Rabies: an old enemy that can be defeated

Human rabies, a zoonotic viral disease, is rare in developed countries but widespread in many parts of the Third World. The virus can affect many wild animals, including the fox. The incidence of rabies in this species has declined markedly in Switzerland and the Federal Republic of Germany since the use of baits containing vaccine was introduced in the 1970s. Bats carrying the virus present a particular threat in countries trying to become or maintain themselves as rabies-free areas. Among domestic animals, the dog is the principal source of rabies in humans. Diagnostic techniques have been greatly improved, and humans as well as animals can be protected with vaccines. Control is possible, and the challenge now is to tackle the disease effectively in the developing countries.

It has been suggested that the first written reference to rabies was in the ninth century BC, when Hector was compared to an enraged dog in Homer’s *Iliad*. By the fourth century BC the works of Aristotle left no doubt that rabies was a topic of the ancient writers, and Celsus, in the first century BC, referred to rabies as “a most wretched disease, in which the sick person is tormented at the same time with thirst and the fear of water, and in which there is but little hope”. As we celebrate the 100th anniversary of the founding of the Pasteur Institute, which was established two years after Louis Pasteur’s historic rabies vaccine treatment of nine-year-old Joseph Meister of Alsace, we have the opportunity to review the present global picture of the disease, to reflect on some of the accomplishments of the recent past, and to look to the future.

Rabies is one of the main zoonotic diseases in many countries. It is caused by a virus which is unique in that death nearly always follows once an animal or human has become clinically ill with the disease. Only three people who have been stricken with rabies have survived. The first was a nine-year-old boy in the USA, who was bitten on the thumb by a bat in 1970, developed symptoms of rabies, yet made a complete recovery. The second was a 45-year-old woman in Argentina who was bitten by a rabid dog in 1972, developed symptoms indicative of rabies, and made a complete recovery after 13 months of intensive therapy. The third, a 32-year-old rabies laboratory worker in the USA, developed clinical signs of rabies in 1977; he survived but unfortunately was left with neurological complications.

In both animals and humans the symptoms include irritability and agitation, often with aggressive behaviour that quickly goes on to
paralysis, coma and death. In animals, the cardinal sign is a change in behaviour so that often a wild animal loses its fear of people, or the mild-mannered domestic animal or timid, elusive wild animal becomes very aggressive.

Although millions of people receive rabies vaccine each year because of exposure to animals known or suspected to be rabid, it remains true that, once clinical illness is apparent, there is no known treatment. Fortunately, vaccines have been developed in recent years do not have to be administered in 14 to 21 daily injections under the skin of the abdomen or back, as the older vaccines do. Instead, only five intramuscular injections, spaced over 28 days, are needed. However, the more recent vaccines, produced in tissue culture cells, are expensive. Investigators are working on vaccine schemes which will reduce even the five-dose schedule, and newer, less expensive, tissue culture vaccines may be on the horizon, offering the prospect that everyone in the world will be able to afford adequate protection.

Global surveillance

National control programmes for any disease rest on surveillance. For a number of years, the World Health Organization has carried out world surveys of rabies, the most recent one being that for 1984–85, in which 112 countries and territories responded to a questionnaire. This is the only instrument available for assessing trends in the global incidence of rabies. In some countries, unfortunately, rabies is not a reportable disease and exact data on human and animal mortality caused by the disease do not exist.

Each region of the world has unique circumstances and differing parameters have to be used for measuring the success of anti-rabies campaigns. One paramount index is the number of cases of human rabies. In the African area there has been an increase in the reported number of human deaths per biennium from 64 to 154 between 1982 and 1985. On the other hand, the Americas have witnessed a decrease in human cases from 247 to 168 during the same period. What do these numbers mean? For Africa, there are reports from 18 countries in 1984–85 and from only 10 in 1982–83. However, the figures for the Americas come from 22 countries in 1984–85 and from 17 in 1982–83, suggesting that the decrease is real. Asia, which for the purpose of the surveys includes much of the eastern Mediterranean region but excludes rabies-free Oceania, has the highest incidence in the world. India alone has an estimated human mortality of 25,000 a year. Europe, like North America, has very few human cases each year, due primarily to the elimination of dog rabies, although wildlife rabies is still present.

Given today’s improved diagnostic techniques and the production of vaccines for both humans and animals, it might be expected that rabies would be under control. In fact the global problem is probably becoming worse.

In Africa, increases in the numbers of cases and expansion of the range of animal rabies are reported from Kenya, Madagascar, Senegal and Uganda. Countries in Asia reporting increased numbers of cases include the Lao People’s Democratic Republic and the Yemen Arab Republic but fortunately there is a reported decrease in Sri Lanka and
the last reported case from Hong Kong was
in August 1984. Only one case of dog rabies
has been reported from the Republic of
Korea.

The Americas have seen various trends.
While wildlife rabies has predominated in
North America in recent years, canine rabies
is the main problem in Central and South
America, as it is in most tropical regions of
the world. In the Americas, vampire bat
rabies makes the disease a potential threat
on even the many rabies-free islands of the
Caribbean. Costa Rica witnessed an increase
in cattle rabies due to vampire bats in 1985.

The wildlife rabies situation has taken some
interesting turns in North America. Raccoon
rabies, previously limited primarily to the
south-eastern United States, has expanded
up the east coast into Maryland and
Pennsylvania. Whereas in the USA the
skunk has, in recent years, been the main
vector of rabies, in Canada this role has
passed from the skunk to the fox and vice
versa from one year to the next.

Europe, like North America, is affected
mainly with wildlife rabies, primarily in the
fox, and this has generated a new control
technique that is proving highly effective.
This involves immunizing wild foxes by
placing rabies vaccine in baits.

Oral vaccination for wild animals

In the early 1970s it was discovered that
foxes could be immunized against rabies by
placing modified live virus vaccine directly
into the mouth. This did not appear to work
in other vectors such as the dog, skunk and
raccoon. Swiss investigators then put liquid
vaccine into capsules that were fixed
between the skull and skin in chicken head
baits, which were successfully used to
vaccinate foxes. Following safety trials on an
island in the River Rhône to assess if the
modified live vaccine would affect other
animals, especially small rodents, field trials
were undertaken. Between 1978 and 1982,
52,000 baits were distributed. There has
been a steady decrease in the incidence of
fox rabies in Switzerland since 1979; the
disease is now largely restricted to the Jura
mountains in the west of the country, where
baiting campaigns are being instituted.

Meanwhile, investigators in the Federal
Republic of Germany developed a “mass
production” oral bait that works very
effectively in the wild. The incidence of fox
rabies has diminished in areas of the country
where vaccination campaigns have been
carried out.

The apparent safety and efficacy of oral
vaccination in the Federal Republic of
Germany and Switzerland has prompted
Austria, Italy, and Luxembourg, among
other European countries, to begin such
campaigns. It is hoped that continuing
efforts will result in the elimination of
wildlife rabies in Europe. However, it
should be noted that a significant decrease
in rabies has occurred in Poland since 1983
and that there have been recent decreases in
Czechoslovakia, the Democratic Republic of
Germany, and Yugoslavia, in the absence of
oral vaccination campaigns. Greece has had
only one case of dog rabies since 1983,
thanks to an extensive campaign against
canine rabies.

Rabies-free areas

Some areas have achieved rabies-free status
by vigorous campaigns of elimination, while
in others the disease has never been
introduced. Geographical boundaries play an
important role here. Water appears to be the
most effective natural barrier to rabies, since
Australia, China (Province of Taiwan),
Control of rabies

Cyprus, Iceland, Ireland, Japan, Malta, New Zealand, the United Kingdom, and the islands of the western Pacific are all free of the disease. The Iberian peninsula and Finland, Norway and Sweden are also rabies-free.

However, the defence of rabies-free status requires great diligence. Some governments have very strict regulations on the importation of live animals, stipulating long quarantine periods in conjunction with vaccination.

The discovery that bats could transmit rabies was made in the early years of the twentieth century in South America. A paralytic disease of cattle was observed to be causing severe economic losses, and eventually it was shown that the animals were suffering from rabies transmitted by vampire bats. These are restricted to Central and South America and to some of the Caribbean islands. In Trinidad between 1929 and 1931, 20 people, predominantly children, died of rabies transmitted by these bats. Most of the cases were in people who slept outdoors and were unaware that they had been bitten.

Most bats are elusive and wary fruit- or insect-eaters that do not normally suck blood. However, in the 1950s it was discovered that such bats could become rabid and then bite people and animals. Subsequent studies have shown that rabies is transmitted widely in the Americas in this way. Recent evidence suggests that rabies may be established in some bat populations in Europe, where, between 1954 and 1984, only 14 bats had been diagnosed as rabid. In 1977 a 15-year-old girl in the USSR died of a rabies-like disease five weeks after being bitten on the finger by a bat.

The virus affecting European bats is not the classical rabies virus but one that is very closely related; it was first isolated in southern Africa. This virus, termed the Duvenhage virus, has been confirmed as a cause of rabies-like disease in over 150 bats in northern Europe between 1984 and 1986 and it caused the deaths of an 11-year-old girl in the USSR and a Finnish biologist in 1985. Fortunately, the European bat virus is so closely related to the classical rabies virus that the vaccines and serum used for the treatment of people bitten by suspectedly rabid animals can be used in persons bitten by bats in Europe.

Although technological advances have made it possible to demonstrate which virus is involved in a suspected bat infection, the similarity of the viruses and the lack of certainty as to whether the rabies-like virus can be naturally transmitted to other animals are matters of paramount importance to regulatory authorities responsible for the control of rabies at the national level. It is interesting to speculate whether the discovery of a bat infected by the Duvenhage virus in the United Kingdom would mean that the long-standing prevention of the reintroduction of rabies into the country would be jeopardized.

Canine rabies

Canine rabies remains the principal concern of the World Health Organization's global rabies programme, because almost all cases of human rabies occur in areas where canine
Dog–bite?
Then here’s what to do

Stimulate bleeding; promptly wash with soapy water

Tie up and observe dog for 10 days

Seek medical advice: if ordered, take injections

If dog remains alive it is free of rabies

If dog dies, rush carcass to diagnostic laboratory

Based on: Guidelines for dog rabies control (WHO document VPH/83.43 Rev.1, 1987) available on request from the Chief, Veterinary Public Health, Division of Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland
rabies persists. Most of the areas concerned lie in the tropics. Surveillance data indicate that south-east Asia has the greatest human mortality attributable to rabies, but the death toll in Africa and South America, although apparently much less, is also a cause for great concern.

It is vital that many of the countries or territories in these regions formulate plans for the elimination of the disease. That this can be achieved has been demonstrated by the Pan American Health Organization’s programme for the elimination of urban rabies in Central and South America by 1990. Many cities in the area have already seen a significant reduction in canine rabies following mass dog vaccination campaigns.

National rabies campaigns should firstly involve education and should go on to surveillance, diagnosis, vaccine production, and dog control. Education should proceed at all levels; its tasks range from inducing a national sense of purpose to teaching villagers that dog bites should be washed immediately, even if no soap or vaccine is available (see figure).

Surveillance and diagnosis are vital, for without knowing the extent of the problem the success of a programme cannot be evaluated. The systems employed should be simple, grass-roots approaches leading to information on the species and numbers of animals involved, and, most importantly, on where and in what numbers people are contracting rabies.

Vaccine production and dog control should be coordinated, since the best way of dealing with the threat from dogs is to vaccinate them. Whether vaccines are locally produced or imported matters less than their delivery to the animal population. Although in some isolated incidents the capture and destruction of large numbers of stray dogs has resulted in a decrease in canine rabies, this is usually an exercise in futility. In order to break the chain of transmission in a density-dependent disease such as rabies, the percentage of dogs that must be removed is very high — some scientists suggest as high as 70%. This necessitates a tremendous amount of labour. Furthermore, in many countries, dogs that appear to be strays are often privately owned or owned and protected by the communities, and mass destruction campaigns are met with hostility. Compounding these problems is the increasing density and mobility of both human and dog populations. Dog populations are no longer restricted to major urban areas but are increasing in rural areas as well.

Clearly, strategies for rabies control must change. The most obvious solution lies in the vaccination of dogs, but this is not an easy task. Research is continuing with a view to producing a potent canine rabies vaccine in quantities and at a price that will assist governments of developing countries. It is necessary to show that the cost benefits of canine vaccination are worth the effort. Preliminary studies carried out in a few developing countries indicate that the cost of vaccinating a dog can be as low as a third of that of catching and destroying it. Even the use of strychnine baits, which is dangerous and often illegal, is no more sparing of labour than is the use of locally produced vaccines. If vaccination campaigns are successful, the destruction of the few truly unwanted or stray dogs is much more easily accomplished with local participation.

Rabies can be controlled, as evidenced by the rarity of human rabies cases in the developed world. The challenge now is to defeat the disease in the developing countries as well. Existing methods of control hold out the prospect of eliminating canine rabies at an affordable price.