's goal was to put Giese into an induced coma to essentially protect herself from her brain, with the hope she would survive long enough for her immune system to produce the antibodies to fight off the virus. Giese was given a mixture of ketamine and midazolam to suppress brain activity, and the antiviral drugs ribavirin and amantadine, while waiting for her immune system to produce antibodies to attack the virus. Giese was brought out of the coma after six days, once signs of the immune system's progress became apparent. After 31 days in the hospital, Giese was declared virus-free and removed from isolation.

The reasons for Giese's survival under the Milwaukee protocol remain controversial.

Recent WHO expert consultation did not recommend this protocol to be tried.

O. Rabies Websites

158. What are the important websites on Rabies?

Important rabies websites are:-

1. <http://rabies.org.in/>
2. <http://www.who-rabies-bulletin.org/>
3. www.who.int/rabies
4. www.cdc.gov.in
5. www.apcri.org
6. www.rabiesinasia.org
7. www.rabiescontrol.net
8. www.worldrabiesday.org
9. www.drakgupta.in

Although utmost care is taken to provide updated information through this book, ultimately the decision to treat the patient lies solely with the physician.