Human rabies: managing animal bite

An Information Booklet

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President's Message

It is a great honour to take on this endeavour of making India Rabies free with the start of this organisation 'Consortium Against Rabies'. The aim of this consortium is to focus on the issues related to Rabies ,which is an often neglected disease.

Rabies is a preventable viral disease of mammals most often transmitted through the bite of a rabid animal. In India, about 15 million people are bitten by animals, mostly dogs, every year and need post exposure prophylaxis. There is at present no comprehensive national rabies control program in India or a policy frame work. I find that in Rabies, the challenges and opportunities are both great.

I think we need more advocacy and research on rabies in order to deal with it.

I welcome all who intend to fight against this menace to join this movement and make their contribution towards this cause.

We are on to make full on efforts to prevent and control Rabies.

I wish my team all the very best !

The consortium would like every one of you to hold hands and give the organization a big boost and fillip.

Dr A T Kannan.
President Consortium Against Rabies.

Hony Secretary's Message

Rabies is a significant medical and veterinary health problem in developing countries especially India where approximately 20,000 people loose their life to this illness. This figure is just the tip of the iceberg as most cases go unreported. Moreover the awareness regarding this illness and its data collection is extremely poor amongst the health professionals and the general public. A lot of media attention has been generated in recent years whenever rabies related deaths are reported. This has led to some increase in political commitment and public awareness.

Shifting to intradermal technique has led to a massive decrease in vaccine requirement per person.

The basic problem in this country is not advanced scientific research but spreading awareness on management of animal bite such as wound washing and serum and vaccine administration at grass root level.

Being clinicians, the biggest problem faced by us sitting in the OPD or casualty is how to tackle various issues in patient management on animal bite and the lack of awareness in the colleagues and general public. Keeping this in mind we, a group of practicing clinicians, got together and organized a movement called CONSORTIUM AGAINST RABIES.

This is the sincere effort of our team of dedicated doctors that we have tried to bring out this publication useful as a quick reference in the busy OPD and casualty where a variety of patients report.

I request all to come forward and join hands in eradicating the menace of rabies in India as many of countries has already done.

Dr. Anurag Agarwal.

Hon. Secretary Consortium Against Rabies.

Acknowledgement

I am highly thankful to Dr. A.T.Kannan for rendering his efforts towards prevention and management of rabies in India. His whole hearted support and cooperation has led to the formation of this informative booklet.

I hope that this booklet will be of help to all those involved in managing animal bite cases with reference to rabies.

Comments, suggestions and feedback for improvement of this endeavor are most welcome.

Dr. Khan Amir Maroof

A. Rabies – An epidemiological overview

Rabies is a viral zoonosis of which a number of carnivores and bat species serve as natural reservoirs. In humans, rabies is almost invariably fatal once clinical signs occur. Bites by rabid domestic dogs cause 99% of human deaths globally. More than 3.3 billion people live in regions where rabies is enzootic. Approximately 55 000 people die from rabies each year, the vast majority of these deaths occurring in Asia and Africa.

However, deaths from rabies are likely to be grossly underreported in a number of enzootic countries, particularly in the youngest age groups. The estimated 55 000 (90% confidence interval (CI): 24 500–90 800) deaths per year may be an underestimate.

Although all age groups are susceptible, rabies is most common in children aged below 15 years, with 30–50% of post-exposure prophylaxis given to children aged 5–14 years, the majority being male.

Annually, more than 10 million people, mostly in Asia, receive postexposure vaccination against rabies. Post-exposure rabies prophylaxis is estimated to prevent 330 304 (90% CI: 141 844–563 515) deaths in Asia and Africa. It is estimated that rabies is responsible for 1.74 (90% CI: 0.25–4.57) million disability-adjusted life years lost each year. The annual global expenditure for rabies prevention is, by conservative estimates, >US$ 1 billion.

B. Rabies – The disease

Infection usually occurs from a transdermal bite or licks on mucosa by an infected animal. Rarely, transmission by aerosol route and organ transplantation have been reported. The virus after entering the body, through the peripheral nervous system reaches the central nervous system and finally the brain. Multiplying rapidly in the brain

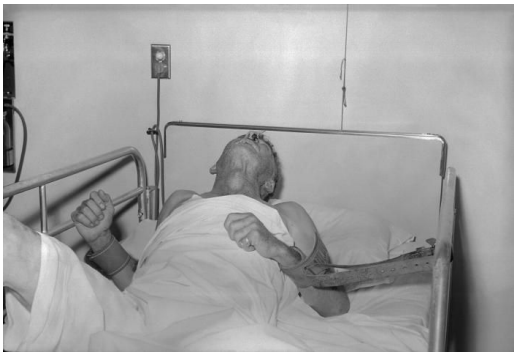

Photo 1: A patient suffering from Rabies

(Photo available from CDC website photo id: pID#:2539 http://phil.cdc.gov/phil/quicksearch.asp)

tissues, it then moves to various tissues of the body mainly the salivary glands. It is present in the saliva of the infected animal/human being. Clinical features are that of acute encephalitis and appear when the virus reaches the CNS. One of the most striking clinical feature is hydrophobia. Once the clinical features set in, this disease is invariably fatal. The incubation period is variable from few weeks to many months. Paralytic rabies is a form of rabies found in about one third of patients affected with rabies and is often misdiagnosed as it runs a less dramatic course and is one of the causes of underreporting of this disease. As the rabies viruses are mainly intraneuronal during infection, it may be concealed from the immune surveillance system of the body.

C. Animals transmitting rabies:

Rabies is a disease that naturally affects only mammals. Mammals are warm blooded animals with fur. Domestic animals like dogs, cats, cattles (cows, buffaloes, camels), horses, sheep, goats, mules;

Photo 2: Dogs: the main reservoir of rabies in India.
(Photo courtesy: Mr. Sameer Joshi)

Wild animals like monkeys, mongoose, bats, coyotes, foxes, raccoons, bears, skunks can transmit rabies. Rodents and squirrels have not been reported to transmit rabies. In India, bats also have not yet been reported to be transmitting rabies. So, bites by rodents and bats do not usually necessitate postexposure prophylaxis but bites by these animals in unusual circumstances may be considered for postexposure prophylaxis in consultation with an expert in the field of rabies. Bites by birds, snakes and fishes do not cause rabies.

D. Wound Toilet:

Since lick on open wounds or mucosa and transdermal bites are responsible for rabies transmission, cleaning the site of wound is of utmost importance. Merely washing the site with copious amount of water and soap/detergent for about 15 minutes reduces the risk of developing rabies by about fifty percent. Care should be taken not to cause any further damage in the process of washing of wound. Touching the wound with bare hands should be avoided. Even if the patient has reported late, wound toilet should be done as the virus can persist and multiply at the site for a long time.

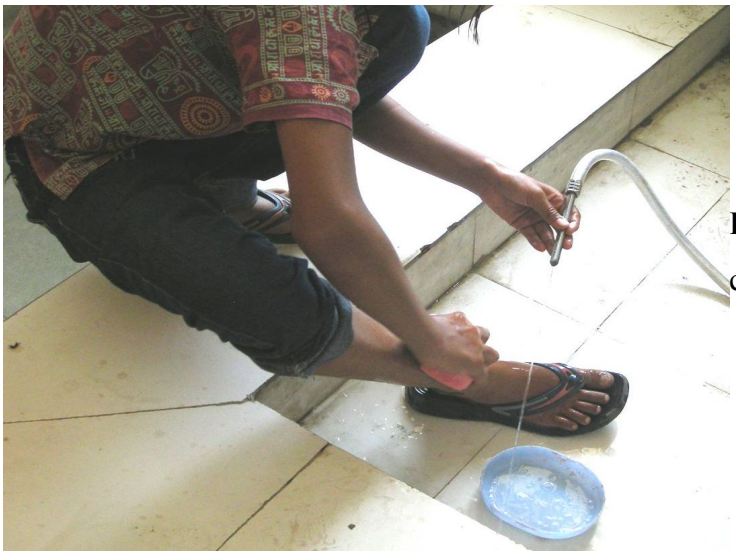

Photo 3: Wound washing. (Photo courtesy: Dr. Anurag Agarwal)

After washing and drying of the wound, chemical agents like Savlon, Dettol, iodine tincture etc. can be applied in recommended dilutions. Application of chilli powder etc. is not of any benefit and being an irritant may increase the risk of infection. Suturing of the wound should not be done. If severe bleeding is there and suturing is unavoidable, minimum stay sutures after administration of rabies immunoglobulin should be given. Other treatments like tetanus immunization and antibiotics should be applied as relevant for bite wounds.

Table 1: World Health Organization (WHO) categorization of type of exposure for management of rabies

WHO category of dog bite exposure	Symptoms/Signs	Management
Category I	Touching or feeding animals, licks on the skin (i.e. no exposure)	➢ No prophylaxis is required
Category II	Nibbling of uncovered skin, minor scratches or abrasions without bleeding	➢ Thorough (for ~15 minutes) washing and flushing with soap/detergent and copious amounts of water of all bite wounds and scratches should be done immediately, or as early as possible. ➢ Immediate vaccination
Category III	Single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva from licks, exposures to bats. Or Bite by any wild animal.	➢ Thorough (for ~15 minutes) washing and flushing with soap/detergent and copious amounts of water of all bite wounds and scratches should be done immediately, or as early as possible. ➢ Immediate vaccination and administration of RIG are recommended

Tip: Any wound that bleeds is category III.

Note: Tetanus immunization should be administered depending upon its past immunization history and antibiotics may be prescribed.

Post-exposure prophylaxis should be converted to preexposure prophylaxis, in the case of domestic dogs or cats where, the animal remains healthy throughout a 10-day observation period, by administering one dose at day 28. Note that the 10 day observation period is only applicable for dogs and cats and not for other animals. In most situations in developing countries, the

vaccination status of the offending animal should not be taken into consideration to withhold prophylaxis.

E. Pre-exposure prophylaxis

PrEP may be performed with any of the modern cell derived vaccines. Pre-exposure immunization is recommended for anyone at increased risk of exposure to rabies virus, either by nature of their residence or occupation, or when travelling. This recommendation includes laboratory staff, veterinarians, animal handlers, wildlife officers with frequent exposure to potentially infected animals, as well as visitors to areas with high risk of rabies.

a. Intramuscular administration

Pre-exposure rabies vaccination requires IM doses of 1 ml or 0.5 ml, depending on the vaccine type, given on days 0, 7 and 28 (day 28 preferable, but administration may be advanced towards day 21 if time is limited). The vaccine should always be administered in the deltoid area of the arm (in adults) and in the anterolateral area of the thigh (for children less than two years). Rabies vaccine should not be administered in the gluteal area, as an adequate immune response may not be reliable.

b. Intradermal administration

ID administration of 0.1 ml volumes on days 0, 7, and 28 (day 28 preferable, but administration may be advanced towards day 21 if time is limited) is an acceptable alternative to the standard IM route. This is to be administered at one site only.

c. Booster injections

Booster doses are not recommended as a routine practice to everyone who has taken a full course of primary immunization against rabies. Periodic booster injections are recommended only for people whose occupation puts them at continuous or frequent risk of rabies exposure. This will depend on the Virus Neutralizing Antibodies (VNA) levels. If it is less than 0.5 IU/ml, then

boosters are recommended. Two doses of modern cell culture vaccines should be administered. They may not be of the same brand which was used in the primary series of vaccination.

F. Post-exposure prophylaxis

a. Rabies Immunoglobulin (RIG):

This provides passive immunity to the individual and is important to protect the individual during the initial phase till the active immunity of the body responds to the rabies vaccine administered. This is administered in the case of category III bites and that too within 7 days of the start of postexposure prophylaxis vaccination. In the case of immunocompromised individuals, RIG should be administered even in the case of category II bites.

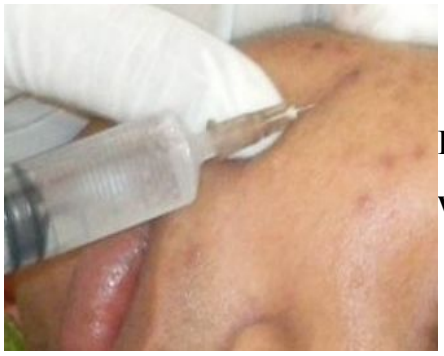

Photo 4: Anti rabies serum injected at the site of wound. (Photo courtesy: Dr. Anurag Agarwal)

The dose for **Antirabies serum/Equine Rabies Immunoglobulin (ERIG)** is 40 IU/kg body weight and for **Human Rabies Immunoglobulins (HRIG)** is 20 IU/kg body weight.. The earlier upper limit for RIG i.e. 1500 IU for HRIG and 3000 IU for ERIG, has been removed as per the latest WHO guidelines and now the whole amount calculated by per kg body weight requirement is to be administered.HRIG are free from the side effects, does not require sensitivity testing and because of their longer half life, are given in half the dose of equine antirabies serum. HRIG should be preferable if it is available and can be afforded. The antirabies sera should always be brought to room temperature (20 - 25^{o}C) before use. Sensitivity testing for ERIG as per the manufacturer's guidelines should be done before administration. However as per latest WHO Recommendations, there are no scientific grounds for performing a skin test prior to administering equine rabies immunoglobulin because testing does not predict reactions, and it should be given whatever the result of the test. The treating physician should be prepared to

manage anaphylaxis which although rare, could occur during any stage of administration (Source: WHO Position Paper 2010). Pregnancy and lactation are not a contraindication for administration of RIGs.

The calculated amount of RIGs should be administered at the site of the wound. If the amount is insufficient to cover infiltration of the wound, it can be diluted with normal saline to 2 or 3 times so that the infiltration of the wound is covered. RIGs should be administered at the site only as much as possible. In cases where after complete coverage of the wound, some amount is remaining, then it should be administered intramuscularly at a site distant from the site where the vaccine is to be administered. Preferably vaccine should be given after half an hour of serum administration. This period can be gainfully utilized to observe the patient for any reactions of the serum.

b. Anti Rabies Vaccines:

i. Intramuscular administration for modern vaccines

The post-exposure vaccination schedule is based on IM doses of 1 ml or 0.5 ml, depending on the manufacturer. The recommended regimen consists of either a 5-dose or a 4-dose schedule.

(i) The 5-dose regimen prescribes 1 dose injected into the deltoid muscle (or anterolateral thigh in children aged <2years) on each of days 0, 3, 7, 14 and 28.

(ii) The 4-dose regimen prescribes 2 doses on day 0 (1 in each of the 2 deltoids or anterolateral thighs in case of children aged < 2 years) followed by 1 dose on each of days 7 and 21.

ii. Intradermal administration

For intradermal administration, three vaccines have been proven to be efficacious:

- Human diploid cell vaccine (HDCV)
- Purified vero cell vaccine (PVRV)
- Purified chick embryo cell vaccine (PCECV

- Note: The vaccines approved by DGCI for intradermal administration should be used by intradermal route. The vaccine package insert should be referred to know whether it can be administered intradermally or not.
- 8-site intradermal method (8-0-4-0-1-1) for use with HDCV and PCECV. *The 8 sites regimen should be particularly considered in emergency situations when no RIG is available.* On day '0' 0.1 ml is administered intradermally at each of the 8 sites i.e. deltoids, lateral thighs, suprascapular region, lower quadrant of abdomen. On day 7, 0.1 ml i.d. at each of the four sites i.e. over deltoids and thighs. On days 28 and 90, 0.1 ml i.d. at one site i.e. deltoid.

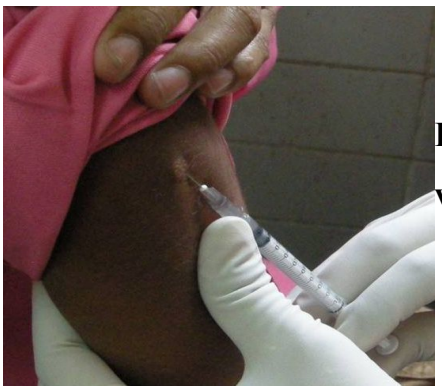

Photo 5: Intradermal administration of Anti rabies vaccine. (Photo courtesy: Dr. Anurag Agarwal)

- 2-site intradermal method (2-2-2-0-1-1 or 2-2-2-0-2) for use with PVRV

and PCECV. 0.1ml i.d. on both deltoids on days 0, 3, 7, 28 and only on one deltoid on 90 or 0.1 ml i.d. on both deltoids on days 0, 3, 7 and 28.

The doses of vaccines are age independent. Pregnancy is not a contraindication to postexposure prophylaxis.

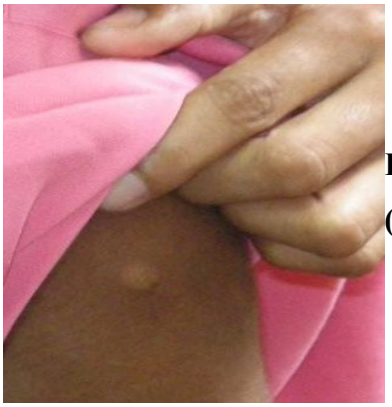

Photo 6: Bleb formation after intradermal antirabies vaccine. (Photo courtesy: Dr. Anurag Agarwal)

In immunocompromised individuals, including patients on immunosupperssant drugs like steroids etc. or with HIV/AIDS, comprehensive wound management and local infiltration with RIG, in combination with a complete intramuscular CCV series, are of utmost importance for the successful prevention of rabies. In these situations, the
people taking chloroquine for treatment or malaria prophylaxis can have a reduced response to ID rabies vaccination. These patients should receive the vaccine by the IM route. VNA response should be determined 2–4 weeks following vaccination to assess the possible need for an additional dose of the vaccine.

For rabies-exposed patients who have previously undergone complete pre-exposure vaccination or postexposure prophylaxis with a Cell Culture Vaccine (CCV), 2 IM or ID doses of such a vaccine administered on days 0 and 3 are sufficient. RIG is not necessary in such cases. The same rules apply to people vaccinated against rabies who have demonstrated Virus Neutralizing Antibodies (VNA) titres of at least 0.5 IU/ml. Vaccination cards carefully recording previous immunizations are invaluable for correct decision-making.

iii. Interchangeability of modern rabies vaccine types and routes for post exposure prophylaxis

- Interchangeability of modern rabies vaccine is not recommended.
- When completion of Post Exposure Prophylaxis (PEP) with the same modern rabies vaccine is not possible, the switch can be done provided that it is one of the WHO recommended cell culture vaccines.
- No study has been done yet on vaccine immunogenicity and change of the route of vaccine administration (eg. From intramuscular to intradermal) during PEP.
- This practice should be the exception.

List of available brands of rabies immunoglobulins and rabies vaccines in the market:

Equine RIG

	Brand	Product	Pharmaceutical company
1	Equirab	Purified Equine RIGs, 5ml vial (300 IU/ml, 1500 IU potency)	Bharat Serums and Vaccines Limited, Mumbai
2	Carig	Purified Equine RIGs, 5 ml vial (300 IU/ml,1500 IU potency)	Cadila Pharmaceutials, Ahmedabad
3	Zyrig	Purified Equine RIGs 5 ml vial (300 IU/ml,1500 IU potency)	Zydus Alidac, Ahmedabad
4	Abhayrig	Purified Equine RIGs, 5 ml vial (300 IU/ml, 1500 IU potency)	Human Biologicals Institute, Hyderabad

Human RIG

	Brand	Product	Pharmaceutical company
1	Berirab-P	Human RabiesImmunoglobulins, 50 IU/ml;2 ml (300 IU) ampoule and 5 ml (750 IU) ampoule	CSL,Bharat Serums and Vaccines Limited, Mumbai
2	Imogamrab	Human RabiesImmunoglobulins, 50 IU/ml;2 ml (300 IU) ampoule and 5 ml (750 IU) ampoule	Aventis Pasteur, France,
3	Kamrab	Human RabiesImmunoglobulins, 50 IU/ml;2 ml (300 IU) ampoule and 5 ml (750 IU) ampoule	Medlife, Thane

Modern Rabies Vaccines

	Brand	Product	Pharmaceutical company
1	Abhayrab	Purified Verocell Rabies Vaccines (PVRV) (0.5ml)	Human Biologicals Institute, Hyderabad
2	Rabipur	Purified Chick Embryo Cell Vaccine (PCEC) (1 ml)	Novaritis Vaccines/sanofi Aventis

3	Rabivax	Human Diploid Cell Culture Vaccine (HDCV) (Liquid) (1ml)	Serum Institute of India, Pune
4	Vaxirab	Purified Duck Embryo Vaccines (PDEV) (1 ml)	Zydus Alidac Ahmedabad
5	Verorab	Purified Verocell Rabies Vaccines (PVRV) (0.5 ml)	Sanofi Pasteur
7	Rabirix	Chromatographically purified PVRV (0.5 ml)	Bharat Biotech, Hyderabad
	Indirab	Chromatographically purified PVRV (0.5 ml)	Bharat Biotech, Hyderabad

Disclaimer: This list has been mentioned just for a quick and handy reference and it is not exhaustive. Consortium Against Rabies does not endorse any brand or is not promoting any particular brand.

Common Questions regarding management of dogbite with special reference to rabies

Q: Can a pregnant women be administered rabies vaccine and serum, if she is exposed ?

Ans: Animal studies regarding this have not been reported. Also there are no such controlled data in human pregnancy. HRIG should only be given to a pregnant woman if clearly needed. Because of the high mortality associated with untreated rabies virus infection and also certain studies showing that rabies vaccines and serum are safe in pregnancy and lactation, pregnancy and lactation is not considered a contraindication to post exposure rabies prophylaxis.

Q: If a rabies vaccine is accidentally kept in the freezer; can it be used ?

Ans: No. The potency of the vaccine is compromised due to freezing and thawing. As rabies is a life threatening disease any chances cannot be taken.

Q: Can we change the type/brand of rabies vaccine with other?

Ans: This is not at all recommended as a routine practice. Only in case of emergency or unavailability this can be done.

Q: A person reports with a history of dog bite 5 years back and no history of any rabies vaccination. Should rabies vaccine be administered?

Ans: Yes, the case should be managed as any other case of dog bite and depending on the type of exposure the management should be done. As the incubation period of rabies is variable, we have no reason not to go for post exposure prophylaxis of rabies.

Q: A person reports with history of dog bite one day back. He also has a past history of receiving a complete course of rabies vaccine five years back. What schedule should be followed in this case?

Ans: For rabies-exposed patients who have previously undergone complete pre exposure prophylaxis or a complete post exposure prophylaxis with a CCV, two doses (IM or ID) of such a vaccine administered on days 0 an 3 are sufficient. RIG is not necessary in such cases. But if the patient has received nervous tissue vaccine earlier, he should be treated as a fresh case and be administered full course of ARV.

Q: Can a rabies vaccine be administered to a lactating mother?

Ans: Yes, rabies vaccine can be administered to a lactating mother. As it is an inactivated vaccine, it is safe for a lactating mother and has no effect on the breastfeeding baby.

Q: If a person is on antimalarials ; what is the schedule?

Ans: People taking chloroquine for treatment or malaria prophylaxis can have a reduced response to ID rabies vaccination. These patients should receive the vaccine by the IM route. Get antibody titre done after day 14.

Q: If a person is suffering from HIV/AIDS; what is the schedule?

Ans: In immunocompromised individuals, including patients with HIV/AIDS, comprehensive wound management and local infiltration with RIG, along with a complete intramuscular rabies vaccine (cell culture) series, are of utmost importance for the successful prevention of rabies. Administer RIG even in Category II exposure. Get antibody titre done after day 14.

Q: Should the dose of RIG be reduced for neonates?

Ans: The dose for RIG depends upon the weight of the patient.

Q: What is the schedule for booster doses of rabies vaccine?

Ans: Periodic booster injections are recommended only for people whose occupation puts them at continuous or frequent risk of rabies exposure. For those persons who are at high risk of getting exposed to rabies virus, it is recommended that they get their virus neutralizing antibody titre level assessed as often as every 6 months. VNA titres above 0.05 IU/ml indicate protection. Booster vaccinations are not recommended routinely to everyone who has taken a full course of primary anti rabies immunization.

Q. : A person with a history of dog bite one day back, tells that he was given an incomplete course of rabies vaccination few years back. What schedule should be followed in such case?

Ans: In case of absence of a well documented and clear evidence of a complete pre-exposure or a post-exposure prophylaxis, full vaccination schedule is to be followed. Incomplete course of vaccination should not be considered as 'previously immunized' persons.

Q. What should be done in case of consumption of milk of a rabid animal by a person ?

Ans: If the milk was boiled before consumption, then no need for further action as boiling destroys the rabies virus. But if it was an unboiled milk that was consumed then full course of rabies vaccine along with the rabies immunoglobulin should be administered.

Q. What should be done if a person gives a history of sexual intercourse with a rabid person or animal ?

Ans: Full course of rabies vaccine along with the rabies immunoglobulin should be administered in such case.

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Setting of a wound washing area:

Wound washing area should consist of a raised platform with multiple sources of water at different heights including pipes with inbuilt jets. (Ref. Photo 3 above) The area should be segregated from the bathrooms attached to toilets, in order to prevent contamination. Privacy should be provided to the patients for washing wounds so that they can wash wounds comfortably, moreso if the bite is near the private parts of the body. The area should be preferably manned by an attendant to guide the patient for

adequate wound toilet. A detergent or carbolic soap should be available to the patient for wound washing, although plain water washing can be done, in case of non availability of a soap. The best practice is washing the wound with soap and water and not just plain water only. If the wound is large, it should be cleaned by a dresser/ staff nurse using antiseptic solution.

Setting of an intradermal rabies vaccination clinic:

- Any centre receiving more than one patient within eight hours can use this technique.
- Any staff trained in intradermal injection technique can easily administer this vaccine. (e.g. staff routinely giving BCG vaccine, doing sensitivity tests before I.M/I.V. injections etc.) No special training is required for this technique.
- The vaccine should be kept at 2-8 degree centigrade after reconstitutioin. Safe injection practices must be followed.
- The vaccine is stable for 8 hours after reconstitution.
- If bleb is not formed while giving intradermal, it means that the drug has entered in the subcutaneous layer, and in this case, the vaccine should be readministered properly by the intradermal route.
- In both the cases, where the anti-rabies vaccine volume is either 0.5 or 1 ml after reconstitution, depending upon the type of vaccine, the dose to be given intradermally is 0.1 ml per site.
- 1 cc syringe with 26 gauge needle is required for i.d. vaccine.
- Vaccine used for i.d. route should be approved by DGCI for i.d. route.

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Consortium against Rabies is a not-for-profit national organization registered in Delhi, India, in 2010 under the Societies Registration Act, 1860.

The aim of this consortium is to focus on the issues related to rabies and work towards raising awareness regarding various aspects of rabies in order to eliminate rabies from India.

For feedback and further details kindly login to

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