RABIES

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Office of Health Economics

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Introduction

Rabies, which is traditionally regarded as a mortal condition in humans once the symptoms have developed, is the best known and most feared of all the diseases which may be passed from animals to man. The course of the illness is usually extremely distressing, both physically and psychologically, although modern medicines can now help to relieve the suffering of its victims. Nevertheless there is still no effective cure. Awareness of this underlines the importance of preventive measures like immunisation and the control of rabies transmission amongst both wild and domestic animals. Hence the disease is a subject of considerable international concern to public health authorities.

Yet it is possible to overstate the seriousness of rabies as a world-wide health hazard. In richer areas, such as western Europe and North America, it currently does not cause a significant loss of human life even where it occurs relatively frequently amongst animals. And in developing countries the mortality estimated to be attributable to rabies is small as compared to the burdens imposed by infections such as malaria, tuberculosis or leprosy. Indeed, it may be argued that a major part of the harm caused by rabies stems not from its immediate effects but from the medical, social and economic risks and costs associated with its prevention. These range from the side effects of vaccination to the ecological damage involved in destroying potential vectors in infected areas.

This paper describes the nature and recent history of rabies and current developments in techniques for its prevention in the context of both its direct and indirect costs to the community. It also attempts to establish a balanced picture of the threat that the disease currently presents to the British Isles, which have been rabies-free for over 50 years.

Nature and transmission

Reports to the World Health Organisation, which conducts an annual world survey of rabies, indicate that between 500 and 1,000 people a year die of the condition and that around a million people a year are vaccinated against it, normally after exposure to an animal vector. Yet as the WHO recognises these figures probably understate the true gravity of the situation, particularly in poorer countries such as India where it has been estimated that the total mortality associated with rabies is nearer 15,000 people per annum (Schwabe 1971).

Rabies is a viral infection which affects primarily the nervous system of its hosts. It is probable that all warm blooded animals are susceptible including birds although these are very rarely recorded as vectors. Because rabies usually kills its hosts it is regarded by some authorities as an example of abberent parasitism. This view, however, has been modified in recent years because there is now some evidence that animals may recover from both inapparent and overt rabies infection (Bell 1975).

The effects of the disease on the nervous systems of its hosts are probably essential to its mode of transmission. Their severity induces marked behavioural changes on the part of affected animals. Although in some instances the course of the illness is characterised by withdrawn behaviour followed by paralysis and death ('dumb' rabies) it more typically involves a 'furious' stage in which sick animals show unusual aggression. The Latin word rabies itself derives from the Sanskrit 'rabhas' – to do violence (Steele 1975).

In particular smaller carnivores lose their natural timidity and attack other creatures indiscriminately. Because rabies virus is present in the salivary secretions it is transmitted by bites and scratches inflicted in such circumstances, although very rarely it may be spread by alternative means such as via the respiratory tract or by the ingestion of infected food. There is also a chance that the disease may be contracted if infected saliva comes into contact with a skin abrasion even if no actual bite takes place.

In around half of all human cases rabies affects the nervous system of the sufferer in such a way that violent spasms of the inspiratory muscles, including those of the larynx, attend attempts to drink. These are in themselves terrifying and lead afflicted individuals to show fear of fluids: hence the historical term for the condition of hydrophobia. Air currents fanned across the throats of rabies victims may cause a similar aerophobic reaction which serves as a useful diagnostic test.

5   **Table 1** *Animal susceptibility to rabies*

| | Susceptibility | | |
extremely high	*high*	*moderate*	*low*
foxes	hamsters	dogs	opossums
coyotes	skunks	sheep, goats and horses	
jackals and wolves	raccoons	nonhuman primates	
kangaroo rats	domestic cats		
cotton rats	bats		
common field voles	bobcats		
	mongooses and		
	Viverridae		
	guinea-pigs		
	other rodents		
	rabbits		
	cattle		

Source WHO 1973

The vectors

There were few records of outbreaks of rabies in Europe until the Middle Ages. By the sixteenth century, however, epizootics[1] of canine rabies had become more frequent and by the eighteenth century they were relatively widespread. This history of increasing rabies outbreaks in Europe over the last millennium may be to a degree a result merely of improved recognition and reporting of the illness coupled with an overall greater prevalence in humans as the population grew. But it may also reflect changes in ecological balances largely brought about by man.

Traditionally 'mad dogs' have been thought of as the most common rabies vectors. Certainly it is true that even today dogs are one of the animals most likely to infect humans with the disease, particularly in areas such as India where rabies is enzootic and where there is a large population of strays. Yet it is now known that dogs are not, as Table 1 shows, particularly susceptible to rabies and that the most significant pool of infection throughout most of the world resides in wildlife populations. The significance of domestic animals like dogs and cats in the transmission of rabies to humans is thus to act as a bridge between infected wild animals and man. When this bridge is destroyed by the immunisation and/or strict control of pets the incidence of human rabies falls dramatically, leaving only those cases where

1 An epizootic of a disease in an animal population is the equivalent of an epidemic in humans; similarly the term enzootic refers to a disease permanently present in an animal population in the same way that endemic does to a disease in humans.

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Figure 1 *Human rabies contracted in the United States by species of vector, 1946–73*
Source Hattwick and Gregg 1975

infection is caused by direct contact with wild creatures. This point is illustrated with regard to the United States in Figure 1.

In central and western Europe the red fox is currently the most important rabies vector. This is in part because it appears to be particularly susceptible to the disease compared with dogs or human beings and in part because of its ubiquitous presence, its habits and population dynamics. Because of its small size it may fail to kill many of the creatures it attacks when rabid. Hence the fox is in some ways a more dangerous vector than stronger animals such as wolves because of the greater risk of secondary dissemination.

In other parts of the world a variety of animals including coyotes, rats, vampire bats, skunks and the mongoose all play significant roles in the spread of rabies, some of which are discussed later in this paper.

Rabies strains and related viruses

Until the beginning of this decade rabies virus was generally considered to be a single antigenic 'species'. Differences in infectivity for other hosts have been recorded in strains isolated from bats and arctic foxes, for example, but all are recognised by the body's immune defences in the same way.[2] Thus only one type of vaccine is used.

This concept of antigenic unity is not now accepted (Shope 1975) and there are today four recognised rabies-related viruses, although the distribution of these appears to be confined to sub-Saharan Africa. The significance of these viruses is that in the case of one of them (known as Mokola virus, first isolated in shrews in Nigeria in 1968) there is evidence that it is associated with human illness. This implies that some cases of vaccine failure amongst humans might be due to infection by rabies-like viruses sufficiently dissimilar to true rabies for the vaccine not to give protection.

It is also possible that certain rabies strains or rabies-like viruses could play a long-term role in the disease's natural history by maintaining a pool of infection in a non-overt form. In Europe, for instance, Czechoslovakian researchers have reported a rabies-like virus in rodents (Sodja *et al* 1971).

Although this cannot immediately cause rabies in animals such as foxes it has been suggested that after serial passaging through mice it becomes sufficiently virulent to cause overt disease.

2 Variations in the hazards of bites from different animals stem from differences in the viral challenge associated with them. Thus a wolf bite, which is usually deep and delivers a large 'dose' of virus, is more dangerous than a bite from a smaller animal like a dog.

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Further information is needed but present knowledge points to the possibility that such viruses could act as a 'smouldering reservoir' of inapparent disease which may in certain conditions be triggered into overt rabies (Turner 1973). It is quite likely, for example, that 'virulence *en passage*' could occur naturally. Yet it should be stressed that in rabies-free areas like Scandinavia and Britain there is no record of any apparently spontaneous outbreaks.

Control of epizootics

Strategies for the control of rabies outbreaks vary from region to region depending on the species involved, ecological considerations and social and economic policy restraints. Generally policies are aimed at keeping population densities of wildlife below the critical levels needed for the widespread transmission of rabies, either by wholesale killing in epizootic areas and/or by the creation of protective zones around the foci of infection. Where domestic and farm animals are involved or at risk vaccination coupled with the strict control of stray animals is employed, particularly in the more affluent nations.

The efficacy of mass canine vaccination (pioneered in Japan and the United States in the 1920s) in protecting not only dogs from contracting rabies but also humans from being exposed to the disease and thus needing possibly hazardous prophylactic treatment is illustrated in Figure 2. The data are derived from experience in Memphis, Tennessee when an outbreak of rabies which had been building up for two years reached alarming proportions in the spring of 1948. An intensive canine vaccination campaign succeeded in immunising 23,000 dogs in about a week, although compliance was voluntary and cost owners one dollar per dog.

In countries like the United Kingdom, Japan and Australia which are currently fortunate enough to be rabies-free and to have a water barrier between themselves and infected areas the risk of importation has been effectively limited by stringent quarantine regulations. Certain other nations, like the Netherlands, have to date resisted its entry across land frontiers whilst Denmark provides one of the most successful examples of rabies eradication in recent years. The disease crossed the Danish frontier in February 1964 and progressed northwards until the first months of 1970, despite the measures taken by the Danish veterinary authorities. However, since that time the controls, which included

Figure 2 *Effect on human uptake of rabies prophylaxis of a canine vaccination campaign (Memphis and Shelby County 1948)*
Source   Tierkel et al 1950

Number of persons vaccinated
and animals reported rabid
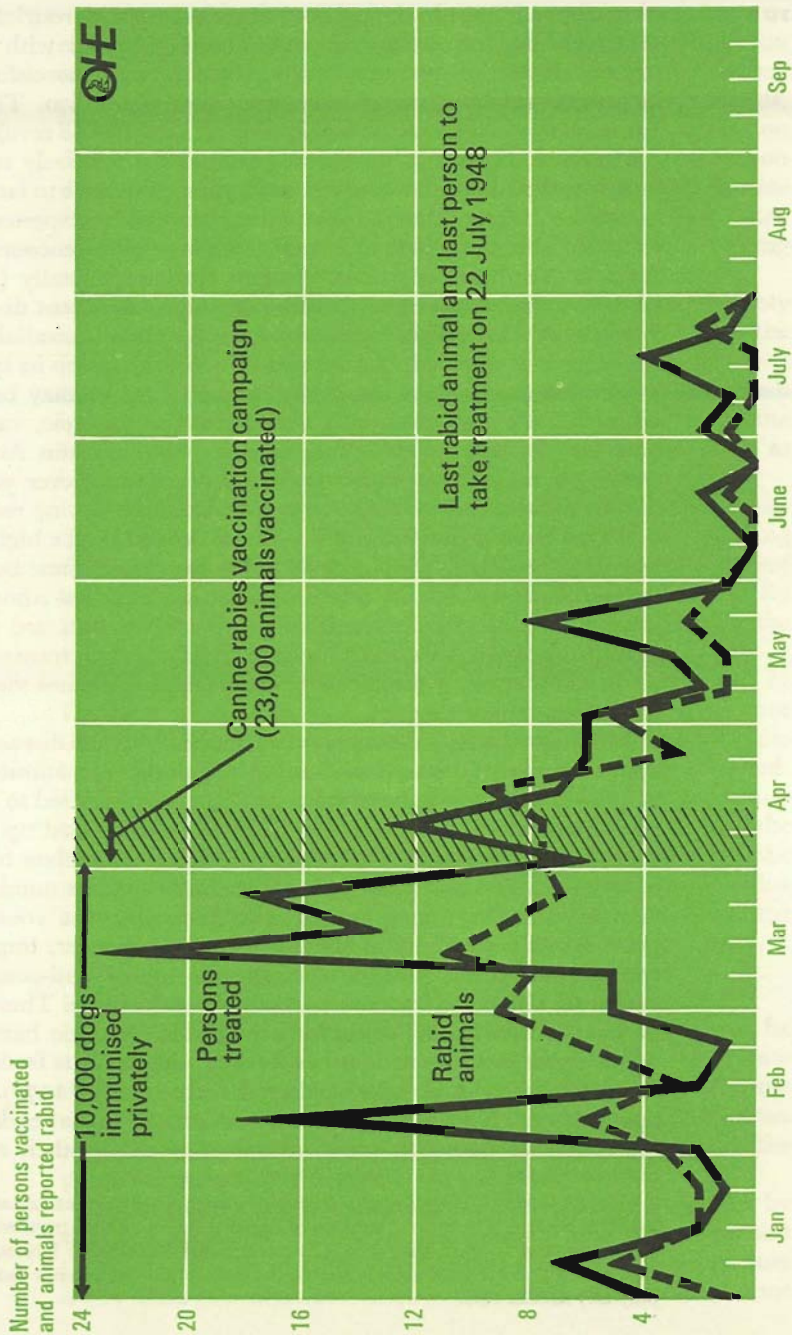
compulsory immunisation of dogs and cats and the restriction of their movements outside controlled areas coupled with other steps such as the gassing of foxes, have proved successful and Denmark has been rabies-free since November 1970. Thus in January 1975 many of the emergency measures were revoked.

However, Denmark has the advantage of a relatively narrow land frontier to 'defend' and did not in the 1960s have to face well established, endemic rabies throughout its wildlife. Experience on continental mainlands under such conditions is less encouraging. Even in North America and Western Europe generally (which have both had to face major rabies epizootics in recent decades) where very considerable resources have been made available for the control of disease it has not proved possible to stop its spread.

In other parts of the world the control of rabies may be even more difficult and potentially expensive. For example, vampire bats are the major vector throughout much of Latin America where bat rabies is estimated to have accounted for over 500,000 cattle deaths a year during the 1960s. Although bovine vaccination may have reduced this toll it is still believed to be high (and largely unreported). Rabies thus inflicts heavy economic burdens on populations which are relatively poor and amongst whom first class protein is often at a premium. Vampire bats are also a significant direct menace to humans to whom they transmit the virus whilst sucking the blood of their sleeping victims via their specially adapted tongues.

Although the bats themselves can succumb to the disease they appear to carry it for a considerable and possibly indefinite time before so doing and may in many respects be considered to be the most 'natural' rabies vectors. In that they usually feed up to ten miles from their roosts (Linhart 1975), which themselves may be in hidden and inaccessible places,[3] limitation of the numbers of vampire bats by searching out and destroying the roosts has proved costly and only of limited efficacy. However, improved control now seems possible through the use of anti-coagulant drugs, to which the bats are particularly vulnerable. These may be injected into cows in doses which do the latter no harm but which cause their blood to prove fatal to vampire bats feeding on them for some days afterwards (Thompson *et al* 1972). This approach also has the advantage of being selective, not endangering beneficial bats with whom vampires may share their roosts.

3 Vampire bat colonies are also relatively small, a further complication for effective control of numbers. Reports of fine droplet or aerosol transmission in bat caves refer to the roosts of non-hemotophagus bats in the United States which may also contract and spread rabies. Bats in Europe are not thought to play any similar role.

It is probable that vampire bats and bat rabies have become more common in Latin America as a result of man's introduction of large numbers of domestic and farm animals. Similar factors played a part in the spread of rabies in some Caribbean islands, like Puerto Rico and Cuba, in that it was human intervention that introduced the mongoose there to control snakes and rats on the sugar plantations. In the late 1940s the mongooses became infected with rabies, perhaps by migrating bats (Bisseru 1972). They now act as vectors and a persistent reservoir of the disease, thriving in an environment where they have no natural competitors.

In Europe the foundations of the present outbreak probably lie in the effects of the Second World War which allowed the fox population to increase rapidly, partly because of reduced hunting. The subsequent ecological effects of post-war European industrialisation and agrarian change have added further to the fox population in that its less adaptable competitors, such as birds of prey, have been adversely affected by them.

Against this changing balance of wildlife population rabies spread across Europe from Poland in the early 1940s reaching the west bank of the Elbe in 1950, the Rhine by 1960 and entering Belgium and Luxembourg in 1967 and France in 1968. By December 1975 it had reached the Côte-d'Or and Jura in the south-east and Oise in the north-west.

The current world distribution of fox rabies is outlined in Figure 3 whilst Figure 4 describes rabies infections in France between 1968 and 1975, showing the numbers of various types of animal reported to be affected by the disease in that period. Figure 5 details the confirmed rabies cases in the United States between 1969 and 1973. Comparison between these and the French statistics underlines the extent to which foxes are the major vector in Europe. The available figures reflect the value of modern vaccines for immunising domestic animals and the need for better means of controlling rabies in other creatures.

Wildlife protection

In cases of isolated introductions of rabies into wildlife it may be argued that the most appropriate response is the immediate slaughter of all animals in the vicinity. This guarantees that the risk of the disease spreading is kept to a minimum and thus serves to protect the wildlife population as a whole as well as the potential human and domestic animal rabies victims.

In the face of rabies epizootics the killing of wild animals by shooting, trapping, poisoning and gassing can sometimes halt the advance of the disease although the value of such techniques is not clear-cut. Examples of successful programmes include one

Figure 3 *World distribution of enzootic fox rabies*
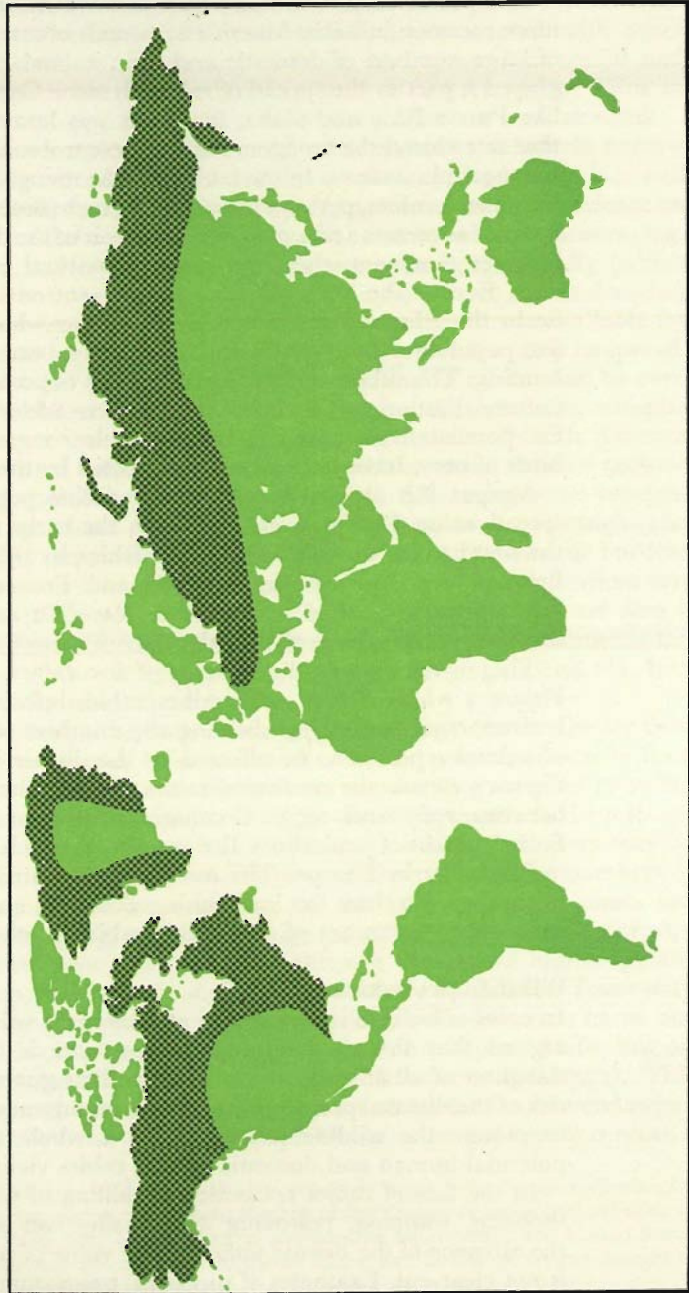*Source* Winkler 1975

Figure 4 *Rabies in France, March 1968 – December 1975 (numbers of confirmed animal cases)*
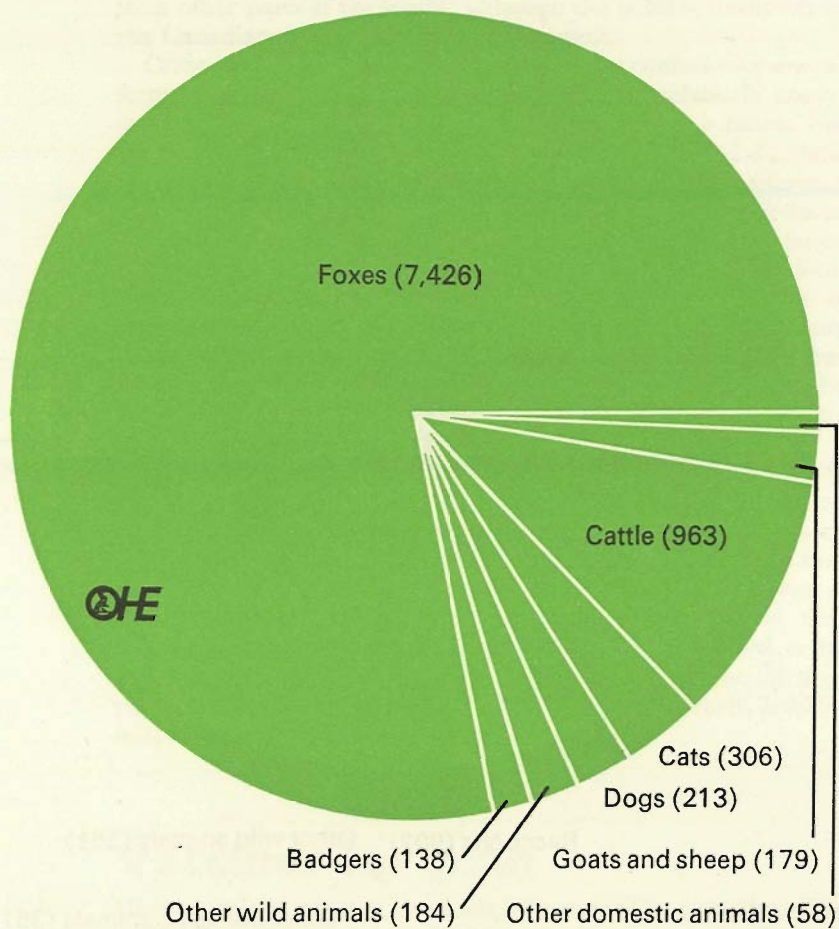*Source* Centre d'etudes sur la rage

Foxes (7,426)

Cattle (963)

OHE

Cats (306)

Dogs (213)

Badgers (138)

Goats and sheep (179)

Other wild animals (184)

Other domestic animals (58)

Figure 5 *Rabies in the United States 1969–73 (number of confirmed animal cases)*

Source   Centre for Disease Control

Skunks (8,355)

Foxes (3,442)

Cats (845)

Dogs (1,088)

OHE

Bats (2,018)   Cattle (1,945)

Raccoons (902)   Other wild animals (361)

Other domestic animals (351)
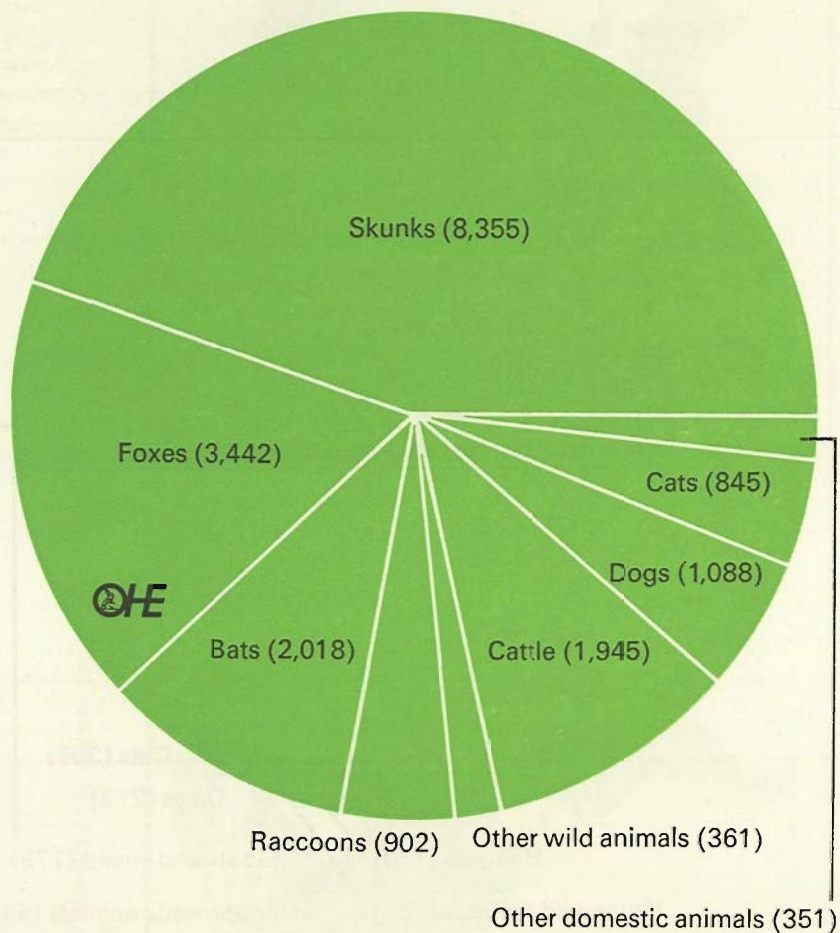
which was credited with the eradication of rabies in southern Alberta in 1952 (Ballantine and O'Donoghue 1954), in which it was estimated that the minimum number of animals killed included 50,000 foxes, 35,000 coyotes, 4,300 wolves, 7,500 lynx, 1,850 bears, 500 skunks, 64 cougar, 1 wolverine and 4 badgers. There are many reports of similar rabies control programmes from other parts of the world, although the wildlife death toll in the Canadian case was higher than in most.

Criticisms of this type of approach to rabies control take several forms. For instance, wildlife extermination is relatively costly, except perhaps in the case of poisoning. But the latter, like trapping, is indiscriminate and endangers humans and domestic animals. Both these techniques may be subject to interference from people who object to them on moral and/or emotional grounds and in the long term any form of wildlife population control based on killing is faced with significant 'public relations' problems. Other considerations include the possible upset of population balances (as happened in Alberta where the moose and deer herds were greatly increased) and also the fact that reductions in the numbers of animals such as foxes may be swiftly made up by increased breeding and survival rates and by migration into population 'vacuums'.

Recognition of these difficulties has led some researchers to look for alternative means for protecting wildlife against rabies. Oral vaccines containing live, attenuated virus have already been shown to be effective in immunising foxes and it is possible that they could be employed via, say, specially treated baits, to protect these and other animals (Baer 1975) provided, of course, that any risks associated with their use can be demonstrated to be acceptable. It is likely that advances in this area, should they prove possible, will be desirable on a direct cost/benefit level as well as from a broad conservationist viewpoint.

Vaccines for man

Human beings are not particularly susceptible to rabies. The probability of contracting the illness varies very markedly with the type of exposure but it may be roughly estimated that on average only 15 per cent of bites from rabid animals result in the development of overt disease in man. Yet even a one in five or one in ten chance of being afflicted with an illness as unpleasant as rabies is of course an alarming one for the individuals immediately concerned.

The only possible protection for exposed individuals before the end of the nineteenth century was prompt bleeding and cleansing of the wound, the value of which probably hinges on the mechanical virtues of vigorous swabbing (Klenerman *et al* 1975). During the 1880s, however, the work of Pasteur made possible more effective protection by immunisation. Although too hazardous for pre-exposure therapy his pioneer vaccine was used in the early treatment of people exposed to rabies. Because the virus spreads slowly in the body a person who has received post-exposure immunisation probably has sufficient time to achieve an adequate immune response, including antibody formation and possibly other immune mechanisms such as cell-mediated immunity and interferon induction.

During the twentieth century numerous attempts to improve rabies vaccine have been made although the available immunising agents are not yet ideal and therapy still centres on dealing with post-exposure crises. Corey and Hattwick (1975) have recently pointed out that in such circumstances there are many factors to be promptly evaluated if the most appropriate possible pattern of treatment is to be achieved. These include the type and circumstances of the exposure, the animal species involved and its role in the local epizootiology of rabies and the treatment alternatives. Figure 6 shows their suggested pattern of decision making for a rational approach to post-exposure rabies prophylaxis.
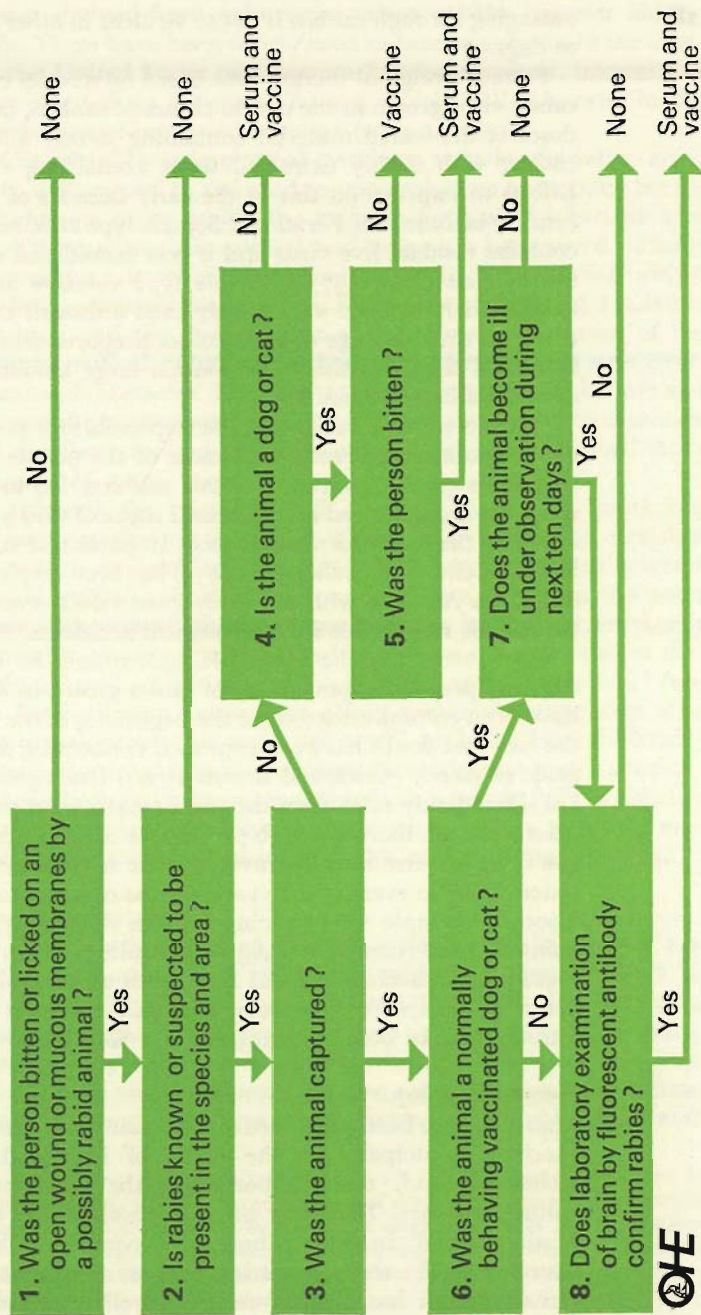
The history of rabies immunisation

The most significant contribution of Pasteur in this sphere does not lie in the immediate value of the vaccine he developed, which is open to some question. In fact it has been argued that up until the Second World War there was little evidence of the efficacy of any of the vaccines in use (Webster 1942) and doubts as to the value of post-exposure prophylaxis with vaccine alone have persisted to the present time.

But what Pasteur unquestionably created was a firm basis for further scientific investigation. It was Pasteur, for example, who postulated that rabies was caused by sub-microscopic microbes which he termed 'viruses' and which he believed flourished in the nervous system of infected animals. He further demonstrated that the 'street' (naturally occurring) virus could be attenuated by 'fixing'[4] it to a certain species. Thus rabies virus subject to serial

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4 The term 'fixed virus' refers to the incubation time of the disease which becomes reduced to a fixed period after the virus is serially passaged through a given species for an adequate period.

Figure 6 *Decision making in post-exposure rabies treatment*
Source Corey and Hattwick 1975

1. Was the person bitten or licked on an open wound or mucous membranes by a possibly rabid animal?

Yes

No → None

2. Is rabies known or suspected to be present in the species and area?

Yes

No → None

3. Was the animal captured?

Yes

No

4. Is the animal a dog or cat?

No → Serum and vaccine

Yes

5. Was the person bitten?

No → Vaccine

Yes → Serum and vaccine

6. Was the animal a normally behaving vaccinated dog or cat?

No

Yes

7. Does the animal become ill under observation during next ten days?

No → None

Yes

No → None

8. Does laboratory examination of brain by fluorescent antibody confirm rabies?

Yes → Serum and vaccine

passaging through rabbits is not so virulent in other animals, such as dogs.

Pasteur's original therapy was based on a series of injections of rabies virus grown in the neural tissues of rabbits, beginning with doses of dessicated material containing mostly killed virus and ending with freshly extracted tissue containing virulent virus. Efforts to improve on this in the early decades of the twentieth century included the Fermi and Semple type vaccines. The former contains residual live virus and is now considered unsuitable for use in man (WHO 1973). Semple type vaccines are completely killed and have been very widely used although they suffer the common disadvantage of all vaccines prepared from rabies virus in neural tissues in that they contain large amounts of myelin-associated host protein.

It is this which is believed to be responsible for potentially fatal encephalomyelitic reactions in some of the people to whom the vaccine is given. Awareness of this problem led to the development of vaccines based on the neural tissue of very young animals in whom the myelin is undeveloped. In particular suckling mouse brain vaccine (Fuenzalida *et al* 1955) has been employed throughout Latin America with relatively good results even though this too can be responsible for neurological accidents.

In countries like the United Kingdom and the United States vaccines prepared from strains of rabies grown in duck embryos have been recommended since the beginning of the 1960s despite the fact that doubt has been expressed concerning their immunogenic efficiency (Crick and Brown 1970). Duck embryo vaccines are significantly safer than the traditional neural tissue preparations although there is a high prevalence of local side effects. The risk of an adverse reaction involving the nervous system is in the order of one in every 30,000 vaccinees as opposed to one in every 2,000 for Semple type vaccine (Rubin *et al* 1973). Yet it was pointed out as recently as 1969 that despite the efforts to improve them rabies vaccines derived from both avian and mammalian neural tissue are 'still the worst biological products ever injected into the human body' (Hummeler and Koprowski 1969).

Recent developments

There has thus been continued research aimed at producing better vaccines, principally in the fields of improved purification techniques and, more importantly, the development of cell culture vaccines. The latter became possible after the success of Kissling (1958) in propagating rabies virus in cultures of non-neural cells. In some countries, such as the Soviet Union and Canada, work has centred on the development of immunising

agents derived from cultures in primary baby hamster kidney cells. These have been widely used in human subjects in the USSR. In the United States and western Europe, however, interest has concentrated on the use of human diploid cell substrates in the production of improved vaccines (HDCS vaccine).

Considerable technological problems exist in the latter area, both with regard to the need to ensure that no potentially harmful changes occur within the cultures (such as the formation of possibly carcinogenic matter) and because it has proved difficult to produce a vaccine of sufficient antigenic concentration within realistic economic parameters. But a combination of academic research and the development and production expertise of the pharmaceutical industry, particularly in France, has now over come such obstacles. The resultant vaccine appears to be safe and powerfully immunogenic, trials in Britain showing it to stimulate an excellent antibody response even when given in small doses (Aoki *et al* 1975).

Although the relatively high cost and theoretical limitations of HDCS vaccine mean that it cannot be considered a complete answer to the problem of rabies immunisation (an ideal vaccine would probably contain only purified antigens from the outer coat of the virus) its advantages over the technology previously available are considerable. Its high immunogenicity means that only a few doses are needed to give satisfactory protection.[5] And its freedom from known side effects means that the range of its legitimate preventive application will probably be considerably greater than that of its predecessors. Nevertheless the new vaccine's suitability for post-exposure prophylaxis is not yet fully established although as yet unpublished data from Germany and Iran may soon help to confirm its value in this context (Turner 1976).

Serum treatment

A further advantage of HDCS vaccine is that its efficacy and safety may also allow vaccinated subjects to donate blood for producing supplies of hyperimmune human antirabies serum. Passive immunisation has since the 1950s been generally recognised to play a key part in the immediate post-exposure treatment of rabies in man, although the first report on this subject dates back to the 1880s. Dramatic confirmation of the value of anti-

5 Previous vaccines have been used much in the manner established by Pasteur, that is to say in large numbers of doses. For example, the normally recommended schedule for duck embryo vaccines involves 14–21 injections. The need for such an approach is, in the light of modern knowledge, questionable even with vaccines less immunogenic than HDCS and there has been a recent trend to modify such schedules.

rabies serum came in 1954 when 29 people were bitten by a rabid wolf in an Iranian village. In a trial conducted under the auspices of the WHO Expert Committee on Rabies some were treated with vaccine alone whilst others received vaccine and serum. Survival amongst these in the latter group was markedly improved (Baltazard *et al* 1955).

Today rabies immune serum is normally infiltrated around serious bites and also injected intramuscularly into the victims. This gives them protection in the period before active immunity to vaccine can be induced, although problems have arisen both because of serum sickness stemming from foreign proteins in serum of non-human origin and also because passive immunisation can suppress active immune responses to vaccine. But the increased availability of human immunoglobulins made possible by the new vaccine coupled with the greater immunogenicity of the latter may well mean that many of the problems associated with the use of immune rabies antiserum can now be overcome more efficiently than in the past.

Hence the research efforts of the past two decades have so improved the available therapies against rabies that in the richer countries of the world it appears likely that in the future everyone exposed to the disease who receives properly controlled, early prophylaxis will survive.

Yet awareness of this achievement should not be allowed to obscure the organisational and economic problems which may restrict people's access to adequate treatment in developing countries. Nor should it detract from the value of efforts aimed at evolving treatments for rabies once it has developed symptomatically; in the recent past there have been two recorded cases of recovery from rabies amongst patients receiving intensive care designed to enable them to survive crises experienced during the illness (*BMJ* Editorial, 3, 1975).

Rabies in Britain

There were outbreaks of rabies throughout Britain during the eighteenth and nineteenth centuries. Attempts to control the disease centred on the destruction of stray dogs, large numbers of which existed in and around the rapidly growing urban areas. However, although such policies met with some local success (as in London in the case of the Metropolitan Streets Act of 1867) there was no effectively co-ordinated national policy and Britain's rabies problem worsened as the twentieth century

approached. In 1874 the reported human death toll reached a peak at 74, despite the fact that Scandinavian countries like Norway and Sweden had already demonstrated that rabies eradication, could be achieved by the regulation of animal movements and the elimination of strays (Bisseru 1972).

In 1887 local authorities were, under the Rabies Order of that year, given extended powers to control the disease. However, they were lax in their enforcement of this legislation (Steele 1975), partly because the practice of muzzling dogs in infected areas was unpopular with much of the dog owning electorate. In 1890 central government took direct control and the numbers of infected dogs began to fall. But in 1892 anti-muzzling feeling amongst the general public led to the restoration of local government control and the disease became more prevalent. In the decade 1889–98 there were over 160 human deaths from rabies.

In 1897 stronger national legislation was brought into effect. As a result rabies was eradicated by 1902. Since that time Britain has remained free of the disease except for one outbreak in 1918 when a rabid dog (or possibly dogs) was smuggled into the country in violation of the quarantine laws, perhaps by a soldier(s) returning home from Europe. It took four years to eradicate the disease again.

In the subsequent half century there have been a number of cases of rabies both in animals and humans who were unfortunate enough to have been infected abroad and whose symptoms became apparent in Britain. The only possibility of infection on home soil occurred at the time of the 'Camberley incident' in 1969, due to cross infection in a quarantine kennel. The incident itself involved an animal in whom the incubation of rabies appeared to take longer than six months, the statutory quarantine period, and it led to a temporary increase in the quarantine time to eight months (since reduced again to six months) and a tightening of the regulations covering kennels.

Concern as to the possibility of importing rabies either from Europe or other parts of the world also promoted more stringent restrictions on the movements of exotic animals as pets and for zoos or laboratory purposes. The value of such regulations is unquestionable as this country's water barrier makes it unlikely that rabies will be transmitted to Britain via wildlife movements. Thus safeguards over the human importation of possible vectors cover the only significant source of danger. In this context it is alarming that in the early 1970s around 200 cases a year of animal smuggling were detected. Increased penalties for such acts under the Rabies (Importation of Dogs, Cats and other Mammals) Order of 1974 (which include unlimited fines, up to one

year's imprisonment and, where necessary, the destruction of illegally imported animals) thus appear fully justified.

Quarantine regulations

Arguments against quarantine for animals entering Britain often appear to be either ill-informed or mischievous, although there may be today some case for suggesting that dogs or cats which can be shown to have been properly immunised by modern vaccines should be allowed some form of preferential treatment. Race horses, it is sometimes pointed out, already enjoy a privileged degree of international movement although the situation in their case is not strictly comparable to that of small domestic pets. For example, their identity (and hence proof of their immunisation) is relatively easy to establish accurately. And even if they do contract rabies horses are not such potentially dangerous vectors of the disease as dogs or cats.

Yet it is interesting to note that Denmark, whose Veterinary Directorate has recently proved very successful in controlling rabies, now only requires a vaccination certificate for dogs or cats accompanying travellers from areas where the disease occurs. The authorities there believe that the development of improved animal vaccines has justified this step.

But in comparing this country with Denmark it should not be forgotten that the latter lacks a water barrier with continental Europe which may increase the difficulty of enforcing strict quarantine regulations and also raises the relative hazard from wildlife importation of rabies.

Current hazards and plans

Some authorities have recently expressed particular fears regarding the risk of rabies entering Britain through animals allowed on shore from small boats harbouring along the south coast of England. The chance of such an occurrence may have increased in recent years because of the growing numbers of privately owned pleasure craft and the provision of yachting marinas.

It has also been suggested that, should rabies establish a foothold in Britain, it may prove harder to eradicate than in the past. This is because it appears that historically wildlife in this country has generally been rabies-free. Even in the Middle Ages there were references to its existence in hounds but not in the game animals they hunted (Cmnd 4696). Yet today the fox population in Britain is larger than before and to a considerable extent the animal's life style has changed to that of an urban, or at least suburban, scavenger. This brings it into closer contact with domestic animals and man.

Figure 7

THE RABIES (Control) ORDER 1974

Place Rules

RABID ANIMALS KNOWN OR SUSPECTED TO BE REPORTED.

ANIMALS TO BE ISOLATED, THEIR DUNG AND BEDDING not TO BE REMOVED.

BANNED TO ALL PERSONS.

INFECTED PLACE TO BE DISINFECTED.

EXIT OF ANIMALS DEAD OR ALIVE IS PROHIBITED.

SIGNS TO BE DISPLAYED.
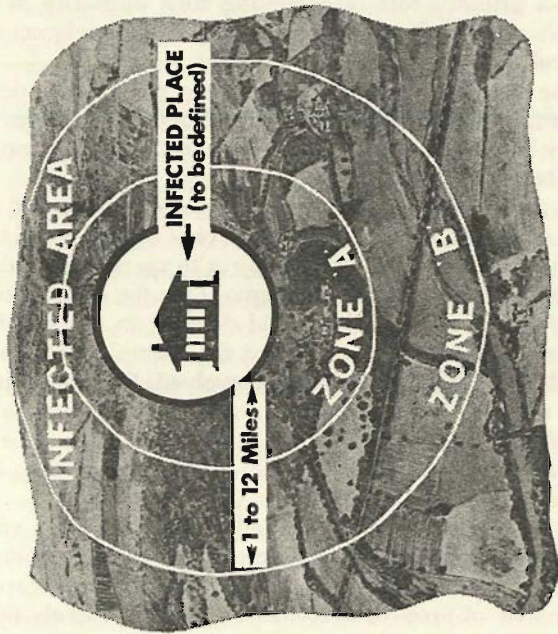
Area Provision

IF NOT UNDER CONTROL ANIMALS TO BE SEIZED.

NO MARKETS OR SALES OF ANIMALS.

FOXES MAY BE DESTROYED AND OTHER DEFINED ANIMALS.

EVERY ANIMAL DEATH TO BE NOTIFIED.

CATS EXERCISED ONLY ON A LEAD.

TRUCKED ANIMALS MAY PASS THROUGH.

EVERY AND ANY ANIMAL MAY BE VACCINATED.

DOGS TO BE ON LEADS AND MUZZLED.

ALL ANIMAL MOVEMENT ON LICENCE except CLOSE-RESTRAINED EXERCISE.

RACING, HUNTING AND SHOOTS BANNED.

EVERY OR SOME CONDITIONS IN EACH ZONE.

AREA TO BE SIGNED.

INFECTED AREA

INFECTED PLACE (to be defined)

ZONE A

ZONE B

◄ 1 to 12 Miles ►

Awareness of the hazards of this situation was largely responsible for the introduction of the Rabies (Control) Order of 1974 and has also led to subsequent efforts to make contingency plans for dealing with rabies in various parts of the country. The 1974 legislation strengthened the Minister of Agriculture's power to intervene in the case of an outbreak, although the Ministry cannot act unilaterally. Local Authorities would necessarily be involved in the administration of contingency plans becasue of their public health role retained after the 1974 NHS reorganisation and their responsibilities as the enforcing agents for Orders made under the Diseases of Animals Act (1950). And in practice the police would play a primary role in exercising such authority as would the health services in protecting the people implementing rabies control measures.[6]

The latter are described in Figure 7, which is derived from explanatory material prepared by officers of the Surrey Constabulary who gained special experience in this field during the 1969 Camberley incident.

As soon as there are grounds to believe that a rabid animal has been identified the premises on which it was kept will be declared an infected place and made subject to special restrictions during the period taken to make a diagnosis. In the event of this proving positive follow-up action would depend on the specific circumstances of the case. It will vary, for example, with the extent to which wildlife may possibly be involved. Generally speaking the next step would be to declare an infected area which again will be subject to special rules, any or all of which may be applied to zones designated within the area. The scope of these is shown in the right-hand side of Figure 7.

In the light of these plans and of the continuing efforts of the Ministry of Agriculture to increase its understanding of rabies hazards (through, for instance, its current research on the behaviour of foxes in mid-Wales) it appears likely that possible outbreaks of the disease would be controlled. However, prompt intervention is clearly desirable and there are some doubts as to whether early co-operation between all the agencies involved in rabies control is assured. Preparedness appears to vary markedly between localities although any part of the UK could be affected at short notice through introduction of the disease by animal smuggling.

6 Vaccines and serum for human protection are available from the PHLS centres in Cardiff, Liverpool, Newcastle and London (Colindale). The latter holds some human serum and cell culture vaccine, although this is not yet licensed for post-exposure use.

Conclusions

Rabies is widely regarded as one of the most terrifying of all illnesses. Death is very probable in man once the symptoms have developed. Despite some encouraging experience in recent years no treatment of the overt disease can be said to offer a reasonable chance of a cure. Hence it is rational for health authorities to regard it with both concern and caution.

But some fears of rabies are exaggerated and may even add to its dangers through encouraging panic or other illogical behaviour amongst people confronted with the threat of the condition. Furthermore they may stimulate or perpetuate primitive terrors regarding other types of ill health, involving symptoms in some ways similar to those of rabies with undesirable consequences.

It is thus to be emphasised that even in the poorer regions of Africa, Asia and Latin America, where health care and allied resources are extremely limited, rabies is only a relatively small threat to human life. The mortality hazard which it presents in richer areas like Europe and North America is still less. Although it is true that even in the latter areas the disease is difficult to control in wildlife the development of efficient vaccines for domestic animals means that the risk of secondary transmission via such creatures from wild animals to man is greatly reduced. As far as overall public health controls are concerned this represents one of the most significant advances in rabies prevention in recent decades.

In addition recent progress in techniques of both passive and active human rabies immunisation means that today virtually everyone receiving prompt and up-to-date prophylactic treatment after exposure will be protected. And the new vaccines derived from human diploid cell substrates offer a much reduced chance of harming or causing pain to vaccinees as compared to their less sophisticated predecessors. They thus provide an outstanding example of the manner in which improved immunological products (or indeed medicines and surgical techniques) may save life not only because of their greater therapeutic efficacy but also of their inherently greater safety. The latter extends the range of employment of vaccination, so allowing a more liberal protective policy for people at special risk. It is also possible that the experiences gained in the production of HDCS rabies vaccines may prove useful to researchers seeking to develop other new forms of immunisation, just as nearly a century ago the first rabies vaccine helped to open up the way to the prevention of many other diseases.

An understanding of the advances in rabies prophylaxis

permits a balanced assessment of the threat that the condition presents to the population of Britain which, unlike many developing countries, is in an economic position to take full advantage of modern immunising techniques should the need arise.

Clearly there is no reason to believe that a rabies outbreak in this country would claim the lives of many, if indeed any, unfortunate human victims. But equally clearly control of the disease would involve considerable economic costs and inconvenience many people in the community. The ecological effects of control measures (not to mention the suffering of infected wildlife) could be at least as serious, if only in that they would reduce the quality of the human environment. Thus although the prospect of a future rabies epizootic in Britain is far less terrifying than such occurrences actually were in the past there are very good reasons for the continuance and strict enforcement of protective regulations such as the quarantining of potential vectors entering this country.

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