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The Invasion, Persistence and Spread of Infectious Diseases within Animal and Plant Communities [and Discussion]

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The invasion, persistence and spread of infectious diseases within animal and plant communities

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Recent theoretical and empirical studies of the population biology of infectious diseases have helped to improve our understanding of the major factors that influence the three phases of a successful invasion, namely initial establishment, persistence in the longer term and spread to other host communities. Of central importance in all three phases is the magnitude of the basic reproductive rate or transmission potential of the parasite. The value of this parameter is determined by a variety of biological properties of the association between an individual parasite and its host and the interaction between their populations. The recent epidemic of acquired immunodeficiency syndrome (AIDS) in North America and Europe is employed to illustrate the factors that promote disease establishment and spread. The frequency distribution of the number of different sexual partners per unit of time within homosexual communities is shown to be of central importance with respect to future trends in the incidence of AIDS. Broader aspects of pathogen invasion are examined by reference to simple mathematical models of three species associations, which mirror parasite introduction into resident predator–prey, host–parasite and competitive interactions. Many outcomes are possible, depending on the values of the numerous parameters that influence multi-species population interactions. Pathogen invasion is shown to have far-reaching implications for the structure and stability of ecological communities.

Introduction

The emotions of fear and fascination often accompany the spectacle of an epidemic, induced by the arrival of a new infectious disease. These are dramatically captured in Daniel Defoe's journal of the 1665 plague epidemic in London.

> 'It was then indeed, that man withered like the grass and that his brief earthly existence became a fleeting shadow. Contagion was rife in all our streets and so baleful were its effects, that the church-yards were not sufficiently capacious to receive the dead. It seemed for a while as though the brand of an avenging angel had been unloosed in judgement.' (Brayley 1722).

The historical and epidemiological literature abounds with similar accounts of disease invading human communities and of the concomitant effects on social organization and the unfolding patterns of historical events (see, for example, Shrewsbury (1970); Henschen (1966); Crawford (1914); Creighton (1894)). Indeed, in a book entitled *Plagues and peoples*, McNeil argues that infectious diseases have had a central influence on the rise and fall of civilizations throughout the history of the human race (McNeil 1976). A catalogue of the number of deaths induced by the major epidemics is staggering and makes the consequences of all past wars almost trivial by comparison (Bailey 1975). In Europe in the 14th century, for example, there were

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some 25 million deaths, out of a population of roughly 100 milllion, from bubonic plague alone. The Aztecs in 1520 lost about half of their population of 3.5 million from smallpox. It has been estimated that Russia suffered about 2.5 million deaths from typhus in the years from 1918 to 1921, and in the world pandemic of influenza in 1919, 20 million people are thought to have died over a brief span of 12 months. These are but a few of the more devastating epidemics (McNeil 1976; see figure 1).

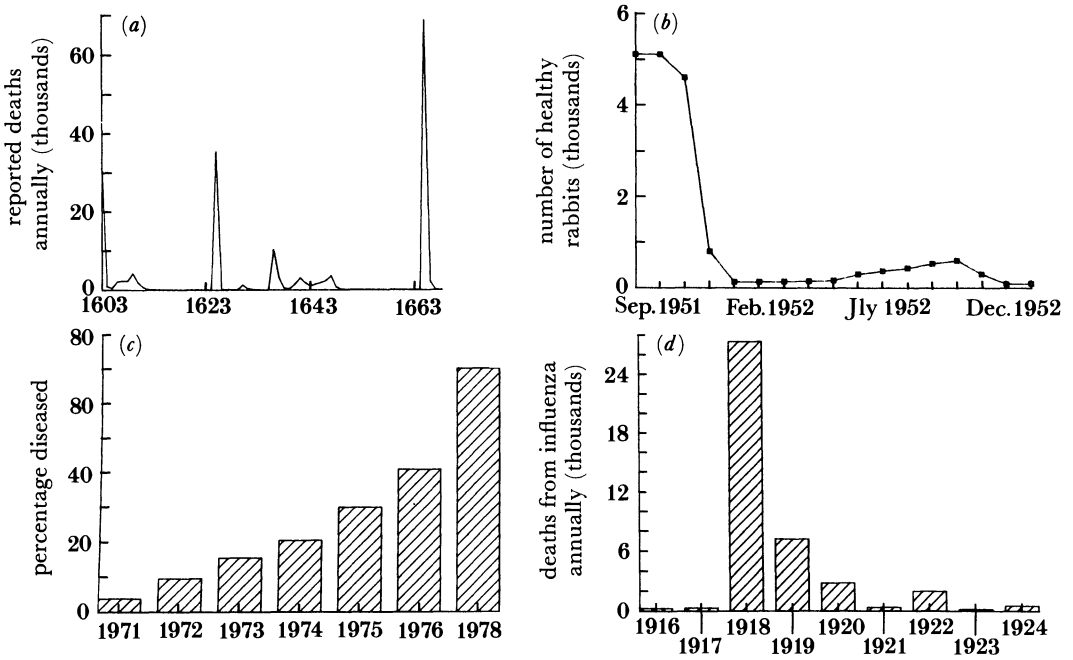

FIGURE 1. Examples of pathogen invasion. (*a*), Reported deaths from bubonic plague in London over the period 1603–1654 (data from Brayley, (1722)). (*b*) The impact of myxoma virus (introduced in late 1951) on the density of rabbits in the Lake Urana region of Australia (data from Myers, *et al.* (1954)). (*c*) The percentage of elm trees (*Ulmus* spp.) in the South of Mersey/Humber region of England infected with the fungus *Ceratocystis ulmi* over the period 1971–1978 (data source: Forest Research Station, Alice Holt). (*d*) Reported deaths from 'Spanish flu' (a 'strain' of the human influenza virus) in Sweden over the period 1916 to 1924 (data from Henschen (1966)).

Invasions by pathogens have also had dramatic effects on non-human animals and plants. The most notorious episodes include the impact of Dutch elm disease (a fungal pathogen) in Europe and North America (Burdekin 1983), the near-extermination of the American chestnut tree by a fungal blight (Soulé & Wilcox 1980), the deliberate introduction of a virulent strain of the myxoma virus into the rabbit populations of Australia and Europe (Fenner 1983) and the rinderpest viral epidemic in Africa in the late 1800s (Sinclair & Norton-Griffiths 1979; figure 1). Many of these invasions had far-reaching consequences, not just for the host species, but also for community structure both with respect to species diversity and relative abundance. The classic work of Elton (1958) on 'The ecology of invasions' and the more recent study of Soule & Wilcox (1980) detail many case histories of the 'knock-on' effects of pathogen invasion.

Aside from the more dramatic and lurid consequences of invasion, the introductions (either deliberate or accidental) of diseases into 'virgin' populations provide us with natural experiments in community manipulation or perturbation. As such, they provide ecologists with unique opportunities, often in very large experimental arenas (such as a continent), to learn

more, not just about the ecology of disease agents but also about community structure and species interactions. They also enable us to test various theoretical notions concerning trophic web stability and resilience against observed patterns. Unfortunately, however, most attention in past episodes has been focused on the host, and quantitative details of indirect effects on other species, such as predators, prey or competitors of the afflicted organism, have rarely been recorded.

This paper does not attempt to give a balanced review of the factors that determine success or failure of an invasion, nor does it focus on cataloguing the potential 'knock-on' effects of pathogen introduction. Instead, we focus on two particular areas of the topic: first, the significance of heterogeneity in transmission between hosts to pathogen invasion, establishment and persistence, as exemplified by the current epidemic of acquired immunodeficiency syndrome (AIDS), in humans; and secondly the consequence of pathogen introduction for established two-species associations such as predator–prey, interspecific competition and host–parasite interactions. In both areas, new research is presented.

The paper is divided into three sections. The first describes some basic properties of host–parasite associations and focuses on the factors that determine the likelihood of establishment, whether or not the infection will persist in the longer term and the rate of spread of the disease to other populations. The next section concentrates on a specific case study, namely the recent epidemic of AIDS in Europe and North America. The third and longest section describes the consequences of disease invasion for resident two-species associations. Mathematical models serve throughout as a template for analysis and interpretation but, where possible, quantitative comparisons are made with observed trends in natural communities.

1. Parasite establishment, persistence and spread

We can distinguish three major phases of a successful invasion: initial establishment, persistence within the invaded host population in the longer term, and spread to other host populations. Observation, combined with the use of simple mathematical models, provides us with an understanding of the key factors involved in each phase.

Basic reproductive rate, R_0

After introduction, the parasite population will initially increase in size provided its basic reproductive rate, R_0, exceeds unity in value. For microparasitic infections (the viruses, bacteria, fungi and protozoa) the parameter R_0 measures the average number of secondary cases of infection generated by one primary case in a susceptible host population. In the case of macroparasites (the helminths and arthropods) R_0 records the average number of offspring (or female offspring in the case of a dioecious species) produced by a single parasite, that attain reproductive maturity within a susceptible population (Anderson 1981; Anderson & May 1979; May & Anderson 1979).

Threshold density, N_T

Host density is an important determinant of the magnitude of R_0, although its precise functional relation with the parameter depends on the structure of the parasite's life cycle (see Anderson 1981; Anderson & May 1979, 1981; May & Anderson 1979). For direct life-cycle parasites that are not sexually transmitted, R_0 is, in the simplest case, directly proportional to

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the density of susceptible hosts. If the parasite is indirectly transmitted between two host species via free-living infective stages, R_0 is usually proportional to the product of both host densities. R_0 is approximately proportional to the ratio of the two host densities if the parasite is indirectly transmitted via a biting vector. In all cases, however, there exists a critical density of hosts, N_T, below which R_0 is less than unity in value. More generally, if the density of susceptible hosts, X, is less than N_T, the initial inoculum of parasites will decay to extinction.

An illustration of the relation between R_0 and N_T in the early stages of invasion is provided by a simple deterministic model of the transmission of a direct life cycle microparasite. If the force of transmission is proportional to the density of susceptibles, X, multiplied by the density of infectives, Y (a 'mass-action' assumption; see Kermack & McKendrick 1927)), then the rate of change in Y with respect to time t is

$$\mathrm{d}Y/\mathrm{d}t = (\beta X - d)Y. \tag{1}$$

Here β is transmission coefficient and $1/d$ denotes the life expectancy of an infective (determined by the rates of host mortality and recovery from infecton (Anderson & May 1981)). After the introduction of a single infective into a wholly susceptible population ($X = N$ initially), (1) reveals that $Y(t)$ will not increase unless $N > d/\beta$. In other words, the critical density of susceptibles (N_T) is simply

$$N_T = d/\beta. \tag{2}$$

The basic reproductive rate or transmission success is defined as the rate of production of new cases per unit of time multiplied by the life expectancy of an infective, hence

$$R_0 = \beta N/d = N/N_T. \tag{3}$$

In the very early stages of invasion (host population largely susceptible), (1) may be rewritten as:

$$\mathrm{d}Y/\mathrm{d}t = d(R_0 - 1)Y. \tag{4}$$

R_0 must clearly be greater than unity if Y is initially to increase in size.

This simple example ignores many complications such as heterogeneous mixing, vertical transmission, latent periods in which hosts are infected but not infectious and genetic variability within both host and parasite population (see Anderson & May 1979; table 1; Anderson & May 1985*a*). However, it captures the essence of the problem. Parasite establishment will not occur unless host density exceeds some critical level whose value is determined by a variety of biological characteristics of both the host and the parasite and

Table 1. Transition types and rates for a simple stochastic model of measles virus transmission ($N = X + H + Y + Z$)

type of transition	rate	event
(1) $X \to X+1, H \to H, Y \to Y, Z \to Z$	μN	birth
(2) $X \to X-1, H \to H, Y \to Y, Z \to Z$	μX	death
(3) $H \to H-1, X \to X, Y, Z \to Z$	μH	death
(4) $Y \to Y-1, X \to X, H \to H, Z \to Z$	μY	death
(5) $Z \to Z-1, X \to X, H \to H, Y \to Y$	μZ	death
(6) $X \to X-1, H \to H+1, Y \to Y, Z \to Z$	βXY	infection
(7) $H \to H-1, Y \to Y+1, X \to X, Z \to Z$	σH	becoming infectious
(8) $Y \to Y+1, X \to X, H \to H, Z \to Z$	Λ	immigration
(9) $Y \to Y-1, Z \to Z+1, H \to H, X \to X$	γY	recovery

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interaction between them. The value of N_T is typically large for directly transmitted microparasites (such as many common viral infections of man), which are horizontally transmitted, are of high pathogenicity and/or induce rapid recovery and lasting immunity in those hosts who do not die from infection. A good example of invasion by such an infection is provided by the history of the arrival in Britain in 1968 of the A/Hong Kong/68 antigenic variant of the human influenza virus. Figure 2 records the proportion of serum samples collected in Sheffield (a large urban centre with a high population density) that had antibodies to the viral strain (Stuart-Harris 1982). The virus rapidly spread in 1968–69 and induced a large epidemic of cases in 1969–70. By 1972 most of the population was immune and virus transmission waned.

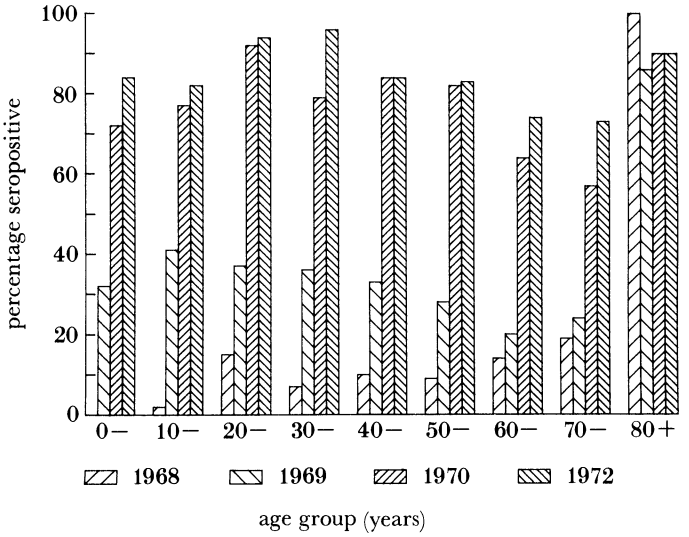

FIGURE 2. Age-stratified serological profiles (haemagglutination-inhibition test) for the percentage of sera, collected from individuals in Sheffield, with antibody to A/Hong Kong/68 influenza virus (data from Stuart-Harris (1982)). Four profiles are displayed (for samples collected in 1968, 1969, 1970 and 1972) to show the creation of herd immunity to the viral strain during three consecutive epidemics (1968–69, 1969–70 and 1971–72). The virus disappeared in 1972 and was replaced by A/Eng/72.

Various mechanisms have evolved to enable parasites to establish within low-density host populations. These include vertical transmission (seen, for example, in many viruses of insects), an ability to evade the host's immunological defences (the slow viruses of vertebrates), transmission by a vector (the arboviruses) and the production of the long-lived infective stages (the nuclear-polyhedrosis viruses of insects). For directly transmitted macroparasites, N_T is invariably low since mature parasites usually produce large numbers of long lived infective stages. A good illustration of this point is provided by the incidences of different types of infectious agent in primitive and isolated human societies such as the South American Indian tribes in the Amazon basin (Black 1975; Tyrell 1977). Endemic infections include the directly transmitted nematodes and persistent or vertically transmitted viruses (such as herpes, Epstein–Barr virus and hepatitis B). Infections which induce rapid recovery and lasting immunity in those who survive, such as measles, influenza and polio, are usually absent in the tribes isolated from frequent contact with developing urban centres (Black 1975).

These considerations might lead us to expect that, in general, macroparasites will be more frequent invaders than microparasites. The literature, however, tends to be dominated by accounts of invasion by microparasites. This is unlikely to be a fair reflection of what actually

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occurs, because the impact of viruses and bacteria is usually more apparent to the casual observer; they tend to be of greater pathogenicity than macroparasites (which are more a cause of morbidity than mortality) and they induce symptoms of disease that are more apparent. On the basis of the critical density for establishment, we might also expect indirectly transmitted species to be more successful as invaders than directly transmitted species. This is not the case, however, since establishment requires the presence of not one but two suitable host species; this requirement reduces the likelihood of success (see Dobson & May 1986). Indirectly transmitted species are often host-specific.

Persistence after invasion

Establishment does not necessarily imply that the parasite will be able to persist within the host population in the long term. Persistence is very dependent on whether or not the interaction between host and parasite is cyclic or epidemic in character. Associations tend to be oscillatory if transmission efficiency is high (the β of equation (1) large), if the infection is short-lived such that hosts rapidly recover to join an immune class or rapidly die from the disease, or if transmission is via long-lived infective stages (Anderson & May 1978, 1979, 1981; May & Anderson 1978, 1979). Many microparasitic infections of vertebrates and invertebrates possess such characteristics and tend to induce large amplitude oscillations in host abundance or the incidence of infection or both. After an epidemic, the reproductive rate of the infection falls below unity in value as a consequence of the removal of a large segment of the susceptible population (either by mortality or by the acquisition of immunity). A further outbreak of infection can only occur when the susceptible population is replenished by new births or the loss of immunity. During the troughs between epidemics, the incidence of infection may fall to very low levels and extinction can occur due to stochastic effects. Whether or not extinction occurs depends critically on the size of the host population and the rate of replenishment of the supply of susceptibles.

A good illustration of this issue is provided by the transmission of measles virus in human communities in cities of differing sizes (Barlett 1960; Black 1966). From studies of cities in North America and island communities before widespread vaccination, the measles virus appears unable to persist endemically in communities of less than a quarter to a half a million people (figure 3). The critical community size for persistence (as opposed to establishment; see equation (2)) is dependent not simply on total population size but also on demographic characteristics such as the net birth rate (the rate of replenishment of susceptibles). A further illustration of the problem of long-term persistence in the absence of repeated invasions is provided by the long-term incidence of measles in a large island such as Great Britain and a smaller community such as Iceland. As is shown in figure 4, the virus persists endemically in England and Wales, exhibiting (before mass vaccination, which started in 1968) two-year recurrent cycles in incidence (Anderson & May 1982, 1985*b*). In Iceland, however, the virus is unable to persist endemically and the infrequent epidemics are triggered by repeated introductions by travellers to and from other countries. Epidemics occur at roughly four-year intervals (presumably dependent on the net birth rate of the community) but between epidemics the virus often vanishes from the island (Cliff *et al.* 1981). Iceland has the lowest population density of any country in Europe. The population sizes of the two communities in 1970 were approximately 49 million for England and Wales and 200000 for Iceland; the net birth rates (per annum) during the 1960–1970 period were between 700000 and 800000 in England and Wales and between 4000 and 5000 for Iceland.

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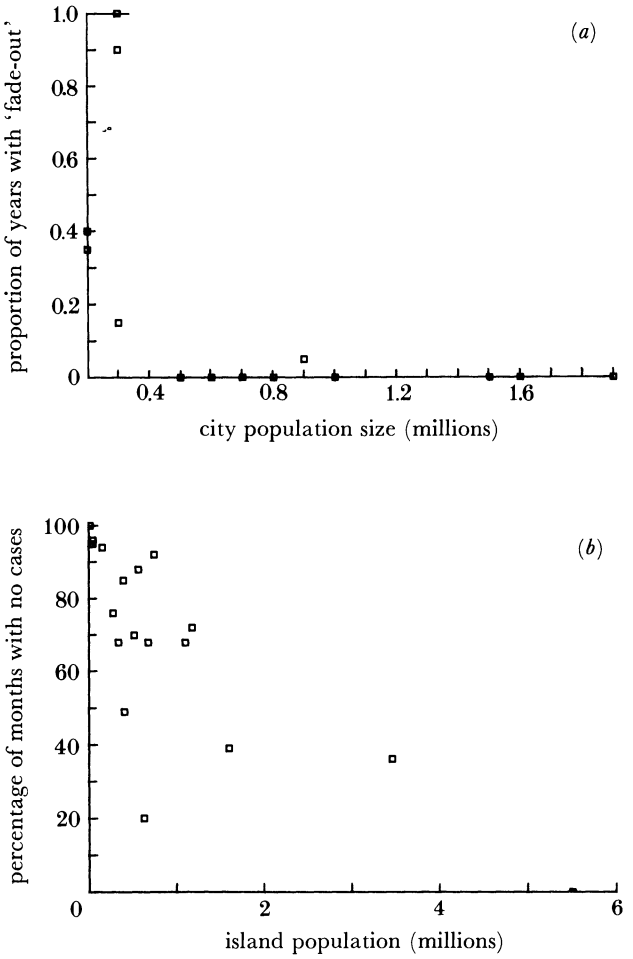

FIGURE 3. The persistence of measles in cities of various population sizes (*a*) in the U.S.A. and (*b*) in island communities. (*a*) Proportion of years in which no cases of measles were reported in one or more months for various cities in North America for the period 1921–1940. The proportion is plotted against population size of the city (data from Bartlett (1960)). (*b*) Percentage of months in which no cases of measles were reported in 19 island communities (data from Black (1966)).

A clearer picture of how community size and net birth rate influence virus persistence can be obtained from numerical studies of stochastic models of virus transmission. For directly transmitted viruses such as measles, which induce life-long immunity on recovery and have short latent and infectious periods (roughly seven days each; Anderson & May 1982), appropriate models of transmission (assuming homogeneous mixing and ignoring the age structure of the community) are compartmental in structure and describe discrete changes in the numbers of susceptible, $X(t)$, infected but not infectious, $H(t)$, infectious, $Y(t)$ and immune, $Z(t)$, individuals. The discrete time stochastic equivalent of the standard deterministic model of recurrent epidemics (Hamer 1906; Soper 1929; Anderson & May 1982) embodies ten transition events and these are summarized in table 1 (see Bartlett (1960) for methods). The parameters are as follows: μ – death rate, β – tranmission coefficient, $1/\sigma$ – latent period, $1/\gamma$ – infectious period and Λ – rate of immigration of infectious people. For simplicity it is assumed that there is no migration out of the community. Denoting the rate of transition of event i as $r_i (i = 1$ to $10)$ then in a small interval of time $(t, t+\Delta t)$ the probability of transition i occurring is $r_i \Delta t + O(\Delta t)$, where $O(\Delta t)$ is a term of infinitesimally

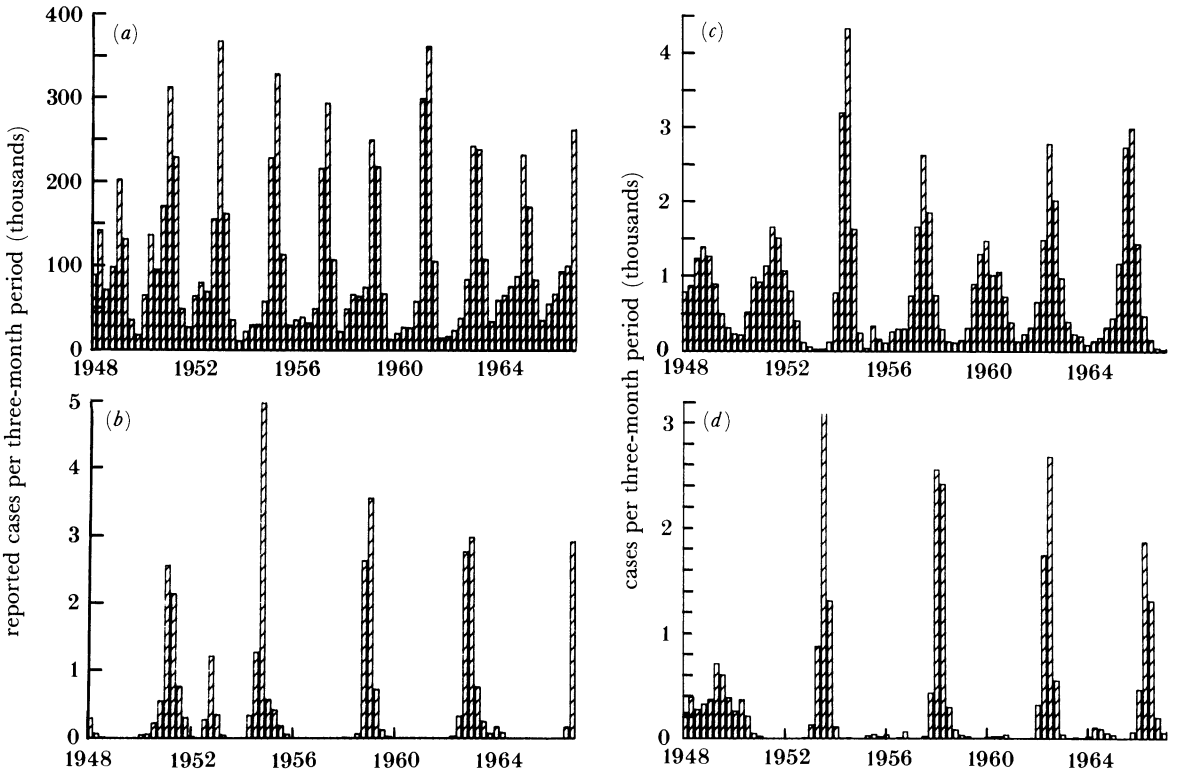

FIGURE 4. Recurrent epidemics of measles: observed patterns and temporal realizations of a stochastic model. (*a*) Reported cases of measles (per three-month period) for England and Wales over the interval 1948–1966. (*b*) Similar data for Iceland. (Sources: (*a*), Registrar-General's Statistical Reviews; (*b*), Cliff *et al.* (1981)). (*c*, *d*) Temporal realizations of a stochastic model (see text for further details) and record cases of measles (per three-month period) for a community of 250000 people (*c*) and a community of 100000 (*d*). Parameter values: incubation and infectious periods, 7 days each; life expectancy, 70 years; rate of immigration of infection, 7 a^{-1}; annual birth rate per community, 3571 (*c*), 1428 (*d*); threshold density of susceptibles (N_T), 15000 (*c*), 6500 (*d*).

small order ($O(\Delta t) \ll \Delta t$). All events are assumed to be independent such that the probability density function, $f(t)$, of the time between any pair of successive transitions is

$$f(t) = r \exp(-rt), \tag{5}$$

where $r = \sum_{i=1}^{10} r_i$. The probability that the next transition is of type i, p_i is $p_i = r_i/r$. This relatively simple model is difficult to study analytically and is best investigated by Monte Carlo simulation techniques (Tocher 1963).

Two examples of stochastic realizations of temporal changes in measles incidence are recorded in figure 4 for community sizes of 250000 and 100000 individuals. Note that in the small community disease 'fade-out' occurs and the recurrent epidemics are induced by the immigration of infectives. Also note that the interval between epidemics is roughly 2–3 years for the larger population (it is roughly 2 years for communities of the order of half a million people) and approximately 4 years for the smaller community (the annual birth rates of the communities were set at 3571 and 1428 respectively, life expectancy was fixed at 70 years ($1/\mu$; type II survival) and the immigration rate of infectives was set at seven per annum) (figure 4). The important point highlighted by such numerical studies is the distinction between

the critical density of susceptibles necessary for parasite establishment (6500 for the numerical simulations recorded in figure 4*d*) and the critical community size necessary for parasite persistence in the longer term (roughly 250000 in the numerical simulations). The demography of the host population (the net birth rate) is an important determinant of the latter; certain biological characteristics of the interaction between an individual host and the parasite (duration of infectiousness and transmission efficiency) are important for the former (the N_T of equation (2)).

In the case of macroparasitic infections (the helminths), which are persistent in character and do not induce lasting immunity or high rates of host mortality, the population interaction between host and parasite is unlikely to be oscillatory in character (Anderson & May 1978; May & Anderson 1978). This being so, establishment usually implies persistence. There are some exceptions to this generalization such as the trichostrongyle nematode (*Trichostrongylus tenuis*) of the red grouse (*Lagopus lagopus scoticus*); this species is highly pathogenic and produces relatively long-lived, free-living infective stages. As recently noted by Hudson *et al.* (1985), this parasite appears able to induce oscillatory fluctuation in grouse abundance. During the troughs in host density the abundance of the nematode declines to very low levels and local extinctions may occur. In this instance, therefore, initial establishment and the induction of an epidemic may not necessarily imply long-term persistence.

Spread to other host communities

After establishment and persistence, the spread of an infection to other communities is dependent on a variety of factors, among which the spatial distribution of host abundance and host migration and dispersal patterns are of particular importance. An excellent example is provided by the current epidemic of rabies in mammalian populations in Europe (see Macdonald 1980; Anderson *et al.* 1981). The epidemic is thought to have originated in Poland in 1939 and is characterized by a high incidence in the red fox, *Vulpes vulpes* (figure 5). The disease has spread outwards from Poland at an average annual rate of 30–60 km, although the rate of spread has varied greatly from one locality to another depending on habitat type and fox density. Mathematical studies of the spread of infectious diseases can be based on the simple assumption of diffusive transmission; a large literature has addressed problems in this area (see Bailey 1975; Cliff *et al.* 1981; Kallen *et al.* 1986). With respect to rabies, Kallen *et al.* (1986) have shown that the velocity of spread, c, of the infection depends on the life expectancy of an infected host (the $1/d$ of equation (1)), the basic reproductive rate, R_0 (whose magnitude is proportional to fox density) and a diffusion coefficient, D (the dispersal and migration rate of the fox, probably related to fox density):

$$c = 2[Dd(R_0 - 1)]^{\frac{1}{2}}. \tag{6}$$

By using crude estimates of the relevant parameter values (Anderson *et al.* 1981) these authors estimated that the average velocity of spread was approximately 50 km a^{-1}, a figure that is in accord with observed trends (Kallen *et al.* 1986). This type of analysis can be employed to help in the design of control programmes based on the killing of foxes in a 'firebreak' area in front of the epidemic wave (Kallen *et al.* 1986). More generally, this case study of rabies spread illustrates techniques that are applicable to the design of control policies for human infections (e.g. 'ring' vaccination around the focus of an epidemic).

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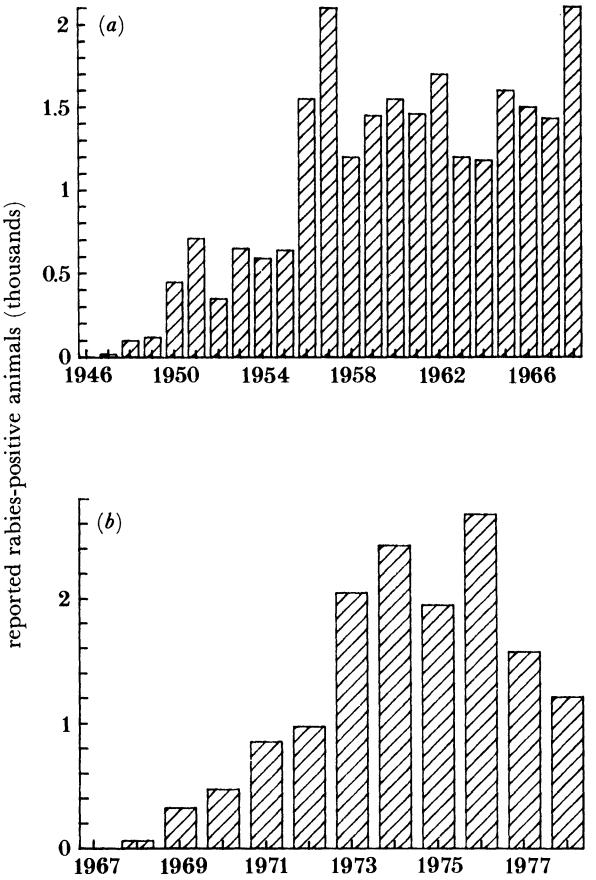

FIGURE 5. The spread of rabies in the German Democratic Republic and France after the introduction of the disease into Poland in 1939. (*a*) Number of reported rabies-positive animals in the G.D.R. from 1947 to 1968 (data from Sinnecker (1976)). (*b*), number of reported cases of rabies in all mammal species in France from 1968 to 1978 (data source: Centre National d'Études sur la Rage).

2. ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

The recent emergence of an apparently new disease syndrome in man, acquired immunodeficiency, provides a fascinating and alarming example of invasion by a highly pathogenic infectious agent. In the period October 1980 to May 1981, five young homosexual men were treated for *Pneumocystis carinii* pneumonia in hospitals in Los Angeles. The cases attracted attention, because *P. carinii* pneumonia was known to be a disease associated with immunosuppression. At the same time, Kaposi's sarcoma was being diagnosed with increasing frequency in young men in New York City and California (Peterman *et al.* 1985). These observations heralded the early stages of the invasion of North America by a previously unknown disease, subsequently termed acquired immunodeficiency syndrome (AIDS). By the end of 1985, over 15000 people in the United States had developed the disease (figure 6). Many thousands more have been infected with the AIDS virus and a substantial proportion of these will probably develop symptoms of disease (figure 6). Most of those reported with AIDS have died within 15 months of diagnosis (Wong-Staal & Gallo 1985). The etiological agent is a lymphotrophic retrovirus, human T lymphotropic virus (HTLV-III) or lymphadenopathy-associated virus (LAV), which can cause a wide range of immunological disturbances and

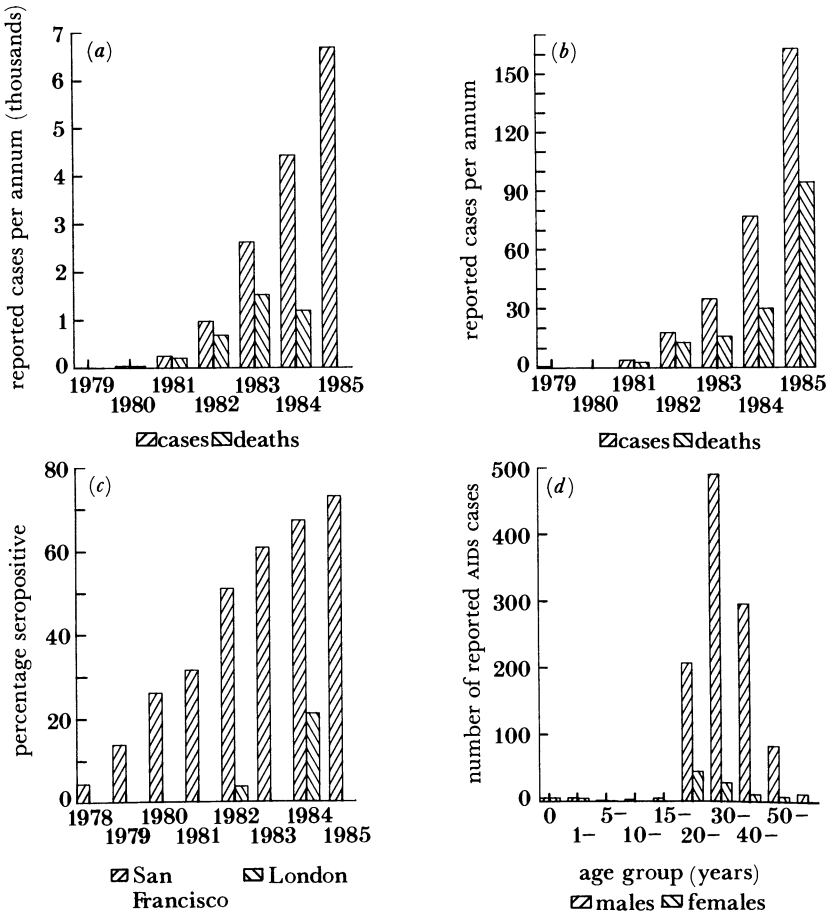

FIGURE 6. AIDS in North America and Europe: (*a*) Reported cases of AIDS per annum and reported deaths from AIDS in the United States over the period 1979–1985 (the 1985 figure only includes cases up to November, the deaths for 1985 are unavailable at present). The reported deaths for the U.S.A. are thought to be a considerable underestimate of the real figure caused by AIDS. (Data source: *Morbidity and Mortality Weekly Reports*, Centers for Disease Control, U.S. Department of Health and Human Services). (*b*) Reported cases of AIDS per annum and deaths from AIDS in the United Kingdom over the period 1979–1985. (Data source: Public Health Laboratory Service, Communicable Disease Surveillance Centre reports.) (*c*) The prevalence of antibody to HTLV-III (LAV) in a cohort of homosexual and bisexual men in San Francisco over the period 1978–1985 (Data source: *MMWR* (1985*b*)). The figures for London in 1982 and 1984 are from a study of homosexuals attending a clinic for sexually transmitted disease. (Data source: Carne *et al.* 1985.) (*d*) The age and sex distribution of reported AIDS cases in 18 European countries up to June 1985 (Austria, Belgium, Czechoslovakia, Denmark, Finland, France, Federal Republic of Germany, Greece, Iceland, Italy, Luxembourg, Netherlands, Norway, Poland, Spain, Sweden, Switzerland and United Kingdom). (Data source: *MMWR* 1985*b*.)

render the host susceptible to opportunistic infections and cancers. Basic research on HTLV-III (LAV) has progressed very fast, due to earlier experience of related animal retroviruses and HTLV-I and -II (leukaemia viruses), and recent progress in the fields of molecular biology and immunology. However, despite the sophistication of our knowledge at the molecular and cellular levels, current understanding of the epidemiology of AIDS remains very limited indeed.

The medical, social and psychological issues associated with AIDS infection have created unprecedented problems for modern medical and public health research. Epidemiological surveillance has identified characteristic groups of people that are at the greatest risk from AIDS, namely, homosexual and bisexual men, intravenous drug abusers, haemophiliacs, recipients of blood transfusions and persons of Central African or Haitian origin (Peterman *et al.* 1985;

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Wong-Staal & Gallo 1985; Moss *et al.* 1985; *MMWR* 1985*a*). These observations, in conjunction with other research, have revealed that the virus is transmitted by sexual contact (mainly between homosexuals but also through heterosexual activity), needle sharing (among intravenous drug abusers), parental exposure to blood or blood products and from mother to child during the perinatal period (*MMWR* 1983) (figure 6). A recent survey of risk factors in homosexual and bisexual men in San Francisco, California, has revealed that certain sexual practices appear to facilitate transmission of HTLV-III (LAV), such as anal intercourse, oral–genital sex and activities involving multiple sex partners (*MMWR* 1985*b*). The extreme promiscuity among homosexual communities in the U.S.A., and to a lesser extent in Europe, appears to have been of central importance to the successful invasion and rapid spread of the virus.

The leukaemia virus (HTLV-I) is thought to have originated in Africa and been brought to Europe and North America by commercial and slave trading activities (Wong-Staal & Gallo 1985). HTLV-III (LAV) is also thought to have originated in Central Africa, but its spread through Haiti (a popular holiday resort for American homosexuals) to California and New York (areas that harbour large homosexual communities) is much more recent. Entry to Europe may have been directly from Central Africa, or from Haiti or the United States (Galbraith 1985; Wong-Staal & Gallo 1985). Most interestingly, Kanki *et al.* (1985) recently discovered a retrovirus (designated STLV-III) closely related to HTLV-III (LAV) in African green monkeys and macaques. In the latter species the virus is also associated with an AIDS-like disease.

The gaps in our knowledge of the epidemiology of HTLV-III are unfortunately many and certain of these are of central importance in any attempt to gain an understanding of the character and persistence of the current epidemic. For example, little is understood at present about: (1) the latent period of the virus (the time from infection to the state of infectiousness to other people); (2) the average duration of infectiousness; (3) the proportion among those seropositive (people with serum antibodies to the virus) who harbour the virus; (4) what fraction of the seropositives will eventually develop symptoms of AIDS (and hence die). Current evidence suggests that, once infected, a host cannot eliminate retrovirus infection (Peterman *et al.* 1985). As such, those found to be seropositive probably harbour the virus. Whether they remain infectious for life is unclear as yet. Seroconversion appears to occur approximately 6–8 weeks after infection (data from donor and recipient transfusion studies of antibodies to HTLV-III (LAV); Esteban *et al.* (1985)). However, virus has been isolated from seronegative persons (Salahuddin *et al.* 1984). The course of virus expression and antibody response from the time of infection through the incubation period (the time of infection to the appearance of symptoms of AIDS) and during different stages of clinical disease has not as yet been clearly established. The serum antibody level to HTLV-III is high in most patients by the time clinical symptoms are recognized and falls to low levels in the advanced stages of the disease. Patients with AIDS appear to have less virus in their blood than 'healthy' seropositives (Wong-Staal & Gallo 1985). The incubation period appears to be very long, being of the order of 3–5 years (Peterman *et al.* 1985). This estimate is probably too low since the epidemic is recent and many of those seropositive 3 or more years ago may develop AIDS in future years. The latent period, by comparison, is probably short, of the order of days to a few weeks.

Simple models of the AIDS epidemic can help in an assessment of the relative importance of these different epidemiological characteristics. In particular, they can help to focus attention

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both on what must be understood to predict the likely pattern of the epidemic in future years and on the question of how much sexual habits must change to induce a decline in the incidence of the disease.

Basic model of AIDS; homogeneous mixing

A very simple model can be constructed on the assumption that a homosexual community of size $N(t)$ at time t consists of five types of individual. The first class is susceptibles of density $X(t)$. On becoming infected (and seropositive), individuals follow one of two possible trajectories. A proportion, p, of those infected move at a rate γ_1 (that is, after a characteristic time $1/\gamma_1$) into the class with clinical AIDS; people with overt symptoms of AIDS are assumed not to contribute to virus transmission within the community. The remaining fraction $(1-p)$ of the infectious class recover into a non-infectious class at a rate γ_2 (that is after a characteristic time $1/\gamma_2$); these non-infectious individuals remain seropositive, but do not develop AIDS. We define $Y_1(t)$, $Y_2(t)$, $A(t)$ and $Z(t)$ to be the densities of infectives who develop AIDS, infectives who will not develop AIDS, people with AIDS and non-infectives who will not develop AIDS, respectively. The total number of infectives at time t is $Y(t) = Y_1 + Y_2$. It is further assumed that infectious and susceptible people mix homogeneously (the mass action assumption), so the net rate of transmission is proportional to the density of susceptibles $X(t)$, multiplied by the probability that any one encounter will be with an infectious individual, $Y(t)/N(t)$. The model is of the form:

$$\mathrm{d}X/\mathrm{d}t = \Lambda - \beta\epsilon XY/N - \mu X. \tag{7}$$

$$\mathrm{d}Y_1/\mathrm{d}t = p\beta\epsilon XY/N - (\mu+\gamma_1)\ Y_1, \tag{8}$$

$$\mathrm{d}Y_2/\mathrm{d}t = (1-p)\ \beta\epsilon XY/N - (\mu+\gamma_2)\, Y_2, \tag{9}$$

$$\mathrm{d}A/\mathrm{d}t = \gamma_1 Y_1 - (\alpha+\mu)\, A, \tag{10}$$

$$\mathrm{d}Z/\mathrm{d}t = \gamma_2 Y_2 - \mu Z. \tag{11}$$

Here, ϵ represents the mean number of sexual partners per unit of time; β characterizes transmission efficiency; Λ is the rate of immigration of susceptibles into the homosexual community; μ is the death rate of non-AIDS people; α is the death rate of AIDS patients; and p, γ_1 and γ_2 are as defined above. The proportion seropositive, q, is $q = (N-X)/N$. Unlike most conventional epidemiological models, in which the total population is constant, here $N(t)$ changes over time as a result of natural and AIDS-related deaths and of immigration:

$$\mathrm{d}N/\mathrm{d}t = \Lambda - \mu N - \alpha A. \tag{12}$$

In the absence of precise knowledge about the characteristic duration of infection in those who go on to develop AIDS and those who do not, we assume the two times are equal, $\gamma_1 = \gamma_2 = \gamma$. Then $Y_1 = pY$, $Y_2 = (1-p)\ Y$, and (8) and (9) simplify to

$$\mathrm{d}Y/\mathrm{d}t = \beta\epsilon XY/N - (\mu+\gamma)Y. \tag{13}$$

This system of equations exhibits damped oscillations to a stable point with the disease maintained within the population, provided the basic reproductive rate of the virus, R_0, exceeds unity. With $\gamma_1 = \gamma_2$, the equilibrium densities, N^* and A^*, are:

$$N^* = \frac{\Lambda(\alpha+\mu+\gamma+(1-p)\ \gamma\alpha/\mu)}{(\mu+\gamma)(\alpha+\mu-\alpha p\gamma/\beta\epsilon)},$$

$$A^* = (\Lambda - \mu N^*)/\alpha.$$

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The predicted pattern of the epidemic after invasion is portrayed in figure 7 for two different sets of parameter values. These patterns are qualitatively similar to those observed in both the United States and Britain (figure 6).

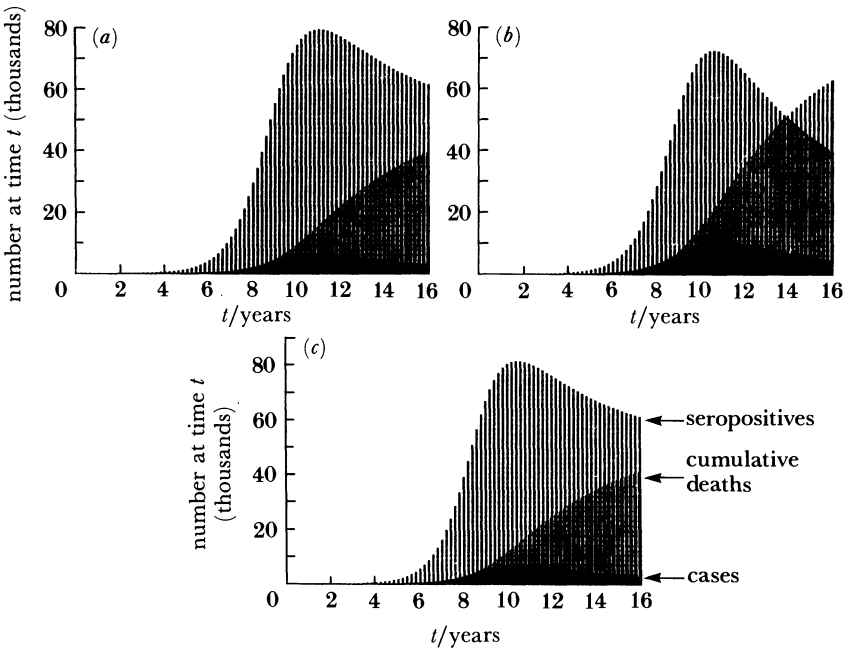

FIGURE 7. Temporal predictions of the basic (homogeneous mixing) AIDS model defined in equations (7)–(11) in the text. The graphs show changes in cases ($A(t)$), seropositives ($A(t)+Y_1(t)+Y_2(t)+Z(t)$) and cumulative deaths from AIDS through time. Parameter values: (*a*) $N(0) = 100000$, $\Lambda = 1333.33$ a^{-1}, $1/\mu = 75$ a^{-1}, $p = 0.5$, $\beta\epsilon = 1.5$ a^{-1}, $1/\gamma_1 = 1/\gamma_2 = 4$ a^{-1}, $1/\alpha = 1.00$ a; (*b*) the same as (*a*) except $p = 0.8$; (*c*) as for (*a*), except $1/\gamma_2 = 10$ a^{-1}.

During the early stages of the epidemic, where the vast majority of the community are susceptible ($X \approx N$), the growth in infectious (seropositive) people, $Y(t)$, is approximately exponential,

$$dY/dt = (R_0 - 1)Y/T. \tag{14}$$

Here, R_0 is the basic reproductive rate and T is the average infectious period ($T = 1/(\mu+\gamma) \simeq 1/\gamma$. This equation has the solution

$$Y(t) = Y(0)\exp[t(R_0-1)/T],$$

where $Y(0)$ is the initial number of infecteds at time $t = 0$. In other words, the intrinsic growth rate of the seropositives, r, is simply $r = (R_0-1)/T$. Similarily, the early growth in the number of people with AIDS, $A(t)$, is given by

$$A(t) = \frac{p\gamma Y(0)}{r+\mu+\alpha}[e^{rt} - e^{-(\mu+\alpha)t}].$$

A rough guide to the value of r can be obtained from a study of seropositivity to HTLV-III (LAV) in a cohort of approximately 6875 homosexual and bisexual men who attended a San Francisco (California) city clinic (*MMWR* 1985*b*). Over the period 1978 to 1985, the prevalence of antibody to HTLV-III (LAV), measured by an enzyme immunosorbent assay, increased from 1.5% to 73.1%. Calculated values of r for each yearly period over the interval

1978–85 are listed in table 2. A single estimate for r over the period 1982–84 in London is also listed in this table. Taking the early stages of the epidemic in the USA (1978–80) gives an average r value of 0.88 a^{-1}, which is similar to the figure for London during the early stages of the spread of AIDS (table 2). A crude estimate of R_0, obtained from equation (14), is around 3–4 given that the incubation period, T, is roughly three to four years. The numerical simulations of the model displayed in figure 7 are based on these crude parameter estimates. It is surprising, however, that the broad pattern predicted by the simple model is similar to the trends

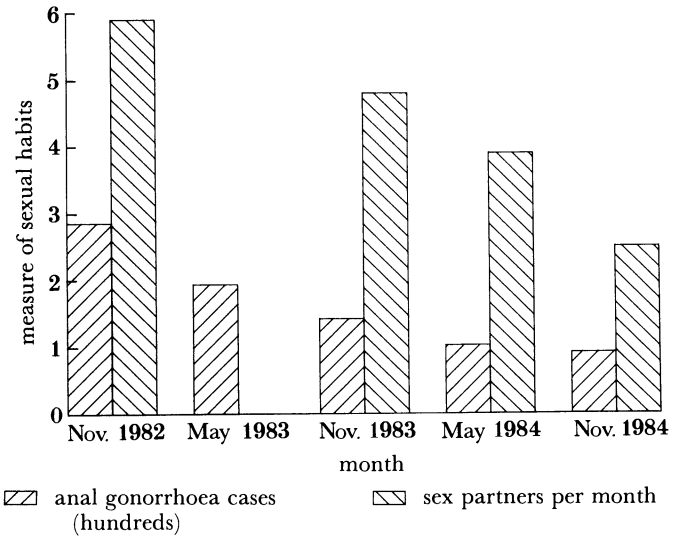

FIGURE 8. Changes in sexual habits among a sample of homosexuals in San Francisco over the period November 1982 to November 1984 (two measures, namely the mean number of different sexual partners per month, and the incidence of anal/rectal gonorrhea (in hundreds)) (*MMWR* 1985*b*).

TABLE 2. THE INTRINSIC RATE OF INCREASE, r, IN THE PROPORTION OF HOMOSEXUALS SEROPOSITIVE FOR HTLV-III (LAV) ANTIBODIES

(Data sources: MMWR 1985*a*; Carne *et al.* 1985.)

period	r/a^{-1}
(*a*) San Francisco, U.S.A.	
1978–79	1.12
1979–80	0.64
1980–81	0.28
1981–82	0.48
1982–83	0.18
1983–84	0.10
1984–85	0.08
(*b*) London, U.K.	
1982–84	0.87

observed in cities such as San Francisco in the U.S.A. (figure 6) both with respect to the timing of the epidemic (reaches its maximum incidence in about 8–12 years from the start of the invasion) and the proportion seropositive in the homosexual community at the peak incidence (70%–80%). Current data from San Fransisco and New York suggest that the incidence of AIDS is beginning to level off. It has been argued that this is a consequence of a change in sexual habits (both with respect to the mean number of sexual partners per unit of time and the type of sexual activity) in the last few years within homosexual communities (figure 8) (Pickering *et al.* 1986). However, the simple model suggests that even with no change in sexual practices,

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the epidemic will reach its maximum intensity in the homosexual community at around 8–12 years after the initial introduction of the infection. This prediction, is of course, dependent on the magnitude of the transmission coefficient, β, and the duration of infectiousness, T. It is striking, however, that the crude parameter estimates of β, based on observed changes in seropositivity, yield a prediction in broad agreement with observation.

In the longer term, the number of deaths arising from AIDS will depend critically on what proportion of those seropositive will eventually develop symptoms of disease. Model predictions (figure 7) were based on the assumption that either 50% or 80% will eventually acquire AIDS. At present the lower figure appears more plausible but, as mentioned earlier, estimates of the incubation period (roughly 3 years) are constantly being revised upwards as data accumulates from longitudinal epidemiological studies (Peterman *et al.* 1985; Wong-Staal & Gallo 1985).

Heterogeneous mixing model

The simple model described above takes no account of the observation that the frequency distribution of the number of different sexual partners per unit of time within homosexual communities is highly skewed, such that most individuals have few partners and a few have very many. For example, a study by McKusick *et al.* (1985) of sexual habits among homosexuals in San Francisco revealed that in 1982 the average number of different partners per month was approximately 5.9 but that the variance within the sample was much greater than the mean. In the early stages of the epidemic (the vast majority of the population remain susceptible), this complication can be crudely mirrored by the following model for changes in $Y_i(t)$, the number of seropositive individuals who have i sexual partners per unit of time:

$$\mathrm{d}Y_i/\mathrm{d}t = i\beta\lambda N_i - (\mu+\gamma)\, Y_i. \tag{15}$$

Here β characterizes transmission efficiency and λ denotes the probability that any one partner is infected. As before, we have assumed $\gamma_1 = \gamma_2 = \gamma$, so that (13) pertains. Assuming that partners are chosen at random, we have

$$q = \Sigma\, iY_i/\Sigma\, iN_i.$$

If $\overline{Y}$ is the weighted sum, $\overline{Y} = \Sigma\, iY_i$, then

$$\mathrm{d}\overline{Y}/\mathrm{d}t = [\beta[(v/\epsilon)+\epsilon] - 1/T]\,\overline{Y}. \tag{16}$$

Here ϵ is the mean number of partners, v is the variance and T is the average incubation period. Note that the intrinsic growth rate, r, of the seropositives now becomes

$$r = [\beta[(v/\epsilon)+\epsilon] - 1/T]. \tag{17}$$

Contrast this with the homogeneous case (equations (7)–(11)), where $r = (\beta\epsilon - 1/T)$. The conclusion to be drawn from this simple model of the early stages of the epidemic is that heterogeneity $(v/\epsilon > 1)$ can enhance the rate of spread of the infection by the activities of the highly sexually active individuals in the tail of the frequency distribution of sexual promiscuity. If the variance:mean ratio (v/ϵ) is large, then the value of r is primarily determined by the degree of heterogeneity as opposed to the mean (ϵ) activities of the individuals within the community.

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More generally, to describe the full course of the epidemic after invasion we require a slightly more complicated model (D. R. Cox & R. M. Anderson, in preparation). Let $X(t, s)$ and $Y(t, s)$ be the number of susceptibles and infectious individuals with sexual habit characteristic s. The definitions of $A(t)$, $Z(t)$ and $N(t)$ remain as defined earlier. Again the duration of infectiousness is assumed to be the same for those who do, and those who do not, go on to develop AIDS ($\gamma_1 = \gamma_2 = \gamma$).

$$(\partial X/\partial t)\ (t, s) = \Lambda(s) - sX(t, s)\ \lambda(t) - \mu X(t, s). \tag{18}$$

$$(\partial Y/\partial t)\ (t, s) = sX(t, s)\ \lambda(t) - (\mu + \gamma)\ Y(t, s). \tag{19}$$

$$\mathrm{d}A/\mathrm{d}t = \rho\gamma \hat{Y}(t) - (\alpha + \mu)\ A(t). \tag{20}$$

Here $\Lambda\ (s)$ is the immigration rate of susceptibles of sexual characteristics (= habits) s. $\hat{Y}(t)$ is the total number of infectives at time t and β is the transmission efficiency coefficient (defined per partner). The probability of infection is defined as;

$$\lambda(t) = \beta \int_0^\infty sY(t, s)\ \mathrm{d}s \Big/ \int_0^\infty sN(t, s)\ \mathrm{d}s. \tag{21}$$

The solution of (18) is

$$X(t, s) = X_0(s)\ \exp\left[-\int_0^t s\lambda(u)\ \mathrm{d}u\right] + \Lambda(s) \int_0^t \exp\left[-\int_\tau^t s\lambda(u)\ \mathrm{d}u\right] \mathrm{d}\tau, \tag{22}$$

where $X_0(s)$ is the number of susceptibles of characteristic s at time $t = 0$.

If s has a gamma distribution within the community, with mean m and variance m^2/b, then with $\hat{Y}(t) = \int_0^\infty sY(t, s)\ \mathrm{d}s$, (19) can be expressed in terms of $\hat{Y}(t)$ and the parameters of the distribution:

$$\frac{\mathrm{d}\hat{Y}}{\mathrm{d}t} + (\mu + \lambda)\ Y = \lambda(t) \left\{X_0\, mb[1 + m\lambda/b(t)]^{-b-1} + \Lambda_0\, mb \int_0^t \left[1 + m/b \int_\tau^t \lambda(u)\ \mathrm{d}u\right]^{-b-1} \mathrm{d}\tau\right\}. \tag{23}$$

Numerical studies of (22) and (23) again suggest that heterogeneity in sexual activity ($m/b > 1$) can act to promote the rapid spread of the epidemic within a segment of the community (figure 9). More intriguing, however, is the observation that heterogeneity tends to induce fewer cases of AIDS than that predicted by the homogeneous mixing model. The highly promiscuous individuals acquire infection early on in the course of the epidemic, and are therefore removed from circulation during the first three to four years after the initial introduction of the infection. They either acquire AIDS and die or move on to the seropositive but non-infectious class. Once they are removed from circulation, the remaining infectives have a lower level of sexual activity and hence the rate of virus transmission declines. In short, heterogeneous mixing models (with a high variance on sexual activity) predict that the epidemic peaks slightly earlier than in the homogeneous case, induces fewer AIDS cases, results in lower levels of seropositivity in the population and induces a longer 'tail' to the epidemic. On the one hand, observation suggests that homosexuals exhibit great heterogeneity in sexual habits, while on the other, heterogeneous mixing models predict epidemic patterns which appear at present to be a poorer match of observed trends than those generated by homogeneous mixing models.

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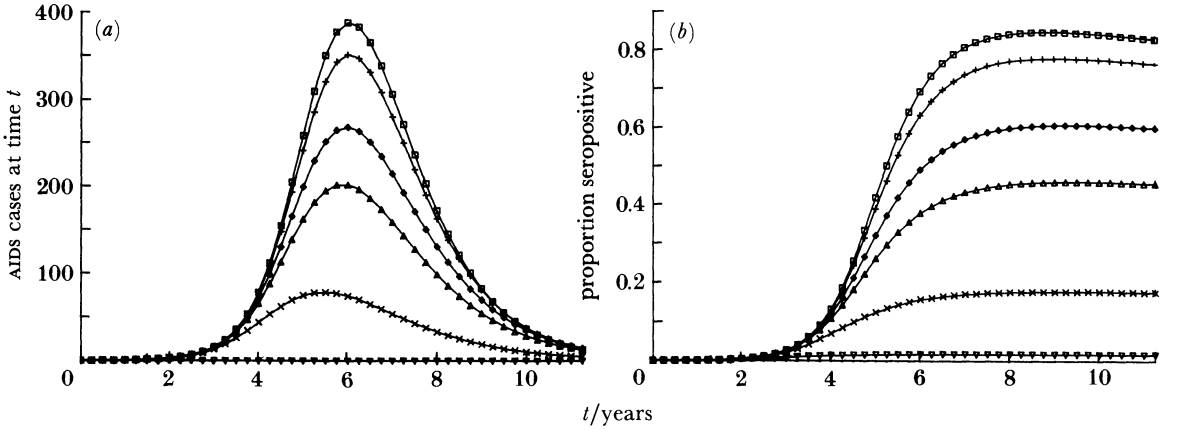

FIGURE 9. Temporal predictions of the heterogeneous-mixing AIDS model (equations (18)–(21) in the text). The graphs show changes in (*a*) AIDS cases $A(t)$ at time t and (*b*) the proportion seropositive at time t, with time for differing degrees of heterogeneity in sexual activity within a homosexual community ($N_0 = 10000$) (the distributions of the number of sexual partners per unit of time for both susceptibles and infectives is assumed to be gamma in form. Parameter values: $\gamma_1 = 0.333\ a^{-1}$, $p = 0.2$, $\alpha = 1.33\ a^{-1}$, $1/\mu = 75$ a, $m = 3.3$. With a fixed mean $m = 3.3$, the variance to mean ratio, m/b, was altered from 0.033 (homogeneous sexual activity) to 200 (highly heterogeneous activity). Symbols for heterogeneity (m/b): □, 0.033; +, 0.5; ◇, 2; △, 4; ×, 33; ▽, 200.

A number of factors could explain this puzzle, not least of which is the accuracy of the compartmental structure of both the homogeneous and heterogeneous models. It may be that a very high proportion of those that become seropositive will eventually develop AIDS such that the average incubation period, T, is much greater than that suggested by current observations (i.e. more than 3 years). Alternatively, those who acquire infection but do not develop AIDS may remain infectious for very long periods of time. A further possibility relates to the accuracy of current beliefs of sexual promiscuity among homosexuals: it may be that homosexuals are more homogeneous in their sexual activity patterns than is suggested by survey data based on interviews with individuals who volunteer information. Furthermore, it may be that the levels of seropositivity recorded in the San Francisco cohort study (figure 6) are much higher than those prevailing in the entire population of homosexuals in this city. Those willing to participate in the study may be the more sexually active individuals. Current and future epidemiological research should help to throw some light on those issues.

In summarizing, it must be stressed that model structure and assumptions remain very tentative at present. Much is unknown concerning the epidemiology of HTLV-III (LAV), and refinements and alterations to the basic structure of the models will undoubtedly be required in the future. Until more epidemiological information on AIDS is available, model construction and analysis simply serve to highlight the gaps in our knowledge and to help guide the interpretation of current trends in disease incidence. Prediction of future events will remain uncertain until more is understood about the basic biology and transmission characteristics of the virus. In the context of invasions, AIDS presents a remarkable example of how a change in the prevailing social and behavioural habits within a host community can facilitate the spread of a lethal pathogen. It is highly probable that, in the early part of this century, sexual promiscuity among homosexuals and the frequency of overt homosexual activity were not of sufficient magnitude to yield an R_0 value for HTLV-III (LAV) of greater than unity. Much earlier introductions of the virus from Central Africa to Europe and North America may well

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have occurred. However, they probably failed to induce a major epidemic as a consequence of low promiscuity and homosexual activity amongst males, by comparison with the prevailing norms today in cities such as San Francisco, New York, Paris and London. In addition to sexual activity there are other aspects of modern society, such as the common use of blood transfusions in medical practice and intravenous drug abuse, that have helped to facilitate the invasion of the heterosexual community. The virus has been isolated from semen and saliva, as well as blood, and transmission between heterosexuals is known to occur (Wong-Staal & Gallo 1985; Des Jarlais *et al.* 1984). In certain parts of Africa, heterosexuals appear to be the major group at risk, although this may be associated with a high frequency of sexual and other practices that facilitate virus transmission in certain societies within developing countries (Biggor *et al.* 1985; Piot *et al.* 1984). To what extent the virus will be able to establish within a wide cross section of adult society in Europe and North America remains to be seen. Once firmly established within the heterosexual community, the virus may be difficult to eliminate unless monogamy (or some approximation to it) becomes more popular than it is at present. The prevailing levels of, and variability in, sexual activity among both homosexuals and heterosexuals will clearly have a central influence on future events.

3. The impact of parasite invasion on community structure

One of the most fascinating, yet little studied, aspects of parasite invasion concerns its significance for community structure and for stability in the invaded locality. The literature contains many anecdotal accounts of the impact of invasion on the abundances of species associated with the host, such as predators, prey or other pathogens. These include the arrival of rinderpest (a viral disease) in Africa and the associated impact on ungulate and predator populations (Sinclair & Norton-Griffiths 1979), the invasion of Europe by Dutch elm disease (a fungal disease) and the consequences of tree losses to the insect fauna (Burdekin 1983), the spread of the rabies virus in Europe and its significance to prey species of the host (Macdonald 1980), the introduction (via host invasion) of a variety of infectious diseases into the Hawaiian island bird community (Warner 1968), the deliberate introduction of myxoma virus into rabbit populations in Australia and Europe and its relevance to predators of the host (Fenner & Ratcliffe 1965), and the spread of the meningeal nematode, *Paralaphostrongylus tenuis*, in Canada and its impact on the relative densities of moose and caribou (Embree 1979; Anderson 1972; Kelsall & Prescott 1971; Telfer 1967). In few instances, however, do such accounts provide quantitative information on species abundance and diversity, both before and after invasion.

Some insights into possible consequences may be obtained by the development and analysis of simple three-species population models. Little research of this nature has as yet been published for food webs that involve one or more parasitic organisms (see Holt & Pickering 1986; Levin & Pimentel 1981; May & Anderson 1983). The following subsections describe the principal conclusions of some new analyses, the technical details of which will be published elsewhere. We examine five food webs whose structures are displayed in figure 10. The webs (labelled (*a*)–(*e*)) represent: (*a*) the introduction of a new pathogen into an established host–pathogen interaction; (*b*) the introduction of a new host (the invader) into an established host–parasite interaction; (*c*) the introduction of a pathogen into an interspecific competitive association between two host species; (*d*) the introduction of a pathogen into a predator–prey

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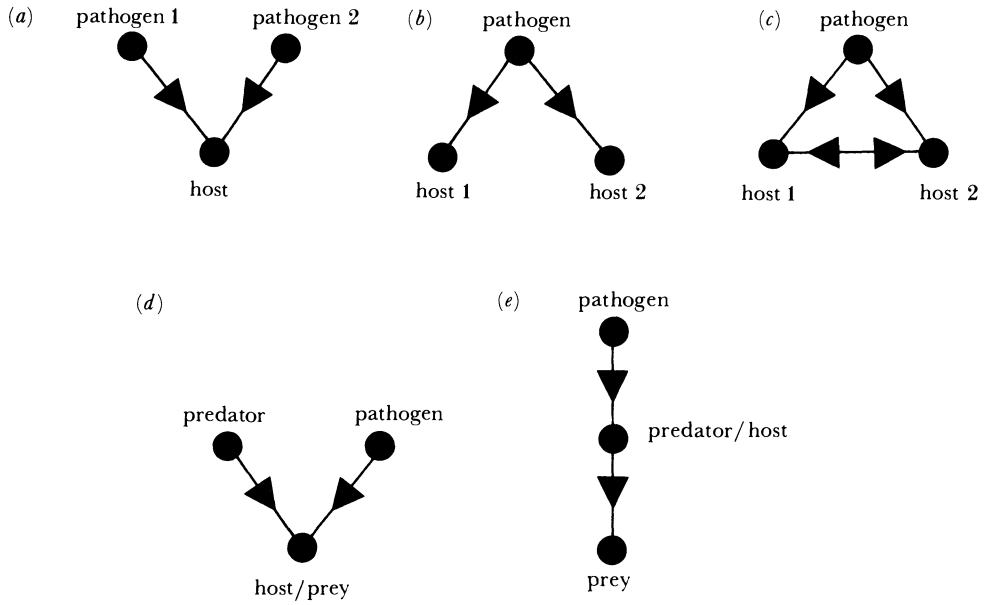

FIGURE 10. Pathogen invasion and its impact on resident two-species associations; the different types of association examined in §3 of the text.

interaction where the pathogen attacks the prey species; and (*e*) the introduction of a pathogen into a predator–prey interaction where the pathogen attacks the predator.

The models employed to examine these five associations make use of the notation defined in the simple model of a direct life cycle microparasite described in §1 (equations (1)–(3)). In all cases the pathogen is assumed to be horizontally transmitted between hosts, to influence host reproduction and/or survival and not to induce lasting immunity to re-infection.

(*a*) *The introduction of a new pathogen species (or strain) into an established host–pathogen association*

In the following model, the subscripts 1 and 2 denote the resident strain and the new invader respectively, and N denotes the total host population (susceptibles and those infected with pathogen species, or strains, 1 and 2). Changes in the densities of X, Y_1 and Y_2 with respect to time may be represented as

$$\begin{aligned} \mathrm{d}X/\mathrm{d}t &= aN - bX - \beta_1 XY_1 - \beta_2 XY_2; \\ \mathrm{d}Y_1/\mathrm{d}t &= \beta_1 XY_1 - d_1 Y_1 - \beta_3 Y_1 Y_2; \\ \mathrm{d}Y_2/\mathrm{d}t &= \beta_2 XY_2 + \beta_3 Y_1 Y_2 - d_2 Y_2; \\ \mathrm{d}N/\mathrm{d}t &= rN - \alpha_1 Y_1 - (\alpha_1 + \alpha_2)\, Y_2. \end{aligned} \tag{24}$$

Here $d_1 = b + \alpha_1$, $d_2 = \alpha_1 + \alpha_2 + b$, $r = a - b$; b denotes uninfected host mortality, α_1 denotes host mortality induced by parasite 1 and $(\alpha_1 + \alpha_2)$ denotes host mortality induced by parasite 2. In equation (24) it is assumed that the invader (parasite 2) can infect hosts already infected with parasite 1 as well as susceptible hosts. In the simplest case where $\beta_3 = 0$ (2 cannot infect hosts already infected with 1), stable coexistence of all three species is not possible if either parasite is able to regulate host population growth (e.g. $\alpha_1 > r$). In these circumstances, which

of the strains 'wins' simply depends on their respective basic reproductive rates R_{0i} (where $i = 1, 2$). The parasite with the greater transmission success (bigger R_{0i}) excludes the other. Put another way, this implies that the parasite with the lower critical density for persistence (N_{Ti}) is able to exlcude the other. These conclusions are summarized in table 3. A high transmission efficiency and/or low pathogenicity and/or slow recovery from infection maximize the parasite's reproductive success.

Table 3. One host and two pathogens

		Interaction (a)					
model	assumptions	pathogen 1 only	stability	pathogen 2 only	stability	both present	stability
(1)	Host cannot harbour dual infection; pathogens always kill host, no recovery possible	$\alpha_1 > r$ $N_{T1} < N_{T2}$ $(R_{01} > R_{02})$	stable	$\alpha_1 > r$ $N_{T2} < N_{T1}$ $(R_{02} > R_{01})$	stable	not possible	unstable
(2)	As for (1), except infected host do not reproduce	$N_{T1} < N_{T2}$ $(R_{01} > R_{02})$	neutral	$N_{T2} < N_{T1}$ $(R_{02} > R_{01})$	neutral	not possible	unstable
(3)	As for (1), except pathogen (2) can establish within hosts infected with pathogen 1 to replace (1); pathogen 2 is more virulent than 1 $(\alpha_2 + \alpha_1 > \alpha_1)$	$\alpha_1 > r$ $a\alpha_2/[(\alpha_1 - r)(\beta_2 - \beta_1) + \alpha_2\beta_1 - r\beta_3]$ $>$ $(\alpha_2 + \alpha_1 + b)/\beta_2$	stable	$\alpha_1 > r$ $a\alpha_2/[(\alpha_1 - r)(\beta_2 - \beta_1) + \alpha_2\beta_1 - r\beta_3]$ $<$ $(\alpha_1 + b)/\beta_1$	stable	$\alpha_1 > r$ $(b + \alpha_1 + \alpha_2)/\beta_2$ $>$ $a\alpha_2/[(\alpha_1 - r)(\beta_2 - \beta_1) + \alpha_2\beta_1 - r\beta_3]$ $>$ $(b + \alpha_1)/\beta_1$	stable

In some instances, however, high pathogenicity is directly associated with high transmission efficiency (e.g. high virulence) (see Anderson & May 1982; May & Anderson 1983). Examples are provided by the high- and low-virulence strains of the fungus *Ceratocystis ulmi*, which causes Dutch elm disease (the pathogen is indirectly transmitted by vectors, various species of elm bark beetles (*Scolytidae*)) and the different virulence grades (I–V, where I is highly virulent and V is of low virulence) of the myxoma virus that infect rabbits (again indirectly transmitted via mosquitoes or fleas). In both instances strains of high virulence appear able to infect hosts already harbouring strains of lower virulence ($\beta_3 \neq 0$ in equation (24)) (Burdekin 1983; Fenner & Ratcliffe 1965).

The model defined in (24) is a rough mimic of the transmission dynamics of both pathogens (the fungus and the virus) under the assumption that the densities of the insect vectors remain relatively constant with respect to the densities of the host species. Once the transmission parameter, β_3, is not equal to zero, stable coexistence between host and the two parasite strains may occur provided certain constraints on parameter values are met. These are detailed in table 3. Other outcomes include the exclusion of the invader (species 1) or the extermination of the resident species (or strain). If $\bar{X}$ denotes the equilibrium density of susceptibles when both parasites coexist, and N_{T1} and N_{T2} denote respectively, the critical host densities for species 1 and 2 to persist within the host population in the absence of the other species, then coexistence requires $N_{T2} > \bar{X} > N_{T1}$. If $\bar{X} > N_{T2}$ then the invader is unable to establish. Conversely, if $\bar{X} < N_{T1}$ the invader eliminates the resident species (figure 11).

The recent history of Dutch elm disease in Europe appears to provide an example of the successful invasion of a high-virulence (= aggressive) strain and concomitant elimination of

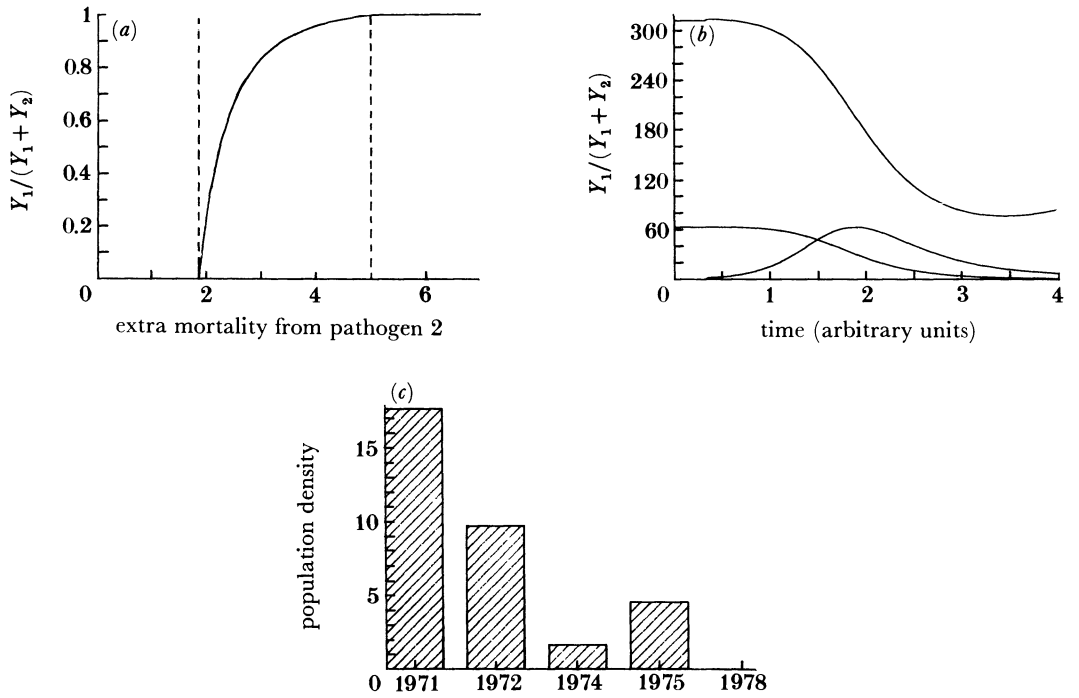

FIGURE 11. One host and two pathogens. (*a*) Proportion of infected hosts that are infected with pathogen 1 at the equilibrium of the model defined in equations (24) ($\hat{Y}_1/(\hat{Y}_1+\hat{Y}_2)$) plotted as a function of the extra mortality, α_2, over that resulting from infection by pathogen 1 induced by infection by pathogen 2 (parameter values: $a=2$, $\alpha_1=1.5$, $b=1$, $\beta_1=0.1$). Stable coexistence of both pathogens in the host population only occurs for a defined range of parameter values (see table 3). (*b*) Numerical solution of (24) illustrating the invasion of an established host–pathogen interaction by a new pathogen of the host. The example records the replacement of the resident pathogen by the invader. The top line at $t=0$ records host density ($N(t)$), the next line records the density of hosts infected with the resident pathogen ($Y_1(t)$) and the bottom line denotes the density of hosts infected with the invading pathogen ($Y_2(t)$). Invasion takes place at time $t=0.35$ (Parameter values, $a=1$, $b=0.4$, $\alpha_1=2$, $\alpha_2=2.2$, $\beta_1=0.01$, $\beta_2=0.025$, $\sigma_1=\sigma_2=0.1$ all per unit of time). (*c*), changes in the percentage occurrence of the non-aggressive strain of *Ceratocystis ulmi* in Britain between 1971–1978 (Dutch elm disease) (data from Brasier (1983)).

the resident low-virulence (= non-aggressive) strain of the fungus *C. ulmi*. When a tree infected with the non-aggressive strain is inoculated with the aggressive strain, the latter seems to be able to colonize the host rapidly, to the detriment of the former (Elgersma & Heybroek 1979). The fungus *C. ulmi* exists as three reproductively isolated sub-populations: the aggressive strain, which consists of two separate races (the Eurasian and North American races), and the non-aggressive strain. The aggressive and non-aggressive strains differ in a series of important biological characteristics and are probably distinct subspecies (Brasier 1982*a*, *b*; Gibbs & Brasier 1973). The current outbreak of Dutch elm disease across Europe is the result of a major shift in the structure of the *C. ulmi* population where the invasion of aggressive strains in the mid-1960s to the early 1970s induced very heavy tree mortalities (some 20 million deaths in Britain in the 1970s) (see figure 1*d*). The areas once occupied by the non-aggressive strain (believed to have been responsible for the early epidemic of Dutch elm disease in the 1920s and 1930s) have slowly been colonized by the aggressive strain and today the former has been virtually eliminated in Britain (figure 11) (Brasier 1983). Whether it will return once the epidemic of the aggressive strain has abated somewhat is difficult to predict. However, the

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simple model defined by equation (24) might suggest that it is unlikely to do so, given that high virulence in the aggressive strain appears to be associated with a high transmission efficiency (i.e. the R_0 of the aggressive strain is probably greater than that of the non-aggressive strain).

The myxoma virus–rabbit interactions in Australia and Europe provide a rather different example. After the introduction of the original highly virulent virus (grade I) into Australia in 1950, a series of less virulent strains (grades II–V) rapidly appeared (Fenner & Ratcliffe 1965; Fenner 1983; May & Anderson 1983). The system appears to have settled, both in Australia and Europe, to a steady state with the predominant strain being the intermediate virulence grades III–IV. In Australian epidemics, where infected mosquitoes are relatively common and several strains of myxoma virus of differing virulence are circulating, some rabbits are probably infected at closely spaced intervals with different strains. Experiments described by Fenner & Ratcliffe (1965; see table 40) suggest that the highly virulent grades usually (although not always) managed to kill rabbits previously infected with an avirulent strain as rapidly as a single infection with just the virulent grade. The model (which is, admittedly, only for two viral strains, but can be easily extended for many parasite strains) suggests that, in these circumstances, stable coexistence of a variety of strains within the host population is possible. This result is in agreement with the observed events in both Australia and Europe (see also Levin & Pimentel 1981). Published analyses of the population dynamics of the myxoma virus–rabbit interaction also suggest that the predominant strain is likely to be the viruses of intermediate virulence grade, since these appear to have the greatest transmission efficiency (the lowest N_{Ti} and highest R_{0i}; May & Anderson 1983).

More broadly, when viral or bacterial strains exhibit a degree of antigenic similarity such that hosts that recover from infection by one strain possess a degree of immunity to other strains, the most successful parasite will be that with the greatest transmission efficiency. However, the degree of antigenic similarity will be of great importance in determining the efficacy of cross-immunity. Understanding the patterns of coexistence of large numbers of different viral strains in human communities, such as the different antigenic types of influenza virus, echovirus, adenovirus and coxsackie virus, is a fascinating topic for future ecological research.

(*b*) *Host invasion: its impact on an established host–parasite interaction*

Population models of the utilization of two non-competing host species or strains by parasites with direct life cycles have recently been analysed by Holt & Pickering (1986) (also discussed in Dobson & May (1986)). In this paper, only a brief sketch of their main properties is presented. The simplest model of a non-host-specific parasite transmitting between two hosts is of the form

$$\begin{aligned} \mathrm{d}X_1/\mathrm{d}t &= r_1 X_1 - \beta_{11} X_1 Y_1 - \beta_{12} X_1 Y_2 + e_1 Y_1; \\ \mathrm{d}Y_1/\mathrm{d}t &= \beta_{11} X_1 Y_1 + \beta_{12} X_1 Y_2 - d_1 Y_1; \\ \mathrm{d}X_2/\mathrm{d}t &= r_2 X_2 - \beta_{22} X_2 Y_2 - \beta_{21} X_2 Y_1 + e_2 Y_2; \\ \mathrm{d}Y_2/\mathrm{d}t &= \beta_{22} X_2 Y_2 + \beta_{21} X_2 Y_1 - d_2 Y_2. \end{aligned} \tag{25}$$

Here β_{ij} denotes the transmission coefficient for the infection of susceptibles of type i by infecteds of type j, e_i denotes the rate of host recovery from infection plus the rate of infected host reproduction and d_i denotes the rate of loss of infected hosts (by recovery and mortality). It is assumed that infected hosts reproduce at a rate equal to or less than that of susceptible

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individuals. Hence $e_i = a_i(1-f_1)+v_i$, where a_i is the reproductive rate, f_1 is the proportional reduction in reproduction and v_i is the rate of recovery from infection. Similarly,

$$d_i = (\alpha_i + b_i + v_i)$$

where α_i is the rate of disease-induced mortality and b_i is the mortality rate not associated with infection.

The properties of this model are summarized in table 4. A variety of outcomes are possible, but stable coexistence is most likely if within-host species transmission is greater than between-host species transmission ($\beta_{11}\beta_{22} > \beta_{12}\beta_{21}$) (Holt & Pickering 1986). The invading host (say species 1) can establish and induce the extinction of the resident species, particularly if the parasite is highly pathogenic to the resident species but of low pathogenicity to the invader that introduced the infection into the new locality. Central to this case is the notion that long-established associations between the invading parasite and host are less antagonistic than that likely to arise in the new association with the native host (no past selection for host resistance to the pathogen). Conditions for the extinction of the resident are outlined in Dobson & May (1986). In brief, it is necessary for the parasite to be able to persist in a low-density population of the invading host, for high pathogenicity in the resident species (r_2/α_2 to be very small) and for efficient cross-transmission between the hosts.

TABLE 4. TWO HOSTS AND ONE SHARED PATHOGEN, NO DIRECT COMPETITION BETWEEN HOSTS

(After Holt & Pickering 1986.)

interaction (b)	condition
(1) both hosts can invade and coexist stably	$\frac{\beta_{22}}{\beta_{21}} > \frac{r_1 d_1 \beta_{22}(d_2-e_2)}{r_2 d_2 \beta_{11}(d_1-e_1)} > \frac{\beta_{12}}{\beta_{11}}$
(2) host 1 can invade when rare, but host 2 cannot	$\frac{\beta_{12}}{\beta_{11}} < \frac{r_1 d_1 \beta_{22}(d_2-e_2)}{r_2 d_2 \beta_{11}(d_1-e_1)} > \frac{\beta_{22}}{\beta_{21}}$
(3) host 2 can invade when rare, but host 1 cannot	$\frac{\beta_{12}}{\beta_{11}} > \frac{r_1 d_1 \beta_{22}(d_2-e_2)}{r_2 d_2 \beta_{11}(d_1-e_1)} < \frac{\beta_{22}}{\beta_{21}}$
(4) each host can exclude the other given that it is initially at its solitary equilibrium	$\frac{\beta_{12}}{\beta_{11}} > \frac{r_1 d_1 \beta_{22}(d_2-e_2)}{r_2 d_2 \beta_{11}(d_1-e_1)} > \frac{\beta_{22}}{\beta_{21}}$

In cases (1)–(4) it is assumed that $(d_2-e_2) > 0$ and $(d_1-e_1) > 0$; $d_i = (\alpha_i+b_i+v_i)$, $e_i = a_i(1-f_i)+v_i$.

One of the most interesting aspects of the Holt & Pickering (1986) analysis is the observation that a shared pathogen can induce 'apparent competition' between the hosts when in reality no direct competition, in the normal ecological sense of the word, is in fact taking place (e.g. competition for resources such as food or space; see also Barbehenn (1969)). Examples of the extinction of the resident host by an invading species, mediated by their shared pathogens, are mainly ancedotal in nature. They include Warner's study of the role of introduced diseases in the extinction of the endemic Hawaiian bird fauna (Warner 1968) and the extinction of caribou in Nova Scotia and New Brunswick after the introduction of white-tailed deer, which harboured a nematode parasite (*Paralaphostrongylus tenuis*) that was highly pathogenic to the caribou (and also moose). In the latter example, the severe neurological disease produced by *P. tenuis* in moose and caribou results from differences in the pathway and speed of larval nematode migration within the host's spinal cord when compared with the normal host, white-tailed deer

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(Anderson 1972; Holmes 1979). A similar example is provided by the filarial nematode *Elaeophora schneideri*, which is relatively non-pathogenic to its normal host, the mule deer, when compared with its effects on elk and sheep (Hibler & Adcock 1971).

In the former example of the Hawaiian bird fauna, the key event appears to have been the introduction of a mosquito vector (*Culex pipiens fatigans*), which played an important role in transmitting viral and malarial parasites between the introduced birds and the resident species. Warner (1968) provides evidence that the diseases were of greater significance in the extinction of the native birds than direct competition with the introduced hosts.

More broadly, the two host models help us to understand parasite transmission between two strains of a given host species. In this context, the mixing between different human races provides us with a number of examples of pathogens' having a dramatic impact on the resident community through introduction by travellers. The Amazonian and American Indians and their contacts with Europeans are a good case. Dobyns (1966), in an analysis of the impact of introduced diseases on the population densities of various races and tribes, produces some remarkable estimates. For the Coastal Mexicans, he gives a depopulation ratio of about 10:1 in less than 60 years. For the Incan Empire in the Andes, rough ratios are between 16:1 to 25:1 after contact with 'the Spanish disease' (smallpox). In Tierra del Fuego, where the natives appear to be headed for biological extinction, the total Indian population has declined from 7000–9000 in 1871 to approximately 200 in 1950; a single measles epidemic in 1884 played a key role in this 40:1 depopulation. A variety of anecdotes yield depopulation ratios, ranging from 20:1 to 200:1, which are thought to have been induced by introduced diseases (May 1984).

(*c*) *Competing hosts and invading pathogens*

The analysis outlined above for a two-host–one-pathogen model (equation (25)) can be extended to encompass the situation in which a pathogen invades and infects one or both antagonists in a direct competitive interaction. The simplest model, where only one host is infected (species 1) and where resource limitation limits either host in the absence of the other (intra-specific competition), is of the form:

$$\begin{aligned}
\mathrm{d}X_1/\mathrm{d}t &= a_1 X_1 - b_1 X_1 - \beta_1 X_1 Y_1 - b_{11} X_1 N_1 - b_{12} X_1 N_2;\\
\mathrm{d}Y_1/\mathrm{d}t &= \beta_1 X_1 Y_1 - (\alpha_1 + b_1) Y_1 - b_{11} Y_1 N_1 - b_{12} Y_1 N_2;\\
\mathrm{d}N_1/\mathrm{d}t &= aX_1 - b_1 N_1 - \alpha_1 Y_1 - b_{11} N_1^2 - b_{12} N_1 N_2;\\
\mathrm{d}N_2/\mathrm{d}t &= r_2 N_2 - b_{22} N_2^2 - b_{21} N_2 N_1. \qquad (26)
\end{aligned}$$

Here, b_{ij} denotes the competition coefficients (both intra- and interspecific). The parasite is assumed to reduce the reproductive rate of infected hosts (Y_1) to zero and to induce mortality at a per capita rate, α_1. The principal properties of this model are summarized in table 5. In the absence of the invading pathogen, competition may result in stable coexistence, either species invariably winning, or an outcome dependent on initial conditions.

An invasion by a parasite can substantially alter the likely outcome. In some cases, infection of a superior competitor can enable an otherwise excluded inferior competitor to coexist. Infection, of course, is unable to change the outcome where the parasite infects the inferior competitor. Also interesting is the case in which, before invasion, the outcome is dependent on initial conditions (the relative densities of the two hosts). In these circumstances, infection

TABLE 5. INTERACTION (c); COMPETITION WHERE ONE OR OTHER COMPETITOR IS INFECTEED BY A PATHOGEN

	pathogen absent	competitor 1 infected	competitor 2 infected
case 1 $r_2 b_{12} > r_1 b_{22}$ $r_2 b_{11} > r_1 b_{12}$	competitor 2 always wins	competitor 2 always wins	stable coexistence
case 2 $r_1 b_{22} > r_2 b_{12}$ $r_1 b_{21} > r_2 b_{11}$	competitor 1 always wins	stable coexistence	competitor 1 always wins
case 3 $r_1 b_{22} > r_2 b_{12}$ $r_2 b_{11} > r_1 b_{21}$	stable coexistence	stable coexistence	stable coexistence
case 4 $r_2 b_{12} > r_1 b_{22}$ $r_1 b_{21} > r_2 b_{11}$	outcome depends on initial conditions	stable coexistence *or* outcome depends on initial conditions; competitor 2 more likely to win	stable coexistence *or* outcome depends on initial conditions; competitor 1 more likely to win

can lead to the uninfected species' always winning, or to stable coexistence being attained from some initial conditions and the uninfected competitor winning from others.

These considerations may have been of some significance in the extinction of the native Hawaiian bird species, since it appears likely that, in the absence of introduced pathogens, they may have been better adapted (and hence superior competitors) in their native habitats, compared with newly introduced bird species. Similar considerations may also have played a role in the competition between the native red squirrel in Britain (*Sciurus vulgaris*) and the introduced grey squirrel, via the action of a shared viral infection, which was highly pathogenic to the resident species (Shorten 1964; Vizoso 1968; Edwards 1962). Perhaps the best quantitative assessments of pathogen invasion on competitors in natural habitats are those concerned with the influence of the myxoma virus on the interactions between hares and rabbits in Europe. Myxomatosis induced a dramatic reduction in rabbit abundance, which often resulted in substantial increases in the densities of hares in given localities. Siriez (1960) quotes estimates of the increase which vary between twofold and tenfold in different areas of France (see also Rothschild (1958)).

The most detailed example of the impact of infection on a competitive association is provided by the classic experiments of Park on competition between two species of flour beetle, *Tribolium confusum* and *T. casteneum* (Park 1948). In the absence of infection by a sporozoan parasite (*Adelina triboli*), *T. casteneum* was the better competitor under the conditions imposed by Park's laboratory experiments, although the outcome of competition was, to some extent, dependent on initial conditions (the starting densities of the two species (case 4 in table 5)). In single-host cultures, the infection had a substantive impact on the abundance of *T. casteneum* but virtually no impact on *T. confusum* (figure 12). In other words, the parasite, although able to infect both species, was primarily parasitic on the superior (in the absence of infection) competitor. When competition was allowed to take place in the presence of the parasite, the inferior competitor usually won, although again the outcome was dependent on initial conditions. The results of a series of Park's experiments, which illustrate these various outcomes, are displayed in

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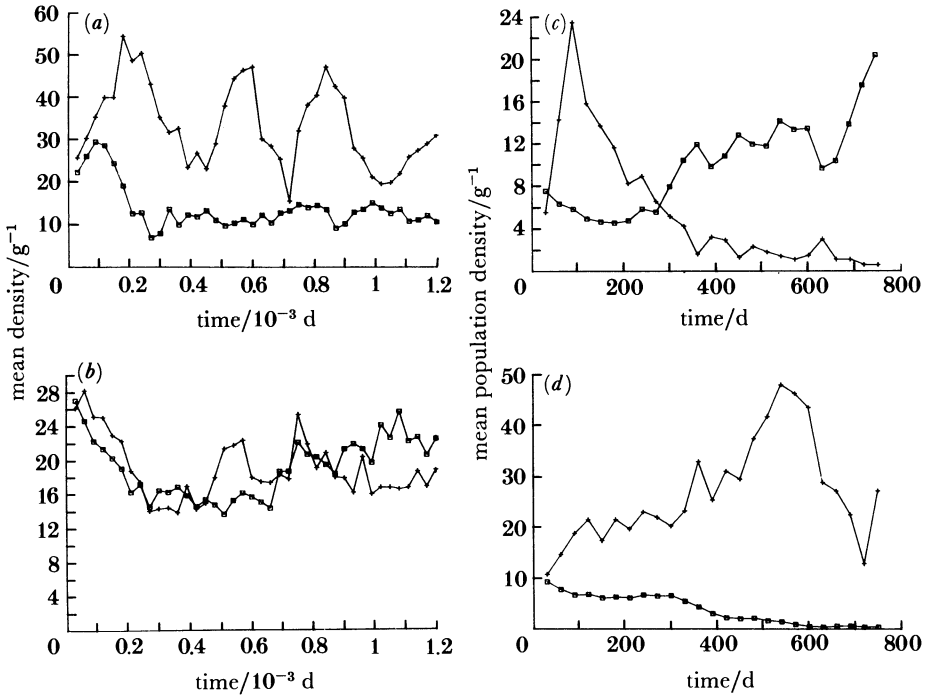

FIGURE 12. Two hosts and one pathogen: the influence of infection by *Adelina triboli* on the population growth of and competition between the beetle hosts *Tribolium confusum* and *T. casteneum* (data from Park (1948)). (*a*) Population growth of *T. confusum* in the presence and absence of infection (tables 2 and 8 in Park (1948)). (*b*) Population growth of *T. casteneum* in the presence and absence of infection (tables 5 and 9 in Park (1948)). (*c*) Competition between *T. confusum* and *T. casteneum* in the presence of infection (table 15 in Park (1948)). (*d*) Competition between *T. confusum* and *T. casteneum* in the absence of infection (table 27 in Park (1948)). Symbols in (*a*, *c*): □, infected; +, uninfected. Symbols in (*b*, *d*): □, *T. confusum*; +, *T. casteneum*.

figure 12. Turning to the simple model of competition and infection detailed in equation (26), crude parameter estimates of the relevant population rates yield predictions that are in qualitative agreement with the experimental results. A series of numerical results, and a phase-plane portrait for competition in the absence of infection, are recorded in figure 13. Quantitative agreement is not to be expected, since age structure (of importance in the competitive interaction) is not incorporated in the simple model defined by (26). In addition, estimates of the transmission efficiency and pathogenicity of the parasite are not derivable from the published details of Park's experiments (rough estimates of β_1 and α_1 were obtained from the degree to which the parasite depressed the abundance of the host). Fairly good data are available to estimate the intra- and interspecific competition parameter values and the respective birth and death rates of the two host species. This example provides a rare opportunity to compare theoretical prediction with detailed experimental observation.

(*d*) *Pathogens of prey species*: *impact on predator–prey associations*

Pathogen invasion can substantially alter the character of a resident predator–prey association (or a plant–herbivore interaction). We consider this aspect under two headings, namely pathogens of the prey and pathogens of the predator.

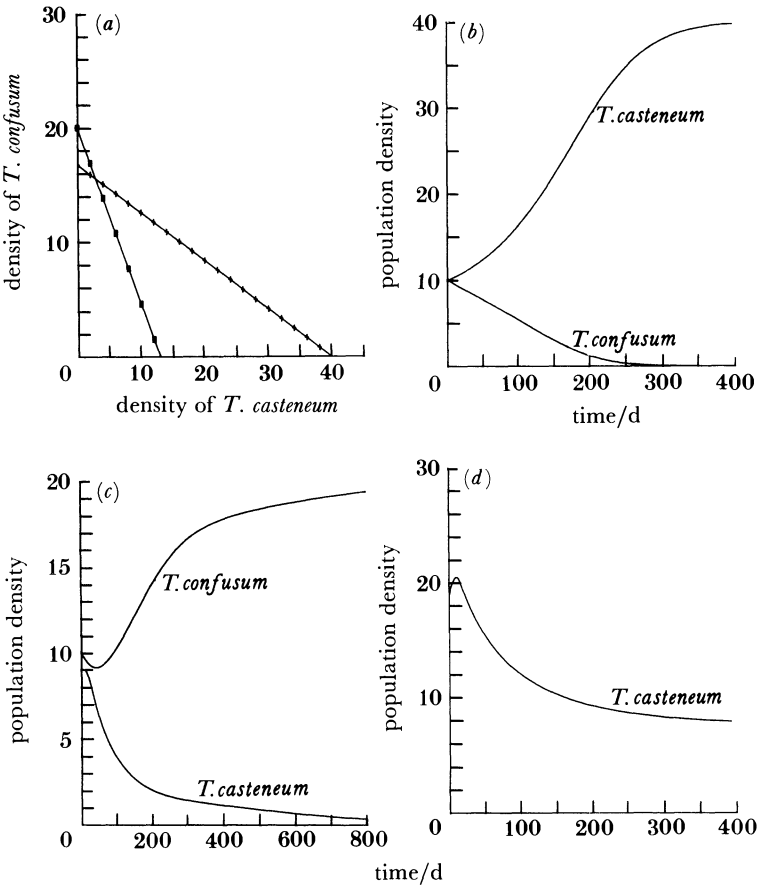

FIGURE 13. Two hosts and one pathogen: model predictions (see text and equation (26)). (*a*) Zero isoclines of the model in the absence of infection (parameter values (subscript 1 denotes *T. casteneum*, subscript 2 denotes *T. confusum*): $r_1 = 0.67$, $r_2 = 0.52$, $b_{11} = 0.01675$, $b_{12} = b_{21} = 0.04$, $b_{22} = 0.026$; all per 30 days). Unstable equilibrium where outcome of competition depends on initial conditions, see Lotka, 1925; Volterra, 1926. Symbols: □, *T. confusum*; +, *T. casteneum*. (*b*) Numerical solutions of (26) for competition in the absence of infection ($N_1(0) = N_2(0) = 10$, other parameter values as for (*a*)). (*c*) Numerical solutions of (26) for competition in the presence of infection ($N_2(0) = 10$, $X_1(0) = 9$, $Y_1(0) = 1$, $\alpha_1 = 0.6$, $b_1 = 0.15$, $\beta = 0.5$, all per 30 days). (*d*) Numerical solution of (26) for the population growth of infected cultures of *T. casteneum* in the absence of *T. confusum* (parameter values as for graphs (*a*) and (*c*)).

With the conventional Lotka–Volterra framework for a predator–prey interaction, the prey pathogen can be easily introduced into the mathematical model:

$$\begin{aligned} \mathrm{d}X/\mathrm{d}t &= (a-b)\,X-\beta XY-c(1-f)\,XP, \\ \mathrm{d}Y/\mathrm{d}t &= \beta XY-(b+\alpha)\,Y-cYP, \\ \mathrm{d}N/\mathrm{d}t &= rX-(b+\alpha)\,Y-c[(1-f)\,X+Y]\,P \\ \mathrm{d}P/\mathrm{d}t &= \delta NP-dP. \end{aligned} \tag{27}$$

N denotes prey density ($N = X+Y$), P represents predator density, δ is the rate of predator reproduction (the net rate is assumed proportional to prey density), d is the predator's death rate and c is the rate of prey consumption by predators; f is a value, between 0 and 1, denoting the possibility of a lower rate of capture of susceptible, as opposed to infected, prey. Note that

in (27), infected prey do not reproduce. The properties of this model, plus a wide range of extensions and modifications to it, are summarized in table 6.

Again, several outcomes are possible, depending on the values of the population parameters. The pathogen will be unable to establish itself if the predators hold the prey population below the threshold density, N_T, required for parasite persistence ($N_T = (\alpha + b)/\beta$). Conversely, the pathogen will induce the extinction of the predator if it regulates the host population at a level too low to sustain the predators ($N < d/\delta$). In between these two limits, a region of stable coexistence occurs (table 6). In certain instances, the introduced pathogen will induce stable limit cycles such that the predator and prey densities oscillate (slightly out of phase, with the peak in predator abundance following that of the prey) in situations where in the absence of the pathogen the interaction would be stable and non-oscillatory. In brief, therefore, parasite invasion can destabilize a predator–prey interaction and, in some circumstances, induce the extinction of the resident predator.

Quantitative examples are again difficult to come by, but several publications provide qualitative description. One of the best concerns the impact of the myxoma virus of rabbits in Europe and Australia on the resident predator populations, such as birds of prey and foxes. After its introduction in Australia and Europe, the virus had a dramatic impact on rabbit abundance (see figure 1*b*). Before the introduction of the virus in England, the rabbit, where abundant, provided 50% or more of the food items of the red fox (*Vulpes vulpes*) (Southern & Watson 1941). It is estimated that 99% of rabbits were killed in England in the first epizootic, which swept the country in 1953–1955 (Lloyd 1970). Following the introduction of the disease, fox densities are thought to have initially declined but to have recovered rapidly, since the predator switched its attention to small rodents (*Microtus agrestis* and *Apodemus sylvaticus*) (Lever 1959). In Southern's study area near Oxford, once myxomatosis invaded, intense predation pressure was imposed on the rodent population by the fox, this pressure had 'knock-on' effects on the density of a bird predator, the twany owl (*Strix aluco*), whose breeding success is very dependent on an abundant supply of voles (Southern 1970; Lever *et al.* 1957; Southern & Watson 1941). Stoat (*Mustela erminea*) abundance also dropped in parallel with that in rabbit density (Jefferies & Pendlebury 1968). The buzzard (*Buteo buteo*) is a predator whose abundance in Britain is also related to rabbit density. Once myxomatosis arrived, the breeding success of the buzzard was dramatically reduced; observations suggest that the bird population has stabilized at a level much lower than that pertaining before the introduction of the disease (Moore 1956, 1965; Parslow 1967). This seems to be an example of stable coexistence between the pathogen, prey (host) and predator, in which invasion substantially decreased the abundance of the predator as well as that of the prey. A similar, but more anecdotal, example is provided by the impact of the maize mosaic virus on the abundance of the maize crop and the Mayan civilization in Guatemala (Brewbaker 1979). Here man is the predator, maize the prey and the plant virus the pathogen. Brewbaker (1979) attributes the collapse of the Maya culture in 900 AD to the spread of the virus and the associated destruction of the agricultural base of the society.

A final example is that of the rinderpest virus and its invasion of Africa from 1889 onwards. The virus is a directly transmitted parasite of ruminants and pigs and was thought to have been introduced into the African continent via domestic cattle. The infection spread extremely rapidly among the native ruminants such as wildebeest, antelope and buffalo. South of the Zambesi, the infection is estimated to have killed over five million animals in two years. In

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Table 6. Interaction (*d*); predator–prey interaction with pathogen infecting the prey species

model	assumptions	predator–prey	stability	predator–prey–pathogen	stability	pathogen–prey	stability
(1)	No density-dependence on prey. Equal predation on infected and susceptible prey. Infected prey do not reproduce. All infecteds die.	$d\beta/\delta < (a+\alpha)$	neutral	cannot persist	unstable	$d\beta/\delta > (a+\alpha)$	neutral
(2)	As for (1), except infected prey reproduce	$d\beta/\delta < (a+\alpha)$	neutral	$d\beta/\delta > (a+\alpha)$ $d\beta/\delta < \alpha+a(\alpha/(\alpha-r))$	stable	$d\beta/\delta > \alpha+a[\alpha/(\alpha-r)]$	stable
(3)	As for (1), except density-dependence on prey.	$d\beta/\delta < (a+\alpha)$ $r/\gamma > d/\delta$	stable	cannot persist	unstable	$d\beta/\delta > (a+\alpha)$	stable
(4)	As for (2), except density-dependence on prey.	$d\beta/\delta < (a+\alpha)$ $r/\gamma > d/\delta$	stable	$d\beta/\delta > (a+\alpha)$ $d\beta/\delta < \theta$	stable or cyclic	$d\beta/\delta > \theta$	stable or cyclic
(5)	As for (3), except only infected prey attacked by predator	predator cannot persist unless infection present	unstable	$d\beta/\delta < r-\gamma(a+\alpha)/\delta$	stable	$[\gamma(a+\alpha)]/\delta > r$ $d\beta/\delta > r-[\gamma(a+\alpha)/\delta]$	stable
(6)	As for (4), except infected prey can recover to become immune.	$d\beta/\delta V < V+\Gamma$ $r/\gamma > d/\delta$	neutral	$d\beta/\delta > V+\Gamma$ $d\beta/\delta < V+\Gamma/$ $[1-(V/\alpha)((V+b)/b)]$	stable or cyclic	$d\beta/\delta > V+\Gamma$ $d\beta/\delta > \Gamma/[1-(V/\alpha)$ $((V+b)/b)]$	stable or cyclic

Where θ given by $(\gamma/\beta)\theta^2+\theta[\alpha-r-\gamma\alpha/\beta]-(b+\alpha)=0$, $\Gamma=(b+V+\alpha)$ and V is the rate of acquisition of immunity.

Table 7. Interaction (*e*); predator–prey interaction with pathogen infecting the predator species

model	assumptions	predator–prey	stability	predator–prey–pathogen	stability
(1)	no density-dependence on prey; infected predators catch prey at rate less than that of susceptibles	$r/c < (d+\alpha)/\beta$	neutral	$r/c > (d+\alpha)/\beta$	neutral
(2)	as for (1), except infected predators reproduce and catch prey at same rate as susceptibles	$r/c < (d+\alpha)/\beta$	neutral	$r/c > (d+\alpha)/\beta$	may or may not be stable; limit cycles possible
(3)	as for (2), except density-dependence on prey	$r/\gamma > d/\delta$ $r/c < [(d+\alpha)/\beta]/[1-d/(k\beta)]$	stable	$r/c > [(d+\alpha)/\beta]/[1-d/(k\beta)]$	may or may not be stable; limit cycles possible

Where k is the carrying capacity of the prey in the absence of the predator and pathogen. The term γ in tables 6 and 7 denotes the severity of density dependence on prey mortality (a logistic assumption).

the Serengeti, when the pandemic eventually abated, the annual survival rate of wildebeest is known to have doubled from 0.25 to 0.5 or higher (Sinclair & Norton-Griffiths 1979). The dramatic reduction of ruminants on the African plains had an immediate impact on populations of predators, such as lions, leopards and hunting dogs. The predator species survived, but population densities were substantially reduced (Spinage 1962).

More generally, we might expect introduced pathogens of prey species to have their greatest impact when the predator species is a specialist as opposed to a generalist feeder. The european red fox, for example, managed to recover rapidly from the introduction of the myxoma virus by switching its predation from rabbits to small rodents. The buzzard, however, was less able to adapt so rapidly.

(*e*) *Pathogens of predator species: impact on predator–prey associations*

The basic Lotka–Volterra model can also be modified along the above lines to mimic the impact of an invading pathogen, which attacks the predator (or herbivore species). A simple model is of the form:

$$\begin{aligned} \mathrm{d}N/\mathrm{d}t &= rN - cN(X + (1-f)\,Y);\\ \mathrm{d}X/\mathrm{d}t &= \delta NX - dX - \beta XY;\\ \mathrm{d}Y/\mathrm{d}t &= \beta XY - (d+\alpha)\,Y;\\ \mathrm{d}P/\mathrm{d}t &= \delta NX - dP - \alpha Y. \end{aligned} \tag{28}$$

The notation is as defined for (27), except that X and Y denote the densities of susceptible and infected predators respectively (where $P = X + Y$), and f denotes the proportional reduction in the rate of prey capture by infected predators. The properties of this simple model, and of models with various refinements, are summarized in table 7. Only two outcomes are possible, namely successful invasion (the predator, pathogen and prey coexist) or failure (predator and prey coexist) (figure 14). In general terms, the latter outcome results if the equilibrium density of predators (r/c), in the absence of the pathogen, is less than the critical density of predators ($N_{\mathrm{T}} = (d+\alpha)/\beta$) required for pathogen establishment. If this is not the case then coexistence occurs. In the latter case, the stability of the association is more complex. Cycles may or may not occur, depending on the parameter values. When intraspecific

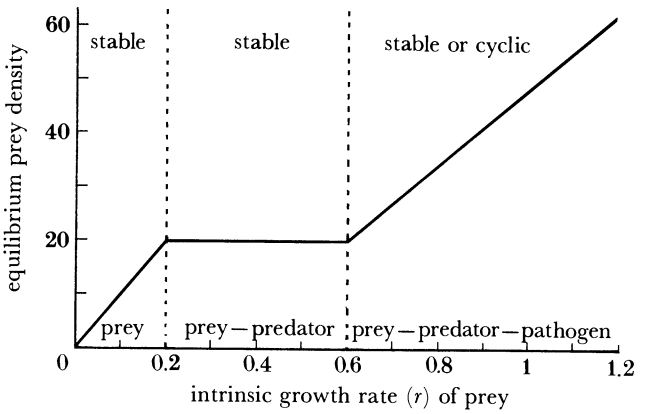

FIGURE 14. Pathogens of predator species: impact on predator–prey associations. An illustration (employing the model defined in equation (28) in the main text) of the possible outcomes of pathogen invasion be reference to the equilibrium prey density, N, as a function of the intrinsic growth rate of the prey, r (defined per arbitrary unit of time; see table 7). Note that where all three species coexist the association may be stable or oscillatory.

competition influences the dynamics of the prey species, pathogen invasion may transform a stable association into an oscillatory one (model 3 in table 7).

Documented accounts of the influence of invasion by pathogens of predators are difficult to find in the literature. Fox rabies in Europe must clearly have had an effect on rodent populations, but these have not been examined in detail. Better accounts exist for pathogens of herbivores (such as the myxoma virus) and the concomitant impact on plant growth and species diversity. The effects of the removal of rabbits by myxomatosis in Britain during the late 1950s and 1960s was often very dramatic. The downland areas in southern England changed from 'smooth-grazed lawn to tussocky field' (Nature Conservancy 1957). Chalk heath areas become dominated by *Festuca rubra* while heather (*Calluna vulgaris*) and other woody species grew tall. In general, the spectacular shows of wild flowers and growth in species diversity were followed by dominance of a few superior competitors, formerly held in check by rabbit grazing (Thomas 1963, 1966; Grubb *et al.* 1969). Similarly, dramatic changes were observed in woodlands and sand dune habitats (Brown 1956; Thomas, 1963). These accounts provide a broad picture of the dramatic and far-reaching consequences of pathogen invasion, not just on the herbivore but on the community structure within the rabbit's habitat.

Conclusions

Three main conclusions emerge from the work described in this paper.

First, the basic reproductive rate (or transmission potential) of the parasite plays a central role in determining the likelihoods of establishment, persistence and spread after introduction. A high transmission potential greatly facilitates establishment and spread but it may or may not enhance persistence. If the parasite induces lasting immunity in those hosts that recover, or if infection is a major cause of host mortality, the relationship between host and pathogen populations is likely to be oscillatory in character with the concomitant risk that the parasite will become extinct during the phase of low parasite abundance after an epidemic. High transmission potential will accentuate the amplitude of such oscillation and hence decrease the likelihood of long-term persistence.

Second, simple population models of three-species associations suggest that a great variety of outcomes are possible following an invasion. The pathogen will alter the numerical abundances of the resident species but it may increase or decrease them, depending on both the type of the invaded association (host–parasite, predator–prey or a competitive interaction) and the magnitude of the numerous population parameters that control the interaction between the species. Similarly, a successful invasion may, or may not, result in the extinction of one of the resident species, again depending on the magnitudes of the population parameters (see tables 3–7). Important determinants of the likely outcome are the critical density of hosts (N_T) necessary for parasite establishment and the equilibrium densities of the resident species before invasion. The principal message to emerge from theoretical work, however, concerns the importance of a quantitative knowledge of the many population parameters involved in multispecies associations to any assessment of the 'knock-on' effects of invasion for community structure and stability. Many accounts of past invasions are qualitative as opposed to quantitative in character. Such natural experiments in community manipulation deserve greater attention in the future. The collection of quantitative information on population abundancies and rate parameter values after disease invasion would not only help in future

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assessments of the likely impact of introduced infections but would also help to further our understanding of community ecology.

Third, the recent epidemic of AIDS provides a striking example of how cultural change in human communities can facilitate pathogen invasion and spread. This example is dramatic because of the lethality of the virus, but it is by no means unique. The rise in the incidences of a broad spectrum of sexually transmitted infections throughout many regions of the world over the past decade reflect the increased mobility of people (via air travel) and greater sexual promiscuity in modern societies (linked to improvements in methods of birth control). In the absence of effective vaccines (none is available at present for the major sexually transmitted infections), cultural change wih respect to sexual practices is the only means of effective control.

Finally, it is important to note that invasion of a community by an animal or plant species can result in evolutionary adjustments of either the invader, or the recipient community, or both. The history of infectious disease invasions provides many examples of evolutionary and coevolutionary responses at the population, individual and molecular levels. Evolutionary changes in the invading parasite population are well illustrated by the example of the influenza viruses of man. Viral strains are classified on the basis of very labile surface haemagglutinin (H) and neuraminidase (N) antigens, which undergo infrequent major 'shifts' (e.g. from H_1 to H_2 to H_3, and from N_1 to N_2; infection by one strain confers little immunity to infection by another strain) and more frequent minor 'drifts' (identified by minor differences in serological tests) (WHO 1980). Major 'shifts' in the antigenic character of the virus facilitate persistence in a population with a high degree of herd immunity to earlier antigenic variants (Nakajima *et al.* 1978). Antigenic variation is an important factor in ensuring the long-term persistence of a virus that is highly transmissible (R_0 large) within its host community. Host evolution in response to pathogen invasion is well illustrated by the history of the introduction of the myxoma virus into the rabbit populations of Australia and Europe (Fenner 1983). This particular case is also a good example of coevolution, because the introduction of the pathogen was followed by genetic changes in both host and parasite populations (May & Anderson 1983).

In any consideration of the impact of a disease invasion it is of particular importance to remember that the association between host and pathogen is likely to evolve in a very dynamic manner. The often strong selective pressures exerted by pathogens on their host populations, and the invariably short generation times of parasites relative to those of their hosts, imply that evolutionary changes may occur fairly quickly after a successful introduction.

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Discussion

K. Joysey (*Department of Zoology, Downing Street, Cambridge*). Please would Professor Anderson expand on his statement about the situation in Central Africa?

R. M. Anderson. I did not go into details because the data are not yet published, but in Zaire, Rwanda and Uganda there is a high level of female infection with HTLV III virus. In this area, a retrovirus in the HTLV group has been identified in macaque monkeys, but we cannot be sure how closely it is related to that present in man. New invasions can occur either through a genetic change in the virus or through a change of host, and AIDS could be the result of the latter, with some later viral evolution. It is clear, in any event, from the African situation, that AIDS is capable of heterosexual transmission, and this is confirmed by the fact that a significant fraction of the heterosexual partners of haemophiliacs infected by blood transfusion in North America have become seropositive. Thus there is a real risk of the persistence of the disease within the heterosexual population.

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D. Mollison (*Department of Actuarial Mathematics and Statistics. Heriot-Watt University, Riccarton, Edinburgh, U.K.*). Did the authors just assume that sexual partners are chosen at random, or did they allow for heterogeneity, such as a preference for other individuals within a group, or at least for other individuals with a similar level of sexual activity?

R. M. Anderson. Our theoretical analysis is designed to include heterogeneity. We accept that there are discrete classes of individual who differ in their sexual activity, but the model assumes a continuous distribution because this is easier to work with. It covers joint distributions, in that members of a high-activity class are assumed to be more likely to choose partners within that class, but with some out-linkages. The models are not predictive, but are designed to stimulate epidemiologists to make the most appropriate measurements.

G. R. Conway (*Imperial College Centre for Environmental Technology, 48 Prince's Gardens, London, U.K.*). I have three questions:

(1) I believe that there is a retrovirus attacking sheep, which is related to the AIDS virus. Have the authors modelled that system, and can any useful conclusions be drawn?

(2) What other major epidemics in history can be attributed to change in human cultural practices?

(3) When Lassa fever first appeared Paul Ehrlich suggested it could become a global pandemic of the kind that has now occurred in AIDS. This did not happen. Have the authors any thoughts as to why, and general observations on the difficulties of predicting such events?

R. M. Anderson.

(1) We have simply addressed the questions of AIDS transmission. We are not aware of any theoretical or mathematical studies of other retroviruses.

(2) There are a number of examples in the literature. Most importantly, the frequency and magnitude of epidemics of various childhood viral and bacterial infections increased during the eighteenth and nineteenth centuries, principally as a result of changing social patterns and the growth of large centres of population in increasingly industrialized societies.

(3) Lassa fever has very different transmission properties to those of the AIDS virus. Sexually transmitted infections clearly have considerable potential for rapid spread throughout the world.

R. Cartwell. Some viruses may persist in the body for long periods and give rise to delayed disease, as chicken pox does with shingles. What does the authors' analysis say about this?

R. M. Anderson. Chicken pox in childhood is dealt with by the immune system, but pockets of virus remain in the nervous system, where they may be evoked in later life by stress. Theoretical studies suggest that the immune system is able to reduce viral abundance to very low levels but it may not always result in elimination of the infectious agent from the host. This may be advantageous in keeping the immune system alert to the virus. This persistence is the key to later flare-up in different forms.

H. V. Thompson. Bats have recently been reported as vectors of rabies in Europe. Does this represent a new phase in that disease?

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R. M. Anderson. It could conceivably permit migration across the Channel, but bats are not thought to be important vectors for rabies in mainland Europe at present. It is worth stressing that rabies is not important as a disease on the global scale; it induces a negligible mortality in Europe.

B. Dixon (81, *Falmouth Road, Chelmsford, Essex, U.K.*). Does the authors' model allow any predictions to be made about the effects of changes in personal habits among the male homosexuals most affected so far in the U.S.A? What importance do the authors assign to health education in curbing the risk of epidemics?

R. M. Anderson. The data suggest that, because of the long latent period, people developing the disease in 1983 were infected in 1980 or earlier. Behavioural changes are unlikely yet to have manifested themselves in the course of the disease because of the three- to five-year lag between infection and symptoms. The changes in sexual habits reported in 1984 will not show for three or four years beyond that date. However, education and changes in habits are likely to be very important and the best way at present of controlling the spread of the disease. It is especially important to focus educational campaigns on the majority of the population rather than just the promiscuous group.

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