Rabies is a viral disease that causes acute encephalitis and is usually transmitted to humans by a bite from an infected animal. It is almost invariably fatal if postexposure prophylaxis is not administered before the onset of severe symptoms.

Rabies is derived from the Latin word *rabere*, to rage. The condition has been known for more than 4000 years. Democritus, in 500 BC, gave a clear description of rabies. In the 4th century BC, Aristotle warned of the danger of being bitten by a rabid dog. In the 16th century, Girolamo Fracastoro, an Italian physician, suggested that rabies occurred in humans only when the skin was broken by an animal bite. In 1793, Samuel Bardsley, a physician at the Manchester Royal Infirmary, published his observations on rabies. He said that rabies was contagious and suggested that all dogs imported into Britain should be put into quarantine. Georg Zink, in 1804, showed that rabies could be transmitted from one dog to another. In 1821, Francois Magendie, in France, showed that a dog would develop rabies if inoculated with saliva from a human case.

Pierre Galtier, Professor of Veterinary Medicine at Lyons, suggested that rabbits should be used for experimental studies of the disease, as they did not develop the furious form of the disease. He was able to transmit rabies from dogs to rabbits, and then from rabbit to rabbit. In 1881 he managed to immunise sheep against rabies. However, Louis Pasteur was the first person to produce a successful vaccine against rabies in the 1880s. He had already shown that infectious material that had been attenuated could be used to protect chickens against chicken cholera, and sheep against anthrax. He developed an attenuated rabies virus in the spinal cords of rabbits. In 1885, inoculation with this material was successful in preventing rabies in a shepherd boy called Joseph Meister who had been bitten by a rabid wolf.

In 1962, Sokolow and Vaney showed that Negri bodies, which had been described by Adelhi Negri in the brains of animals that had died from rabies, consisted of granules of RNA embedded in a matrix of DNA.
VIROLOGY OF RABIES

The rabies virus is the most common rhabdovirus to infect man. Other rhabdoviruses that occasionally infect man include the Lagos bat virus, the Mokola virus, the Duvenhage virus and the European lyssaviruses I + II. Immunisation against rabies gives slight protection against infection with these viruses, with the exception of the Mokola virus.

Rhabdoviruses are readily destroyed by exposure to sunlight and by boiling: they are less easily destroyed by disinfectants.

The virus is excreted in the saliva of infected animals, including man. It is present in the saliva of dogs for up to two days before they exhibit symptoms of the disease.

EPIDEMIOLOGY OF RABIES

Rabies is a cosmopolitan infection. Australia, Antarctica and a few island nations such as Britain are the only countries in which it is not found. At least 100 000 people die each year from rabies, mostly in India and the Far East, in particular Thailand. In the developing countries, domestic and feral animals are the most common reservoirs of infection. Rabies has been eliminated from domestic animals in countries such as North America, so wild animals such as raccoons are reservoirs of infection. In South America, vampire bats transmit rabies to cattle and sometimes man.

Animals vary in their susceptibility to rabies. Wolves and foxes are very susceptible, whereas dogs are less so, though they are responsible for most infections in humans.

PATHOGENESIS OF INFECTION

Though viraemia can be demonstrated in experimental infections, there is no evidence that it is important in the pathogenesis of human disease. The virus disappears rapidly from the site of inoculation, spreading to the brain by retrograde axoplasmic flow through the peripheral nerves. Once it has become established in the brain, it spreads back to the peripheral tissues through the nervous system.

INFECTION IN MAN

Infection usually follows a bite from a domestic or wild animal, though it can occur through the respiratory tract. Speleologists have contracted rabies after exploring caves inhabited by infected bats. A laboratory worker contracted rabies when a flask containing rabies virus broke, releasing viral particles into the atmosphere. However, infection is not inevitable following the bite of a rabid animal.

The incubation period is usually between one and three months, though it can vary from ten days to more than a year. The nearer the bite is to the head, the shorter the incubation period.

At the end of the incubation period, the patient starts to complain of malaise, anorexia and headache, with pain and paraesthesia around the site of the bite. Changes in personality are common. On examination, the patient appears anxious and may have a temperature up to 40°C. Speech gradually becomes impaired. There may be slight neck stiffness, but Kernig’s sign is negative. Muscular tone is altered and convulsions may occur. Retention of urine and constipation are common. The patient often has excessive salivation. Difficulty in swallowing may result in dehydration. Hydrophobia, the old name for rabies, arose from the mistaken belief that the patient was afraid of water. In act it was difficulty in swallowing as a result of muscular spasm that gave the impression of a dislike of drinking. Eventually the patient passes into a coma and dies.

RABIES IN ANIMALS

There are two forms of rabies in mammals, including man. Furious rabies, the most common form, occurs in about 80 per cent of cases. In this form, a usually passive animal becomes aggressive, attacking anything in sight. In the dumb form of the disease, which occurs in about 20 per cent of infections, the animal hides. Dumb rabies is particularly dangerous in wild animals because they are no longer afraid of humans; young children may play with them and subsequently contract the infection.

DIAGNOSIS OF RABIES

Diagnosis on clinical grounds can be difficult, especially if there is no history of an animal bite, or it has occurred several months previously so that the patient has forgotten about it. If convulsions are common, the differential diagnosis will include tetanus and other causes of encephalitis.

The most useful diagnostic test is immunofluorescent staining of a biopsy taken from the skin at the nape of the neck, just above the hairline, as the virus is found in hair follicles.

Techniques using the polymerase chain reaction to detect viral particles are becoming more widely used. They can be done on saliva, cerebrospinal fluid and samples of tissue.

If an animal is thought to have rabies, the head should be sent to a veterinary laboratory equipped to diagnose this infection. Stains can be used to demonstrate Negri bodies in the cells of the hippocampus, a pathognomic feature of this infection.

TREATMENT OF RABIES

Patients with rabies should be barrier-nursed on an intensive care unit, where they will be given symptomatic treatment. The disease is invariably fatal, though a few patients have survived the infection with varying degrees of neurological damage.

In America, Dr R. Willoughby successfully treated a teenager who had rabies, by using drugs to put her into a coma and then administering antiviral agents. It is
too soon to say whether this will become a successful treatment for rabies.

PREVENTION OF RABIES

Pre-exposure prophylaxis

Immunisation using a vaccine made in human diploid cells provokes good immunity against infection. Vaccines in which the virus has been grown in brain tissue are still available in some countries. They should not be used as they can cause severe neurological complications.

Vaccination of visitors to countries in which rabies is endemic is unnecessary unless they are backpacking or visiting remote parts of the country in which there are few or no medical facilities.

Post-exposure prophylaxis

The wound should be thoroughly cleaned with soap and water, and then rinsed with Lotio iodi mitis (tincture of iodine) or a quaternary ammonium compound. Hyperimmune globulin should be administered: half the dose is infiltrated around the wound and the remainder is given by intramuscular injection. The patient should also receive human diploid vaccine.

In the UK, advice can be obtained from an expert on rabies at the Central Public Health Laboratory, Colindale.

If the bite came from a domestic animal, the latter should be kept in quarantine for at least ten days. If the animal remains well at the end of that time, it is unlikely to have rabies.

Declaration of interests

None declared.

REFERENCES


FURTHER READING