महानिदेशक सशस्त्र सेना चिकित्सा सेवा चिकित्सा ज्ञापन क्रमांक 130
DG AFMS MEDICAL MEMORANDUM NO. 130

अलर्क—नियंत्रण एवं उपचार
RABIES—CONTROL AND TREATMENT

(मई 1991 में जारी किया गया)
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RABIES—CONTROL AND TREATMENT—130

INTRODUCTION

1. Rabies is responsible for extensive mortality and morbidity in India. The exact figures are not available but it is estimated that 25,000 persons die of hydrophobia every year. The approximate figure for postexposure immunisation is 500,000 per year in the country.

PRINCIPAL RESERVOIR

2. Rabies is primarily a disease of animals and almost all the warm blooded animals fall prey to it. In India 96% of the persons undergoing antirabies treatment are bitten by dogs.

CAUSATIVE AGENT

3. Rabies virus is a small bullet shaped RNA virus belonging to family Rhabdoviridae. The virus can remain infectious for weeks in the cadavers being highly resistant to cold and dryness. It is inactivated by sunlight, formaldehyde, lipid solvents and various antiseptics. The 'street virus' refers to the virus freshly isolated from naturally occurring cases and it is characterized by a very variably incubation period, and by its capacity to invade the salivary glands. The 'fixed virus', by contrast, refers to strains altered by serial intracerebral passages in laboratory animals which have a fixed incubation period of 4 to 6 days and do not invade he salivary glands. The fixed virus is used for preparation of antirabies vaccine.

RABIES IN MAN

PATHOGENESIS

4. After a bite or lick on broken skin or mucosa, the neurotropic virus spreads mainly along the endoneural lymphatic ducts, thus reaching the brain and the spinal cord where it multiplies in the grey matter. It then passes into salivary glands and other parts of the body through the peripheral nerves. The

incubation period of rabies is exceedingly variable ranging from 10 days to over a year. The time period depends upon the amount of virus introduced, host defence mechanisms, and the actual distance that the virus has to travel from the site of inoculation to he central nervous system.

CLINICAL MANIFESTATIONS

5. The clinical manifestations of rabies can be divided into three stages :

(a) During the *prodromal stage* of 1 to 4 days the symptom suggestive of rabies is the complaint of paraesthesias and/or fasciculations at or about the site of inoculation of virus. It is present in 50 to 80 per cent of the patients.

(b) The *encephalitic* stage is usually ushered in by periods of excessive motor activity, excitation, and agitation. Characteristically, the periods of mental aberration are interspersed with completely lucid periods but as the disease progresses, the lucid periods get shorter until the patient lapses into coma. Hyperaesthesia with excessive sensitivity to bright light, noise or even gentle breeze, is common along with abnormalities of autonomic nervous system and upper motor neuron lesions.

(c) *Brainstem dysfunction* begins shortly after the onset of the encephalitic phase. Cranial nerve involvement cause diplopia, facial palsies, optic neuritis, and the characteristic difficulty with deglutition. The combination of excessive salivation and difficulty in swallowing produces the traditional picture of "foaming at the mouth". Hydrophobia, the painful, violent involuntary contraction of the diaphragam,accessory respiratory, pharyngeal and laryngeal muscles initiated by swallowing liquids is seen in about 50 per cent of cases. The median survival after onset of symptoms is 4 days with a maximum of 20, unless artificial supporting measures are instituted. Recovery is very rare and when it occurs, has been gradual.

LABORATORY DIAGNOSIS

6. The spcific antemortem diagnosis of rabies depends upon the demonstration of viral antigen in infected tissues, e.g. corneal impression smears, and saliva by the use of Fluorescent Antibody Test (FAT). For postmortem diagnosis the virus antigen is demonstrated on brain biopsy.

MANAGEMENT

7. Treatment of rabies consists only of symptomatic therapy. Utmost attention should be given to proper nursing care. The patient has to be protected from external stimuli such as draughts; noise or bright light. To reduce psychomotor excitation, intravenous diazepam can be given. If it is administered along with antithistaminics and analgesics, better results can be obtained.

Due to the dramatic dehydration in all the cases, patients require large quantities of intravenous infusions. Prednisolone and mannitol may be administered to the patients with high intracranial pressure. Respiratory and cardiac support may be given to alleviate the suffering.

Individuals attending on hydrophobia patients should take all the precautions using face masks, gloves and aprons as the virus may be present in the saliva, tears, urine and other body fluids. If the attendant has handled any secretions or excretions, he must be given appropriate ARV immunisation.

PREVENTION OF RABIES IN MAN

8. Prevention of Rabies consists of local management of the wound, post-exposure and pre-exposure immunisations. A summary of antirabies treatment following dog bite is given at Appx 'A'.

CLASSIFICATION OF BITE WOUNDS

9. *Class I*—Slight/negligible exposure i.e. minimum risk. All cases of licks except those on fresh cuts and scratches drawing blood.

Class II—Moderate exposure i.e. definite but moderate risk :—

(a) Licks on fresh cuts and scratches drawing blood.

(b) All bites except those on the head, neck, face palm and fingers; and less than five minor wounds in number.

Class III :—Severe exposure i.e. definite and grave risk.

(a) All bites on the neck or above, palm and fingers.

(b) Lacerated wound anywhere on the body.

(c) Multiple bites (5 or more).

(d) Bite by wolf, Jackal and other wild animals.

MANAGEMENT OF WOUND

10. It is emphasized that local treatment of wound is extremely important and on its own can prevent many cases of rabies by eliminating or inactivating the inoculated virus. It is strongly recommended that the wound must be washed as soon as possible after the bite, as given below :—

(a) Immediate washing and flushing with soap and water, detergent, or water alone are imperative. Then either alcohol. tincture, aqueous solution of iodine or quarternary ammonium compounds such as 1 to 4% benzalkonium chloride or 1% cetrimonium bromide cetavlon should be applied. All traces of soap should be removed before the application of these latter compounds.

(b) Antirabies serum (preferably homologous) should be applied by instillation in the depth of the wound and by infiltration around the wound, where required.

(c) Suturing of the wounds should be postponed by 24 to 48 hours. However, if suturing is necessary, antiserum should be administered locally as described above.

(d) Specific systemic treatment should be adapted for each individual case. For major bites on the face, head neck or fingers by a suspect or confirmed rabid domestic

or wild animal, serum and vaccine should be applied immediately in association, where indicated, Tetanus toxoid and antibiotics must be given. Cauterization with pure carbolic acid or fuming nitric acid is no longer recommended.

ANTIRABIES VACCINES

11. Two types, Nervous Tissue Vaccines and Tissue Culture Vaccines are available.

NERVOUS TISSUE VACCINES

12. This is an inactivated vaccine prepared from sheep brain that are infected with a suitable strain of the 'fixed virus'. It is manufactured by the Central Research Institute (CRI) Kasauli and the Pasteur Institute, Conoor. The vaccine should be stored between 4°C to 10°C. It is only used for post-exposure immunization.

TISSUE CULTURE VACCINES

13. The virus has been cultivated in high concentrations in tissue cultures of non-neural origin. The vaccine thus produced is free from nervous tissue and animal protein and after concentration and purification, it is inactivated by beta-propiolactone. In the HUMAN DIPLOID CELL VACCINE (HDCV) the laboratory strain rabies virus is cultivated in human (embryonal lung fibroblast) diploid cells. In the purified Chick Embryo Cell vaccine (PCEC), the fixed virus strain Flury LEP is grown in primary cultures of chick fibroblasts.

14. The advantages of the Tissue Culture Vaccines are that it has excellent general and local tolerance as compared to the nervous tissue vaccine. It can be given for pre-exposure prophylaxis also to persons at high risk. The total number of injections required is 5 to 6, over a period of one to three months. These are given on day 0, 3, 7, 14, 30 and 90 after the bite. The dose per injection is 1 ml IM irrespective of age and weight of the patient.

INDICATIONS FOR ANTIRABIES VACCINATION

15. Antirabies Treatment should be started immediately when a person is bitten, scratched or licked under the following conditions :—

(a) The animal is suspected of being rabid or is diagnosed as suffering from rabies clinically or by laboratory examination.

(b) In endemic areas following the bite of stray or wild animal that cannot be apprehanded.

SITUATIONS WHERE ANTIRABIES VACCINATION IS NOT INDICATED

16. (a) A bite through clothes without tearing or piercing it and when the skin is unbroken though a bruise may be present.

(b) Handling of animals bitten by a rabid animal, or contact with fomites of rabid animals.

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1. **Monkey bites :** Rabies occuring in wild and free living monkeys has never been reported in literature. However, there is a possibility of rabies occuring in captive or pet monkeys. Anti-rabic treatment is not advocated to persons bitten by free living monkeys. In case of bites by pet monkeys, it is advisable to give 5 injections of ARV (Sheep brain vaccine) or injections of tissue culture vaccine and observe the monkey for any evidence of rabies. Full treatment is indicated if the monkey becomes ill and dies during the observation period.

2. **Man to Man transmission :** Human transmission of rabies is very rare Transmission of rabies from one person to another has been proved only in 5 patients who had received infected corneal grafts. Although virus is secreted in saliva, yespiratory secretions, tears and urine of rabies patient, the disease generally does not spread to people in contact with such patients. A number of women with rabies encephalitis have delivered healthy babies. Hence all those who are in contact with patients suffering from rabies need not be protected with ARV unless they are directly involved in the care of such patients and have doubtful integrity of skin or sustain abrasions during the care of patients suffering from rabies. In such circumstances, complete anti-rabic vaccination to be given. Additionally there is a necessity to protect individuals conducting post-mortem on such cases.

(c) Drinking of boiled milk from animals bitten by a rabid dog.

(d) If the biting animal remains normal and healthy for a minimum period of 10 days after the bite.

ANTIRABIES SERUM

17. The antirabies serum provides passive immunity quickly to tide over the initial phase of the infection. It is given along with vaccine in all class III bites; and where the dog is definitely rabid or cannot be kept under observation. If the patient is seen within 24 hours of the bite, part of the serum should be applied locally by instillation in the depth of the wound and by infiltration around the wound; the rest of the dose should be given intramuscularly (IM). After 24 hours upto 7 days of the bite, the full dose is given IM. After 7 days of bite, use of serum has no role.

18. The equine Antirabies serum is generally used, but the Rabies Immunoglobulin RIG of human origin is preferable, where available. The dose of equine antirabies serum (ARS) is 40 IU/Kg body weight and is given by intramuscular route upto a maximum of 3000 IU, after testing for sensitivity. The dose of rabies immunoglobulin of human origin is 20 IU/Kg body weight and does not require prior sensitivity testing. Treatment for anaphylactic reaction should be readily available for use.

DOSAGE SCHEDULES OF NERVOUS TISSUE VACCINE

19. Two schedules are commonly followed in this country; one propagated by CRI, Kasauli and the second by Pasteur Institute, Conoor. In Class I and Class II bites, the vaccine alone is recommended; while in class III bites combined ARS and ARV should be given. The vaccination is stopped if the animal remains healthy for 5 days and no further

treatment is needed if the animal is alive for 10 days. However, if the animal is definitely rabid, dies within 10 days of observation, or is untraceable, the full course of vaccination must be completed.

DOSAGE SCHEDULE FOR ANTIRABIES VACCINE

	Class of Bite Wound	Dosage per day		Duration	Booster Doses
		Adult	Children under 30 kg.		
CRI	I	2ml	2ml	7 days	
Kasauli	II	5ml	2ml	14 days	5 ml given, 21 day after the 14th injection.
	III	5ml	2ml	14 days	5ml each on 7th and 21st days after the 14th injection.
Pasteur Institute	I	2ml	1ml	7 days	
Conoor	II, III	3ml	3ml	10 days	

NOTE : Follow the manufacturers' instructions as given on each batch of vaccine.

SITE OF VACCINATION

20. The ideal site is the anterior abdominal wall, as this area offers enough space to accommodate 14 injections at different sites. In late pregnancy, the thigh will be a suitable site. The vaccine must be deposited deep substaneously. To ensure success, a fold ot skin is lifted between the thumb and other finger in a patient lying down or standing and the vaccine injected into the base of the fold employing a 37mm long needle. A fresh, sterile syringe should be used for each patient to prevent tansmission of serum hepatitis.

INSTRUCTIONS TO PATIENTS

21. The patient should immediately inform the medical attendant of any symptoms suggestive of neurological complications like difficulty in micturition, tingling, numbness and muscular weakness in the extremities. All patients undergoing antirabies treatment should be advised to avoid undue physical/mental exertion. They should abstain from alcohol for upto a month after completion of vaccination; steriods and other immunosuppressant drugs should be avoided.

COMPLICATIONS

22. The complications following ARV immunisation with Semple Vaccine may be local, general or neuroparalytic.

LOCAL

23. Moderate pain, redness and itching at the site of inoculation may occur locally after 5 to 6 injectiors. Treatment consist of hot fomentation, and antihistaminics.

GENERAL

24. Reactions may be mild or severe. Mild systemic reactions consist of fever, headache, insomnia, giddiness, palpitations and diarrhoea which require only symptomatic treatment. Uncommonly generalised urticaria and angioneurotic oedema may occur. Rarely sudden shock may result after antirabies vaccination and is seen during the last phase. Treatment consists of parenteral administration of adrenaline and corticosteroids along with other measures of resuscitation.

NEUROPARALYTIC ACCIDENTS

25. The incidence of the neuroparalytic accidents in India has been between 1:5500 to 1:11000 of treated cases. These are due to sensitization of the patient to some factor present in the sheep brain, and occur usually after 6th or 7th injection of the vaccine. Prodromal symptoms like headache, muscular aches, and pain in the neck may be followed by any of the neurological manifestations as given below.

NEURITIC TYPE

26. Temporary paralysis of one or more, spinal or cranial nerves, may occur. The commonly affected nerves are facial, ocular, glossopharyngeal or sciatic and rarely the optic nerve.

LUMBODORSAL TYPE

27. This is the commonest complication which is characterized by severe pain in the limbs followed by paralysis of legs and difficulty in micturition and/or evacuation. The patient may complain of diminished sensation in the affected limbs. The disease may not progress further and recovery may ensue. About 5% mortality has been reported.

LANDRY TYPE

28. It is more severe and the mortality rate is 20—40%. It starts with fever and backache. Flaccid paralysis sets in both the legs along with retention of urine and faeces. In a day or two the paralysis ascends upwards and involves muscles of face, neck and tongue. It further progresses to medulla oblongata resulting in paralysis of the respiratory muscles and death follows.

TREATMENT

29. As soon as the diagnosis is suspected, stop the vaccine administration and hospitalise the patient with absolute bed rest. Symptomatic treatment, oral steroids, and in severe cases use of plasmapheresis where available, is recommended. Further vaccination, if needed, should be carried out with tissue culture vaccines.

PRE-EXPOSURE IMMUNISATION FOR RABIES

30. With the availability of safe and potent tissue culture vaccines, it is possible to recommend use of these vaccines for pre-exposure prophylaxis in individuals at high risk i.e. animal handlers, veterinarians, wildlife officers and laboratory staff handling infected material. The dose is three injections of tissue culture vaccine with a potency of not less than 2.5 IU per ml on days 0, 7 and 28. Further booster injections are

given at intervals of 1 to 3 years as long as the person remains at risk. The virus neutralising antibody titre should be more than 0.5 IU/ml, and if the level is less, further booster must be given. Post-exposure prophylaxis in an individual protected by pre-exposure immunisation consists of Tissue Culture Vaccine alone. Two doses of Tissue Culture Vaccine on days 0 and 3 are usually adequate.

EXPOSURE AFTER ANTIRABIES VACCINATION

31. Exposure after 6 months of completion of a course of Semple vaccine, should be considered as a fresh case. Re-exposure to Class I risk within 6 months of a course of treatment should be treated with one booster injection of 2ml vaccine. If within 6 months a patient of Class I group has been inflicted Class II or III wound, a full course for that type ef Class is indicated. However, if the patient had been treated earlier for class II or III and the next exposure (within 6 months) also falls in either Class II or III, only two booster injections of 5 ml each of ARV one immediately on reporting and second after a week stould be given.

RABIES IN ANIMALS

DOGS

32. Rabies in dogs may manifest in two forms furious and dumb rabies. Furious rabies is characterised by change in the normal disposition with tendency to attack and bite without provocation, running amuck, excessive salivation and change in voice. Dumb rabies is characterised by predominantly paralytic features and the irritative stage is lacking. Once the symptoms of rabies develop, the dog dies within 10 days.

CATS

33. Generally the disease is of furious type just like furious rabies in dogs. Paralysis of posterior third of body follows 2 to 4 days after the appearance of excitation symptoms.

MONKEYS

34. Monkeys encountered in urban dwellings are capable of contracting and transmitting the disease; and a bite by these monkeys is to be managed in the same way as is done for dog bite.

OTHER ANIMALS

35. Other prominent vactors of the disease in different parts of the world are, the wolf (Eastern Europe, Arctic region), the mongoose (South Africa, Caribbean), the fox (Western Europe), and the vampire bat (Latin America), in India mongoose is known to suffer from rabies and the possibility of transmission of disease from infected mongoose to other rodents and human beings cannot be ruled out. Therefore, cases of bites by rodents which show a tendency to be unusually aggressive, must be viewed with suspicion and treated on the merit of the individual case.

POSTMORTEM DIAGNOSIS

36. Any animal suspected of having rabies should be sacrificed immediately and sent to the laboratory for examination. If a pet animal with no signs of illness bites a human or another animal and there is no other reason to suspect that the animal has rabies, it can be confined for 10 days. If symptoms develop during this period of observation the animal must be killed immediately and sent to laboratory for testing. If no symptoms develop during these 10 days, the exposed person is not considered at risk. The animal should be killed with care not to damage the brain. The brain, spinal cord and salivary glands should be immediately taken out, refrigerated and sent to the laboratory. The rest of the body should be incinerated. The list of laboratories is given in Appx 'B'.

37. Apart from transporting the specimen packed in ice (Wet or dry), it can be also preserved in 50% glycerol saline. The specimen should be placed in a suitable water tight container, placed inside a larger similar container packed

with ice. Specimens should never be shipped or sent to the laboratory in formalin, because formalin makes the specimen unsatisfactory for rabies testing. The specimen is examined by the following methods:—

(a) Detection of Negri-Bodies by Seller's stain.

(b) Detection of viral antigen by Fluorescent Antibody Test (FAT).

38. The sensitivity of Seller's staining for Negri-Bodies, is about 75 per cent. It is a rapid and cheap test and report is available in 2 hours. If it is negative, the Fluorescent Antibody Test (FAT) is performed after fixing the smears in acetone for 18 hours in cold. It is 95 to 99 per cent sensitive.

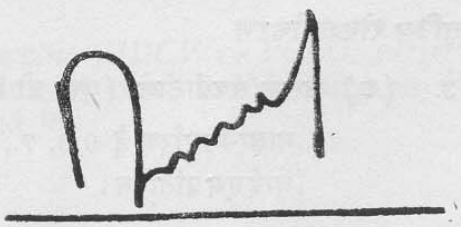
CONTROL OF RABIES

39. Three important components of the programme are:—

(a) Pre-exposure immunization of pet animals as advised by Veterinary Surgeons.

(b) Elimination of stray dogs.

(c) Extensive health education to procure cooperation in fulfilling the above mentioned components.



Date : ....., 1992.

(NC SANYAL)
Lt Gen
Director General
Armed Forces Medical Services

APPENDIX 'A'

SUMMARY OF ANTIRABIES TREATMENT FOLLOWING DOG BITE

(Copies to be displayed in MI Riom/RAP/OPDs)

Treatment of the Wound

(a) Wash with soap and water or water alone.

(b) Apply Cetavlon or Tincture of Iodine.

(c) Instil antirabies serum in the depth of the wound and infiltrate around the wound.

(d) Do not suture the wound up to 48 hours.

ANTIRABIES IMMUNISATION

Passive Immunisation

2. Antirabies Serum (ARS) or Rabies Immunoglobuline (RIG) is required in class III Bites.

(a) Within 24 hours after the bite—Give half the dose of ARS locally and other half IM.

(b) From 24 hours to 7 days after the bite—Full dose of ARS given IM only. —

Active Immunisation

3. (a) *Tissue Culture Vaccine (HDCV or PCEC) perferred* The dosage schedule is one ml IM daily on days 0, 3, 7, 14, 30 and 90.

(b) *Semple Vaccine*

(Only if tissue culture vaccine is not available).

DOSAGE SCHEDULE

	Class of wound	Dosage per day		Duration	Booster Dose
		Adult	Children (less than 30 kg)		
CRI Kasauli	I	2ml	2ml	7 days	
	II	5ml	2ml	14 days	5ml given 21 day after the 14th injection.
	III	5ml	2ml	14 days	5ml each on 7th and 21st days after the 14th injection.
Pasteur Institute Conoor	I	2ml	Iml	7 days	
	II, III	3ml	1ml	10 days	

NOTES :—

1. Follow the manufacturer's instructions given on each batch of the vaccine.
2. All serving personnel receiving antirabies treatment with Semple vaccine should be hospitalised.
3. For further details read relevant parts of the Memorandum.

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