

# Rabies

## **General introduction**

Rabies, present on all continents and endemic in most African and Asian countries, is a fatal zoonotic viral disease, transmitted to humans through contact (mainly bites and scratches) with infected animals, both domestic and wild. Rabies is estimated to cause at least 55 000 deaths per year worldwide, about 56% of which occur in Asia and 44% in Africa, particularly in rural areas on both continents. In Africa and Asia, these deaths are responsible for 1.74 million disability-adjusted life years (DALYs) lost each year. The estimated annual cost of rabies is US\$ 583.5 million, most of this cost being borne by Asian countries where large amounts of postexposure prophylaxis are administered. Most postexposure prophylaxis needs are borne by patients who can least afford to pay. An estimated 10 million people worldwide receive post-exposure treatment after being exposed to animals suspected of rabies.

There is no specific treatment for rabies, which is a fatal disease. (Supportive treatment alone has been successful in one recently-reported confirmed case of human rabies in the United States of America.) WHO promotes:

- human rabies prevention through:
  - well-targeted postexposure treatment using modern vaccine types and, when appropriate, antirabies immunoglobulin;
  - pre-exposure prophylaxis using modern vaccine types for certain professional groups at higher risk and also if vaccines are easily accessible, of children aged under 15 in areas where rabies is hyperendemic;
  - increased access of safe and effective rabies vaccines.
- dog rabies elimination through mass vaccination of dogs and dog-population management.

## **Causal agent and main modes of transmission**

**Causal agent:** Lyssaviruses of the *Rhabdoviridae* family.

**Main modes of transmission:** Hosts are usually *Canidae*, including dogs (responsible for more than 99% of all human deaths from rabies), foxes, coyotes, wolves and jackals; also cats, skunks, raccoons, mongooses, bats and other biting animals. A bite or a scratch introduces virus-laden saliva from a rabid animal. The incubation period ranges from a few days to several years (most commonly 3-8 weeks).

## **Clinical description and recommended case definition**

### **Clinical description**

- Paresis or paralysis, delirium, convulsions.
- Without medical attention, death in about 6 days, usually caused by respiratory paralysis.

**Clinical case definition:** a person presenting with an acute neurological syndrome (encephalitis) dominated by forms of hyperactivity (furious rabies) or paralytic syndromes (dumb rabies) progressing towards coma and death, usually by respiratory failure, within 7-10 days after the first symptom if no intensive care is instituted.

### **Laboratory criteria**

*One or more* of the following:

- Detection of rabies viral antigens by direct fluorescent antibody test (FAT) or by ELISA in clinical specimens, preferably brain tissue (collected post mortem).
- Detection by FAT on skin biopsy (ante mortem).
- FAT positive after inoculation of brain tissue, saliva or CSF in cell culture, or after intracerebral inoculation in mice or in suckling mice.
- Detectable rabies-neutralizing antibody titre in the serum or the CSF of an unvaccinated person.
- Detection of viral nucleic acids by PCR on tissue collected post mortem or intra vitam in a clinical specimen (brain tissue or skin, cornea, urine or saliva).

### **Case classification (humans)**

#### *Human rabies*

**Suspected:** A case that is compatible with the clinical case definition.

**Probable:** A suspected case plus history of contact with a suspected rabid animal.

**Confirmed:** A suspected case that is laboratory-confirmed.

#### *Human exposure to rabies*

**Possible exposure:** A person who had close contact (usually a bite or scratch) with a rabies-susceptible animal in (or originating from) a rabies-infected area.

**Probable exposure:** A person who had close contact (usually a bite or scratch) with an animal displaying clinical signs consistent with rabies at time of the exposure, or within 10 days following exposure in a rabies-infected area.

**Exposed:** A person who has had close contact (usually a bite or scratch) with a laboratory-confirmed rabid animal.

## **Surveillance**

### **Rationale for surveillance**

Surveillance of both human and animal rabies is essential to detect high-risk areas and outbreaks quickly and to monitor the use of vaccine.

### **Recommended types of surveillance**

#### ***Surveillance in human populations***

- *Surveillance of human exposure to rabies.* Reports of patients with a history of animal contact (usually a bite/scratch), especially in rabies-infected areas, to be investigated at once. Case-based and aggregated data must be sent regularly from the local level to the intermediate and central levels.
- *Surveillance of cases of human rabies.* Immediate reporting of suspected and confirmed cases from the local level (by diagnosing physician and laboratory) to the intermediate and central levels.
- Rapid exchange of information with services in charge of animal rabies surveillance and control is required.
- Epidemiological investigation of outbreaks: investigation of all rabies foci, identifying sources of infection as well as humans and animals exposed or possibly exposed.

#### ***Surveillance in animal populations***

Where the disease is endemic or could be reintroduced, undertake surveillance of animal rabies and similar conditions in wild and domestic species most likely to be reservoirs of disease. Surveillance is laboratory-based. There should be immediate submission of a brain specimen of the suspected animal for laboratory diagnosis when human exposure occurs. Suspected domestic animals at the origin of human exposure that cannot be killed must be kept under observation for 10 days. Rapid exchange of information between services in charge of human and animal rabies surveillance and control is required. In circumstances where samples cannot be collected from the suspected rabid animal or a laboratory diagnosis cannot be made, cases to be recorded as suspected animal rabies cases on the basis of clinical signs; and these data should also be collected and exchanged with public health authorities.

### **Recommended minimum data elements**

#### *Human rabies exposure*

**Case-based data.** Unique identifier, name, age, geographical information, date of onset of symptoms, date(s) of bite/scratch, geographical information, (location) of biting episode(s), category of exposure, local wound treatment, vaccination history, previous serum treatment, current treatment, outcome; details of biting animal, vaccination history, samples taken, samples outcome, outcome.

#### ***Aggregated data reporting***

- Exposures by geographical information on biting episode, biting animal, outcome in animal and human populations.
- Surveillance of deaths from human rabies:

#### **Recommended data analyses, presentation, reports**

- Number of human rabies deaths and rabies cases in animals (by species), by date of presentation.
- Human exposures by location and dates of biting/scratch episode, animal species at origin of exposure and by outcome in human and in animal populations.
- Cases by geographical area (e.g. district), dates of biting/scratch episode, type of animal, occupation and outcome.

## **Control activities**

### **Case management of bitten patients**

- Immediate and thorough cleaning of the wound with soap, followed by ethanol or aqueous iodine.
- Postexposure prophylaxis (PEP) if required: administration of rabies immunoglobulin in case of severe exposure (WHO category 3).
- PEP to be applied as soon as possible – vaccines with a potency at least 2.5 IU per single immunizing intramuscular dose according to one of the following schedules: (Volume of 1 intramuscular dose after reconstitution may vary according to vaccine brand.)
  - *Intramuscular schedules*
    - Essen regimen: 1 dose on days 0, 3, 7, 14 and 28. All intramuscular injections to be given into deltoid region or anterolateral area of thigh muscle in small children. Never inject the vaccine in the gluteal region.
    - 2-1-1 regimen: 2 doses on day 0 (one in the deltoid region of the right arm and the other in the deltoid region of the left arm). 1 dose in the deltoid region on day 7 and 1 on day 21. This regimen is particularly recommended when no immunoglobulin is required, i.e. when contact consists in nibbling of uncovered skin, minor scratches or abrasions without bleeding, or licks on broken skin.
  - *Intradermal schedules*. The following intradermal regimens have been shown to be immunogenic:
    - *2-site intradermal method* (2-2-2-0-1-1 and 2-2-2-0-2) for use with purified vero cell vaccine (PVRV), purified primary chick embryo cell vaccine (PCECV) and human diploid cell (HCDV) at 0.1 ml per intradermal injection site – days 0, 3 and 7: 0.1 ml at each of 2 sites, intradermally on upper arm, over each deltoid. Days 28 and 90: 0.1 ml at 1 site, on upper arm. The single dose of vaccine given on day 90 of the original Thai Red Cross regimen (2-2-2-0-1-1 regimen) can be replaced if two doses of vaccine are given on day 28 (2-2-2-0-2 regimen).
    - *8-site intradermal method* (8-0-4-0-1-1) for use with human diploid cell vaccine HDCV, and PCECV. Regimen: day 0: 0.1 ml at each of 8 sites. Inject intradermally over deltoid, lateral thigh, suprascapular region and lower quadrant of the abdomen. Day 7: 0.1 ml of vaccine at each of 4 sites over deltoids and thighs. Days 28 and 90: 0.1 ml of vaccine at 1 site, over deltoid.
  - Intradermal injections must be given by staff trained in this technique. Vaccine vials to be stored between 2 °C and 8 °C after reconstitution and total content to be used as soon as possible, at least within 8 hours. Rabies vaccines formulated with an adjuvant should not be administered intradermally. The standard dose per id injection site is 0.1 ml. It should be noted however that the volume of one single immunizing intramuscular dose after reconstitution may vary according to vaccine brand.

### **Prevention**

- Immunize all dogs and cats owned by an individual or by the community and reduce the size of the ownerless dog population by reproduction control, reduction of the carrying capacity of the environment and law enforcement when needed.
- Immunize any person with proven or probable exposure to rabies and administer rabies immunoglobulin in case of severe exposure (WHO category 3).
- Humans at high risk (e.g. laboratory personnel, professions at high risk) must receive pre-exposure immunization: 3 injections of an intramuscular dose on days 0, 7, and 28.
- Pre-exposure vaccine regimen: 1 dose of a cell culture or purified duck embryo vaccine on days 0, 7, 28. A variation of a few days is acceptable. The dose is 1 standard intramuscular dose (1 ml or 0.5 ml according to vaccine type). vaccine may be given intradermally (0.1 ml on days 0, 7, 28) but intramuscular injections are preferable if antimalarial chemoprophylaxis (e.g. chloroquine) is being used concurrently or there is a possibility of an immune-compromised state (antibody response may be impaired if the intradermal method is used).

### **Epidemics**

#### ***Conditions under which epidemics may occur***

- Introduction of the virus into a rabies-free area with a fully susceptible animal population.
- Affected areas where the dog/human population ratio is high, with little dog supervision and immunization.
- Affected areas with animal outbreaks where no human rabies vaccines/immunoglobulin are available.

#### ***Management of epidemics***

If an epidemic arises from a new introduction at one site, intensive vaccination of dogs in combination with dog-

population control and movement restriction to be implemented immediately. Public health authorities, particularly in isolated rabies-free island communities, should have a contingency plan for such an event.

#### *In animals*

- Undertake a dog immunization campaign: 75% of the dog population must be vaccinated within 1 month.
- Immunize domestic animals and (through bait) wild animals as appropriate.
- Enact/ enforce legislation on dog movement restriction.
- Selective and humane capture and elimination of dogs not in compliance with legislation may be conducted in outbreak situations.

#### *In humans*

- Ensure availability of vaccine and immunoglobulin in the affected area.
- Train medical staff in defining when PEP is needed, categories of exposures and in the use of the intradermal technique.
- Investigate animal outbreaks and identify human contacts with suspect animals.
- Immunize any person with proven or probable exposure to rabies.

### **Other aspects**

#### **Procurement of equipment and drugs**

- A 1-ml syringe and a needle for each intramuscular injection (intradermal needles and syringes for intradermal vaccination).
- Vaccine amounts: between 2 and 5 vials, depending on the method used.
- Only the following vaccines meet WHO safety, potency and efficacy requirements when used for postexposure intradermal treatment of rabies:
  - human diploid cell vaccine (HDCV): Rabivac™;
  - purified vero cell vaccine (PVRV): Verorab, Imovax, Rabies vero, TRC Verorab™;
  - purified chicken embryo cell vaccine (PCECV): Rabipur™.

#### **Special considerations/other interventions**

- It is theoretically possible for person-to-person rabies transmission to occur since secretions may contain the virus; this has not been described. As a precaution, medical and nursing staff must wear mask, gloves, and goggles. In hospitals and other institutions caring for several rabid patients, pre-exposure vaccination of medical and nursing personnel should be considered. Do not use organs of patients with rabies or any neurological disease for transplantation.
- Intersectoral cooperation of medical and veterinary services, community involvement and participation are required for targeted response and control in animal reservoirs.

### **Contacts**

WHO Headquarters 20 Avenue Appia, CH-1211 Geneva 27, Switzerland

Communicable Diseases Surveillance and Response (CSR)

E-mail: [meslin@who.int](mailto:meslin@who.int) and [zoonotic\\_alert@who.int](mailto:zoonotic_alert@who.int) Tel: (41 22) 791 2575/2111, Fax: (41 22) 791 4893 attn CSR

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