The Threat of Rabies

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Britain faces the threat of a reintroduction of rabies. Fox rabies is spreading inexorably across Europe. The increase in cross-channel traffic resulting from Common Market membership seems to invite an accidental invasion, and those misguided sentimentalists, the pet animal smugglers, will continue to break the quarantine regulations despite the more severe penalties recently imposed. During the last 15 months, the deaths of three men in Britain from rabies contracted abroad have reminded us forcibly of the almost inevitably fatal outcome of the disease.

The History of Rabies in Britain

The earliest references to rabies in Britain are in Saxon herbals of the early tenth century which contain many cures for mad dogs and their bites (Fleming, 1872; Shrewsbury, 1952). Discussion of these mythical remedies formed the bulk of the first English book on rabies by Thomas Spackman, published in 1613 (Fig. 1). Dogs were always the main vector of rabies in Britain. There are many accounts of rabies in packs of hunting hounds (e.g. Hopkinson, 1793), the earliest being by Edward, the second Duke of York, in 1430. Lloyd (1976) cites two reports of human rabies following fox bites in 1684 and 1708, and a third possible case of a rabid fox in the late nineteenth century, but there are no other records of rabies in wild animals, apart from some outbreaks in deer near Barnsley in 1856 and in Richmond Park in 1886. The wolf is still an important cause of human rabies in Iran and elsewhere, but no cases were described in Britain before it became extinct in England (early 1400s), Scotland (1680) and Ireland (1770) (Shrewsbury, 1952).

During the second half of the eighteenth century and the nineteenth century mad dogs were reported with increasing frequency, and the number of human deaths from rabies in Britain rose to 74 in 1874. In the 1750s local authorities had attempted to control the disease by ordering that all dogs should be kept indoors for a period during which generous rewards were offered for the shooting of any dogs that escaped the curfew. After a failure to achieve national legislation in 1831, the muzzling of dogs, control of their movements and destruction of strays were still left to local authorities. The Metropolitan Police Act of 1839 and its subsequent amendments allowed policemen to kill dogs that appeared to be rabid. The Rabies Orders of 1887, 1890 and 1897 helped to enforce these measures, and...
the Importation of Dogs Order of 1897 prevented further introduction of rabid animals. In response to these efforts the number of rabid animals dwindled rapidly. After Pasteur’s successful introduction of anti-rabies vaccination with live attenuated virus in 1885, several hundred British people travelled to Paris for the treatment (Barclay, 1958). The last two patients who contracted rabies in this country died in 1902. The eradication of rabies had proved remarkably easy because the infection had been confined to domestic animals, mainly dogs, and had not established itself in a wild animal reservoir.
Rabies was reintroduced to Britain in 1918 when servicemen returned from the war with smuggled dogs. Before the disease was again eliminated in 1922 there had been 328 confirmed cases in domestic animals but none in man or wild animals.

In 1969 and 1970 two imported dogs developed rabies after completing the statutory six months' quarantine period. One of them, called Fritz, was free for 50 minutes on Camberley Common after becoming rabid. Because of the danger that a wild animal had been infected, a shoot was organised in the vicinity.

**THE PRESENT EUROPEAN EPIZOOTIC OF FOX RABIES**

Outside Britain, Europe has known frequent epizootics of fox rabies, recorded since the thirteenth century. Rabies was also common in wolves, badgers, bears and other wild animals. In 1939 there was an outbreak of rabies in foxes and badgers at the Polish-Russian border. Since then, the infection has spread in all directions at a rate of about 20 to 60 km each year, entering Germany in 1947, the Netherlands in 1962, Belgium and Luxembourg in 1966, and France in 1968 (Fig. 2). Wartime relaxation of controls on stray dogs and foxes has been blamed.

![Fig. 2. The progress of fox rabies through France.](image-url)
for the early growth of this epizootic. The red fox (*Vulpes vulpes*) has been the principal vector and victim, but the relatively small overspill into the domestic dog population has accounted for three-quarters of the cases of human exposure to rabies. There have been surprisingly few human deaths: 37 in Germany from 1945-1966 (Stottmeier, 1970), and 38 in Europe, excluding USSR and Turkey, from 1966-1973 (Kauker, 1975); but in the latter period 5.5 million people were given post-exposure anti-rabies vaccination. In 1974, 22 deaths in Europe were reported to the World Health Organisation. Most of the recent deaths have been in Poland, Rumania and Yugoslavia.

Extensive and expensive efforts have been made to halt the progress of the epizootic but, apart from limited successes in Denmark, Holland, and parts of Germany, these have failed. At the present rate of advance, rabies will have reached the English Channel by the early 1980s.

**HOW RABIES MIGHT BE REINTRODUCED TO BRITAIN**

The defence of Britain against rabies relies on a quarantine period for imported animals. Although all species of warm-blooded animals, including birds, are susceptible to rabies infection, only 10 of the 17 mammalian orders are thought sufficiently likely to transmit rabies to require a full six months in quarantine. The two orders of hoofed mammals, including the privileged racehorse, are subject to less stringent regulations. In 1969, 4,000 dogs and 1,000 cats were legally imported and quarantined in Britain. This number is increasing each year. Between 1922 and 1971, 27 animals developed rabies while in quarantine. The development of rabies in two dogs, 10 days and three months after the completion of their six month's quarantine led to a reappraisal of the adequacy of this system (Report of the Committee of Inquiry on Rabies, 1971). Since the incubation period for rabies in dogs is nearly always less than six months, it seems unlikely that rabies could be reintroduced by an animal that had been properly quarantined, especially now that anti-rabies vaccination is given to prevent infection within the quarantine kennels. The smuggled pet animal is the greatest threat. There are between 100 and 200 detected cases each year. Recent prosecutions have been widely publicised and penalties have been increased. In August 1976 two people were imprisoned for four months for smuggling in a dog and two cats. Warnings about Britain’s ban on imported mammals should be displayed at points of embarkation on the Continent. No reliable technique is available for the rapid screening of vehicles for concealed sedated animals.

Airborne invasion by migrant birds or insectivorous bats from Europe (*Myotis myotis*) or even North America (*Lasiurus cinereus*), and the risk of infection by shipborne rats are exciting but very unlikely possibilities.

If rabies were reintroduced into Britain its spread to a wild animal reservoir would pose the greatest obstacle to its eventual eradication.

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CONTROL OF FOX RABIES

Within the rabies enzootic area in Europe up to 86 per cent of the animals affected are foxes. This may be the result of the fox's extreme susceptibility to the virus. The fox is also the principal species responsible for the spread of rabies. At fox population densities of more than one per 250 hectares there seems to be sufficient contact between individuals to support a rabies epizootic. Spread of the disease increases in the late autumn, which is the mating season and the time when young male foxes must leave home and travel up to 46 km in search of a new territory of their own (Lloyd, 1976). The technique of radiotelemetry has been extremely useful in the study of these fox movements.

To offer any hope of success, control measures against fox rabies must be based on an understanding of fox behaviour and ecology. All attempts so far have been aimed at reducing the population density below the critical level in a zone ahead of the advancing epizootic. Achieving this is extremely difficult. Any method has to contend with the fox's fabulous cunning. Traditional techniques such as hunting, trapping, snaring and shooting are useless. A combination of cyanide gassing, strychnine poisoning and shooting was successful in Denmark along a narrow front facing the rabies invasion from Germany, but has failed in France. Contrary to popular belief, foxes spend little time underground. Gassing of earths will be effective only during the period April to June when the vixen is with her cubs. Indiscriminate killing of foxes may have some unexpected results. The fox is a territorial animal, a family group of one dog fox and five or six vixens occupying an area of from 20 to more than 1,000 hectares, depending on available food (D. W. Macdonald, unpublished). Destruction of foxes will encourage outsiders to move in and recolonise the area—the 'vacuum' effect. Anything that increases movement of foxes near the epizootic area will promote the spread of rabies. Shooting and hunting will also help to disperse foxes. In areas where the fox population has been reduced there is an immediate increase in fertility to restore the original population density (Lloyd, 1976). Recent research (D. W. Macdonald, personal communication) suggests that in each family group of foxes only one 'dominant' vixen breeds each year. Killing this vixen might unsuppress the breeding of one or more of her younger and more fertile sister vixens, finally increasing rather than decreasing the population.

Other means of reducing the numbers of foxes are the use of anti-fertility drugs, which is not yet technically possible, and the introduction of another lethal fox disease such as canine distemper or hepatitis. Such ecological tampering could prove disastrous if the introduced infection spread to dogs and other animals.

Epidemics of fox rabies might be prevented if 70 per cent of the fox population in the danger zone could be vaccinated each year. This may sound extremely fanciful, but effective attenuated live virus vaccines have been developed, which can be incorporated into sausage baits and have proved acceptable at least to captive foxes (Winkler and Baer, 1976). Immunity from
rabies might cause an undesirable increase in the numbers of foxes, and the live virus might cause disease if ingested by animals other than foxes. Many practical problems as well as these dangers must be considered before mass immunisation of wild foxes can be contemplated.

When rabies spreads into a new area 20 to 60 per cent of the foxes die of rabies. About 3 per cent of the animals may develop immunity to rabies and survive (Winkler, 1975). The dramatic reduction in population resulting from the disease virtually eradicates rabies until, after three to five years, the numbers of foxes are again adequate for spread of another major epidemic. More rabid foxes seem to be 'dumb' than 'furious' and, unlike rabid dogs, do not wander farther than usual. The behaviour of rabid foxes in the wild will affect spread of the virus to other foxes and to other animals including man, but very little is known about this important subject. Within the endemic area foxes are responsible for most cases of rabies in domestic animals, including cattle and other farm animals, but only 25 per cent of humans who died from rabies had been bitten by foxes (Kauker, 1975). Some people have been attacked and bitten by aggressive rabid foxes, but the confused animal, which is unnaturally tame and appears friendly, is the commoner source of infection.

Once rabies becomes established in a wild animal reservoir, such as the skunk in North America, it is virtually impossible to eradicate it. The Report of the Committee of Inquiry on Rabies (1971) has recommended intensive attempts to reduce fox and other wild animal populations up to a radius of 24 miles from the site of a confirmed case of wild animal rabies. Yet, during centuries of rabies in Britain, the wild animal population was scarcely affected. The reasons for this are unknown. There is no reason to believe that British foxes were inherently resistant to rabies. Perhaps foxes were too scarce in those days. There is some evidence that foxes have increased their numbers and range (Report of the Committee of Inquiry on Rabies, 1971; Lloyd, 1976). From 1750 onwards foxes were actually imported and released for the sake of sportsmen. It seems likely that by the nineteenth century there were adequate numbers of foxes in Britain for an epizootic. Rabbits are a major prey of foxes. The myxomatosis epidemic, which reached its peak in the 1950s, may have forced foxes to invade built-up areas where they can collect worms on suburban lawns, windfall apples in neglected orchards, and do some scavenging around dustbins. This change of habitat could be important in increasing contact between wild foxes and domestic dogs and cats in the event of a rabies epidemic. Now that rabbits have become immune to myxomatosis and are enjoying a population explosion, an accompanying surfeit of foxes may be predicted. Conditions in Britain may now be more favourable for an epizootic of fox rabies than at any time in the past.

Recently it has been argued that all cats and dogs in Britain, and perhaps other domestic animals, should be vaccinated against rabies immediately (Bahmanyar, 1976; Edsall, 1976). A killed-virus vaccine would have to be used because of the
unknown dangers of vaccination with live attenuated virus on such a wide scale. Against this scheme are the enormous expense involved, the difficulties in persuading animal owners to bring their animals for vaccination, of capturing stray animals, the fact that a very large proportion (more than 70 per cent) would need to be vaccinated to make such a campaign effective, and finally the fact that wild animals could not be protected in this way and would still be a susceptible potential reservoir of infection.

RABIES IN MAN
Since 1946 there have been 11 cases of human rabies in Britain. In all cases the infection was acquired abroad (Macrae, 1969; Maton et al., 1976; Cohen et al., 1976; Parker and Mandal, 1976).

Rabies infection usually results from inoculation of virus-laden saliva through the skin by a dog bite. Penetration of intact mucous membranes is also possible. Infection by inhaling virus aerosol is exceedingly rare. Bites by rabid dogs can be extremely disfiguring, especially when children, who are likely to be seized by the face, are the victims (Fig. 3). Bites even by non-rabid dogs are common events. The incidence of dog bites in Liverpool and Sunderland was 500 and 400 (children under the age of 15 years) per 100,000 population per year (Robinson, 1976; Lillington and Ross, 1976). These figures would increase if rabies became endemic in dogs. All dog bites should be vigorously cleaned with soap and water, rinsed with plain water and then irrigated with a 0.1 per cent solution of cetrimide or some other quaternary ammonium compound. The risk of secondary bacterial infection and tetanus should be considered. If there is a risk of rabies,
wounds should be left unsutured and uncovered whenever possible. Assessing the probability of infection and, hence, the need for anti-rabies vaccination and antiserum or human anti-rabies globulin, can be difficult (World Health Organisation, 1973; Corey and Hattwick, 1975), especially when the patient first seeks medical advice on returning to Britain, weeks or months after being bitten in some distant country. Travellers abroad should be advised to ask for medical help locally if they are bitten by an animal. This may allow assessment of the biting animal and, if necessary, the immediate start of post-exposure immunisation. The risk of developing rabies after exposure to infection by a rabid dog or wolf can be reduced approximately tenfold to about 5 per cent by the approved combination of active and passive immunisation (Veeraraghavan, 1968-69; Fathi et al., 1970).

After an incubation period that is usually one to two months but occasionally much longer, rabies presents with a few days of non-specific influenza symptoms and abnormal sensation at the site of the healed bite wound. The more common furious form of the disease is characterised by hydrophobia, which is a response of overwhelming terror, with spasms of the inspiratory and pharyngeal muscles, provoked by attempts to drink or by a variety of other stimuli (Warrell et al., 1976). Episodes of extreme excitation are interspersed with lucid intervals of calm comprehension. Within a few days the patient becomes generally paralysed, lapses into coma, and dies. Common misdiagnoses include psychosis, upper respiratory tract infection, and tetanus (Warrell, 1976). About one-fifth of rabies patients, especially those bitten by rabid vampire bats (Hurst and Pawan, 1931), present with an ascending paralysis with sensory disturbances. Death from bulbar and respiratory paralysis occurs after one to three weeks, a slower and less hectic clinical course than in furious rabies. Paralytic rabies may be confused with post-vaccinal encephalomyelitis (following anti-rabies vaccination), poliomyelitis, and other causes of ascending paralysis.

Rabies is a horrifying disease because its symptoms are mentally and physically agonising and because it is virtually always fatal.

TREATMENT OF RABIES ENCEPHALITIS
Immunisation, antiviral agents, interferon, corticosteroids, and other tested remedies are all useless once rabies virus has invaded the central nervous system. Cardiorespiratory failure, electrolyte disturbances, raised intracranial pressure and convulsions can be prevented by intensive care, which has prolonged the life of patients with proven rabies for up to 133 days after their first symptom (Hattwick and Gregg, 1975). Two patients, with probable rabies diagnosed immunologically, have recovered completely under this regime in the U.S.A. and Argentina (Hattwick et al., 1972; Porras et al., 1976). There have been no further successes. Recent studies have re-emphasised the severity of the encephalitis (Warrell et al., 1976; Maton et al., 1976), but intensive care remains the only known method for...
prolonging the life of rabies patients. The promising results may bring about an increased demand for this treatment by Britons who develop rabies overseas.

PREVENTION OF RABIES
Since the outlook for patients with rabies encephalitis is so hopeless, prevention is the only reasonable approach to the problem. Information about the prevalence of rabies in animals, elimination of stray cats and dogs, vaccination of domestic animals, control of wild animal vectors, and adequate treatment of human patients bitten by animals are essential ingredients in any prevention campaign. Health education is of the utmost importance.

Recently, a vaccine made from virus grown in human fibroblast tissue culture and subsequently inactivated has proved to be highly antigenic in man (Turner et al., 1976). This is called human diploid cell strain vaccine. Unlike the older nervous tissue vaccines its use carries no risk of post-vaccinal (allergic) neuroparalytic complications. This will become the vaccine of choice for pre-exposure vaccination of those people whose occupation places them at particular risk. The staff of a centre designated for the treatment of rabies patients in Britain could be given pre-exposure vaccination against the disease and then look after patients without risk. Vaccination after exposure can never be as effective as pre-exposure vaccination in preventing rabies.

CONCLUSION
Rabies encephalitis in man cannot be cured and so must be prevented. Rabies can be kept out of Britain by enforcing quarantine regulations and preventing the smuggling of pet animals. If rabies were reintroduced there would be a severe risk of the virus becoming established in wild foxes. The traditional methods of dealing with fox rabies should be critically re-examined. They have proved largely unsuccessful in Europe, they are indiscriminate and fail to take into account what is known about fox ecology.

If rabies were to become endemic in Britain, the post-exposure treatment of patients bitten by animals would become a major medical problem. Even if rabies can be kept out, a designated centre is needed for the treatment of imported rabies patients. This unit would be run by a staff fully protected against rabies by pre-exposure vaccination.

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