Management of Rabid Dog bites: Guidelines

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Scope:

Rabies is included in WHO's 2021–2030 Roadmap for the global control of neglected tropical diseases, which sets regional, progressive targets for the global strategic plan to end human deaths from dog-mediated rabies by 2030. The national strategic framework aims at zero human dog-mediated rabies deaths by 2030, a goal consistent with the global action plan set in 2015 by WHO, OIE, and FAO. WHO and its global partners aim to end human deaths from dog-mediated rabies through a comprehensive One health approach promoting mass dog vaccination, ensuring access to post exposure prophylaxis, health worker training, improved surveillance, and bite prevention through community awareness.

Introduction:

Rabies is an acute viral disease, which causes encephalomyelitis in virtually all the warm blooded animals including man. The causative agent is found in domestic and wild animals, and is transmitted to other animals and to humans through close contacts with their saliva (i.e. bites, scratches, licks on broken skin and mucous membranes). Rabies is an important zoonotic infection in which man is dead end host and therefore it does not play any role in its spread to new hosts. Rabies occurs in all continents with the exception of Australia and Antarctica. Several countries are currently free of rabies. In Africa rabies is prevalent in almost whole of the territory with a stable pattern. In most of the developing countries, dogs are the principal reservoirs of rabies (**canine rabies**) whereas sylvatic rabies involving animals such as foxes are principal wild animals' reservoirs of this disease in Egypt. It is a viral, zoonotic, neglected tropical disease that causes tens of thousands of deaths annually, with 40% being children under 15. Worldwide the number of human rabies deaths is estimated to be between 35,000 and 50,000 annually. Regarding animal bite incidents in Egypt, a total number of cases of reported animal bites were 482,040 in 2018, compared to 431,917 in 2017 and 355,373 in 2016. It seems that this trend of increased number of reported incidents of animal bites is continuing with 574149 cases reported in 2019 indicating a 20% increase from the previous year. According to the WHO, in the late 1990s, the average number of rabies deaths was reported to be 30-40 persons per year, and in 2000, were about 35 persons per year [12]. Stray dogs bites are considered as the most common source of the disease. Virus is excreted by the rabid animal mainly in saliva. It is present in the

saliva of the dogs for 2-3 days before the appearance of clinical features. It remains in the saliva till the animal dies. Death usually occurs within one week of onset of clinical manifestations.

The Target audience

This guidance was developed for the veterinarians, clinical staff and personnel as well as dog owners to provide information on prevention of rabies as well as clinical management and post-exposure prophylaxis. There is a need for educational campaigns and mass media programs in Egypt to increase the awareness of the community about rabies.

Susceptibility to physical and chemical agents

The rabies virus is highly resistant against cold, dryness and decay. In cadavers, it remains infectious for weeks. This virus is highly thermo-labile with a half-life of approximately 4 hours at 40℃ and 35 seconds at 60℃.

In brain tissue at room temperature it can survive up to 1-2 weeks. The rabies virus remains stable for several days at 0-4℃, indefinitely at -70℃ and when freeze dried. The virus cannot withstand pH less than 4 or more than 10. It is also susceptible to the action of oxidizing agents, most organic solvents, surface acting agents, and quaternary ammonium compounds. Proteolytic enzymes, ultraviolet rays and X-rays rapidly inactivate rabies virus. Soaps and detergents are effective against rabies virus because of their lipid eliminating property, which destroys the outer envelope of the virus.

Excretion of rabies virus

Virus is excreted by the rabid animal mainly in saliva. It is present in the saliva of the dogs for 2-3 days before the appearance of clinical features. It remains in the saliva till the animal dies. Death usually occurs within one week of onset of clinical manifestations.

Mode of transmission

Rabies virus is predominantly neurotropic and kills the host in short period after it has entered the neurons. Before death, from the brain virus reaches salivary glands and is excreted in saliva. The saliva gains entry into another host through licking or contamination is adequate or the bite of the rabid animal creates a mechanical breach of skin through which the rabies virus gains entry. Virus may be present in the saliva for many days before clinical signs appear and it may be steadily or intermittently secreted until just before death. Report of pre-clinical periods of virus secretion in saliva range from 3 days in cats, 12 days in Mexican free tail bats, 14 days in dogs infected with an Ethiopian virus isolate to 29 days in foxes. Infection has been documented in personnel receiving corneal grafts and organs from rabies cases.

PATHOGENESIS

On entering into human body, rabies virus multiplies at local site of inoculation prior to its spread towards brain via the nerves. Within the brain, virus spreads from infected to contagious cells. The main areas affected are usually the cerebellum, hypothalamus, hippocampus and scattered neurons in the reticular formation. It may be that aggression in rabies is related to the presence of virus in mid brain raphe nuclei and hypothalamus, since these are two inhibitory centers of aggressive behavior.

Incubation period:

The average incubation period is between 30-90 days. Factors which may influence the length of the incubation period include the site of bite, the amount of virus in saliva of the batting animal, the virus strain, and the age and immune status of the victim. It is shorter in case the bite is closer

to brain and massive dose of virus has been inoculated. Incubation period as short as 10 days and as long as 2 years have been reported.

CLINICAL FEATURES IN MAN

The first symptom to appear may be pain and tingling in the affected limb, especially around the site of bite. This is seen in 35-65% cases. Hydrophobia is the best known symptom of this disease and is pathognomonic for rabies.

RABIES IN ANIMALS

Clinical features in dogs

After an incubation period of around 3 months (range 10 days to 6 months), dog may manifest one or more of the following clinical features. There may be change in behavior of dog, change in bark tone, change in feeding habits, the animals may go off feed and eat abnormal objects. They may develop fever, vomiting, excessive salivation, paralysis of lower jaw, anxiety, restlessness, convulsions, paralysis leading to death within 5-7 days on onset of disease. There is however no hydrophobia in animals. Rabies in dogs is also classified as dumb (predominantly paralytic manifestation with docile behavior of animal) or furious (mainly convulsions and aggressive behavior with greatly exaggerated biting tendencies).

Clinical features in cats and cattle

Rabid cats show extreme aggressiveness, great sensitivity to touch/voice, profuse salivation and may attempt to attack dog or man. In cattle, rabies is manifested as abnormal movements of posterior extremity, foamy yellow froth from mouth and decrease in yield of milk. Milk of rabid cattle has been shown to have viable rabies virus and its ingestion in raw form may require post exposure treatment in those individuals who have ulcers or abrasions in mouth or pharynx. Otherwise the gastric juice destroys the rabies virus. Pasteurization and cooking also kill the virus.

POST-EXPOSURE TREATMENT IN HUMANS

This must be started at the earliest to ensure that the individual will be immunized before the rabies virus reaches the Central Nervous System.

Decision to treat

In rabies endemic countries, where every animal bite is potentially suspected as a rabid animal bite the treatment should be started immediately. To bring out uniformity globally, the WHO recommended classification of animal bite for post-exposure treatment should be followed

WHO Guide for post-exposure treatment against rabies

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

	scratches Contamination of mucous membrane with saliva (i.e. licks)	vaccine immediately [b] Stop treatment if animal remains healthy throughout an observation period [c] of 10 days or if animal is killed humanely and found to be negative for rabies by appropriate laboratory techniques
a Exposure to rodents, rabbits and hares seldom, if ever, requires specific anti-rabies treatment **b** If an apparently healthy dog or cat in or from a low-risk area is placed under observation, the situation may warrant delaying initiation of treatment **c** This observation period applies only to dogs and cats. Except in the case of threatened or endangered species, other domestic and wild animals suspected as rabid should be killed humanely and their tissues examined using appropriate laboratory techniques		

Source**:** Guidelines for post-exposure treatment in 8th Report of the WHO Expert Committee on Rabies, WHO Technical report Series 824, 1992

Although unvaccinated animals are more likely to transmit rabies, vaccinated animals can also do so if the vaccination of the biting animal was ineffective for any reason.
The treatment should be started immediately after the bite. The treatment may be discontinued if animal involved (dog or cat) remains healthy throughout an observation period of 10 days. The observation period is valid for dogs and cats only. Bite by all wild animals should be treated as category III exposure. It should be noted that bites by rats, mice, squirrel and rabbits seldom require treatment. It is re-emphasized that the treatment should be started as early as possible after exposure, but it should not be denied to person reporting late for treatment.
The post-exposure treatment includes three equally important approaches and should be done simultaneously.

- Management of wound
- Passive immunization
- Active immunization.

Management of animal bite wound

Wound toilet

Since the rabies virus enters the human body through a bite or scratch, it is imperative to remove as much saliva, and thereby the virus, from the wound as is possible by an efficient wound toilet. Since the rabies virus can persist and even multiply at the site of bite for a long time, wound toilet must be performed even if the patient reports late. This can be done by prompt and gentle thorough washing with soap or detergent and flushing the wound with running water for 10 minutes. If soap and detergent are not immediately available wash with running water for at least 10 minutes. Avoid direct touching of wounds with bare hands.
It should be noted that the immediate washing of the wound is a priority. However, the victim should not be deprived of the benefit of wound toilet as long as there is an unhealed wound, which can be washed even if the patient reports late. The maximum benefit of the wound washing is obtained when fresh wound is cleaned immediately. **Suturing** of wound should be **avoided** as far as possible. If unavoidable, minimum loose sutures should be applied after adequate local treatment along with proper infiltration of anti-rabies serum.
Cauterization of wound is no longer recommended as it leaves very bad scar, and does not confer any additional advantage over washing the wound with water and soap. Inj. tetanus toxoid should

be given to the unimmunized individual. To prevent sepsis in the wound, a suitable course of an antibiotic may be recommended.

Application of antiseptic

After thorough washing and drying the wound, any one of the available antiseptic agents should be applied: Savlon (in appropriate recommended dilution), Dettol (in appropriate recommended dilution), povidone iodine, alcohol etc.

Local infiltration of rabies immunoglobulins

In category III bites rabies immunoglobulins should be infiltrated in the depth and around the wound to inactivate the locally present virus.

Passive Immunization by rabies immunoglobulin

Anti-rabies serum: The anti-rabies serum provides passive immunity in the form of readymade anti-rabies antibody to tide over the initial phase of the infection. Anti-rabies serum (ARS) has the property of binding with the rabies virus, thereby resulting in the loss of infectivity of the virus.

Human Rabies immunoglobulins (HRIG): HRIG are free from the side effects encountered in a serum of heterologous origin, and because of their longer half- life.

Dose of rabies immunoglobulins : The dose of equine anti rabies serum is 40 i.u. per kg body weight of patient and is given after testing of sensitivity, up to a maximum of 3000 i.u. The dose of the human rabies immunoglobulins (HRIG) is 20 i.u. per kg body weight (maximum 1500 i.u.). HRIG does not require any prior sensitivity testing.

In Category III of animal bites, the anti-rabies serum after sensitivity test is infiltrated in and around the wound even if the lesion has begun to heal followed by administration of anti-rabies vaccine.

Active immunization – Anti-rabies vaccines

The currently available anti-rabies vaccines can be grouped on the basis of the substrate used to grow the vaccine virus strain.

Name of the vaccine	Fixed virus strain	Substrate
1. Neural tissue vaccine BPL inactivated sheep brain vaccine (Semple type)	PV – 11	Sheep brain
Cell Culture vaccines i) Human Diploid Cell Vaccine (HDCV)	Pitman Moore (PM)	MRC-5
ii) Purified Chick Embryo Cell Vaccine (PCEC)	LEP-Flury	Primary SPF chick embryo cells
iii) Purified Vero Cell Rabies Vaccine (PVRV)	Pitman Moore (PM)	Vero Cells
3. Purified Duck Embryo Vaccine	Pitman Moore (PM)	Duck Embryo

Neural Tissue Vaccine (NTV)

The Neural Tissue Vaccines (NTV) have been effective but as it contains less antigen, daily injections for 10-14 days followed by boosters are required to produce a protective level of antibody. The production of NTV has been stopped in Egypt in view of serious Neuroparalytic reaction.

Tissue Culture Vaccines (TCV)

Three types of vaccines that are currently available are:

- Human diploid cell strain vaccine (HDCV)
- Purifed chick embryo cell vaccine (PCEC)
- Purified Vero cell vaccine (PVRV)

As recommended by the WHO Expert Committee on Rabies (1992), the course for post-exposure prophylaxis should consist of five injections (Day O, 3, 7, 14 and 28) and the sixth injection (D90) should be considered as optional. (Should be given to those individuals who are immunologically deficient, and are at the extremes of age and on steroid therapy). Day 0 indicates date of first injection.

The dose of the vaccine per injection is 1 ml for HDCV and PCEC vaccines and 0.5 ml for PVRV irrespective of age and weight of vaccine.

Indications: All cases of animal bites, irrespective of severity of exposure, require the same number of injections and dose per injection. The Category III requires administration of rabies immunoglobulins.

Site of inoculation: The deltoid region is ideal for the inoculation of these vaccines. Gluteal region is not recommended because the fat present in this region retards the absorption of antigen and hence impairs the generation of optimal immune response.

Protective level of anti-rabies antibody: Humoral antibodies are believed to play important role in protection against rabies and a titre of 0.5 i.u./ml or more in serum is considered as protective.

Adverse effects with tissue culture vaccines: The tissue culture vaccines are widely accepted as the least reactogenic rabies vaccines available today. Various studies have now shown that adverse effects can be either general in nature or allergic in origin. The general adverse reactions include sore arm, headache, malaise, nausea, fever and localized edema at the site of injection. Symptomatic treatment may be needed.

Purified Duck Embryo Vaccine (PDEV)

A purified version of duck embryo vaccine (PDEV) has been prepared because of the excellent yield of rabies virus obtained from embryonated eggs and the economy in production. The PDEV has been claimed to be as immunogenic and safe as other anti-rabies Tissue Culture Vaccine. Its dosage and schedule is similar to that of tissue culture vaccine.

Post exposure therapy for previously vaccinated persons

Managing re-exposure following post-exposure treatment with TCV

If re-exposed, persons who have previously received full post-exposure treatment with a potent cell-culture vaccine should be given only two booster doses, intramuscularly on days 0 and 3, but no rabies immunoglobulin.

Managing exposure following pre-exposure prophylaxis with TCV

If after recommended pre-exposure prophylaxis, a vaccinated person is exposed to rabies, a proper wound toileting should be done and two IM doses of Tissue Culture Vaccine be given on days 0 and 3. Treatment with RIG is not necessary.

Approach to a patient requiring rabies immunoglobulins when none is available

In circumstances where no immunoglobulins are available greater emphasis should be given to proper wound toileting followed by Essen schedule of Tissue culture vaccine with double dose on day 0 at 2 different sites intramuscularly (0 day – 2 doses on left and right deltoid, 3, 7, 14 and 28 days).

Management of animal bite exposure to pregnant women and lactating mothers

Post-exposure prophylaxis against rabies takes preference over any other consideration since it is a life-saving procedure. Moreover, rabies vaccine does not have any adverse effect on fetus, mother-to-be and the course of pregnancy. Hence complete post-exposure treatment should be given depending on the category of the exposure.

PRE-EXPOSURE PROPHYLAXIS

Pre-exposure prophylaxis may be offered to high risk group like laboratory staff handling the virus and infected material, clinicians and para-medicals attending to hydrophobia cases, veterinarians, animal handlers and catchers, wildlife wardens, quarantine officers and travellers from rabies free areas to rabies endemic areas. Pre-exposure immunization should be three full IM dose of TCV given on day 0, 7 and 28 or 0, 28 and 56 followed by booster at one year and then a booster every three years.

Laboratory staff and others at high continuing risk of exposure should have their neutralizing antibody titres checked every 6 months. If it is less than 0.5 i.u./ml a booster dose of vaccine should be given. Such individuals on getting exposed to rabies virus after successful pre-exposure immunization require only two booster injections of vaccine given on days 0 and 3 without any anti rabies serum.

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