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REVIEWS AND SYNTHESES

Seasonality and the dynamics of infectious diseases

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Abstract

Seasonal variations in temperature, rainfall and resource availability are ubiquitous and can exert strong pressures on population dynamics. Infectious diseases provide some of the best-studied examples of the role of seasonality in shaping population fluctuations. In this paper, we review examples from human and wildlife disease systems to illustrate the challenges inherent in understanding the mechanisms and impacts of seasonal environmental drivers. Empirical evidence points to several biologically distinct mechanisms by which seasonality can impact host–pathogen interactions, including seasonal changes in host social behaviour and contact rates, variation in encounters with infective stages in the environment, annual pulses of host births and deaths and changes in host immune defences. Mathematical models and field observations show that the strength and mechanisms of seasonality can alter the spread and persistence of infectious diseases, and that population-level responses can range from simple annual cycles to more complex multiyear fluctuations. From an applied perspective, understanding the timing and causes of seasonality offers important insights into how parasite–host systems operate, how and when parasite control measures should be applied, and how disease risks will respond to anthropogenic climate change and altered patterns of seasonality. Finally, by focusing on well-studied examples of infectious diseases, we hope to highlight general insights that are relevant to other ecological interactions.

Keywords

Annual cycle, climate variation, host–parasite interaction, population dynamics, transmission.

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INTRODUCTION

Seasonal changes are cyclic, largely predictable, and arguably represent the strongest and most ubiquitous source of external variation influencing human and natural systems (e.g. Fretwell 1972; Wingfield & Kenagy 1991; Blank 1992). Despite the pervasive nature of seasonality, exploring its consequences for population dynamics poses a challenge for ecologists, in part because seasonal mechanisms can be difficult to pinpoint empirically and can generate complex population fluctuations. One area where the role of seasonality has been relatively well explored is in the population dynamics of infectious diseases. The incidence of many pathogens and parasites varies conspicuously by season (Table 1, and reviewed in Dowell 2001) with examples in humans ranging from increases in cases of influenza and respiratory infections during the winter months to peaks in the incidence of malaria following seasonal rains in warmer regions. Together with these empirical patterns, conceptual approaches for capturing seasonal variation in epidemiological models provide a natural framework for exploring the role of seasonality in population ecology.

Annual changes in host and parasite biology can generate outbreaks that occur around the same time each year, although it is important to distinguish observed seasonal outbreaks of infectious diseases from seasonal drivers of epidemic parameters. Indeed, in nonlinear systems, response frequencies and driving frequencies need not be the same, and there is growing awareness that seasonality can cause population fluctuations ranging from annual cycles to multiyear oscillations, and even chaotic dynamics (Dietz 1976; Aron & Schwartz 1984; Greenman *et al.* 2004). In addition to driving temporal patterns, epidemiological

Table 1 Parasites and pathogens from humans and vertebrate animals for which seasonal drivers generate annual peaks or longer-term variation in incidence

Pathogen/disease	Host	Timing of outbreaks	Mechanism of seasonality	Reference
Vector-borne diseases				
Malaria (*Plasmodium vivax* and *Plasmodium falciparum*)	Humans	Peak transmission during warm or rainy seasons	Rainfall and temperature affect mosquito vector abundance, biting rates and parasite development within vectors	Hoshen & Morse (2004)
Dengue haemorrhagic fever (dengue viruses type 1–4)	Humans	Peak case rates during hot-dry and rainy season	Rainfall and temperature affect mosquito vector abundance, temperature influences parasite replication in vectors	Watts *et al.* (1987)
West Nile virus	Avian hosts, humans, other vertebrates	Human cases peak in summer and early fall in temperate regions	Temperature and rainfall affect mosquito vector abundance; temperature influences parasite replication in vectors	Campbell *et al.* (2002)
Tick-borne encephalitis virus	Rodents, humans	Transmission during spring and summer; persistence depends on seasonality	Virus occurs in areas with seasonal synchrony of larval and nymph ticks as determined by rapid fall cooling	Randolph *et al.* (2000)
Diarrhoeal diseases				
Cholera (*Vibrio cholerae*)	Humans	One or two annual peaks in spring and fall	Rainfall and temperature influence pathogen survival and transmission	Pascual *et al.* (2002)
Rotavirus infections	Humans	Winter peaks; timing shifts with latitude	Aggregation of children could elevate contacts and transmission	Cook *et al.* (1990)
Respiratory-aerosol and contact-borne pathogens				
Measles (morbillivirus)	Humans	Increases in fall or spring	Host aggregation during school terms increases transmission	Fine & Clarkson (1982)
Pneumococcal disease (*Streptococcus pneumoniae*)	Humans	Increases during fall and winter	Possibly photoperiod-dependent host susceptibility; fall aggregations among school children	Dowell *et al.* (2003)
Influenza (influenza A and B viruses)	Humans	Winter months in colder climates	Unknown: possibly winter aggregation increases transmission	Dushoff *et al.* (2004)
Respiratory syncytial virus (hRSV virus)	Humans	Winter months in colder climates	Possibly host crowding, or seasonal shifts in immunity	White *et al.* (2005)
Meningococcal meningitis (*Neisseria meningitidis*)	Humans	Winter (February to May) in western Africa	Wind speed and low humidity affect respiratory/aerosol transmission	Sultan *et al.* (2005)
Ebola haemorrhagic fever (EHV viruses)	Humans, gorillas, chimpanzees	During dry conditions following the rainy season	Possibly tree fruiting patterns or increased numbers and aggregation of insects and mammals	Pinzon *et al.* (2004)
Bacterial conjunctivitis (*Mycoplasma gallisepticum*)	House finches	Fall and winter (September to March)	Seasonal host births and flocking increase transmission during fall and winter, partial immunity is also important	Altizer *et al.* (2004b) and Hosseini *et al.* (2004)
Pneumocystis carinii (pulmonary protozoan)	Voles and shrews	Late autumn peak	Possibly seasonal changes in immunity or host density	Laakkonen *et al.* (1999)

Rabies (lyssavirus)	Skunks	Autumn peak in eastern US; early spring peak in central US	Dispersal of juveniles during fall could increase contact rates with raccoons; early spring peak coincides with breeding activity	Gremillion-Smith & Woolf (1988) and Guerra *et al.* (2003)
Helminths and other macroparasites				
Intestinal nematodes (incl. *Haemonchus contortus*)	Sheep, other livestock	Most transmission during spring and summer	Warm temperatures and moisture needed for development outside of host; larvae arrest in hosts during winter and mature after periparturient drop in immunity	Waller *et al.* (2004)
Intestinal nematode (*Trichostrongylus retortaeformis*)	Wild rabbits	Mean intensity highest during autumn months	Warm temperatures are needed for development of parasite free-living stages; periparturient drop in immunity increases transmission	Cattadori *et al.* (2005)
Oestrids (warble fly and bot fly)	Reindeer	Transmission during July and August	Warm temperatures needed for adults flies to mate and transmit eggs and larvae	Nilssen (1997)
Tapeworm (*Caryophyllaeus laticeps*)	Cyprinid fishes	Intensity peaks during summer months	Greater host feeding activity in warmer temperatures; higher parasite mortality in winter	Anderson (1974)

Seasonal outbreaks are especially common among many respiratory-borne acute infections, diarrhoeal diseases, vector-borne parasites, and helminth infections. These selected pathogens are not intended as an exhaustive list, and in some cases the importance of seasonal drivers depends on the host species affected and geographical regions sampled.

studies of humans and wildlife systems show that seasonality can generate geographical variation in the timing and severity of epidemics, with latitudinal and altitudinal gradients in the onset and persistence of infections (Cook *et al.* 1990; Randolph *et al.* 2000). From an applied perspective, clarifying the mechanisms that link seasonal environmental changes to diseases dynamics will aid in forecasting long-term health risks and in developing strategies for controlling parasites across a range of human and natural systems. This is especially important because longer-term environmental changes caused by climate warming and complex events like El Niño/Southern Oscillation (ENSO) will alter seasonality in ways that influence parasite spread (e.g. Harvell *et al.* 2002; Pascual *et al.* 2002).

In this review, we begin by examining the mechanisms by which seasonality operates on host–pathogen interactions, focusing primarily on examples from humans and wildlife. Seasonal changes can affect hosts, pathogens and vectors in ways that alter components of the basic reproductive number that determines the rate at which infected hosts are produced. These mechanisms include those that influence parasite transmission, in part by altering the behaviour of hosts, the biology of vectors or parasite infectious stages in the environment. Seasonality can further cause shifts in the base of susceptible hosts through annual variation in host births and deaths, or cause changes in underlying immunity to infection – and in natural systems it is likely that multiple seasonal drivers will interact in complex ways. From a modelling perspective, approaches are available for incorporating periodic forcing into epidemiological models, and we review how seasonality can be described mathematically and several important dynamical consequences. Finally, we consider the implications of seasonality for predicting longer-term changes in the risk of infectious disease, and highlight several priorities for future research.

MULTIPLE SEASONAL PROCESSES INFLUENCE HOST–PARASITE SYSTEMS

Seminal work during the last century uncovered multiple environmental drivers that can generate periodical variation in the biology of hosts and pathogens (Table 1; Fig. 1), including human-imposed annual changes driven by school terms and the management of crops and livestock. A useful framework for considering the mechanisms by which seasonality affects epidemiological systems is to examine variation in R_0, the basic reproductive number of a parasite. In a deterministic system, R_0 defines a break-even point (i.e. $R_0 = 1$) above which a pathogen can spread and below which a pathogen declines to extinction (Anderson & May 1991). Expressions for R_0 capture processes that give rise to new infections multiplied by the duration over which infectious stages are produced. For directly transmitted

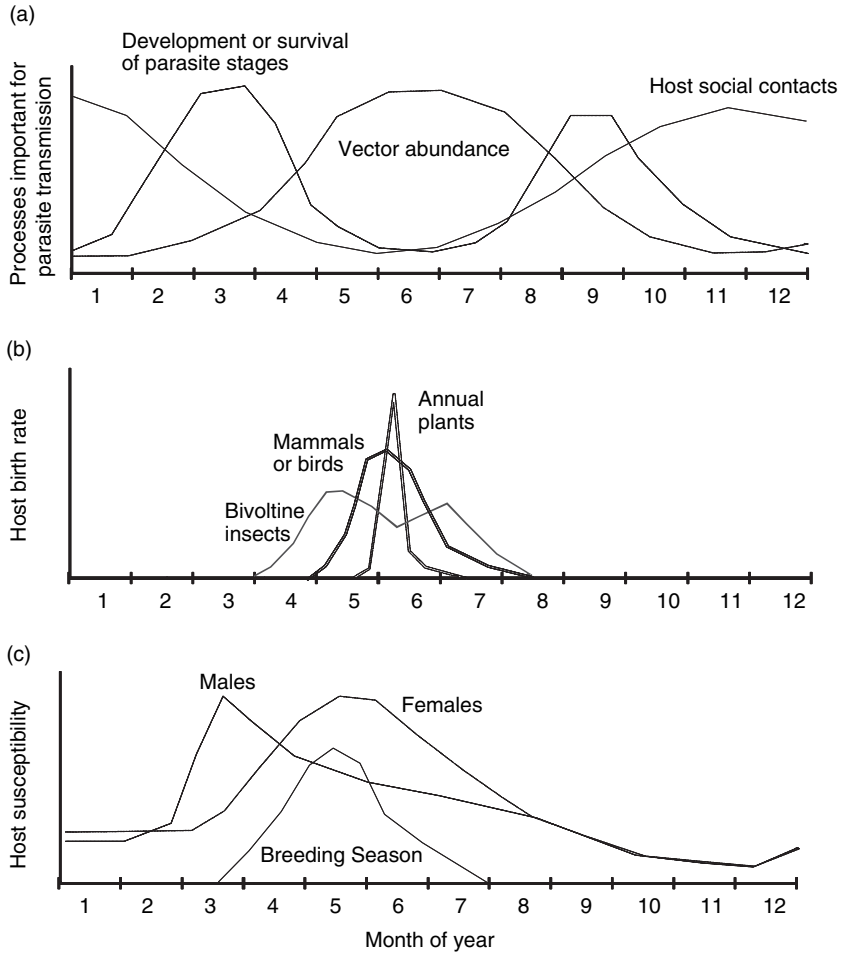


Figure 1 Types of annual variation in host and pathogen biology important to infectious disease dynamics, including: (a) variation in parasite transmission, such as might be caused by host aggregation and increased contact rates, seasonal changes in vector abundance or biting rates, and the development and survival of parasite-free living stages in the environment; (b) seasonally pulsed births, as might be represented by different types of host species, should lead to annual increases in the abundance or density of susceptible hosts; (c) seasonal changes in host stress and lowered immunity can increase susceptibility to infection; these changes might covary with the breeding season for adult males and females. In all three graphs, factors that increase the parasite's basic reproductive number (R_0) are shown as increasing along the *y*-axis, and time of year is shown along the *x*-axis. For many pathogens, different seasonal mechanisms can operate in- or out-of-phase with others and each of these mechanisms can be incorporated in different ways into epidemiological models (Box 1).

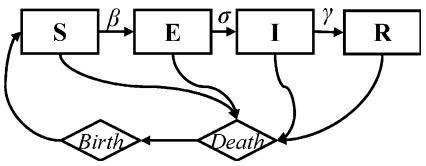
pathogens such as measles virus, the value of R_0 depends on the product of the transmission coefficient (β) and the duration of the infectious period (Anderson & May 1991). Values for R_0 can vary over time and space, even for the same host–pathogen system (Anderson & May 1982; Dietz 1993), and once an epidemic is underway, a measure called R tracks the number of subsequent new cases ($R = R_0\, s$, where s is the remaining fraction of susceptible hosts).

Pinpointing the relative importance of seasonal drivers that increase or decrease R_0 represents a crucial first step towards understanding their roles in the dynamics of infectious diseases. Seasonality of transmission, specifically the probability of contacting infected hosts or encountering infectious particles, has received the most attention from epidemiological models (e.g. Box 1). Yet even though multiple mechanisms (including changes in host contact rates and the per-contact probability of transmission) are often subsumed in the transmission parameter β, these need not vary synchronously (Fig. 1). In the case of vector-borne diseases like malaria, transmission becomes a function of the relative size of the vector population, vector biting rates and parasite development within vectors (Macdonald 1957; Hoshen & Morse 2004; Smith *et al.* 2004). For many intestinal parasites and diarrhoeal diseases, transmission depends on the production of and host encounters with parasite stages in the environment and the decay rate of parasite particles – all of which can vary seasonally. In addition to seasonal changes in parasite transmission, periodical changes in host demographic rates, and especially seasonal pulses of births, can expand and contract the abundance and proportion of susceptible hosts with concomitant impacts on R and R_0. Less appreciated is the role of seasonal variation in host immunity that will alter per-contact transmission probabilities and the duration of the infectious period.

Seasonal forcing in host social behaviour and aggregation

Annual changes in host social interactions can alter the transmission coefficient for many directly transmitted contagious infections (Table 1). In humans, a range of calendar events mediate the timing of contacts that propagate contagious diseases such as mumps, chicken

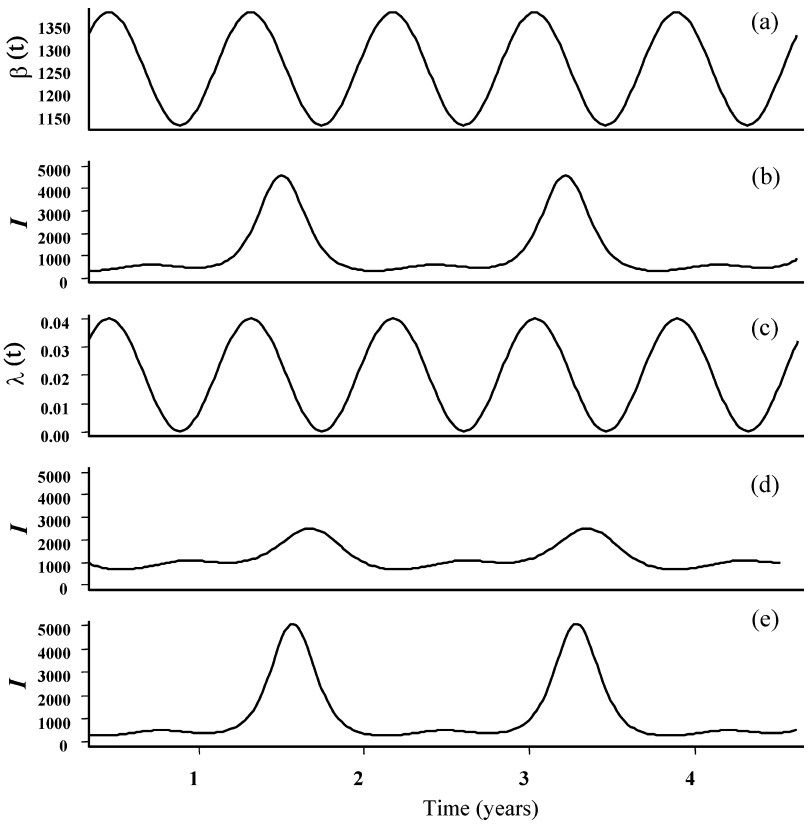
Box 1 Effects of seasonal forcing on susceptible, exposed, infected and recovered (SEIR) systems



$$\frac{dS}{dt} = \lambda(t)(N - S) + \mu I - \beta(t)S\frac{I}{N}$$
$$\frac{dE}{dt} = \beta(t)S\frac{I}{N} - \lambda(t)E - \sigma E$$
$$\frac{dI}{dt} = \sigma E - (\gamma + \mu + \lambda(t))I$$

$$R = N - (S + E + I)$$
$$\beta(t) = \beta_0(1 + \beta_1\cos(2\pi t))$$
$$\lambda(t) = \lambda_0(1 + \lambda_1\cos(2\pi t))$$

Seasonality in either transmission or births can yield complex dynamics in SEIR systems. In the box diagram, seasonality can operate on processes including transmission β, recovery γ, birth λ and death. In this example, the nonlinearity interacts with the seasonality to produce biennial cycles. Note that the relatively strong seasonal fluctuation in births ($\lambda_1 = 1$) produces a weaker fluctuation than the lower amplitude fluctuation in the transmission rate ($\beta_1 = 0.1$), which dominates the dynamics when the two are combined.



Here, the graphical outputs illustrate (a) seasonal fluctuation in transmission rate, (b) resulting biennial dynamics in infected individuals given constant birth rate, (c) seasonal fluctuations in birth rate, (d) resulting biennial dynamics given constant transmission rate, and (e) dynamics resulting from varying both birth and transmission rates. Parameters $\lambda_0 = 0.02$, $\lambda_1 = 1$, $\beta_0 = 1250$, $\beta_1 = 0.1$, $N = 5 \times 10^6$, $\gamma = 73$, $\mu = 0$, $\sigma = 45.625$.

pox and influenza (London & Yorke 1973; Fine & Clarkson 1982; Bolker & Grenfell 1995; Dushoff *et al.* 2004). This is vividly illustrated by the dynamics of measles, a communicable childhood disease that represents one of the most comprehensively studied data sets in population ecology (e.g. Bjørnstad *et al.* 2002; Grenfell *et al.* 2002; Fig. 2). In one of the earliest studies of seasonality in infectious disease dynamics, Soper (1929) noted that simple deterministic models of measles predicted damped oscillations, whereas case report data showed large sustained oscillations. Soper suggested that a missing ingredient in the basic model was seasonal change because of 'perturbing influences, such as might be brought about by school break up and reassembling, or other annual recurrences'. Focusing on measles notifications in Glasgow from 1901 to 1917 (Fig. 2a), he proceeded to estimate the effective contact coefficient through time. Results (shown in Fig. 2b) demonstrated a clear peak in transmission in October, coinciding with the start of the school calendar. Since then, a number of researchers (London & Yorke 1973; Fine & Clarkson 1982; Finkenstädt & Grenfell 2000) have employed more refined methodology and examined additional data sets with the general conclusion that patterns of transmission for childhood diseases reflect a regular increase in contact rates during the opening of school terms and a decrease during vacations. Variation driven by the school year can also affect the degree of spatial heterogeneity, as mixing patterns tend to be spatially local during school terms and better-mixed during vacation periods when people visit relatives and friends (Finkenstädt & Grenfell 2000).

As with humans, seasonal changes in the behaviour and contact rates of wildlife can generate pulses of high

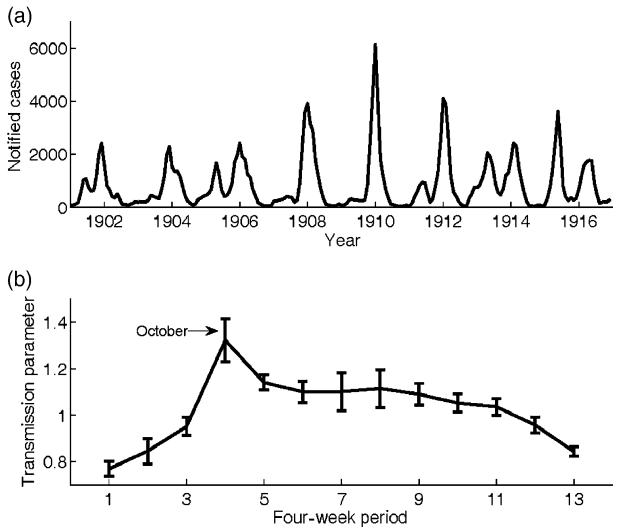


Figure 2 (a) Fluctuations in monthly case reports of measles in Glasgow, as documented by Soper (1929). (b) Soper's (1929) estimates of the parameter that summarizes the 'the influence of season' over the entire 16-year span of the data. The mean values and SE of four weekly contact rates demonstrate a clear peak in transmission coinciding with the start of the school calendar, followed by a gradual decline through the rest of the year. Data are from Soper (1929).

transmission for directly transmitted pathogens (Table 1; Hosseini *et al.* 2004). Although the epidemiological consequences of natural variation in animal social aggregations have been less well studied, changes in social grouping have been demonstrated for a wide range of species in response to variation in resources (e.g. Newton-Fisher *et al.* 2000). Thus, animals might concentrate at water sources or fruiting trees during the dry season, or in dens or feeding sites during the winter months (e.g. Fig. 1a). Regular increases in the incidence of rabies in skunks during the winter and spring could be driven by seasonal host crowding (Gremillion-Smith & Woolf 1988), and outbreaks of phocine distemper virus in seals have coincided with the period when animals haul out and aggregate on beaches (Swinton *et al.* 1998). In both of these cases, closer host proximity and greater local density could lead to higher rates of contacts both within- and between species.

Seasonality and the transmission of vector-borne diseases

Vector-borne diseases, including those caused by viruses, protozoa and filarial nematodes, are among those parasites most likely to covary with environmental conditions (Dobson & Carper 1992; Hay *et al.* 2000). In many regions, seasonal variation in temperature limits the abundance of mosquitoes, ticks and other arthropod vectors that die, fail to develop or become less active below temperatures common to many temperate winters (e.g. Rogers & Randolph 1988; Fig. 1a). For example, longer winters and colder temperatures can reduce the numbers of host-seeking nymphs present to transmit Lyme disease and other tick-borne infections during the summer and autumn months (Ogden *et al.* 2006). By comparison, in the case of tick-borne encephalitis (TBE) in Europe, effects of rapid autumn cooling on the development of tick larvae and nymphs has been suggested as a cause of the persistence of TBE foci (a point discussed in more detail below).

In warmer regions, seasonal rainfall can increase the abundance of mosquitoes and other vectors with aquatic larval stages, where reproduction depends on the availability of breeding sites (Muir 1988; Linthicum *et al.* 1999). Furthermore, mosquitoes reach sexual maturity earlier and feed more frequently at warmer temperatures, potentially increasing the rate of parasite transmission. In addition to effects on vector abundance and behaviour, temperature influences rates of parasite development within vectors. For example, the replication rates of mosquito-transmitted dengue viruses and malaria parasites increase at warmer temperatures (Focks *et al.* 1995; Hoshen & Morse 2004). This is important because during cool autumn or spring conditions, parasites might not mature quickly enough to be transmitted before adult mosquitoes die, hence lowering the proportion of infectious mosquitoes and the average risk of infection.

Seasonal changes that affect parasite stages in the environment

For many intestinal parasites, infectious stages released into the environment are vulnerable to variation in temperature, rainfall and humidity before they encounter new hosts (e.g. Gordon *et al.* 1934; Gillett 1974). Thus, it has long been known that annual changes in the intensity of gastrointestinal nematodes in sheep and cattle are predictable based on seasonal variations in the weather (Levine 1963; Donald 1968). In fact, before the regular application of anthelmintic drugs, 'bioclimatographs' that combined local data on moisture and temperature were historically used to monitor, predict and avoid outbreaks of nematodes of sheep and cattle (Gordon *et al.* 1934; Smith 1990). For parasites where eggs are deposited in faeces, temperature can influence both rates of parasite development and the survival of external stages (Fig. 1a). For larval stages to develop, first the temperature must exceed a critical threshold, and then parasite development rates further increase with temperature above this threshold. Moisture is also critically important for the development, survival and movements of helminth larvae. Dry conditions can limit transmission and cause larvae to migrate into the soil, although excessive rainfall can wash away eggs and infectious stages (Stromberg 1997). These seasonal changes can alter R_0 through effects

on host encounter rates with infectious stages or by changing the overall abundance and decay rates of parasites in the environment (e.g. Roberts & Grenfell 1992).

Studies of cholera, caused by the bacterium *Vibrio cholerae*, illustrate the difficulties in uncovering seasonal mechanisms operating on diarrhoeal diseases for which infectious stages are released into the environment. Cholera dynamics in endemic regions show both marked regular seasonal cycles and longer-term fluctuations (Pascual *et al.* 2002; Fig. 3). One major challenge in explaining seasonal cholera outbreaks is that almost all environmental variables, particularly rainfall and temperature, are under the pervasive influence of monsoons themselves. Thus, moisture appears to be important for transmission, particularly in dryer regions, but seasonal flooding can also lower the concentrations of bacteria in the environment and reduce salinity to unfavourable levels (Pascual *et al.* 2002). Seasonal changes in temperature can further affect pathogen growth rates and plankton blooms in aquatic habitats in ways that might increase the pathogen's survival through its attachment to copepods and cyanobacteria (Colwell 1996). Ultimately, uncovering mechanisms behind cholera seasonality will point to the relative importance of two main routes of cholera transmission necessary for developing mathematical models: primary transmission from aquatic reservoirs to the human population, and secondary or human-to-human spread via faecal–oral transmission.

Seasonal timing of reproduction and pulses of susceptible hosts

Mechanisms described thus far highlight environmental drivers that influence parasite transmission by affecting host contacts, vectors or the parasites themselves. Annual reproduction is a separate form of periodic change that should have strong effects on host–parasite dynamics across a range of host species (White *et al.* 1996; Fig. 1b). Concentrating host births into a short breeding season can generate a pulse of new hosts that are recruited into the population at approximately the same time each year, thus effectively expanding host abundance as a factor of crucial importance to R and R_0 (Fig. 1b; Box 1). Furthermore, juveniles recruited into the population are likely to be immunologically naïve and more susceptible to a variety of parasites. Several predictions arising from this mechanism are that disease incidence should increase following juvenile recruitment, that the magnitude of annual outbreaks should covary positively with the numbers of new births, and that the majority of new infections following the breeding season should occur among relatively young hosts. Levels of herd immunity could also decline when a pulse of new juvenile hosts enters the population, leading to greater risks of infection among susceptible adults.

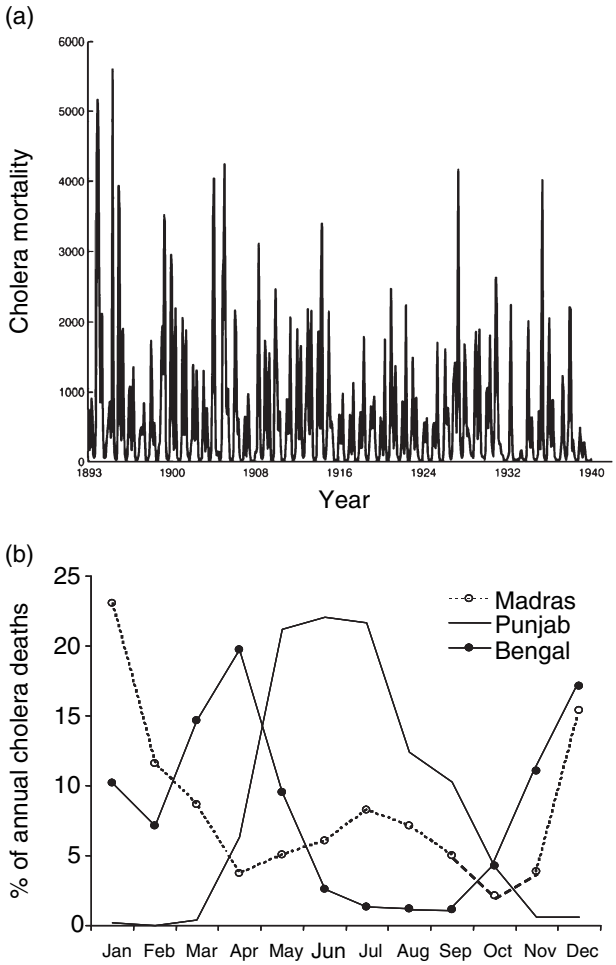


Figure 3 Monthly cholera deaths in the Dhaka district between 1893 and 1940 from historical records for former British India. The typical seasonal pattern with two peaks per year is modulated by longer cycles with considerable variation in total deaths from year-to-year. (b) Average monthly changes in cholera cases from provinces with two peaks per year (Bengal and Madras, with higher annual rainfall) and in the drier province of Punjab (with a single peak per year). The relative shift in the bimodal seasonal cycles in Bengal and Madras depends on the seasonal timing of the south-west monsoon in Bengal, and the north-east monsoon in Madras. Figures are redrawn from Pascual *et al.* (2002).

The role of seasonal host breeding for disease dynamics is illustrated by cycles of *Mycoplasma gallisepticum* infecting wild House Finches in North America. This recently emerged bacterial eye disease shows predictable fall–winter outbreaks separated by low prevalence during the summer months (Altizer *et al.* 2004a). Fall epidemics of mycoplasmal conjunctivitis appear to be caused by a combination of factors, including the recruitment of immunologically naïve juveniles into the population towards late summer. In line with this hypothesis, during fall outbreaks both the

prevalence and severity of infection are higher among juvenile birds (Altizer *et al.* 2004b), consistent with the observation that birds retain partial immunity following initial exposure and recovery (Kollias et al. 2004). Other animal–pathogen systems implicate seasonal births, possibly in combination with changes in social behaviour, as a factor important to the dynamics of pathogens, with examples including cowpox virus and macroparasites infecting voles and wood mice (Montgomery & Montgomery 1988; Begon *et al.* 1999) and phocine distemper virus in seals (Swinton *et al.* 1998). Studies of nematode outbreaks in Soay sheep have shown that magnitude of late-summer peaks in worm larvae depended on the number of lambs produced earlier that year (Gulland & Fox 1992). Even relatively continuous breeders like humans exhibit seasonal variation in reproduction, with potential consequences for infectious diseases. As with social contact, this mechanism should be most important for directly transmitted parasites whose transmission is limited by the abundance or proportion of susceptible hosts.

In addition to births, seasonal variations in host mortality can also influence host–pathogen interactions. If periods of unfavourable conditions lead to a homogenous increase in death rates for all hosts, this can effectively lower both R_0 and R in two ways: by shortening the infectious period, and by lowering the abundance of susceptible hosts (Dobson 1982). Seasonal host mortality can also interact with disease in ways that cause rapid host population declines. For example, stress associated with harsh winters, combined with the competitive social interactions that occur at high population densities, can impair immune defences and allow pathogens to enhance the background seasonally induced mortality (Lafferty & Holt 2003). In support of this hypothesis, the high winter mortality of Soay Sheep on St Kilda probably reflects interactions between population density, parasite loads and severe winters (Coulson *et al.* 2001).

Seasonal changes in host susceptibility and immune defence

Hosts often exhibit yearly rhythms that influence immune function (Dowell 2001; Nelson *et al.* 2002; Fig. 1c). Recent studies of rodents, birds and humans suggest that immune systems are weakened during the winter (reviewed in Dowell 2001), and by harsh weather conditions, poorer nutrition or investment in reproduction (Lloyd 1995; Nelson *et al.* 2002) in ways that could affect their ability to defend against infectious diseases (Hillgarth & Wingfield 1997). Several mechanisms could cause seasonal variation in host defences, including investment in reproduction that can lower host immune responses (Sheldon & Verhulst 1996; Klein & Nelson 1999). For example, increased reproductive effort in several bird species correlates with higher parasite burdens and lower antibody production and cell-mediated immunity (e.g. Hillgarth & Wingfield 1997; Moreno *et al.* 2001). These changes in immunity can influence parasite spread by increasing per-contact transmission probabilities or by lowering host recovery rates (and hence extending the duration of the infectious period).

During peak mating activity, males can experience lowered immunity from testosterone and mating displays, and females from pregnancy, lactation and offspring care (Festa-Bianchet 1989). Annual periods of high aggression or stress can increase host susceptibility to a wide range of parasites, partially through activation of glucocorticoid hormones prior to and during the breeding season (Nelson & Demas 1996; Padgett & Glaser 2003). Interactions between immunity and host breeding behaviour were recently explored in the red grouse-*Trichostrongylus tenuis* system. Grouse males given testosterone implants experienced greater infection rates, but also held larger territories – leading to more mates and higher mortality rates (Mougeot *et al.* 2004). Further experimental work involving testosterone implants and subsequent inhibitors indicated that testosterone was most likely influencing susceptibility to infection, rather than exposure through behavioural changes (Mougeot *et al.* 2005).

Among placental mammals, pregnant females actually lower their own immunity to prevent harming their fetuses (Lloyd 1983); this process is known as the periparturient rise, and provides a strong seasonal increase in R_0 by affecting host recovery or per-contact transmission probabilities. As one example, seasonal shifts in female immunity have been shown to occur in the European rabbit, *Oryctolgaus cuniculus*. Non-pregnant females acquire a strong immune response to the gastrointestinal nematode *Trichostrongylus retortaeformis*, so that the age intensity curve peaks in juveniles and declines in older rabbits as a consequence of acquired immunity (Cattadori *et al.* 2005). When females become pregnant, their immunity is suppressed, and the age intensity curve for *T. retortaeformis* no longer declines in older animals. This results in elevated numbers of infective stages being produced by females at the same time as their young begin foraging in habitats where parasites can accumulate, thus generating seasonal increases in transmission during and just after the peak breeding season.

Approaches for modelling seasonal dynamics

Given that seasonal factors can influence epidemiological parameters, a major aim is to understand how environmental drivers alter the dynamics of infectious diseases. Many population models have incorporated seasonality in phenomenological ways, either by dividing time into discrete intervals (e.g. May 1976), by adding time delays into continuous-time models. Other modelling approaches have

used 'forced oscillators' to show that systems subject to periodical external forcing can exhibit a range of interesting dynamics – from directly tracking the timing of forcing through a hierarchy of more complex behaviours (e.g. Grenfell *et al.* 1995; Vandermeer 1996; Earn *et al.* 2000; Pascual *et al.* 2000; Keeling *et al.* 2001; Greenman *et al.* 2004). Here, we briefly review how mechanisms behind seasonality can be represented mathematically and their effects on resulting dynamics.

Incorporating seasonal forcing into models

One conceptual approach for exploring how environmental drivers influence pathogen spread is to examine the long-term average of R_0, estimated as the arithmetic mean of pathogen fitness (Williams & Dye 1997). In many cases, seasonality will cause R_0 to vary above and below 1, thus affecting the window of time over which parasites can spread, and hence the probability of establishment and persistence. But more explicit modelling approaches are needed to explore how multiple seasonally varying parameters interact with one another and with other perturbations, including long-term environmental change and stochastic noise.

Building on compartment models of host–pathogen interactions that divide the host population into susceptible, exposed, infected and recovered classes (Boxes 1 and 2), a number of researchers have captured seasonality in a phenomenological way by making transmission periodic in time (Dietz 1976; Aron & Schwartz 1984). Thus the transmission parameter β can be described as oscillating around a baseline rate β_0 with a forcing term β_1 that is coupled to a seasonally changing term (usually a sinusoidal function; Boxes 1 and 2). Depending on the natural history of host and parasite, seasonal mechanisms can be considered by coupling external forcing to processes including host contact rates, host birth or mortality, recovery and host immunity, or the biology of vectors or free-living stages (e.g. Fig. 1; Box 1).

An important question is how the application of seasonality to different model parameters influences the resulting dynamics. It has been well established seasonal forcing of the transmission parameter, β, can generate complex dynamics for directly transmitted pathogens (Fig. 4; Aron & Schwartz 1984). By comparison, host birth rates tend to require a greater degree of seasonality to produce similar dynamics (cf. Box 1). This result arises because the effects of host birth rates on population turnover and abundance generally occur over slower timescales than transmission. It is also important to note that seasonality in transmission is linked with nonlinear effects (arising from the βSI transmission term), relative to the linear effects of fluctuations in birth rates on epidemiological systems. Another issue related to the dynamical outcomes of seasonality concerns the timing of multiple seasonal processes relative to one another – such as the timing of births relative to social grouping and contact rates. As a case in point, for some wildlife species such as the house finches described earlier, summer breeding and winter social aggregations are out-of-phase, and thus each seasonal factor has its own relatively separate effects, with a potential outcome manifested as two annual epidemics (Hosseini *et al.* 2004). For other species like harbor seals, breeding and seasonal aggregation occur at the same time, thus creating a much larger, but single, seasonal effect (Swinton *et al.* 1998).

The shape of the seasonal forcing function will further influence the ability of ecologists to separate factors associated with seasonal changes in prevalence with those causing longer-term cycles. Box 2 illustrates how the shape of the forcing function can have subtle but important effects on dynamics. A relevant example is provided by the case of measles, where the use of simple and intuitively appealing sinusoidal forcing functions can lead to unrealistically deep epidemic troughs, even for seemingly reasonable parameter values (Bolker & Grenfell 1993). As an alternative, in his seminal 1984 paper, Schenzle treated term-time forcing as a step function, assuming that contact rates were uniformly high during school terms and low during the school holidays (Keeling *et al.* 2001). This more detailed function predicted measles dynamics that were highly consistent with observed case reports (Bolker & Grenfell 1995; Earn *et al.* 2000). These findings were explained by the work of Keeling & Grenfell (2002), who parameterized both sinusoidal and term-time forcing functions using measles time-series data.

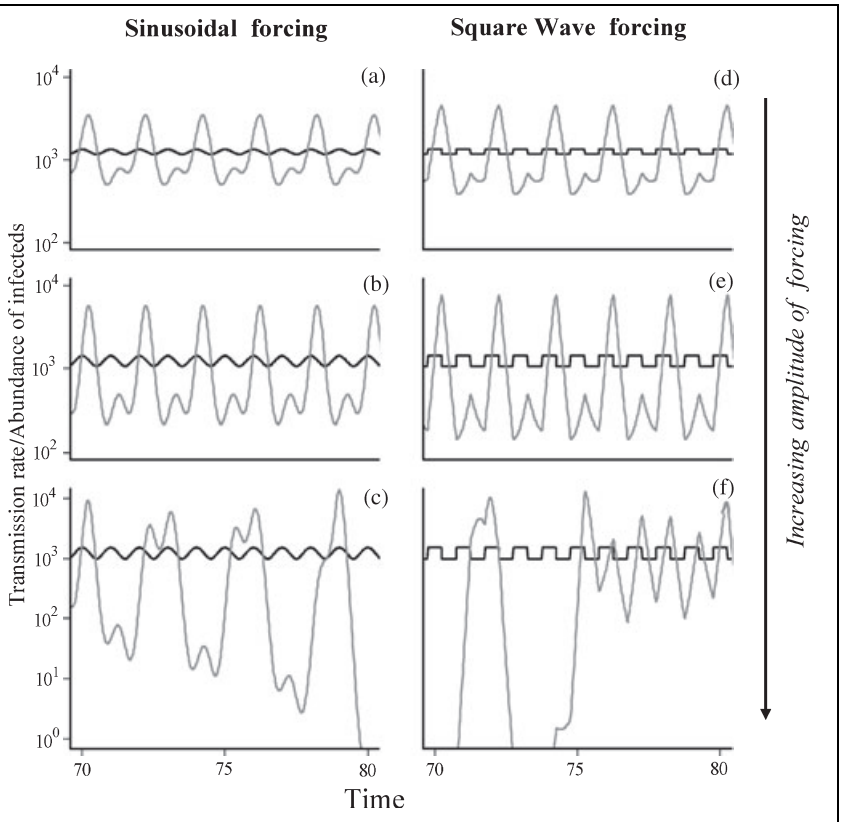
Finally, although the effects of seasonality are pervasive, it is important to note that not all types of host–parasite systems will respond strongly to environmental forcing. As one example of how modelling approaches can point to systems most sensitive to seasonality, Bolzoni *et al.* (L. Bolzoni, A.P. Dobson, M. Gatto and G. De Leo, unpublished manuscript) described an allometric approach that incorporates seasonally forced dynamics into the standard 'susceptible, exposed, infected and recovered' (SEI) and (SEIR) models for microparasites. Their results suggest that the potential of wildlife systems to respond to seasonal forcing depends on host body size and on the presence of host immunity. Specifically, small host species with relatively high birth and death rates will replenish their pool of susceptible individuals more rapidly, which in turn makes them more likely to exhibit short-period cycles in response to seasonal variation. For longer-lived host species with slower birth rates, seasonal births should have less of an effect on the numbers and proportions of susceptible hosts entering the population at any given time, leading to longer-period cycles that arise primarily from larger degrees of seasonal forcing.

Box 2 Linking seasonal forcing to model parameters: size and shape matter

Both the shape and amplitude of seasonal forcing can contribute to how seasonality affects host–parasite dynamics. Building on the same susceptible, exposed, infected and recovered model of Box 1, as the amplitude of the forcing term (black lines) applied to transmission increases, the realized dynamics (grey lines) change from biennial to chaotic fluctuations, a well-known result from the measles literature. The first column (a–c) shows sinusoidal forcing, where the transmission term is given by

$$\beta(t) = \beta_0(1 + \beta_1 \cos(2\pi t)).$$

The second column (d–f) shows forcing with a square wave: replacing the cosine function with 1 when it would be positive, and with -1 when it would be negative. Here, the realized dynamics fluctuate more sharply and with greater amplitude. However, except in the case of chaotic dynamics (c, f), the general pattern remains similar. Note that once seasonal forcing causes chaotic dynamics, the number of infected hosts can periodically fall below 1, even for this rather large system ($N = 5 \times 10^6$). Parameters used were as follows: (a) $\beta_1 = 0.07$ (b) $\beta_1 = 0.14$, (c) $\beta_1 = 0.21$, (d) $\beta_1 = 0.07$ (e) $\beta_1 = 0.14$ and (f) $\beta_1 = 0.21$. Model equations and all other parameters are as in Box 1.



SEASONAL EFFECTS ON LONG-TERM DYNAMICS

In addition to causing annual outbreaks of disease, seasonal forcing can be a crucial determinant of longer-term fluctuations in host–parasite systems. One way to illustrate the direct influence of seasonality on long-term dynamics is to compare the multiyear cycles arising from seasonal forcing of measles to annual outbreaks of mycoplasmal conjunctivitis in house finches. In the case of house finches, a high rate of influx of susceptible hosts and higher rate of turnover in the host population (Hosseini *et al.* 2004) leads to a process known as 'harmonic oscillation', whereby forcing drives regular cycles each year. However, when population turnover is lower, susceptible hosts are in short supply and the model exhibits greater density dependence, as exemplified by human measles during the 1950s–1960s (Finkenstädt *et al.* 1998). In this case, 'subharmonic resonance' is possible, whereby seasonal forcing of specific parameters gives rise to interepidemic periods that are integer-multiples of the period of forcing (Keeling *et al.* 2001; Greenman *et al.* 2004). To illustrate this complexity, Dietz (1976) demonstrated how changes in the amplitude of seasonal forcing can generate a cascade of dynamical bifurcations, with resulting population cycles of 1, 2 and 4 years and eventually to chaos (Fig. 4). It is also known that the precise dynamics of seasonally forced childhood infections depend on the length of the infectious period (Rohani *et al.* 1999). As demonstrated in Fig. 5, very short infectious periods can generate pronounced multi-annual oscillations when transmission rates vary seasonally. As the infectious period increases, however, the influence of seasonality shrinks to small amplitude annual variation.

Disease dynamics are also influenced in important, although subtle, ways by demographic and environmental noise. In non-seasonal population models, it has long been

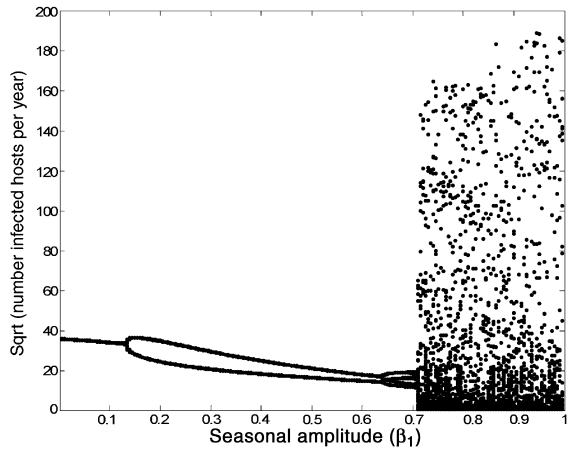


Figure 4 Bifurcation diagram summarizing the increasingly unstable dynamics of measles as the amplitude of seasonality is increased. The diagram is produced by running a 'susceptible, exposed, infected and recovered' model with term-time forcing (dates given in Keeling *et al.* 2001) and $n = 5 \times 10^6$, $\mu = 0.02$, $1/\sigma = 8$ days, $1/\gamma = 5$ days and $R_0 = 17$. For each value of the control parameter (b_1), 150 years of transients were discarded before disease incidence on 1 January was recorded for 50 years. The figure shows a series of period doubling bifurcations with increased seasonal forcing, leading eventually to chaos.

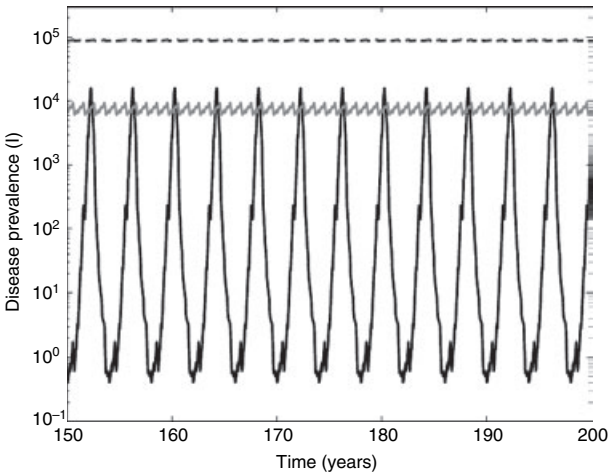


Figure 5 Time-series plots demonstrating that the dynamical consequences of seasonality are sensitive to the infectious period, or duration of time that infected hosts can transmit disease. The three curves represent infection prevalence through time from a term-time forced model (as used in Fig. 4) with infectious periods of 5 days (black line), 1 month (solid grey line) and 1 year (dashed grey line). For all cases, $R_0 = 10$, population size $= 5 \times 10^6$ and the *per capita* birth rate $= 0.02$ year^{-1}.

known that noise can sustain cycles that would otherwise decay to equilibrium (Nisbet & Gurney 1982; Greenman & Benton 2003). The magnitude of effects caused by stochasticity, however, depends on the type of noise and on which life history stage it operates. When the infectious period is long, 'phase locking' with seasonality is reduced because the infection can more successfully persist during the periods of low contact. This allows stochasticity to play a stronger dynamical role, with potentially interesting consequences for outbreak dynamics and the spatial synchrony of epidemic patterns (Rohani *et al.* 1999). For other systems like cholera, seasonal mechanisms provide a key pathway for the effects of year-to-year variation in climate as another form of environmental noise. Specifically, climate phenomena such as ENSO can modify the seasonal cycles of regional environmental variables and generate year-to-year variation in the size of outbreaks (Koelle *et al.* 2005a).

SEASONAL VARIATION AND SPATIAL PATTERNS OF DISEASE

Geographical shifts in seasonality across the range of a host can generate spatial variability in parasite–host dynamics – in some cases limiting the parasite's distribution and also causing regional variation in observed dynamics. TBE is one vector-borne disease that illustrates how geographical variation in seasonality affects vector feeding behaviour and the spatial distribution of disease. The disease is caused by a virus that circulates in yellow-necked mice (and leads to fatal infections in humans). One route of TBE transmission occurs when infected nymphal ticks feed close to susceptible tick larvae (termed co-feeding; Labuda *et al.* 1993). In parts of Europe that show less seasonality, TBE infections do not occur even though both the ticks and mice are abundant (Randolph *et al.* 2000), whereas in colder, more seasonal environments, TBE persists enzootically. Under climatic conditions observed in western Europe, potentially infected nymphs emerge earlier in the year than most larvae, and the probability of co-feeding on mice is relatively rare. In parts of mountainous Europe, by comparison, rapid autumn cooling prevents the development of larvae into nymphs before the winter, leading to infected nymphs questing for hosts at the same time as larval ticks in the spring (Randolph *et al.* 2000). If this hypothesis is correct, then persistence of TBE is highly unlikely in areas with a long summer season, whereas regions with a truncated summer (leading to synchronous co-feeding of larvae and nymphs) should show enhanced disease persistence.

Geographical variation in environmental drivers can also generate changes in annual patterns of disease outbreaks. In the case of house finch conjunctivitis, latitudinal variation in the duration of the breeding season could drive observed geographical variation in the timing and magnitude of epidemics. Fall outbreaks start earlier and are more severe in the milder southern climate (Altizer *et al.* 2004b), consistent

with an earlier onset of breeding in the south and more rapid recruitment of susceptible juveniles hosts (e.g. Hosseini *et al.* 2004). Cholera dynamics in the Indian subcontinent provide a more extreme example of regional variation in annual outbreaks, as wetter regions experience two annual peaks in cholera incidence whereas dryer provinces show only a single peak (Fig. 3b). In dryer provinces, the single yearly peak in cholera cases co-occurs with the onset of the monsoons, whereas the two peaks in wetter regions tend to occur during the dry months (with a decrease in incidence during monsoon rains). The patterns are probably caused by different environmental drivers: in the wetter regions, temperature has been implicated in the rise of the spring peak and the diluting effect of rainfall as a cause of the summer decline (Pascual *et al.* 2002). In dryer regions, rainfall could have the opposite effect of increasing transmission. Importantly, a key test for mechanisms that underlie cholera transmission will be their ability to predict geographical variation in the seasonal patterns of the disease, including the shift in timing of outbreaks, the number of peaks per year, and the different phases relative to the monsoons.

In addition to determining regional variation in the persistence of infections and timing of epidemics, latitudinal changes in seasonality can affect the temporal dynamics of host populations. This point is illustrated by the interactions between red grouse and *T. tenuis*, a directly transmitted caecal nematode. Red grouse tend to show large fluctuations in abundance, with the period of the oscillations ranging from 4 years in the southern part of the host's range to *c.* 12 years in areas farther north (Haydon *et al.* 2002). Field experiments coupled with detailed monitoring have shown that periodical declines in red grouse numbers are caused by high intensities of nematode infections (Hudson 1986; Hudson *et al.* 1992, 1998). Standard macroparasite models applied to this system show that cycles are caused primarily by negative effects of parasites on host fecundity, and that the duration of these cycles is determined jointly by the survival of free-living stages and the duration of hypobiosis in the parasite (Dobson & Hudson 1992). In more northern latitudes with longer winters, parasite survival in the environment is reduced and the duration of parasite arrestment is longer, leading to population cycles of longer periods. Thus, predictions from models regarding the effects of more extreme seasonal environments operating on parasites are consistent with observed latitudinal variation in the population cycles of the host.

IMPLICATIONS FOR DISEASE EMERGENCE AND CONTROL

Many diseases of concern to humans, domestic livestock and wildlife species have strong seasonal components to their transmission or biology (Table 1). Even periodically emerging outbreaks of Ebola haemorrhagic fever appear to have been clustered around dry periods that followed the rainy season in parts of central Africa (Pinzon *et al.* 2004). Among wildlife populations, vector-borne pathogens including West Nile virus and avian malaria (linked to marked losses in Hawaiian forest birds and North American corvids; van Riper *et al.* 1986; O'Leary *et al.* 2002) are favoured by warm temperatures and higher precipitation during key times of the year. Although exact connections between weather and infectious disease patterns are the subject of much debate (Hay *et al.* 2005), detailed information on annual variation in disease processes is becoming important for tracking outbreaks and understanding how pathogens respond to seasonal variability and long-term climate change (Harvell *et al.* 2002).

Forecasting how infectious diseases might respond to climate warming requires understanding how pathogens respond to different annual environmental changes; in many ways this is more important than simply estimating optimal environmental conditions. For example, seasonal changes in host biology driven by photoperiod might not respond to climate warming as strongly as other changes driven by temperature or rainfall. A better understanding of the mechanisms behind seasonal cycles of infectious diseases such as cholera and malaria will allow the development of increasingly better tuned early warning systems that predict disease risk in response to specific seasonal changes in climate. As a case in point, nonlinear time-series models have recently been developed to consider the interactions between intrinsic processes (such as levels of population immunity) and extrinsic factors (seasonal and longer term climate changes) in determining the size of yearly cholera outbreaks (Koelle & Pascual 2004; Koelle *et al.* 2005a).

How can knowledge of annual variation and infectious disease patterns inform policy and methods for disease prevention and control? One obvious strategy is that vaccinations for seasonal pathogens can be concentrated into a period several months prior to the onset of regular outbreaks. For example, influenza vaccination programmes are most active during the fall, and are repeated annually due to the limited duration of efficacy. Yet such programmes pose additional challenges, such as timing vaccine delivery to maximize both the time over which the vaccine is effective, and the likelihood that the vaccine will protect against the dominant strain. Knowledge of seasonal drivers could also improve control policies for vector-borne diseases like West Nile virus. In this case, concentrating spraying efforts during the spring when most transmission occurs among birds could be more effective in preventing human cases (and less environmentally damaging) than the current practice of responding

when human cases peak in the late summer and early fall – when mosquito numbers are already in decline. Ultimately, models and management practices that incorporate the seasonal timing of key events such as vector reproduction and pathogen development are essential to develop more cost effective and successful control strategies for infectious diseases.

FUTURE CHALLENGES FOR MODELLING AND EMPIRICAL STUDIES

Despite the pervasive nature of seasonality and the interesting dynamics that result from seasonally forced systems, we are only beginning to understand how seasonal external drivers influence the majority of host–parasite systems. One major difficulty in uncovering seasonal patterns and drivers of infectious diseases is identifying the relevant spatial scale for analysis (Pascual & Dobson 2005). Some patterns of seasonality only become obvious at large spatial scales, particularly in systems where significant numbers of random factors can impact disease incidence at local scales. Furthermore, epidemiologically relevant factors that operate on different time scales, such as changes in the pool of susceptible hosts or El Niño periods, can produce strong seasonal outbreaks in some years, and little or no disease in other years. With these challenges in mind, we identify several research priorities for improving our understanding how seasonal variation modifies the population dynamics of infectious diseases.

Identify how seasonality affects processes mechanistically

Examples highlighted in this review point to a diversity of mechanistic drivers of seasonality from human and wildlife systems, but for many infections, these mechanisms are unknown. Thus, while it has been well established that influenza outbreaks are highly seasonal, the particular causes remain uncertain and could range from human crowding to low humidity, cold weather or cycles in host immunity (Dushoff *et al.* 2004). Similarly, annual outbreaks of mycoplasmal conjunctivitis in wild house finches could be caused by a multitude of factors including seasonal reproduction, fall and winter flocking behaviour or annual variation in hormones and host defences (Hosseini *et al.* 2004; Lindstrom *et al.* 2005). As models that incorporate seasonality are sensitive to which parameters are externally forced, there is a pressing need to identify these mechanisms. A key problem here is that seasonality is so ubiquitous in nature that identifying the relevant environmental drivers and the parameters they influence becomes extremely difficult. It is also important to determine whether multiple mechanisms, such as seasonal breeding and social aggregations, are operating either in or out of synchrony. To that end, combining experimental and modelling approaches will become increasingly important in teasing apart the roles of multiple environmental drivers and the processes they influence.

Incorporate seasonality into mathematical models

Most infectious disease models tend to incorporate seasonal forcing phenomenologically as a simple sine wave that operates only on parasite transmission. However, seasonality in many systems will neither conform to an idealized sinusoidal pattern, nor will its impact be focused on transmission. It is therefore important to understand how the shape and duration of seasonal forcing influences dynamics, and to incorporate patterns of forcing that most closely correspond to biologically realistic assumptions (e.g. Fig. 1, Box 2). Recent models for childhood diseases have demonstrated that this level of detail matters (Bolker & Grenfell 1993; Earn *et al.* 2000), as the shape and magnitude of effects on host contact rates significantly alter the long- and short-term dynamics of measles. Similarly, new models of malaria transmission have incorporated the details of how seasonal changes in temperature influence mosquito reproduction and development rates of parasites within the vectors, allowing more accurate forecasting of malaria outbreaks based on weather changes (Hoshen & Morse 2004).

Examine how processes interact, and potentially resonate, with stochastic, nonlinear dynamics

Mathematical models show that once forcing is applied, complicated dynamics can result (e.g. Greenman *et al.* 2004). Previous work has already shown that multi-annual epidemics are more likely in long-lived hosts experiencing a relatively short-lived disease, but are less likely for short-lived hosts or pathogens associated with long infectious periods. However, we are only beginning to understand the complex interactions between noise, both demographic and environmental, and the nonlinear dynamics of disease. For example, two well-studied childhood infections, measles and whooping cough, are modelled with essentially the same equations, and yet they show different dynamics in the presence of noise, with major impacts on how each pathogen has responded to vaccination in time and space (Rohani *et al.* 1999; Earn *et al.* 2000). It also remains an open question to determine how different host–pathogen systems respond to environmental drivers (including seasonality) when the host population is spatially structured (Rohani *et al.* 1999).

Describe patterns of seasonality in time-series data

Better statistical approaches and more long term data sets are needed to understand the intrinsic and extrinsic factors

that influence the temporal dynamics of disease. Of particular relevance here are statistical methods that can: (i) fit models in continuous time; (ii) incorporate different forms of stochasticity; and (iii) handle hidden variables such as the number of susceptible individuals in the population. These approaches are crucial to bridge the gap between the differential equation models currently used in theoretical approaches relative to those used for fitting actual data, which are typically formulated in discrete time (Bjørnstad *et al.* 2002; Koelle & Pascual 2004). For example, several ecological time series show temporal patterns that are extremely regular in the timing of peaks but highly irregular in the amplitude of these outbreaks. Models have outlined several explanations for these patterns, from the so-called quasi-cycles (Nisbet & Gurney 1982) to Uniform Phase Chaotic Amplitude dynamics (UPCA; Blasius *et al.* 1999). Yet better statistical techniques are needed to distinguish which models best explain these patterns. Given the need to tease apart the effects of the many variables that influence epidemic patterns, one factor limiting studies of seasonality is the need for more long-term time-series data on host and pathogen occurrence. Not surprisingly, the most important insights have emerged from a small number of systems where sufficient replication has been obtained, almost all focused on human case data.

Develop manipulative field and laboratory approaches

A crucial next step will be to use a combination of field and laboratory experiments to perturb processes that covary with seasonal environmental changes and quantify the resulting effects on dynamics. These experiments can take one of several forms. First, researchers can capitalize on existing geographical variation within specific host–pathogen systems to reveal variation in the presence, timing and strength of seasonal mechanisms, host and parasite responses to environmental drivers, and observed temporal dynamics. Second, field-based experiments can be used to manipulate the potential responses of hosts and parasites to seasonally varying parameters across replicated populations. For example, treatments might use contraceptives or culling to limit seasonal recruitment through births, or alter host susceptibility or the infectious period by treating animals with immunosuppressive hormones. Finally, truly artificial systems grown in chemostats or growth chambers could be used to actually manipulate the seasonal parameters themselves and observe their effects on host and parasite biology.

Be aware of evolution

Host parasite dynamics have great potential to evolve in part because of the short generation times and high mutation rates of pathogens, and because pathogens impact both their own fitness and that of their hosts (Altizer *et al.* 2003; Galvani 2003). Seasonality might play a role in pathogen evolution by causing alternating periods of high transmission and population bottlenecks that simultaneously limit strain diversity and cause rapid genetic shifts (e.g. Ferguson et al. 2003), particularly given that even small amounts of seasonal forcing can generate tremendous oscillations in prevalence. The response of pathogens to environmental variation might evolve if particular strains are well suited to capitalizing on seasonal increases in potential transmission (Kamo & Sasaki 2005; Koelle *et al.* 2005b), or if pathogens adapt to persist during unfavourable conditions. Thus, in response to seasonally unfavourable conditions, many parasites have evolved adaptations such as seasonal reproduction, hypobiosis, and liver or deep tissue stages (e.g. Meade 1984). Although much work has been carried out on the evolution of virulence (Lipsitch & Nowak 1995; Frank 1996; Levin 1996), and multistrain dynamics (Dobson 1985; Gupta *et al.* 1994; Gog & Grenfell 2002), very few studies consider the ways that seasonality might affect pathogen evolution.

In summary, while seasonality is a ubiquitous force in nature, the complexity of its role has required the development of much theoretical work to gather even a basic understanding of how seasonality affects population dynamics. To completely understand many infectious disease systems it will become increasingly important to understand how seasonality affects multiple processes, including host behaviour, reproduction, immune function, and parasite transmission and survival in the environment. Basic processes important to host–parasite interactions are also seasonal in many other ecological systems; thus, it is likely that seasonality plays a much broader role in general population dynamics than we currently know – and the prospect that global climate change will rapidly modify current patterns of seasonality provides a major and immediate challenge for future ecological research.

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GLOSSARY

Bifurcation diagram: a summary diagram showing dynamical transitions (or bifurcations) that result from changes in a key parameter.

ENSO: describes global climate fluctuations every 2–7 years associated with shifts in air pressure between regions of the tropical Pacific Ocean. ENSO is a major source of interannual climate variation in many parts of the world marked by warmer 'El Niño' phases and cooler 'La Nina' phases.

External forcing: a factor affecting a dynamical system which is not internal, with no feedback to system variables of interest.

Herd immunity: protection from an infectious disease conferred by lower transmission when a high proportion of hosts in the population are immune; this lower abundance of susceptible hosts reduces the probability that any 'unprotected' individuals will acquire the disease.

Hypobiosis: a period of arrested development of parasitic worms, during which time larvae remain inactive within their hosts following infection; arrestment usually occurs when external temperatures are too low or conditions are too dry for egg development.

Multi-annual cycles: cycles with a period of more than 1 year; also called interannual cycles.

Nonlinearity: behaviour of a system in which the observed output does not vary in direct proportion to changes in input parameters; nonlinear behaviour can often be complex, unpredictable or chaotic.

Harmonic oscillation: fluctuations with a period entrained on regular external forcing, also called parametric resonance.

Periparturient: period of time around birth events.

Phase locking: periodic dynamics that are observed when the ratio of natural to forced frequencies is a rational number.

Quasi-cycles: a sustained pattern of cyclic dynamics caused by the introduction of stochasticity into a system that would otherwise experience under-damped oscillations to a stable equilibrium.

Subharmonic resonance: fluctuations with a period that is an integer multiple of the period of the external forcing.

Term-time forcing: assuming high contact rates between susceptible and infected hosts during the school terms and low contact rates during the holidays.

UPCA: a dynamical outcome whereby the phases of individual cycles appear to be entrained, but their amplitudes show a chaotic pattern.

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