# II.9

# Ecological Epidemiology

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## OUTLINE

1. Parasites, pathogens, and other definitions
2. The importance of ecological epidemiology
3. The dynamics of parasites within populations: Transmission
4. The population dynamics of infection
5. Parasites and the dynamics of hosts
6. Shared parasites—zoonoses

Strictly speaking, *epidemiology* is the study of the dynamics of disease in a population of humans. In ecology, however, the term takes on a slightly different meaning. Ecologists tend to expand the usage to cover populations of any species, animal or plant, but they then restrict it to infectious diseases (as opposed to, say, cancers or heart disease). Studies of human epidemiology usually treat the host (human) population as fixed in size and focus on the dynamics of disease within this population. What distinguishes "ecological" epidemiology is an acknowledgment that the dynamics of the parasite and the host populations may interact. Hence, we are interested in the dynamics of parasites in host populations, that may themselves vary substantially in size, and also in the effects of the parasites on the dynamics of the hosts.

## GLOSSARY

**basic reproductive number.** Usually denoted $R_0$, for microparasites, the average number of new infections that would arise from a single infectious host introduced into a population of susceptible hosts; for macroparasites, the average number of established, reproductively mature offspring produced by a mature parasite throughout its life in a population of uninfected hosts

**critical population size.** The population size of susceptible hosts for which $R_0 = 1$, where $R_0$ is the basic reproductive number, and which must therefore be exceeded if an infection is to spread in a population

**density-dependent transmission.** Parasite transmission in which the rate of contact between susceptible hosts and the source of new infections increases with host density

**frequency-dependent transmission.** Parasite transmission in which the rate of contact between susceptible hosts and the source of new infections is independent of host density

**herd immunity.** Where a population contains too few susceptible hosts (either because of natural infection or immunization) for infection to be able to establish and spread within a population

**macroparasite.** A parasite that grows but does not multiply in its host, producing infective stages that are released to infect new hosts; the macroparasites of animals mostly live on the body or in the body cavities (e.g., the gut); in plants, they are generally intercellular

**microparasite.** A small, often intracellular parasite that multiplies directly within its host

**transmission threshold.** The condition $R_0 = 1$, where $R_0$ is the basic reproductive number, which must be crossed if an infection is to spread in a population

**vector.** An organism carrying parasites from one host individual to another, within which there may or may not be parasite multiplication

**zoonosis.** An infection that occurs naturally and can be sustained in a wildlife species but can also infect and cause disease in humans

## 1. PARASITES, PATHOGENS, AND OTHER DEFINITIONS

A parasite is an organism that obtains its nutrients from one or a very few *host* individuals, normally causing harm but not causing death immediately. This distinguishes parasites from predators, which kill and consume many prey in their lifetime, and from grazers, which take small parts from many different prey. If a parasite infection gives rise to symptoms that are clearly harmful, the host is said to have a

disease. *Pathogen*, then, is a term that may be applied to any parasite that gives rise to a disease (i.e., *is pathogenic*).

The language used by plant pathologists and animal parasitologists is often very different, but for the ecologist, these differences are less striking than the resemblances. One distinction that *is* useful is that between microparasites and macroparasites. Microparasites are small, often intracellular, and they multiply directly within their host where they are often extremely numerous. Hence, it is usually impossible to count the number of microparasites in a host: ecologists normally study the number of infected hosts in a population. Examples include bacteria and viruses (e.g., the typhoid bacterium and the yellow net viruses of beet and tomato), protozoa infecting animals (e.g., the *Plasmodium* species that cause malaria), and some of the simpler fungi that infect plants.

Macroparasites grow but do not multiply in their host. They produce infective stages that are released to infect new hosts. The macroparasites of animals mostly live on the body or in the body cavities (e.g., the gut) of their hosts. In plants, they are generally intercellular. It is often possible to count or at least to estimate the numbers of macroparasites in or on a host. Hence, ecologists study the numbers of parasites as well as the numbers of infected hosts. Examples include parasitic helminths such as the intestinal nematodes and tapeworms of humans, the fleas and ticks that are parasitic in their own right but also transmit many microparasites between their hosts, and plant macroparasites such as the higher fungi that give rise to the mildews, rusts, and smuts.

Cutting across the distinction between micro- and macroparasites, parasites can also be subdivided into those that are transmitted directly from host to host and those that require a vector or intermediate host for transmission, i.e., are either simply carried from host to host by another species (aphids carrying viruses from plant to plant) or need to parasitize a succession of two (or more) host species to complete their life cycle (both mosquitoes and humans being parasitized by the malaria *Plasmodium*).

## 2. THE IMPORTANCE OF ECOLOGICAL EPIDEMIOLOGY

Parasites are an important group of organisms in the most direct sense. Millions of people are killed each year by various types of infection, and many millions more are debilitated or deformed. When the effects of parasites on domesticated animals and crops are added to this, the cost in terms of human misery and economic loss becomes incalculable. Parasites are also important numerically. A free-living organism that does *not* harbor several parasitic individuals of a number of species is a rarity.

Thus, ecological epidemiology is important from an entirely practical point of view. If we wish to control the diseases that have afflicted us and our domesticated species historically—malaria, tuberculosis—and those that have emerged recently or threaten us—HIV-AIDS, SARS, avian influenza—then we must seek to understand their dynamics. But it is also the case that a major question in ecology that not only remains unanswered but has only recently been seriously addressed is: To what extent are animal and plant populations and communities in general affected by parasitism and disease? Ecologists have long been concerned with the effects of food resources, competitors, and predators on their focal species; only recently have parasites and pathogens been afforded similar attention.

## 3. THE DYNAMICS OF PARASITES WITHIN POPULATIONS: TRANSMISSION

Transmission dynamics, in a very real sense, is the driving force behind the overall population dynamics of pathogens. Different species of parasite are of course transmitted in different ways between hosts, the most fundamental distinction being between parasites that are transmitted directly (either through close contact between hosts or via an environmental reservoir to which infectious hosts have contributed) and those that require a vector or intermediate host for transmission.

Irrespective of these distinctions, the rate of production of new infections in a population depends on the per capita transmission rate (the rate of transmission per susceptible host "target") and also on the number of susceptible hosts there are. That per capita transmission rate depends on the infectiousness of the parasite, the susceptibility of the host, and so on, but it also depends on the *contact rate* between susceptible hosts and whatever it is that carries the infection.

For directly transmitted parasites, we deal with the contact rate between infected hosts and susceptible (uninfected) hosts; for hosts infected by long-lived infective agents, it is the contact rate between these and susceptible hosts; with vector-transmitted parasites it is the contact rate between host and vector. But what determines this contact rate? Essentially, two factors are determinative: the contact rate between a susceptible individual and *all* other hosts, and the proportion of these that are actually infectious.

For the first of these, ecologists have tended to make one of two simplifying assumptions: either that this contact rate increases in direct proportion to the density of the population (density-dependent transmission) or that it is utterly independent of population density

(frequency-dependent transmission). The former imagines individuals bumping into one another at random: the more crowded they become, the more contacts they make. The latter, by contrast, assumes that the number of contacts an individual makes is a fixed aspect of its behavior. Frequency-dependent transmission has therefore conventionally been assumed for sexually transmitted diseases—the frequency of sexual contacts is independent of population density—but it is increasingly recognized that many social contacts, territory defense for instance, may come into the same category. It has also become increasingly apparent that real contact patterns usually conform to neither of these simplifying assumptions exactly, but they nonetheless represent two valuable benchmarks through which real data sets can be understood.

There has also often been an assumption that the "infectious proportion" can be calculated from, and also applies throughout, the whole host population. In reality, however, transmission typically occurs locally, between adjacent individuals. Thus, there are likely to be hot spots of infection in a population, where the infected proportion is high, and corresponding cool zones. Transmission, therefore, often gives rise to spatial waves of infection passing through a population rather than simply an overall, global rise.

## 4. THE POPULATION DYNAMICS OF INFECTION

We begin by looking at the dynamics of disease within host populations without considering any possible effects on the total abundance of hosts. We then take the more "ecological" approach of considering the effects of parasites on host abundance in a manner much more akin to conventional predator–prey dynamics (see chapter II.7).

### The Basic Reproductive Number and the Transmission Threshold

In the study of the dynamics of parasites, there are a number of particularly key concepts. The first is the basic reproductive number, usually denoted $R_0$. For microparasites, this is the average number of new infections that would arise from a single infectious host introduced into a population of susceptible hosts. For macroparasites, it is the average number of established, reproductively mature offspring produced by a mature parasite throughout its life in a population of uninfected hosts.

The transmission threshold, which must be crossed if an infection is to spread, is then given by the condition $R_0 = 1$. An infection will eventually die out for $R_0 < 1$ (each present infection or parasite leads to fewer than one infection or parasite in the future), but an infection will spread for $R_0 > 1$. Insights into the dynamics of infection can be gained by considering the various determinants of the basic reproductive number. We do this in some detail for directly transmitted microparasites with density-dependent transmission (see above) and then deal more briefly with related issues for other parasites.

### Directly Transmitted Microparasites and the Critical Population Size

For such microparasites, $R_0$ can be said to increase (1) with the average period of time over which an infected host remains infectious, $L$; (2) with the number of susceptible individuals in the host population, $S$, because greater numbers offer more opportunities for transmission; and (3) with the transmission coefficient, $\beta$, the strength or force of transmission. Thus, overall:

$$R_0 = S\beta L. \psi \qquad (1)$$

Note immediately that by this definition, the greater the number of susceptible hosts, the higher the basic reproductive number of the infection. But in particular, the transmission threshold can now be expressed in terms of a critical population size, $S_T$, where, because $R_0 = 1$ at that threshold:

$$S_T = 1/\beta L. \psi \qquad (2)$$

In populations with numbers of susceptibles less than this, the infection will die out ($R_0 < 1$). With numbers greater than this, the infection will spread ($R_0 > 1$). These simple considerations allow us to make sense of some very basic patterns in the dynamics of infection.

Consider first the kinds of population in which we might expect to find different sorts of infection. If microparasites are highly infectious (large $\beta$s), or give rise to long periods of infectiousness (large $L$s), then they will have relatively high $R_0$ values even in small populations and will therefore be able to persist there ($S_T$ is small). Conversely, if parasites are of low infectivity or have short periods of infectiousness, they will have relatively small $R_0$ values and will be able to persist only in large populations. Many protozoan infections of vertebrates, and also some viruses such as herpes, are persistent within individual hosts (large $L$), often because the immune response to them is either ineffective or short lived. A number of plant diseases, too, such as club-root, have very long periods of infectiousness. In each case, the critical population size is therefore small, explaining why the diseases can and do survive endemically even in small host populations.

On the other hand, the immune responses to many other human viral and bacterial infections are powerful enough to ensure that they are only very transient in individual hosts (small $L$), and they often induce lasting immunity. Thus, for example, a disease such as measles has a critical population size of around 300,000 individuals and is unlikely to have been of great importance until quite recently in human biology. However, it has generated major epidemics in the growing cities of the industrialized world in the eighteenth and nineteenth centuries, and in the growing concentrations of population in the developing world in the twentieth century.

### The Epidemic Curve

The value of $R_0$ itself is also related to the nature of the *epidemic curve* of an infection. This is the time series of new cases following the introduction of the parasite into a population of hosts. Assuming there are sufficient susceptible hosts present for the parasite to invade (i.e., the critical population size, $S_T$, is exceeded), the initial growth of the epidemic will be rapid as the parasite sweeps through the population of susceptibles. But as these susceptibles either die or recover to immunity, their number, $S$, will decline, and so too, therefore, will $R_0$. Hence, the rate of appearance of new cases will slow down and then decline. And if $S$ falls below $S_T$ and stays there, the infection will disappear—the epidemic will have ended. Not surprisingly, the higher the initial value of $R_0$, the more rapid will be the rise in the epidemic curve. But this will also lead to the more rapid removal of susceptibles from the population and hence to an earlier end to the epidemic: higher values of $R_0$ tend to give rise to shorter, sharper epidemic curves. Also, whether the infection disappears altogether (i.e., the epidemic simply ends) depends very largely on the rate at which new susceptibles either move into or are born into the population because this determines how long the population remains below $S_T$. If this rate is too low, then the epidemic will indeed simply end. But a sufficiently rapid input of new susceptibles should prolong the epidemic or even allow the infection to establish endemically in the population after the initial epidemic has passed.

### Cycles of Infection

This leads us naturally to consider the longer-term patterns in the dynamics of different types of endemic infection. As described above, the immunity induced by many bacterial and viral infections reduces $S$, which reduces $R_0$, which therefore tends to lead to a decline in the incidence of the infection itself. However, in due course, and before the infection disappears altogether from the population, there is likely to be an influx of new susceptibles into the population, a subsequent increase in $S$ and $R_0$, and so on. There is thus a marked tendency with such infections to generate a sequence from many susceptibles ($R_0$ high), to high incidence, to few susceptibles ($R_0$ low), to low incidence, to many susceptibles, etc., just as in any other predator–prey cycle. This undoubtedly underlies the observed cyclic incidence of many human diseases, with the differing lengths of cycle reflecting the differing characteristics of the diseases: measles with peaks every 1 or 2 years, whooping cough every 3 to 4 years, and so on.

By contrast, infections that do not induce an effective immune response tend to be longer lasting within individual hosts, but they also tend not to give rise to the same sort of fluctuations in $S$ and $R_0$. Thus, for example, protozoan infections tend to be much less variable (less cyclic) in their prevalence.

### Immunization Programs

Recognizing the importance of critical population sizes also throws light on immunization programs in which susceptible hosts are rendered nonsusceptible without ever becoming diseased (showing clinical symptoms), usually through exposure to a killed or attenuated pathogen. The direct effects here are obvious: the immunized individual is protected. But by reducing the number of susceptibles, such programs also have the indirect effect of reducing $R_0$. Indeed, seen in these terms, the fundamental aim of an immunization program is clear: to hold the number of susceptibles below $S_T$ so that $R_0$ remains less than 1. To do so is said to provide "herd immunity."

In fact, a simple manipulation of equation 2 gives rise to a formula for the critical proportion of the population, $p_c$, that needs to be immunized in order to provide herd immunity (reducing $R_0$ to a maximum of 1, at most). This reiterates the point that in order to eradicate a disease, it is not necessary to immunize the whole population—just a proportion sufficient to bring $R_0$ below 1. Moreover, this proportion will be higher the greater the "natural" basic reproductive number of the disease (without immunization). It is striking, then, that smallpox, the only known disease where in practice immunization seems to have led to eradication, has unusually low values of $R_0$ (and hence $p_c$).

### Frequency-Dependent Transmission

Suppose, however, that transmission is frequency dependent. Then there is no longer the same dependence for spread on the number of susceptibles, and hence, no

threshold population size. Such infections can therefore persist even in extremely small populations, where, to a first approximation, the chances of sexual contact, say, for an infected host are the same as in large populations.

### Vector-Borne Infections

For microparasites that are spread from one host to another by a vector, the life-cycle characteristics of both host and vector enter into the calculation of $R_0$. In particular, the transmission threshold ($R_0 = 1$) is dependent on a ratio of vector:host numbers. For a disease to establish itself and spread, that ratio must exceed a critical level; hence, disease control measures are usually aimed directly at reducing the numbers of vectors and are aimed only indirectly at the parasite. Many virus diseases of crops, and vector-transmitted diseases of humans and their livestock (malaria, onchocerciasis, etc.), are therefore controlled by insecticides rather than chemicals directly targeting the parasite.

### Directly Transmitted Macroparasites

The effective reproductive number of a directly transmitted macroparasite (no intermediate host) is directly related to the length of its reproductive period within the host (i.e., again, to $L$) and to its rate of reproduction (rate of production of infective stages). Most directly transmitted helminths have an enormous reproductive capability. For instance, the female of the human hookworm *Necator* produces roughly 15,000 eggs per worm per day. The critical threshold densities for these parasites are therefore very low, and they occur and persist endemically in low-density human populations, such as hunter–gatherer communities.

### Indirectly Transmitted Macroparasites

Finally, for macroparasites with intermediate hosts, the threshold for the spread of infection depends directly on the abundance of both (i.e., a product as opposed to the ratio, which was appropriate for vector-transmitted microparasites). This is because transmission in both directions is by means of free-living infective stages. Thus, because it is inappropriate to reduce human abundance, schistosomiasis, a helminth infection of humans for which snails are intermediate hosts, is often controlled by reducing snail numbers with molluscicides in an attempt to depress $R_0$ below unity (the transmission threshold). The difficulty with this approach, however, is that the snails have an enormous reproductive capacity, and they rapidly recolonize aquatic habitats once molluscicide treatment ceases.

## 5. PARASITES AND THE DYNAMICS OF HOSTS

It is part of the definition of parasites that they cause harm to their host, and although it is not always easy to demonstrate this harm, there are numerous examples in which all sorts of parasites have been shown to affect directly the key demographic rates: birth and death.

### Parasites Interact with Other Ecological Processes

On the other hand, the effects of parasites are often more subtle than a simple reduction in survival or fecundity. For example, infection may make hosts more susceptible to predation. For example, postmortem examination of red grouse (*Lagopus lagopus scoticus*) carried out by Peter Hudson and colleagues showed that birds killed by predators carried significantly greater burdens of the parasitic nematode *Trichostrongylus tenuis* than the presumably far more random sample of birds that were shot. Alternatively, the effect of parasitism may be to weaken an aggressive competitor and so allow weaker associated species to persist. For example, a study by Pennings and Callaway showed that dodder (*Cuscuta salina*), a plant parasitic on other plants, which has a strong preference for *Salicornia* in a southern Californian salt marsh, is highly instrumental in determining the outcome of competition between *Salicornia* and other plant species within several zones of the marsh.

Thus, parasites often affect their hosts not in isolation but through an interaction with some other factor: infection may make a host more vulnerable to competition or predation; or competition or shortage of food may make a host more vulnerable to infection or to the effects of infection. This does not mean, however, that the parasites play only a supporting role. Both partners in the interaction may be crucial in determining both the overall strength of the effect and which particular hosts are affected.

### Parasites Affect Host Abundance/Dynamics

What role, if any, do parasites and pathogens play in the dynamics of their hosts? Data sets showing reductions in host abundance by parasites in controlled, laboratory environments, in which infected and uninfected populations are compared, have been available for many years. However, good evidence from natural populations is extremely rare.

### Red Grouse and Nematodes

The difficulties of finding such evidence are illustrated by further work on the red grouse—of interest both because it is a "game" bird, and hence the focus of an industry in which British landowners charge for the right to shoot at it, and also because it is a species that often, although not always, exhibits regular cycles of abundance (repeated increases and crashes): a pattern demanding an explanation. The underlying cause of these cycles has been disputed, but one mechanism receiving strong support, especially from Hudson and his colleagues, has been the influence of the parasitic nematode *Trichostrongylus tenuis* occupying the birds' gut caeca and reducing both survival and fecundity.

Mathematical models for this type of host–macroparasite interaction are supportive of a role for the parasites in grouse cycles (i.e., the results of the models are consistent with field observations), but they fall short of the type of "proof" that can come from a controlled experiment. Hudson and others therefore carried out a field-scale experimental manipulation in the late 1990s designed to test the parasites' role. In two populations, grouse were treated with an anthelmintic (worm killer) in the expected years of two successive population crashes; in two others, grouse were treated only in the expected year of one crash; and two further populations were monitored as unmanipulated controls. Grouse abundance was measured as "bag records": the number of grouse shot. The anthelmintic had a clear effect in the experiment—population crashes were far less marked—and it is therefore equally clear that the parasites have an effect normally: that is, the parasites affected host dynamics. The precise nature of that effect, however, remained a matter of some controversy. Hudson and his colleagues believed that the experiment demonstrated that the parasites were responsible for both the existence of the host cycles and their amplitude.

Others, however, felt that rather less had been fully demonstrated, suggesting for example that the cycles may have been reduced in amplitude in the experiment rather than eliminated, especially as the very low numbers normally observed in a trough are a result of there being no shooting when abundance is low. That is, the worms may normally have been important in determining the amplitude of the cycles but not for their existence in the first place. Redpath, Hudson, and others therefore carried out a very similar field experiment, almost 10 years after the first, but with a greater proportion of experimental birds treated for worms and with abundances measured more accurately. This time, the demonstrable effect of worms was far less profound, and the conclusion drawn was that the parasites appear to be part of a much larger web of interactions, molding host dynamics. As evidence accumulates, this seems likely to be a much more general conclusion: that parasites may play a neglected but important role in determining host dynamics, alongside and interacting with many other factors.

## 6. SHARED PARASITES—ZOONOSES

Finally, we turn from systems comprising one host to those with more than one host species, and to a subset of these interactions that is of particular importance to humans. For any species of parasite (be it tapeworm, virus, protozoan, or fungus), the potential hosts are a tiny subset of the available flora and fauna. The overwhelming majority of other organisms are quite unable to serve as hosts.

The delineation of a parasite's host range, moreover, is not always as straightforward as one might imagine. Species outside the host range are relatively easily characterized: the parasite cannot establish an infection within them. But for those inside the host range, the response may range from a serious pathology and certain death to an infection with no overt symptoms. What is more, it is often the "natural" host of a parasite, i.e., the one with which it has coevolved, in which infection is asymptomatic. It is then often "accidental" hosts in which infection gives rise to a frequently fatal pathology. (*Accidental* is an appropriate word here because these are often dead-end hosts that die too quickly to pass on the infection, within which the pathogen cannot therefore evolve, and *to* which it cannot therefore be adapted.)

These issues take on not just parasitological but also medical importance in the case of *zoonotic infections*: infections that circulate naturally, and have coevolved, in one or more species of wildlife but also have a pathological effect on humans. Good examples of zoonotic infections are bubonic and pneumonic plague, the human diseases caused by the bacterium *Yersinia pestis*. *Y. pestis* circulates naturally within populations of a number of species of wild rodent: for example, in the great gerbil, *Rhombomys opimus*, in the deserts of Central Asia, and probably in populations of kangaroo rats, *Dipodomys* spp. in similar habitats in the southwestern United States. (Remarkably, little is known about the ecology of *Y. pestis* in the United States despite its widespread nature and potential threat.) In these species, there are few if any symptoms in most cases of infection. There are, however, other species where *Y. pestis* infection is devastating. Some of these are closely related to the natural hosts. In the United States, populations of prairie dogs,

*Cynomys* spp., also rodents, are regularly annihilated by epidemics of plague, and the disease is an important conservation issue. But there are also other species, only very distantly related to the natural hosts, where untreated plague is usually, and rapidly, fatal. Among these are humans. Why such a pattern of differential virulence so often occurs—low virulence in the coevolved host, high virulence in some unrelated hosts, but unable even to cause an infection in others—is an important unanswered question in host-pathogen biology. But it is a question that urgently requires an answer as the list of zoonotic infections threatening us—HIV-AIDS, Ebola, avian influenza—grows ever larger.

## FURTHER READING

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