CHAPTER 8

Health ecology: a new tool, the macroscope

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8.1 Introduction

Epidemiologists and parasitologists studying transmissible diseases tend to take an interest in direct causes, the visible modes of spread, and disease prevention. Usually, these disciplines show little interest in the physical, ecological, or evolutionary processes which occur on larger time and space scales. Epidemiologists and parasitologists have for a long time also considered the individual host as the only frame of reference for understanding the causes and consequences of infections. However, recent studies on the impact of global environmental changes and the dynamics of pathogens and their geographical distributions perfectly illustrate the relevance of large-scale studies for a better understanding of the persistence and dynamics of micro-organisms in host populations of humans, animals, or plants. As in classical mechanics, changing our frame of reference allows us to highlight important but previously unsuspected phenomena for a better understanding of the modes of transmission of pathogens within and between host populations.

In this chapter, using several recent examples, we illustrate the need to use a new instrument in **epidemiology** and parasitology, the 'macroscope' (de Rosnay 1975), in parallel with the conventional use of the microscope, to analyse on a more global scale the forces and parameters implicated in the emergence and spread of infectious or parasitic agents. As the scale of study (spatial or temporal) grows, one begins to see the involvement of parameters and mechanisms more usually thought to belong to academic disciplines other than epidemiology and parasitology. Solution of the world's health problems requires an opening up the conventional frames of reference in which host–pathogen interactions are usually analysed; the importance of non-causal or distal factors or processes having a direct, or more often indirect, influence on the nature and quality of the associations cannot be ignored.

8.2 Interactions between host populations and natural systems marked by exponential human growth

The current exponential growth in the human population, and the consequent huge and increasing impact that humans have on natural ecosystems, is one of the major problems facing human society today. The need for ever-increasing amounts of food has led to the rapid intensification and industrialization of agricultural production systems. This has had negative consequences for the viability of natural ecosystems (Aron and Patz 2001; Aguirre *et al.* 2002). The development of industrial-scale ruminant or poultry breeding in periurban areas has significant consequences for the quality of life and health of urban populations. Modern breeding plants pollute the water table and act as 'time bombs' for the spread of pathogens, which may be dangerous to humans. The present fears about propagation of the H5N1 bird flu virus in human populations will be even more justified if we offer such viruses favourable conditions for their spread; indeed, a large concentration of poultry (often genetically homogeneous) close to an urban community offers ideal

conditions for H5N1. We are, in effect, reorganizing natural systems to make them less favourable to our quality of life and at the same time more dangerous as conditions because more suitable for the spread of numerous diseases. Growth of the human population also leads to the search for new areas of land to colonize and on which to build new communities, structures, and infrastructures; again, most of these settlements are established at the expense of natural ecosystems. The example of the Amazon forest in Brazil is illustrative; deforestation of the primary forest for the purpose of farming and stock breeding has led to the emergence of several **infectious diseases**, including malaria and leishmaniasis, because the environmental destruction has provided suitable habitats for the **vectors** and/or **reservoirs** for these diseases.

Socio-economic measures and political decisions often have unforeseen negative environmental consequences—affecting soil and plants and increasing pollution and the proliferation of pathogens. The structure and dynamics of the networks used by micro-organisms to move from a reservoir to a vector, then from a vector to another reservoir, and even to tangential hosts including humans, are integral parts of ecosystems, each having its own mechanics. We are therefore compelled to consider in a more integrated way the research on communicable diseases: a single fact about the molecular features of a virus, for instance, is not sufficient to explain an epidemic disease. The word 'macroscope' comes from the famous book by Joël de Rosnay (1975), and we have chosen to use it in the title of this chapter. It has become necessary nowadays to develop this concept in public, veterinary, and plant health. We recommend here the use of a 'macroscope' together with the more usual 'microscope' in epidemiology and parasitology. The microscope and macroscope are both useful and valuable, but are used to answer some very different questions and investigate mechanisms occurring at different levels of organization.

8.2.1 Complex relationships between ecosystems, hosts, and pathogens

Recent years have seen the emergence or re-emergence of an increasing number of transmissible diseases. But why? Is there a single common explanation for all these epidemic diseases or, alternatively, is each unique regarding its mechanism of transmission/spread? Are there any common factors behind the Chikungunya epidemic on Réunion Island in 2006, and the intense more or less recurrent bursts of **Ebola fever** observed in Central Africa? The first epidemiologists were accused of being naïve because they acknowledged the major importance of a pathogenic organism and its distinctive features in the spread of a new epidemic even if the organism was already present before the disease outbreak! Emergences and recent re-emergences (some examples are given in this chapter) show that many factors, and even some interactions between these factors, can favour the outbreak of a pathogen in a host population which previously seemed to be disease free. A wider vision of what pathogenic micro-organisms are, of the interactions they have with their hosts, reservoirs, or vectors, and of the influence that the environment can have on the interactions between such partners is necessary. This integrative, interdisciplinary approach is necessary if one wants to try to solve the problems of population health. To paraphrase Morange (2005): '[a] fuller vision of what an epidemic is… takes into account the existence of other organisms which are their natural reservoirs, and of changes in the ecological environment or the behaviour of human populations which are bound to create new niches for the bacteria or the virus, and new ways of spreading'.

Numerous infectious diseases, particularly those that spread through a vector and/or a reservoir, depend on particular environmental conditions to develop. For many this can be the proliferation of a species of rodent, encouraged by meteorological and ecologically favourable conditions, as in the case of the **hantavirus** spread by rodents of the Muridae family in South America (Suarez *et al*. 2003). Other diseases are spread by tick vectors: large numbers of tick larvae hatch during the rainy season, followed by a peak in the adult population, leading to increased incidence of tick-borne disease (Gardon *et al*. 2001). **Lyme disease** is one such tick-borne disease present in Europe, but there are many others. The recent example of cases of **legionnaires' disease** in France is interesting

because this involves neither a reservoir *per se* nor a vector. The *Legionella* bacterium, responsible for occasional outbreaks of legionnaires' disease, is naturally present in water and soil, and can spread via plumbing and hot water systems when the conditions are favourable, particularly at temperatures varying between 25°C and 45°C. Industrial and domestic hot water systems and cooling systems using water make artificial ecosystems suitable for the development of these bacteria. Death occurs in 15% of cases of legionnaires' disease.

We shall now illustrate the complex relationships between the environment, micro-organisms, and hosts with some examples.

8.2.2 Different explanations

Even if we have learned much about transmissible diseases, their natural potential hosts, their reservoirs and vectors, and their interactions with the environment, there is no denying that many questions remain unanswered.

First let us take the example of cholera, a disease which until recently we thought we fully understood. The epidemiology of cholera can be looked at from two very different viewpoints. One explanation gives particular importance to the transmission of the two pathogenic strains (O1 and O139) of *Vibrio cholerae*, the bacterium responsible for the disease, and the consequences of these strains for **morbidity** and mortality in human populations. These aspects are the ones generally studied and analysed by molecular biologists who identify the **virulence** genes on isolated bacteria, and by epidemiologists who describe the evolution of outbreaks and intervene to stop their effects. A second type of explanation, a more recent addition to our understanding of this human disease, dates from the beginning of the 1980s. This considers that the two strains that are pathogenic in humans cannot be distinguished in a larger environmental context, in which a large number of *V. cholerae* strains coexist in the aquatic environment. Here, we need to understand the interactions between the environment and the bacterium, humans being a possible host for some of the bacterial forms. What is our current knowledge of the ecology of *V. cholerae*?

Cholera, or 'blue death', is an infectious diarrhoeic bacterial disease with an epidemic character. The pathogenic agent of cholera, as already mentioned, is *V. cholerae*, a Gram-negative motile bacillus belonging to the family Vibrionaceae. Not all strains of *V. cholerae* are responsible for cholera. In fact, the *V. cholerae* strains can be classified according to the O **antigen**, and, at present, nearly 200 serogroups are known; only the strains belonging to serogroups O1 and O139 have been linked to major cholera outbreaks. *V. cholerae* strains belonging to the other serogroups can cause sporadic diarrhoea, abscesses, or **septicaemia**. Cholera is the result of the absorption, by ingestion, of the cholera bacterium in water or food, but can also be transmitted from person-to-person by contact with pathological products (faeces, vomit, sweat). The experimentally determined **infectious dose** is of the order of 10^8 to 10^{11} bacteria, but it can be less, of the order of just 10^4 to 10^6 bacteria. After the passage through the gastric barrier, the bacteria become fixed to the proximal part of the small intestine, cross the mucous layer, and exude the choleric toxin. It is this toxin which modifies water and electrolyte exchange preventing the entry of sodium into the body cells; this results in the passage in the lumen of the digestive tract of a huge quantity of water, leading to severe dehydration of the patient. After an incubation period varying from a few hours to a few days, cholera manifests itself with violent diarrhoea and vomiting, but without fever. The water leakage leads to acute cramps propagating throughout the whole body, making the eyes sink in their sockets and contracting the orbicular muscle of the mouth, giving a cyanotic aspect to the patient's face ('blue death'). The expression 'to get a blue fear' (meaning to be scared out of one's wits) also originates from these symptoms.

It is the production of the cholera toxin from the *V. cholerae* O1 and O139 strains which is responsible for the expression of the disease. The **pathogenicity** of these strains is the result of the joint action of a set of factors favourable to the colonization of the intestine and the production of toxins by the bacterium. An environmental filamentous **bacteriophage** called CTXΦ, a virus attacking the cholera bacterium, has the ability to lyse the bacterial cell

wall and integrate its genome into the bacterial genome. An inserted bacteriophage gene *ctxAB* produces the cholera toxin. Another important factor implicated in the virulence of the pathogenic strains of *V. cholerae* is slightly co-regulated with the toxin. Its role was first identified in the colonization by *V. cholerae* of the host intestinal wall, but seemed to be more directly linked to the development of pathogenicity, being used as a receptor by the CTXΦ bacteriophage.

Recently, Faruque and his collaborators (Fig. 8.1) offered a new synthesis to account for the re-emergence of cholera cases and the pathogenicity

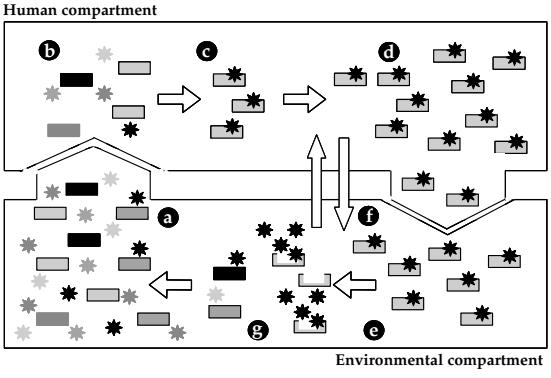

Figure 8.1 Diagram showing the way in which the epidemiology of cholera is currently interpreted. The aquatic environment maintains the phenotypic and genetic diversity of the strains of the bacterium *Vibrio cholerae* that are not very pathogenic for humans. Aquatic ecosystems also host a multitude of bacteriophages (viruses that naturally attack bacteria). Human populations form a selective filter, responsible for the better adaptation of the two pathogenic strains of the *V. cholerae* bacterium (O1 and O139) to the intestinal tract, by acquiring virulence genes from the bacteriophages. In some ways, humans are responsible for the disease that can be fatal to them. (a) Different environmental strains of *V. cholerae* (rectangles in different shades of grey and black) and of bacteriophages (stars) coexist in nature. (b) Bacteria and bacteriophages in the human small intestine; the bacteriophages can insert virulence genes into the bacterial genome. (c), (d) The now pathogenic bacteria are better adapted to the intestinal tract and spread; they are discharged with the diarrhoea to the external environment. (e) The aquatic environment is preferably loaded with pathogenic strains coming from the infected humans that 'selected' them. (f) An epidemic cycle is set up in which human populations, when drinking the water, take in the pathogenic strains which are the most abundant in the environment. (g) The spread of the pathogenic bacteria is followed by a population burst of lysogenic bacteriophages, a process that reinstates the initial conditions of the cycle. Adapted and interpreted from Faruque *et al.* (2005a,b).

of this disease in human populations (Faruque *et al*. 2005a, b). Locally, for example in the Bay of Bengal, the coastal and estuary waters, and even fresh water, naturally shelter a great variety of environmental strains of *V. cholerae*. So there is good reason to think, even if we have no direct evidence yet, that other tropical areas house a greater variety of these strains than waters situated further north. Several environmentally occurring non-pathogenic strains of *V. cholerae* can be ingested during contact or by swallowing water, and CTXΦ bacteriophages, naturally present in the water, can also be ingested. Besides, bacterial populations and bacteriophage dynamics can be observed and they are identical to what has been observed in prey–predator systems, i.e. an increase in bacteria in the aquatic environment is followed by a peak abundance of the bacteriophage (Faruque *et al*. 2005a,b). The small intestine therefore becomes a 'partners' crossroads' where contacts and exchanges between bacteria and their bacteriophages are greatly facilitated. Two strains of *V. cholerae*, O1 and O139, have indeed been more successful in infecting human populations, with tragic consequences. But why is this so? And how can we account for the visible antagonism between this increased ability of the O1 and O139 strains to develop, but also to bring about morbidity and mortality in human populations?

Let return briefly to what happens in the small intestine when *V. cholerae* strains and bacteriophages have been ingested. Some contacts and associations occur between some bacterial cells and the 'predator' bacteriophages, by chance or following some principles we are not yet aware of. In any event, the insertion of bacteriophage genes into the bacterial genome (a process called transduction) leads to an advantage for those bacteria carrying the pathogenicity gene *ctxAB*. From then on, these bacteria start to produce the gel-like toxin which has a devastating effect on the intestinal walls as well as on the natural intestinal flora, but forms a protective cocoon for the *V. cholerae* bacteria enabling the bacterial population to increase inside it. The significant diarrhoea provoked by the toxin then ejects the bacteria into the external environment which gradually becomes loaded with bacteria selected in the intestines, i.e. the pathogenic O1 and O139 strains exclusively. A 'reactor' is

created, and humans eat or absorb some elements which are contaminated by the pathogenic strains which are ever more present in the environment as the cholera epidemic spreads. In other words, the human population, and the miniature ecosystems formed in thousands of small intestines, generate the pathogenic bacteria that are responsible for their own misfortune. A sad fate for the hosts, but just a survival strategy for the micro-organisms which have to adapt to survive, or die. But in that case, why doesn't the epidemic continue to make progress as more and more pathogenic bacteria are poured into the external environment? Faruque and his colleagues once more have a rational explanation for this.

The pathogenic strains of *V. cholerae*, better adapted to the environment of the intestinal tract, are much less viable in the external environment: there, they meet other environmental strains of the same species, but also other species of potentially competitive micro-organisms, and even predators. The relatively rapid input of the O1 and O139 strains to the external environment during an epidemic also leads to the proliferation of bacteriophages in the aquatic environment which attack the bacteria by lysis. Progressively, or more suddenly, the O1 or O139 strains in the aquatic environment disappear, and a bacterial microfauna consisting of environmental strains returns. The Vibrionaceae are Gram-negative bacteria, and this bacterial group includes bacteriophages associated with the different species. There is good reason to believe that many diseases caused by these Gram-negative bacteria could also follow such a scenario (Fig. 8.1).

There are of course many other explanations for the outbreak and spread of cholera within human populations; interestingly, the explanation given by Faruque and colleagues matches the more traditional view of cholera epidemiology. The different explanations are not antagonistic but complementary, the traditional explanation finding its place within a novel and more integrated approach. The continual coming and going between *V. cholerae* bacteria and bacteriophages would, according to Faruque and colleagues, be the explanation accounting for the very marked seasonal variation of the epidemic episodes of cholera in the endemic zones. We are not that certain, but we do admit that such an ecologically based explanation is quite attractive. It could also be that particular oceanographic and climatic conditions are responsible for the exponential growth of the bacteria and their bacteriophages, as suggested in several recent works by Colwell and colleagues in the USA (Colwell 1996). Other factors also affect the impact of cholera, such as sanitary facilities and the level of poverty, the public health services, population demography, changes in the use of soil, and urbanization and travel. These causes are those that are usually cited to explain the outbreaks of cholera epidemics and their dispersal within populations. The model of Faruque and colleagues provides interesting possibilities: an appreciation of the existence of two compartments, on one side the environment that shelters a large diversity of *V. cholerae* strains and on the other human populations that unintentionally select the virulent strains; this model readily allows us to understand where action is needed to control or prevent the disease—in other words, within the environmental compartment that is upstream in the causal chain. We are obviously not questioning the critical contribution that medicine and public health care make in fighting outbreaks of communicable diseases, but we think that consideration of this kind of integrative approach in epidemiology can help us find alternative solutions to existing problems.

This observation leads us directly to the second example we wish to address in this section, which concerns the importance of economic exchange in the transmission of contagious diseases. Many examples feature the importance of sea and air travel as a driver behind the initiation and dispersal of epidemics (Ferguson *et al*. 2005). We shall mention a few of them here. One quite conclusive example concerns the seemingly trivial importation into the USA of several specimens for the pet trade that almost caused a major health crisis.

During the spring of 2003, several cases of monkey pox—caused by a simian orthopoxvirus provoking a disease clinically undifferentiated from smallpox—were reported in small pets in Texas (Di Giulio and Eckburg 2004). A few sporadic cases of monkey pox had already been reported in humans living in tropical forest areas in Central

and West Africa, where the major reservoirs of this disease are squirrels of the genus *Funisciurus* and *Heliosciurus*, Gambian rats of the genus *Cricetomys*, and several species of monkeys. Monkey pox had never previously been reported in the Northern Hemisphere. The introduction of this virus into the USA took place when some small African mammals were imported. Within the six different classes of rodents introduced, at least one Gambian rat, two squirrels, and three dormice (genus *Graphiurus*) were identified by the American medical authorities as having been infected with the monkey pox virus. Native prairie dogs cohabitating with Gambian rats in pet shops were then infected, and several people who bought these pets were infected in turn. Fortunately, none of the humans identified became seriously ill and the outbreak of a new **zoonosis** was averted. The occurrence of an **epizooty** originating from a few prairie dogs infected in a pet shop could have had dramatic consequences for the wild animals of the southern USA if they had come into contact with the virus. Undoubtedly, the transfer of animals, and thus probably of the pathogens hosted by them, is very disquieting given our current understanding of the susceptibility of other animal species and humans to infectious or parasitic agents of animal origin. This is also the case for the trade in food products and plants.

In order to deal with these 'new biological invasions', it will be necessary for there to be greater cooperation between national and international health services, doctors, veterinarians, and scientists. Imagine the consequences of the introduction—intentional or unintentional—to a conurbation of an animal that is a reservoir for a virus such as the one causing Ebola fever. Indeed, in Central Africa, where cases of Ebola fever are often reported, the spread of the virus is nonetheless limited by the small number of humans living in the forest villages.

The importance of worldwide exchanges of goods and humans today makes the rapid dispersal of infectious agents from their original area almost inevitable. Infectious diseases are very likely to be one of the priorities for the 21st century, and we must plan in order to better foresee the potential hazards and deal with the expected consequences.

8.2.3 Ecosystem dynamics and infectious diseases—or the snowball effect

Each new human or animal epidemic (surprisingly we seldom hear about the true devastation caused by infectious diseases of crops) is followed by many public and media arguments regarding its origin. The example of the epidemic outbreak of avian flu in Asia at the end of 2003 and beginning of 2004 is enlightening regarding the fact that wild birds, especially aquatic birds, were said to be responsible for the disquieting spread of the disease in Asia, while domestic ducks were blamed for having played a major role in the origin and the persistence of the flu virus (Li *et al*. 2004). The Thai political authorities even ordered the selective slaughter of the Asian openbill—a species of migratory bird of the same family as the stork—even though the decision was later revoked. Facing panic, the Food and Agriculture Organization of the United Nations (FAO) valiantly advised the Asian public authorities against the slaughter of wild birds, since there was no direct evidence of their being responsible for spreading of the disease between different epidemic centres and given that these wild birds represent a major component in the dynamics of aquatic ecosystems (see http://www.fao.org/newsroom/en/news/2004/48287/index.html). Recent observations in birds, but also in humans, of avian flu in Europe, Asia Minor, and Africa have also illustrated our total ignorance regarding the biological cycle of the viruses responsible. It is now thought that certain avian flu viruses—without knowing exactly which ones—have an exceptional capacity to survive for several months in the cold water of ponds and marshes; this upsets our knowledge about this zoonosis to such a degree that the role of the migratory birds or the domestic bird trade seems questionable. To illustrate this, imagine that a political decision had been taken in Thailand to exterminate the Asian openbill under the pretext that it was responsible for the spread of the avian flu virus. What would have been the epidemiological and ecological effects of such a suppression of predatory birds from the ecosystem?

One of the best documented examples today on the relationship between ecosystem dynamics, animal communities that coexist in the ecosystem,

and microbial agents is that of Lyme disease (Ostfeld and Keesing 2000a,b). Lyme disease is a disorder conveyed by a tick, *Ixodes scapularis*, in North America, and caused by micro-organisms called *Borrelia burgdorferi* (a spirochaete bacterium). Most often, it gives rise to a ring-shaped skin rash and **erythema**, accompanied by non-specific symptoms such as fever, discomfort, headache, or muscle and joint pain. Lyme disease is considered as an emerging disease in Western countries. In the USA, it has been shown that the risk of transmission of the pathogen is closely linked to the local diversity of small vertebrate species, certain ones of which can act as reservoirs for its growth and circulation. It seems that a small rodent, *Peromyscus leucopus*, is the reservoir species most likely to host and re-transmit the bacterium when a tick bites humans and other species. The environmental conditions, in particular the reforestation taking place in several north-eastern regions of America, have greatly modified the biological diversity of the resident species. Richard Ostfeld and collaborators have studied the risk of transmission of Lyme disease to humans according to the animal species composition of the forest fragments of different areas. In those forest segments with sufficiently large areas they found a large biological diversity, including predators and competitors of the rodent *P. leucopus* which regulate the population dynamics of this small mammal. On the other hand, in small forest systems, the lack of predators and competitors favour larger populations of *P. leucopus*. The increase in the numbers of *P. leucopus*—an excellent reservoir for *B. burgdorferi*—in this environment causes an increase in the general circulation of the pathogen within the ecosystem, and thus an increased probability of transmission to other animals and humans. American scientists have called this phenomenon the 'dilution effect'—a true functional role played by biological diversity in the transmission of a zoonosis to human populations.

According to this very original study, the main question that immediately arises is how does an infectious agent spread within a community of reservoir species? Is this situation also true for vector-borne diseases that show different transmission capacities? The work on Lyme disease represents a fascinating first study, that is not only focused on the relationship between a pathogen and a reservoir or vector species, but also tries to understand the circulation of a micro-organism within the ecosystem (Fig. 8.2). At the moment we generally lack

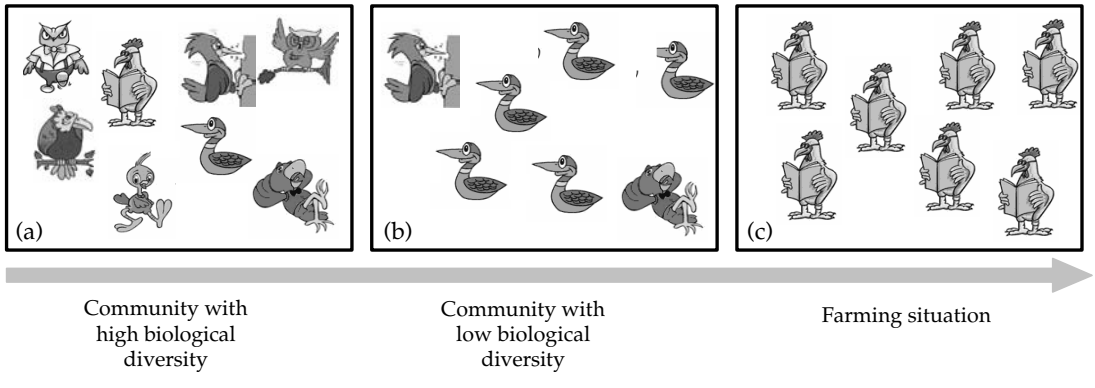

Figure 8.2 Depending on the diversity of species within a community the same infectious agent will present very different transmission modes (for example bird species that are reservoirs for a virus such as the one responsible for West Nile fever). (a) In the presence of diverse reservoir species with very different virus-transmitting capabilities, the pathogen has many possible modes of transmission with a resulting dilution of its effects. The dilution phenomenon increases with increasing proportions of weak reservoir species. (b) In communities with fewer reservoir species, where one or several strong reservoir species have taken advantage of the environmental conditions to reproduce, the transmission of the infectious agent is facilitated and its effects are more apparent. A similar situation exists when bird migrations occur with a flow of some strong reservoir species into a local community where the virus did not previously exist. (c) This illustrates an extreme situation where the individuals of a single bird species, often very capable of transmitting a virus, or alternatively have weak resistance to its invasion, are concentrated in large numbers, as in farms.

this kind of wholesale understanding of the ecological and evolutionary mechanisms implied in the emergence of pathogenic agents. Future work should focus on other examples of infectious diseases for which the dynamics of biological diversity and ecosystem change play a major role.

Undoubtedly, it is now obvious that human interaction can easily upset the equilibrium of ecological systems to a greater extent than in the past (Lebel 2003). As shown by many examples, only a few of which are given here, the emergence of infectious diseases or of certain epidemics with a zoonotic or vectorial origin is often the result of upsetting the equilibrium between a pathogen, the vector or reservoir populations, and the human populations that are often unfortunately the target but also actors in the situation. Epidemic phenomena are themselves complex and cannot be reduced to a simple explanation involving the presence and virulence of the pathogen, as was stressed early on by Duclaux (1902). An understanding of the dynamic equilibria occurring within ecosystems, where micro-organisms are a fundamental part of these giant puzzles, and to describe their changes to anticipate potential impacts in terms of health risks should today be part of our scientific culture from school upwards, and should receive more attention in undergraduate medical and scientific college courses.

8.2.4 A new school of thought: ecomedicine or health ecology

A new field of 'conservation medicine' has developed in recent years, almost exclusively in Anglo-Saxon countries (see http://www.conservationmedicine.com/). Its main objectives are to better understand the relationships and interactions between human health, animal health, and ecosystem dynamics (see Fig. 8.3), and also, of course, to promote these ideas to policy-makers, economists, and other leaders at national and international levels (Aguirre *et al*. 2002). The examples presented in this chapter are representative of this expanding line of research because the health of human populations cannot currently be dissociated from environmental conditions on the one hand ('ecosystem health') and animal health on the other. The example of avian flu is a perfect illustration of this. The reader will find much information on conservation medicine in the literature of Aguirre and colleagues (e.g. Aguirre *et al*. 2002) and of Lebel (2003; a free copy of Lebel's book is available in French from the site of the Canadian Development and Cooperation Agency http://www.idrc.ca/openebooks/012-8/). A programme initiated by the present authors in France contains sufficient material to keep several young and brilliant scientists in work. The stakes for

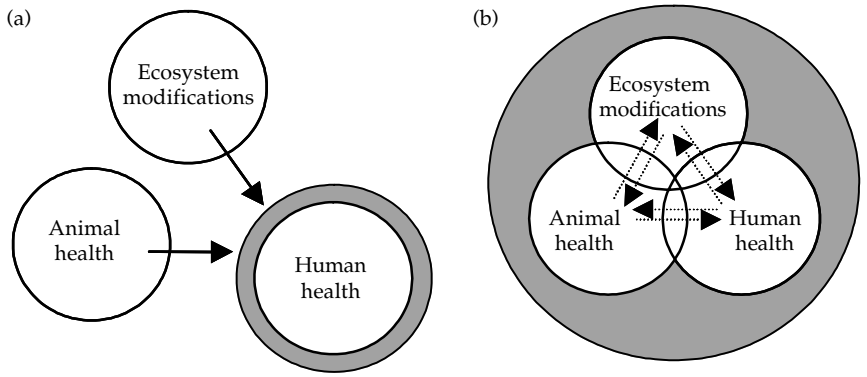

Figure 8.3 (a) The classical epidemiological view of the relationships between human health, animal health, and ecosystem modifications. Human health problems are interpreted according to a view where only the effects of changes in the ecosystem on human health are considered (see the arrows). (b) Potential multiple relationships between human health, animal health, and ecosystem health, where all the components interact with one another; a serious epidemic affecting whole populations of large ruminants in the East African savannah, for example, can have major consequences on the stability of this particular ecosystem as a whole.

population health are too high for this synthesis to be dismissed. Surprisingly enough, the field of epidemiology is probably one that is most in need of multiple explanations (Morange 2005), and yet where real joint research between disciplines is still very hard to implement.

8.3 The ecology of infectious diseases

For the reasons discussed in this chapter, we have a limited knowledge of the geographical distribution of the major pathogens in human populations (Jones 1990). This is also the case for animal and plant pathogens. What are the factors and mechanisms that are responsible for the present distribution of pathogens in human populations around the world? What role does climate and its variability play in the distribution of these microorganisms? What are the quantitative relationships between biological diversity and pathogens? What are the main factors responsible for the emergence, re-emergence, and dispersal of a pathogen, excluding the socio-economic reasons generally put forward? Are the globalized economy and modernization still paramount in explaining the spread of diseases and, if so, of what diseases? We have not yet found convincing answers for many questions of this type. The article by Tony McMichael (2004) gives an overview of the major causes of the emergence/re-emergence of current human diseases, and below we give a few examples of situations illustrating the relationships—often inextricable, but always complex—between ecosystem mechanics and population health.

8.3.1 What happened first: biology or socio-economics?

Two questions seem to dominate the traditional epidemiological approach to the study of communicable diseases—Where do they develop? Why do they develop there? Parasitology has the same questions. Determination of the 'where' has needed a considerable amount of observation, identification, and description. Understanding the 'why' has focused on the importance of social, economic, and technological organization to explain the occurrence, development, and distribution of infectious and parasitic diseases. There have been few works in the literature with an ecological or biogeographical approach.

Recent statistical studies of the large-scale spatial distribution of human infectious and parasitic diseases have provided interesting predictions concerning the different mechanisms that are responsible for the observations. Through a modelling approach based on a large set of data (332 human pathogen species with a worldwide distribution), Guernier *et al*. (2004) have shown, after correction for disturbance variables, that the species diversity of human pathogens is highly correlated with latitude: human communities that live in the intertropical regions generally host a larger diversity of pathogens than populations living in temperate regions (Fig. 8.4). In other words, the species diversity of human pathogens is consistent with the rule that applies to other free-living species (Hawkins *et al*. 2003; Chown *et al*. 2004; Hillebrand 2004). Is this geographical distribution the rule for all groups of pathogens? The study showed that pathogens that are transmission via a vector or a reservoir have a distribution based on latitude. It is the presence and the distribution of the vector, or of the reservoir, that determines that of the pathogen. Thus, many vectorial or reservoir diseases are present in intertropical regions because the diversity of the vector or reservoir hosts is very high in these regions. A single group of pathogens does not follow this general trend—pathogens with direct transmission, i.e. those for which infection takes place from one human to another and for which no animal reservoir exists. Many viruses and bacteria fall into this group, for instance the viruses responsible for measles and chickenpox and the bacterium responsible for whooping cough. As a matter of fact, these were originally animal diseases that were transmitted to the first organized human populations in the Neolithic age. These diseases, with progressive selection for forms adapted to humans, were then distributed by humans during colonizations, conquests, and displacement and economic exchange. Nowadays these pathogens are present almost everywhere on Earth apart from the two poles. They take advantage of large-scale transportation by air, rail, or sea to disseminate worldwide and their host resource is global, i.e. the human population.

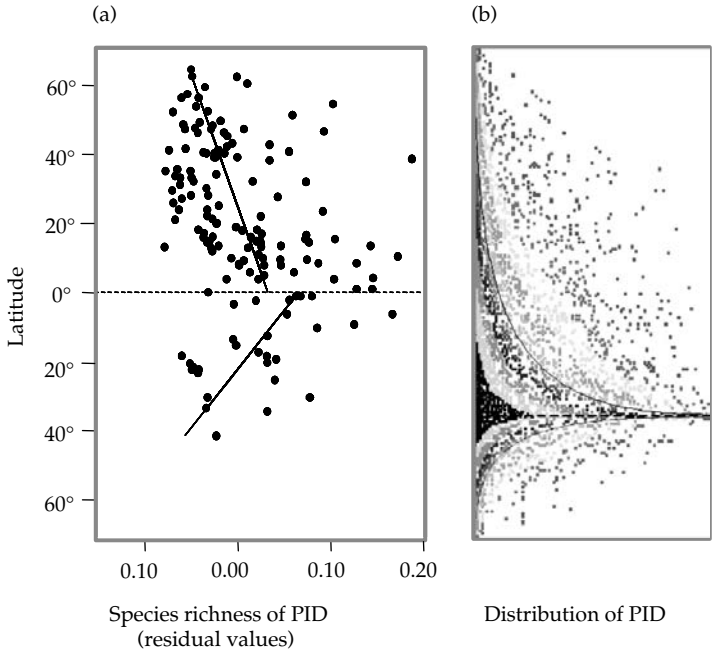

Figure 8.4 (a) Trend of the species diversity of pathogens for human parasitic and infectious diseases (PID) according to latitude. We can see a negative correlation between pathogen species diversity, after correction for disturbance factors to estimate diversity, and latitude for both the Northern and Southern hemispheres. (b) Presence/absence distribution matrix for 332 PID pathogens in both hemispheres. The spatial distribution of the aetiological agents, based on real data, was computed using random permutation statistics (Monte Carlo tests). The presence/absence matrix provides information on the distribution of the presence of a species in a given location (indicated by a dot) and deduces its absence elsewhere. Part (b) shows that the PID diversity decreases from the equator to the north or to the south. Furthermore, the PID pathogens present in a temperate region also tend to be present in human populations of the intertropical region. The opposite situation, where a pathogen is present in temperate regions and absent in intertropical regions, is very seldom observed. The spatial distribution of human pathogens follows an interlocked spatial model called a nested pattern (Guernier *et al.*, 2004).

Apart from that group of pathogens transmitted only from human to human, this study shows that the worldwide spatial distribution of human pathogens strongly depends on climatic conditions. Two factors are paramount: the temperature and especially the variation in precipitation during the year, which statistically explains the observed spatial distributions (Guernier *et al*. 2004). Undoubtedly, the particular ecological conditions acting on vector or reservoir species are those that limit the spatial distribution of these pathogens. Other pathogenic micro-organisms that, strictly speaking, lack reservoir or vector species also depend for their survival on the bioclimatic conditions that prevail in the ecosystem. In the next section we will discuss the example of the bacterium *V. cholerae*. We can then speculate about how these disease agents will evolve, either directly or indirectly, when faced with the expected changes in global climate.

8.3.2 Global climate change and the spread of infectious diseases

For efficient disease control it is essential to have a grasp of the ecology of infectious diseases and particularly of the role of environmental parameters in the evolution of interactions between hosts, vectors or reservoirs, and parasitic or microbial agents. By the contingent displacement of vectors and reservoirs, global climate change will undoubtedly contribute to major changes in the distribution of infectious diseases. A direct consequence will be the exposure of new human populations to exogenous pathogens against which they will

have no protection. Several recent examples show a trend toward an increase in the **incidence** and a change in the spatial distribution of infectious diseases of plants and animals in response to local climate change (Harvell *et al*. 2002). But what about diseases affecting humans? Are there any convincing demonstrations of the action of climate and its variability on the behaviour of microbial and parasitic agents? Let us look at the example of cholera epidemics in Bangladesh, which to date is one of the best documented studies in the literature (Rodó *et al*. 2002).

Through an analysis of the historical data on the incidence of cholera in Dhaka, the capital of Bangladesh, Rodó *et al*. (2002) found a close relationship between the El Niño phenomenon [more particularly the set of physical parameters measured by oceanographers and climatologists in the Indian Ocean (the Southern Oscillation Index, or SOI)] and the temporal dynamics of cholera cases in Dhaka. Figure 8.5 shows that the dynamics of cholera cases tend to change with the SOI, showing a strong match between the cholera peaks and the SOI minima for the period 1980–2002 (on the right of the figure). The nearly quadrennial cycle (between 4 and 5 years) of cholera epidemics in Dhaka since 1980 is interpreted as the result of the major climatic role played by the El Niño/Southern Oscillation (ENSO) phenomenon for the last two or three decades. But what links the cases of cholera in Dhaka to the ENSO phenomenon in the Southern Pacific Ocean as measured by the SOI? Physicists explain that the Earth's water masses are linked by teleconnections and that there are large-scale energy transfers from one ocean to the others. The disruptions linked to the ENSO phenomenon in the South Pacific then have consequences for the Indian Ocean. As was said above, environmental bacteria of the genus *Vibrio* are very sensitive to the physico-chemical conditions of the water they live in. For instance, temperature modifications at the surface of the Indian Ocean tend to favour these bacteria in coastal environments where human populations are concentrated. The work of Rodó *et al*. (2002) is one of the first contributions based on a mathematical/statistical approach to demonstrate a link between climate change (under way since 1976 according to climatologists) and the temporal dynamics of cases of an infectious disease (see also Speelmon *et al*. 2000).

In the same vein, let us take another example—flu epidemics in France. Using two independent sets of data for the period between 1971 and 2002, Viboud *et al*. (2004), showed a statistical relationship between mortality and morbidity due to flu epidemics in France, and the ENSO oscillations discussed above. During the study period, flu mortality in France was significantly higher for the 10 winters marked by cold ENSO periods compared with the 16 more temperate winters. Another study on the same subject confirms the overall influence of climate on the number of flu (due to the influenza virus) and viral pneumonias (other types of virus) hospitalizations in Sacramento, California (Ebi *et al*. 2001).

Although no hypothesis about the mechanism linking climate to the dynamics and size of flu epidemics has been put forward, the authors suggest

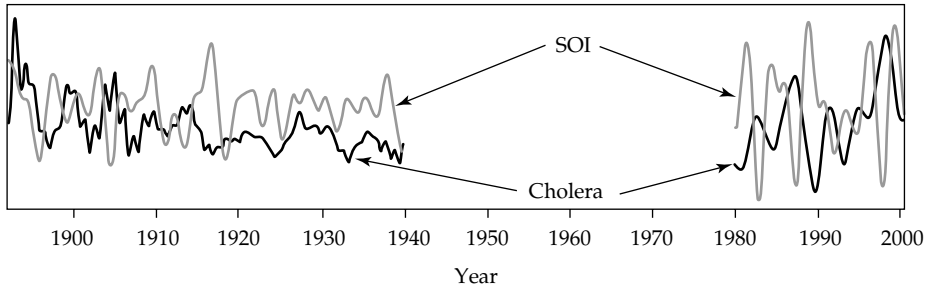

Figure 8.5 Relationship between the Southern Oscillation Index (SOI) and cholera cases in Dhaka (Bangladesh). Since the beginning of the 1980s, cholera epidemic peaks have occurred when the SOI index is at its lowest levels, and vice versa (see Rodó *et al*., 2002). ©*PNAS* (2002).

that climate change could favour the emergence of new **genotypes** of flu viruses that are better able to survive and spread in the new conditions. Another hypothesis, that does not exclude the first, suggests that lower temperatures and higher humidity rates, as observed during the very cold ENSO periods in Europe, could affect the physiology of individuals, making them more vulnerable to certain diseases due to immune deficiencies. There is currently no study demonstrating the better capacity of certain genotypes of flu virus to spread in particular environmental conditions, reflecting our present lack of knowledge about the ecology and evolutionary biology of the large majority of pathogens. This observation should generate new paths for research and draw young talent into this expanding discipline.

Climate and its variability have well-known consequences for living organisms, and ecologists would not omit bioclimatic parameters from their studies. Unfortunately, and somewhat surprisingly, very little importance has been attached to climate in explanations of the survival and viability of micro-organisms. The present unprecedented rate of global warming underlines the urgent need to develop adequate research in order to understand the adaptations taking place in microbes. Only such research will allow us to understand this process and predict the responses in the face of climate and anthropogenic changes. Further information on this topic can be found in a report from the American Society for Microbiology (King *et al*. 2001).

8.3.3 Ecosystem changes and health

Many examples of the emergence of infectious or parasitic diseases are consequences of human-induced ecosystem changes and habitat disruption. The epidemics of infectious or parasitic diseases, such as Lyme disease, schistosomiasis, and infections caused by Hantaviruses in Latin America, represent striking examples of the way in which ecosystems can affect the emergence of new diseases. This emphasizes the importance of developing pictures of ecosystem dynamics, the evolution of biological diversity, and their respective effects, or synergy, on health (see Section 8.2.3). We will illustrate this chapter with two new examples: one concerns the recrudescence of schistosomiasis in an East African lake, and the other the increase in malaria cases following the unprecedented deforestation of a major part of the Amazon plain in South America. Let us start with Africa.

Most infectious diseases have complex life cycles that require a reservoir host or a vector. One such disease, schistosomiasis, or bilharziasis, is one of the most serious tropical diseases. The helminths causing this disease are transmitted by gastropods (intermediate hosts) that are re-emerging in different African and Southeast Asian countries despite an improvement in the sanitary and socio-economic conditions of these regions. The worms in the larval stage (called cercaria) leave the snails and enter humans in contact with fresh water. The adult worms live in the human blood system and feed on blood cells. Their eggs are deposited in several human organs and tissues (liver, bladder, gut, etc.). The blood vessel damage they cause, and the corresponding physiological complications, give rise to the symptoms of the disease (Combes 2001). A key element in the re-emergence of schistosomiasis is the increasing number of habitats that are favourable to the different snail species that are compatible with the transmission of the parasite. Snails develop in rice fields, dams, and areas set aside for fish farms. For example, widespread large water reservoirs in Africa, e.g. the Aswan Dam that gave rise to Lake Nasser, have greatly increased the parasite's transmission, and consequently human morbidity and mortality in the region.

Changes in trophic webs due to the introduction of new species have also facilitated the increase in snail populations that are responsible for the transmission of schistosomiasis. For example, let us discuss the epidemic of schistosomiasis on the banks of Lake Victoria in East Africa. Lake Victoria has hosted a great diversity of cichlid fish species for several thousand years, and this exceptional diversity has led to spectacular specializations in several fish species. In particular, several cichlids have adapted to feed exclusively on molluscs, thus regulating gastropod populations and keeping their densities low enough to slow down the transmission of the parasite to humans. However, the Nile perch, *Lates niloticus*, was introduced to

stimulate the local economy—with such 'success' that we can now find Nile perch on sale in nearly all fish markets or supermarkets in France some 10 years after it was introduced into Lake Victoria. The consequences of the introduction of the Nile perch are many and have been the subject of a documentary film called *Darwin's Nightmare*. Two such consequences have been a drastic reduction in the biological diversity of native cichlid species and the consequential explosion of the mollusc populations on the lake's banks. The increase in the human population seeking to take advantage of the new local economy linked to fishing thus generated new centres for the transmission of schistosomiasis (Ogutu-Ohwayo 1990). If the introduction of the Nile perch in Lake Victoria did indeed lead to direct short-term economic benefits for the local population, the loss of biological diversity that it caused has led to considerable health problems for humans in the long run.

Another example that illustrates the way hosts and agents of infectious diseases interact with their ecosystems is that of malaria in the Amazonian equatorial forest. The deforestation associated with agricultural development and the construction of the trans-Amazonian highway has favoured the development of the mosquito *Anopheles darlingi* that is the main vector for two pathogens, *Plasmodium falciparum* and *Plasmodium vivax*, responsible for malaria in South America (Tadei *et al*. 1998; Conn *et al*. 2002). *A. darlingi* is known to occupy a specific ecological niche in the canopy of the humid forest. Deforestation has opened new habitats favouring the irruption, development, and establishment of populations of this mosquito species (Vittor *et al*. 2006). The arrival of human communities to the newly developed agricultural areas was accompanied by the introduction of the *Plasmodium* parasite by infected persons. The presence of larges numbers of *A. darlingi* then efficiently contributed to the creation of new centres for the transmission of malaria. In Peru, the areas deforested for agriculture have an almost 400-fold higher risk of malaria transmission than the forest zones (Vittor *et al*. 2006). The ecological disruption of the equatorial forest ecosystem due to deforestation for agriculture, the proliferation of the vector, and the settlement of human communities form a complete picture for understanding the spread of centres of malaria within the Amazonian plain. The role and importance of environmental and socio-economic factors are easy to identify in this example, but they are also closely related. Another example of the role of deforestation on the emergence of diseases is given by the recrudescence of cases of **hookworm**, an important human pathogen in Haiti (Lilley et al. 1997).

Over the past 50 years, industrial and agricultural changes, economic and social changes, and the rapid growth of the human population and international travel have all contributed to modification of the occurrence profiles and spatial distribution of infectious and parasitic diseases. However, for a large number of known pathogens, and probably also for thousands of other unknown ones, the role of the ecosystem is fundamental in explaining the emergence or recrudescence of diseases, as shown here. It is crucial that national and international organizations start to implement an ecosystem approach to health problems (Rapport and Lee 2003).

8.3.4 Land use, agricultural development, intensive farming, and health

The huge increase in population that began in the 20th century necessitates a permanent increase in the production of food products. The soil and the ecosystems are already being vastly over-exploited in order to satisfy these needs: to feed the 6.6 billion people that currently live on Earth (Aron and Patz 2001; Patz *et al*. 2005). (For further information seven very interesting seminars on 'Medical Ecology: Environmental Disturbance and Disease' by Dickson Despommier of Columbia University may be accessed at http://ci.columbia.edu/ci/eseminars/1111_detail.html.)

What might be the ecological consequences for human health of these land use practices, intensive farming, and agronomic systems? Are our practices also re-creating new types of ecosystems which will facilitate the development and circulation of new pathogens? Let us look at several examples of infectious diseases whose recent emergence is linked in part to land use or intensive practices in agronomy.

The Japanese encephalitis virus has represented a serious public health problem in several Southeast Asian countries since its emergence at the beginning of the 1970s. This virus is transmitted by mosquitoes of the species *Culex vishnui* which preferentially breeds in rice fields. The intensive cultivation of rice in the Tamil Nadu region of India, as in many regions of developing countries, has strongly determined the recrudescence of these insects in rice fields (Sunish and Reuben 2001). We know today that the use of fertilizers such as nitrates has a positive effect on the abundance of mosquito larvae in rice fields, namely on the propagation of aquatic micro-organisms on which the mosquito larvae feed. Likewise, for the same agrosystem but in north-eastern Argentina, the abundance of molluscs of the genus *Biomphalaria* (possible vectors for the transmission of schistosomiasis) is linked to concentrations of nitrates and nitrites in rice fields (Rumi and Hamann 1990). Similar scenarios have been observed for Korean haemorrhagic fever, caused by a virus of the Hantaan group, and for the Argentinean haemorrhagic fever caused by the Junin virus (Morse 2004). The virus causing Korean haemorrhagic fever infects the vole, *Apodemus agrarius*, in several Southeast Asia countries and in particular in the People's Republic of China. This pathogen can infect humans. The expansion of rice fields has created favourable conditions for an explosion in the vole population, which thus increases the risk of transmission of the disease to humans, mostly farmers. Moreover, it is supposed that the conversion of prairies into corn fields in several regions of Argentina has facilitated the proliferation of a reservoir of host rodents for the Junin virus (Morse 2004).

Ecological change subsequent to agricultural development are is of the factors most frequently identified with the emergence of a new disease. Avian flu caused by the influenza virus is another example of the way in which intensive animal production can play an important role in the origin and circulation of a disease. Indeed, the intensive production of birds and pigs represents an artificial ecosystem favourable to the circulation and transmission of this type of virus, because the organisms are present in high densities and they are often physically compromised. One can imagine how a viral epidemic could spread through the intensive concentrations of such farm animal in periurban areas of megacities such as Bangkok or Mexico City, for example. Let us also recall the recent outbreak of severe acute respiratory syndrome (SARS) in the south of China, caused by a coronavirus from a small civet-like mammal sold in markets and eaten by the local population (Guan *et al*. 2003). The intensive production of cattle and the methods used to feed them have facilitated the transmission of prion agents causing bovine spongiform encephalopathy (BSE) in ruminants, linked to a new variant of Creutzfeldt–Jakob disease in humans (Ghani *et al*. 2000; Valleron *et al*. 2001). Intensive farming and related industrial production methods favour the increase of contamination and accidental amplifications, as was observed in the case of BSE. Indeed, animal by-products—mainly ovine and bovine—were used to feed the cattle, thus creating a new 'artificial food chain' and an occasion for cannibalism in otherwise strictly herbivorous animals.

The intensification of agriculture and animal rearing represent major sources of new infectious agents. Given that many pathogens have displayed a natural ability to overcome the species barrier, we must also reflect on the consequences, in terms of public health, of allowing the spatial coexistence of thousands or even millions of animals for human consumption in the vicinity of large cities where millions of inhabitants are sometimes concentrated. This is what the next section deals with.

8.3.5 Human population growth and the evolution of infectious diseases

In their respective conclusions, McMichael (2004) and Morse (2004) underline the fact that the human demographic explosion and its consequences are responsible for the many emergences and/or re-emergences of infectious or parasitic diseases. What is in store for the future then? What does theoretical and empirical epidemiology have to say?

There were 2.5 billion people on Earth in 1955, 6.5 billion in 2006, and a predicted 9 to 10 billion 50 years from now. This increase in the 'host population' can only favour the persistence and evolution of a greater diversity of pathogens (Guégan and Broutin 2008). Indeed, even if we do not have a

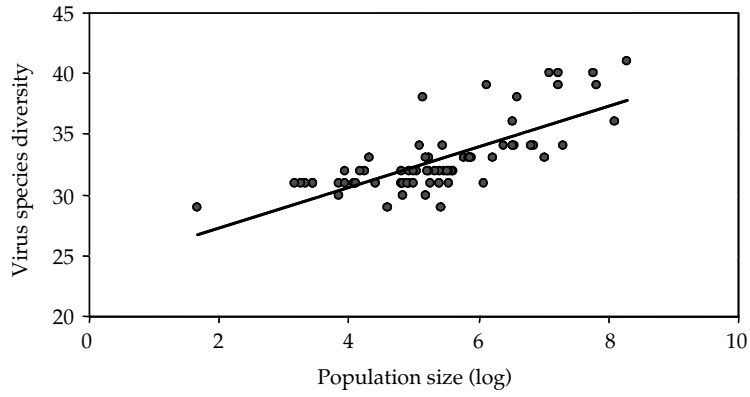

Figure 8.6 Linear relationship between the size of a human population (number of individuals) and the diversity of viral species in 71 human communities living on oceanic islands. The linear regression is $y = 1.67x + 23.97$, $r^2 = 0.551$, $P < 0.0001$. The 'population size' variable is log-transformed. From Guégan and Broutin (2008).

comprehensive grasp of the biological diversity of pathogens hosted by human populations, it is quite easy to understand that larger human populations with more individuals will display increased hosting possibilities for a larger number of pathogens than smaller and less numerous populations (Fig. 8.6).

There are still many uncertainties about the mechanisms that regulate pathogen diversity, particularly in human communities. The examples above give quite a convincing demonstration that simple laws of population and community ecology are perfectly adaptable to communities of pathogenic micro-organisms. Indeed, recent works tend to show that free-living micro-organisms such as planktonic algae or microscopic fungi (Finlay 2002; Green *et al*. 2004) as well as bacteria and viruses infecting human populations (Guernier *et al*. 2004; Guégan and Broutin 2008) are not randomly distributed, but display organized and predictable spatial distributions. This type of results offers new possibilities for a synthetic understanding of the way in which pathogens organize and become structured in host communities.

The population size, i.e. the number of people within a community, is an essential factor for the persistence and spread of a contagious pathogen, such as a virus or bacterium. Many studies have thus shown the existence of a critical threshold for the number of individuals in human populations (critical community size, CCS) below which the pathogen cannot persist (Grenfell and Harwood 1997; Grenfell *et al*. 2001; Broutin *et al*. 2004). In the case of the virus responsible for measles, the critical threshold is estimated to be 250,000–300,000 inhabitants, and in the case of the bacterium responsible for whooping cough, the threshold value is 400,000–450,000 individuals. Inspired by the **metapopulation** theory, Rohani *et al*. (1999) showed that the measles virus and whooping cough bacterium spread in the United Kingdom from certain urban centres such as London, Liverpool, and Birmingham toward peripheral rural areas. Several urban areas function as sources or reservoirs that allow these infectious diseases to persist and give rise to new epidemics (Fig. 8.7).

As shown by that work on the spread of the measles virus and whooping cough bacterium, it is critical to consider the regional scale (in this case England and Wales) in order to understand events at the local scale, i.e. a city or a town. Once again, the use of the macroscope allows a broader vision of the way infectious agents spread within a web of cities and towns. These ideas, developed from the concept of metapopulation ecology, are crucial in epidemiology and public health because they allow, once the special dynamics of a pathogen are understood, new means of control and vaccination. Indeed, wouldn't it be better to vaccinate populations in several 'source' areas when the case

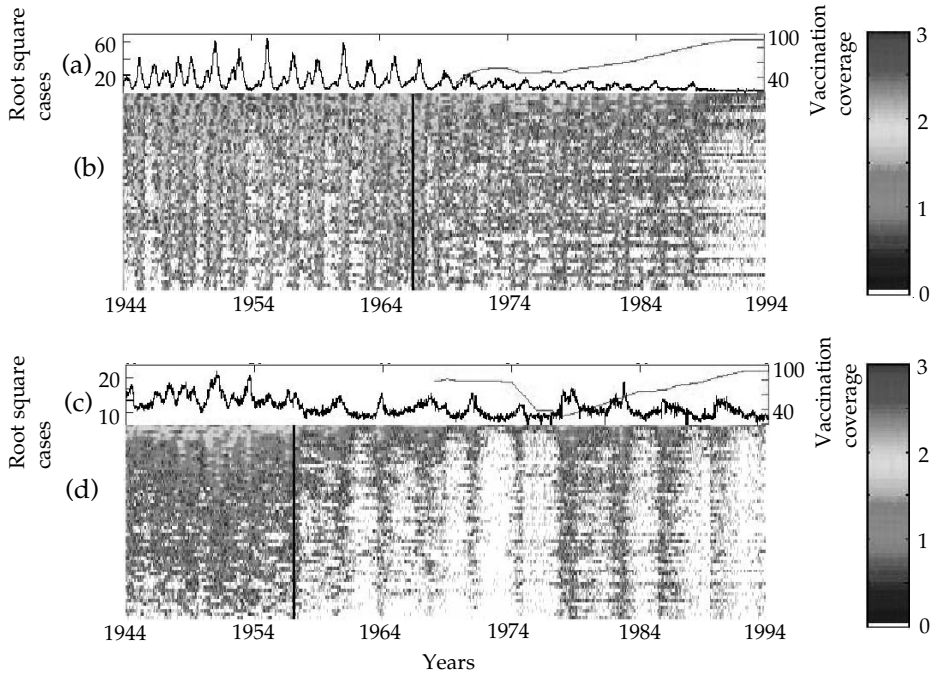

Figure 8.7 Parts (a) and (c) show the dynamics of the number of individuals infected by the pathogens that cause measles (a) and whooping cough (c) in England and Wales. The grey curve shows the evolution of the vaccination coverage (per cent) for these two diseases. Parts (b) and (d) show the spatial organisation of the number of cases from the largest city (London (on top) to the smallest town Teignmouth (on the bottom). The greyscale show the incidence rate of the disease. The spatial distribution of the cases in (b) and (d) show that both these early childhood diseases persist in time in the largest towns of England and Wales (red). This spatial organization is particularly clear in the cases of measles (b). Modified from Rohani *et al.* (1999) with the permission of the first author.

dynamics are at the inter-epidemic stage, i.e. when the number of cases is reduced? This is an important issue, and the question remains as to whether or not these ideas will be tested or adopted in the near future. We have analysed the dynamic behaviour of a pathogen at the scale of a country; the following section analyses what happens on a worldwide scale.

8.3.6 International travel and trade

Of all the species on the planet, humans probably have the most extraordinary abilities to adapt and survive. Modern technologies have facilitated access to and colonization of geographical areas that had remained isolated for a long time. Transcontinental flights and sea transport, and economic and business exchanges have contributed to this. This almost total colonization of the planet by human populations has also been profitable to 'aliens', i.e. free riders, such as parasites and microbes (Spielman *et al*. 2004). The development of air transport now favours the transmission of pathogens between opposite sides of the globe (Fig. 8.8). This is an unprecedented situation in human history. Pathogens such as many viruses and bacteria that are transmitted in this way can readily spread and infect human populations that were previously free from infection. The recent avian flu epidemic in Southeast Asia should teach us many lessons; by generating worldwide panic, it showed that global action was needed to manage an issue with a global outcome (Li *et al*. 2004). Instead of choosing one or two particular diseases with which to finish this section and chapter, we will present new data provided by Smith *et al*. (2007) regarding the degree of homogenization of nearly 320 human pathogens. The issue here is to

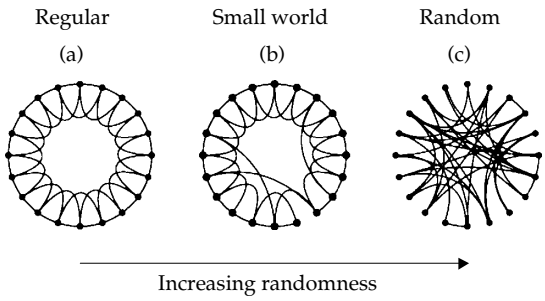

Figure 8.8 Diagram of the levels of homogenization of human populations. (a) In ancient times human communities were only in contact with their nearest neighbours. (b) When transcontinental exchanges were still limited several decades ago, local human populations were in contact with other neighbouring ones, and occasionally with other communities farther away (notion of a *small world*). (c) Each local community is in contact with the others, illustrating a globalized world. Infectious diseases could take advantage of such a strongly interconnected world to spread and develop in host populations. Modified from Watts and Strogatz (2004).

determine which human pathogens display global dynamics as opposed to more local mechanisms (Fig. 8.8).

Based upon a set of data from 317 infectious diseases affecting human populations, Smith *et al*. (2007) first sought to classify the different **aetiological agents** according to the type of reservoir hosts: (1) pathogens that are strictly specific to humans; (2) pathogens that use human and non-human reservoirs (called multi-reservoir pathogens); and (3) pathogens whose reservoir is an animal, i.e. a zoonosis, and that are occasionally transmitted to humans. Based on a similarity index, identical to those commonly used in community ecology, and measuring the degree of homogenization between geographical areas, the authors showed that contagious agents of the first category displayed the highest degree of similarity between regions, followed by the infectious multi-reservoir agents, and finally zoonoses (Fig. 8.9).

The homogenization of directly transmitted pathogens suggests that their host resource is global. The local and global diversities of this type of pathogen and their specific types are almost identical; a locality like Montpellier displays both the same number of pathogen species and the same species composition as another locality far away, such as Los Angeles, for example. Furthermore, the richness and diversity of these pathogens in Montpellier are not very different than what is observed at the global scale. The immigration/colonization/extinction processes are the ones that are in a large part responsible for the local diversities observed. Colonizations originate from a continental or even global colonization pool. On the contrary, aetiological agents having more complex cycles do not achieve this degree of homogenization. This is more obvious for zoonoses (Fig. 8.9). Two adjacent geographical areas can shelter of very different pathogen communities. In this chapter, we have already discussed the reasons for this phenomenon. It is the endemic nature of the host reservoir species, and very often the related pathogens that explain this situation. These pathogens display very marked local or regional spatial distributions, whereas directly transmitted pathogens have a global spread. The processes that explain their spatial distribution and those of their hosts are more related to habitat heterogeneity and whether it is favourable or not to their development. Since for directly transmitted pathogens the host resource is global and 'finite', we think that the reservoir pathogens are those that today represent the biggest danger to human populations if they are given the chance to spread (like the monkey pox example given earlier). The increasing rate of introduction of exotic species, as already pointed out above, greatly facilitates the arrival of these new 'aliens'. What should we do? How can we prevent these new invasions? Shouldn't we exert stricter control on the introduction of species by targeting animal groups that are known to be important disease reservoirs, such as rodents, birds, or ungulates for example?

International traffic and trade, like the tyre trade responsible for the spreading of disease vectors (Renaud *et al*. 2005) or the pet trade, are today especially alarming. They have played—and will probably still play in the future—an important role in the spread of pathogens in regions that were previously free from them. This issue in itself requires quick decisions on trade regulations and worldwide transportation.

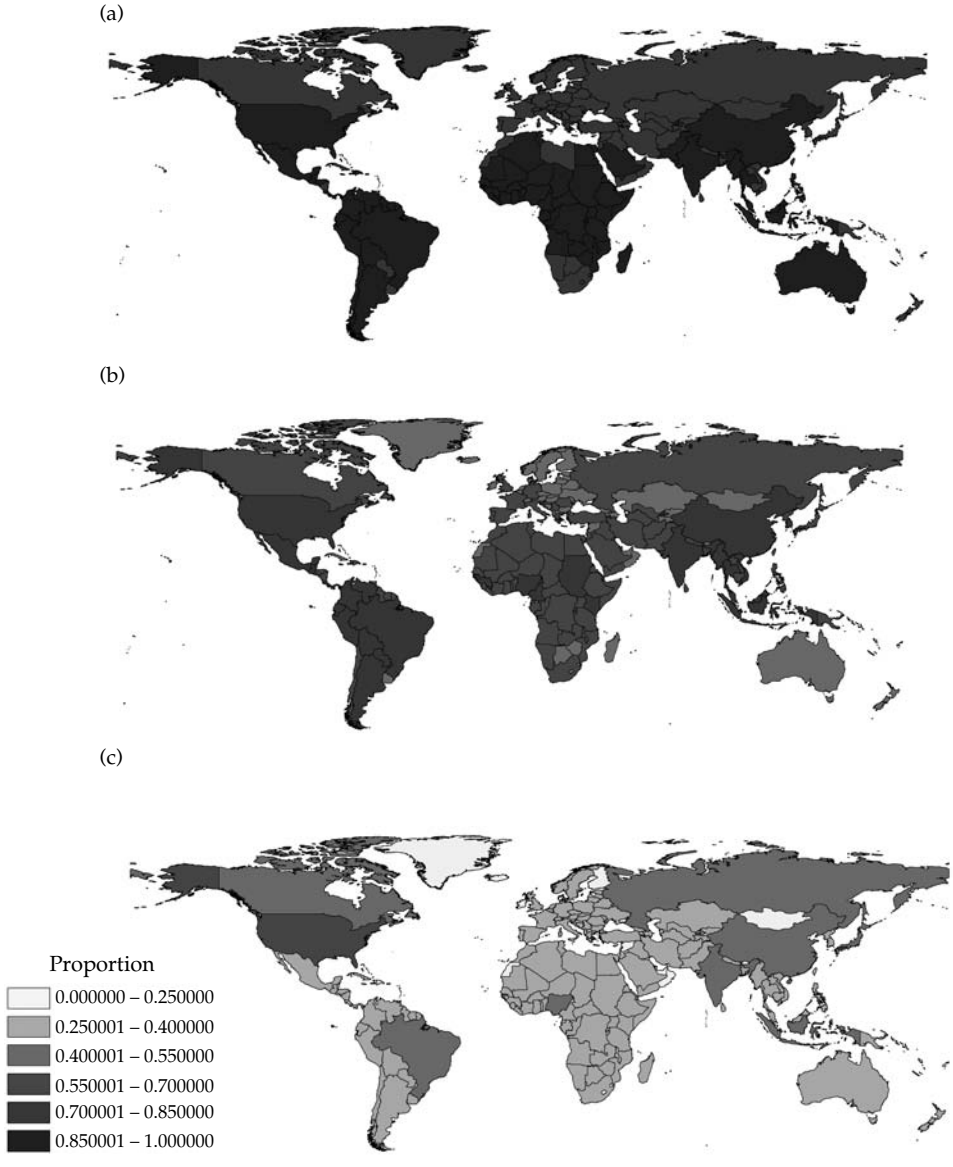

Figure 8.9 Degree of homogenization of human pathogens at the global scale, according to their life cycle: (a) for pathogens with direct transmission; (b) for pathogens that have both human and non-human reservoirs (multi-reservoirs); and (c) for pathogens with an animal reservoir. The classification according to the degree of homogenization is based on the Jaccard similarity index which varies between a low value (lightest) and a high value (darkest). From Smith *et al.* (2007).

8.4 Conclusion and proposals for new research perspectives

We have analysed and summarized in this chapter several issues concerning the relationships that exist between environmental changes and health problems, and the challenges arising from this new global context in terms of public health issues. This contribution is by no means an exhaustive review of the scientific literature on the subject. In fact we have deliberately selected just a few examples that

give a good illustration of the scientific and health situation. Our selection was intended to give the reader a broader vision of the health issues, using a new tool we call the 'macroscope'. The same kind of reflection and approach should of course be followed in plant health and agronomy (due to lack of space our selection of the literature has omitted to include many situations of interest in these fields).

Many epidemiologists think that we have learnt enough about infectious diseases; this chapter seeks to convince even the most sceptical that we must improve our understanding of infectious diseases and change the way we think and work. The challenge for modern epidemiology is to change scales and adopt a global ecological perspective on health issues. Lawton (2000) has identified four fields in which he thinks that community ecology has not yet found a happy medium. These fields can easily be transposed to modern epidemiology: (1) too big an investment in field experiments or short-term laboratory research, often with a reductionist character; (ii) too much importance given to research in processes involved at a local scale rather than processes taking place at larger spatial or temporal scales; (3) lack of synthesis between molecular ecology, populations genetics, and population and community ecology to better understand infectious and parasitic diseases; and (4) a lack of statistical and mathematical models.

What can we do to change this research trend? We can summarize the possible actions and priorities as follows:

1. Develop a multidisciplinary approach. Develop research favouring interdisciplinarity and an exchange of views. Reconcile explanatory molecular–mechanistic, neo-Darwinian schemes and non-causal physical mechanisms with one another. Avoid setting disciplines against one another, but rather use their complementarity to express different points of view on the same phenomenon.

2. Carry out containment research in pilot zones. We must concentrate our research efforts on a given number of geographical areas, or observatories, and on studies of biological systems. Research on infectious diseases cannot do without such an approach, which will ultimately allow a comparative intersite analysis.

3. Develop long-term epidemiological study sites, particularly in intertropical regions where the impact of the environmental changes on health issues is apparent, and where the risk of infection is greatest.

4. A consequence of point (3) is the need to standardize the protocols in the different epidemiological disciplines. The inability to standardize protocols during recent decades has virtually excluded any attempts at meta-analysis and comparative analyses in epidemiology. Quite surprisingly too, the reason mentioned to justify this was the lack of standardization.

5. More coordinated research programmes at the national and international level. National and international scientific institutions must promote coordinated multidisciplinary research. For example, in the USA, the experience with the joint project of the National Science Foundation and the National Institutes of Health represents an important effort toward better collaboration between medical scientists and ecologists/evolutionists.

6. Promote population and community epidemiology. In epidemiology as in other disciplines, there is an actual trend to consider molecular biology as the only true science, namely because it takes the molecular-deterministic approach. The same trend can apply to field epidemiology with regard to theoretical epidemiology. We must encourage a diversity of approaches that will provide different points of view and information that is essential to the understanding and modelling of how a local outbreak may happen. We must also take interest at the population level, which is the fundamental basis of the approach in public health, and the community level, more in phase with the natural circulation of pathogens within ecosystems.

At the end of this chapter, we are convinced that by broadening the approaches of our studies, i.e. using the 'macroscope' as much as we do the microscope, we will be able to answer some of the questions about the issues concerning the emergence or re-emergence of pathogens. Our ability to react and to adapt our research largely depends on the eventual answers to these questions. Additional or complementary information on this topic is available in the United Nations Environment Programme Geo Year Book (2004/5) *Emerging challenges—new*

findings. emerging and re-emerging infectious diseases: links to environmental change.

Important facts

- Each species of bacteria or virus in the environment has an important phenotypic and genetic diversity, but only some rare forms are pathogenic for humans (see Faruque *et al*. 2005a, b).
- Potentially infectious organisms are often present in the environment before the onset of an epidemic (see Morange 2005).
- The health of humans, animals, and ecosystems are closely related (see Lebel 2003).

Questions for discussion

- How do we explain the current outbreak of epidemics in populations?
- Does the determination of the virulence genes of an infectious organism help us understand its ability to spread?
- How can we make a compromise between the traditional vision of cholera epidemiology and a more integrative approach considering the aquatic environment as a natural reservoir for bacteria?
- Why is it important to switch spatial and temporal scales in epidemiology and infectious disease ecology?
- Why is it important to adopt an approach based on community ecology when studying the emergence of new pathogens?

Further reading

- Further information on the effects of environmental global changes on the health and well-being of humans can be on the World Health Organization website at http://www.who.int/globalchange/en/
- Information on the policy of the Canadian International Development Research Centre regarding health ecology can be found at http://www.idrc.ca/ecohealth.
- Chivian, E. (ed.) (2002). *Biodiversity: its importance to human health*. Harvard Medical School, Center for Health and the Global Environment, Cambridge, MA.
- An introduction to health ecology: Guégan J.F., Renaud F. (2004). Vers une écologie de la santé. In: *Biodiversité et changements globaux* (ed. R. Barbault and B. Chevassus-au-Louis), pp. 100–135. ADPF/MAE Editions, Paris (in French).
- Collinge S.H., Ray C. (2006). *Disease ecology*. Oxford University Press, Oxford.
- Patz J., Confalonieri, U. (coordinators) *et al*. (2005). Human health: ecosystem regulation of infectious diseases. In: *Ecosystems and human well-being: current state and trends: findings of the Condition and Trends Working Group*, Millennium Ecosystem Assessment Series, pp. 393–415. Island Press, Washington, DC.