

Emerging infectious disease: what are the relative roles of ecology and evolution?

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Despite important successes in the control and treatment of infectious diseases, bacterial and viral infections remain the leading source of mortality worldwide¹. Following the discovery of antibiotics, focus in the developed world on cancer and heart disease shifted medical research away from microbial infections although they continued to pose serious problems in developing countries. However, diseases that could be effectively controlled in the past by anti-microbial drugs and public health measures are currently re-emerging as menaces in both the developed and developing worlds (e.g. tuberculosis, cholera). In addition, in the past 15 years, a number of seemingly new diseases have posed serious threats^{2,3}. The HIV epidemic, newly described viral hemorrhagic fevers, Lyme disease, Legionnaires' disease and toxic shock syndrome (TSS) are all examples of 'emerging diseases', diseases that are currently increasing in human populations. The potential for isolated outbreaks to develop into pandemics has increased significantly with the invention of rapid transportation, transforming the problem of disease emergence into a global concern. Furthermore, this concern extends beyond human populations to domestic and wild populations of animals and plants.

What are the relative contributions of ecology and evolution to the emergence of disease? The vast literature on genetic bases of pathogenicity, along with a resurgence of interest in the evolution of virulence^{4,5}, might suggest that genetic characteristics of pathogens lie at the heart of disease emergence. However, for currently emerging diseases ecological factors may play the primary role. Here, we survey recent emergence patterns of a number of microbial infections to illustrate the interplay of ecology and evolution in the spread of disease.

Verifying that diseases are truly emerging

We define disease emergence broadly as any disease that is currently spreading within host populations¹. This definition does not require an emerging disease to be newly evolved. In fact, the vast majority of currently emerging diseases have surprisingly long histories. Many have either persisted at low levels in host populations for some time, or

The increasing threat of infectious diseases in humans has renewed interest in factors leading to the emergence of new diseases and the re-emergence of familiar diseases. Examples of seemingly novel diseases currently spreading in human populations include HIV, dengue hemorrhagic fever and Lyme disease; drug-resistant forms of well-known diseases such as tuberculosis are also increasing. The problem of disease emergence also extends to other animal and plant populations. In most current epidemics, ecological factors (e.g. migration, climate, agricultural practices) play a more significant role in disease emergence than evolutionary changes in pathogens or hosts. Evolutionary biologists and ecologists have much to offer to the development of strategies for the control of emerging diseases.

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recently invaded new hosts from reservoir populations where they have coexisted for some time. Traditionally, determining whether a pathogen is newly evolved or simply newly identified has been difficult. Recently, however, DNA sequencing and PCR have led to rapid progress in disease detection and identification. These techniques can also shed light on features of disease epidemiology and evolution that may play a role in disease emergence⁶. Additionally, serological surveys and clinical records can often distinguish between truly emerging diseases and newly identified pathogens that have a history of stable association with host populations.

The key role of ecology in disease emergence

Changes in pathogen and host ecology may be primarily responsible for the emergence of the majority of currently spreading diseases (Table 1). Seemingly minor changes (e.g. the implementation of a new farming technique

or long-distance travel of infected hosts) can significantly alter transmission and exposure patterns, leading to sudden proliferation of disease. Exposure of pathogens to new environments within the host may also result in emerging disease. While each disease has its unique story of emergence, pathogens with similar modes of transmission often share similar emergence patterns.

Arthropod-borne disease

Weather conditions, availability of suitable breeding sites and increased migration (in particular, increased opportunities for pathogens and their arthropod vectors to hitchhike with humans or cargo over long distances) have contributed strongly to emergence of arthropod-borne diseases. The emergence of Oropouche fever (symptoms include fever, headache and muscle aches) in human populations in South America demonstrates how simple changes in ecology, in this case increased cacao and banana farming, can lead to rapid increases in arthropod-transmitted disease⁷. The primary vector of Oropouche virus, a segmented RNA virus in the family Bunyaviridae, is a midge (*Culicoides paraensis*) that preferentially breeds in rotting organic matter. The first case of Oropouche fever was identified in Trinidad in 1955; since then, a series of epidemics has

Table 1. Examples of currently emerging diseases

Disease type	Disease name (Taxon)	Distribution	Reservoir hosts	Probable factors in emergence
Virus ^a	Influenza (Orthomyxoviridae) ^b	Worldwide	Aquatic birds	Integrated pig-duck farming
	HIV (Retroviridae) ^b	Worldwide	Humans (originally from primates?)	Sexual transmission; intravenous drug use; medical technology (blood transfusion); travel
	Marburg, Ebola (Filoviridae)	Africa	Unknown	In Europe and USA, monkey importation
	Dengue (Flaviviridae) ^b	Throughout tropics	Mosquitos, humans	Urbanization; factors favouring increased mosquito populations
	Rift Valley fever (Bunyaviridae)	Africa	Mosquitos, ungulates	Dams, irrigation
	Oropouche fever (Bunyaviridae) ^b	Brazil, Trinidad, Panama	Midges	Agriculture
	Junin (Arenaviridae)	South America	Rodents	Agriculture
	Hantaan (Bunyaviridae)	Asia, Europe, USA	Rodents	Agriculture
	Hantavirus (Bunyaviridae) ^b	S.W. USA	Rodents	Climate-mediated increases in rodent populations
	Seal plague (Paramyxoviridae) ^{b,c}	Northern Europe		
Canine parvovirus type 2 ^c	Worldwide	Canids (originally from felines or foxes?)	Unknown; possibly mutation of a feline or fox parvovirus	
Bacteria	Legionnaires' disease (<i>Legionella</i>) ^b	Worldwide	Natural component of water flora	Technology: air conditioning, water-cooling towers, water-storage units
	Lyme disease (<i>Borrelia</i>) ^b	Worldwide	Deer, rodents, birds	Reforestation
	Toxic shock syndrome (<i>Staphylococcus</i>) ^b	Worldwide	Human nasal passages; elsewhere?	Technology: high absorbency tampons
	<i>E. coli</i> O157:H7 ^b	USA, Europe, possibly worldwide	Cattle	Unsanitary food production
	Plague (<i>Yersinia</i>)	Worldwide; mostly southeast Asia	Rodents	Unsanitary urban environments
	Antibiotic-resistant pathogens ^b	Worldwide	-	Medical technology: human use of antibiotics
Fungi	Dogwood anthracnose disease (<i>Discula</i>) ^c	USA	?	?

^aInformation on viral diseases is based on Tables 2.1 and 2.2 in Ref. 2.

^bDenotes diseases that are discussed in more detail in text.

^cDenotes diseases that are emerging in animals or plants, as opposed to human populations.

occurred throughout the Amazon River basin in Brazil. Local farming practices in northern Brazil (where *C. parvovirus* is abundant) involve stacking banana tree stumps and cacao husks on the ground to decompose after harvest. Because the stumps and husks are often placed near homes, this practice leads to increased contact between midge and human populations, resulting in greater likelihood of transmission of Oropouche virus to humans.

Larger-scale changes in ecology can lead to widespread increases in disease, as demonstrated by the recent emergence of dengue fever, now an important arthropod-borne virus in humans⁸. Dengue fever (classic symptoms include fever, skin rash and muscle and joint pain) is caused by an RNA flavivirus – transmitted by mosquitos (*Aedes aegypti*) – that has been present in human populations for over 200 years. During that time dengue has caused intermittent, slowly spread pandemics in Asia and the Americas. Increases in the incidence of dengue fever in the past 20 years result from conditions following World War II. Increased air travel, urbanization and poor sanitation conditions all facilitated mosquito transmission of dengue virus⁸. At the same time, mosquito populations increased because of relaxation of mosquito control programs in Asia and the Americas⁸, and the emergence of insecticide resistance. Furthermore, a new dengue mosquito vector, *Aedes albopictus*, spread from Asia to the Americas in the 1980s.

Recent increases in the severity of dengue infections, in particular the appearance of a new form of the disease

called dengue hemorrhagic fever/dengue shock syndrome (DHF) in 1954, can also be traced to World War II. During the war, infected military personnel spread antigenically different strains of dengue (which has four distinct serotypes) to new areas, increasing rapidly the number of regions where multiple serotypes overlapped. DHF, which can be fatal if hemorrhagic symptoms are not treated, often occurs in people who have recovered from dengue fever and are subsequently infected with a different dengue serotype. As regions containing multiple dengue serotypes become common, DHF has spread to 11 countries in the Americas. In addition to the strong impact of ecology on dengue emergence, there is suggestive evidence that evolution of virulence in the RNA virus may also have contributed to the emergence of DHF (Ref. 8).

Mammal-mammal transmitted disease

Changes in the densities of wild mammal populations, agricultural practices and urbanization may lead to increased contact between humans and other mammals, increasing opportunities for transmission of mammal-borne disease. The May 1993 outbreak, in the southwestern USA, of hantavirus pulmonary syndrome (HPS) – a severe respiratory illness (fatal in approximately half of diagnosed cases¹) – demonstrates how this can lead to disease emergence. The syndrome is caused by a segmented RNA virus, Sin Nombre virus (SNV; family Bunyaviridae). Its primary reservoir is deer mice (*Peromyscus maniculatus*), one of the most

common mammals in North America. A probable case of HPS occurred in New Mexico, USA, in 1975, implying that the virus-rodent association is at least that old⁹. The fairly large genetic diversity in SNV is also consistent with a long, well-established relationship between the virus and rodents¹⁰. If the virus-rodent association is quite old, why has the disease only now been identified? The recent outbreak appears to have resulted from abnormally high densities of deer mice owing to two particularly wet springs in a row. Oral history from the Navajo Indian tribe supports a past association between similar disease outbreaks and years with particularly high rodent populations (S. Nichol, pers. commun.). Epidemics in non-human animals (epizootics) have also been linked to mammal-mammal infectious transmission (see Box 1).

Disease transmission from other primates to humans accounts for the most devastating human epidemic of recent times. Based on phylogenetic analysis, it appears that HIV1 and HIV2 (the latter is found primarily in Africa) were independently transferred from African primates to humans. HIV1 is most closely related to a simian immunodeficiency virus (SIV) in chimps (*Pan troglodytes*), and HIV2 is most closely related to SIV found in the sooty mangabey (*Cercopithecus atys*)^{11,12}. Transfer of HIV-like lentiviruses (named for their association with slow, progressive diseases) from other primate species to humans may occur periodically because of close human-primate contact (e.g. via hunting and exportation). Many important questions related to the evolutionary history of HIV remain unresolved: (1) How old are the primate lentiviruses? (2) How long have HIV1 and HIV2 been in human populations? (3) Are genetic changes involved in the emergence of one or both of these pathogens (most SIVs do not cause disease in their natural hosts¹¹)? (4) How can we account for the nearly simultaneous emergences of HIV1 and HIV2 in humans? Lentiviruses have been found in several groups of African primates and are extremely diverse in some groups (e.g. African green monkeys, *Cercopithecus aethiops*), implying a long association¹¹. However, there is no consensus on the age of the entire group or on the divergence times within or between HIV1 and HIV2 lineages (estimates of the divergence time between HIV1 and HIV2 range from 40 years to several thousand¹³). With respect to the role of genetic changes in the emergence of HIV, there are differences in latent period and transmissibility of HIV1 and HIV2 (Ref. 13). However, the epidemiological impact of these differences is not yet understood. Moreover, while genetic changes could have increased pathogenicity in HIV lineages relative to their simian counterparts, it appears more likely that ecological changes (including increased mobility of humans, promiscuous sexual behavior and intravenous drug use) provided the necessary conditions for the simultaneous expansion of both immunodeficiency viruses in human populations.

HIV/AIDS differs from HPS in that the pathogen can be sustained and reach epidemic proportions in humans without the need for additional contact with the reservoir population. Diseases, like AIDS, that do not require reservoir hosts or vectors for transmission have greater potential to develop into epidemics.

Diseases requiring vectors and reservoir hosts for transmission

When two intermediate vectors are involved in disease-transmission cycles, the complexity of disease dynamics increases and ecological changes affecting either vector population can lead to disease outbreaks. The recent emergence of Lyme disease, now the most common vector-borne

Box 1. Example of an epizootic

In 1987-1988, over 18 000 harbor seals (*Phoca vitulina*) in northern Europe and several thousand Lake Baikal seals (*Ph. sibirica*) in Siberia died in two isolated epizootics of morbillivirus (a genus of RNA viruses that includes canine distemper virus, CDV, measles and rinderpest)²⁴. A similar outbreak caused severe mortality in striped dolphins (*Stenella coeruleoalba*) in 1990 (Ref. 25). The cause of the harbor seal outbreak was identified as phocine distemper virus (PDV). To trace the source of this PDV epizootic, other seal species were tested for serological evidence of exposure to morbilliviruses. A large percentage of asymptomatic harp seals (*Ph. groenlandicus*) tested positive for antibodies specific to PDV (Ref. 26). Harp seals participated in a large-scale migration in 1986-1987 from the Arctic to northern Europe, during which time they could have infected harbor seals²⁷. If so, transmission may have been associated with selection for increased virulence or expanded host range of the virus. The virus that caused the Lake Baikal outbreak appears to be more closely related to CDV than to PDV, and thus did not have the same harp seal origin²⁸. It is possible that the Siberian epizootic was transmitted from dogs or other terrestrial carnivores infected with CDV to Lake Baikal seals. The Lake Baikal outbreak and an outbreak of PDV in minks (*Mustela vison*) in 1990 suggest that transfer of morbilliviruses between terrestrial and aquatic hosts is not uncommon.

disease in the USA¹⁴, demonstrates how agricultural practices influencing vector and reservoir populations can lead directly to increased disease incidence (Box 2).

Technology-transmitted disease

Technology can lead to unsuspected modes of disease transmission, providing new opportunities for disease emergence. Intravenous drug use has played a key role in the transmission of HIV. Further examples of technology-transmitted disease are described in Box 3.

Evolutionary changes that can lead to disease emergence

Recent promotion of the idea that disease can be controlled by selection for decreased virulence rests on the assumption that evolution drives disease emergence. However, clearly identified cases where evolutionary forces have significantly influenced disease emergence are strikingly rare relative to the dramatic contributions of ecology (Table 1). Nonetheless, evolutionary changes in microbial pathogens and their hosts have the potential to lead directly to disease emergence, as the following examples illustrate.

Box 2. Factors behind the recent emergence of Lyme disease in northeastern USA

Lyme disease rose to public attention in 1975 because of a cluster of cases in Lyme, CT, USA, but a similar syndrome was described clinically in Europe as early as 1883 (Ref. 29). Lyme disease is caused by the bacterium *Borrelia burgdorferi* and is transmitted by ticks in the *Ixodes ricinus* complex. Humans (not a natural part of the transmission cycle of the disease) can develop infections in regions where bacteria, ticks and reservoir host ranges overlap²⁹. In recent years, such regions have been increasing, both in the USA and in Europe. After the agricultural center of the USA shifted to the midwest, reforestation of suburban areas in New England led to sudden increases in density of reservoir hosts of *B. burgdorferi*, in particular mice (*Peromyscus* species) and white-tailed deer (*Odocoileus virginianus*^{14,30}). As these populations increased, so did tick and bacteria populations. *Borrelia burgdorferi* infection has been detected retrospectively in a tick collected 50 years ago on Long Island, NY, USA, suggesting that before the recent epidemic, bacteria populations persisted in isolated areas that were not severely deforested²⁹. Migration of infected deer or rodents from such refuges may have played a role in current disease emergence²⁹.

Molecular data suggest that some *B. burgdorferi* strains are probably native to North America while others may have come from Europe³¹. In Europe, three major *Borrelia* lineages (including *B. burgdorferi*) cause Lyme disease¹⁴. European transmission cycles appear more closely linked to farm animals and humans. Lyme disease is now recognized to have a worldwide distribution; the pattern of disease radiation is still unknown, but there is a great variety in reservoir hosts and epidemic cycles across geographic regions^{29,30}.

Box 3. Examples of technology-transmitted diseases

The emergence of Legionnaires' disease, a pneumonia caused by the bacterium, *Legionella pneumoniae*, demonstrates how technology can provide new routes of disease transmission. Legionellae bacteria are part of the normal commensal flora of aquatic habitats where they are either free-living or parasites of protozoa³². *Legionella pneumoniae* strains do not cause disease in humans unless they are inhaled into the lungs via aerosols or aspiration of water³². It has been suggested that the ability of Legionellae to parasitize protozoa serves as a pre-adaptation for the invasion of human pulmonary macrophages³³. Epidemics of Legionnaires' disease, which have been traced retrospectively to the 1940s, have often been linked with proximity to water-cooling towers or exposure to *L. pneumoniae* aerosols via water storage, heating and/or air conditioning systems in hospitals, office buildings and shopping malls³⁴.

The association between the emergence of toxic shock syndrome (TSS; late 1970s in the USA) and the use of highly absorbent tampons demonstrates how technology can allow microbes to reach new tissues within hosts. Toxic shock syndrome results from vaginal infections of toxin-producing strains of the bacterium, *Staphylococcus aureus* (TSS can also result, in rare cases, from non-vaginal infections). Strains with toxin-producing genes (that are sometimes found on plasmids) are commonly carried by humans, especially in the nasal passage³⁵. Toxin production, however, appears to occur only under certain conditions. In the recent emergence of TSS, *S. aureus* was presumably hand-transmitted to the vagina³⁶, where in the presence of super-absorbent tampons, the bacteria flourished and produced high toxin concentrations. It has been proposed that tampon use creates biochemical environments conducive to toxin production³⁷. Because the ability to produce the toxin causing TSS has been identified retrospectively in *S. aureus* as early as 1956 (Ref. 38), an evolutionary explanation for the recent disease emergence (e.g. a newly evolved toxin) has been ruled out.

Box 4. Potential sources of genetic variability in bacteria and virus populations

Bacteria

Bacteria can be altered genetically by mutation or by infectious transfer of chromosomal genes or accessory elements. These elements include plasmids (small, circular DNA that exists within cells) and bacteriophages (bacterial viruses).

Mutation: mutation rate in bacteria is approximately 10^{-9} – 10^{-6} per DNA base pair. Point mutations as well as deletions, insertions and inversions can lead to significant changes in virulence factors (e.g. adhesion ability, toxin production). Antigenic drift resulting from point mutations in genes coding for surface proteins can allow bacterial pathogens to 'hide' from mammalian immune systems.

Transposition: transposons are segments of DNA that can be integrated into new sites on the same or different DNA molecules from their origin; conjugative transposons are elements that can promote their own transfer from one bacterial cell to another.

Transformation: uptake and integration into bacterial chromosome of exogenous DNA.

Plasmid exchange: transfer of plasmids between bacterial cells; for example, plasmids encoding antibiotic resistance or virulence factors.

Conjugation: plasmid-mediated chromosome transfer between bacterial cells.

Lysogeny: incorporation of phage genes into bacterial genome via phage integration; for example, *E. coli* O157.

Transduction: phage-mediated transfer of small portions of bacterial DNA.

Viruses

Viruses are cellular parasites that have genes that encode their ability to replicate. Their genetic material can be either RNA or DNA. Some viruses can integrate into the chromosomes of their hosts. RNA viruses that do so need the ability to reverse transcribe themselves into DNA and are called retroviruses. Most viral pathogens of humans are RNA viruses.

Mutation: RNA viruses have significantly higher mutation rates than DNA viruses or bacteria, because of the greater instability of RNA molecules and the higher error rates of RNA replication enzymes. Point mutations can generate rapid antigenic variation (e.g. HIV).

Recombination between viruses: intra- and interspecific recombination has been observed in some DNA and RNA viruses.

Recombination with host genes: can occur in DNA viruses that integrate into host chromosomes, or in the DNA proviral step of retroviral replication; if the host chromosome has previously incorporated pieces of viral DNA, recombination can result in the integration of both host and viral genes into viral genetic material.

Reassortment of viral segments: in RNA viruses with segmented genomes (e.g. influenza), reassortment of segments among progeny rapidly leads to high levels of genetic variability within populations.

Emergence resulting from pathogen evolution

If variation in pathogen virulence, transmission rates, survivability or host ranges has a genetic basis, natural selection on pathogen populations can facilitate disease spread. Selection within hosts for colonization of new tissues can also lead to disease. Potential sources of genetic variation in bacteria and viruses, which both have generation times typically much shorter than their hosts, are shown in Box 4.

Influenza, the cause of the most severe pandemic of this century (killing at least 20 million people in 1918–1919; Ref. 15) and currently the sixth most important cause of death in the USA¹⁶, is a classic example of how selection can lead to epidemics and pandemics. Influenza is an RNA virus composed of eight segments, each of which corresponds to a major gene; influenza A has the highest mutation rate of the major influenza strains and has caused most human flu epidemics. Gradual accumulation of point mutations in two proteins (haemagglutinin, HA; neuraminidase, NA) that act as antigens to the host immune system has led to contained flu epidemics every other year this century¹⁶. Incorporation of new HA and NA variants into human influenza strains can cause more-dramatic changes in disease virulence and has caused all major influenza pandemics. These new variants have often been traced to aquatic ducks and shore birds, a large asymptomatic reservoir that contains all known subtypes of influenza virus. Segments of avian influenza virus can be incorporated directly into human strains, but most often recombination of segments between human and avian strains occurs in pigs, which can act as hosts to both varieties¹⁶. With such a large avian reservoir of influenza, the opportunity for new HA and NA variants to enter the human population poses a constant threat. Human agricultural practices, in particular combined pig and duck farming (common in China) further increase the opportunity for recombination between avian and human strains¹⁶.

Evolutionary factors have also played a role in the emergence of *E. coli* O157:H7, the pathogenic enterobacterium responsible for food-related outbreaks in North America and the UK. The majority of outbreaks have resulted from contaminated beef (farm cattle are known to carry the bacterium). The largest outbreak in January 1993 was associated with fast-food restaurants in the northwestern USA. Strains identified serologically as O157:H7 may produce one or both of two 'Shiga-like' toxins (similar to those produced by *Shigella dysenteriae* type I)¹⁷. It is these toxins that lead to the symptoms of the infection, hemorrhagic colitis. Genes for both toxins are encoded by phage that have integrated into the *E. coli* chromosome¹⁸. While many strains of *E. coli* have one or both toxin genes (assayed by molecular probe), only a small subset actually produce the toxins, at least to a level high enough to cause disease. A possible explanation for this pattern is that phage integration is fairly common but phage integrate at a position in the chromosome where the genes are expressed at high levels only in a minority of cases (R. Tauxe, pers. commun.). The large reservoir of toxin-producing genes (it is estimated that up to 40% of non-O157 *E. coli* in healthy cattle have one or both genes¹⁷) and the apparently large potential for phage integration make *E. coli* O157:H7 and other Shiga-like-toxin-producing *E. coli* a serious public health risk.

Emergence resulting from host evolution

Evolution in host populations, in particular, genetic changes affecting disease susceptibility, can also significantly influence disease emergence patterns. Strong artificial selection in domestic plants has facilitated disease emergence,

as demonstrated by the rapid spread of southern corn leaf blight in 1970–1971, which resulted in the most serious agricultural epidemic to date (Box 5).

Post-emergence opportunities for disease evolution

Even if ecology often plays a larger role than evolution in the initial phases of disease emergence, as diseases increase in host populations, opportunities arise for them to evolve in response to selection pressures exerted by hosts. The evolution and rapid spread of antibiotic resistance in pathogenic bacteria following the discovery of antimicrobial drugs 60 years ago is a dramatic example. The evolution of drug resistance also poses a problem for the treatment of fungal, protozoan and viral infections. Antibiotic-resistant strains of previously treatable diseases (TB, pneumococcus, staphylococcus infections) are currently increasing in prevalence and pose a serious medical threat worldwide. For example, 90% of staphylococci today can produce β -lactamase, an enzyme that allows bacteria to overcome the effects of penicillins, cephalosporins and related antibiotics¹⁹. Some forms of antibiotic resistance in bacteria can arise by chromosomal mutation; in many cases, however, genes for antibiotic resistance are encoded in conjugative plasmids that can be rapidly transferred within and across bacteria species. While some antibiotic-resistance genes appear to pre-date the antibiotic era (it has been proposed that they evolved in antibiotic-producing bacteria²⁰), recent use of antibiotics has been responsible for their proliferation.

Conclusions

It is clear that both ecological and evolutionary changes can contribute to emergence (and re-emergence) of infectious diseases. However, despite the potential for rapid genetic changes in microorganisms, ecological change appears to be a more general explanation for new epidemics. Why is this? Ecological changes impacting strongly on disease dynamics may be less constrained than evolutionary changes in pathogens or hosts. For example, even if mutants with greater virulence arise frequently, if such mutations are negatively associated with fitness, they will be rapidly eliminated. It also appears that evolutionary changes resulting in new disease often require ecological 'cofactors' (e.g. a microbe that evolves an expanded host range cannot emerge in a new host unless it also reaches that host). Regardless of the relative roles of ecology and evolution, emergence patterns of nearly all the epidemics described here were influenced significantly by human activity. Examples include agricultural practices (Oropouche fever, Lyme disease, influenza, O157:H7, corn blight), travel (dengue fever, HIV), invention (antibiotic-resistant bacterial pathogens, TSS, Legionnaires' disease) and urbanization (pneumonic plague, hantavirus). Therefore, any general approach to reducing the threat of emerging diseases must focus on human behavior.

Recommendations

The dynamics of emerging diseases are of clear scientific interest. However, while writing this review, we began to ask ourselves how population biologists can contribute to developing strategies to control these diseases. There are five major areas where ecologists and evolutionary biologists can have an impact. First, well-established methods of superimposing host and pathogen biology onto epidemiological models²¹ can be used to evaluate control measures in the case of newly emerging diseases. Applications of such models to vaccine assessment look especially promising

Box 5. Disease emergence resulting from genetic homogeneity of host populations

The southern corn leaf blight epidemic of 1970–1971 in the USA is a striking case where genetic homogeneity of a host population led to one of the most severe agricultural epidemics. The use of hybrid seed corn on a commercial scale began in the 1940s and by 1970, 85% of hybrid seed corn in the USA consisted of lines containing a particular genetic background (Texas cytoplasm male sterility, Tcms), which was beneficial for large-scale farming³⁹. However, Tcms was also hypersusceptible to a rare physiological race of fungus, *Helminthosporium maydis*, which causes southern leaf blight. This race of fungus, which is closely related to a common race of *H. maydis* recognized for years worldwide, has been detected retrospectively at low levels in Iowa, USA, in 1968 and has now been observed in Asia, Africa, Europe and South and Central America³⁹. It is speculated that the race either arose by spontaneous mutation in the US cornbelt in the late 1960s or was imported there in infected seeds. Weather conditions in 1970 in the USA were favorable for pathogen population growth and because of the high density of hypersusceptible hosts, southern corn leaf blight quickly spread to almost every state east of the Mississippi and some states further west. In the southern USA, where weather conditions were most favorable, virtually 100% of corn crops were destroyed. Infection in subsequent years was reduced by eliminating Tcms corn and increasing the genetic variability in agricultural corn crops³⁹.

(e.g. HIV vaccines²²). Second, as the recent rise in drug-resistant pathogens dramatically illustrates, strategies for controlling diseases must begin to take into account the evolution of resistance in pathogens and vectors²³. Third, phylogenetic analyses of pathogen sequence data can now be used to uncover disease transmission routes, both within and between species, and to estimate rates of transmission⁶.

Because pathogen evolution rarely leads directly to disease emergence, investigations of disease ecology will also be essential to the control of emerging diseases. Public health planning for well-established diseases like malaria and schistosomiasis²¹ has integrated information related to vector natural history, breeding biology, population and community dynamics for some time. Similar studies of vectors of currently emerging diseases will be important in limiting disease spread. Finally, studies of host–pathogen interactions can suggest measures that reduce population growth and transmission of emerging pathogens (e.g. intercropping). A focus on controlling pathogen populations is likely to have a broader impact on disease control than attempts to select for lowered virulence⁵. Historically, population biologists have left the study of disease to the fields of medicine and public health. The dramatic resurgence of infectious disease highlights the urgent need for collaboration between these disciplines.

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The molecular basis of quantitative genetic variation in natural populations

Thomas Mitchell-Olds

Natural populations evolve and adapt. Genetic variation affects fitness in wild populations adapting to different environments and during the process of speciation. If we could identify these genes, we would be able to address many ecological and evolutionary questions of long-standing interest. How often does adaptation involve major genes? Is pleiotropy responsible for genetic trade-offs among components of fitness? What maintains levels of quantitative genetic variation? What causes heterosis? What are the genetic mechanisms and evolutionary consequences of genotype–environment interaction? Are changes in regulatory genes important during speciation? Using mapped molecular markers, it is feasible to attack these problems now.

Genes affecting quantitative trait variation (i.e. quantitative trait loci, or QTL) have been mapped in plant and animal populations¹. Genes of large effect have not been considered important for adaptation in natural populations, since most major mutations have deleterious pleiotropic effects on fitness. However, rare major mutations without deleterious effects may sometimes occur. When such mutations occur they may play an important role in the evolution of natural

DNA markers allow us to study quantitative trait loci (QTL) – the genes that control adaptation and quantitative variation. Experiments can map the genes responsible for quantitative variation and address the evolutionary and ecological significance of this variation. Recent studies suggest that major genes segregate within and among natural populations. It is now feasible to study the genes that cause morphological variation, life history trade-offs, heterosis and speciation. These methods can determine the role of epistasis and genotype-by-environment interaction in maintaining genetic variation. QTL mapping is an important tool used to address evolutionary and ecological questions of long-standing interest.

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populations. Alternatively, strong selection or genotype–environment interaction may permit major genes to persist in natural populations. The frequency of such loci is an empirical question that can be determined by QTL mapping in the wild.

Practical matters

Our ability to understand molecular quantitative genetics is constrained by molecular and statistical technology. Only in the past few years has it become feasible to map quantitative trait loci in natural populations. I will repeatedly refer to the relative costs of these methods, since financial resources are the primary limitation on molecular quantitative genetics. For QTL mapping, expenditures are roughly proportional to the length of the linkage map, so species with many chromosomes will be difficult to study. Molecular

and statistical technology is changing rapidly, and improved methods can be expected in the coming years.

Molecular methods

DNA-based markers are essential to obtain polymorphic markers throughout the genome. Rafalski and Tingey² have reviewed molecular markers suitable for mapping. Most