## CHAPTER 10

# Parasitism in man-made ecosystems

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*Technological and cultural change in human populations is opening up new ecological niches for pathogens and parasites. The organisms that cause many of these "diseases of progress" have opportunities for global spread and access to host population densities unprecedented in human history. Understanding the natural history and evolutionary ecology of these pathogens needs to become a key part of public health planning.*

## 10.1 Introduction

Like free-living organisms, parasites and pathogens can colonize and evolve in new environments. In this way, travel and technical developments (e.g. air conditioning, plane, boats, new economic links, etc.), medical and surgical developments (e.g. catheters, fibroscopy, prosthesis, organ transplants associated with anti-rejection medicine, immunosuppressive drugs, etc.) are generating new environments in hospital ecosystems which are colonized now by new parasite and pathogen flocks. Elsewhere, agricultural processes have widely disturbed ecological parameters in natural ecosystems for food development; they are responsible for the emergence and development of new parasite and pathogen species, and also for changes in host–parasite interactions. Through different examples, the aim of this chapter is to present and to discuss some phenomena and processes involved in the conquest by parasites and pathogens of man-made ecosystems. We could name diseases which are the result of pathogens colonizing man-made ecosystems as 'progress infectious diseases'.

To pass from 6 billion to 10 or 12 billion human inhabitants by the end of the twenty-first century represents one main subject of anxiety for scientists. Ten billion humans could not live on the earth with the lifestyle enjoyed by the 750 million people presently living in developed countries, because of lack of water, energy, quality, and quantity of space. Developed countries must contribute to the development of all countries to balance economy and life conditions. However (indeed, *if* ever) this is achieved, substantial environmental modification seems likely. Throughout history, mankind has severely modified the biosphere. Human impacts on ecosystems are as old as the human species. However, following industrialisation, the consequent increase in numbers of people and their ability to modify the biosphere, the extent and consequences of human impacts on ecosystems have accelerated. Impacts resulting from human activities occur in all parts of the biosphere, and at all kinds of temporal and spatial scales. (Dickinson and Murphy 1998). The ecological consequences of the unavoidable modifications of the future are hard to predict: we simply do not have a thorough understanding of the impact of global change on local environmental conditions and the evolution of biodiversity.

### 10.1.1 But what is an ecosystem?

Let us imagine a pond, for example. What animals might live here? Insects, worms, birds, fish, mice, muskrats, ducks, deer, wolves. What do these animals need to eat? Insects eat plants, fish eat

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worms and insects, birds eat fish, worms, and insects. Mice eat grain. Muskrats eat ducks, eggs, and chicks. Ducks eat insects and worms. Deer eat grass. Wolves eat mice, muskrats, and deer. All these animals rely on the pond for the water they need. The deer cut the grass, wolves remove the sick and weak deer from the herd. Muskrats regulate the duck population. All these animals rely on each other. Just like people in a human community. An ecosystem is a community too. Consider a pond community, with all its variety of plants, insects, birds, and other living things. What would happen to the community if the water vanished? What if the ducks all disappeared?

Other examples of ecosystems include forests, rivers, oceans, deserts, cold arctic tundra, high mountains, and rain forests. Different plants and animals grow in different ecosystems. Normally, the living things in the ecosystem balance in such a way that no living things take over the whole ecosystem and destroy it, at least not for a while. For example, the production of $O_2$ by the first photosynthetic algae had dramatic consequences on the anaerobic life that predominated at that time.

### 10.1.2 But why some deer are sick and weak within the herd?

May be they could be parasitized? We just want to underline here that the above description of an ecosystem, as we can read it in numerous books or websites, disregards systematically the fundamental role that parasites play in ecosystem functioning! Indeed, it is less poetic to speak about a tapeworm or a virus than a duck or a deer! Nevertheless, parasites are present in a large part of ecosystems, and the liver, kidneys, lungs, gills, gut, and pharyngeal sphere of a host constitute as many ecosystems for parasites and pathogens as do rivers, oceans, desert, high mountains, and jungles for free-living organisms.

### 10.1.3 But what is a parasite and/or a pathogen?

'An organism in or on another living organism obtaining from it part or all of its organic nutriments, commonly exhibiting some degree of adaptive structural modifications, and causing some degree of real damage to its host' (Price 1980). So, the parasite/pathogen lives at the expense of the host, and this host's exploitation has automatic consequences on host biology and physiology, on host evolutionary biology and on evolutionary relationships between hosts and parasites (Renaud and De Meeüs 1991). Because the host represents the 'habitat/resource' system of the parasite, each modification on host ecosystem will have consequences on the parasite ecosystem, and because parasites affect host fitness, they act on host ecosystem too. Because living organisms are parasitized, we cannot consider ecosystem evolution without parasites (see Chapter 9).

It is undeniable that humans greatly disturb ecosystem equilibrium (deforestation, eutrophication, overgrazing, etc.), but the aim of this chapter is not to consider anthropogenic ecosystem disturbances and subsequent evolution of parasites and diseases which are presented in other chapters of this book (see Chapter 7). Instead, we will illustrate and discuss, through different examples, the impact of technical progress by humans on the evolutionary ecology of parasites and pathogens. How have parasites exploited new 'human-made' ecosystems, especially those concerning public health?

### 10.1.4 What is a 'human made' ecosystem?

It is an ecosystem artificially elaborated by humans in order to enhance their quality of life.

For example, let us imagine that the wheel was never invented! The wheel is everywhere on our cars, trains, planes, machines, wagons, and most factory and farm equipment. What could we do without wheels? But as important the wheel is, we do not know who exactly invented it. The oldest wheel found in archaeological excavations was discovered in Mesopotamia, and is believed to be more than 5500 years old. Eventually, wheels became covered with tyre in order to make the trip more easy and pleasant. But, it is almost impossible remove all the water a worn-out tyre contains. Consequently, old tyres become excellent habitat for the larvae of different mosquito species, especially *Aedes* spp. which are the vectors of the Dengue virus. Worn and waste tyres are being traded throughout the world, and are

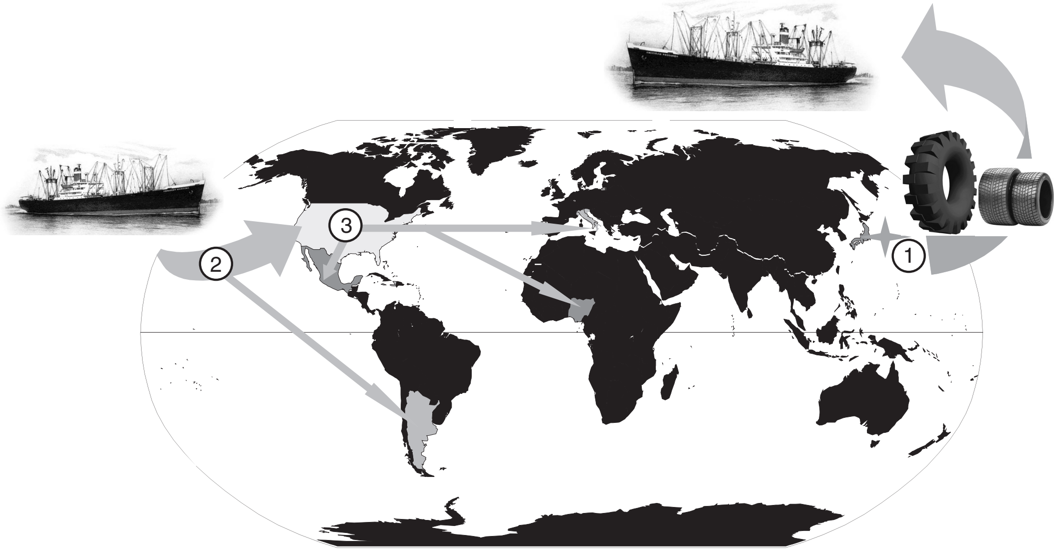

**Figure 10.1** Example of hypothetical main routes of *Aedes albopictus*- infested tires.

*Notes*: 1: Japanese origin; 2: first colonization wave: US and South America in 1985/1986; 3: second colonization wave: Mexico, Africa, and Europe in 1990/1991.

*Source*: Data from Reiter (1998: 93, table 10).

responsible for the introduction of mosquitoes in different countries (Fig. 10.1). 'In short, it seems we must accept the establishment of exotic species as an inevitable consequence of modern transportation technology' (Reiter 1998). For example, inspections of containers arriving in US ports showed the presence of living *Aedes albopictus* and four other mosquito species in worn tyres from Japan (Craven *et al.* 1988). Japan is the biggest exporter of worn tyres in the world. *Ae. albopictus* is capable of vertical and horizontal transmission of the Dengue virus, and other important human arboviruses (Shroyer 1986). Thus pathogenic agents can take advantage of tyre trade. We can imagine that such trades could have also consequences on other vectors, such as the *Anopheles* mosquitoes which transmit malaria.

## 10.2 Economic and touristic human travels: enhancement of human contacts!

Boats not only carry the worn tyres which constitute new ecosystems for mosquito larvae, but they also have bilge. The classic bacterial disease, cholera, entered both North and South America during the last century from the bilge-water of an Asian freighter. Indeed, molecular typing showed that the South American isolates were pandemic genotypes previously observed in Asia. Water bilge seems to constitute a very good ecosystem for the transported pathogens such as bacteria (Anderson 1991; Morse 1995). Cholera is not the only opportunistic pathogen which use such kinds of transport: an epidemic strain of *Neisseria meningitidis* seems to have disseminated rapidly along routes by travelling in ballast waters (Moore and Broome 1994).

Malaria parasites use mosquitoes to transmit between vertebrate hosts. For example, different mosquito species belonging to the genus *Anopheles* are the definitive hosts of the malaria agent *Plasmodium vivax* , one of the four species of human malaria. Human malaria is currently absent in western Europe, but an autochthonous case of *P. vivax* malaria occurred in Tuscany (Italy) in August 1997, decades after malaria eradication (Baldari *et al.* 1998)! The disease was diagnosed in a woman with no travel history who lived in a rural area where indigenous *Anopheles labranchiae,* the former main malaria vector in Italy, was abundant (Romi *et al.* 1997). A molecular epidemiological investigation concluded that this was an introduced malaria case, and indicated a girl recently immigrated from Punjab (India) and living about 500 m away from the patient, as the source of *P. vivax* infection (Severini *et al.* 2002). The parasite was able to pass from Asia to Europe because an infected host took a plane to visit a family member. Planes and boats constitute new opportunities for vector and pathogen dispersion, in the same way as when a pathogen is using different hosts for its dispersal. Parasites and pathogens are able to colonise new environments and to adapt locally to new hosts and vectors through human-made transportation. Similarly, epidemics of malaria in NE Brazil in the 1930s occurred because of the introduction of *Anopheles gambiae* , one of the most efficient malaria vectors, which probably arrived from a boat bringing mail from Africa (Killeen *et al*. 2002).

But what could be the consequences ever more frequent travel? What would be the possible consequences on pathogens evolution as regards to resistance and virulence? Vector-borne diseases such as malaria and water-borne diseases such as cholera are generally more virulent than diseases spread by direct infection (Ewald 1994). One reason for this may be that vector or water-borne diseases to spread over long distances, and causing infection of susceptible individuals distant from the infected individual. In a spatially structured host population, the ability of the pathogen to infect distant individuals leads to the evolution of a more virulent pathogen (Boots and Sasaki 1999). Developing travel alters the connections between different towns or areas (Fig. 10.2). We could have passed from a regular lattice between the different points to random net-connections which are permitted by long and frequent travels. From their analyses on the consequences of the modification and the evolution of connections, Watts and Strogatz (1998) suggested that infectious diseases spread more easily in small-word networks than in 'regular' lattices. We can predict that the increase in world travel would have strong consequences on

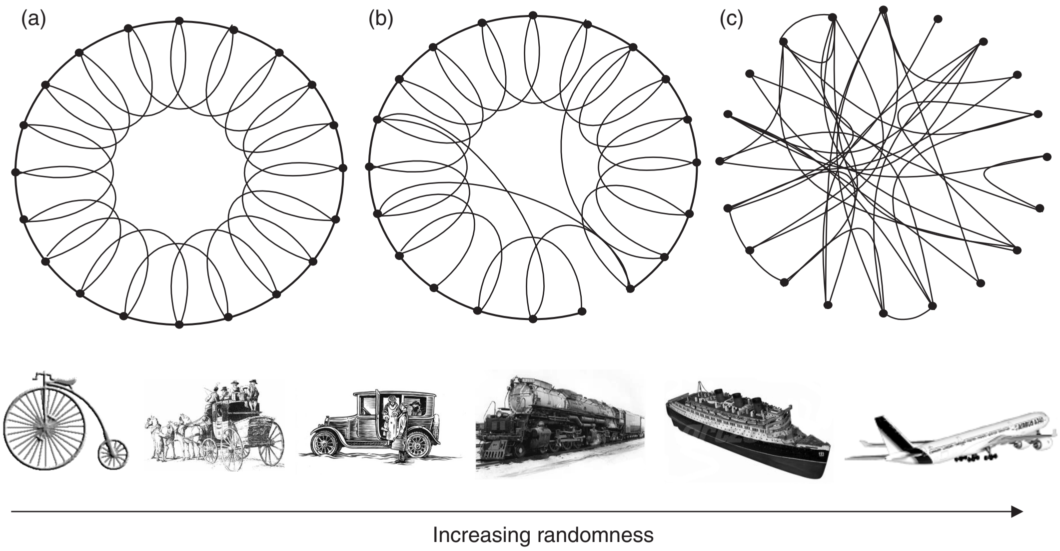

**Figure 10.2** Connection topology from (a) regular ring lattice, to (b) small-world, to (c) a random network.

*Notes*: The intermediate connection is called 'small world' network, and infectious diseases spread more easily in small-world networks that in regular lattices. The different means of transport are presented in order to try to illustrate the development of 'travel man-made ecosystems' which permit to link different geographical points and modify the connections within and between populations. No company or factory could be incriminated here for disseminating pathogens.

*Source*: Modified from Watts, D. J. and Strogatz, S. H. (1998).

pathogens dispersal and consequently on the evolution of infectious diseases virulence and resistance, but this could be also applied for all categories of vectors which are responsible of pathogen carriages. It seems reasonable to assume that human societies in the past lived in larger with more isolated communities. But, modern social networks (Wasserman and Faust 1994) are known to be small words (Watts and Strogatz 1998), and it follows that infection networks may also show 'small world' connections in modern societies. When infections occur predominantly locally we predict a lower virulence than when transmissions occur predominantly randomly throughout within and between populations (Boots and Sasaki 1999).

## 10.3 Human comfort and industrialization

Throughout human evolution, people have always tried to enhance their comfort. Temperature and humidity have a significant effect on human comfort and health. The most comfortable humidity range is 40–60%, but air temperature and humidity are related in respect to comfort or perceived temperature. The combination of temperature and humidity where people report comfort is termed the 'comfort zone'. At the time we are writing this chapter, an epidemic legionnaire's disease occurs in North of France (Pas de Calais). Indeed, 85 persons where infected during January and February 2004, and among them 13 died (Fig. 10.3).

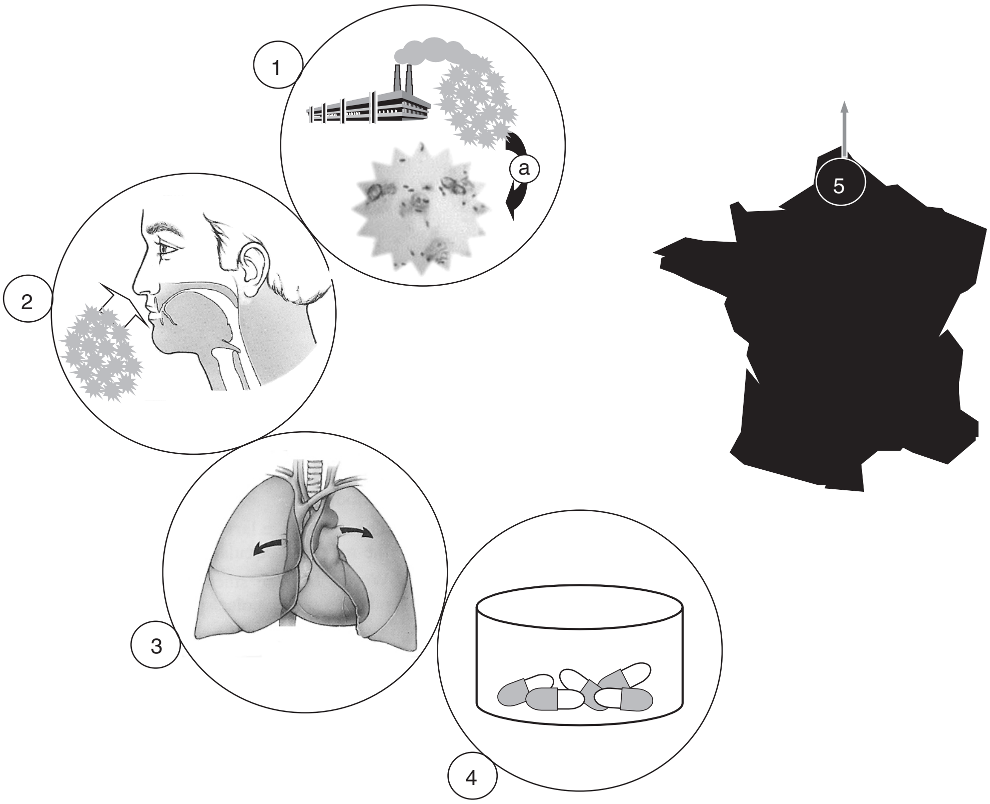

**Figure 10.3** Persons exposed to Legionnaires' disease the case of factory cooling towers which could constitute a potential reproductive ground for *Legionella* bacteria, Pas de Calais—France 2004: >80 cases of *Legionella* disease.

*Notes*: 1: Technical personal intervening near the cooling towers; 2: persons working near the smoke; 3: persons living in buildings and houses near the factory: the contaminated air penetrating through windows and new air intakes.

Legionnaires' disease is a lung infection pneumonia) caused by a *Legionella pneumophila.* The name of this bacterium was derived from the original outbreak at the 1976 American Legion Convention in Philadelphia (Hlady *et al.* 1993). These bacteria are readily found in natural aquatic environments and some species have been recovered from soil. *Legionella* parasitize Amoeba, and spread through cysts of these protozoans (Fliermans 1996). The pathogen can survive in a wide range of conditions, including temperatures of 0–63 °C, pH of 5.0–8.5, and dissolved oxygen concentrations of 0.2–15 ppm in water. Temperature is a critical determinant for *Legionella* proliferation. *Legionella* and other micro-organisms become attached to surfaces in an aquatic environment forming a biofilm. *Legionella* has been shown to attach to and to colonize various materials found in water systems including plastics, rubber, and wood. But, crucially from the public health perspective, *Legionnella* are not only found in natural habitats. These bacteria develop particularly well in human infrastructures where water is present as saunas, for example (Den Boer *et al.* 1998). But the main human-made ecosystem they colonize seems to be the cooling systems found, for example, in factories, hotels, and hospitals (Alary and Joly 1992; Pedro-Botet *et al.* 2002; Sabria and Yu 2002). For instance, in January 2000, WorkSafe Western Australia reported a case of Legionnaires' disease from a teacher who had worked in a room supplied with cooled air from an evaporative air-conditioning unit, and had also used potting mix while gardening at home. Both potting mix and warm water allow multiplication of these bacteria.

Figure 10.3 describes the different steps of human infection by *Legionella*. But, not only workers who live in the contaminated building are concerned, indeed people working or living around the *Legionella* source can be infected (Fig. 10.4). For example, during the 2004 French epidemic discussed above, the infected patients were people living near a factory where the bacteria were identified in the cooling systems. Even though the link between the presence of the bacteria and human infections was not clearly established, the French government decided to stop immediately the factory activity.

Other microbes can contaminate air-conditioning units and cooling towers which can result in other health problems for workers and visitors such as respiratory sensitization and building related illness, or 'sick building syndrome'. It is thus essential to maintain a good indoor air quality at all times.

Water is essential for life! But drinking water networks are heterogeneous and constitute real biological reactors, that is to say an ecosystem between a mobile phase (i.e. water) and an appointed phase (i.e. biofilm). These networks are continually contaminated by microorganisms (i.e. bacteria, algae, protozoans, fungi, yeast, metazoans) and nutrients (i.e. organic dissolved matter) that passed through the treatment systems or gather from accidental procedures (i.e. breaks and repairs). Drinking water networks thus bring together all the favourable conditions for the maintenance and the spread of microbial systems diversified and organized in different trophic levels, and thus constitute real food webs.

Another example which could well illustrate the phenomenon of disease induced by the human desire for comfort is wastewater such as those encountered near houses in septic tanks. Septic tanks were designed to improve sanitation. Bacteria, viruses, protozoans, and worms are the types of pathogens in wastewater that are hazardous to human. Bacteria are responsible for several wastewater related diseases, including typhoid, bacillary dysentery, gastroenteritis, and cholera. Depending on the bacteria involved, symptoms can begin hours to several days after ingestion. Viruses cannot multiply outside their hosts, and wastewater is a hostile environment for them. But enough viruses survive in water to make people sick. Hepatitis A, polio, and viral gastroenteritis are a few of the diseases that can be contracted from viruses in wastewater. A protozoan is the cause of amoebiosis, also known as amoebic dysentery. Parasitic worms also dwell in untreated sewage. Tapeworms and pinworms are the most common parasites found in these wastewaters, from where their eggs can be ingested. Children and the elderly are the groups the most significantly affected by wastewater related diseases.

**Figure 10.4** *Legionella* disease: infection routes.

*Notes*: 1: The pathogen responsible for the disease is a bacteria living in fresh water. The optimal growth temperature is between 35 and 40 °C. This pathogen is present in sanitary facilities (showers, taps, etc.), air conditioning, fountains, greenhouse, cooling towers, etc. For example, bacteria are presents in droplets coming from factory steam; 2: Bacteria contained in 'contaminated droplets' are inhaled by humans, and clinical symptoms arise after 2–10 days of incubation; 3: The serious form of the disease named 'Legionnaire's disease' generally arise in weakened patients (elderly, immunocompromised, etc.) which can evolve to a lethal pulmonary infection in about 15% of cases; 4: The treatment is based on antibiotics; 5: While writing this chapter, a *Legionella* epidemic was raging within the north of France (Department: Pas de Calais). More than 80 cases were registered during January 2004.

## 10.4 Humans get sick, age, and die!

Modern humans try to live better and longer. These days, this desire has culminated in massive pharmaceutical and medical industries and associated science base, as well as on going interest in alternative medicine. Unsurprisingly, some pathogens take advantage of human illness and death, and of the new openings provided by medical science.

### 10.4.1 Sickness

'Despite a century of often successful prevention and control efforts, infectious diseases remain an important global problem in public health, causing over 13 million deaths each year. Changes in society, technology and the microorganisms themselves are contributing to the emergence of new disease' Cohen (2000). During the twentieth century, many medical and public health officials were optimistic that most of infectious diseases could be eradicated. This has patently not occurred, and indeed that the ongoing emergence of new pathogens is a reality (Liautard 1997). Pathogens have plunged into the new ecological niches provided by new human behaviours and customs. It would be impossible and tedious to make an exhaustive review of these diseases, because they are so numerous. The development of medical technology in hospital ecosystems lead to the development of cohorts of opportunistic pathogens which exploit these new ecosystems. Diseases emerging in hospital ecosystems are known under the terminology 'Nosocomial infections' (hospital-acquired infections), derived from the

Greek ‘nosokomeion’, which means hospital. Hospitals are the source of many diseases because patients are often immunocompromised, and because infected people come to hospitals. The majority of nosocomial infections have an endemic origin (i.e. inside the hospital), where infection comes from a microorganism present in the ecosystem, and the surgical intervention renders it infectious. In an important article, Cohen (2000) reviewed the causes of nosocomial infections in modern medical environments. The classical case is represented by an inoffensive bacterium that is brought by the surgeon’s lancet into the body of a patient and evolves to a septicaemia. Figure 10.5 illustrates different origins of nosocomial infections where medical tools can be incriminated. These infections can be due to microbes that have lived on or in (i.e. colonized) the patient for many years without harm before healthcare procedure provides a means of bypassing the patient’s host defences (Farr 2003).

Nosocomial infections have been known for a long time in hospital ecosystems: Oliver Wendell

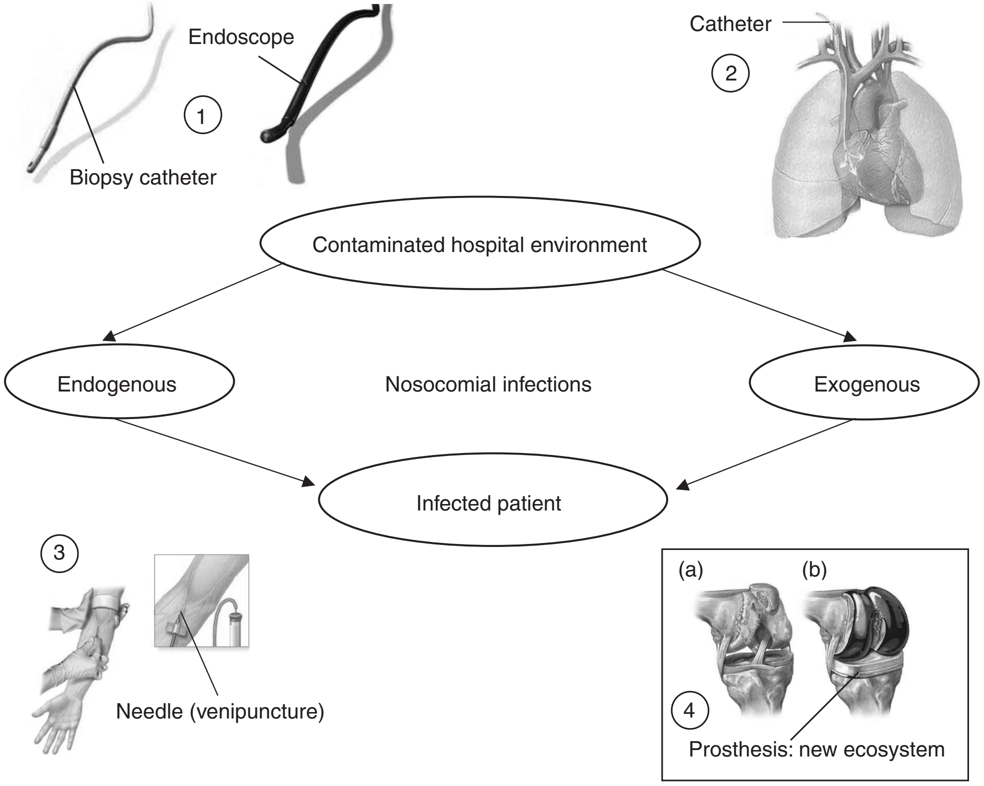

**Figure 10.5** Nosocomial infections.

*Notes*: Following an invasive surgery (i.e. through the skin as illustrated in 1, 2, 3, for example), a patient can be infected by germs coming from an:

*Endogenous origin*: patient is infected by its own germs following a surgical act and/or because he displays a particular weakness. For example, a patient under artificial breathing can develop pneumonia from a germ of its own digestive tract, which can go up to the respiratory ways. The same phenomenon can be observed for an urinary infection from an urinary probe carrier.

*Exogenous infection*: Cross infections transmitted from a patient to another through hand contacts or medical tools. These infections can be originated from the germs inhabiting hospital workers, or linked to the contamination of the hospital environment (water, air, material, foods, etc.).

Prosthesis constitutes new ecosystems for pathogens. The figure shows a knee prosthesis (4): (a) before; and (b) after.

Holmes published a paper on this topic as early as 1843. Nosocomial infections can be directly linked to medical treatment, or can simply occur during hospitalization, independently of any medical act. They concern patients, but also workers present in this ecosystem. They can occur because the immune system is busy fighting some other chronic illness, or for people who are immunocompromised. People can be immunocompromised from certain diseases (e.g. AIDS), certain medications (e.g. immunosuppressants or chemotherapy), surgical recovery, or other serious medical complaints that limit the person's ability to fight against these infections (Berche *et al.* 2000).

These infections can spread by endogenous or exogenous ways (Fig. 10.5). Many types of pathogens are involved, including fungal infections (e.g. *Candida, Aspergillus, Fusarium*), bacterial and viral pneumonia (e.g. influenza, Staphylococci, *Pseudomonas*) which can be found in different organs, giving rise to urinary tract infections, surgical site infections, respiratory tract infections, blood stream infections, skin infections, gastrointestinal tract infections, central nervous system infections, and so on. Numerous surgical acts can initiate nosocomial infections, these fall into three main types: (i) urogenital probes lead to urinary infections, (ii) catheters are sources of systemic and local bacterial and viral infections, and (iii) artificial breathing systems are responsible of pulmonary infections. For a lead into the extensive literature on nosocomial infections see Arnow *et al.* (1993), Scheckler *et al.* (1998), Lucet (2000), Lemaitre and Jarlier (2000), Korinek (2000), and Joly and Astagneau (2000).

The frequency of nosocomial infections in France is typical of industrialized countries, with about 7% of hospitalized patients developing a nosocomial infection. In other countries it ranges from from 5% to 12%. In the United States, more than 2 million cases of nosocomial infections have been reported, leading to about 80,000 deaths and to 8000 additional days in hospital for 1000 infected patients, all at a cost of $US5 billion dollars in 1985 (Wenzel 1985; Haley 1991).

In this section on human sickness, we can illustrate the Machiavellianism of pathogens exploiting a human health problem: *drug addiction*. Many pathogens from viruses to worms use insect as vectors in order to infect new hosts. In the same way, we could do a comparison with medical tools that pathogens use as vectors. The best and saddest example could be the syringe which represents a wonderful vector for pathogens to pass from host to host. A non sterilized syringe represents a very efficient ecosystem exploited by many pathogens. One terrible recent example was provided by HIV and drug addiction. The HIV virus can be passed through different venous injections from different individuals sharing the same syringe. Unfortunately, this problem does not only occur within drug addicts; nurses in hospital have been contaminated by this parasite when taking a blood sample from infected patients. AIDS is one of the major diseass at the beginning of the twenty-first century, and we have to keep in mind the public scandal which occurred in France at the end of the twentieth century with contaminated HIV blood. Indeed, haemophiliacs need recurrent blood transfusions, and before the use of warmed blood elements, many of them were infected by HIV through the needle which served to transfuse them (Fig. 10.5). Most of them died, and this scourge continues to kill a lot of people in the world.

### 10.4.2 Ageing

Modern humans live longer, at least in industrialized countries, where the number of the elderly is rapidly increasing (Morris and Potter 1997). This leads to an increasingly large group of hosts ripe for exploitation. For example, ageing results in senescence of the gut-associated lymphoid tissue, and decreasing in gastric acid secretion (Feldman *et al.* 1996). The consequences of these physiological disturbances lead to an increase of susceptibility to pathogens. Indeed, as a low pH of the stomach represents an important barrier to entry of enteric pathogens, reduction in gastric acidity can increase the susceptibility to infection by these pathogens (Morris and Potter 1997). The communal living environment of some elderly, exacerbated by problems such as incontinence, further creates an habitat in which enteric and food-borne pathogens can spread rapidly (Benett 1993). In a study between 1968 and 1979 in the United States, Blaser and Feldman (1981) showed that the frequency of *Salmonella* bacteremia increased dramatically in the elderly compared with other age groups. *Salmonella* infections increase the risk of death, and elderly are often immunocompromised and they are assisted by a large cohort of medications. This treatment undeniably leads to the selection of drug resistance in many categories of pathogens. The grouping of patients in 'elderly care homes' may constitute production units of 'pathogen resistant ecosystems', which will represent a new and complex public health problem as the population ages. We expect that pathogens produced in these ecosystems, many of which may be drug resistant, will spill out to attack other age groups of the population (i.e. babies, toddlers, and children)? To our knowledge, policies have not yet considered this ecological problem. It is well known in evolutionary parasitology that an increase in the number of susceptible hosts can have dramatic consequences for the spread of pathogens in the whole population (Bird Influenza Virus below).

### 10.4.3 Death

Even if human have largely improved health care and have lengthened life expectancy, particularly in industrialized countries, death always occurs. Humans worship death and we can observe a lot of flower vases in some cemeteries. These vases can constitute ideal ecosystems for the development of different mosquito species larvae. In a very interesting paper, Lancaster *et al.* (1999) related the invasion of *Ae. albopictus* into an urban encephalitis focus, where flower vases ecosystems found in cemeteries could play an important role. Elsewhere, O'Meara *et al*. (1995) investigated the competition between *Aedes aegypti* and *Ae. albopictus* in a US cemetery named Rose Hill, and showed that until the summer of 1990, only *Ae. aegypti* inhabited vases at Rose Hill. *Ae. albopictus* was first collected that summer and by 1994, had become the most prevalent species (i.e. greatest percentage of vases occupied). Juliano (1998) sampled three cemeteries in Southern Florida where *Aedes* inhabit water-filled stone cemetery vases. From manipulative field experiments, he analysed the mechanisms involved in the competition between *Ae. aegypti* and *Ae. albopictus*. He showed that, at least at the three sites tested, *Ae. albopictus* was more competitive than *Ae. aegypti*. This invader superiority was attributed to better resource acquisition in these ecosystems. Knowing that these mosquito species are vectors of different pathogenic viruses, these cemetery ecosystems can play an undeniable role in mosquito transmitted diseases, at least in the area concerned.

### 10.4.4 Surgical progress

Like different mechanical parts of our car, many organs of our body can be replaced by better functioning parts. Xenotransplantation is the graft (i.e. skin, tissue) or the transplant (i.e. organ) into humans of tissue or organs from animals (Wadman 1996). Xenotransplantation seems a very real possibility now that the generation of transgenic pigs as potential organ donors for humans has been achieved. Baboons are also likely to be used, especially so for bone marrow grafting. But, both baboons and pigs may silently harbour a great variety of viruses belonging mostly but nor exclusively to the *Herpesviridae*, *Retroviridae*, and *Papoviridae* families. All these viruses are potentially able to infect deeply immunocompromised patients. This may lead to the emergence of deadly viral infections, the so-called 'xenozoonosis', among the recipients and/or the general population (Chastel 1996). Indeed, the majority of viruses that emerged during these last 30 years displayed a zoonotic (mainly simians) origin (Morse and Schluederberg 1990). For example, the *Herpesvirus simiae* , specific to asian cerpothitecicidae of the genus Macaca and where it seems to be a largely benign virus, becomes very dangerous for human when injected by biting or by accidental injection by infected syringe or needle (Artensein *et al.* 1991). DNAs represent a well-established molecular species ecosystem where a large number of selfish DNAs (including number of viruses) are evolving and pass through generations. Each species harbours its own selfish DNAs, and they constitute, for example, a large part of the human genome (De Meeûs *et al.* 2003). Therefore, transmission of virus through grafts is confirmed, and allografts were reported to be at the origin of primary infections by, at least, the cytomegalovirus, Epstein–Barr virus, VIH, and hepatitis C (Chastel 1998). We could be thus confronted to a new virulent variant of these viruses or to a genetic matching between close human and simians viruses (i.e. Herpesvirus, Retrovirus). We cannot exclude the possibility of an outbreak of a genetic chimera between human and animal viruses, or of the 'complementation' of a defective virus. Xenotransplants can come from transgenic animal in order to avoid graft rejection by human recipient. 'I view xenograft tissues as essentially very complex vectors for shuttling new viruses in humans' (Allan 1995).

Prostheses are another example of surgical progress. The addition of exogenous material leads to the establishment of new ecosystems inside the body (Fig. 10.5). These new niches can be colonized by pathogens. For example, prosthetic joints, prosthetic implants, and vascular prosthetic materials are a 'nest' for many pathogens such as group C *Streptococcus*, *Staphylococcus epidermidis, Staphylococcus aureus*, *Mycobacterium tuberculosis, Histoplasma capsulatum* (Gillespie 1997; Kleshinski *et al.* 2000).

### 10.4.5 Hygienic progress

Polio was almost unknown until the dramatic epidemics that terrorised the developed countries in the twentieth century. This terror led to irrational responses, such as aggression to immigrants of shantytowns. Before hygiene was common, infants were safely immunized against polio by maternal milk. However, once hygiene standards were high in developed countries, individuals were first exposure to polio occured at older ages, when the clinical complications are likely. Thus, changing hygiene habits has allowed the poliovirus to the exploitation of new habitats, with dramatic consequences for the host (Schlein 1998; Seytre and Schaffer 2004).

Medical progress has led to women being attacked by pathogens due to menses (i.e. tampon use) and contraceptive methods (i.e. Intra-Uterine contraceptive Devices—IUDs or coil). The insertion of tampons or coils in female genital systems represents a new opportunity for pathogens. Urinary tract infections of women are common, and a source of considerable expense. The possibility that tampon usage is a risk factor for recurrent urinary tract infection has not been studied in detail, but it has been associated with bacterial vaginosis. The tampon may facilitate the spread of bacteria from the vagina to the urethra and bladder (Doran 1998). Elsewhere, it was thought that IUD infections spread through lymphatic canals to produce a perisalpingitis similar to that of postabortal or postpartum infections. Even if it was not demonstrated that IUDs are directly responsible of these infections, their role remains to be determined (Schwarz 1999).

## 10.5 Human need to eat!

Life, reduced to its simplest expression, could be caricatured through two main functions for each individual in each plant and animal species: survival and reproduction. Food is the fuel for this, but eating is not without risk. Our new food habitats have opened up new niches for many pathogens.

### 10.5.1 Tinned food

A major problem to which human populations were and are still confronted is to food preservation. Different methods of food conservation were developed in human societies, but two of them are the more used, at least in industrialized countries: tinned and cooled food.

Listeriosis, a serious infection caused by food contaminated by the bacterium *Listeria monocytes,* has recently been recognized as an important health problem in the United States and European countries (Lorber 1997; Silver 1998). Listeriosis is a disease that is enhanced by alimentary progress. This bacterium is frequently found in soil and water, and becomes pathogenic for human when ingested at high densities. Naturally contaminated food never presents dangerous densities of this bacterium, but this pathogen experiences an increase of its population demography at low temperatures. Refrigerators constitute a favourable ecosystem for these bacterial populations where they can reach the infectious quantity dose for human.

Human brucellosis or 'Bang's disease' which was discovered a century ago remains poorly known and difficult to treat. Pathogens responsible for the disease are bacteria belonging to the genus *Brucella,* a strictly aerobic coccobacillus. *Brucella* can enter the body via the skin, respiratory tract, or digestive tract. Once there, this intracellular organism can enter the blood and the lymphatic canals where it multiplies inside the phagocytes. The disease spreads through animal contacts or contaminated food, especially cheese! Cheese permits milk to be preserved, and several hundred of people are infected each year in France. The disease causes nausea, meningitis, hepatitis, and miscarriages (Straight and Martin 2002).

Botulism is a food-borne disease; the agent of the disease is an anaerobic bacteria *Clostridium botulinium* with a spore-forming rod that produces a neurotoxin. The spores are heat-resistant and can survive in foods that are incorrectly or minimally processed. The disease is caused by the neurotoxin produced by *C. botulinium* that is present in the food (Smith and Sugiyama 1988). The organism and its spores are widely distributed in nature (e.g. cultivated and forest soils, coastal waters, gut of fish and mammals, gills and viscera of crabs and other shellfishes), but the types of foods involved in botulism vary according to regional food preservation and eating habits. Almost any type of food that is not too acidic (pH above 4.6) can support the growth and toxin production of *C. botulinium*. Botulinal toxin has been evidenced in a considerable variety of foods, such as canned corn, soups, ham, sausage, smoked, and salted fish. The incidence of the disease is low, but the mortality is high if not immediately and properly treated.

### 10.5.2 Intensive farming

High intensity farming has been very good at producing large amounts of cheap food, but has also opened up new parts of the human–pathogen ecosystem. Salmonellosis is one of the most common food-borne illness causing enteric infections in developed countries. The pathogens are bacteria (*Salmonella)* which consist of a range of very related bacteria, many of which are pathogenic to humans and animals (Thorns 2000). The strains which are implicated in the diseases are generally different serovars of *Salmonella enterica* that caused diseases of the intestine, as suggested by their name. For example, *S. enterica* serovar typhi is the causative agent of typhoid fever. It is very common in developing countries, where it causes a serious and often fatal disease. *Salmonella* bacteria primarily invade the wall of the intestines causing inflammation and damage. Infection can spread in the body through the bloodstream to other organs such as liver, spleen, lung, joints, placenta, or foetus, and the membrane surrounding the brain. Toxic substances produced by bacteria can be released and affect the rest of the body. *Salmonella* has evolved mechanisms to escape our immune system (Olsen *et al*. 2001). In the liver, bacteria can grow again, and be released back into the intestine. *S. enterica* serovar enteritidis has become the single most common cause of poisoning in the United States in the last 20 years. *Salmonella* are found in contaminated food, with recent increases in the number *S. enteritidis* a consequence of mass production chicken farms. When tens or hundreds of thousands of chickens live together, die together and are processed together, a *Salmonella* infection can rapidly spread throughout the whole food chain, and hence *Salmonella* can be rapidly dispersed among million of people.

Changed farming practices have also led to new opportunities for non-food-borne human pathogens. In the Asillo zone, located at a very high altitude of 3910 m in the Peruvian Altiplano, high levels of human infection by *Fasciola hepatica* (i.e. the liver fluke) were linked to man-made irrigation zones. Man-made irrigation areas are built only recently to which both liver fluke and lymnaeid snails (i.e. the first intermediate host of the liver fluke) have quickly adapted. Such man-made water resources in high altitude of Andean countries dangerously inflate the parasitic risk, because the lack of drinking water and running water inside dwellings forces inhabitants to obtain water from irrigation canals and drainage channels (Esteban *et al.* 2002). Elsewhere, it is largely recognized that a significant amount of malaria transmission in Africa and Madagascar is due to human activities. Modifications of the environment resulting from land use often create or alter habitats for mosquito vectors, and may indirectly affect parasite development rates, and the lifespan of mosquito (Service 1991; Ault 1994; Coluzzi 1994).

Marine ecosystems are also on the danger list due to pollution and aquaculture which modify all parameters of natural equilibrium. The organic pollution exerts both oppressing and stimulating influences, with industrial waste depressing the formation and function of parasite systems. Some current aquaculture practices are environmentally benign, others, especially those in some of the fastest growing portions of the industry, can degrade water quality, transmit diseases to wild populations, disrupt marine ecosystems, and spread invasive parasites and pathogens species (Maender 2002; Young 2003, see also Chapter 7).

We think that it is now important to present a current very deep problem which links public and veterinary health. At the time we are writing this chapter at the beginning of 2004, public opinion and World Health Organization is strongly focused on two animal zoonotic diseases which have arisen recently, particularly in Asia. 'The terror of the unknown is seldom better displayed than by the response of a population to the appearance of an epidemic, particularly when the epidemic strikes without apparent cause'. This quote from Kass (1977) concerned the emergence of legionnaires' disease, and it well describes public response to the recent emergence of an atypical pneumonia named as Severe Acute Respiratory Syndrome (SARS). SARS was first recognized in the Guangdong Province of China, in November 2002. Subsequent to its introduction in Hong Kong in mid-February 2003, the virus spread to more than thirteen countries and caused disease across five continents. According to the World Health Organisation (WHO) in January 2004, a cumulative total of eight thousand SARS cases with more than 800 deaths had been reported. A novel coronavirus was identified as the human etiological agent of SARS, causing a similar disease in cynomolgous macaques (Peiris *et al.* 2003). Because cases where SARS was first diagnosed occurred in restaurant workers handling wild mammals and exotic food, scientists focused on wild animals recently captured and marketed for consumption. Their work provides evidence that SARS shifts from animals to humans, possibly frequently (Guan *et al.* 2003). Elsewhere, Stanhope *et al.* (in press) have confirmed this host shift, because they could identified that SARS-CoV has a recombinant history with lineages of types I and III virus, concomitant with the reassortment of bird and mammalian coronaviruses. Food marketing trades could thus provide the opportunity animal ScoV-like viruses to amplify and to be transmitted to new hosts, including humans. Even if the natural reservoir is not clearly identified, market animals (civets, raccoon dog, and ferret badgers for example) might be compatible hosts that increase the opportunity for transmission of the virus to humans. Markets constitute thus man-made ecosystems favourable to a new set of pathogenic agents. Thousand of these aforesaid animal species have been slaughtered as a preventive measure. But, is it the most efficient solution?

The Avian Influenza outbreak which is currently raging in south east Asia is related to SARS only in demonstrating how the so-called zoonotic diseases in animals can become a threat to human health. It clearly illustrates how man-made intensive farming ecosystems can represent spring boards for new pathogens. Highly pathogenic avian influenza A viruses of subtypes H5 and H7 belong to the Orthomyxoviridae family, and are the causative agent of fowl plague in poultry. Type A influenza viruses are those which affect humans, but also pigs, horses, and some marine mammals (whales and seals). There are three types (A, B, and C) of influenza viruses, depending on the antigens detected in the virus capsid. The antigens that are used to recognize the different viruses belong to two kinds of glycoproteins, hemagglutinin (HA), and neuramidase (NA). There are fifteen different HA antigens (H1 to H15) and nine different NA antigens (N1 to N9) for influenza A. Human disease historically has been caused by three subtypes of HA (H1, H2, and H3) and two subtypes of NA (N1 and N2), which were responsible for million of deaths around the world, through different pandemics. All known subtypes of influenza A can be found in birds, but only subtypes H5 and H7 have caused severe disease outbreaks in bird populations (Fouchier *et al.* 2004). Figure 10.6 illustrates the life cycle and possible routes taken by these pathogens; migratory birds and waterfowl are thought to serve as reservoir hosts for influenza A virus in nature (Murphy and Webster 1996), but waterfowls generally do not suffer from the disease when infected with avian influenza.

The viruses easily circulate among birds worldwide as they are very contagious for birds, and can be deadly, particularly for domesticated birds like chickens and turkeys. The disease spreads rapidly within poultry flocks and between farms. Direct contact of domestic flocks with wild migratory waterfowls has been implicated as a frequent cause of epidemics, and live bird markets are implicated in the spread of the disease. Avian influenza A virus may initiate new pandemics in humans because the human population is serologically naive toward most HA and NA subtypes (Fouchier *et al.* 2004). Until recently, it was considered that pigs were the obligate intermediate host for transmission of these virus types to humans (Yasuda *et al.* 1991; Webster 1997, Fig. 10.6). Past influenza pandemics have led to high levels of illness, death, social disruption and economic loss (Fig. 10.6), but in general, avian influenza viruses do not replicate efficiently or cause disease in humans (Bear and Webster 1991). However, the highly pathogenic influenza virus subtype H5N1, first documented in Hong Kong in 1997, was transmitted in 2003 from bird to humans, and was responsible for a very serious outbreak, the seriousness of which is still unclear at time of writing. Nevertheless, this epidemic is an illustration of how intensive poultry farming ecosystems (i.e. increasing host density to increase food productivity) are responsible for these new outbreaks, at least in the countries where this influenza H5N1 virus finds its origin (Fig. 10.6).

### 10.5.3 But how can viruses of high and low virulence coexist?

This is a case of a classical question in evolutionary biology: what conditions are required to maintain polymorphism (genetic and/or phenotypic variability), in space and time, within and among populations of all kind of species? Literature on the topic is rich (e.g. De Meeüs *et al.* 1993 and 1995; De Meeüs and Renaud 1996 for examples). We will not attempt here to make a review on this topic, but in their paper published in 2004, Boots, Hudson, and Sasaki developed a theoretical model to envisage the conditions for maintenance and spreading of low versus high virulent type of pathogens (e.g. viruses). The model clearly shows that large shifts in pathogen virulence are related to host population structure (i.e. demography and genetic). Poultry flock structures managed by humans represent new ecological and demographic configurations for the evolution and emergence of new virulent pathogen strains, which enter more and more in contact with human populations.

> Given the increasing long-distance movement of people and domestic animals around the modern world, our results have important implications for emerging diseases in general. Recombination among avirulent (and therefore possibly previously undetected) strains of viruses and other pathogens may produce new virulent strains that may spread through vertebrate host populations because they have shifted to a new evolutionary stable state. (Boots *et al*. 2004)

What is happening with the current influenza outbreak has been clearly predicted by theoretical population biology models. This stresses the need there is that such approaches should be taken now into account in future public and veterinary health control.

Pathogens and parasites can use different man-made ecosystems to spread and threaten human's health. Indeed, as illustrated in the case of influenza virus, the pathogen can first exploit the intensive farming processes (i.e. food production) in order to emerge and rapidly infect humans (Fig. 10.6), and second, hitch-hike the man-made 'travel ecosystems' (i.e. plane, boat, or train) to spread among populations and become pandemic (Fig. 10.2).

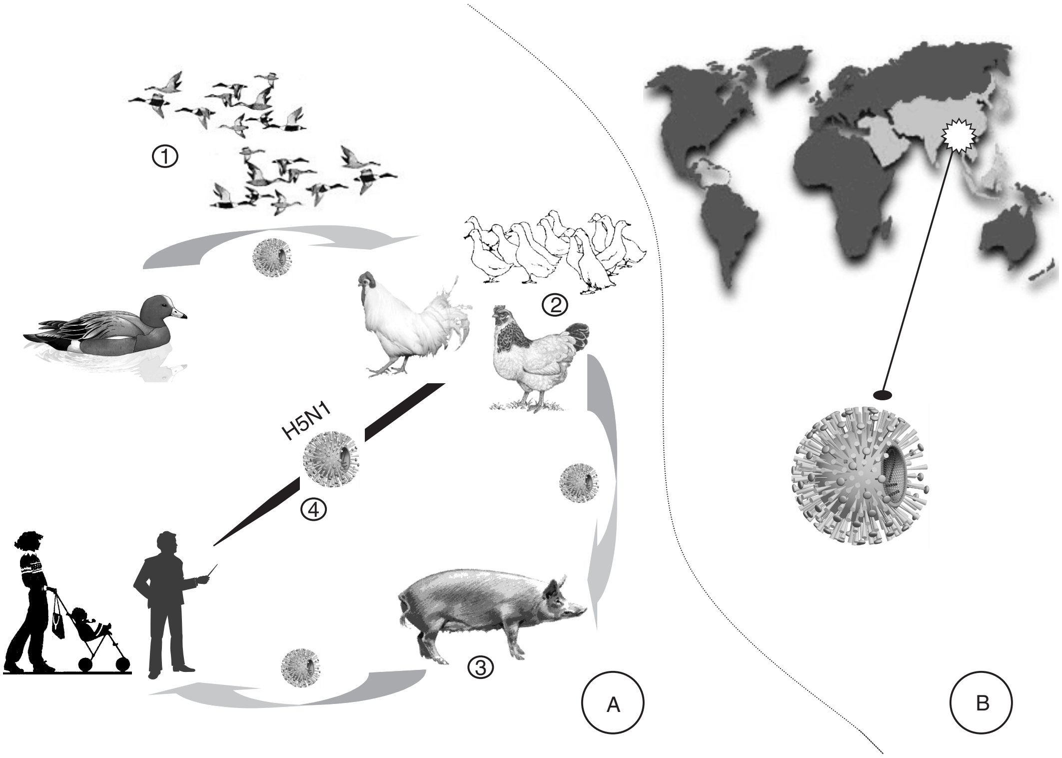

**Figure 10.6** Avian influenza: (a) infecting routes and (b) geographical outbreaks in 2004 and the Avian influenza virus.

*Notes*: (a) Waterfowl are thought to be the natural reservoir of Avian influenza A viruses (1). Viruses replicate in the intestines as well as the respiratory tract of birds.

During migratory processes of birds, poultry flocks become infected when contacts between them and naturally infected birds are established. In the 2004 outbreak, very large quantities of virus were excreted in the faeces of infected farming birds, resulting in widespread contamination of the environment (2). This presence of numerous H5N1 subtype created one of the most important risks for human exposure and subsequent infection.

Some findings support the hypothesis that the pig was a 'mixing vessel', able to produce new virus subtypes by genetic reassortment that can infect humans. Until recently, it was supposed that pigs were obligatory intermediate hosts for human infections (3). Nevertheless, epizoonose of Avian Influenza in different Asian countries in 2004 confirmed the possibility of direct human infection from birds, via the H5N1 Influenza virus subtype (4). Indeed, if Avian Influenza viruses lack the receptors needed to infect mammals efficiently, the infection of humans observed during the 2004 and two previous H5N1 outbreaks demonstrates that transmission from birds to mammals, including humans, can occur despite the lack of receptors. (b) The influenza outbreak in 2004 affected more than ten Asian countries.

From the 20 February 2004, Thai authorities reported that 147 patients were admitted in the hospital since the beginning of the zoonotic outbreak, and eight died. The main problem for all countries around the world is that this Asian influenza outbreak became pandemic. There were three pandemics in the twentieth century. All of them spread worldwide within one year:

- 1918–19: 'Spanish flu' [H1N1]: 20–50 million people died worldwide. Nearly half of those who died were young, and healthy adults.
- 1957–58: 'Asian flu' [H2N2]: First identified in China, the Asian flu spread in the United States and caused about 70,000 deaths.
- 1968–69: 'Hong Kong flu' [H3N2]: First identified in Hong Kong, the virus spread in the United States and caused about 35,000 deaths.

More than seven billion poultry were slaughtered in infected Asian countries which suggest the farming of billions of bird in this geographic area. This demographic situation is favourable for (i) the emergence and the spread of highly virulent strains of pathogens within and between stock breeding, and (ii) the transfer between host species, including humans.

In front of such processes, we do not know which zoonoses will become important in public health in the future, and we must be vigilant over the emergence of new pathogens.

## 10.6 Concluding remarks

It was not our intention to produce an exhaustive review of all situations where pathogens and parasites found new infectious routes associated with human customs, development, and technology, and we are conscious of many gaps (for instance, Western beds provide an excellent ecosystem for ectoparasites such as lice, fleas, ticks, sarcoptes, bed bugs, etc.). But our goal was to present some aspects which we believe will become more and more topical given current trends. We believe future key questions will be how societies could and should manage (i) population ageing, (ii) need of food access, (iii) earth demographic growth, (iv) people density and urbanization, (v) new technical and medical tools. This is a challenge for which we must get prepared. Pathogens are everywhere and can adapt to a wide panel of environments (even computers). Indeed, we may be just at the beginning of the evolution of pathogens and parasites evolution in our biosphere ecosystem.