Current Guidelines on Prevention of Rabies

An Information Booklet (2nd edition)

CONSORTIUM AGAINST RABIES

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Honorary President's Message

The very idea of publishing this booklet **on "Current Guidelines on Prevention of Rabies"** by **Consortium Against Rabies,** is intended for all interested clinicians in updated, evidence based knowledge about the subject. This pocket-sized reference consolidates information from nationally recognized associations and government agencies into concise recommendations for prevention of 100% fatal yet equally preventable disease –Rabies.
In this era of ever-changing science, one has to remain updated about the current concepts, available options and of course scientifically sound evidence-based recommendations/ guidelines from nationally recognized authorities/ bodies.

The authors have really worked hard so as to make this a comprehensive document for quick reference to the primary clinicians. Here I would appreciate the efforts of **Dr. Anurag Aggarwal and Dr. Amir M Khan** for their untiring efforts in compilation of this booklet incorporating updated knowledge about the subject.

This booklet is organized into topics related to general information and current burden of disease, pre-exposure & post-exposure prophylaxis and the products available in the market for such preventive strategies. Hope this will be of great help in spreading the right knowledge and practices and will certainly have positive effect in prevention of this dreaded disease.

Wish you happy reading,

Long live Consortium Against Rabies (CAR)!

Dr. G. P. Kaushal
President, Consortium Against Rabies® (2019-20)

Honorary Secretary General's Message

Rabies is a significant medical and veterinary health problem in developing countries especially India where approximately 20,000 (2004) people lose 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 country is coming out of a massive shortage of Rabies vaccine for the past more than a year due shut down of supply from a major manufacturer. This shows the vulnerability of total dependence on few major players from the private sector. The Public Sector Units (PSUs) need to be rebooted to keep a continuous supply of essentials ready.

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.

Due to exciting new research, WHO has modified the schedules and has done away with IM injection of RIG. Besides a new product, i.e. monoclonal antibody is available in the market. We have tried to include the latest changes in our guidelines, though Indian data is lacking.

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 Agrawal
Honorary Secretary General
Consortium Against Rabies®.

Message from Dr. G. Gongal, WHO SEARO

Rabies is one of the most horrific diseases and bite by a mad dog has been known as a primary source of rabies transmission to humans. Even today, a medical doctor is helpless in front of a rabies patient although it is one of the oldest zoonotic diseases ever known to mankind. Rabies is well known as a fatal disease and any negligence made by a patient after rabies exposure will become a blunder mistake leading to painful death experience. Even today, many medical practitioners and health professionals are confused when someone is talking about rabies and its prophylaxis. Production and use of rabies vaccine of nerve tissue origin in public hospitals is limited in medical textbook and introduction of cost-effective intradermal rabies vaccination has made modern rabies vaccine easily accessible and affordable in public hospitals.

I am very pleased to go through an information booklet on Rabies prevention written by Dr. Anurag Agrawal and Dr Khan Amir Maroof and published by the Consortium Against Rabies. I hope that it will be a best guide for medical practitioners and paramedics as it has updated information on rabies vaccination and rational use of immunobiologicals as per recent recommendations of the WHO expert consultation.

India has the highest burden of human rabies and this country has everything to fight against rabies, i.e. expertise, vaccine and immunobiological production potential, workforce and plan of action for rabies control and subsequent elimination. The World Health Organization and international partners have appealed all rabies endemic countries to move towards elimination of human rabies by 2030 and India has embarked on mission for zero human rabies death. Awareness and education for rabies prophylaxis is critical and we all must join hands together to provide better and timely post-exposure rabies prophylaxis to those people exposed to rabies.

Dr. Gyanendra Gongal
Scientist
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Foreword

Consortium Against Rabies has always been in forefront to tackle the problem of rabies by educating the public and training doctors regarding latest in the field. This booklet is a very good exercise by the Rabies experts from Consortium Against Rabies and would be useful for anyone who wants to know about rabies in brief. The pics and tables are very illustrative and QA section is nicely written. The latest 2018 guidelines by WHO have been incorporated for the benefit of the readers.

I congratulate authors for their interest and hard work to enable the reader know the complexities of dreaded disease like rabies because Rabies is the disease that is 100% fatal but almost 100% preventable if proper containment measures are taken as soon as person is exposed to animal bites. Bites by dog, cat, mongoose, monkey and squirrel or by any other domestic animal like cow, buffalo or horse and wild animal like fox, jackal, leopard or bear etc can cause rabies.

It is important to remember that tiny pups and vaccinated dogs can also transmit rabies and bites or minor scratches from them should be taken seriously and would require proper prophylaxis with appropriate injections. Vaccinating a pup before bringing one home, even if pup is below three months, is necessary and it is better if we give preventive rabies vaccination to all household members before bringing a pup home to protect family members from rabies.

Let's join hands to make Rabies elimination a reality by 2030 as is the goal of the WHO.

With Best Wishes,

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Rabies – An epidemiological overview

Rabies is a viral zoonosis of which several 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 55000 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. The recent Global burden of disease study estimates approximately 4500 deaths per year from India. This is the tip of the iceberg as most cases go unreported. Islands like Andaman and Lakshadweep are reported to be rabies free. Goa is also submitting zero rabies status for last few years. Efforts are being made to make rabies a notifiable disease to have improved surveillance. A global target of zero human rabies deaths by 2030 was set in line with the Sustainable Development Goals (SDG) 3.3 to end Neglected Tropical Diseases by 2030 and SDG 3.8 to achieve Universal Health coverage.

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.

Rabies is a major burden in Asia, with an estimated 35 172 human deaths per year. India accounts for 59.9% of rabies deaths in Asia and 35% of deaths globally. 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 cost of Post Exposure Prophylaxis (PEP) is highest in Asia, with estimates up to US$ 1.5 billion per year.

As a part of its mandate to provide guidance, World Health Organization (WHO) issues a series of regularly updated position papers on vaccines against diseases that have an international public health impact. The WHO currently published a proposed position paper prepared by the SAGE Working Group on Rabies vaccines and immunoglobulins on September 22, 2017. This was finally accepted and published as Weekly epidemiological record in April 2018. This replaces all the previously published position papers on rabies prevention. The following article is based on these papers and national guidelines. It discusses strategies to prevent infection with rabies after being bitten or exposed to an infected animal or suspected animal and pre-exposure prophylaxis.

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 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 features 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.

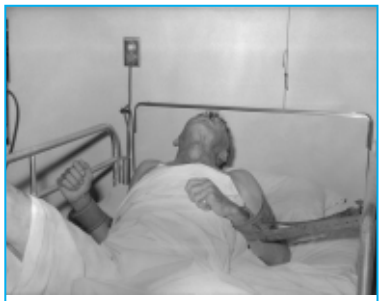

Photo 1: A patient suffering from Rabies
(Photo available from CDC website: https ://phil.cdc.gov/details.aspx?pid=2539)

Animals transmitting rabies

Rabies is a disease that naturally affects only mammals. Domestic animals like dogs, cats, cattle (cows, buffaloes, camels), horses, sheep, goats, mules and wild animals like monkeys, mongooses, bats, coyotes, foxes, raccoons, bears, skunks can transmit rabies. Rodents and squirrels have usually not been reported to transmit rabies in India, although there have been reports of dead squirrels being found to be positive for Rabies virus from Sri Lanka. 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.

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

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 for about 15 minutes reduces the risk of developing rabies by more than 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 Agrawal)

After washing and drying of the wound, chemical agents like savlon, dettol, iodine tincture, spirit, or alcohol 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 suturing after wound cleansing cannot be avoided, the wound(s) should first be thoroughly infiltrated with human or equine RIG or RmAb and suturing delayed for several hours to allow diffusion of the immunoglobulin through the tissues before minimal sutures are done. Secondary sutures are less likely to become infected and present better cosmetic results if done under optimal conditions. An infected bite wound is not a contraindication to injection of RIG or RmAb. Other treatment like tetanus immunization with TT/Td-vaccine and antibiotics should be applied as relevant for bite wounds.

Wound washing area: A separate wound washing area should ideally be a part of every animal bite management clinic. Soap and water should be available to wash the wound. As most of the bites are on the lower extremities the water hose or tap should be such that flowing water can be used to directly wash the wound area. If needed, a connecting pipe should be attached to the tap so that the patient can comfortably wash the wound site. In case of multiple wounds, care must be taken to wash all the wounds.

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

WHO category of 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 and copious amounts of water of all bite wounds and scratches should be done immediately, or as early as possible. When available, a topical virucidal application such as povidone iodine should be applied. • 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 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

RIG: Rabies Immunoglobulin. Tip: Any wound that bleeds is category III.

Note: Tetanus immunization with TT/Td-vaccine should be administered depending upon past immunization history. Antibiotics may be prescribed as needed.

Post-exposure prophylaxis can be discontinued if the suspect animal is proved by appropriate laboratory examination to be free of rabies, or, in the case of domestic dogs or cats, the animal remains healthy throughout a 10-day observation period. This 10-day observation period is not applicable for animals other than dogs and cats. The vaccination status of the offending animal should not be taken into consideration to withhold prophylaxis.

People with category III exposure who have not received at least two doses of PrEP or PEP and severely immunocompromised people with category II exposure (e.g. AIDS patients or transplant recipients) should receive both an effective rabies vaccine and rabies immunoglobulin

Pre-exposure prophylaxis

Rationale for pre-exposure prophylaxis

- May protect children who do not receive postexposure prophylaxis, for example, after unremarked exposure (i.e. if their antibody titer at exposure is ≥ 0.5 IU/mL)
- May protect patients when postexposure prophylaxis is delayed
- Accelerates antibody responses to postexposure prophylaxis
- Reduces the cost of postexposure prophylaxis by removing the need for rabies immunoglobulin and reducing the number of postexposure prophylaxis doses required from 8 to 2

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, children from endemic countries, families keeping pets 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, and 7. Day 21/28 dose has been removed by WHO guidelines but still recommended in National guidelines. 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

i. Intradermal 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.

ii. Recent WHO guidelines also recommend a two-site intradermal vaccination schedule with 0.1 mL per site on days 0 and 7.

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.
- Persons working with live rabies virus in diagnostic laboratories, research laboratories, vaccine production laboratories, at permanent risk of exposure to rabies should have one serum sample taken every six months and booster dose when the titre falls below 0.5 IU/mL
- Other professions (veterinarians, animal handlers, wildlife officers etc) working in rabies endemic areas should have one serum sample taken every two years and booster dose when the titer falls below 0.5 IU/mL.
- Healthy subjects do not require boosters on re-exposure to suspected rabies exposure for up to 3 months after pre-exposure or previous postexposure prophylaxis.

The booster doses (1 mL i.m. or 0.1 mL i.d one-site) should be given every two years or when the RVNA titers are below 0.5 IU/mL to persons such as veterinarians, animal handlers, and laboratory technicians who are continually at risk. They may not be of the same brand which was used in the primary series of vaccination.

People who discontinued a PEP series after administrations of at least two doses of vaccine may be considered to have completed their pre-exposure prophylaxis. But if they have a severe unprovoked bite, it will be better to give them a complete course, till further data is available from India.

Immunodeficient patients should receive an intradermal or intramuscular PrEP regimen as mentioned above plus a third administration of vaccine on days 21–28. Immunodeficient patients who are clinically monitored and well managed, such as HIV-infected people receiving antiretroviral therapy, are considered not to be immunocompromised and have been shown to respond to rabies and other vaccines in the same way as healthy individuals. Although immunocompromised patients, who have been given pre exposure prophylaxis, on re exposure a complete regimen is preferable, including RIGs, as their antibody titres and immune response to vaccine is doubtful.

d. Re-exposure management

For animal bite exposed patients who have previously undergone complete pre-exposure vaccination or postexposure prophylaxis with a Cell Culture Vaccine (CCV), One-site two visit schedule vaccine to be given on days 0 and 3. Intradermal: one site 0.1 mL at each visit OR Intramuscular: 1 mL or 0.5 mL depending upon the vaccine. RIG is not necessary in such cases.

An alternative regimen is a four-site intradermal vaccination with 0.1 mL at each site, on day 0.

Vaccination cards carefully recording previous immunizations are invaluable for correct decision-making.

Post-exposure prophylaxis

a. Rabies Immunoglobulin (RIG) or Rabies Monoclonal Antibody (RmAb):

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.

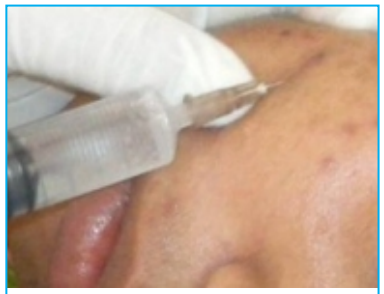

Photo 4: Anti rabies serum injected at the site of wound.
(Photo courtesy: Dr. Anurag Agrawal)

The dose for **Anti-rabies serum/Equine Rabies Immunoglobulin (ERIG)** is 40 IU/kg body weight); for **Human Rabies Immunoglobulins (HRIG)** is 20 IU/kg body weight and for **Rabies monoclonal antibody (RmAb)** is 3.33 IU/kg body weight. There is no maximum ceiling dose for Immunoglobulins including RmAb. RmAb and HRIG are usually free from side effects and do not require sensitivity testing. The dose requirement is lower than that of ERIG due to higher potency and longer half-life. For HRIG, the required dose is half the dose of equine anti-rabies serum. Due to its much higher potency, the dose of RmAb is significantly lower than ERIG and HRIG with advantage of lower infiltration volume compared to ERIG or HRIG. RmAb or HRIG should be preferable over ERIG if they are available and can be afforded. The antirabies sera should always be brought to room temperature (20 - 25°C) before use. Sensitivity testing for ERIG as per the manufacturer's guidelines may be done before administration though WHO guidelines have done away with its

requirement. Even if the sensitivity testing shows a negative skin test, preparation for managing anaphylactic reactions should be ready as there is still a possibility, although remote that the anaphylactic reaction may occur. For RmAb, or HRIG sensitivity testing is not recommended.

The calculated amount of RIGs/RmAb 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 sterile normal saline to 2 or 3 times so that the infiltration of the wound is covered. Care should be taken in case of multiple wounds so that no wound is left without RIG/RmAb infiltration. RIGs/RmAb should be administered at the site only as much as possible till the administered product oozes out from the wound.

Evidence suggests that injecting the remaining RIG/RmAb volume intramuscularly at a distance from the wound provides no or little additional protection against rabies as compared with infiltration of the wound alone. WHO guidelines have removed the recommendation of administration of RIG/RmAb by IM route, whereas NCDC guidelines have retained the IM route pending more data from India and the world. Doing away of IM injection of RIG will bring down the cost of PEP drastically.

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.

Rabies monoclonal antibody (RmAb)

RmAb manufactured by Serum Institute of India Pvt. Ltd. is a recombinant human IgG1 antirabies monocolonal antibody developed with MassBiologics, USA to replace serum derived immunoglobulin. This monoclonal antibody is a 4th generation fully human monoclonal type which is currently most advanced type of monoclonal. The advantage of fully human monoclonal antibody is higher safety and extremely low risk of immunogenicity, which may be seen with other monoclonals of older generations like Murine (mouse) or Chimeric (part mouse and part human) monoclonals. RmAb has been approved for use by WHO and DCGI and is being distributed in 18 countries across the world.

The advantages of RmAb over RIG are:

a. Unlimited easy availability

b. Standardized production quality

c. No requirement of animal or human serum in its production

d. Lesser adverse events as compared to equine products

e. Lesser cost as compared to HRIG

f. Lesser volume requirement as compared to RIG as it is more potent and

g. No risk of blood borne pathogens

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 2-week or a 3-week regimen.

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

WHO guidelines recommend a reduction in the number of doses from five to four, whereas NCDC guidelines have retained the fifth dose, pending more data from India and the world.

ii. Intradermal administration

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

- Purified vero cell vaccine (PVRV)
- Purified chick embryo cell vaccine (PCECV)
- 1 week 2-sites intradermal regimen (2-2-2-0-0) for use with PVRV and PCECV: 0.1 mL i.d. on both deltoids on days 0, 3, and 7 only.

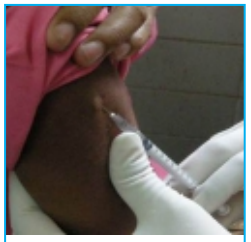

Photo 5: Intradermal administration of Anti rabies vaccine. (Photo courtesy: Dr. Anurag Agrawal)

WHO guidelines have reduced the number of doses from four to three, by doing away with the day 28 dose of the vaccine, whereas NCDC guidelines have retained the day 28 dose, pending more data from India and the world.

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

In immunocompromised individuals, including patients on immunosuppressant 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. The recommendations need to change as intra dermal route is found to give equal if not less antibody titers as compared to IM route. VNA response should be determined 2–4 weeks following vaccination to assess the possible need for an additional dose of the vaccine. Immunodeficient patients who are clinically monitored and well managed, such as HIV-infected people receiving antiretroviral therapy, are considered not to be immunocompromised and have been shown to respond to rabies and other vaccines in the same way as healthy individuals. In the event of re-exposure, a complete PEP course, including RIG, is recommended.

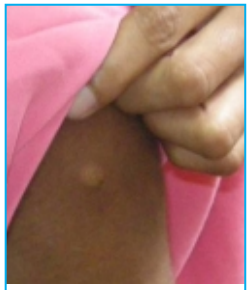

Photo 6: Bleb formation after intradermal antirabies vaccine. (Photo courtesy: Dr. Anurag Agrawal)

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 enough. RIG is not necessary in such cases. The same rules apply to people vaccinated against rabies who have demonstrated Virus Neutralizing Antibodies (VNA) titers 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/or routes for post exposure prophylaxis

- Interchangeability of modern rabies vaccine should not be a routine practice.
- 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 vaccine.
- In case of route change, PEP need not be restarted, and the schedule of the new administration route should be adopted.

Table 2: Changes between old and new WHO position on animal bite management guidelines for rabies control

Component	2010	2018
Post exposure prophylaxis duration	**3-4 weeks and 4-5 visits** Intradermal: 2-2-2-0-2: on days 0, 3, 7, and 28 Intramuscular: 1-1-1-1-1: on days 0, 3, 7, 14 and 28	**One week and 3-4 visits** Intradermal: 2-2-2 on days 0, 3 and 7 Intramuscular: 1-1-1-1 on days 0, 3, 7, and 14-28
Pre-exposure prophylaxis duration	**Four weeks and three visits** Intradermal: One-site, three visits on days 0, 7, and 28 Intramuscular: One-site, three visits on days 0, 7, and 28	**One week and two visits** Intradermal: Two-site, two visits on days 0, and 7 OR Four-site, one visit on day 0 Intramuscular: Two-site, on days 0, and 7
Rabies immunoglobulin mode	In the wound as much as anatomically feasible and remaining to be given intramuscular	In the wound itself as much as anatomically feasible
Rabies Monoclonal antibody	—	Recommended
Consumption of milk of animal suspected to be suffering from rabies	Lack of clarity in the guidelines	No postexposure prophylaxis recommended for boiled or raw milk.

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

Table 3: Equine RIG brands available in market

S. no	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 (not available)	Purified Equine RIGs, 5 mL vial (300 IU/mL, 1500 IU potency)	Cadila Pharmaceutials, Ahmedabad
3	Zyrig (not available)	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
5	VINRIG	As above	Vins Pharma Pvt Ltd, Hyderabad

Table 4: Human RIG brands available in market

S. no	Brand	Product	Pharmaceutical company
1	Berirab-P	Human Rabies Immunoglobulins, 150 IU/mL; 2 mL (300 IU) PFS and 5 mL (750 IU) ampoule	CSL, Bharat Serums and Vaccines Limited, Mumbai
2	SUYA-HRIg	Human Rabies Immunoglobulins, 150 IU/mL; 2 mL (300 IU) ampoule	Prosper Life Sciences, Delhi
3	Kamrab not available presently	Human Rabies Immunoglobulins, 150 IU/mL; 2 mL (300 IU) ampoule and 5 mL (750 IU) ampoule	Medlife, Thane

Table 5: Recombinant Rabies Monoclonal brands available in market

S. no	Brand	Product	Pharmaceutical company
1	Rabishield	Fully Human Rabies Monoclonal Antibody, 40 IU/mL; 2.5 mL (100 IU) vial	Serum Institute of India Pvt Ltd, Pune
2	Rabishield-50	Fully Human Rabies Monoclonal Antibody, 40 IU/mL; 1.25 mL (50 IU) vial	Serum Institute of India Pvt Ltd, Pune

Table 6: Modern Rabies Vaccines available in market

S. no	Brand	Product	Pharmaceutical company
1	Abhayrab	Purified Vero cell Rabies Vaccines (PVRV) (0.5mL)	Human Biologicals Institute, Hyderabad
2	Rabipur/ Chirorab	Purified Chick Embryo Cell Vaccine (PCEC) (1 mL)	Sanofi Aventis/ Chiron Behring/ Bharat Biotech
3	Rabivax-S	Purified Vero Cell Vaccine (1mL)	Serum Institute of India, Pune
4	Vaxirab	Purified Duck Embryo Vaccines (PDEV) (1 mL)	Zydus Alidac Ahmedabad
5	Vaxirab	Purified Verocell Rabies Vaccines (PVRV) (0.5 mL)	Sanofi Pasteur
6	Rabio	Purified Verocell Rabies Vaccines (PVRV) (0.5 mL)	Prosper Channel Life Sciences India Pvt Ltd, Delhi
7	Rabirix	Chromatographically purified PVRV (0.5 mL)	Bharat Biotech, Hyderabad

Disclaimer: This list has been mentioned just for a quick and handy reference for healthcare practitioners. Consortium Against Rabies® does not endorse and does not promote any particular brand of vaccine or immunoglobulin or medical product.

Common Questions regarding management of animal bite with special reference to rabies

Q1. Can a pregnant woman be administered rabies vaccine and serum if she is exposed?

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 certain studies showing that rabies vaccines and serum are safe in pregnancy and lactation, pregnancy and lactation is not considered a contraindication to postexposure rabies prophylaxis.

Q2. If a rabies vaccine is accidentally kept in the freezer; can it be used?

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.

Q3. Can we change the type/brand of rabies vaccine with other?

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

Q4. A person reports with a history of dog bite 5 years back and no history of any rabies vaccination. Should rabies vaccine be administered?

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.

Q5. A person reports with history of dog bite one day back. He also has a history of receiving a complete course of rabies vaccine five years back. What schedule should be followed in this case?

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 and 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.

Q6. Can a rabies vaccine be administered to a lactating mother?

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.

Q7. If a person is on antimalarials; what is the schedule?

People taking chloroquine for treatment or malaria prophylaxis or on any other suppressant can have a reduced response to ID rabies vaccination. These patients should receive the vaccine by the IM route along with RIG / RmAb. If possible, its ideal to get antibody titer done after day 14.

Q8. If a person is suffering from HIV/AIDS; what is the schedule?

In immunocompromised individuals, including patients with HIV/AIDS, comprehensive wound management, and local infiltration with RIG / RmAb, 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 titer done after day 14. Immunodeficient patients who are clinically monitored and well managed, such as HIV-infected people receiving antiretroviral therapy, are considered not to be immunocompromised and have been shown to respond to rabies and other vaccines in the same way as healthy individuals.

Q9. Should the dose of ARV be reduced for neonates?

The antirabies vaccine (ARV) dose is age independent. However, the dose for RIG depends upon the weight of the patient.

Q10. What is the schedule for booster doses of rabies vaccine?

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 titer level assessed as often as every 6 months. VNA titers above 0.5 IU/mL indicate protection. Booster vaccinations are not recommended routinely to everyone.

Q11. 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?

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.

Q12. What should be done in case of consumption of milk of a rabid animal by a person?

Post-exposure prophylaxis is not recommended in cases where milk (either boiled or raw) is consumed by a person. This is the current recommendation based on the available evidence that no rabies virus has not been isolated from rabid animal milk.

Q13. What should be done if a person gives a history of sexual intercourse with a rabid person?

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

Q14. A patient has completed pre or post exposure prophylaxis. For how long s/he does not need post exposure prophylaxis on being exposed to a potentially rabid bite?

If a patient has completed pre or post exposure prophylaxis, then for the next three months no re-exposure prophylaxis is needed for any potentially rabid exposure/s. After three months, if re-exposed, s/he should be administered two doses of anti-rabies vaccine i.e. one dose i.d (0.1 mL) or i.m (1 mL) on days 0, and 3.

Q15. What will be the dose of an intradermal injection, if the vial is of 0.5 mL?

The intradermal dose of is 0.1 mL per site, irrespective of whether the vial is of 1 mL or 0.5 mL.

Q16. Is it necessary to give the remainder RIG (the RIG remaining after the wound infiltration has been done) intramuscularly at a distant site?

WHO 2018 guidelines mention that there is no evidence to support administering the remainder RIG intramuscularly. However, the current guidelines from the Government of India and also the product insert instructions require that the remainder RIG should be given intramuscularly at a distant site. We recommend that the Government of India guidelines and the product insert instructions should be followed and the remainder RIG should be given intramuscularly at a distant site from the wound. This is also relevant to safeguard a practitioner from Consumer Protection Act, in case any adverse event happens to the patient later.

Q17. What to do in case the mucosa (eyes, oral mucosa, genitalia) is exposed to saliva of a suspected rabid animal?

Rinse it with RIG/ RmAb. If more volume is needed to cover the area, dilute RIG/ RmAb with sterile normal saline and then rinse the area with RIG/ RmAb.

Q18. What if the wound is infected? Can RIG/RmAb be infiltrated in the wound then?

Clean the infected wound and then infiltrate RIG/ RmAb.

Q19. What if I follow a schedule or a technique which is different from what is mentioned in the product package insert?

The product package insert usually in the form of a small page with instructions about its use is approved by the DCGI and is important to be followed by all. The only exception is when there is a written order by the government stating otherwise. Off-label use (any deviation from the product package insert) is not recommended. It can even invite action as per the Consumer Protection Act.

Q20. What should I do if by mistake, I administer the antirabies vaccine subcutaneously instead of intradermally?

If such a thing happens, it is advisable to give another injection intradermally at another site. But if you think it is not possible for you to give the injection

intradermally, then administer the injection intramuscularly, taking care of the dose recommendations.

Q21. What to do in case if a patient misses a dose of antirabies vaccine? Should the whole course be repeated, or should the schedule be resumed from where it was left?

The whole schedule should not be repeated. The injections should be resumed from where it was left. The later dates should be revised accordingly.

Q22. If one patient has received the antirabies vaccine, but not the RIG/RmAb, till when can RIG be administered?

Till 7th day of receiving of the first dose of the antirabies vaccine. After that, there is no additional benefit by giving RIG/ RmAb; in fact, it will reduce the efficacy of ARV.

Q23. What vaccination schedule must be followed for pet dogs to prevent rabies?

In case of puppies, the rabies vaccine is to be given at 3 months, 9 months, and then yearly boosters. In case of adopting an adult dog, the first vaccination should be given as soon as possible and then a veterinarian should be consulted.

Q24. Can PEP fail?

Most cases where PEP failed in case of rabies were due to delay in ARV, incomplete schedule, incorrect procedure of administering RIG or ARV, or in immunocompromised patients. But in certain cases, even when everything was done correctly apparently, failure of PEP has been reported.

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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.

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