CHAPTER 33

Epidemiology in a Changing World: The Need for a Bigger Picture!

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"... Quite properly, the medical epidemiologist's main concern is often with the recondite biological and medical details that make each infection unique ... In the absence of [such] a unified framework each infection tends to develop its own, often arcane, literature."

—Anderson and May, 1991

33.1 INTRODUCTION

Medical epidemiologists studying infectious diseases generally prefer to deal with their primary causes, propagation and prevention, rather than bothering with the possibility–when a communicable disease conforms to biological laws–of the existence of physical, ecological, or evolutionary processes that might affect the organisms in question. Epidemiology can be defined in a number of ways (there are many examples in this *Encyclopedia*), but traditionally it deals with epidemic manifestations, that is, the study of outbreaks of infectious diseases, their incidence and prevalence in human communities, and with establishing disease patterns and their aggravating factors. To use a simple comparison that should facilitate the task of the reader in understanding where we are headed in the present chapter, the study of infectious diseases until very recent times consisted only of examining the visible part of the iceberg, with the assumption that its nonvisible part was negligible and that the dynamics of the total ice mass did not interact with sea surface winds, marine currents and swells, or sea surface temperatures. This is a sensible attitude, because studying the interactions between, for example, disease spatial distribution and climate variability is already complicated, and necessitates collaboration with at least geographers and climatologists. Indeed, an enormous influx of nationally and internationally funded research resources have been targeted toward promoting sophisticated molecular tools such as genomics, proteomics, and nanotechnology (see many chapters in this volume). Clearly, this is of crucial importance in developing diagnostic tests, vaccines, and therapeutic tools, but what is really being studied is the health and diseases of individuals rather than populations and groups. Likewise, the traditional approach in medical epidemiology and parasitology has been to focus research attention on the understanding of local phenomena, considering that the unit of study is the individual, thus pinpointing the critical importance of sociocultural influences on disease patterns. We are not contesting here that socioeconomical parameters are not important in influencing the distribution and prevalence of disease, but we are arguing that some disease patterns can, in some cases, be attributed to the natural environment, as illustrated by the examples that will follow. Finally, there exists an individual-centered approach on the part of medical epidemiologists, which does not consider the effects of large-scale or global environmental influences; these

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can only be understood through the development of focused, comparative studies. However, the study of the health of human populations lacks a comparative health perspective, whereas major research developments have been made recently in other fields of life science, such as population dynamics and community ecology, that have benefited from such a comparative approach. Recent studies of the impact of global environmental changes on disease population dynamics and their spatial distribution [36,37,55,58] provide several good examples of how large-scale studies are of particular relevance to both wildlife and human epidemiology.

Several decades ago, scientists were still skeptical about the existence of a global environmental crisis; at present, however, they increasingly recognize the consequences of global changes in terrestrial, marine, and freshwater environments in the developed and developing worlds [2,3]. Evidence is also accumulating that global environmental changes may have a strong impact on the health of humans and even wildlife [15,20,34,36,60,77]. The issues involved are numerous [54,58] and highly complex; indeed, many different parameters acting at different spatial and timescales may be intimately interconnected in their effects [4], and these problems constitute a growing challenge not only for scientists and physicians but also for governments, international institutions, and societies [2,3].

Large-scale global environmental hazards to human and wildlife health include climatic change, ozone depletion, loss of biodiversity and ecosystem modifications, changes in hydrological systems and freshwater supplies, land degradation, and stresses occurring within food production systems [4].

In this chapter, we attempt an objective, though not exhaustive, analysis of global environmental changes and their impact upon disease patterns. We will concentrate on parasitic and infectious diseases, also referred to as communicable diseases, including emerging and reemerging diseases; we will not include noncommunicable and noninfectious diseases such as heart disease and hepatocellular carcinoma, for instance. Although primarily meant as a review, this chapter does contain some new information. The analysis of large-scale global environmental hazards in epidemiology requires integrating knowledge of different disciplines, thus necessitating a holistic research approach. The health consequences of global environmental changes are pervasive, and the different causes of the observed health patterns are often intimately interconnected. Clearly, problems of human health (and that of wildlife as well!) are complex, with many factors acting at different spatial and temporal scales. Our ultimate goal here is to convince readers, medical practitioners, research scientists, and even policy makers of the potential usefulness of enlarging the "window" of disciplines and subdisciplines so as to better understand and potentially control diseases. The implications are important for global public health issues, and this perspective should contribute to the design of public health programs in the very near future. As a title for this chapter, we chose to paraphrase that of a now-seminal contribution by Professor John Lawton [47], head of the Natural Environment Research Council (NERC) in the United Kingdom and one of the leading international ecologists, and to adapt it to the present exercise. As already stated above, major contributions have recently been made in macroecology and community ecology by adopting a comparative research approach; this is why our chapter is entitled "Epidemiology in a Changing World: the Need for a Bigger Picture!".

33.2 THE INTERACTIONS BETWEEN HUMAN POPULATIONS AND NATURAL SYSTEMS

Basic ideas and developments in medical epidemiology were developed in a world of "small, local communities," in which research priorities were given to case accounts of infectious diseases affecting human population groups, and their consequences for morbidity and mortality. With the appearance of large-scale global environmental hazards such as those we face today (some of which no doubt existed in the past, but which have been amplified by anthropogenic factors), the basic principles of medical epidemiology are being seriously questioned in light of their effect on local human health. This section is devoted to a brief description of why subjects in medical epidemiology are only rarely considered within a broad perspective, and why modern events such as global warming and other environmental changes due to a stronger human imprint on Earth should induce new ways of thinking in modern epidemiology. This section will end with an exploration of the different global environmental changes that may affect public health in the near future.

33.2.1 Human Psychology and Our Mental Perception of the Environment

Throughout the course of man's intellectual evolution, human societies have constantly been confronted with a range of problem-solving skills primarily based on local observations of natural phenomena. The first human societies were faced with the effects of lightning striking their houses or dreaded diseases; they tended to attribute such events to a local, perceptible mechanism, or else to an extraterrestrial, ideological phenomenon involving the intervention of a god or a spirit. The term "locus" is used in epistemology [35] to describe a scene in which human societies elaborate, in a preliminary state, the core of their societal organization: In other words, a clearing in the forest was the "locus" for Stone Age Celtic populations, and even now for native Amerindian tribal communities; populations were unaware of the role of potential external effects–outside the "locus"–upon their own living conditions. As human populations grew, they were faced with new events, and thus were obliged to take into account this external context for explaining local living conditions. The impacts of man-made global changes is now clearly recognized, as is the fact that such changes have yielded a vast array of problems, including those involving health. However, current trends in human transformation of the planet, including habitat destruction and climatic change, because they take place on

a large spatial scale, are not easily perceptible in modern human psychology. Our mental perception of the environment more efficiently copes with the directly proximal and perceptible causes. It must be recognized that the largest spatial scales–and this also is true for time scales–which cannot be easily evaluated from a locus-orientated perspective, may strongly influence lower hierarchical levels; this is indeed a prerequisite for modern science [57]. At the heart of any solution-oriented program is the need for training and convincing modern societies of the potential impact of global changes taking place at a lower level. In ancient Egypt, at the time of the Pharaohs, the wrath of God was evoked to explain major natural catastrophes. At present, a sudden explosion of locusts in Africa may have a lot to do with climatic variability at a continental or global level.

33.2.2 A Changing World, Changing Human Mentalities, and the Role of Science

Conceptually, much of our mental perception of the environment takes root in the direct connections we observe between cause and effect on a very fine spatial scale. However, the consequences of global changes constitute a reality that we can no longer ignore; we need to readjust our thinking when confronted with complex environmental problems. As already stated, the issues are numerous, of great complexity and often interrelated [1,87].

Human health systems are complex entities characterized by the diversity of their components, dynamic interactions within and between these components, and their relationship with the environment. None of the standard entities usually employed in epidemiology, for example, genes, individuals, communities, are completely separate from the others, and any one of them is embedded in a continuous hierarchy of structural organization (Fig. 33.1). Most epidemiologists would agree that it is not an easy task to use observations at a small, individual level to predict what will happen within a larger ecosystem, or, *vice versa*, or to determine which macro-level process is responsible for micro-level patterns. For instance, in epidemiology, the many problems we face, for example, vaccination and herd immunity, or the role of climate change in disease dynamics, cannot be solved without properly addressing the complexity of host–pathogen interactions, including their global environmental and human dimensions. Modern epidemiology is now confronted with the problem of how to identify the relevant spatiotemporal and organizational scales that might be relevant in explaining disease patterns and processes. A new integrative approach and a theory of up and down environmental scaling, involving both abiotic and biotic phenomena, is needed in epidemiology [33]. Epidemiology today must deal with problems associated with linking processes on very different spatial, temporal, and organizational scales (Fig. 33.1), and with health-related inducers of global environmental change probably representing the forgotten dimension in global health [1,4,33].

One major problem faced by human societies, and by the host planet Earth itself, is that of increasing population

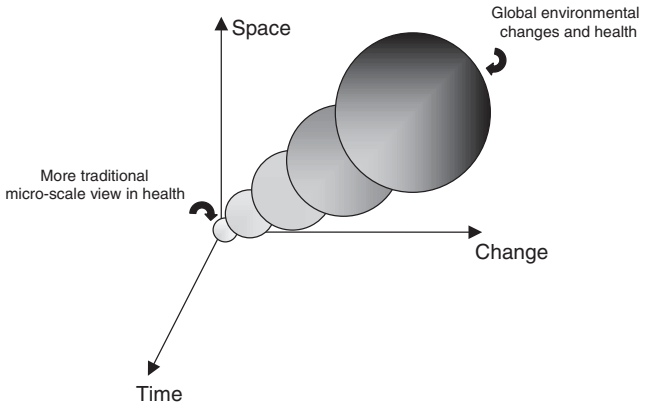

Fig. 33.1. Human (and wildlife) health concerns intervene on a three-dimensional scale, that is, space, time, and change. Because of this hierarchical organization, in any health system, scaling laws must be taken into account for health research and public health strategies.

numbers and expanding human footprints exerted upon the planet. Humanity as a whole has seriously exploded in size, meaning that human consumption requirements will not be fulfilled by the resource capacities of the planet in the very near future. In other words, we are at present in a state of rupture in the global production-ecological capacity of the Earth's equilibrium [1,95]. At the heart of any global health planning policy is the consideration that humanity cannot increase in size as it is currently doing because the global support capacity must not be exceeded. But, how did we arrive at this critical point?

In earlier times, human populations–and this is also true for certain, now rare populations on remote islands and native tribes in the rain forests of Amazonia, Papouasia-New Guinea, and Central Africa–lived in harmony with their natural ecosystem, which was able to meet the community needs (Fig. 33.2a). As human populations exponentially grew in modern times with the appearance of community settlement encroachments in new areas, the impact exerted by human societies on ecosystems (Fig. 33.2b) became greater and greater. Human ecological footprints on the planet, defined as the extent to which human consumption can be supported by local ecological capacity [1,95], has grown in such a manner that there is no comparison in time. Deforestation, habitat fragmentation, land use, and agricultural systems, coastal zone and watershed management, climate change, ecotourism, transportation trade and transcontinental traffic, added to new behavioral practices, have created new conditions for more direct contact between humans, ecological communities and ecosystems (Fig. 33.2c). The emergence of new viruses and bacteria, as recently observed in some human communities [60], is the immediate manifestation of the fact that human and animal disease interactions have become more frequent and human societies are strongly impacting on the ecosystem equilibrium (Fig. 33.2c). The ecological effects exerted by humans may have dramatic consequences that extend throughout a cascade of ecological

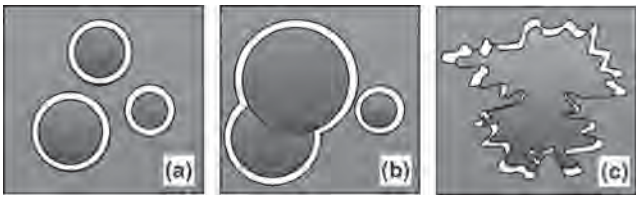

Fig. 33.2. Schematic illustration representing the relationships between human populations and their environment. Grey forms indicate human communities, grey squares natural habitats such as rainforests, and white forms the contact margins between the two domains: (a) ancient human populations, and even some present-day native populations or isolated populations on remote islands, living in harmony with their natural habitats; (b) with the population explosion and new community settlements, the interactions between humans and ecosystems have increased, creating more and more contact areas between the two domains; (c) current situation in which human populations strongly increase in size and natural ecosystems largely interact, as the human footprint on the planet expands.

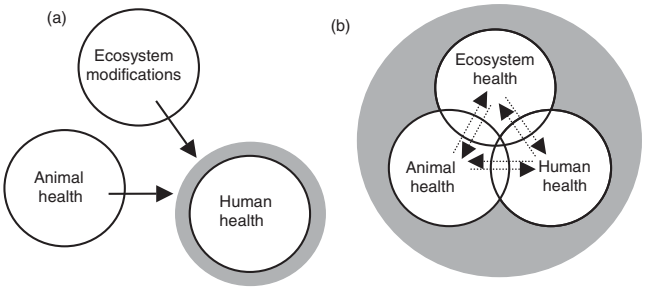

Fig. 33.3. Schematic diagram illustrating: (a) the traditional view, in epidemiology, of the links between human health, ecosystem modifications and animal health; human health problems are seen in a downstream perspective where only the impacts of ecosystem modifications on human health are considered (see arrows); (b) conceptual diagram of possible multiple two-way links between human health, animal health and ecosystem health, in which all the components interact. Conservation medicine as an interdisciplinary field addresses the complex interrelationships between health and ecological concerns. Modified from Ref. [1].

responses. Clearly, these problems raise questions about the scientific and social attitudes required in order to meet the challenge created by such complex issues.

Thus, traditional health concerns have been oriented toward the downstream effects of environmental impact [87], such as those of pollutants or toxic substances upon human health, or habitat modifications upon disease dispersion, notably in occidental industrialized countries. This cultural habit of examining downstream events in medical epidemiology instead of upstream events, for example, understanding the proximate and ultimate causes of disease (re)emergence, needs to be reinterpreted (Fig. 33.3). The true impact exerted by global environmental changes on health should compel medical scientists to rethink several basic assumptions, and notably that of the "bottom-up" approach as a single research perspective in the search for more general proximate causes for observed morbidity and mortality in local communities.

Looking to the future, a key goal is to move from a consequence-oriented method to an "ecological-context-of-health" framework (Fig. 33.3), in which we would take into consideration the multiple two-way interactions between pathogens and disease, and between the many host, vector, reservoir, and microbe species that may be involved within ecosystems [32].

This requires a better integration of knowledge of different disciplines and subdisciplines in order to elucidate complex relationships between health and the environment. This intellectual trend is referred to as *Conservation Medicine* [1]. A move in this direction clearly requires an interaction on the part of medical science and related disciplines. The plethora of findings described below clearly suggest the need for extending health questions to other disciplines such as climatology, oceanography, physics and mathematics, population biology and genetics, or community ecology, for instance.

Finally, as already discussed in previous sections, the many problems we are facing today, for example, climate change and disease dynamics (see examples hereafter), cannot be solved without properly addressing the complexity of host–pathogens interactions, including the appropriate scaling law level of resolution at which specific processes may happen. Interestingly, recent studies on the impacts of global environmental changes on disease population dynamics and their spatial distribution [20,34,60,77] have provided good examples of how large-scale studies are of particular relevance in coping with human health problems. In order to deal with large-scale patterns and processes, comparisons between data and model outputs are required in order that a "bigger picture," to use the terminology of Lawton [47], may emerge. Although major research developments have come about recently in other fields of life sciences such as population dynamics, community ecology, and macroecology [7,57,80], largely due to the use of comparative research perspectives, epidemiology continues to suffer from the absence of comparative studies, because of the individually focused-research dimension given to health problems. We must go beyond local details upon which traditional health investigations have usually focused, and search for more general and rigorous disease patterns [6,79], thus providing a consistent framework upon which to build a true predictive discipline (see Fig. 33.4).

As recent understanding of some infectious disease patterns such as environmentally persistent, zoonotic and vector-borne diseases, have clearly shown the impact of large-scale climate variability on the geographic spread of these infections [39,60,77,78], medical epidemiology clearly needs to go one step further in developing comparisons between local data (Fig. 33.4). Recent investigations into childhood diseases have also provided clear evidence of how large-scale studies on a nationwide or global scale are of particular relevance for public health concerns in the characterization of the many processes involved in disease behavior (from Refs. [6,79], see also Chapter 12 in this volume).

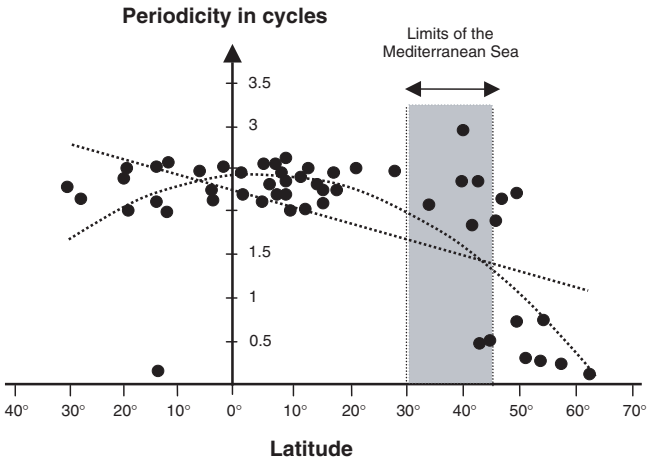

Fig. 33.4. The comparative approach based on comparison of independent data sets at lower scale, for example, time series for cholera at a nationwide scale, is a way to characterize disease patterning at larger scale. Data show the evolution of cholera population time series dynamics in terms of shape of dynamics, that is, highly regular and periodic to erratic. Dots synthesize the form of the disease population dynamics on a double-axis gradient: On the *x* axis is the position in latitude, at which the disease cases come from; on the *y* axis is an index value with estimates near 2 representative of cyclic population dynamics of cholera, and near 0 of highly erratic dynamics. The figure shows that the evolution of cholera population dynamics from southern Africa to northern Europe shows cyclic fluctuations in tropical and subtropical areas of Africa, and when moving toward southern and northern Europe disease cases are rare to extremely rare. Population dynamics of cholera cases is transient in the Mediterranean basin (see grey rectangle), with epidemics of cholera more or less regular on the seashores of northern African countries (data from Guégan and Constantin de Magny). Another illustration of the comparative approach in epidemiology is given by Broutin et al. [6]).

From traditional investigations focusing on very small-scale case studies in medicine, there is a growing scientific tendency, under the impetus of population biologists, to go one step beyond the idiosyncratic details at a lower local scale and to move to a broader perspective of epidemiological systems in order that only the important disease generalities or patterns remain [6]. Because medical epidemiologists primarily focused their research investigations on local qualitative details in explaining disease patterns, they did not consider, or else totally neglected, the importance of large-scale processes, arguing that comparison across localities was impossible due to data heterogeneities. On the contrary, the main focus of comparative analysis is to compare data acquired at a lower spatial scale–and thus not to decide *a priori* that comparison is totally impossible–and to consider that emerging patterns may exist at a larger scale encompassing the total dataset under study. The basic idea in comparative analysis in epidemiology is to describe the different spatiotemporal patterns that may be at work at the different hierarchical scales under scrutiny and then to explore the corresponding processes responsible for the observed patterns. Comparative analysis is thus a promising approach to public health concerns in infectious disease population dynamics, in that it offers a much broader perspective on health and a more quantitative approach to predicting and controlling disease evolution.

33.2.3 Global Environmental Changes: New Health Threats for the Foreseeable Future

Medical doctors, researchers, policy makers, and the general public are relatively unfamiliar with the nature of global environmental changes and with the very complex links that may exist between these global changes and human well-being and health.

Global environmental changes refer to planetary-scale, largely human-induced alterations that affect the environmental capital of the planet to support life, and which modify the structure, composition, or function of large-scale biophysical and ecological systems [1,55,58]. They are by-products functions of an unprecedented situation in which the overall population size of the planet is dramatically increasing at an unprecedented rate, and in which economic activities and technological choices are beginning to considerably modify aspects of the planet (see above). Global human-induced environmental changes may be either those environmental changes that impact on global process, for example, the aggregation of greenhouse gases, which amplify the worldwide greenhouse effect, or widespread local changes, for example, ecosystem modifications or desertification, which by accumulation on a large scale, may modify ecosystem functioning. What is common between all these human-induced environmental changes is their "global" dimension and the uncertainty as to their possible consequences for human societies, as their existence is new. They differ as such from localized toxicological and microbiological environmental hazards, the consequences of which never cross the upper scales.

Global climate change is undoubtedly the most well-known pattern of global environmental change, but other types of global changes exist that pose serious problems for the future of our planet's life. The main types of global environmental changes induced by humans are (i) changes in the atmospheric composition with stratospheric ozone depletion and greenhouse gas accumulation, (ii) biodiversity loss and changes (e.g., biological invasion and extinction), (iii) disruption of elemental cycles, for example, nitrogen, sulfur, and phosphorus, (iv) changes in the hydrological cycles and depletion of freshwater supplies, (v) changes in food-producing ecosystems (e.g., land cover, soil fertility, coastal, and marine ecosystem stocks), (vi) global dissemination of persistent organic pollutants, (vii), urbanization, and (viii) desertification [1,55,58,87].

As we have already stated, the health of human communities is strongly influenced by large-scale conditions from beyond the boundaries of those communities' living space, that is, the locus. Consequences of global environmental changes on health may be complex because many different effects may interact with each other and with lower scale changes that make their understanding and prediction highly

difficult. Although more and more researchers are currently working on global human-induced changes in health, this domain is quite new. Modern-day environmental threats and the risks they may induce in human societies should thus stimulate more research initiatives so as to provide new skills, new tools, and new vision of global health.

33.3 DYNAMIC PROPERTIES OF MICROBES, THEIR HOSTS AND THE ENVIRONMENT

There exist many diseases and disorders that are environment-dependent; we can here cite the heat-wave-related mortality that occurred in France in the Summer of 2003, or the numerous parasitic and infectious diseases that have increased, or will increase, in prevalence, incidence, and geographical range distribution. In this chapter, we will focus only on communicable diseases, but the readers may refer to [4,52,55,58] for further details on noncommunicable diseases. They will also find more information on the effects of global environmental changes upon health and human well-being at the World Health Organization website at http://www.who.int/globalchange/en/.

But, how can global environmental changes affect human health? Even though the connection between natural history and medicine is generally accepted–at least in recent textbooks–this paragraph is devoted to a general presentation of the linkages that really exist between ecological processes on Earth and health. We will begin this section by describing the broad ecological context of infectious diseases. Then, we will explore the many two-way interactions that truly exist between ecological processes, microorganisms, and health. We will conclude this section by discussing the emerging field of *Conservation Medicine*, which brings together environmental sciences and the many disciplines of health.

33.3.1 The Ecological Context of Infectious Diseases: The Three-Piece Puzzle

Although much has been learned about parasitic and infectious diseases, their potential natural hosts, reservoirs and vectors, and their interactions with the environment, many questions remain. An ecological perspective in health science will reveal that we are still ignorant of the complexity of interactions such as those of food chains, and the diversity of microorganisms that truly exist on Earth, some of them being potential human pathogens [32,91].

A recent outbreak of a very rare zoonosis attributed to the monkeypox virus (MPV) in the Spring of 2003 in the central United States, which caused an illness clinically indistinguishable from smallpox, made the headlines [16]. Sporadic cases of monkeypox virus had been previously reported in human individuals only from the rainforest areas of central and western Africa, where the main reservoirs (throughout primary origin remains unknown) are squirrels (*Funisciurus* and *Heliosciurus* genera), Gambian giant rats (*Cricetomys* genus), and certain species of monkeys. This outbreak had never been recorded in the northern hemisphere before and was occasioned by the international shipment of small African mammals from Ghana to Texas, thereby constituting the source of disease introduction. From the six different categories of rodents introduced in the United States for pet distribution, at least one Gambian giant rat, two squirrels, and three dormices (*Graphiurus* genus) were identified by medical authorities to be infected by monkeypoxvirus. Native prairie dogs (*Cynomus* genus) co-housed with Gambian giant rats in pet shops were contaminated. Fortunately, none of the human cases identified in the United States resulted in death, and most of the patients did not fall seriously ill [16]. The establishment of a new zoonotic disease in the United States was avoided. Because its initial clinical features are indistinguishable from those of smallpox, a dreadful mutilating, and even killer agent for humans before its eradication in the 1970s, lessons were learned from the latter. Recently, Smith and collaborators, using an impressive dataset of information on human infectious diseases, have demonstrated that disease categories that are limited by the export of their host species between nations and continents, that is, multi-reservoir and zoonotic infectious diseases, are most likely to emerge in entirely new regions of the world [83]. This is particularly alarming in the face of increased rates of exotic species introductions, notably in developed countries (see Section 33.4.6).

The relationships between microorganisms or parasites, their hosts and the environmental conditions, both physical and biological, under which all these components interact, have developed throughout a long history of community coevolution [97]. As explained by community ecology and population dynamics, local animal communities–and within them the important components known as microorganisms–are constantly exchanging fluxes of energy and materials with the surroundings [32,71,92]. Local communities, and thus pathogens within them, are ultimately dependent upon a balance between the rates of migration and extinction throughout ecological times. This necessitates a consideration of balance in nature as a starting point of discussion on infectious disease dynamics in space and time (Fig. 33.5).

As illustrated in Figure 33.5, the conventional statical view of health is now replaced by a more complex, dynamic three-piece puzzle in which the component parts, that is, the host, the agent and the environment, abiotic or biotic, strongly interact with each other and where multiway interactions, feedbacks and loops may intervene in disease behavior in time and space. As such infectious diseases cannot be viewed as a separate, independent entity apart from the whole ecosystem–the conventional downstream approach to health–but rather, need to be considered as a piece of a more complicated puzzle in which all components are extensively interdependent on each other; in other words, any effect on one subset may potentially lead to consequences for the others [97]. Because of the reality of this diversity of interactions and other linkages between the agent, the host and the environment, health problems, at least when it concerns communicable diseases, have much to do with complexity, rather than

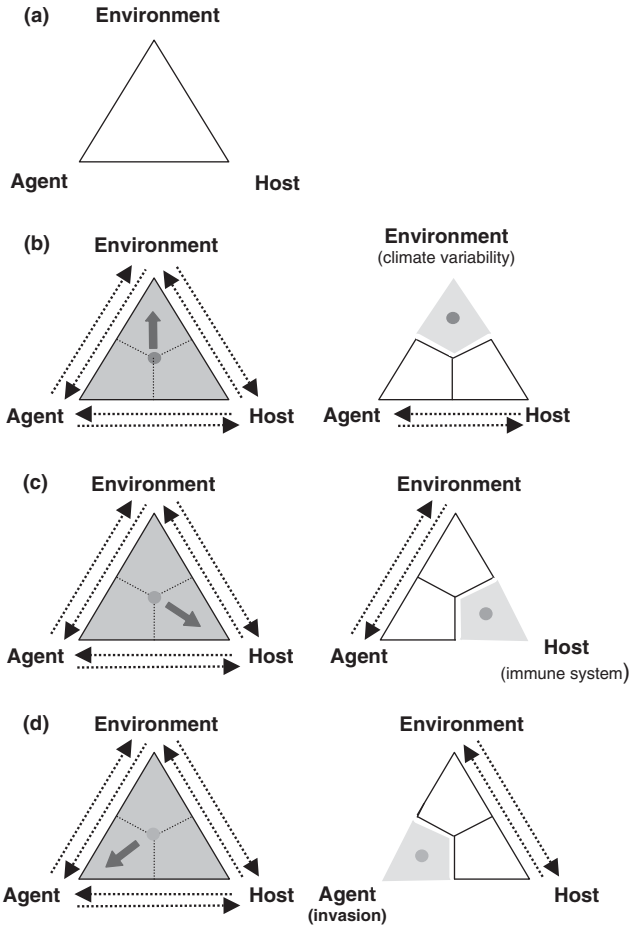

Fig. 33.5. Schematic representation of the infectious disease triad of agent, host, and the environment: (a) classic, static representation of the three-pieces triangle; (b)–(d) dynamic illustrations of the three-pieces triangle which considers two-way multiple interactions between components of the triad (on the left); dots illustrate a given disease, and the arrows the major force explaining disease patterns. On the right side of the figure: (b) case where the environment, for example, climate change, is important for explaining disease patterns such as for many vector-borne diseases; (c) case where host biological conditions, for example, immune properties, are preponderant, for example, HIV spread; (d) case where intrinsic factors of the etiological agent are important in disease dispersion such as for influenza virus. Modified from Ref. [97].

being simple cause-and-effect relationships. One pertinent example of such complexity is the demonstration of how the interplay between environmental forces and ecological responses may mould the population dynamics of disease. A cogent illustration is that of the cholera epidemic resurgence in certain populations, which clearly shows the existence of cyclic fluctuations in disease case numbers (Fig. 33.6).

One important question is whether cholera outbreaks in human populations are simply the acquisition, by specific bacteria strains, of virulence genes, that is, genes for the phage-encoded cholera toxin and the toxin-regulated pilus factor [21], responsible for better transmission dynamics,

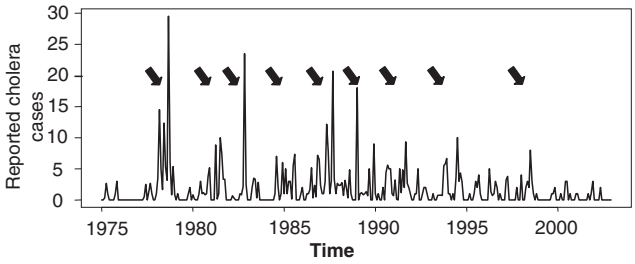

Fig. 33.6. Evolution of the number of reported cholera cases (monthly data) declared to the World Health Organization by national health authorities of Singapore as a function of time (1975–2002). Cholera population dynamics shows somewhat seasonal patterns of epidemic resurgences and interannual largest epidemics each 5–7 years (see black arrows). From de Magny and Guégan' compiled data.

which clearly represents a fine-scale, direct cause-and-effect approach on health, or whether they are due to a complexity of factors involved at different time and spatial scales that determine disease reemergence, which in fact constitutes a holistic perspective on health [11]. Studying disease from the unique small-scale molecular perspective seems incomplete, because it does not totally explain why recurrent epidemic waves occur in time (but see Ref. [22]).

First, the variation in fraction of susceptible individuals in the population over time as the result of immunity acquired by previous infection, and by the input of births and migrants into the pool of susceptible hosts, may result in that the population dynamics of cholera fever intrinsically oscillates and creates annual to biennial epidemic outbreaks. But, in addition, when strong couplings between climate and transmission occur like during *El Niño* events, a second outbreak is then observed each 5–7 years like in Bangladesh [67]. There is considerable evidence by now linking cholera outbreaks to climate [11,68,69,84], yet mechanisms explaining this coupling are not well understood [67]. Temperature, rainfall, and plankton blooms among others have been proposed to explain the seasonal nature of cholera. Magny and collaborators have recently provided a mathematical model for cholera population dynamics in human communities that incorporates the seasonal dynamics of phytoplankton blooms–a potential reservoir for bacteria–and *Vibrio* concentration in aquatic environments [53]. The readers will find an excellent report from a scientific committee by the US National Academy of Science on the impacts of climate and weather on infectious disease at http://www.nap.edu/catalog/10025.html.

Obviously, other environmental parameters are important in the emergence, incidence, and intensity of cholera outbreaks. Studies have shown that avirulent environmental strains of the *Vibrio cholerae* bacteria are maintained within the ecosystem, and may be associated with phyto- and zooplankton organisms, algae, crustaceans, and fish [12,41–44,56,82,90]. Thus, the ecology and transmission

biology of *Vibrio* forms are twofold: (i) probably many environmental avirulent forms live in natural ecosystems, but there is limited understanding of their exact life cycle; and (ii) certain particularly virulent strains are selected to invade human populations. The second phase, that is, transmission from person-to-person, which in fact represents an evolutionary "dead end" for the bacteria, is familiar to the public, and it is generally that which is studied by medical epidemiologists, and it forms what we have called the emerging part of a larger iceberg. In reality, what is currently poorly understood, that is, the environmental phase, should in a very near future prove to be the cornerstone for a better understanding of bacterial evolution, for example, genetic polymorphism, gene transfer, and strain adaptation to specific contexts. Recent findings [22,23] have clearly shown that bacterial viruses in both the environment and the intestine of cholera patients might strongly influence cholera cases seasonality in that *in vivo* bacteriophage amplification in infected individuals and hence bacteriophage predation on environmental *V. cholerae* during the cholera epidemic yielded the collapse of the disease. These data suggest that bacteriophages in the aquatic environment are an additional factor that causes disease population dynamics in human. However, it seems also likely that specific climatic conditions may lead to the explosion of bacteriophages in aquatic environments that may cause changes in the abundance of *V. cholerae* bacteria, a phenomenon recently observed for gastrointestinal nematodes of red grouses [8]. The incidence of cholera is also affected by many other factors like sanitation and level of poverty, public health services, population demography, land use changes and urbanization, and travel exchanges, for example, the pilgrimage to Mecca, and these are commonly invoked to explain cholera outbreaks and dissemination within populations (see Chapter 37 in this volume). Thus, the assembly of the different extrinsic and intrinsic factors into a perspective–in a multiple pathway diagram with both direct and indirect connections between the many parameters involved on different spatiotemporal scales–should be a prerequisite for better capturing the complex web of causation that shapes cholera epidemic resurgence over time. This leads us directly to the next section on the linkages between ecosystem dynamics and infectious diseases.

33.3.2 Ecosystem Dynamics and Health, or the Snowball Syndrome

Any new outbreak in a population usually generates much public and media speculation on the possible causes underlying such phenomena. The avian flu outbreak in Asia between late 2003 and the beginning of 2004 is informative in that wild birds, particularly waterbirds, have been blamed for the serious spread of the disease in Asia, whereas poultry ducks are considered to have played a central role in the generation and maintenance of the flu virus [49]. Policy authorities in Thailand even got to the point of ordering a cull of openbill storks, a long-distance migratory bird species, although this decision was then called off. Confronted with panic, the Food and Agriculture Organization (FAO), the animal health service of the United Nations, urged Asian public authorities not to cull wild birds, because there was no direct evidence that they were responsible for disease spread between the different outbreaks, and "wild birds are an important element of the ecosystem and should not be destroyed" (see FAO news at http://www.fao.org/newsroom/en/news/2004/48287/index.html). Although it is entirely natural to search for the more plausible factors involved in these issues, it should be emphasized that a complex web of causative factors with multiple interactions and environmental forcing may intervene, and thus the political decision making openbill storks the scapegoats was unwarranted!

The relationships between ecosystem dynamics and infectious disease are obviously, highly complex in the patterns and processes involved, and totally underestimated or poorly understood because of the lack of research studies that could help to disentangle this natural biological complexity [15]. In addition, the links between ecosystems, communities, and health are often strongly dependent on local factors, for example, local conditions, which predispose the spread of an emerging zoonotic disease to human communities, whereas these links are more vague on larger spatial scales, for example, the aggregation of deforestation surface areas, which might amplify the risk of new infectious diseases emergence–but all this needs to be formally demonstrated. Changing ecosystems, that is, due to modifications, instabilities or perturbations, induced or not by climate change, land use changes and stress, loss of biodiversity, species dislocation and alien invasion, may have strong connections with public health problems in that any effect on the planet's ecosystems could have repercussions, in a cascade-and-effect scenario, upon human beings [9]. This is what we call here the "snowball" syndrome, in which tiny local effects may produce bigger problems on a larger scale.

One of the best-documented illustrations on the link between ecosystem dynamics, community, and health issues is Lyme disease [65,66]. Lyme disease is a tick-borne disease caused by the spirochete bacteria, *Borrelia burgdorferi*, and it most often presents with a "bull's-eye" rash and erythema, accompanied by nonspecific symptoms such as fever, malaise, fatigue, headache, muscle and joint aches. Lyme disease is considered to be an emerging disease in western countries. In the United States, where the spatial dynamics of Lyme disease has been investigated [65,66], it was shown that the risk of disease transmission strongly depends on local vertebrate-species diversity. In habitat patches with high vertebrate-species richness, many vertebrate species may be bitten by infected ticks (from the *Ixodes* scapularis species), feeding from a wide variety of mammalian, avian, and even reptilian host species. However, all these potential hosts strongly differ in their probability of infecting a feeding larval tick. In eastern North America, the white-footed mouse is highly efficient at infecting feeding mites, but other species are poorly capable of, or totally incompetent at, transmitting the bacteria to feeding tick larvae, thus impeding or interrupting the disease life cycle [66]. High-order vertebrate-species diversity effectively

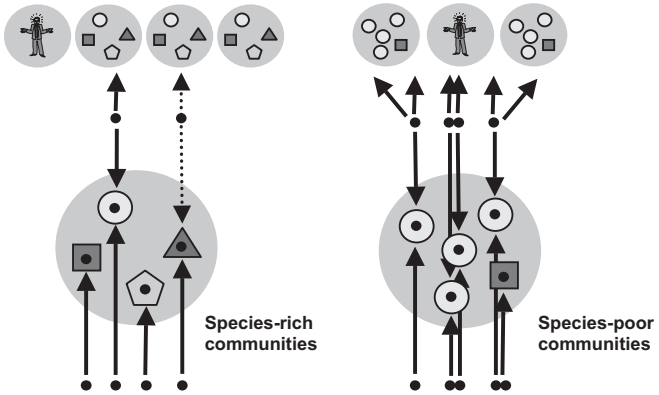

Fig. 33.7. Schematic representation of the ecology and epidemiology of transmission of Lyme vector-borne disease. On the left, in local species-rich communities of vertebrate hosts, potential host reservoirs do not transmit the bacterial agent with the same probability. Some host species (green disk) are more efficient at transmitting the disease to biting ticks, whereas others are poorly able to do so (red triangle and dashed arrows) or unable to do so (blue square and yellow hexagon). On the right, in local species-poor communities, where a more efficient host reservoir occurs (green disks) the disease is transmitted at a higher rate to feeding tick larvae, and thus the probability of human contamination is higher. Ostfeld and Keesing [65,66] have called this ecological phenomenon a "buffering effect" conferred by biological diversity, which tends to dilute the disease agent. See color plates.

locally dilutes the disease agent, and risk of disease transmission to humans is thus less likely (see Fig. 33.7).

Richard S. Ostfeld and Felicia Keesing [65,66] have referred to the potentiality that biological diversity may exert on infectious disease transmission as a "buffering effect" conferred by effectively diluting large fluxes of disease germs into poor or nonefficient hosts vertebrates. A by-product of this within-local-community disease agent dilution is that it is less likely, in terms of probability, for an infected tick to transmit the Lyme disease to humans (Fig. 33.7). On the contrary, when local communities are species-poor and a more efficient host reservoir comes into being, larger fluxes of disease agents are generated, which increases the risk of disease contamination to humans (Fig. 33.7). Another complementary but not exclusive explanation proposed by these authors is that competitors and/or predators of the main Lyme disease reservoir keep local mice populations low, thus reducing the risk of disease transmission. Ostfeld and Keesing [65,66] have opened up a new and fascinating avenue of research on the role exerted by biological diversity, community composition, and wealth on infectious disease ecology and epidemiology. Based on basic knowledge, we thus suspect that many other infectious diseases (around 63% of current human infectious diseases are zoonotic), and animal diseases as well, might be driven to some extent by the same ecosystem dynamics rules, suggesting that practitioners, policy makers, and the public should more carefully evaluate interconnections between ecosystem, biodiversity and health concerns in coming years [15,48,72,73,88].

Humanity is degrading Earth's ecosystems at an incomparable rate, disrupting their functioning while human populations continue to live at the expense of a number of ecosystem services: nutrient recycling on land and in the oceans, detoxification of many dangerous substances, air purification, fossil energy production, or food production [48,72,73,88]. Both ecosystem functioning and biological diversity are cornerstones of the Earth's magnificent architecture, and it is up to humans to find their exact place in this system.

33.3.3 The Emergence of Conservation Medicine

The many aspects of research on ecosystem health and human health discussed above, in which our safety and wealth strongly depend on the ecosystem and on community health as a whole have helped to define a current of thinking now known as "*Conservation Medicine*" (see website at http://www.conservationmedicine.com/), the main goals of which are (i) a better understanding on the many inextricable interrelationships that may exist between human health, animal health and ecosystem functioning and dynamics; and (ii) the promotion of such thinking in different arenas such as those of policymakers, economists and the public [1]. The many examples that we have chosen to show below are representative of this promising field. The reader will also find more details on *Conservation Medicine* in excellent books by Aguirre and collaborators [1] and Lebel [48], (see also http://www.idrc.ca/ecohealth). A free online French version of Lebel's book is available at http://web.idrc.ca/en/ev-32399-201-1-DO_TOPIC.html. Previous important publications by the *Consortium of Conservation Medicine* include contributions to two books on conservation biology [88] and world sustainability [72], respectively.

33.4 THE ECOLOGY OF INFECTIOUS DISEASES IN PRACTICE

Although medical epidemiology has focused on the socioeconomic determinants of disease patterns, we still have a very limited quantitative picture of the geographic distribution of the main disease agents in human populations throughout the Earth [45]. To what extent are they climate-dependent, and how many of them are there? What are the quantitative linkages between organism biodiversity and human pathogens? What are the main drivers of disease emergence or reemergence and dispersion, excluding the generally invoked socioeconomical drivers? Are socioeconomy and modernization really important in explaining disease spread, and for which diseases are they pertinent? Recently, McMichael [59] has provided some examples of emerging infectious diseases considered under major categories of environmental and socioeconomical influences, and we recommend the reader to refer to this contribution. The following sections deal with how to disentangle the complexity of the many interrelationships that truly exist between ecosystem

functioning and its impacts on health. Examples may come from the general published literature or they may be new illustrations from personal findings by the authors of this chapter.

33.4.1 What Came First: Biology or Socioeconomy?

As the roots of current epidemiology are strongly embedded in the socioeconomic development of western countries [45], what we call "mimetic epidemiology," epidemiologists have primarily focused their research efforts on the importance of modern conditions, for example, sanitation, urbanization, and economic activities, in infectious disease patterns. Two questions tend to dominate the traditional approach by the epidemiologist to disease study: where? And, why there? Determining the "where" has led to considerable work in observing, identifying, and depicting qualitative patterns of disease spatial distribution. Understanding the "why" focuses on the importance of social and technological organization and rapid environmental changes–the so-called economically based approach –as major processes influencing infectious disease distribution and occurrence. Very few studies have attempted to study in a thorough manner the spatial distribution of the many pathogen species in humans as a group, and to analyze the factors affecting their geographical ranges. The most important developments in modern epidemiology involve the search for epidemiological–ecological patterns, regularities and order in space, and then explaining these observed patterns by the many abiotic and biotic processes, which are interactive and which operate differentially in space and time, generating, modifying, replacing, and eventually destroying such patterns.

Recent statistical insights into the spatial distribution of infectious and parasitic diseases in humans on a large scale have enabled robust predictions of the different mechanisms responsible for the observed patterns. Using extensive datasets on up to 332 different human pathogens throughout the world, Vanina Guernier and co-workers [34] have shown that, after correcting for covariates, they still observe that species richness in human pathogens is strongly correlated with latitude and, in general, human communities in intertropical areas harbor greater pathogenic diversity than human populations living in subtemperate conditions (Fig. 33.8). In other words, the species richness of human pathogens follows the same pattern seen

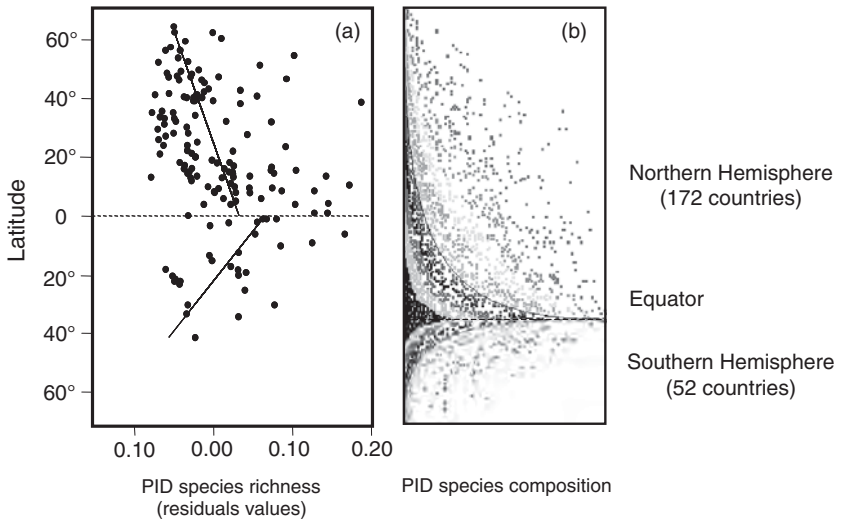

Fig. 33.8. (a) Evolution of parasitic and infectious disease (PID) species richness with latitude across the two northern and southern hemispheres. Dotted lines express the negative relationships between total species richness in human etiologic agents, after correcting for the effects of confounding factors on richness estimates, and the degree of latitude for the two hemispheres. (b) Presence/absence matrix for the 332 distinct PID species across the two hemispheres. The spatial distribution of PID species based on real data was run using a statistically rigorous method for model selection, that is, Monte-Carlo randomized permutations. The presence/absence matrix provides distributional information about which species occurs at each site (recorded by a point), and which does not. Figure (b) indicates that PID species diversity decreases as we move northward or southward from the equator, with pathogen species present in any human community living in a temperate area tending also to be present in richer intertropical human populations. Based on this test, the actual spatial distribution of human pathogens on Earth shows a clear nested pattern where some pathogens are restricted to the tropics, whereas others, more ubiquitous, are widely and regularly distributed throughout human populations. Such a distribution pattern provides information on the processes that are involved in generating the current geographical distribution and spatial range of human diseases. From Ref. [34]. See color plates.

in other free-living organism species [10,38,40]. But, to what extent, this geographical pattern might be the rule or the exception for such microbial human disease diversity? Many epidemiologists have treated this human pathogen diversity as a black box with no spatial structure, but it clearly appears that a large part of human microbes are not randomly distributed, notably those that are involved with multireservoir and zoonotic infectious diseases, and which strongly depend on the presence of their obligate hosts and/or reservoirs. One group of pathogens is obviously not conform to the general trend of spatial distribution observed, that is directly transmitted diseases specific to humans, which may quickly spread throughout the Earth with the potential to impact millions of people, and so which exhibits a high degree of homogenization. Many diseases like whooping cough and measles (see Chapter 12 in this volume) have made extraordinary evolutionary adjustments to coexist with humans over thousands and thousands of years, having originated in wildlife and then domesticated animals. Such diseases that have been around for a long time have extended progressively following humankind on its travels, migrations, and colonizations all around the world.

Clearly, many factors, often interacting with each other, can influence the actual spatial distribution and range of human pathogens. Thus, what is the relative importance of biological and socioeconomical factors? For human diseases, the causal geographical configuration seems obvious in that a large part of human pathogens originally comes from wildlife animals, a category that will continue to produce new infectious diseases particularly in the tropics where the biological diversity is the highest. The underlying initiating event of host switching from the "environment" as the source may then be amplified by some human social practices, human migration, continental and intercontinental exchanges that are circumstances that may facilitate the diffusion of microbes. However, it is difficult to attribute clear-cut impacts to one specific driver as recent emergence of new infectious diseases such as HIV, Lyme disease, and West Nile virus are due to human migration into new environments, specific cultural human behaviors or land modification as well [59]. Figure 33.8 gives an idea of the actual spatial distribution of human microbes in the world with most of species concentrated in the tropics thus in conformity with a common biogeographic rule [33], but the globalization of air travel and economic trades, global climate change, or land use and habitat modifications will accelerate the rate of human pathogens globally. The picture as illustrated in Figure 33.8 could be then progressively replaced by a new "global" picture where most of microbes are everywhere [59].

What the study by Guernier and collaborators [34] adds to our understanding of human disease biogeography is the knowledge that, quantitatively, their actual spatial distribution ranges, with the exception of the group of directly transmitted diseases specific to humans, strongly depends on climatic conditions. Again, this pattern is due to the strong associations that exist between indirectly transmitted pathogens such as dengue virus and the *Plasmodium* protozoan, or viruses causing viral hemorrhagic fevers, their vector or reservoir hosts, and habitat conditions. Undoubtedly, many human diseases are associated with environmental climatic conditions, and we might then ask how they will respond to the plausible range of global climate change over the coming five decades. This is exactly what the next section will deal with.

33.4.2 Enhanced Global Warming and the Spread of Infectious Diseases

The ecology of infectious diseases, and notably the manner in which hosts, vectors or reservoirs, and parasites interact with each other and their natural environment, represents a cornerstone in controlling disease, as global climate change could have far reaching effects on global patterns of disease distribution, with vectors, reservoirs and diseases once relegated to the tropics migrating to temperate zones. What Guernier et al.'s study tells us [34] that the influence of annual precipitation range and, to a lesser extent, of monthly temperature range is much more crucial than temperature and humidity *per se* in the occurrence and spatial range of numerous human parasitic and infectious disease agents. Examples of infectious diseases in plants and animals that have expanded their frequency and geographical ranges over recent years in response to partial global climate change have now been documented [37]. Indeed, one of the most convincing demonstrations of how recent climate change may intervene in health concerns lies in the incidence and frequency of cholera outbreaks in human communities in Bangladesh [76].

When analyzing historical data on cholera prevalence in Dhaka (Bangladesh), and *via* the use of sophisticated statistical procedures, Rodó and his colleagues [76] found a strong association between the *El Niño*/Southern Oscillation Index (SOI), a measure of ENSO, and the temporal dynamics of cholera. This signature was highly visible for the period between 1980 and 2001, corresponding to the well-documented Pacific basin shift of 1976. This signal was not visible or was too poorly pronounced to be detected for the period between 1893 and 1940 for which data were available. Figure 33.9 captures this tendency, during the more recent interval of time, of cholera population dynamics to oscillate with the SOI index, with strong correspondence of maxima of cholera to minima of SOI. From 1980 to 2001, a quasi-quadriennal cycle (a period of between 4 and 5 years) of more severe cholera outbreaks in Dhaka human communities was observed, and can be interpreted as being the result of a more prominent role of climate forcing by ENSO in cholera population dynamics during the last two to three decades. The consequences of climate change in terms of infectious diseases of both humans and animals (this is also true for plants!) are only now beginning to be evaluated and foreseen. The work by Rodó and his collaborators [76] is probably one of the first epidemiological contributions providing quantitative evidence of the impact of climatic change upon the interannual variability of an infectious disease (see also Ref.

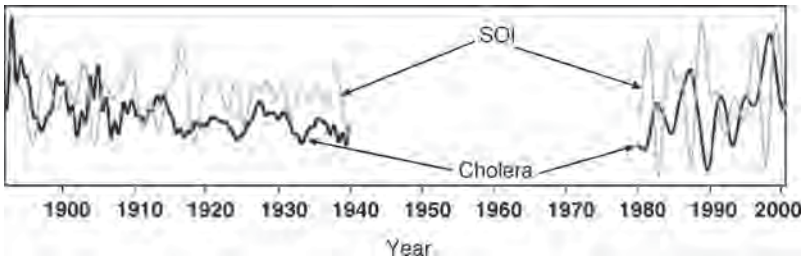

Fig. 33.9. Relationship between the Southern Oscillation Index (SOI) and cholera cases in Dhaka (Bangladesh). Data time series as illustrated in the figure are from the reconstruction of principal components based on original SOI and cholera cases in order to remove seasonal variation and isolate the dominant interannual variation in dynamics (see Ref. [76] for further details) [© *PNAS* (2002)].

[84]). The reader will find further details on statistical and mathematical techniques in Chapter 22 in this volume.

Interestingly, one study has gone a step beyond in the demonstration of an association between global climate change and disease. Viboud and colleagues found an association between the mortality and morbidity impact of influenza epidemics in France and ENSO oscillations for two independent influenza datasets over the period 1971–2002 [94]. The mortality impact of influenza in France was significantly higher during the 10 winter seasons with cold ENSO conditions than during the 16 winter periods with warmer conditions (Fig. 33.10). Another previous work also evidenced an important association between ENSO and hospitalization cases for influenza and viral pneumonia in Sacramento, California [18].

Although no biological mechanisms have yet been characterized to explain the influence of climate variability on both influenza dynamics and the amplitude of outbreaks in terms of number of cases affected by the disease, the authors argued that environmental conditions caused by global climate change might interfere with the emergence and spread of new epidemic flu virus variants, making them better adapted to surviving and propagating under prevailing conditions. Another important, nonmutually exclusive, group of arguments infer that local conditions associated with lower temperature and higher humidity rate, as observed during strong cold ENSO phases in Europe, might affect human body conditions, rendering them more prone to acquiring the disease, that is, *via* immunosuppression or individual behaviors, with more indoor crowding, thus facilitating flu transmission between individuals and across groups of people. There is at present no clear evidence for the existence of an evolutionary scenario of flu virus adaptation driven by environmental or climatic conditions. Some evidence suggests that rapid patterns of evolutionary change in viral antigen properties may be driven by intense selection from the host immune system itself, that is, antigenic drift [17], and the intervention of short-lived immunity that would act as a density-dependent constraint upon overall infection incidence [24], thus giving no or very little support today to the hypothesis of climate-driven selection in influenza virus diversity. However, a more complete explanation of differences between influenza virus variants in the future should also provide insight into whether climatic variability on a wide scale influences the survival of dominant flu virus variants.

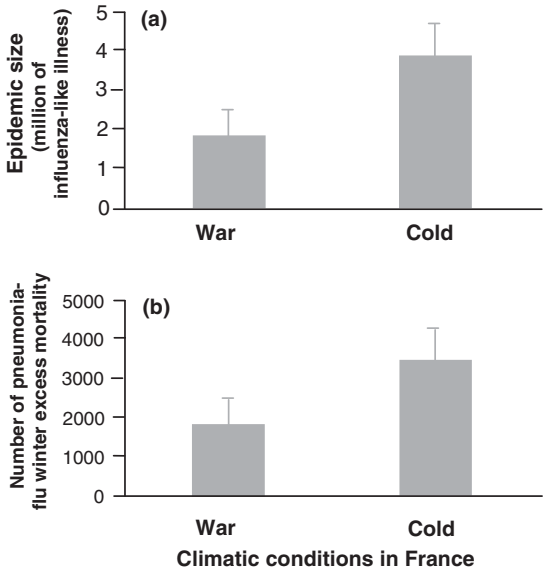

Fig. 33.10. Relationships between influenza-like syndrome morbidity (a) and mortality (b), and climatic conditions during cold and warm seasons in France. (a) Winter epidemic size average values and standard errors for 1984–2002. (b) Winter excess mortality due to pneumonia and influenza average values and standard errors for 1971–1997 (redrawn with permission from Viboud et al. [94]).

Man has long been aware of the fact that climatic conditions affect diseases, and there is much evidence for associations between climatic conditions and infectious diseases. As climate also has an effect upon host and parasite body physiology, host and microbe life cycles, their habitat, and numerous other environmental parameters, the unprecedented rise in temperature underscores the urgent need for developing appropriate research in order to understand adaptations occurring within the microbial world, and for predicting responses in the face of such anthropogenically induced changes. The reader will find further information in national and international reports (from Refs. [2,3,46], and the numerous references cited above), and a very recent book [63] on global environmental change and health/ecosystems issues.

33.4.3 Ecosystem Changes and Health

There exist many documented cases of infectious and parasitic diseases that illustrate the effect of ecosystem changes upon health. Relationships between ecosystem changes, including habitat modifications and host species imbalances, and human, animal, and plant health merit our close attention. Outbreaks of infectious diseases like Lyme disease, schistosomiasis, and hantavirus infections in Latin America are clear illustrations of how ecosystem modifications may strongly impact upon the emergence of new infectious diseases. Because much of this chapter is concerned with the links between biological diversity and disease risk, that is, the reduced dilution effect of biodiversity upon disease transmission (see concerned Section 33.3.2), we here illustrate this by two other examples of the influence of species composition within an ecosystem and habitat alteration, and the resulting shifts in host species.

Many infectious diseases have complex life cycles requiring a reservoir or vector host. One such infectious disease, schistosomiasis, constitutes one of the most debilitating tropical infectious diseases. These snail-transmitted trematodes are reemerging in different African and Southeast Asian countries despite the undisputable improvement in sanitary and socioeconomical conditions in these areas. Larval worms, called cercariae, leave snails and penetrate humans in contact with freshwater. Adult worms live in the circulatory system of humans, consuming blood. Their eggs lodge in various tissues of their final human hosts, leading to organ failure [13]. A key to this reemergence is the creation of habitats for the several species of snails that serve as initial intermediate host for human schistosomes. Snails proliferate in ricefield cultures, dams, and aquaculture extensions. For instance, large impoundments throughout Africa, notably construction of the Aswan Dam that created Lake Nasser, have substantially increased schistosome transmission, resulting in increased human morbidity and mortality [19].

Trophic cascades driven by species introduction may also favor snail population increases. One example is the recent reemergence of schistosomiasis in Lake Victoria in East Africa. An amazing species flock of endemic Cichlid fish had evolved in Lake Victoria, and a few highly specialized species, adapted to feeding on mollusks, along with the resulting low snail density, thus hampered transmission of schistosomes to humans. But, fishery biologists then introduced the Nile perch, *Lates niloticus*, in an attempt to stimulate the local economy. The Nile perch drastically reduced the abundance of native cichlids. The subsequent explosion of mollusk populations on the lakeshores and an increase in human settlements, which sought to benefit from the new fish economy in the area, created foci for schistosomiasis transmission [64]. Thus, introduction of the Nile perch resulted in both direct economic profits for local populations and the loss of biological diversity of endemic Cichlid fauna, thereby creating indirect human health problems over the long run.

Another good example of how hosts, vectors, and infectious disease agents interact with each other and with their ecosystem is that of malaria in the Amazonian rainforest. Deforestation due to intensified farming and agriculture and the trans-Amazonian highway construction provided the environment necessary for one specific mosquito, *Anopheles darlingi*, to flourish in disturbed habitats [14,89]. *A. darlingi* is known to occupy a particular ecological niche in the rainforest canopy, but habitat changes have offered new opportunities for this insect to rapidly adapt to lower habitat layers in these man-made open ecosystems. Human encroachments have thus moved *Plasmodium* protozoans into those areas in which mosquitoes were accidentally highly competent at malaria maintenance and transmission. Deforestation and its resulting ecological niche shift by free-pathogen insects, increased urbanization, and human migration are all implicated in the observed changes in malaria dynamics in the Amazon basin. Human disturbance of the rainforest due to intensified agriculture, proliferation of the highly important insect vector, and the introduction of the disease agent near human populations clearly show the intricacy of environmental and social factors contributing to amplification of disease spread. Changing environmental conditions like deforestation have also contributed to the emergence of hookworms, an important human pathogen in Haiti, for instance [51].

Over the past 50 years, industrial and agricultural changes, along with economic and social changes, rapid population growth and international travel, have inevitably contributed to changing the profile of infectious disease occurrence and distribution. At the same time, we have either forgotten or neglected the initial events underlying the emergence of infectious diseases. The complex dynamics of environmental and social factors should force us to take into account ecosystem approaches to human health programs in the very near future [74].

33.4.4 Land Use, Agricultural Development, Intensified Farming, and Health

In the recent history of our society, successive human settlements and encroachments, along with growing human populations at the planetary level, are requiring huge supplies of food for sustenance, along with land for providing essential ecosystem services to meet that need [4,70]. At present, these services are being disrupted by the "eruption" of a dominant species on the planet, that is, man, who needs more and more resources and facilities, often to the detriment of ecosystem stability and sustainability. The reader has free access to a series of seven very fascinating e-seminars on *Medical Ecology: Environmental Disturbance and Disease* by Dickson Despommier of Colombia University, USA at http://ci.columbia.edu/ci/eseminars/1111_detail.html.

What then are the ecological implications of agricultural land use and intensified farming and husbandry for human health? Are we in fact creating modern artificial ecosystems that may contribute to the spread of new invasive pathogens by breaking down natural barriers?

Patz and Confalonieri [70] listed the environmental factors associated with land use that may have an impact upon

emerging diseases. These include (i) agricultural development, (ii) urbanization, (iii) deforestation, (iv) population movements, (v) introduced species/pathogens, (vi) biodiversity loss, (vii) habitat fragmentation, (viii) water and air pollution, (ix) road building, (x) HIV/AIDS, (xi) climatic changes, and (xii) hydrological changes including dams [59]. In addition, land use for agricultural development, intensified farming and husbandry have strongly affected biodiversity and climate at rates that have no equivalent in the history of human societies.

Some examples of emerging infectious diseases due to land use changes and intensified practices in agronomy can be illustrated as follows.

The Japanese encephalitis virus has been a serious public health problem in many countries of Southeast Asia since the time it emerged in the early 1970s. The virus is a natural infection transmitted by mosquitoes of the *Culex vishnui* group as found in Indian ricefields, their most prolific breeding sites. Intensified rice paddies in the Tamil Nadu district, as in many other regions of developing countries, and the physical and chemical properties of ricefield waters, that may change in response to natural drivers or by anthropogenic actions, have strongly affected the abundance of culicines in ricefields [86]. The larval density of mosquitoes and their rate of development may depend on a series of biological factors, for example, dilution by rain, surface area size for cultivation practices, and agricultural operations, for example, use of fertilizer. With the development and extension of ricefield cultures, which represent the food staple for the many millions of people living in those areas, human-induced environmental changes have created foci for the development of vector and reservoir hosts. In particular, use of fertilizers with nitrate nitrogen has exerted a positive influence upon larval abundance of mosquitoes *via* a mediated-effect upon the multiplication of microorganisms in the ecosystem, which constitute the main diet of mosquito larvae. Similarly, in the same type of agroecosystem, but in northeastern Argentina, a strong correlation has been found between the abundance of *Biomphalaria* species, which are potential vectors for schistosomiasis transmission to humans, and, among other environmental parameters, nitrate and nitrite concentrations in ricefields due to fertilization [81]. Man-made creation of new habitat conditions in ricefields, through the addition of compounds such as calcium, the main component of the snail shell, has caused vector hosts to flourish, and humans usually contract the disease during the rice harvest *via* contact with infected snails. Similar scenarios have been observed for both Korean hemorrhagic fever, caused by a Hantaan virus, and Argentine hemorrhagic fever due to the Junin virus [61]. The virus responsible for Korean hemorrhagic fever is a source of natural infection in the field mouse, *Apodemus agrarius*, in many countries of Southeast Asia, particularly the People's Republic of China. Ricefield extension has created favorable conditions for the explosion of field mouse populations, thus increasing the risk of disease transmission to the population, and especially farmers. It is suspected that the conversion of grassland to maize cultivation, as seen in many districts of Argentina, has facilitated the proliferation of a rodent reservoir that is the natural host for this virus [61]. Additional examples exist of new areas subject to intensive cultivation, which witness the development of potential vector or reservoir host species [4,61]. Ecological changes due to agricultural development are among the most frequently identified factors in disease emergence, and it is important to consider that the need for more food supplies as human populations continue to grow will inevitably precipitate the emergence of new diseases, by placing more and more populations in close proximity to a natural reservoir or host.

Pandemic influenza is another illustration of how agriculture and intensified farming play an important role in disease outbreak. In general, communities are afflicted by annual or biennial epidemics of influenza caused by virus mutant strains highly selected to propagate in human hosts [17]. However, recent evidence shows that man, despite his relative resistance, may also be exposed to new influenza viruses from avian hosts [49,50], thus contradicting the more general belief that host switching is only occasional [62]. Waterfowl, such as ducks, constitute an important natural reservoir of influenza, but what is even more extraordinary is the high susceptibility of pigs to these avian influenza viruses. Recent findings [49,50] show that pigs might serve as "mixing vessels" [61] for the recombination of avian and human influenza viruses, thus generating novel influenza recombinants highly virulent for humans. It is now suspected that the ancient influenza pandemics might have resulted from the propagation of mammalian influenza recombinant strains [61]. But, what changes in human ecology facilitated the acquisition of avian influenza viruses by pigs, and the diffusion of new, highly virulent mixed influenza strains to humans? It now appears clear that influenza viruses benefit from a community of potential host species, rather than a single species, so as to evolve and select new forms better adapted to propagation. Intensified pig–duck farming, meant to provide food supplies to human populations, as is the case in Southeast Asia, has undoubtedly contributed to creating new "man-made ecosystems" [75] highly favorable to the diffusion and mixing of disease strains. As pointed out by Morse [61], these human influenza infections with complex zoonotic pathways have recently received much attention from public health authorities on intensified farming and in other settings, where different potential host species may be close together at high densities, as in live animal markets. Here we cite the recent outbreak of SARS in southern China, caused by a coronavirus from a small mammal,[1] which serves as a food source for the local population, as another illustration of the introduction of a new disease agent into human populations [31]. High-intensity production of food animals like cattle, along with rendering processes, have facilitated the transmission of the scrapie agent from sheep to cattle, causing bovine spongiform encephalopathy, later associated with a new variant of Creutzfeldt–Jakob disease in humans [26,93]. Intensified production of food and industrial

[1] A scientific discovery published after manuscript writing has shown that Chinese horseshoe hat was a reservoir for SARS disease-agent. See Li et al. (2005).

processes in our modern societies will clearly increase the incidence of accidental contamination and amplification, as observed for BSE, in which mammal by-products, mainly from sheep and cattle, were fed to cattle, thus forming a new "artificial food chain" and providing the opportunity for cannibalism to herbivorous cattle.

As human populations grow, agricultural development and intensified settings, as in poultry farms, will be important causes of both ecological disruption and interaction with the environment, thus providing suitable conditions for exposure to novel pathogens. There is now increasing concern about the many uncertainties surrounding the environmental origins of microbes; indeed science over the past decades has concentrated only on understanding the human side of this question. The flu epidemic in Southeast Asia is one recent illustration of the need to enhance our "window of knowledge" of the natural ecology of infectious diseases.

33.4.5 Human Population Growth and Behavioral Practices

Having discussed at length the imprint of humans on the Earth's ecosystems (see above), we will here concentrate on the potential effects exerted by increasing human population size and density on disease emergence and spread. In their respective conclusions, both McMichael [59] and Morse [61] agreed that current living conditions have created a situation in which the causes of disease emergence and spread are more prevalent than ever.

Indeed, the human population of the planet is now much greater than at the beginning of the twentieth century, creating a greater diversity of microbes existing in these increased populations [32]. Though we have little or no idea of how many pathogen species are hosted by human communities, it is now clear that larger populations may harbor a greater diversity of pathogens than smaller populations (Fig. 33.11).

Much remains to be understood on the mechanisms regulating the diversity of pathogens in human communities.

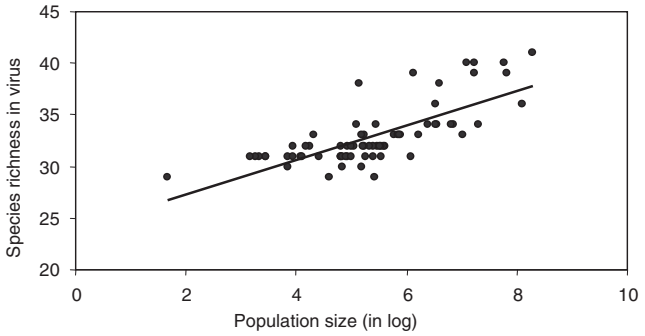

Fig. 33.11. Linear relationship between human population size and species diversity in viruses across 71 human communities living on different islands. Linear regression is $y = 1.67\ x + 23.97$, $r^2 = 0.551$, $p < 0.0001$. Population size variable is log-transformed. From Ref. [32].

The example above provides clear evidence of how the spatial scaling theory and community ecology rules might be best applied to pathogen microorganisms in humans. Many epidemiologists and public-health scientists have treated the "tiny world of human pathogens" as a "black-box" with no spatial structure or biogeography [25], but recent findings [25,34,83] illustrate that, like macroorganisms (see many references above) and other microorganisms, for example, microalgae, and fungi [27], human pathogens are not randomly distributed, but rather exhibit predictable spatial patterns. This offers exciting potential for a more synthesized view of human pathogen distribution and organization, and ultimately a new means of understanding and thus controlling infectious diseases.

Moreover, the effect of population size, that is, the number of susceptible persons within a community, on both disease persistence and spread is particularly important, and many recent studies have clearly shown its role in childhood diseases [5,28–30]. First, there exists a community size threshold, referred to as the critical community size (CCS), according to which disease probability extinction is high due to demographic and environmental heterogeneities. Thus, the disease can only persist with time in only human communities over a given population size, that is, around 250–300,000 inhabitants for both measles and whooping cough. Rohani and co-workers [79] showed that both measles and whooping cough (see also Chapter 12 in this volume) diffuse progressively from urban centers to the surrounding rural areas, with, for England and Wales, the three biggest cities, that is, London, Liverpool, and Birmingham, acting as sources of disease retransmission (Fig. 33.12).

Thus, many recent advances in the ecology of infectious diseases have led to the fascinating finding that numerous infectious diseases faced local fade-outs, but enjoyed regional persistence at the metapopulation level (see Chapter 12 for a definition), indicating that disease dynamics behavior in space and time cannot be understood without considering the importance of large spatial scales. Despite the public health importance of such findings, little is known about the regional influence of space in shaping disease incidence and prevalence within local communities. Major advances made during the recent decade in the metapopulation dynamics theory of infectious diseases clearly point to the fact that we need to adopt a macroscopic view of disease. It remains to be seen whether these ideas will be adopted in the very near future as our world progressively becomes a "small-village." We will deal with this in the final section.

33.4.6 International Travel and Trade

The historical processes that gave rise to the preponderant role of humankind on Earth are continuing. Humans, members of a common, ubiquitous species highly resilient to diverse habitat alterations, have exploded in size on the planet because modern living conditions have ensured their survival and reproduction. Modern technologies are a compound ingredient in the success of the "human saga," and have

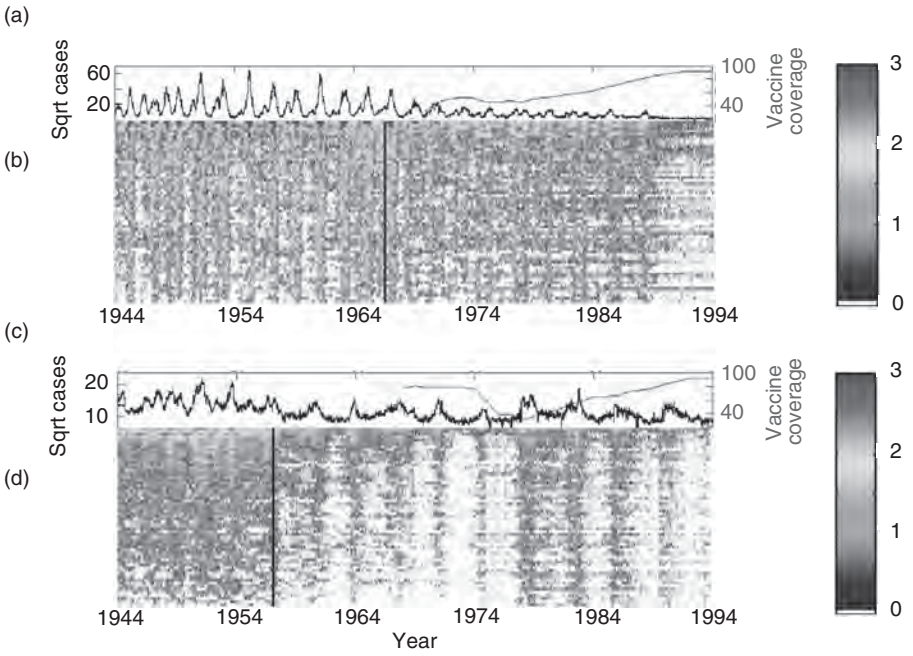

Fig. 33.12. a and c illustrate the population dynamics in number of infected cases for measles and whooping cough, respectively, for England and Wales. Gray curve shows the evolution of vaccine update for both diseases. (b) and (d) show the spatial patterning of number of disease cases ranked from the largest city, that is, London, at the top of subfigures to the smallest one, that is, Teignmouth, at the bottom of subfigures. Variability of gray (clear to dark) colors indicate the level of disease incidence. Spatial patterning on subfigures (b) and (c) indicates that both childhood diseases persist with time in the largest cities in England and Wales. This pattern is highly visible for measles on subfigure (b). Modified from Ref. [79] with permission from the senior author.

facilitated the transfer and encroachment of new populations into unoccupied areas of the world. Transcontinental air travel and maritime transport, along with global economic trade, have contributed to the success story, but evidence is now accumulating that supports the adverse effects of globalization upon the rapid spread of emerging infections and the diffusion of infectious diseases [85]. Today, speed of travel and global reach enable rapid access of disease to uninfected populations: Any population on Earth, with the possible exception of native tribes in the rainforest, is at risk of contracting any disease (Fig. 33.13). The recent avian flu epidemic in Southeast Asia and the world-wide panic it created is a crude example of the new artificial world we, as humans, have generated, thus facilitating the spread of infections [49]. Instead of choosing one or two specific diseases to illustrate this section, we present new findings here by Smith and coworkers, who have begun to quantify the degree of global homogenization of human diseases and have categorized the taxonomic groups of diseases at risk of contaminating human communities in the future [83].

Based on an extensive dataset of around 317 human infectious diseases affecting human populations on Earth, Smith and contributors [83] have categorized these different diseases according to the collection of reservoir hosts utilized: (i) infectious diseases specific to humans, (ii) infectious diseases that utilize human and nonhuman reservoir hosts (multireservoir), and (iii) zoonotic infectious diseases. Then, using a similarity index to measure the degree of homogenization across regions, the authors have revealed that infectious diseases specific to humans exhibit the greatest degree of similarity among nations and continents, followed by multireservoir infectious diseases, and finally zoonotic infectious diseases (Fig. 33.14).

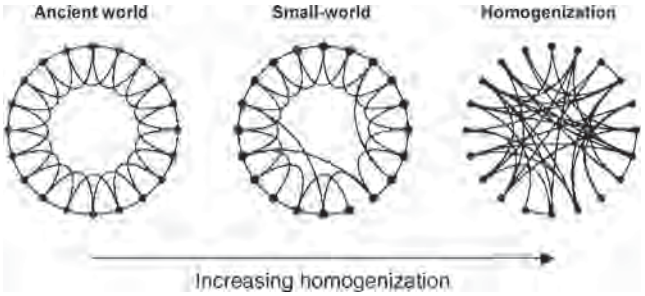

Fig. 33.13. Schematic illustration of (i) early conditions in which local communities were in contact with nearest neighbors only (on the left); (ii) small-world conditions (middle) where, in addition, a given local community was in occasional contact with another distant community, thus mimicking transcontinental exchanges; and (iii) global homogenization (on the right) where "any community is in contact with the others," illustrating a global world. Infectious diseases may benefit from this strongly interconnected world so as to proliferate and expand in host populations. Modified from Ref. [96].

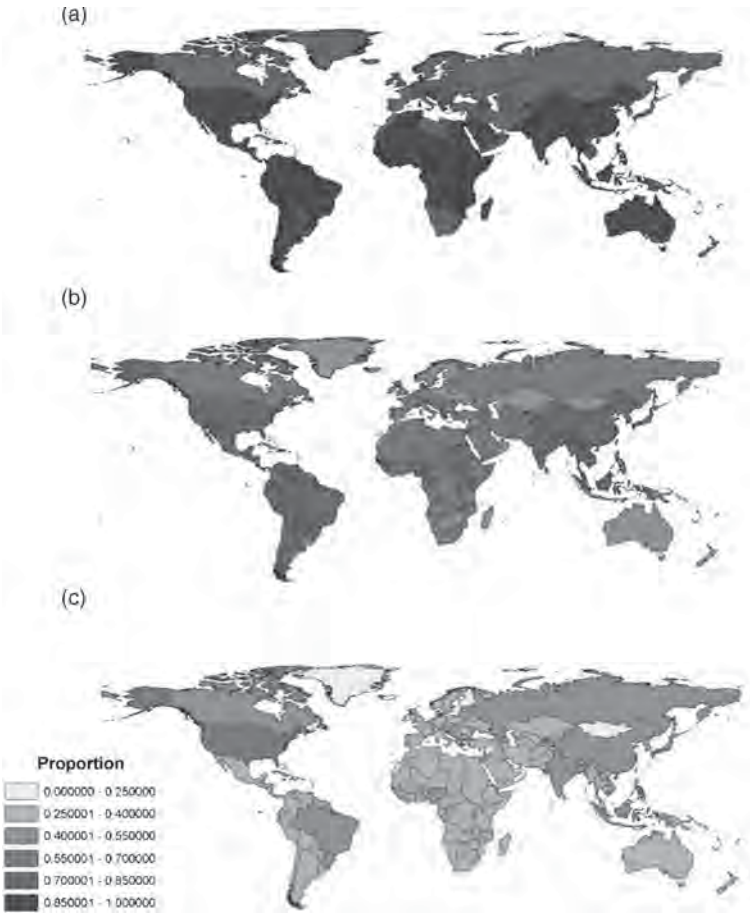

Fig. 33.14. Degree of homogenization at the national scale of human infectious diseases based on the range of hosts utilized: (a) infectious diseases specific to humans; (b) infectious diseases that utilize human and nonhuman reservoir hosts (multireservoir); and (c) zoonotic infectious diseases. The degree of homogenization ranking is based on Jaccard's similarity index from low (gray) to high (dark). With permission from Ref. [83].

At the national scale, the near global homogenization of infectious diseases specific to humans suggests that there is little scope for further expansion in their spatial distribution. However, although many multireservoir and zoonotic infectious diseases are also broadly distributed, far more remain localized to specific regions and localities of the world. As a consequence, infectious diseases with direct lifestyles represent the most likely candidates for spread in nations in which they are absent today. The spatial distribution of infectious diseases that utilize nonhuman hosts is likely due to the geographic distribution of their reservoir hosts. As in the case of the emergence of monkeypox disease in the United States, the increasing rate of introduction of exotic species will probably facilitate an increase in geographic scope of the infectious diseases they may host in the years to come. This raises a serious concern for public health, as pointed out by Smith and collaborators [83], how to target public health strategies, as human nonspecific infectious diseases might have the greatest potential for crossing frontiers and becoming established in new areas. Admittedly, this is not a new phenomenon. Humans have facilitated the spread of disease to novel and susceptible populations across the planet for hundreds, of thousands, of years [83]. The magnitude of these introductions has created a world in which many historically localized diseases are now broadly distributed and shared between regions. International travel and economic trade, particularly that of exotic pets (though it has since been demonstrated that the tire trade is also highly responsible for diffusion of disease vectors [75]), are particularly alarming, as they play a strong role in the diffusion of diseases in new regions, and as such, require immediate decisions when regulating trade and transport at the global level.

33.5 CONCLUSION AND SUGGESTED RESEARCH PERSPECTIVES

This chapter has explored and summarized topics on the links between global environmental changes and health concerns, and the problems and challenges posed by this new global context in terms of actual health issues. It is not, nor was it

intended to be, an exhaustive review of the numerous examples that now exist on the interrelationships between global changes and health. For instance, we deliberately decided not to include considerations on microbe adaptation and evolution, or the socioeconomic drivers of disease, as many chapters in this volume will deal with that matter. We also hope to have proposed an important list of references, which the reader can consult for further reading. Rather, we have selected topics that illustrate, for scientists, policy makers, and the public, the nature of scientific and health challenges posed by global change and implications from a global health perspective, giving "a broad picture" to show how health scientists, and national and international health authorities need to consider the complex nature of two-way interrelationships that truly exist between the environment and health.

Many academic epidemiologists believe that we have learned enough about infectious diseases, and this chapter tries to convince the more skeptical of them that we might take more important crucial steps in understanding disease by changing the way we work. The challenge for modern epidemiology is to open "the window," and to adopt a broader perspective on health. On page 166 of his book, Lawton has identified four areas in which he feels contemporary community ecology has got the balance wrong. These areas can be easily transposed to current epidemiology. They are (i) too great an emphasis on short-term, highly reductionist experiments or laboratory research; (ii) too great an emphasis on local, often tiny, processes at the expense of larger-scale regional ones; (iii) the absence of a connection between molecular ecology, population genetics, and population and community ecology of infectious diseases; and (iv) a nearly total failure in exploiting the power of model systems.

What then can we do to reduce uncertainty about the health responses to global environmental changes? Such an approach will require a shift in the way we operate as "epidemiologists," from field epidemiologists to computer-science epidemiologists. This volume may constitute a current demonstration that breaking with tradition in health can be a source of confusion, but it is also the means, and this was the intention of our scientific publisher, of bringing together different disciplines and subdisciplines for fruitful exchanges. What we need, then, are the following:

(i) *A plurality of approaches*: We need field observations, theory, experimental designs in the laboratory and in the field, hypothesis testing, molecular ecology, and global epidemiology.

(ii) *Fewer systems studied, but in greater depth*: We need to concentrate our research efforts on fewer places and biological systems in which to place our resources. As pointed out by Lawton, people hate this idea, but as two population and community ecologists, we can state here that health research will considerably benefit within the next years from this decision, and it is in the interest of epidemiology to adopt such an approach.

(iii) *Development of long-term epidemiological survey sites*: It is particularly true in tropical regions of the world where the impact of global environmental changes on health concerns will be the most substantial.

(iv) *Embedded into item (iii) is the need for standardization of protocols*: It is particularly true in different disciplines of epidemiology. Failure to standardize protocols over the past decades virtually destroyed any attempts at meta-analysis and comparative analysis in epidemiology. Curiously, the excuse of not being able to develop a comparative approach in epidemiology stems from the fact that no standardization of protocols has been decided.

(v) *Institutions and research*: There is a strong need on the part of national and international health institutions to promote more coordinated multidisciplinary research. The experience in the United States of a joint *National Science Foundation-National Institutes of Health* project represents an effort toward better collaboration between health scientists and those working on other fields of science.

(vi) *More nationally and internationally coordinated research programs*.

(vii) *Promoting community contributions instead of individual work*: There is a current tendency in epidemiology to consider molecular ecology as a "primer" in modern science, and to relegate other fields of research to second position. The same can be said for field epidemiology as related to theoretical epidemiology. We need to encourage a variety of approaches that will provide different points of view on disease.

Despite considerable research efforts made toward understanding patterns and processes that explain the occurrence, emergence, geographic spatial distribution, and extension of infectious diseases, epidemiologists are still not able to predict in detail how, where and when particular diseases will respond to environmental change. This represents a major research challenge for epidemiology in a changing world. We strongly feel that such a challenge can be met, widening our approaches and state of mind so as to join together in fighting disease.

33.6 SUMMARY

Recent studies of the impact of global environmental changes on the health of humans, and even wildlife, have provided several good examples of how large-scale investigations are of particular relevance to epidemiology. However, health study lacks both a broader "picture" and a comparative perspective, whereas major research developments have been made recently in other fields of life science, such as population dynamics,

community ecology, and macroecology, that have benefited from enlarging scales under scrutiny. In this chapter, we attempt an objective, though not exhaustive, analysis of global environmental changes and their impact upon infectious disease patterns. The analysis of large-scale global environmental hazards in epidemiology requires integrating knowledge of different disciplines, thus necessitating a holistic research approach. This chapter provides with numerous examples of how large-scale patterns may intervene with local-scale health concerns, and thus it tries to convince the more skeptical among public health-scientists and authorities that we might take more important crucial steps in understanding infectious disease by changing the way we work. Such a challenge can now be met, widening our approaches and state of mind so as to join together in fighting disease.

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