

Rabies: A Highly Fatal But Preventable Disease

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ABSTRACT

Rabies is a highly infectious viral disease of central nervous system caused by rabies Lyssa virus type-1. It is also known as hydrophobia and is transmitted to human being mostly by the rabid carnivorous animals. **Objectives:** 1-To understand the pathogenesis of the disease rabies and be able to manage this problem most effectively. 2- To be able to avoid preventable deadly complication of this disease. 3- To give awareness about right treatment and remove wrong concepts among the public about this highly fatal disease. **Conclusion:** treatment

Rabies can be managed effectively with various modalities like wound management, vaccination and use of Rabies immune-globulins (RIG) as active & passive immunization according to the category of the exposure. **Prognosis and outcome:** With tissue or cell cultured vaccine the results are good while nerve tissue vaccines have too many disadvantages and are of uncertain efficacy. Failure to use RIG in category iii bite is often a reason for failure of therapy. **Key Words:** Rabies, Photophobia, Lyssa virus, Vaccination, Immune-globulins, Carnivorous animals.

INTRODUCTION

Rabies, also known as hydrophobia is an acute, highly (100% fatal), viral disease of Central Nervous System^{1,2}. It is primarily a zoonotic disease of warm blooded animals. Carnivorous animals such as dogs, cats, jackals, wolves, foxes, monkeys, mongoose and also bats are the main reservoir and transmitters of rabies^{1,5}. The main source of infection to man is the saliva of rabid animals. The urine and other secretions of the rabid animals are other sources of this viral infection².

EPIDEMIOLOGY

Rabies is the 10th most common cause of death among the human infections in the world. Canine rabies exist in 87 countries of the world & accounts for 99% of all human rabies cases. World-wide the human death toll is about 60,000 per year. Globally each year, 10 million people require post-exposure treatment¹. In Pakistan each year, about 80,000 to 90,000 people require post-exposure treatment. About 40,000 human deaths occur due to rabies each year in South East Asian countries. Rabies is endemic in Pakistan and around 2000 to 5000 rabies deaths occur per year³. In the United States domestically acquired rabies cases are rare but probably under reported, eight human cases of rabies were reported in 2004⁴.

HOST FACTORS

All warm blooded animals including man are susceptible to rabies. All age groups are susceptible, but rabies is most common amongst children between 5-15 years. Rabies in man is a dead-end infection. Laboratory staff working with rabies virus, veterinarians, dog handlers, hunters, wild life officers & field naturalists faces high risks of rabies^{1,2}.

Mode of Transmission

- **Animal Bites:** Transmission to man is particular through rabid dog bites. There is possibility of contracting rabies from other animals besides dog (e.g. cats, monkeys, horses, donkeys, sheep, goats, cows and buffalos) Note. Rats, Mice, Squirrels or birds do not transmit rabies.
- **Licks:** Licks on abraded skin and mucosa (abraded or un-abraded) can transmit the disease.
- **Aerosols:** Aerosol (respiratory) transmission has been observed in nature only in certain caves harboring rabies infected bats. In the laboratory, where aerosols are created during homogenization of infected animal brains, can infect laboratory workers.

- **Person-to-Person:** Man to man transmission, although rare, is possible. There are also reports of transmission of rabies by corneal and organ transplants¹.

INCUBATION PERIOD

The incubation period in man is highly variable, commonly 3-8 weeks following exposure but may vary from 4 days to many years.

The incubation period depends on;

- The site of the bite
- Severity of the bite
- Number of wounds
- Amount of virus injected
- Species of the biting animal
- Protection provided by the clothing and treatment undertaken¹.

PATHOGENESIS

Rabies virus (Lyssa virus type-1) multiplies locally in muscle or connective tissue cells at or near the site of introduction before attaching to nerve endings and then enters the peripheral nerves. It travels in side the nerves towards the Central Nervous System. The virus does not travel through blood^{1,2}.

RABIES IN MAN

Clinical Picture: Rabies in man is called hydrophobia. Prodromal symptoms such as headache, malaise, sore throat, pain / tingling at the site of the bite and slight fever last for 3-4 days. It is followed by widespread excitation and stimulation of all parts of nervous system usually involving, the sensory, the motor, the sympathetic and central nervous system. Aerophobia (fear of air), violent spasms of the pharyngeal and neck muscles. Mental changes, depression, fear of death, anger, irritability, paralysis, coma and death¹.

Diagnosis

Clinical diagnosis of hydrophobia.

- History of bite by a rabid animal.
- Characteristic signs & symptoms as stated above as fear of drinking water due to violent spasms of the pharyngeal and neck muscles¹.

Rabies is confirmed by

- Antigen detection by immuno-fluorescence of skin biopsy, Fluorescent Rabies Antibody (FRA) Test.
- Direct Fluorescent Antibody (DFA) assay is the standard test of choice and requires few hours to perform.
- ELISA for serum or CSF
- RFFIT (Rapid Fluorescent Focus Inhibition Test)
- RT-PCR (Rapid Test-Polymerase Chain Reaction) Amplification of small quantities of viral nucleic acid.
- Virus isolation from saliva & other secretions^{1, 5, 6}.

TREATMENT: There is no specific treatment for rabies up-till now. **Referral Hospital in Punjab is, Infectious Diseases Hospital Bilal Gang, Lahore.**

Case management is as follows:

- The patient should be isolated in a quiet & dark room protected from external stimuli such as bright light, noise or cold draughts.
- Relieve anxiety and pain by liberal use of sedatives.
- If spastic muscular contractions are present use drugs with curare-like action.
- Ensure hydration and diuresis.
- Intensive therapy in the form of respiratory and cardiac support.
- Medical and Nursing personnel attending rabid patients should wear face masks, gloves, goggles and aprons to protect themselves.
- Persons having bruises, cuts or open wounds may not be entrusted to look after the patient¹.

PREVENTION OF HUMAN RABIES

This may be considered under 3 heads.

- Post – exposure prophylaxis
- Pre – exposure prophylaxis
- Post – exposure treatment of persons who have been vaccinated previously¹.

POST EXPOSURE PROPHYLAXIS

General consideration

Every human exposure should be treated as a medical emergency. Irrespective of the class of wound, the combined administration of a single dose

of anti-rabies serum with a course of vaccine & local treatment should be given ¹.

Local treatment of wound

- **Cleansing:** Immediate flushing and washing of the wounds, scratches and the adjoining areas with plenty of soap and water is of paramount importance in the prevention of human rabies.
- **Chemical treatment:** Whatever residual virus remains in the wound, after cleansing, should be inactivated by irrigation with virucidal agents – either alcohol (400 – 700 ml/liter) or Dettol, Savulon or Povidone. Do not use Iodine, or house hold applicants like salt, chilies, spices or other powders. These cause local irritation and push the virus deeper in to the wound.
- **Suturing & Bandage:** Bite wounds should not be immediately sutured to prevent additional trauma which may help spread the virus in to deeper tissues. If suturing is necessary, do it after 24 to 48 hours. No tight bandage of the wounds is recommended.
- **Anti-rabies serum:** The local application / infiltration of anti-rabies serum on the wound will be highly effective in preventing rabies
- **Antibiotics and anti-tetanus measures:** The application of antibiotics and anti-tetanus procedures when indicated should follow the local treatment ¹.
- **Observe the animal for 10 days:** The rationale for this is that the animal incubating rabies generally becomes ill in 3-4 days and dies in another 3-5 days. To determine if the individual bitten by a rabid animal is at risk of developing rabies or not. The only limited course of action is to observe the biting animal for at least 10 days from the day of bite. If there is any doubt about the state of the animal, the series of the vaccination may be started and If the animal remains alive and healthy at the end of 10 days, the series may be stopped. However, since the patient may already have received 3 doses (0,3,7) and only 2 doses remain, one may as well continue with the last 2 doses, or give only the 4th dose, and convert to pre-exposure prophylaxis (0,7,21 or 28 days) ^{1,2}.

IMMUNIZATION

Indications for Anti Rabies Treatment:

If the animal shows signs of rabies or dies within 10 days of observation.

- If the biting animal cannot be traced or identified.
- Unprovoked bites.
- Laboratory tests (e.g., fluorescent rabies antibody test or test for Negri bodies) of the brain of the biting animal are positive for rabies.
- All bites by wild animals ^{1,2}.

WORLD HEALTH ORGANIZATION (WHO) CLASSIFICATION OF EXPOSURES

Category-i Touching or feeding animal or licks on intact skin, Consumption of un-boiled milk of suspected animal , scratches without oozing of blood. (Mild risk)

Category-ii Licks on fresh cuts, scratches with oozing of blood ,minor wounds and less than 5. (Moderate risk)

Category-iii All lacerated wounds , scratches with oozing of blood, on head ,neck, face or hands, wounds more than 5, Bites from wild animals. (High risk) ^{1,2}.

VACCINES FOR IMMUNIZATION OF MAN

1. Nervous tissue vaccines (NTV)

- Derived from adult animal nervous tissues
- Derived from suckling mouse brain

2. Duck Embryo Vaccine (DEV)

3. Cell-culture vaccines

- Human Diploid Cell (HDC) vaccine
- “Second generation” tissue culture (animal cell) vaccines ^{1,2}.

Schedule for Inactivated Nervous Tissue Vaccine			
Class of treatment	Dosage per day		Duration of treatment
	Adult	Children	
Class- I	2 ml	1 ml	7 days
Class- II	3 ml	3 ml	10 days
Class- III	5 ml	3 ml	10 days

Technique of Administration Nervous Tissue Vaccine S/C

The ideal site for vaccination is the anterior abdominal wall, this offers enough space to the large quantity of vaccine to be injected.

Duration of Immunity

Serum antibodies appear approximately 7 days after vaccination; it takes at least 30 days to achieve a maximum level. The protection lasts for about 6 months from the date of completion of the course ¹.

Adverse Reactions

General: Headache, Insomnia, Giddiness, Palpitation, Diarrhea.

Local: Itching irritation, Pain, Tenderness, Redness and Swelling at the site of injection.

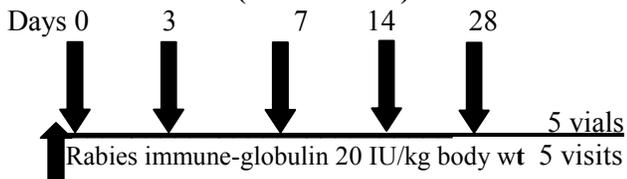
Allergic: Urticaria, Syncope, Angioneurotic oedema, Anaphylactic reaction.

Neuroparalysis: Post-vaccinal paralysis due to sensitization ¹

Cell-cultured vaccine Schedule I/M ¹

The WHO recommended vaccination schedule consists of 6 doses (1 ml each) on day 0,3,7,14 and 28 and a booster dose on day 90. Injections are given I/M into deltoid. The major advantages of cell-cultured vaccines over conventional vaccines are their efficacy and safety.

Dose one i/m dose (1.0 or 0.5 ml) into deltoid

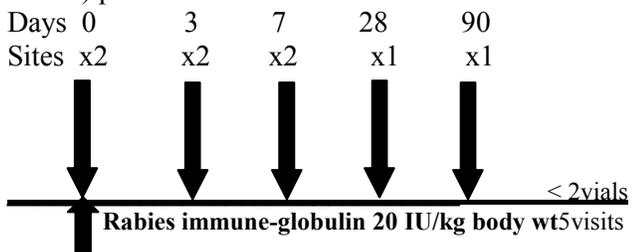


Intradermal Schedules: ¹

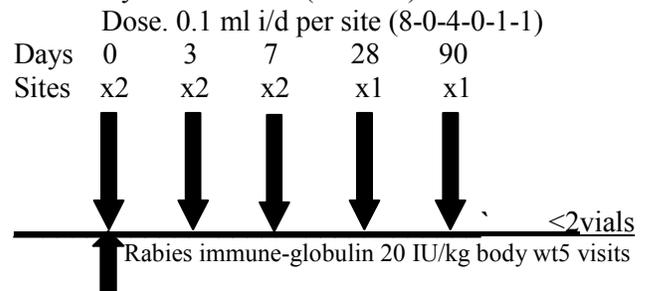
Two intradermal regimens have been recommended.

- **2 site intradermal schedule:** With purified primary chick embryo cell vaccine (PCECV) and purified duck embryo vaccine (PDEV). (2-2-2-0-1-1)

Dose. one i/d = one fifth of i/m dose (1.0 ml or 0.5ml) per site



- **8 site intradermal method:** With human diploid cell vaccine (HDCV) and purified chick embryo cell vaccine (PCECV) ¹.



Three approved tissue culture vaccines are available in Pakistan and are very effective.

Cost may only be the consideration.

- 1- Purified Chick Embryo Cell (PCEC, Rabipur®, Chiron)
- 2- Purified Vero Cell Vaccine (PVRV, Verorab®, Aventis)
- 3- Purified Duck Embryo Vaccine (PDEV, Lyssavac®, Berna) ².

Rabies Immune-Globulins (RIG) for passive, immediate protection: Rabies Immune Globulin must be given in all category iii bites, and whenever there is high suspicion of a rabid animal bite, even if it is category ii.

Two types are available

- (a) Human, which is very expensive but risk free. Dose 20 IU/kg body weight.
- (b) Equine, which is less expensive and occasionally can produce adverse effects. Dose 40 IU/kg. skin test must be done for hypersensitivity reaction before injecting.

Failure to use RIG in a category III bite is often a reason for failure of therapy, despite correct vaccine use ^{2,7}. If immune globulin (human) is not available equine rabies anti-serum (20-40 IU/kg) can be used if available, after appropriate tests for horse serum sensitivity ⁸. Neither the passive nor the active form or post exposure prophylaxis is associated with fetal abnormalities and the pregnancy is not considered a contraindication to vaccination ^{9,10}. Rabies vaccine should be given on the deltoid muscle and not on the gluteus muscle because the danger of nerve damage and long distance of brain from the gluteus. Rabies immune-globulin and rabies vaccines (HDCV) should never be

given in the same syringe or at the same site ^{1,5}.

Rabies in Dogs/Cats may be Suspected if:

- Any change in normal behavior aggression or depression.
- Running aimlessly and attacking without provocation.
- Animal is drowsy and withdrawn.
- Excessive salivation.
- Refusal to eat.
- Eating unusual objects like wood, stone, metal.
- Death of the animal due to illness ^{1,2}.

There are two forms of rabies.

- **Furious Rabies:** Very aggressive, running amuck, change in voice, growling, excessive salivation.
- **Dumb Rabies (paralytic):** Excitatory or irritative stage is lacking. Disease is predominantly paralytic. It lapses into a stage of sleepiness and death in about three days ¹.

IMMUNIZATION OF DOGS/CATS

Inactivated Nervous tissue vaccine.

- Single dose 5 ml for dogs.
- Single dose 3 ml for cats.
- Re-vaccination after 6 months and every subsequent year ¹.

Oral Vaccines

The successful introduction of oral vaccines for immunization of foxes is a great advancement in the rabies prophylaxis of wildlife ^{1,12}.

CONTROL ACTIVITIES

Control of Animal Rabies:

- The animal reservoir mostly dogs by population management (destruction, reproductive control, sterilization) as well as dog vaccination.
- Immunization of dogs should reach at least 80% in highly endemic areas.
- A good surveillance system.
- Dog registration and responsible pet ownership.

- Quarantine /strict implementation of national and international regulation on movement of animals.
- Community participation during vaccination campaign ^{12,13}.

Control of Human Rabies

- Ensuring pre-exposure treatment of personnel at high risk (dog vaccinators, hospitals personnel)
- Post-exposure treatment of bitten persons.
- Availability of immunoglobulin for treatment of severe cases.
- WHO guidelines about rabies should be followed.
- Training of health personnel for management of cases
- Health education of the public.
- Pre-exposure treatment of children, who may come in contact with dogs/cats ¹².

Applied Research

In animals the following areas require attention

- Dog ecology and human-dog relationship.
- Oral rabies immunization especially among inaccessible owned dogs.
- Use of traditional plants with birth control effects and development of anti-reproduction vaccine for dogs.
- Rabies surveillance in wild life in rabies free areas
- In humans study the immunogenicity of current vaccines and regimens in immune-compromised individuals ¹².

International Measures

Quarantine and vaccination of dogs intended to be conveyed to rabies free areas should be done ¹³.

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