Krebs, C. 2008. The Ecological World View
Univ. of California Press

Chapter 8

NEGATIVE SPECIES INTERACTIONS—INFECTION AND PARASITISM

IN THE NEWS

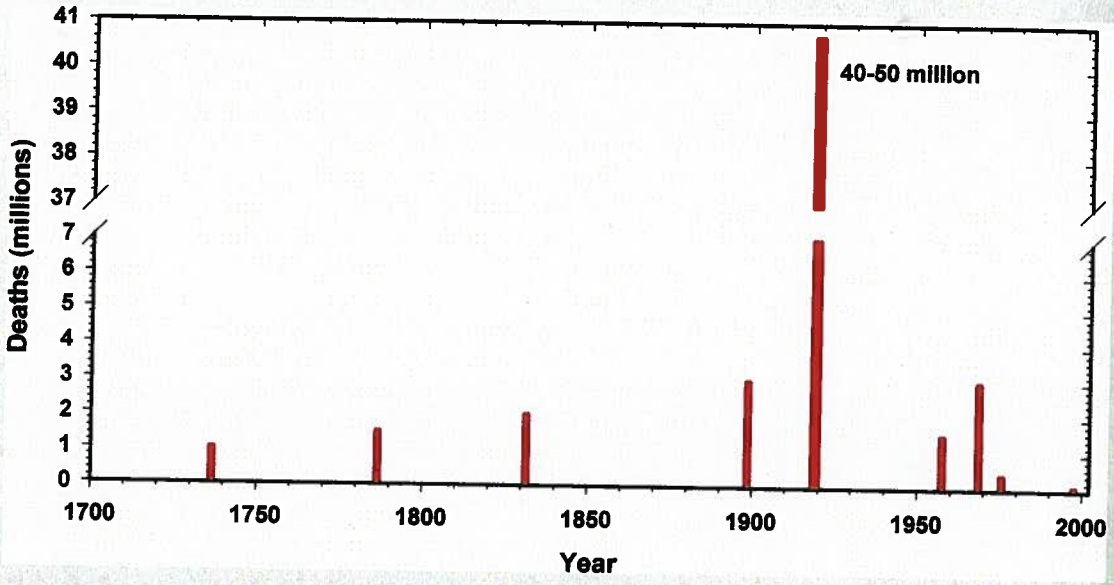
Influenza in its many forms is one of the most common diseases affecting humans each year, and many people underestimate its potential for harm. Avian influenza, or 'bird flu,' is caused by type A strains of the influenza virus. First identified in Italy more than 100 years ago, avian influenza occurs worldwide, and all species of birds are thought to be susceptible to the 15 forms of this virus. However, some birds are more resistant than others. Ducks and geese are the natural reservoir of the avian influenza viruses, but they are also very resistant to the viruses, which produce only a mild illness in them. By contrast, chickens and turkeys are extremely susceptible to bird flu and typically die from the highly pathogenic forms of this virus. Transmission of bird flu virus seems to occur when domestic flocks of chickens or turkeys have contact with waterfowl. Quarantine of infected chicken farms and destruction of exposed flocks are the standard means of preventing spread of the disease.

Because the influenza virus is unstable and genetically labile, a relatively harmless flu virus can mutate into a highly pathogenic virus. That happened during a 1983–1984 outbreak of bird flu in the United States. The subtype H5N2 flu virus, which initially caused a mild disease in chickens, mutated within 6 months to a form that killed 90% of infected chickens. Poultry farmers had to destroy 17 million chickens to end this epidemic.

The global concern is that these lethal bird viruses will cross over and infect humans. Influenza viruses can shift hosts by an exchange of genetic material between two subtypes. For example, the human flu virus in a person could acquire genetic material from the avian strain of the virus in a chicken. Highly pathogenic avian flu viruses can remain infective on farm equipment, cages or clothing, especially when temperatures are low. Pigs can be infected with both avian flu and human flu strains, so they may serve as a medium for the shift of highly pathogenic avian strains into forms that will readily infect humans.

The ability of the flu virus to jump from birds to humans was responsible for the 'Spanish flu' pandemic[1] of 1918–1919, which killed at least 40 million people. Influenza pandemics have occurred every 10–50 years during the last 300 years:

1 A pandemic is an epidemic that affects a large number of individuals on a global scale.



Deaths from influenza pandemics for the past 300 years

Outbreaks in 1957 and 1968 claimed 4.5 million lives. In 1997, chicken flu caused about 6 million birth deaths in Asia and within three days all of Hong Kong's poultry had to be killed. Given the close contact between large numbers of people and domesticated animals in developing countries and the speed of international travel, conditions are now favourable for another major pandemic. However, we do not have the ability to predict where or when new flu virus strains will appear. Vaccination is the major weapon we have against the flu virus, but, because the virus can mutate so rapidly, immunity gained to one strain will not confer immunity against a new strain. Flu vaccines take 4–8 months to produce and are expensive. Consequently, medical response teams are constantly racing to stay ahead of the ever-changing targets for vaccination. Newly emerging diseases such as bird flu are now one of the most pressing medical threats to humans.

CHAPTER 8 OUTLINE

8.1 PATHOGENS AND PARASITES HAVE NEGATIVE IMPACTS ON SPECIES

Dealing with disease resulting from infection has been one of the great preoccupations of humans throughout our recorded history, from the Black Death of the 14th century to the smallpox plague of the 19th century and the Spanish flu pandemic of 1918–1919. Today's scourges include AIDS, drug-resistant tuberculosis, West Nile virus and mad-cow disease. Generations of children succumb to common diseases such as measles, and each winter brings another flu epidemic.

Infection is a negative interaction in which a pathogen (disease-causing agent) lives on or in a host organism, to the benefit of the pathogen and the detriment of the host. Pathogens include microorganisms, such as some bacteria and fungi, as well as viruses and prions (protein bodies), which are non-living. Parasitism has much in common with infection as a negative biotic interaction, but it differs from infection mainly because parasites are often large, multicellular organisms, such as tapeworms. Large parasites are called **macroparasites.** Some parasites, such as the spirochete bacteria that cause syphilis, are also pathogens. Pathogenic microorganisms are called **microparasites.**

The **virulence** of a pathogen depends on the intensity of the disease it causes and is measured by host mortality. Although people are often very concerned about the lethal effects of pathogens and parasites, the **sublethal effects**—any effects that reduce well-being without causing death—are probably more important for plants and animals in ecological settings. Infected or parasitized animals may produce fewer offspring, be captured more easily by predators, or be less tolerant of temperature extremes. Infection and parasitism can thus interact with competition and predation in affecting population dynamics. Almost every individual plant and animal harbors both pathogens and parasites.

8.2 COMPARTMENT MODELS ARE USEFUL FOR ANALYZING HOW DISEASES AFFECT POPULATIONS

One way to begin to understand a disease is to build a simple model that describes how the disease spreads

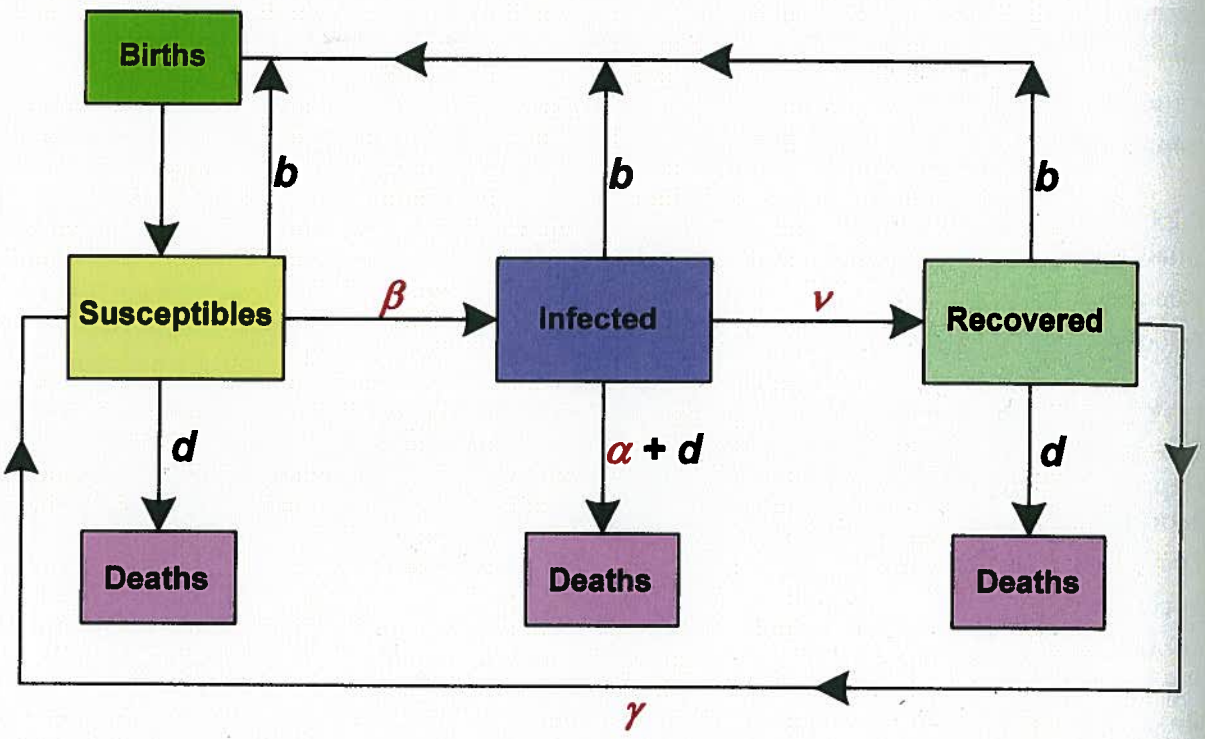


Figure 8.1. Compartment model for a directly transmitted microparasitic disease such as syphilis. Each box represents a number of individuals and, in each time step in which the model is run, individuals move between the boxes at the rates given by the symbols alongside the arrows. (Modified from Anderson and May 1979.)

among individuals and what happens to individuals that become infected. Many types of models have been used in the study of disease. **Compartment models** are box-and-arrow models that show simplified population dynamics, and they are a good starting point for learning to think about epidemics. The boxes in these models represent groups of individuals in the population, and the arrows represent the movements of individuals from one group to another (Figure 8.1). For example, a susceptible individual may move into the infected category if it contracts the disease, or an infected individual may die or recover from the disease. In their simplest form, compartment models assume a constant host population, and because this assumption is valid for the human population in the short term, these models have been used extensively for exploring human diseases.

Parameters of Compartment Models

We will use microparasites that are directly transmitted between hosts and that reproduce within the host to illustrate a compartment model. Microparasites have short generation times and thus have very high reproduction rates. Hosts that recover from infections typically acquire some immunity against reinfection, sometimes for life. In many cases, the duration of the infection is short relative to the lifespan of the host.

For microparasitic infections, we can divide the host population into three groups of individuals: susceptible, infected and recovered. As shown in Figure 8.1, the host population has a natural birth rate (b) and death rate (d). The rates of four processes determine the progression of a disease caused by a microparasitic infection:

1. the rates at which infected individuals die from the disease (α)
2. the rates at which infected individuals recover from the disease (ν)
3. the rate of transmission between infected and susceptible individuals (β)
4. the rate at which recovered individuals lose their immunity to the disease (γ).

This model is relatively simple because it does not consider the abundance of the microparasite in the host (individuals are either infected or not infected) or

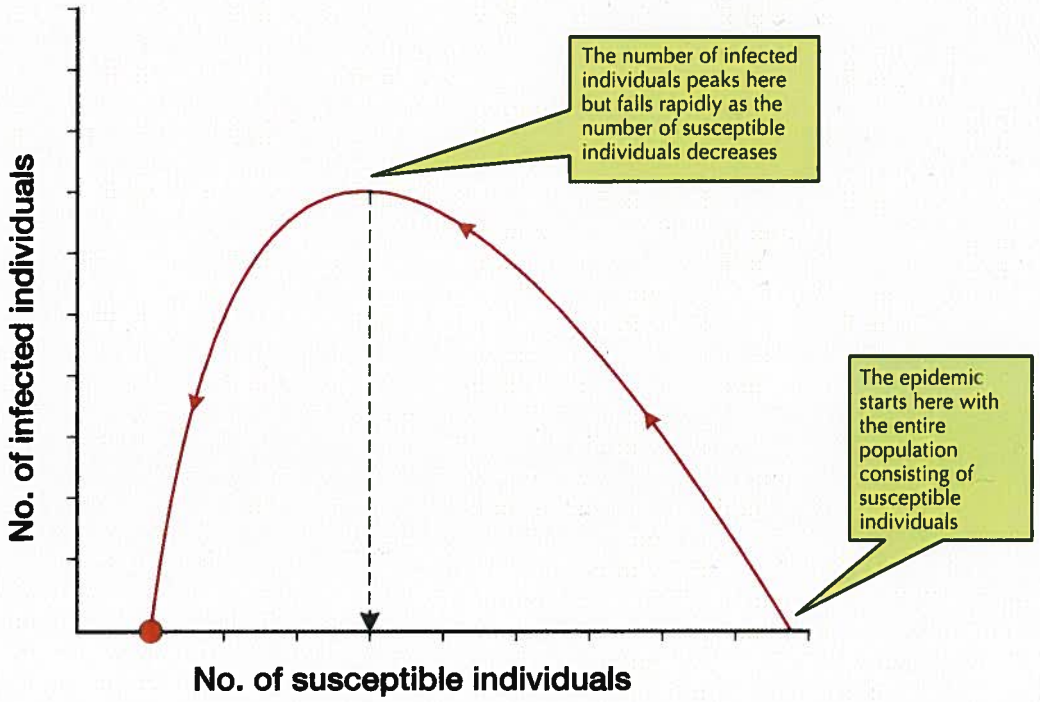


Figure 8.2. Trajectory for an epidemic described by the compartment model in Figure 8.1. The number of infected individuals rises to a peak and then falls to zero at the threshold of transmission (red dot). (Modified after Heesterbeek and Roberts 1995.)

variations in host susceptibility due to genetic or nutritional differences.

Q How would a compartment model for macroparasites differ from that shown in Figure 8.1 for microparasites?

Compartment models are useful for answering questions about the stability of the host–microparasite interaction. Will the disease persist in a population or will it disappear? How do the proportions of susceptible and infected individuals change as the disease moves through a population? The answers to these important questions are the keys to understanding the effects of disease in populations.

Epidemics

The general course of an epidemic described by a simple compartment model is shown in Figure 8.2. An epidemic spreads through a population until the number of susceptible individuals falls below a threshold of transmission. At the threshold, the susceptible population becomes so small that it is unlikely an infected individual will contact a susceptible individual. Individuals can become immune to the disease, or die from it, as the epidemic progresses. In populations that are growing due to births or immigration, the disease may persist as new susceptible individuals come into the population.

Culling and vaccination are two methods for reducing the size of the susceptible population below the threshold of transmission. The more transmissible a pathogen or parasite is, the higher the fraction of individuals in a population that must be culled or vaccinated to prevent an epidemic. For example, the virus that causes German measles is highly transmissible among children, and a vaccination rate of 95% is needed to prevent an epidemic of this disease.

Q Which method—culling or vaccination—would be preferable for preventing an epidemic in a wild population of animals?

Simple compartment models can be elaborated upon to account for the specific details of different diseases. We turn now from these models to consider the

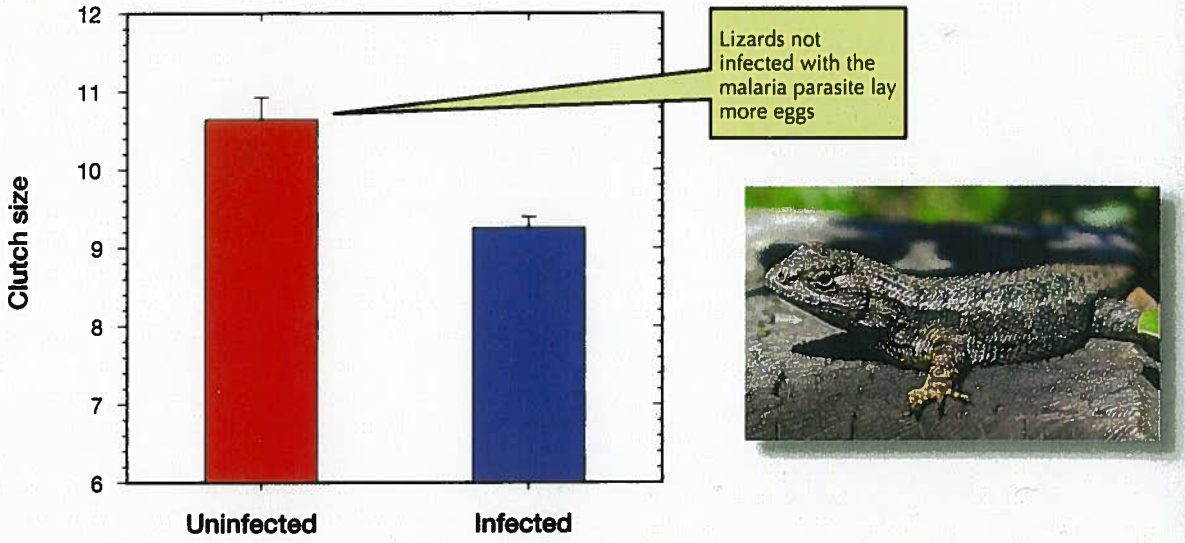


Figure 8.3. Effect of lizard malaria on clutch size in western fence lizards from 1978 to 1982. (Data from Schall 1983, photo courtesy of Bob Dyer.)

impacts that pathogens and parasites have on individual plants and animals and on populations.

■ 8.3 PATHOGENS AND PARASITES AFFECT INDIVIDUAL ORGANISMS BY REDUCING REPRODUCTIVE OUTPUT AND INCREASING MORTALITY

Individual hosts are like islands or patches of habitat that must be colonized by pathogens or parasites if a disease is to spread. Much more is known about the impact of infection and parasitism on domestic animals and humans than about their impact on wild animals and plants. One reason few studies on this topic have been carried out in the wild is that many biologists have assumed that evolution causes pathogens and parasites to become relatively harmless to their hosts, and so we would not expect infection and parasitism to have severe impacts on wild organisms. But this assumption is probably not correct—an increasing number of studies are finding that parasites and infections have significant effects on the reproduction, survival and growth of organisms.

Effects on Reproduction

Because food is not unlimited and most organisms have a limited amount of energy available, it is not surprising to find that pathogens and parasites can reduce reproductive output. For example, about 25% of western fence lizards (*Sceloporus occidentalis*) in California are infected with *Plasmodium mexicanum*—the parasite that causes lizard malaria. Malaria-infected lizards lay clutches of eggs that are about 20% smaller than those produced by uninfected lizards (Figure 8.3). Infected lizards store less fat in the summer and therefore have less energy available the following spring to produce eggs.

Effects on Mortality

Bird chicks are often attacked by parasites and, if parasite infestation is severe, the chicks may die in the nest. For example, ticks may reduce chick survival by causing blood loss and by transmitting pathogens. One study on a colony of cattle egrets in Queensland, Australia, found that chicks infested with ticks (*Argas robertsi*) grew more slowly and were more likely to die than those without ticks (Figure 8.4). The degree of tick infestation was sensitive to fluctuations in the tick population due to environmental factors. In the 1991–1992 breeding season, tick infestations were severe—an average of 24 ticks per chick—and chick mortality was significant. During the 1992–1993 breeding season, however, rainfall was low and ticks did not survive well. There were fewer ticks (an average of 5 per chick) that season, and chick mortality was much lower. This type of result is common in studies of parasitic diseases,

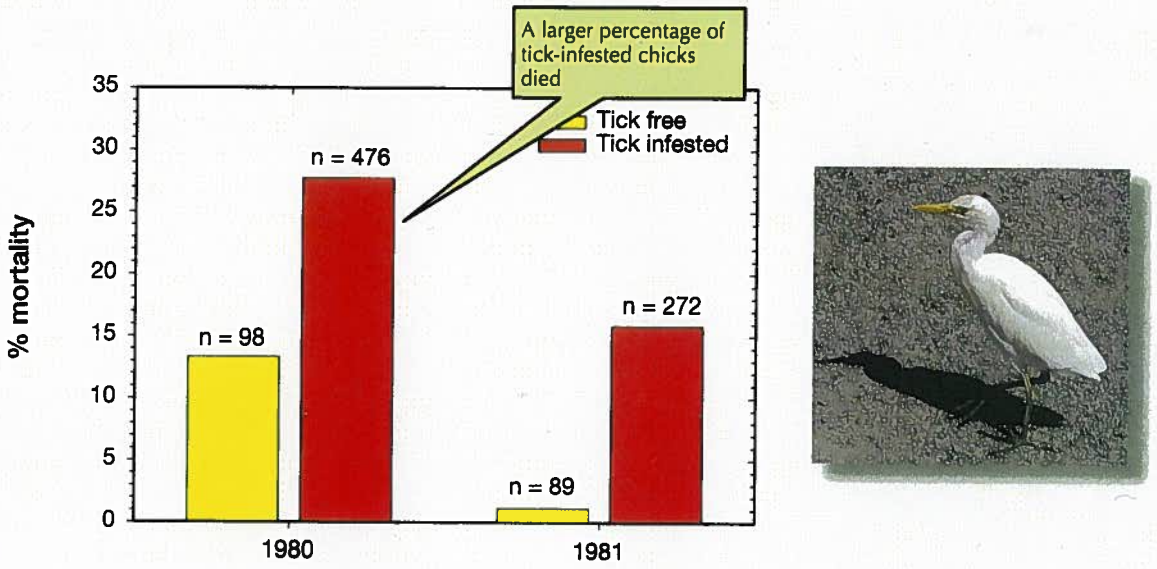
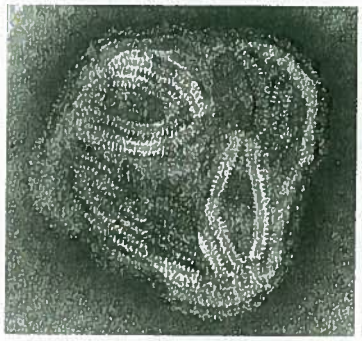


Figure 8.4. Effect of tick infestation on mortality of cattle egret (*Bubulcus ibis*) nestlings in Queensland during two breeding seasons. The numbers of chicks studied are given above the bars. (Data from McKilligan 1987, photo courtesy of David Cook.)

which may have strong effects on host populations in some years and insignificant effects in others.

No one doubts that diseases kill animals, and numerous veterinary examinations of dead animals have suggested that a parasite or pathogen was the immediate cause of death. However, a population ecologist needs to know more. What fraction of mortality in a population is caused by disease? To answer this question, we must examine disease outbreaks in natural populations.



A paramyxovirus similar to the phocine distemper virus. The ribonucleoprotein capsid has a 'herring-bone' appearance. These viruses are single-stranded RNA viruses. This family includes the viruses that cause measles and mumps in humans.

In the spring of 1988, harbor seals (*Phoca vitulina*) in the North Sea began to die in large numbers. Dead seals were first noticed in the waters between Denmark and Sweden, but within a few months they were found near the Netherlands, Great Britain, and Ireland (Figure 8.5). Harbor seals are distributed throughout the North Atlantic and North Pacific, and before 1988 there were approximately 50,000 harbor seals in European waters. The massive epidemic in 1988 claimed an estimated 60% of the harbor seal population in the Baltic Sea, and the deaths accumulated very rapidly (Figure 8.6). The cause of the deaths was not clear initially, but a virus was suspected because the dying seals showed symptoms—including aborted pregnancies—similar to those of canine distemper—a viral disease. Eventually, the causative agent was indeed identified as a virus similar to canine distemper virus; it was named phocine distemper virus (PDV). Within 2 weeks of infection by the virus, seals developed symptoms and typically died of pneumonia and associated secondary bacterial and viral infections.

The incidence of infection for this epidemic could not be measured directly, but indirect estimates suggest that that 95% of the harbor seals in the North Sea were infected with the virus. Deaths from PDV seemed

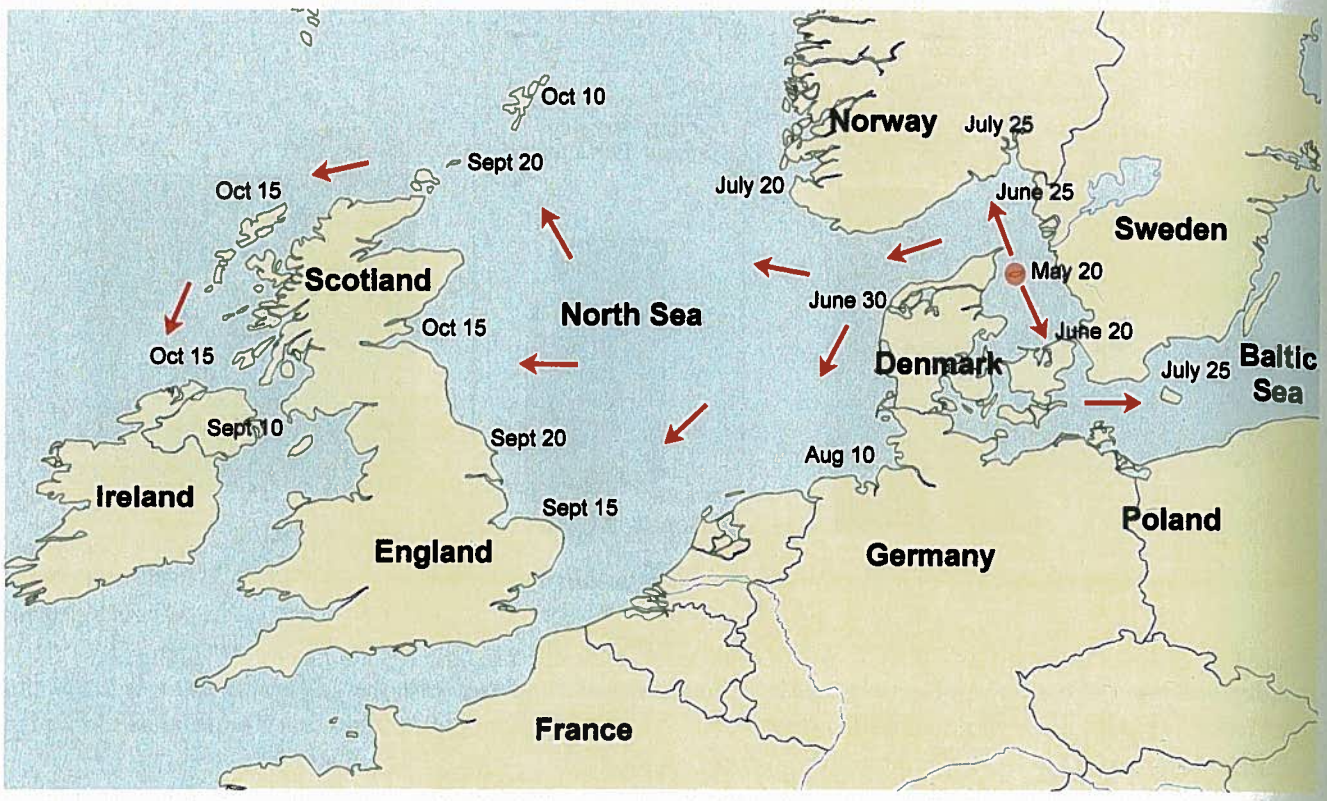


Figure 8.5. Map of the spread of harbor seal deaths in the North Atlantic in 1988. These deaths were part of the first well-documented epidemic among free-ranging marine mammals. (Data from Swinton *et al.* 1998.)

to be more common in males than females, although both sexes were infected. The disease spread so rapidly that dispersal of infected seals between colonies must have been frequent. Small colonies were as likely to become infected as large colonies, and the main predictor of a colony's chance of becoming infected was its proximity to other colonies. Harbor seal colonies in northern Norway and Iceland escaped the epidemic, presumably because no infected seals dispersed to these distant colonies.

Could this viral disease persist in the harbor seal population? Infected individuals that recover are immune for life, but, because births occur each year, there is a continual source of susceptible seals in the population. In the Baltic Sea, pups constitute about 20–22% of the harbor seal population. Using this information, ecologists constructed a compartment model of the 1988 epidemic, which showed that PDV could not be maintained in harbor seal populations as a persistent infection. Then how did the disease originate in the North Sea harbor seals in 1988? It may have been introduced by another species of seal—the harp seal (*Phoca groenlandica*)— in which the virus causes a relatively innocuous disease. Harp seals are normally rare in southern waters, but in 1987 and 1988 harp seals moved south in large numbers from northern Norway into the North Sea. PDV may have crossed species boundaries at this time, triggering the 1988 epidemic among the more susceptible harbor seal population.

Despite the large number of harbor seal deaths in 1988, the harbor seal populations of Western Europe were only temporarily affected and quickly returned to their former numbers. Another less severe epidemic reduced the harbor seal population in the North Sea in 2002. The seal epidemics of 1988 and 2002 raise the general question of how often a disease can exert a long-term effect on a population—a question we turn to next.

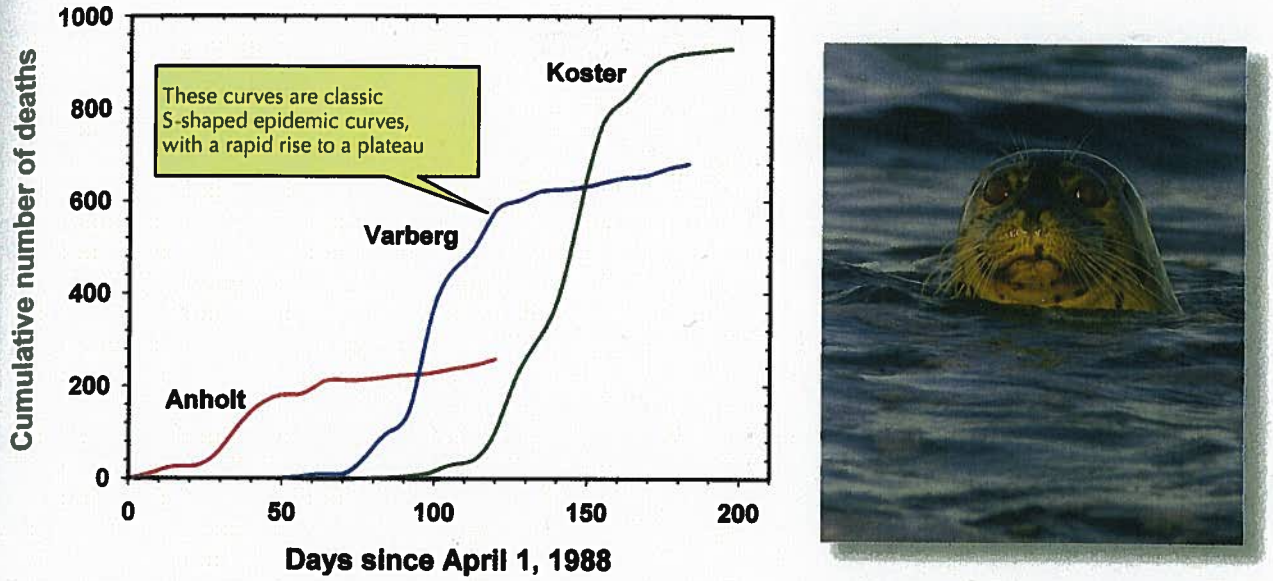


Figure 8.6. Cumulative number of harbor seal deaths in three colonies between Denmark and Sweden in 1988. The epidemic started at the small Anholt colony in April, at the larger Varberg colony in mid-May and at the Swedish Koster colony in late June. On average, an estimated 60% of the seals died in each colony. (Data from Heide-Jørgensen and Härkönen 1992, photo courtesy of Tom Grey.)

8.4 DISEASES CAN REDUCE POPULATIONS

There are few studies of plant or animal diseases in which the history of each individual in a closely monitored population is known. Most often the available data are estimates of seroprevalence—the percentage of individuals in a population that have antibodies to a particular pathogen. Seroprevalence measures how widespread a disease has been in a population in the recent past. Consequently, the impact of a disease on a population is usually not well understood. Three examples illustrate the range of problems ecologists face when they try to measure the population impacts of disease.

Brucellosis in Ungulates

Brucellosis is a highly contagious disease of ungulates (hoofed mammals) caused by the bacterium *Brucella abortus*. The disease is prevalent in cattle throughout the world and, because it manifests itself in pregnant females by causing abortion, it is commonly called 'contagious abortion'. The livestock industry has made a huge effort to eradicate brucellosis, but the disease persists in the western United States in wild populations of bison and elk, which can transmit it back to domestic cattle. Transmission occurs most readily through exposure to an aborted fetus or other birth materials. As Figure 8.7a shows, about 50–60% of adult bison in Yellowstone National Park have antibodies to *Brucella*, indicating that they must have had the disease and have become immune. There is considerable controversy over whether brucellosis is a native disease of bison or was introduced into North America by cattle (it is most likely that brucellosis was not present in bison before 1917 and was contracted from domestic cattle).

Q Could social organization in herding animals affect disease transmission rates?

Andy Dobson and Mary Meagher constructed a simple model of the spread of brucellosis through bison populations to determine whether the disease could be eliminated by a culling program. Brucellosis has a sharply defined threshold of transmission equal to about 200 bison, above which the proportion of

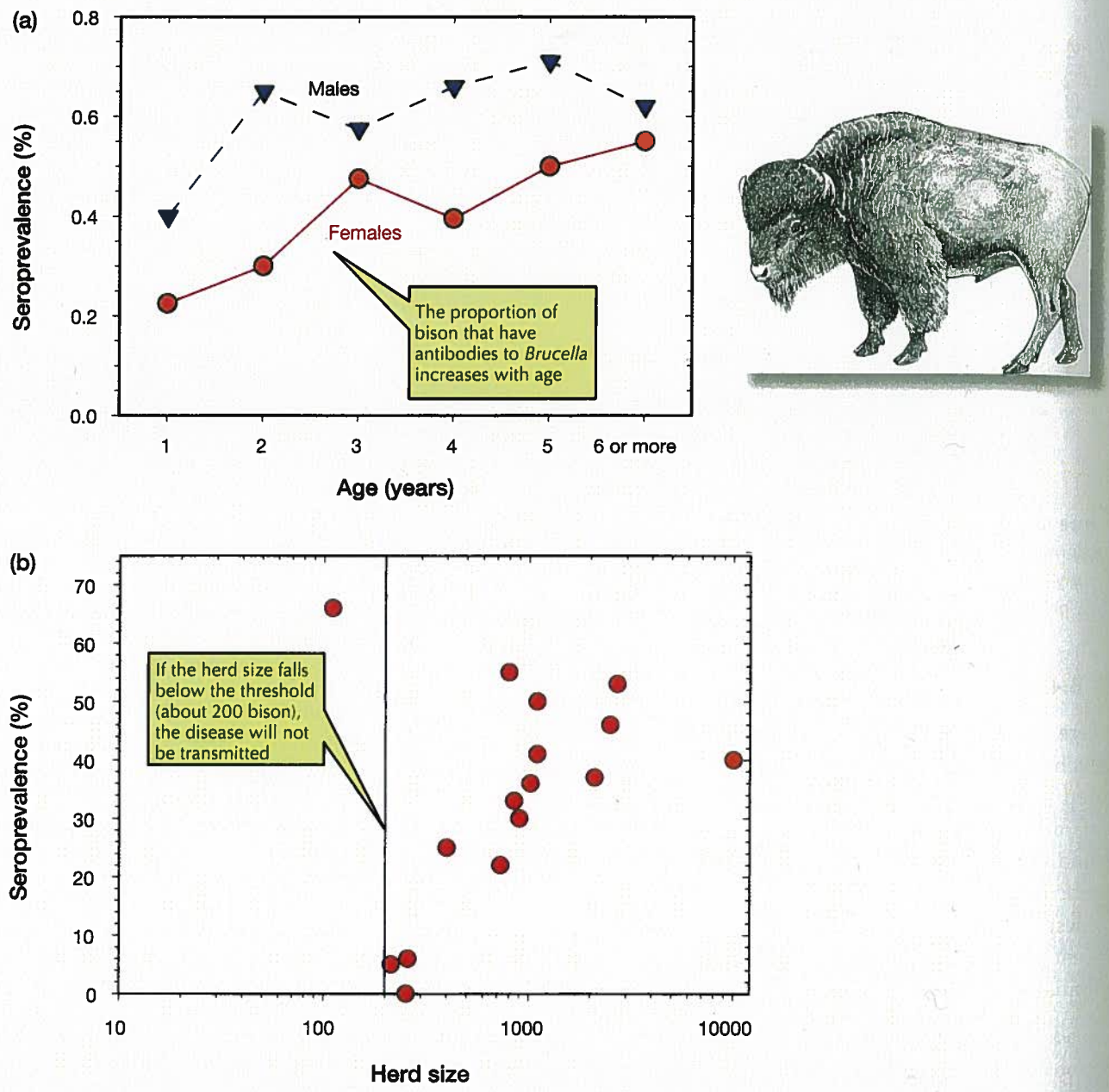


Figure 8.7. Brucellosis in bison as measured by seroprevalence. (a) Relationship between seroprevalence and age of male and female bison in Yellowstone National Park in the winter of 1990–1991. (Data from Pac and Frey 1991.) (b) Relationship between seroprevalence and size of bison herds in six national parks in Canada and the western United States. (After Dobson and Meagher 1996.)

infected individuals rises smoothly with population size (Figure 8.7b). There are now about 4,000 bison in Yellowstone National Park. While it would be possible to reduce the population to 200 through culling, doing so would put Yellowstone bison in danger of extinction and would undoubtedly be very unpopular. Therefore, it is unlikely that culling will be a viable strategy for eliminating brucellosis in Yellowstone bison. An alternative strategy—vaccination—works well in cattle, but is not very effective in bison.

Brucellosis reduces the growth rate of bison populations, and herds with brucellosis are smaller than herds

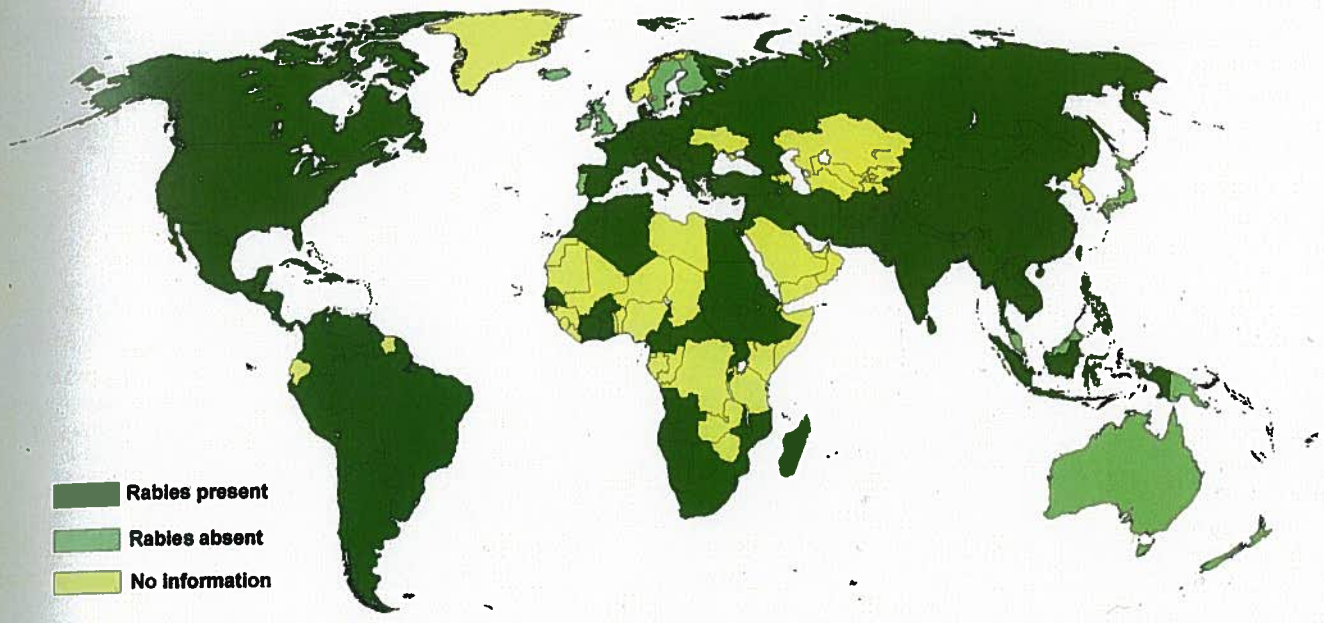


Figure 8.8. World distribution of rabies. There are only a few countries in which rabies is absent. The annual number of deaths worldwide caused by rabies is estimated to be 55,000, mostly in rural areas of Africa and Asia. An estimated 10 million people receive post-exposure treatments each year after being exposed to rabies-suspect animals. (Data from World Health Organization for 2001–2006.)

that are infected with the disease. The detrimental impact of brucellosis on elk and bison populations has been studied much less than the transmission of the disease between domestic cattle and wildlife in areas surrounding national parks, such as Yellowstone.

Rabies in Wild Mammals

Rabies is one of the oldest known diseases, and one of the most terrifying for humans. Democritus described rabies around 500 BC and, 200 years later, Aristotle wrote about rabies in his *Natural History of Animals*. Rabies is a directly transmitted disease of the central nervous system caused by a number of viruses of the genus *Lyssavirus* in the family Rhabdoviridae[1]. All mammals are susceptible to the disease, but carnivores are the viruses' essential hosts. The viruses are usually transmitted in saliva by the bite of an infected animal, although a few cases of aerosol transmission from bats in caves have been reported. Rabies is widespread in the world (Figure 8.8) and only a few countries are free of this disease. About 55,000 people contract rabies each year, mostly in India and the Far East. In many parts of the world, rabies infects humans via domestic dog bites, but vaccination of dogs has cut this link to humans in North America and Europe. The incubation period in humans is highly variable, ranging from less than 10 days to more than 6 years. There is no cure for rabies, which is almost always fatal once symptoms appear. Between 1994 and 2002, 28 people died in the United States from rabies, and 79% of the confirmed cases in humans were caused by viruses carried by bats.

Among wild animals, rabies is particularly common in foxes, wolves, coyotes, skunks, raccoons, bats and jackals. In Europe, the red fox is the main reservoir for rabies; in North America, the main reservoirs are raccoons, skunks, foxes and bats. The major vectors of rabies vary in different regions of the United States (Figure 8.9), and these vectors carry a diverse set of rabies viral genotypes. Foxes accounted for most reported cases of rabies in the United States before 1960, skunks from 1960 to 1990, and raccoons since 1990 (Figure 8.10). Little is known about the

1 Virologists have established a classification system for viruses that includes orders, families, genera, and species. This system is separate from the one used to classify organisms.

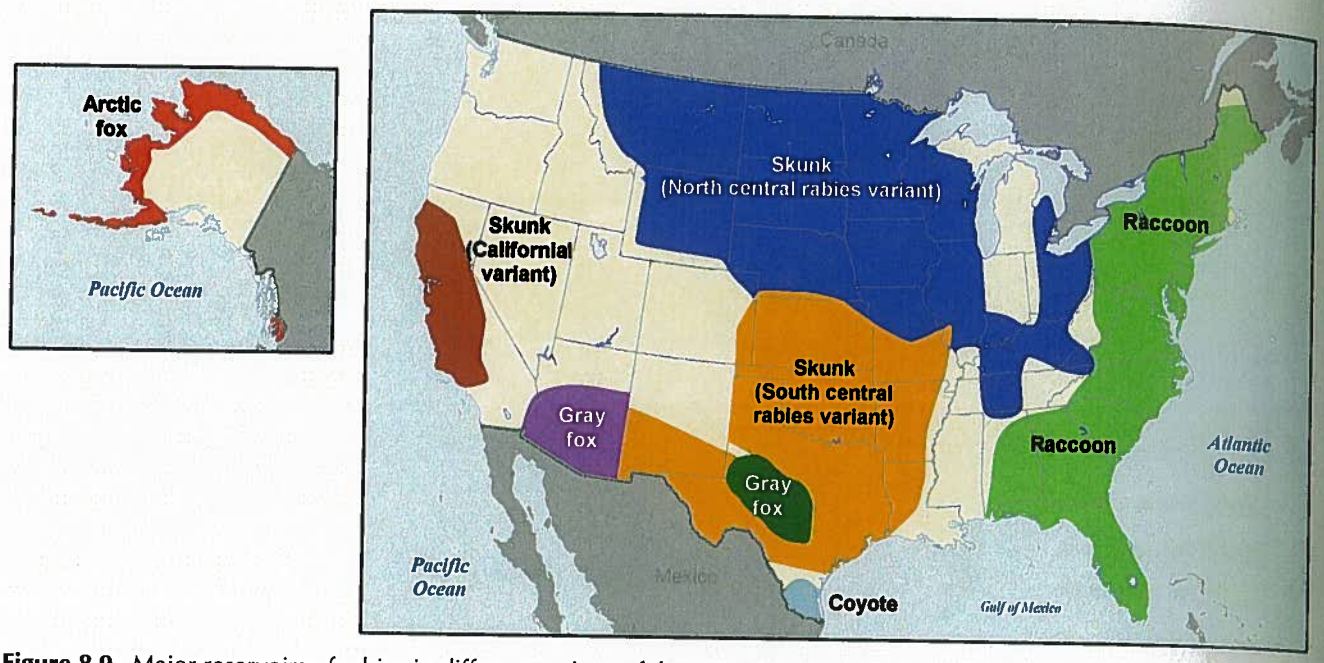


Figure 8.9. Major reservoirs of rabies in different regions of the United States. Other mammals serve as minor reservoirs of the disease in each region. The geographic ranges of these five species are much wider than the areas shown here. There are several variants of the rabies virus that are spread by specific mammals. (Modified from Krebs *et al.* 2005.)

quantitative incidence of rabies in bats or the impact of rabies on bat populations.

An epidemic of rabies in eastern North America began in the 1970s in Virginia and has been spreading for more than 30 years (Figure 8.11). This epidemic probably started when humans brought diseased raccoons into the area from the south-eastern states. Raccoon rabies crossed the border into Ontario, Canada,

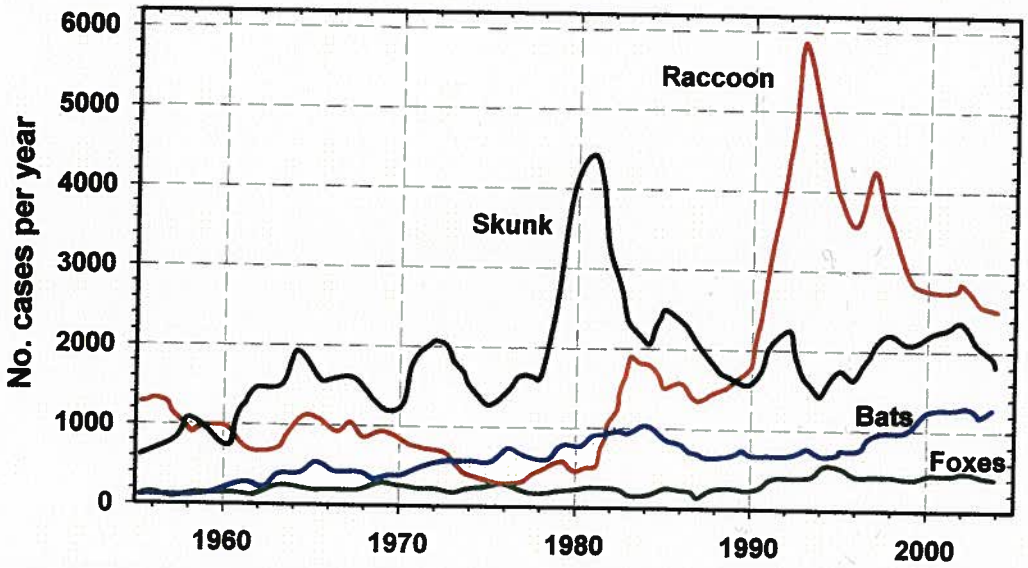


Figure 8.10. Number of rabies cases reported to the Centers for Disease Control in the United States from 1955 to 2004. The rise in the number of raccoon rabies cases since 1980 has resulted from an epidemic that spread through the eastern United States. (Data from Krebs *et al.* 2005.)

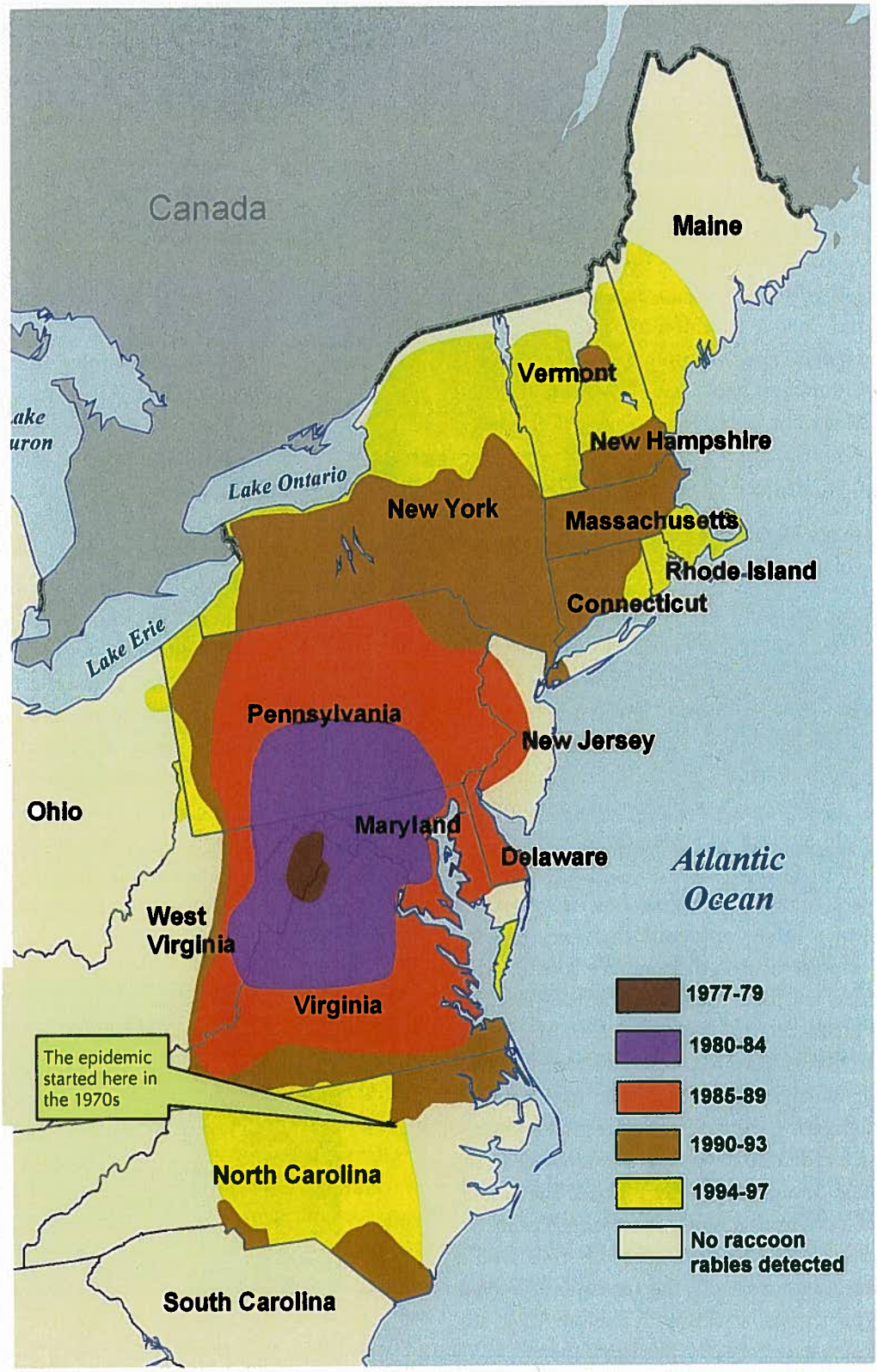


Figure 8.11. Spread of a rabies epidemic in raccoons in the eastern United States since 1977. (From the Centers for Disease Control, courtesy of John W. Krebs.)

in 1998 and has also spread south, meeting another epidemic coming north from Florida.

Because raccoons are so common, particularly around human habitations, rabies in raccoons has been particularly targeted by control agencies in the United States and Canada in recent years. Health officials are attempting to reduce the incidence of raccoon rabies by vaccinating wild raccoons, using a recombinant virus vaccine approved in April 1997. Some raccoons are trapped, injected with the vaccine, and released. However, most of the vaccine is added to bait consisting of small cubes of fish oil and wax polymer, which the raccoons eat. Millions of baits have been distributed annually in Massachusetts, New York, New Jersey, Vermont and Ontario, but it is not yet clear how effective this program has been.

- **Could a disease like rabies ever die out naturally in wild populations?**

A major epidemic of rabies came out of Russia in the 1930s and was first reported in Poland in 1939. It has moved westward at a rate of 20–60 km per year, reaching the northern coast of France in the late 1980s (Figure 8.12). More than 70% of the infected animals have been red foxes. One feature of this epidemic is that it appears to show a 4–5 year cycle, rather than being a constant disease problem.

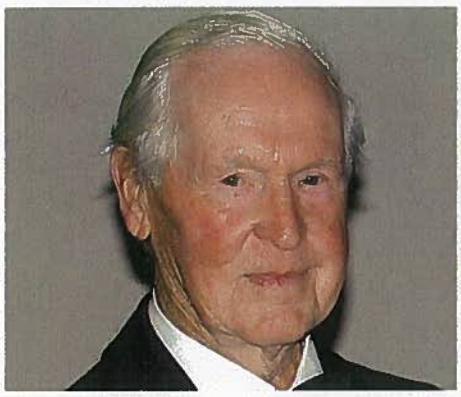
Roy Anderson and his colleagues have developed a simple model of a rabies epidemic that encapsulates much of the ecology of this disease. We can use this model to address a critical management question: can we eliminate rabies from a fox population by culling or vaccination? Foxes have high rates of reproduction and dispersal, which makes culling an unsuccessful strategy for controlling the disease unless the foxes are in poor habitat or the rate of culling is extremely high.

In contrast, vaccination directly reduces the size of the susceptible pool and is much more effective in the control of rabies. The proportion of foxes that would have to be vaccinated to break the transmission cycle and eradicate the disease varies with the density of the fox population. At a density of 2 per km^2, about 50% of the population would need to be vaccinated. Extensive programs of vaccination of wild foxes with baits have been carried out in Switzerland, Austria, Hungary, France, Belgium and Germany. These programs have been highly successful: by 1999 rabies was much reduced in Western Europe and Switzerland was rabies free.

At present we have no quantitative data on the impact of rabies on mammalian host populations. The amount of mortality rabies causes in natural populations of foxes, raccoons and skunks is believed to be high, and the resulting population declines are often commented on, but have not been measured rigorously. Arctic foxes and wolves in northern Canada have periodic outbreaks of rabies that reduce their populations to low numbers. All of these animals have high reproductive rates so, even if rabies kills a large fraction of their populations, they recover from epidemics fairly quickly.

Myxomatosis in the European Rabbit

The European rabbit (*Oryctolagus cuniculus*) was introduced into Australia in 1859, and within 20 years it had reached very high densities throughout the continent. Beginning in 1950, the Australian government attempted to reduce rabbit numbers by releasing the myxoma virus—a pox virus of the genus *Leporipoxvirus*. The European rabbit had no prior evolutionary exposure to this virus, whose original host is the South American jungle rabbit (*Sylvilagus brasiliensis*). The disease is transmitted passively by the bites of arthropod vectors, principally mosquitoes and fleas. The virus does not replicate in the vectors.



Frank Fenner (1914–) Professor of Microbiology, Australian National University, Canberra. Dr Fenner was instrumental in studying the evolution of the myxoma virus and the European rabbit in Australia.

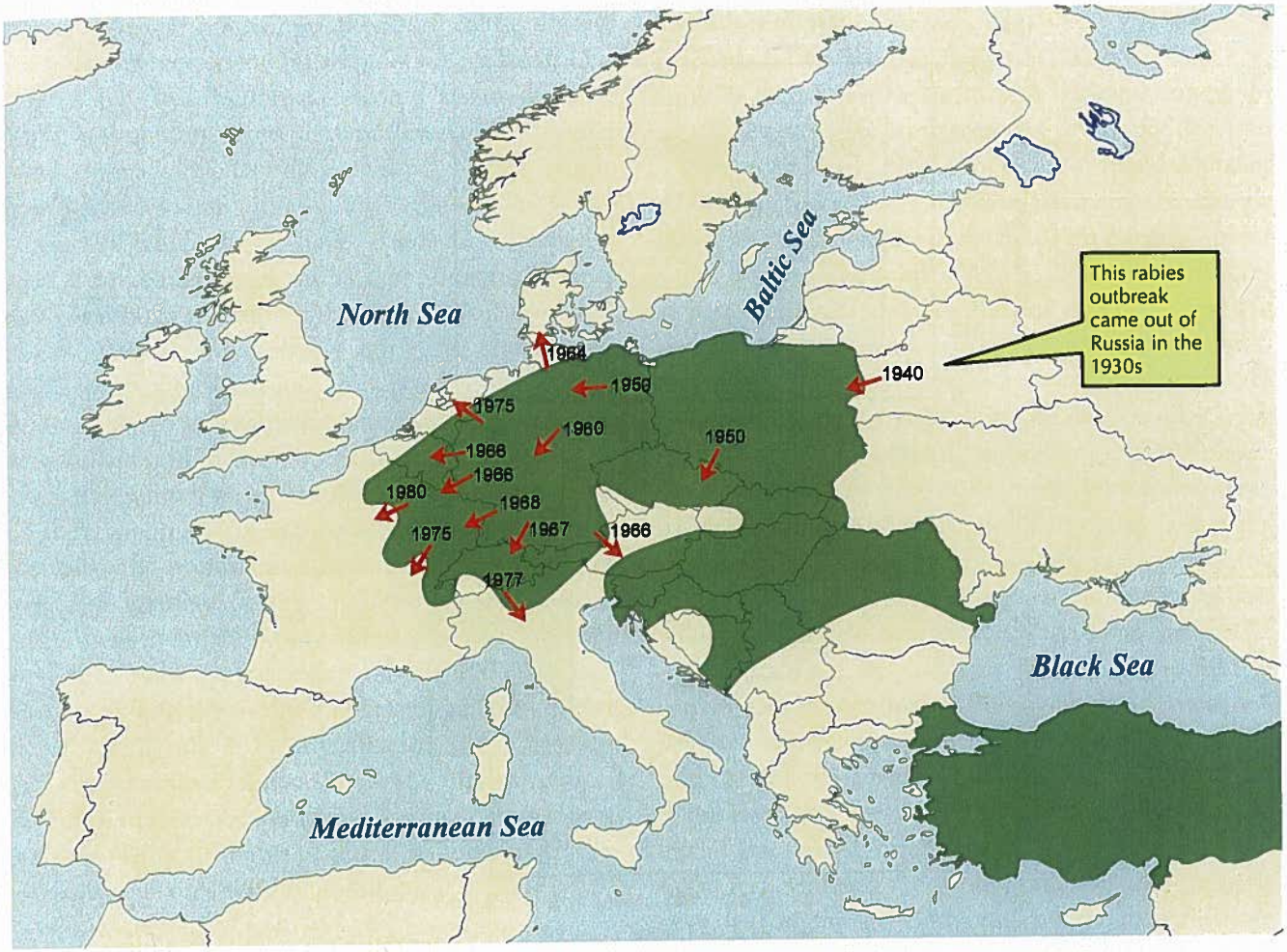


Figure 8.12. Spread of a rabies epidemic in Europe. There has been no westward movement of the epidemic since 1983, probably due to oral vaccination of foxes with baits. (After Macdonald and Voigt 1985.)

The myxoma virus causes myxomatosis, a disease that rarely kills South American jungle rabbits, but is highly lethal to European rabbits. After its introduction into Australia, it killed more than 99% of the rabbits it infected. Figure 8.13a shows the precipitous crash in rabbit numbers that followed the release of myxomatosis in one area in south-eastern Australia in 1951. Myxomatosis was also introduced to France in 1952, from where it spread throughout Western Europe. In Great Britain, 99% of the entire rabbit population was killed in the first epidemics from 1953 to 1955. This type of extreme mortality is common when pathogens infect new host species, and introducing the pathogen can be a useful strategy if the host species are pests.

Both the myxoma virus and the European rabbit have been evolving since the virus was introduced into Australia and Europe. More virulent strains of the virus have been replaced by less virulent strains, which kill fewer rabbits and take longer to cause death. Because the host remains alive longer while infected with less virulent strains, the virus has a higher probability of being spread by vectors than with more virulent strains. At the same time, rabbits have become more resistant to the more virulent strains of the virus (Figure 8.13b).

What impact do these changes in the virus and the rabbits have on the population dynamics of the rabbits? Because myxomatosis causes less mortality now than it did immediately after the virus was

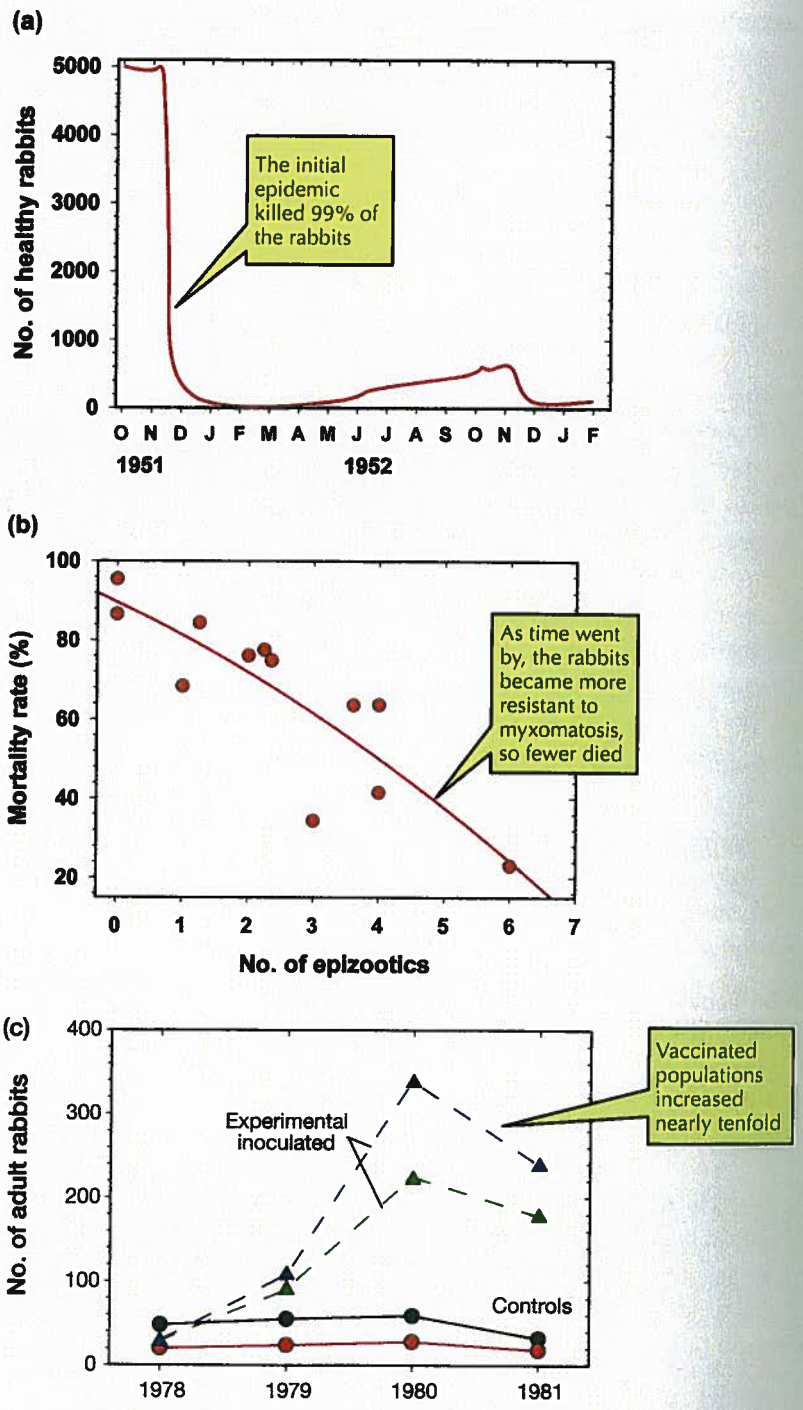


Figure 8.13. Effects of myxomatosis and vaccination on European rabbits. (a) Crash of the rabbit population at Lake Urana, New South Wales, after the myxoma virus was introduced in 1951. Numbers of healthy rabbits were counted on standardized transects. (After Myers *et al.* 1954.) (b) Decline in mortality rates of wild rabbits near Lake Urana as a function of time since the myxoma virus was introduced. Mortality was measured after infection with a virulent strain of the virus. (After Fenner and Myers 1978.) (c) Effect of vaccination on the numbers of adult rabbits in four fenced areas in south-eastern Australia. Rabbits in two areas (triangles) were vaccinated with an attenuated strain of the myxoma virus that produced immunity to virulent strains. Rabbits in the other two areas (dots) were inoculated with a virulent strain. (Data from Parer *et al.* 1985.)

introduced, you might hypothesize that the disease has little impact on rabbit numbers at present. One way to test this hypothesis would be to compare rabbit populations with and without myxomatosis, but it is impossible to find a field population of rabbits that does not already have the disease. Two groups of researchers have tried an alternative approach: reducing the impact of myxomatosis by making rabbits immune or by eliminating transmission by vectors. In Australia, Ian Parer and his colleagues compared four fenced populations of rabbits, two inoculated with an attenuated strain of the virus (to produce immunity with little mortality) and two inoculated with a virulent strain. They found that the immune populations increased approximately tenfold over the populations that had been inoculated with the virulent strain (Figure 8.13c). A similar experiment in England reduced the numbers of rabbit fleas (the main vector) using insecticides: this produced a two- to three-fold increase in rabbit numbers. These results show clearly that myxomatosis still limits rabbit populations despite the virus's reduced virulence in field populations. Myxomatosis is a good example of the strong impact that an introduced disease can have on a wild population.

■ 8.5 PATHOGENS CAN BECOME MORE OR LESS VIRULENT THROUGH EVOLUTION, AND THEIR HOSTS CAN EVOLVE RESISTANCE

How do pathogens and their hosts evolve? This simple question has become critical now that we know that some pathogens, such as the viruses that cause AIDS and bird flu, appear to have moved into the human population from other animals. One idea is that pathogen–host systems become stable as they evolve because natural selection changes the characteristics of both pathogens and hosts in a direction that produces population stability. In particular, the conventional wisdom about these systems is that virulence is selected against, so that pathogens and parasites become more benign and thus persist. But does natural selection really work that way? What can we say about the evolution of virulence?

Evolution of Virulence

One way to study the evolution of pathogen–host systems is to perform a serial passage experiment, in which a pathogen is transferred from one host to another in a chain. Host properties are held constant so that evolutionary changes in the pathogen can be monitored. Because the pathogen is propagated under defined laboratory conditions, the biological attributes of pathogen individuals at the end of the experiment can be compared with those of individuals that started the experiment. Serial passage experiments were developed for vaccine studies, but can be used very effectively for investigating the evolution of virulence. A general result of such experiments with many viral, bacterial, fungal and protozoan pathogens is that the pathogens become more virulent with each generation in their native host species. Figure 8.14 illustrates this result for the bacterium *Salmonella typhimurium*.

The increase in pathogen virulence observed in serial passage experiments does not occur in most natural disease systems, presumably because natural host populations are genetically more variable. According to the **Red Queen hypothesis**, genetic variation is beneficial because it hinders pathogen adaptation (see *Essay 8.1*). The Red Queen hypothesis states that any selective advantage that one species might obtain through evolutionary change may be offset by evolutionary changes in other species in the community. If hosts are genetically variable, pathogens will be on average less virulent than if hosts are genetically uniform (as is the case for some crops).

Coevolution in Disease Systems

The evolution of pathogens and their hosts is a classic example of **coevolution**, or reciprocal evolutionary change. For example, the evolution of resistance to the myxoma virus in European rabbits is easily explained by selection operating at the individual level: rabbits that are more resistant to the virus leave more offspring. It is more difficult to explain the evolution of reduced virulence in the virus, however. Virulence in a virus is related to fitness because more virulent viruses make more copies of themselves. But if more virulent viruses kill rabbits more quickly, there will be less time available for transmission of the virus by mosquitoes

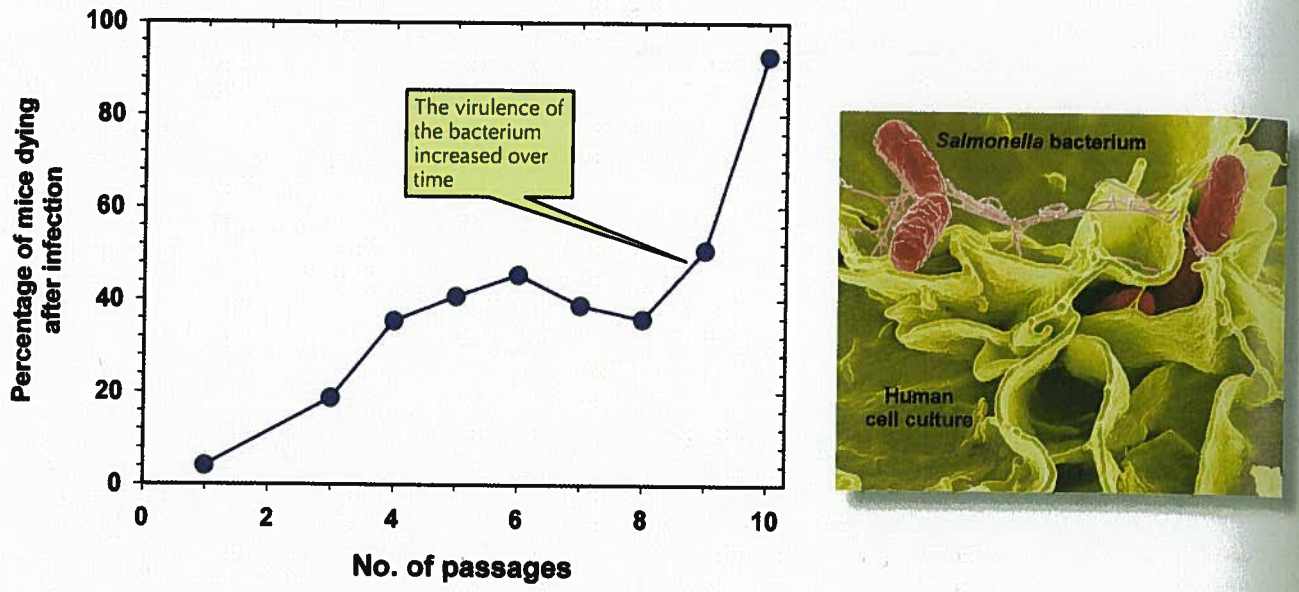


Figure 8.14. Change of virulence of the mouse typhoid bacterium *Salmonella typhimurium* after ten serial passages in laboratory mice. *Salmonella typhimurium* (red, rod shaped bacterium) is a common cause of food poisoning in humans. It uses its whip-like flagella to sense a cell and then attach to the cell wall. (Data from Ebert 1998, photomicrograph courtesy of National Institutes of Health.)

or fleas. Thus, there is a trade-off between virulence and transmissibility in the myxoma virus, and natural selection favors a moderate level of virulence, which maximizes the reproductive rate of the virus.

We do not know if the myxoma virus–rabbit system has reached a stable equilibrium or if continuing evolution will allow the rabbit population to slowly recover to its former levels. There is some evidence that the interaction between the virus and the rabbit is changing in Britain, and the size of the rabbit population seems to be slowly increasing there. Evolutionary changes in the myxoma virus–rabbit system in Australia have been complicated by the introduction in 1997 of another viral disease, rabbit hemorrhagic disease, which has further reduced the rabbit's average population density. There is still much to be learned about how pathogens and their hosts interact and evolve.

SUMMARY

Pathogens and parasites are involved in negative interactions with host organisms in which the host loses and the pathogen or parasite gains. Much of our understanding of the dynamics of pathogen-caused diseases has come from studies of human diseases, such as influenza and measles.

Compartment models can be used to visualize the interactions between pathogens or parasites and hosts. The host population is usually broken down into susceptible, infected and recovered individuals. These simple models are characterized by a few rates that define the outcome of the interactions. Pathogen–host systems have a threshold of transmission below which the disease will be eliminated from the population. The objective of much of the study of applied disease ecology is to determine how best to move the host population below this threshold. In general, vaccination has been more effective than culling in meeting this objective for wild animals.

Pathogens and parasites can affect the reproductive rate or the mortality rate of their hosts. Many studies show impacts on mortality, but few measure how large these impacts are in nature or indicate whether the average density of the host species has been reduced. Pathogens and parasites often have debilitating effects on their hosts and make them more susceptible to predators, bad weather or food shortage.

ESSAY 8.1 WHAT IS THE RED QUEEN HYPOTHESIS?

In Lewis Carroll's *Alice in Wonderland*, there is a scene in which Alice and the Red Queen have to run as fast as they can to get nowhere because the world is running by at the same speed. Lee Van Valen used this metaphor in 1973 to illuminate biological evolution. Any selective advantage that one species might obtain through evolutionary change may be offset by changes in other species in the community. For example, if a prey species evolves the ability to run faster, it will gain no advantage in surviving predation if the predators also evolve this ability. Therefore, pathogen–host systems, plant–herbivore systems and predator–prey systems may continually undergo evolutionary change without affecting the overall balance in the system. Increasing fitness in one species is always balanced by increasing fitness in all other species. The characters run and run and run, but get nowhere. This idea is called the Red Queen hypothesis.

"A slow sort of country!" said the Queen. "Now, here, you see, it takes all the running you can do, to keep in the same place. If you want to get somewhere else, you must run at twice as fast as that."

Evolution can be much faster in pathogens and parasites whose generation times are short relative to those of their hosts. If the success of a pathogen or parasite is determined by its ability to infect a host, the main selection pressures will come from the most common host genotypes. A host species whose genotype changes over time can present a moving target that the pathogen or parasite cannot catch. This is one possible reason for the evolution of sexual reproduction, in which recombination in each generation presents a new array of host genotypes to the coevolving array of pathogens and parasites. The Red Queen hypothesis thus predicts continually changing dynamics in the evolution of pathogens, parasites and hosts—not a stable equilibrium in which there is one winner and one loser.

The evolution of virulence has progressed from the idea that well-adapted pathogens and parasites are benign to a more dynamic view. Virulence will increase through evolution if that enables a pathogen to increase its fitness by producing more copies of itself. One of the main factors limiting disease virulence is host genetic variability; genetically uniform populations are particularly susceptible to virulent disease outbreaks. Much remains to be done to link epidemiology and ecology in disease studies.

SUGGESTED FURTHER READINGS

Diamond, JM (1999). *Guns, Germs, and Steel: The Fates of Human Societies.* W. W. Norton & Company, New York. 480 pp. (A best-selling book that discusses the role of diseases in European colonization of the world.)

Ebert D and Bull JJ (2003). Challenging the trade-off model for the evolution of virulence: Is virulence management feasible? *Trends in Microbiology* **11**, 15–20. (A good discussion of whether humans can manipulate the evolution of diseases toward harmless ends.)

Ewald PW (1995). The evolution of virulence: a unifying link between parasitology and ecology. *Journal of Parasitology* **81**, 659–669. (An evaluation of the idea that diseases become benign in their hosts through evolution.)

Grenfell BT and Dobson AP (Eds) (1995). *Ecology of Infectious Diseases in Natural Populations.* Cambridge University Press, Cambridge, UK. (A good overview of the effects of disease on populations.)

Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson AP, Ostfeld RS and Samuel MD (2002). Climate warming and disease risks for terrestrial and marine biota. *Science* **296**, 2158–2162. (A discussion of how global warming will affect disease transmission.)

Weiss RA (2002). Virulence and pathogenesis. *Trends in Microbiology* **10**, 314–317. (An evaluation of the critical question of why viruses cause disease.)

Wills C (1996). *Yellow Fever, Black Goddess: The Coevolution of People and Plagues.* Addison-Wesley Publishers, Reading, Massachusetts. (A timely discussion of how and why some human diseases rise and fall.)

QUESTIONS

1. Anthrax is a disease caused by the bacterium *Bacillus anthracis*, which is lethal to most mammalian herbivores. Within a few months in 1983–1984, an anthrax epidemic wiped out 90% of the impala population of Lake Manyara National Park in Tanzania. Discuss the biological mechanisms that would permit an epidemic of this type to appear suddenly in a population and then disappear for decades. Prins and Weyerhaeuser (1987) discuss this particular epidemic.
2. Rabies is a disease with interesting spatial spread patterns (Figures 8.11 and 8.12). Foxes defend discrete, non-overlapping territories. How might territorial behavior affect the spatial dynamics of rabies spread?
3. The myxoma virus has been introduced into European rabbit populations on islands to eradicate the rabbits for conservation purposes. What factors might affect the success of this eradication program? Flux (1993) considers this issue.
4. Male bison show a higher prevalence of antibodies to brucellosis than do female bison (Figure 8.7a). Suggest two conditions under which this situation might be produced.
5. McNeill (1976), Wills (1996) and Diamond (1999) discuss the idea that the introduction of diseases by Europeans made possible their conquest of aboriginal peoples in the Americas, Africa and Australia. Review the arguments supporting this idea for an area of the world that interests you and discuss their validity.