



FREQUENTLY ASKED QUESTIONS ON RABIES



FREQUENTLY ASKED QUESTIONS ON RABIES



© World Health Organization 2013 All rights reserved.

Requests for publications, or for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – can be obtained from Bookshop, World Health Organization, Regional Office for South-East Asia, Indraprastha Estate, Mahatma Gandhi Marg, New Delhi 110 002, India (fax: +91 11 23370197; e-mail: sebookshop@who.int).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

This publication does not necessarily represent the decisions or policies of the World Health Organization.

Printed in India

Photo credit: WHO Indonesia/Budhi Chandra

FREQUENTLY ASKED QUESTIONS ON RABIES

FAQs

Se	ectio	n 1: For the general public	2
Q	1:	What is rabies?	2
Q	2:	How is rabies transmitted?	2
Q	3:	How does one treat an animal bite?	4
Q	4:	What should not be done with an animal bite wound?	4
Q	5:	How does rabies develop in humans?	5
Q	6:	What are the factors that influence development of rabies?	5
Q	7:	How long does it take for dogs and cats to develop rabies, and how long does a rabid animal survive?	5
Q	8:	What are the clinical features of rabies in dogs?	6
Q	9:	What are the signs and symptoms of rabies in humans?	6
Q	10:	Is there any specific treatment for a rabies patient?	7
Q	11:	Is rabies always fatal?	8
Q	12:	Is simply observing the biting dog or cat for 10 days without starting treatment justified?	8
Q	13:	Under what conditions do we have to take anti-rabies vaccination after being bitten?	8
Q	14:	Do you have to take vaccination against rabies if a vaccinated dog bites you?	9
Q	15:	If I am bitten by a rat do I require post-exposure prophylaxis (PEP)?	10
Q	16:	What should be done if I am bitten by a bat?	10
Q	17:	Is PEP necessary if milk or milk products from an infected animal are consumed?	10
Q	18:	Can consumption of meat from an infected animal transmit rabies?	10
Q	19:	Is there a single-dose human rabies vaccine which will provide life-long immunity?	11
Q	20:	Is it possible to develop rabies from the vaccination?	11
Q	21:	What can be done for rabies prevention and control?	11
0	22:	What is the rables vaccination schedule for net dogs?	12

Se	ectio	n 2: For health providers	12
Q	1:	How does one treat an animal bite?	12
Q	2:	What should not be done with an animal bite wound?	13
Q	3:	What are the indications for post-exposure rabies prophylaxis (PEP)?	14
Q	4:	How should anti-rabies vaccines be stored to maintain safety and potency before administration?	15
Q	5:	Can the rabies vaccine and immuno-globulin be given to a pregnant woman or a lactating mother?	15
Q	6:	What type of rabies vaccines are used in rabies-endemic countries of the South-East Asia Region?	15
Q	7:	What are the comparative advantages of using the modern rabies vaccines?	16
Q	8:	What are the rabies vaccines recommended by WHO?	16
Q	9:	What is the standard vaccination schedule for rabies prophylaxis?	17
Q	10:	Are there any shorter intradermal (ID) PEP regimens?	20
Q	11:	What are the important points to be considered while administering modern rabies vaccines?	20
Q	12:	Do we need to consider specific vaccine potency for ID vaccination?	21
Q	13:	How does ID rabies vaccination work when the dose is so small? Does it fully protect against rabies exposure?	21
Q	14:	What is rabies immunoglobulin (RIG) and how it is used?	22
Q	15:	Is it necessary to perform a skin sensitivity test while using ERIG?	23
Q	16:	What precautions should be taken while administering RIGs?	24
Q	17:	Is it necessary to perform an antibody test on the patient following anti-rabies vaccination?	25
Q	18:	Are there any adverse effects of rabies vaccination?	26
Q	19:	Are there any contraindicated drugs or dietary restrictions during anti-rabies vaccination?	26
Q	20:	If one rabies vaccine has been used for PEP and it is not available for the last two doses, is it possible to interchange rabies vaccine or vaccination route (IM versus ID)?	27
Q	21:	Is there any possibility of failure after PEP?	27
Q	22:	If a previously immunized person is bitten by a rabid dog again, what is the re-exposure vaccination schedule?	28



Rabies is one of the oldest diseases known to mankind. There is still no treatment available once a patient develops the symptoms of rabies. There has been confusion among the general public because of historical fears and the painful injections of anti-rabies vaccination (nerve tissue vaccine administered over the abdomen) given in the past.

These FAQs are an attempt to provide accepted and evidence-based answers to common questions about the disease. Although efforts have been made to include all possible situations, the reader is advised that these FAQs are by no means exhaustive and they may need to consult an infectious disease/rabies expert in situations where their doubts are not addressed.

These FAQs are presented in two sections. The first section provides information for the general public. The second section gives advice to health providers on dealing with wounds from potentially rabid animals, and the administration of anti-rabies vaccines.

Section 1: For the general public

Q 1: WHAT IS RABIES?

Rabies is a disease transmitted from animals to humans, which is caused by a virus. There are two clinical manifestations of rabies – frantic and paralytic. Frantic rabies is most common form of human rabies.

Q 2: HOW IS RABIES TRANSMITTED?

The rabies virus invades the nervous system of mammals. It is primarily transmitted from the rabid animal's saliva when it bites or scratches someone. Licks to wounds or grazed and broken skin, or to



the lining of the mouth and nose, can also transmit the disease.

Dogs are responsible for 96% of human rabies cases in South-East Asia, but there are also reports of human rabies due to bites of cats, mongooses, jackals, foxes, wolves and other carnivorous animals. Rabies due to monkey and rat bites are rare. Horses and donkeys get aggressive and bite ferociously when they are rabid. Cattle and buffaloes do not bite when they are rabid, but precautions should be taken while examining sick animals that are salivating.

Sometimes livestock owners confuse rabies with foot-and-mouth disease, haemorrhagic septicaemia or choking and may attempt to administer drugs by hand, and thus get infected with rabies virus.

There are no evidence-based reports of human rabies occurring due to consumption of milk. Individuals or professionals who slaughter rabies-infected animals and handle brain and other infected

material may be at risk, but there are no human cases due to consumption of cooked meat.

Human-to-human transmission of rabies through corneal or other organ transplantation is rare but possible. Such transmission has occurred among recipients of transplanted corneas and recently among recipients of solid organs and vascular tissue. Therefore corneas or organs should not be collected from a patient who died due to rabies encephalitis or any undiagnosed neurological disease.

Although rabies patients are extremely unlikely to bite other people, caregivers should be watchful and alert when looking after them, and avoid contact with the patient's saliva.

Q 3: HOW DOES ONE TREAT AN ANIMAL BITE?

If a person is bitten by an animal:

- Wounds should be washed and flushed immediately with soap and water for 10–15 minutes. If soap is not available, flush with water alone. This is the most effective first-aid treatment against rabies.
- Wounds should be cleaned thoroughly with 70% alcohol/ethanol or povidone-iodine, if available.
- As soon as possible, take the person to a healthcare facility for further treatment.

Q 4: WHAT SHOULD NOT BE DONE WITH AN ANIMAL BITE WOUND?

Avoid:

- Applying irritants to the wound such as chilli powder, plant juices, acids or alkalis.
- Covering the wound with dressings or bandages.

Q 5: HOW DOES RABIES DEVELOP IN HUMANS?

After entering the human body, the rabies virus progresses from the innermost layer of tissue below the human skin (called subcutaneous tissue), or from muscle, into peripheral nerves (i.e. the nerves in the body which are outside the brain or spinal cord).

The virus migrates along nerves to the spinal cord and brain at an estimated speed of 12–24 mm a day. The infected person exhibits behavioural changes and clinical signs when the virus reaches the brain. The incubation period ranges from a few days to several months, and can be as long as 1 year.

Q 6: WHAT ARE THE FACTORS THAT INFLUENCE DEVELOPMENT OF RABIES?

Factors that may influence development of rabies infection include:

- type of exposure
- severity of the bite
- the amount of rabies virus introduced
- the animal responsible for the bite
- the immune status of the victim
- site of the bite head and neck wounds, as well as wounds in highly innervated areas such as fingers, generally have shorter incubation periods due to the proximity of the viral inoculation to nerve tissue.

Q 7: HOW LONG DOES IT TAKE FOR DOGS AND CATS TO DEVELOP RABIES, AND HOW LONG DOES A RABID ANIMAL SURVIVE?

The incubation period ranges from a few days to several months, whereas the duration of illness – until death – varies from 1 to 7 days.

Q 8: WHAT ARE THE CLINICAL FEATURES OF RABIES IN DOGS?

Dog rabies is characterized by changes to its normal behaviour, such as:

- biting without any provocation
- eating abnormal items such as sticks, nails, faeces, etc.
- running for no apparent reason
- a change in sound e.g. hoarse barking and growling or inability to make a sound
- excessive salivation or foaming at the angles of the mouth – but not hydrophobia (fear of water).

Q 9: WHAT ARE THE SIGNS AND SYMPTOMS OF RABIES IN HUMANS?

Human rabies has the following signs and symptoms:

- pain or itching at the site of the bite wound (in 80% of cases)
- fever, malaise, headache lasting for 2-4 days.
- hydrophobia (fear of water)
- intolerance to noise, bright light or air
- fear of impending death
- anger, irritability and depression
- hyperactivity
- at a later stage the mere sight of water may provoke spasms in the neck and throat
- the duration of illness is usually 2–3 days, but might stretch to 5–6 days or more when receiving intensive care support.

Q 10: IS THERE ANY SPECIFIC TREATMENT FOR A RABIES PATIENT?

There is no specific treatment once rabies develops. There is almost nothing that can be done apart from keeping the patient comfortable, and free from physical pain and emotional upset.

- Precautions should be taken by the caregiver to avoid bites and saliva contamination of mucous membranes and wounds by using personal protection equipment.
- Keep the patient in a quiet room with subdued light and protect them from stimuli (e.g. loud noises, cold air) that are likely to increase spasms and convulsions.
- Sedation with diazepam 10 mg every 4–6 hours, supplemented by chlorpromazine 50–100 mg, or intravenous morphine if necessary, will help to control muscular spasms and excitability.
- Feeding orally is usually impossible. Fluids should be given intravenously.



Q 11: IS RABIES ALWAYS FATAL?

Human rabies caused by the classical rabies virus continues to be almost 100% fatal, with no specific treatment available anywhere in the world.

There are only seven recorded cases of human rabies survivors in the world, who received intensive nursing care. Almost all of them received preventive/ pre-exposure rabies vaccination that might have modified the course of illness. Only one case of human rabies caused by a bat bite did not receive pre-exposure vaccination but survived. However, this case was not caused by the classical rabies virus.

Q 12: Is simply observing the biting dog or cat for 10 days without starting treatment justified?

No. In countries where rabies is prevalent in a large population of dogs and cats, it is compulsory to start treatment and keep the biting dog/cat under 10 days of observation. If the animal remains healthy during the observation period then post-exposure prophylaxis (PEP) can be converted into pre-exposure regimen, i.e. the vaccine taken will be to prevent rabies if bitten in the future.

Q 13: Under what conditions do we have to take anti-rabies vaccination after being bitten?

Post-exposure rabies prophylaxis (PEP) is compulsory if you are bitten by a dog, cat or other animal that is rabid or is suspected to be infected with rabies.

PEP is required under following conditions:

 If the bite has broken the skin and the wound is bleeding.



- If a mucous membrane has been exposed to saliva from a suspect animal.
- If the animal that has bitten someone
 - 1. is killed
 - 2. disappears during the observation period
 - 3. displays unusual, erratic behaviour
 - 4. if laboratory tests of brain material from the suspected or rabid animal is positive.

Q 14: DO YOU HAVE TO TAKE VACCINATION AGAINST RABIES IF A VACCINATED DOG BITES YOU?

No, not if the dog is properly vaccinated against rabies and the efficacy of the vaccine is confirmed by laboratory evidence. Otherwise an appropriate post-exposure prophylaxis (PEP) should be given.

Q 15: If I AM BITTEN BY A RAT DO I REQUIRE POST-EXPOSURE PROPHYLAXIS (PEP)?

Rat rabies has been reported from some Asian countries but is extremely rare. It is not necessary to take PEP in bite cases by house rats. However, it is prudent to take PEP in consultation with an infectious disease physician when bitten by wild rats/rodents.

Q 16: What should be done if I am bitten by A bat?

There is no evidence-based information on human rabies cases due to bat exposure in the South-East Asia Region. However, there are reports of seropositivity against bat rabies virus in the bat population in Thailand. Therefore, it is recommended that you thoroughly wash the bite wound and consult an infectious disease physician. It is also recommended not to play with or handle sick or dead bats.

Q 17: IS PEP NECESSARY IF MILK OR MILK PRODUCTS FROM AN INFECTED ANIMAL ARE CONSUMED?

No. There is no laboratory or epidemiological evidence that the consumption of milk or milk products from rabid animals transmits the disease. However, it is not advisable to consume milk from rabid animals.

Q 18: CAN CONSUMPTION OF MEAT FROM AN INFECTED ANIMAL TRANSMIT RABIES?

The consumption of raw meat from an infected animal requires PEP. Cooked meat does not transmit rabies; however, it is not advisable to consume meat from an infected animal.

Q 19: IS THERE A SINGLE-DOSE HUMAN RABIES VACCINE WHICH WILL PROVIDE LIFE-LONG IMMUNITY?

No. There is no single-dose rabies vaccine available anywhere in the world which can provide lifelong immunity. Single-dose vaccines are available, but they only provide immunity for a limited period of time.

Q 20: IS IT POSSIBLE TO DEVELOP RABIES FROM THE VACCINATION?

No. All rabies vaccines for human use are inactivated. Human rabies vaccines undergo a series of quality control tests such as potency, toxicity, safety and sterility. It is not possible for the rabies vaccination to cause the disease.

Q 21: WHAT CAN BE DONE FOR RABIES PREVENTION AND CONTROL?

Be responsible by vaccinating pet dogs or cats against rabies, as recommended by veterinarians or animal health workers.



- Keep the dog vaccination certificate safe and present it during annual vaccination.
- Do not sell or consume milk or meat from rabid or suspected rabid cows or buffalos.

Q 22: WHAT IS THE RABIES VACCINATION SCHEDULE FOR PET DOGS?

Puppies are often obtained from reliable dog breeders where bitches are vaccinated against rabies. These puppies get maternal antibodies against rabies for 3 months and therefore it is recommended to vaccinate at 3 months of age, then at 9 months of age and revaccinate annually. Puppies and dogs must be given anthelmintic drugs regularly before vaccination.

If the puppies adopted are street dogs, the first vaccination should be given as the same protocol (at 3 months of age, 9 months, and yearly boosters). Alternately, first vaccination can be given as early as 2 months of age. Precautions should be taken in first 3 months of age.

If adult street dogs are adopted, then the first vaccination should be given as soon as possible, and a local veterinarian should be consulted.

Section 2: For health providers

Q 1: HOW DOES ONE TREAT AN ANIMAL BITE?

If a person is bitten by an animal:

 Wounds should be washed and flushed immediately with soap and water for 10–15 minutes. If soap is not available, flush with water alone. This is the most effective first-aid treatment against rabies.

- Wounds should be cleaned thoroughly at the health care facility with 70% alcohol or povidoneiodine.
- Assess the vaccination status: e.g. whether diphtheria, pertussis, tetanus (DPT) or tetanus toxoid vaccination has been given in the past. Tetanus toxoid should be inoculated when necessary.
- Antimicrobials should be prescribed to prevent possible bacterial infection.

Q 2: WHAT SHOULD NOT BE DONE WITH AN ANIMAL BITE WOUND?

Avoid:

- Covering the wound with dressings or bandages.
- Suturing which facilitates further inoculation of rabies virus.
 - If necessary for closing large wounds, suturing should be done after infiltration of wound with rabies immunoglobulin (RIG). Rabies immunoglobulin of human origin (HRIG) is expensive and only limited amounts are available. Rabies immunoglobulin of equine origin (ERIG) is available in many countries and is considerably cheaper than HRIG.
 - The sutures should be loose and not interfere with free bleeding and drainage. It is well established that secondary suture of bite wounds results in better cosmetic outcomes.

Q 3: WHAT ARE THE INDICATIONS FOR POST-EXPOSURE RABIES PROPHYLAXIS (PEP)?

The WHO Expert Consultation on Rabies (2013) has categorized rabies risk based on category of exposure and made recommendations for PEP, as shown in Table 1.

Table 1: Categorization of exposure and indications for post-exposure rabies prophylaxis¹

Category of exposure	Type of exposure to a domestic or wild animal suspected or confirmed to be rabid, or animal unavailable for testing	Recommended post-exposure Prophylaxis
I	Touching or feeding animals Licks on intact skin Contact of intact skin with secretions or excretions of a rabid animal or human case	None, if reliable case history is available
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding	Administer vaccine immediately ^b . Stop treatment if animal remains healthy throughout an observation period of 10 days ^c or is proven to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques.
III	Single or multiple transdermal bites ^d or scratches, licks on broken skin Contamination of mucous membrane with saliva (i.e. licks) Exposure to bats ^e	Administer rabies vaccine immediately and rabies immunoglobulin, preferably as soon as possible after initiation of post-exposure prophylaxis. Rabies immunoglobulin can be injected up to 7 days after first vaccine dose administration. Stop treatment if animal remains healthy throughout an observation period of 10 days or is proven to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques.

World Health Organization (2013). WHO Expert Consultation on Rabies. WHO Technical Report Series 982. Second Report. Geneva.

Exposure to rodents, rabbits or hares does not routinely require rabies postexposure prophylaxis.

b If a n apparently healthy dog or cat in or from a low-risk area is placed under observation, treatment may be delayed.

^c This observation period applies only to dogs and cats. Except for threatened or endangered species, other domestic and wild animals suspected of being rabid should be euthanized and their tissues examined for the presence of rabies antigen by appropriate laboratory techniques.

d Bites especially on the head, neck, face, hands and genitals are category III exposures because of the rich innervation of these areas.

Post-exposure prophylaxis should be considered when contact between a human and a bat.

Q 4: HOW SHOULD ANTI-RABIES VACCINES BE STORED TO MAINTAIN SAFETY AND POTENCY BEFORE ADMINISTRATION?

Modern rabies vaccines are freeze-dried, giving them a longer shelf-life and stability. The vaccine vial should be kept cool and stored in a refrigerator at 2°C to 8°C. The reconstituted vaccine should be used as soon as possible as it is single-dose vaccine. If it is used for intradermal rabies vaccination, the reconstituted vaccine must be used within 6 hours and kept at 2°C to 8°C.

Q 5: CAN THE RABIES VACCINE AND IMMUNO-GLOBULIN BE GIVEN TO A PREGNANT WOMAN OR A LACTATING MOTHER?

Yes. All modern rabies vaccines are inactivated, safe and potent and can be given to pregnant women or lactating mothers. It has no effect on fetal development during pregnancy or breastfed infants during lactation. The rabies virus is not known to cross the placental barrier in women and healthy babies have been born via caesarean section.

Q 6: WHAT TYPE OF RABIES VACCINES ARE USED IN RABIES-ENDEMIC COUNTRIES OF THE SOUTH-EAST ASIA REGION?

Rabies vaccines in use can be categorized on the basis of their origin, as follows:

- tissue culture origin
- embryonated egg origin.

Modern rabies vaccines are commercially available as human diploid cell vaccine (HDCV), purified Vero cell rabies vaccine (PVRV), purified chick-embryo cell vaccine (PCECV) and purified duck embryo vaccine (PDEV).

WHO is encouraging countries to promote the cost-effective intradermal (ID) rabies vaccination schedule – which is safe and efficacious – to improve accessibility, availability and affordability of modern rabies vaccines.

Q 7: WHAT ARE THE COMPARATIVE ADVANTAGES OF USING THE MODERN RABIES VACCINES?

Modern rabies vaccines are highly potent, safer to use and provide immunity for a longer period of time – which is important, considering the long incubation period of rabies infection.

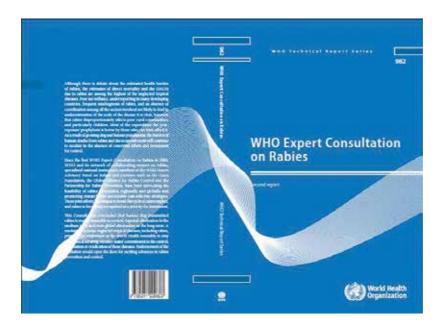
- These vaccines are available in freeze-dried form so that they have a longer shelf-life and remain very stable.
- The vaccines are produced in vials with a disposable syringe and diluents for single intramuscular (IM) use.
- They can be given to high-risk groups such as children and animal handlers for pre-exposure vaccination.
- They are also given after animal bites, and are known as post-exposure rabies prophylaxis (PEP).
- A person is either given anti-rabies vaccination for pre-exposure or PEP. This leads to added protection by inducing memory cells to cause an accelerated immune response when a booster dose of vaccine is administered.

Q 8: WHAT ARE THE RABIES VACCINES RECOMMENDED BY WHO?

WHO maintains a list of WHO-prequalified rabies vaccines which are commercially available on the international market, which concerns only vaccines administered by the IM route.

WHO also maintains another list of vaccines proven to be safe and efficacious by the ID route, using the WHO-recommended ID regimen.

WHO encourages pharmaceutical companies to undergo the WHO prequalification procedure to ensure good manufacturing practices and quality assurance.



Q 9: WHAT IS THE STANDARD VACCINATION SCHEDULE FOR RABIES PROPHYLAXIS?

Modern rabies vaccines are administered for preexposure and post-exposure prophylaxis and the vaccination schedule is determined accordingly.

Pre-exposure prophylaxis

Intramuscular administration: One dose of vaccine is administered intramuscularly on each of days 0, 7 and 21 or 28.

Intradermal administration: One intradermal injection of 0.1 ml is given on each of days 0, 7 and 21 or

28. To maximize savings, sessions of intradermal pre-exposure prophylaxis should involve enough individuals to use all opened vials within 6 hours.

Three doses/three visits

IM or ID one dose each on day 0, day 7, and day 21 or 28.

Day 0 means day of first vaccination, not necessarily day of bite.

Post-exposure prophylaxis (PEP)

There are three vaccination schedules for this purpose:

Five- versus four-doses IM regimen ("Essen" regimen)

One dose of vaccine is administered intramuscularly on days 0, 3, 7, 14 and 28. Injections must be given in the upper arm (deltoid region) or, in small children, into the anterolateral thigh muscle. Vaccines should never be administered into the gluteal region or the buttocks, where absorption is unpredictable.

The reduction in doses (four doses IM regimen) for PEP recommended by the Centers for Disease Control and Prevention (CDC) in Atlanta, USA, was based in part on studies that indicated that four vaccine doses in combination with rabies immune globulin (RIG) elicited adequate immune responses, and that a fifth dose of vaccine did not contribute to more favourable outcomes. (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm)

Full Essen regimen (five visits/with or without RIG)

IM one dose each on day 0, day 3, day 7, day 14 and day 28.

IM one dose each on day 0, day 3, day 7 and day 14.

Shortened Essen regimen (four visits/four doses with or without RIG)

IM one dose each on day 0, day 3, day 7 and day 14.

Rabies PEP should be administered using a fivedose IM regimen for persons with immunosuppression.

The first dose should be administered as soon as possible after exposure (day 0).

Day 0 means day of first vaccination, not necessarily day of bite.

Abbreviated multisite IM regimen (Zagreb regimen), four doses/three visits (2-1-1) regimen

One dose of vaccine is administered intramuscularly into the left and one into the right upper arm (deltoid region) on day 0 followed by one dose into the upper arm (deltoid region) on days 7 and 21. This schedule saves two clinic visits and one vaccine dose.

Multisite intradermal (ID) vaccination schedule Updated Thai Red Cross (TRC) regimen/twosite ID schedule (2-2-2-0-2)

One dose each (0.1 ml) is given at two sites, on both arms (over deltoids) on day 0, day 3, day 7 and day 28.

The standard schedule is recommended in designated health-care facilities by trained health professionals under the supervision of a medical officer.



Q 10: ARE THERE ANY SHORTER INTRADERMAL (ID) PEP REGIMENS?

There are clinical trials to shorten PEP in order to improve patient compliance for the full course of vaccination. A four-site one-week PEP regimen (4-4-4) has been proposed to replace the Thai Red Cross (TRC) regimen, given by four-site ID injections on days 0, 3 and 7. The immunogenicity study results are promising. WHO has recommended further assessment of this regimen through a well-designed study.

Q 11: WHAT ARE THE IMPORTANT POINTS TO BE CONSIDERED WHILE ADMINISTERING MODERN RABIES VACCINES?

All rabies vaccines are available as single-dose vials for IM use and must be given in the deltoid region (i.e. upper arm, near the shoulder) or, in small children, into the anterolateral area of the thigh muscle (on the upper thigh). As with other injections, the rabies vaccine should not be given in the gluteal region (buttocks) because of low absorption due to the presence of adipose (fat) tissue.

- The IM or ID dose is same for all age groups.
- It is desirable to use the same type of modern rabies vaccine for the full course of vaccination, such as HDCV, PVRV, PCECV or PDEV.
- All the rabies vaccines can be used for IM regimen, but only PVRV and PCECV are approved for ID.
- Antibody response to ID regimen has been unsatisfactory in some groups receiving chloroquine for anti-malarial chemoprophylaxis, therefore an IM regimen should be used in such cases.

Q 12: DO WE NEED TO CONSIDER SPECIFIC VACCINE POTENCY FOR ID VACCINATION?

No. There has been concern as single IM doses are reconstituted in different volumes depending on manufacturers. The WHO-recommended minimum potency is 2.5 IU per IM dose and the WHO-recommended volume of a single dose of rabies vaccine administered per ID site is 0.1 ml.

Q 13: HOW DOES ID RABIES VACCINATION WORK WHEN THE DOSE IS SO SMALL? DOES IT FULLY PROTECT AGAINST RABIES EXPOSURE?

It is a multisite (upper arms, lateral thighs, suprascapular or upper trunk region, and lower quadrant of abdomen) vaccination technique which elicits a prompt and highly protective immune response with a small dose. Initially eight-site and four-site ID inoculation were conducted but clinical trials and immunological studies clearly demonstrated that two-site ID inoculation is sufficient and is

also user-friendly and cost-effective. The immune response induced by ID rabies vaccination is the same as with the IM regimens. Rabies antigen is inoculated into the dermis of the skin which helps trigger a high immune response. It has been shown that the antigen presenting cells in the skin are more effective than the ones in muscle.

Q 14: WHAT IS RABIES IMMUNOGLOBULIN (RIG) AND HOW IT IS USED?

RIG is a biological product which is used to provide immediate readymade antibodies until the patient's own immune system responds to immunization. RIG may be of human or animal origin.

- Equine rabies immunoglobulin (ERIG)
- Human rabies immunoglobulin (HRIG).

The dose calculation is done as follows:

- ERIG 40 IU/kg body weight with a maximum of 3000 units
- HRIG 20 IU/kg body weight with a maximum of 1500 units.

For all category III bites, RIG should be given immediately after the incident. RIG should be infiltrated as much as possible in and around all wounds. After infiltration of the wounds, if there is any remaining RIG, it should be given intramuscularly on the anterolateral region or deltoid region. Anti-rabies vaccines should then be administered, preferably on the same day, but at a different site (right arm for vaccine and left arm for serum, or vice versa).

 RIGs remain in short supply throughout the world, but new technology capable of producing monoclonal antibodies (MAbs) against rabies might help increase the supply of RIGs globally.

Q 15: IS IT NECESSARY TO PERFORM A SKIN SENSITIVITY TEST WHILE USING ERIG?

Most ERIG products currently being manufactured are highly purified and the occurrence of adverse events has been significantly reduced. There are no scientific grounds for performing a skin test prior to administering ERIG because testing does not predict reactions, and it should still 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. However, some manufacturers of ERIG still recommend performing a skin test. It should be kept in mind that a negative skin test does not guarantee that anaphylaxis would not occur.



Q 16: WHAT PRECAUTIONS SHOULD BE TAKEN WHILE ADMINISTERING RIGS?

All emergency drugs and facilities for managing any adverse reactions must be available.

- The RIG vial(s) taken out from refrigerator should be kept outside for a few minutes before administration to the patient (to warm to room/ body temperature).
- RIG should preferably be administered before administering the anti-rabies vaccination. It should, however, never be administered later than 7 days after start of vaccination as it then will suppress native antibody production.
- RIG should not be administered in the same syringe as the vaccine, or at the same site as the vaccine.
- While infiltrating RIG into bite wounds, care must be taken to avoid injecting into blood vessels and nerves. Anatomical feasibility must always be kept in mind while injecting RIG.
- While injecting into finger tips, care must be taken to avoid compartment syndrome*.
- In small children with multiple bites, if the volume is insufficient for infiltration in and around all wounds, RIG should be diluted with sterile normal saline to double or three times the volume.
- Keep the patient under observation for at least 1 hour after ERIG administration before sending him or her home.

^{*} If an injection is administered into a region that is compartmentalized (fingers etc.) and the volume is more it will cause pressure effects which will include pain, pallor and parasthesia.



- The patient should not be given RIG on an empty stomach.
- Pregnancy is not a contraindication for RIG and anti-rabies vaccination.

Q 17: IS IT NECESSARY TO PERFORM AN ANTIBODY TEST ON THE PATIENT FOLLOWING ANTI-RABIES VACCINATION?

It is not necessary on a routine basis when human rabies vaccines are properly stored and given according to the approved schedule in a healthy individual. It is recommended only under special medical conditions, such as for immunocompromised patients, or in cases of delayed vaccination, or cases of frequent exposure to the rabies virus. Such patients require special wound care and careful immunoglobulin infiltration into the wounds.



Q 18: ARE THERE ANY ADVERSE EFFECTS OF RABIES VACCINATION?

Mild symptoms such as pain, redness, irritation or swelling at the site of injection may occur. Generalized symptoms such as headache, fever and influenza-like illness might be observed in some patients.

All these adverse effects are temporary and selflimiting and rarely need medication. All patients should be told about the possible adverse effects, but they must be advised that it is essential to continue vaccination – even if there are local or mild systemic adverse reactions.

Q 19: ARE THERE ANY CONTRAINDICATED DRUGS OR DIETARY RESTRICTIONS DURING ANTI-RABIES VACCINATION?

All immunosuppressive drugs are contraindicated during vaccination such as steroids, chloroquine (anti-malarial drug) and anti-cancer drugs. If these drugs cannot be avoided and the patient is in an immunocompromised state, the IM regimen must be followed by infiltration of site of bite wound with RIG. Monitoring of antibody titration is recommended in such patients where possible.

There are no dietary restrictions during the course of vaccination.

Q 20: If one rabies vaccine has been used for PEP and it is not available for the last two doses, is it possible to interchange rabies vaccine or vaccination route (IM versus ID)?

If completion of PEP with the same modern rabies vaccine is not possible, the switch can be made. This practice should be the exception.

No study has been done yet on vaccine immunogenicity and change of the route of vaccine administration from IM to ID during PEP.

Q 21: IS THERE ANY POSSIBILITY OF FAILURE AFTER PEP?

There are occasional human rabies cases reported despite PEP, due to various factors related to negligence and individual health status. Most cases have been reported due to delayed vaccination, or non-use of rabies immunoglobulin in category III exposure, or incomplete course of vaccination. Some cases are related to immunocompromised status such as HIV/AIDS, cirrhosis or use of chloroquine, steroids or anti-cancer drugs. Unexplained failure in cases where everything was apparently done correctly have also been documented.

Q 22: If a previously immunized person is bitten by a rabid dog again, what is the reexposure vaccination schedule?

If a person has been previously fully vaccinated against rabies using a modern rabies vaccine, either for pre-exposure or post-exposure vaccination by IM or ID route, only two doses of vaccines are given on days 0 and 3. (However, a full vaccination course is recommended for those previously vaccinated with nerve tissue vaccine.)

Persons previously immunized against rabies have two distinct comparative advantages.

- It is not necessary to administer RIG, even in a category III exposure.
- Pre-vaccination leads to added protection by inducing memory cells causing an accelerated immune response when a booster dose of vaccine is administered. This is the reason why parents are encouraged to vaccinate their children against rabies, because they are most vulnerable to dog bites and category III exposure.

Rabies is one of the oldest diseases known to humans, and is a serious public threat in many countries in South-East Asia. There is still no treatment available once a patient develops the symptoms of rabies. These FAQs are an attempt to provide accepted and evidence-based answers to common questions about the disease.

If a person is bitten by an animal:

Wounds should be washed and flushed immediately with soap and water for 10–15 minutes. If soap is not available, flush with water alone. This is **the most effective first-aid treatment** against rabies.

Wounds should be cleaned thoroughly with 70% alcohol/ethanol or povidone-iodine, if available.

As soon as possible, take the person to a health-care facility for further treatment.

To download this booklet and other FAQs about infectious diseases, please visit:

http://www.searo.who.int/about/administration_structure/cds/en/index.html



Regional Office for South-East Asia World Health House Indraprastha Estate Mahatma Gandhi Marg New Delhi-110002, India

