Could rabies be eliminated?

How to eradicate a disease

AQA: 3.2.4 Cell recognition and the immune system
Edexcel A: 6 Immunity, infection and forensics
Edexcel B: 6 Microbiology and pathogens
OCR A: 4.1.1 Communicable diseases, disease prevention and the immune system
OCR B: 3.2 Pathogens, immunity and disease control
WJEC Eduqas: Option A Immunology and disease

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Rabies is one of the oldest-known diseases and also one of the deadliest. Here veterinary scientist Sarah Cleaveland reveals the natural history of rabies and the research that has underpinned the global target of achieving zero human rabies deaths by 2030

Key words
Elimination
Epidemiology
Rabies
Vaccination
Zoonosis

Every year, rabies is a death sentence for nearly 60 000 people worldwide, who develop this horrifying disease after being bitten by rabid animals. In most cases, the bite is from a domestic dog, and the people who die come from the poorest communities in Asia and Africa.

Rabies is caused by viruses in the genus *Lyssavirus*, named after Lyssa the Greek goddess of madness and frenzy, and is in the family of *Rhabdoviridae*. The disease has been known for thousands of years, and the link between the bite of a rabid dog and the development of a fatal disease has been recognised since ancient times.

The virus is transmitted in the saliva of a rabid animal (see Figure 1). Curiously the incubation period, defined as the interval from the time when a person is bitten to the onset of clinical signs, is highly variable. It is typically around 1 month, but can last several years. Not all bites result in development of the disease. However, if the virus has made its way to the central nervous system and the disease starts to take hold, it only takes a few days to progress from the early signs, a rather vague, flu-like illness, to death, which is the inevitable outcome. The distinctive and terrifying symptoms, such as hydrophobia (fear of water), aerophobia (fear of a breeze or draught over the skin), aggressive behaviour, convulsions and progressive paralysis, convey an almost gothic horror. It is possible that the disease is the basis for the myths of vampires and zombies.

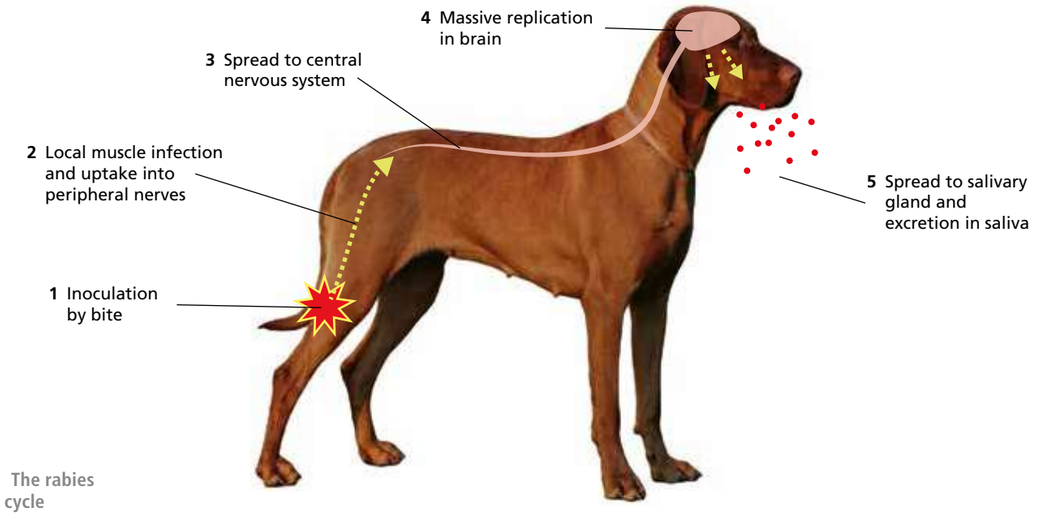


Figure 1 The rabies infection cycle

What is the threat from rabies?

No one should ever die from rabies. Since the time of Louis Pasteur, who developed the first immunisation protocol (see Box 1), we have had excellent vaccines to control and prevent the disease. This can be achieved in two ways.

- The first approach is known as **post-exposure prophylaxis (PEP)**. It prevents rabies developing in people who have been exposed to the rabies virus and is given after the exposure (usually a bite). PEP involves a series of vaccinations, which need to be started within 24 hours of the bite and are given over the course of several weeks through intramuscular or **intradermal injections** in the arm.
- The second approach is based on the **mass vaccination** of the animal **reservoir of infection**. This controls rabies in the animal population and reduces the risk of transmission to people.

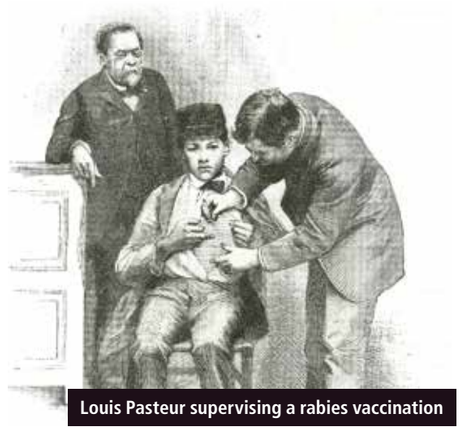
For those of us living in western Europe, rabies is not as much of a threat as it was in the past, largely due to great success in controlling the disease in foxes. In the 1980s, there was a huge campaign to vaccinate foxes against rabies. This involved dropping millions of vaccine-laden baits across huge areas twice a year. It was ambitious, but it worked. Foxes literally took the bait and the disease has now been **eliminated** entirely from western Europe.

Box 1 Vaccination

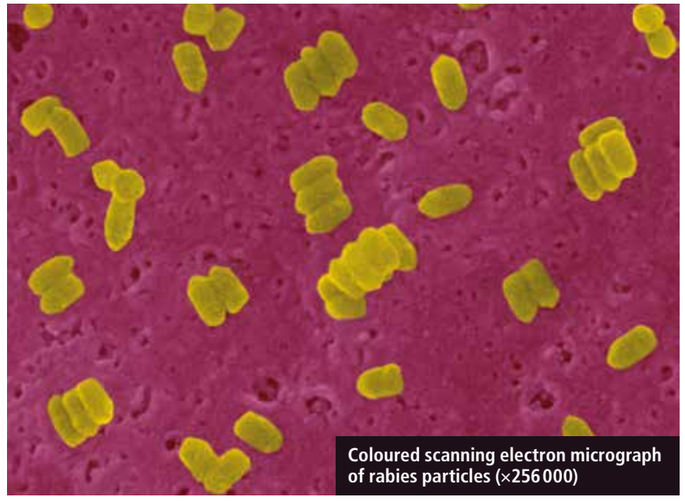
Louis Pasteur (1822–95) was a visionary scientist who took the remarkable first steps towards ridding the world of rabies.

After witnessing the horrifying deaths of several people who were attacked by a rabid wolf in his village, Pasteur held a lifelong fear of and fascination for the disease. Following a series of experiments, he had the brilliant insight that rabies could be treated by a preventive vaccine given *after* the exposure. This is a very different approach from traditional vaccination. It exploits an opportunity to attack the rabies virus during the interval after a person is bitten but before the virus enters the nervous system, where it is protected from the immune response.

It is critical that post-exposure vaccination is started immediately after a person is bitten. Once the virus enters the nervous system it is too late. Pasteur developed a way of producing weakened strains of the rabies virus which stimulated the immune system to attack rabies and, in 1885, he first used the new vaccination technique on a 9-year-old boy, Joseph Meister, who had been severely bitten by a rabid dog. Pasteur administered a course of 12 injections to Meister, and he survived. For the first time, people had a way of combatting this fatal disease.



Louis Pasteur supervising a rabies vaccination



Coloured scanning electron micrograph of rabies particles (×256 000)

Rabies reservoirs

The oral vaccination campaign of foxes was heralded as a major public health success. It demonstrated an important **epidemiological** principle, that if you can control rabies in the reservoir host population, it will disappear from all other species. In western Europe, the reservoir for rabies was the red fox. However, in North America, other wild carnivores, including raccoons, skunks and arctic foxes can sustain rabies as reservoirs. Bats are also an important reservoir for Lyssaviruses and are probably the original ancestral hosts of the rabies virus.

Nevertheless, the most important host species in terms of global public health is the domestic dog. Dogs are the principal reservoir of rabies across Asia, Latin America and Africa, even in areas with abundant wildlife, and by far the most important species in causing human deaths.

Although many mammals can be infected by animals in the reservoir, they cannot all sustain the onward transmission of the virus. This can be explained with reference to the epidemiological term R_0 — the basic reproduction number. This describes the number of new hosts that are, on average, infected by a single infected host (see Box 1). If R_0 is higher than 1 (meaning an infected host transmits the virus to one susceptible host) the chain of transmission will be sustained and the disease will persist. But if R_0 falls below 1, the disease will eventually die out.

Terms explained

Elimination Reduction to zero incidence of infection caused by a specific **pathogen** in a defined geographic area.

Epidemiological Relating to epidemiology: the patterns of diseases in human and animal populations and how they can be controlled.

Eradication Permanent reduction to zero of the worldwide incidence of infection caused by a specific pathogen.

Intradermal injection An injection administered into the skin layers.

Pathogen A microorganism that can cause disease.

Post-exposure prophylaxis A combination of rabies immunoglobulin and rabies vaccine given to people exposed to rabies to prevent the onset of clinical disease.

R_0 Basic reproduction number. The average number of secondary cases caused by a single infected individual in a completely susceptible population.

Reservoir of infection One or more epidemiologically connected populations or environments in which an infection can be permanently maintained and from which infection is transmitted to a defined target population.

Zoonotic A disease that normally exists in animals but that can infect humans.

Why do people still die from rabies?

Although human rabies is entirely preventable, the sad truth is that rabies has not been tackled effectively in many international and national health programmes. This is probably because the disease affects disadvantaged communities, often in rural areas, where rabies deaths may pass unnoticed by policy-makers and health professionals.

There are a number of reasons for this.

- People with rabies often die at home because they are too ill to travel to hospital.
- In some cases, people recognise the futility of treatment and may not seek conventional medical care at health facilities.
- In other cases, rabies is not perceived as a disease, but as a form of witchcraft, which is still widely believed in parts of Africa.
- Despite the distinctive clinical signs, health workers can still misdiagnose rabies, sometimes misinterpreting it as malaria.

Policy-makers will only act if a disease is recognised as a problem, and because only a small number of human deaths are officially reported, rabies has often been considered of little significance. Further, where there are no survivors of rabies, the stories of the victims are not heard, which also contributes to the cycle of neglect.

Recent research has focused on generating more reliable estimates of human deaths, using data collected from health centres on bite injuries inflicted by suspected rabid animals. From this, it is estimated that 59 000 people die from rabies every year, 40% of them under 15 years old.

Rabies incurs a high economic burden because PEP is very costly. Yet even with high expenditure on PEP, deaths still occur in places where people face difficulties in accessing treatment in time, particularly poor people in rural areas. To protect these communities, we need to invest in vaccinating dogs. By tackling the problem at the main animal source, everyone can be protected, both rich and poor. This approach can ultimately result in elimination of the disease.

The terror of dog bites

Although dogs can bite people anywhere in the world, people bitten in rabies-affected areas face huge anxiety, uncertainty and costs, because of the urgent need to seek PEP. Imagine the stark choice of a poor, rural family with a recently acquired puppy that developed rabies and licked or bit every one of the six children in the family. The children's parents could only afford to send one child to the health centre for PEP. Which child should receive the treatment? This is a horrific choice that no parent should have to make.

This is only one example, but worldwide around 30 million people every year receive PEP for potential rabies exposures. Each one of these cases represents a family crisis and a medical emergency.

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www.hoddereducation.co.uk/bioreviewextras

How feasible is rabies elimination?

Total **eradication** of the rabies virus is not feasible because of the circulation of bat species in some areas, such as the Americas. To date, we have no means of effectively vaccinating bats. However, there are several reasons why we believe that it would be feasible to eliminate canine rabies, which causes the vast majority of human deaths from rabies.

There are several criteria that determine whether it might be feasible to eliminate a disease. First, we need to understand the epidemiology of the disease. Infection can only be eliminated if we can disrupt transmission in the reservoir population (to bring R_0 below 1), and have effective tools and strategies to achieve this. Where diseases only affect people, for example smallpox and measles, eradication can be achieved by mass vaccination of the human population. For diseases that are sustained in animal reservoirs, the situation is more challenging. However, we know where to target vaccination to tackle rabies. We have excellent animal vaccines, and we have tried-and-tested delivery strategies.

How many have to be vaccinated?

The number of individuals that need to be vaccinated to disrupt transmission is determined by the value of R_0. The higher the value of R_0, the higher the proportion of individuals in the population that must be vaccinated. As a result of herd immunity, not all individuals have to be vaccinated. Herd immunity was first recognised in the 1930s following childhood measles vaccination, when it was noted that the number of new infections decreased not only in the vaccinated population, but also in unvaccinated children. If herd immunity drops, as occurred recently due to unwarranted concerns around childhood vaccination, measles can rapidly re-emerge, as is being seen in several parts of the world.

In terms of rabies elimination, the good news is that the value of R_0 is relatively low. Indeed it is much lower than for measles, and typically falls between 1.1 and 2.0. This means that dog rabies can be brought under control, at any point in time, if at least 40% of the dog population is immune.

When working out how many dogs need to be vaccinated during an annual campaign, we need also to take into account the rate at which dogs die and puppies are born (the turnover rate). In most areas where canine rabies occurs, dog birth and death rates are both high. In the interval between vaccination campaigns, many new susceptible puppies are born, and some vaccinated (immune) dogs die. Herd immunity will therefore decline progressively until the next campaign is carried out. To ensure that immunity never falls below 40%, at least 70% of dogs must be vaccinated in annual campaigns.

Further reading

Many educational resources are available through the Global Alliance for Rabies Control website: **www.rabiesalliance.org**

The World Health Organization fact sheets on rabies can be found at: **www.tinyurl.com/9cgoh**

A popular science book that has some fascinating insights into the cultural history of rabies: Wasik, B. and Murphy, M. (2012) *Rabid: A Cultural History of the World's Most Diabolical Virus.* Penguin Books.

Herd immunity and measles from the World Health Organization: **www.tinyurl.com/ybnetnpq**

From the BBC on measles vaccination: **www.tinyurl.com/y9ncdwtd**

Can rabies be eliminated?

It may seem as though it would be difficult to vaccinate enough dogs in Africa and Asia because so many of them roam freely around communities. These dogs are often assumed to be strays, without owners, but this is far from the truth. Most dogs have owners and can be handled for vaccination — usually enough to achieve the required level of population immunity.

Disease elimination is never simple, but all the evidence points to the feasibility of eliminating canine rabies and removing this horrifying disease as a global public health concern. The international health agencies have now committed to a target of 2030 for achieving zero human deaths. We know it can be done, but do we have the commitment and will to see it through?

Points for discussion

- Which two infectious diseases have we been able to completely eradicate?
- What other diseases are targets for global eradication?
- Can you think of any other **zoonotic** diseases?

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Key points

- Rabies is one of the world's deadliest diseases. Once a person or animal starts to get sick, there is no treatment or cure.
- Rabies is 100% preventable. Vaccines can control and eliminate disease in animal reservoirs, and post-exposure vaccination can prevent rabies in people bitten by rabid animals.
- More than 99% of human rabies deaths are caused by dogs.
- Dog rabies remains widespread throughout Asia and Africa, but it can be controlled and eliminated through mass dog vaccination.
- The international health agencies have agreed a target date of 2030 for reaching zero human deaths from dog-mediated rabies.