Introduction

Some optimistic scientists of the 20th century imagined that it might be possible with interventions such as antimicrobials and vaccines to close the book on infectious diseases. Unfortunately, infectious diseases remain among the leading causes of death worldwide, despite remarkable advances in medical research and treatments during the 20th century. Some of the main reasons why infectious diseases couldn't and cannot be eradicated are: (1) emergence of new infectious diseases; (2) re-emergence of old infectious diseases; and (3) persistence of intractable infectious diseases.

Emerging infectious diseases (EIDs) are diseases that (a) have not occurred in humans before (this type of emergence is difficult to establish and is probably rare); (b) have occurred previously, when they affected only small numbers of people in isolated places, but have emerged in new populations due to human behaviors or modifications to natural habitats (AIDS,
Ebola hemorrhagic fever); or (c) have occurred throughout human history but have only recently been recognized as distinct diseases due to an infectious agent (Lyme disease, *Helicobacter pylori*). Applied to animals, this definition includes newly recognized diseases such as Nipah virus infection of swine, old diseases that acquire new properties such as enteritis caused by multidrug resistant *Salmonella enterica typhimurium* DT104, and well-known diseases that appear in a new geographic region such as the recent introduction of West Nile virus (WNV) into North America.

Environmental changes are related to the emergence of many infectious diseases. For example, Lyme disease, Hantavirus pulmonary syndrome (HPS), and Lassa fever all emerged when humans began encountering the insect vector (for Lyme disease) or rodent host (for HPS and Lassa fever) of the causative agents in greater numbers than ever before. The Legionnaire disease emerged as a result of the changing technologies (air conditioning systems).

Emergence may also be used to describe the reappearance (or „reemergence”) of a known infection after a decline in incidence: **re-emerging infectious diseases** are diseases that once were major health problems globally or in a particular country, and then declined dramatically, but are again becoming health problems for a significant proportion of the population, usually due to microbiological adaptation and change; this includes previously-identified microorganisms exhibiting new patterns of antimicrobial drug resistance and pathogenic properties. Examples are West Nile virus in the Western hemisphere, Monkey pox in the United States, dengue (rebounding in Brazil and other parts of South America and working its way into the Caribbean).

**Tuberculosis** has re-emerged due to evolution of the causative bacteria. The pathogen has acquired resistance to the antibiotics used to treat tuberculosis (either through mutation or genetic exchange), and the long-term use of antibiotics (both within one individual and across the population) has selected for the pathogen’s proliferation.

**Malaria** has also become drug resistant, and the vector mosquito has acquired resistance to pesticides as well. The re-emergence of diseases such as diphtheria and whooping cough (pertussis) is related to inadequate vaccination of the population (when the proportion of immune individuals in a population drops below a particular threshold, introduction of the pathogen into the population leads to an outbreak of the disease).

**Deliberately emerging diseases** are those that are intentionally introduced. These are agents of bioterrorism, the most recent and important example of which is anthrax.

Causal factors contributing to the emergence and re-emergence of infectious diseases include: economic development and land use, human population growth (resulting in human encroachment on wildlife habitats), human behavior (contributing to emerging zoonoses through wildlife trade and translocation, live animal and bush meat markets, consumption of exotic food, development of ecotourism) and international travel and commerce.

Travelers are an important factor in the global dissemination of EIDs due to the increased frequency and speed of both local and international travel. International travel related to tourism, commerce, relief efforts, work and study means that humans are increasingly in direct or indirect contact with previously isolated, remote populations and ecosystems. Travelers returning home may harbor exotic infections that are still in the incubation stage. Thus, infections acquired during travel may be transmitted to others in the community by returned travelers before the diagnosis of disease can be made. In addition to international travelers, imported animals, birds, foods and insects from abroad, especially from tropical developing countries, can also pose a significant threat to the public health of receiving countries by serving as means of transportation for pathogens into new geographical areas. Human behavior contributes to emerging zoonoses through wildlife trade and translocation, live animal and bush meat markets, consumption of exotic food, development of ecotourism and ownership of exotic pets, as noted by Chornel et al (2007). (1)

Almost all of these factors reflect in some measure the encroachment of human civilization on the environment and on the microbial species that inhabit our environment. The human species lives in a delicate balance with microbial species; there is an ever-present tension between the two. If we perturb this balance, microbes almost always figure out a way to counterbalance the effect. Lyme disease emerged as we developed land near forests; changes in social structure and human behavior contributed to the emergence of HIV/
AIDS; and monkey pox emerged in the United States when people started adopting exotic pets such as Gambian rats.

**Zoonoses**

Emergence of new zoonotic pathogens seems to be accelerating for several reasons: global human and livestock animal populations have continued to grow, bringing increasingly larger numbers of people and animals into close contact; transportation has advanced, making it possible to circumnavigate the globe in less than the incubation period of most infectious agents; ecologic and environmental changes brought about by human activity are massive; and bioterrorist activities, supported by rogue governments as well as organized amateurs, are increasing, and in most instances the infectious agents of choice seem to be zoonotic. It is important to note that most emerging diseases of humans are zoonotic (Taylor, Latham, and Woolhouse 2001). (2)

According to a comprehensive literature review performed by Taylor et al. (2001) at the Centre for Tropical Veterinary Medicine at the University of Edinburgh, 1415 species of infectious organisms known to be pathogenic to humans were identified. The majority of these (61%) were zoonotic infections. Of the 175 pathogenic species associated with diseases considered to be “emerging”, 135 (75%) were zoonotic. An updated literature survey from the Centre for Infectious Diseases at the same institution (University of Edinburgh) was published in 2005 by Woolhouse and Gowtage-Sequeria. This study identified 1407 species of human pathogens, 58% of which were zoonotic. Of the total, 177 were regarded as “emerging” or “re-emerging” pathogens. The authors noted that although zoonotic pathogens constitute a significant source for emerging and re-EIDs, only a small minority of them would prove capable of causing major epidemics in the human population— but the H1N1 influenza strain could prove to be an exception. (3)

Two transmission patterns have been described for transmission of pathogens from wild animals to humans by Bengis et al. (2004). One pattern consists of rare events when direct animal-to-human transmission of an animal pathogen occurs, but then direct human-to-human transmission maintains the infection in the human population for a limited time or permanently (human immunodeficiency virus (HIV), influenza A, severe acute respiratory syndrome (SARS), Ebola virus). The secondary pattern of transmission is where human infections with animal pathogens result from repeated episodes of direct animal-to-human transmission or of repeated vector-mediated animal-to-human transmission and the infections are not usually propagated by human-to-human transmission (rabies, Nipah virus, West Nile virus, Hantavirus, Lyme borreliosis, plague, tularemia, leptospirosis, ehrlichiosis). (4)

**Vectored diseases**

Numerous arboviral outbreaks during the past decade have demonstrated that arthropod-borne pathogens continue to be significant public and animal health threats. Contributing to the emergence of zoonotic diseases is the capacity of microorganisms and viruses to adapt to extremely diverse and changing ecologies. When ecosystems are altered, disease problems of humans and animals follow. Population movements and the intrusion of humans and domestic animals into arthropod habitats have resulted in emergent disease episodes (example: the emergence of yellow fever when humans entered the Central American jungle to build the Panama Canal). An important ecologic factor contributing to arthropod-borne zoonotic viral disease emergence is uncontrolled urbanization. The mega cities of the tropics, with their lack of sanitary systems, serve as incubators for emerging zoonoses. Fortunately, scientific research, including advances in rapid detection of this diverse group of pathogens, has also been progressing. While arboviruses are likely to continually emerge and re-emerge, improved scientific technologies and approaches will hopefully make each future epidemic less likely to occur.

Emerging mosquito-borne viral illnesses, endemic in rural areas of tropical South America, such as Mayaro and Oropouche virus infections were found in Brazilian woodcutters who cleared the Amazonian forest in recent years, pointing out that deforestation and settlement of new tropical forest are also risk factors for the emergence of this kind of infections. (5)

Increased long-distance air travel facilitates the movement of infected persons and exotic arthropod vectors around the world. The introduction of the Asian mosquito *Aedes albopictus* to the United States in water contained in used tires represents an unsolved problem of this kind.
Some arboviruses cause sporadic outbreaks in areas where they have previously been documented. Recent examples of this re-emergence phenomenon include yellow fever virus (YFV) epidemics in South America, as well as outbreaks of Rift Valley fever in parts of Africa.

A large outbreak of Chikungunya virus (CHIKV) emerged in 2005 in the Indian Ocean islands of Mayote, Mauritius, the Seychelles and particularly in Reunion Island where 35% of 770,000 inhabitants were infected in 6 months. The virus is transmitted to human by the bite of infected *Aedes* and *Culex* mosquitoes, including the day-time biting. Circulation of this virus has been documented in Madagascar, India and Sri Lanka. The disease has been reported among travelers returning from endemic areas as a cause of acute illness characterized by sudden onset of fever, chills, headache, nausea, vomiting, joint pain with or without swelling, low back pain and rash, similar to the symptoms of dengue fever. (6,7)

Relatively recent dengue fever virus outbreaks in the Hawaiian Islands and Ningbo, People's Republic of China, were linked to importation of the virus in infected travelers from Samoa and Thailand, respectively, and the presence of *Aedes aegypti* mosquitoes in the local environment that promoted subsequent human-to-human spread in the local populations.

Another type of emergence occurs when a virus not only expands to novel geographic regions, but also changes its pattern of illness as it moves. A very specific and well-known example of this scenario involves West Nile virus (WNV). WNV is now considered enzootic in North America, causing seasonal human outbreaks of neuroinvasive disease after being introduced 10 years ago; disease in both humans and equines is also documented in the original geographic range of Africa and Europe, where prior to the 1990s, the pathogen was considered to be a minor threat.

Malaria is considered to be an emerging disease because it is undergoing movements into more temperate areas; there have been recent changes in the distribution of a number of potential malaria vectors along Europe's eastern borders and the development of trans-Saharan routes that potentially bring both the disease and its vectors closer to her southern borders. The social, economic, and human toll exacted by malaria globally is widespread and profound. Each year, acute malaria occurs in >300 million people and results in >1 million deaths worldwide. Most of these deaths occur in young children who live in sub-Saharan Africa. (8) Whereas malaria appeared to have been almost eradicated in the 1960s, re-emergence of this has occurred over the following decades due to many factors, including parasite resistance to antimalarial drugs, decreased effectiveness of insecticides used for mosquito control and changes in social/financial infrastructures necessary for treatment and prevention programs in highly endemic areas. Recently a new strain of *Plasmodium*, longtime misdiagnosed as *P. malariae* has been discovered; it is called *Plasmodium knowlesi* and human infections with this parasite are widely distributed across Malaysian Borneo and extend to Peninsular Malaysia. A study carried out by Cox-Singh et al. which analysed through PCR methods 960 samples from malaria patients hospitalized in Sarawak, Malaysian Borneo from 2001-2006 revealed that 266 (27.7%) were infected with *P. knowlesi*. These had been misdiagnosed by microscopy, with 228 (85.7%) being reported as *P. malariae* but only four (0.4%) containing *P. malariae* DNA. Four fatal cases were identified among these patients, all diagnosed as *P. knowlesi* DNA. (9)

**Airborne diseases**

Pathogens that are transmitted directly or indirectly through droplet nuclei disseminated in the air have a high potential for rapid global spread. Microorganisms spread by this mode include avian (H1N1) influenza virus, recently the new strain of H1N1, extremely drug-resistant tuberculosis (XDR TB) tuberculosis (TB), severe acute respiratory syndrome (SARS) Corona virus.

It is important to bear in mind that respiratory diseases are closely linked to overcrowded places, whenever a susceptible person is in close proximity to an infectious person.

Direct transmission (ex. from contaminated fingers to mucosal surfaces) is also an important route of transmission of respiratory pathogens.

Given the high risk of transmission of airborne pathogens, aggressive prophylactic measures need to be taken, such as vaccines, personal protection equipment, reliable screening tests and, if available, medication for prophylaxis and treatment.

Mandatory screening and isolation of infected individuals should play an important role in preventing the transmission of airborne infections. The general believe is that airplane cabins provide a unique environment for transmission of
air-borne infectious agents. Nevertheless, human factors rather than strictly environmental factors promote transmission of infectious diseases during long airplane flights.

**Food - and water - borne diseases**

Emergence in food borne diseases has the same causes as emergence in other infectious diseases: changes in human behavior, industry, and technology; the shift toward a global economy; microbial adaptation through natural selection. The most important emerging food-borne zoonotic pathogens include Salmonella species (multidrug-resistant *Salmonella typhimurium* DT 104, *Salmonella enteritidis* (SE), *Campylobacter* species, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Toxoplasma gondii* and *Cryptosporidium parvum*.

Some foodborne diseases are well known, but are emerging because they have recently become more common. For example, within the past 25 years there has been an increase in the incidence of salmonellosis outbreaks on many continents. In Europe SE has become the predominant strain and is related to consumption of poultry or eggs.

Other emerging food borne pathogens are new microorganisms or have been only recently documented as transmitted through food: *Escherichia coli* serotype O157:H7 was first described in 1982 and has been since a major cause of bloody diarrhea and acute renal failure. Outbreaks of infection, generally associated with beef, have been reported in Australia, Canada, Japan, United States, in various European countries, and in southern Africa.

*Listeria monocytogenes* (Lm) is considered emerging because the role of food in its transmission has only recently been recognized. Outbreaks of listeriosis have been reported from many countries, including Australia, Switzerland, France and the United States. Two recent outbreaks of *Listeria monocytogenes* in France in 2000 and in the USA in 1999 were caused by contaminated pork tongue and hot dogs respectively.

Norwalk virus and Norwalk-like viruses are also considered emerging agents; they cause mild to moderate disease with gastrointestinal symptoms. Outbreaks have been associated with the consumption of contaminated drinking water and food, especially raw or undercooked shellfish.

Prevention of food-borne and water-borne diseases involves personal precautions and further development and implementation of food safety programs. The Food and Agriculture Organization (FAO)/ World Health Organization (WHO) have recently established a new framework of microbiologic risk assessment to guide efforts of member countries in reducing pathogen contamination at relevant points in food production chains. The appropriate international organizations, with the assistance of their members, need to elaborate a plan of action for global food safety control to encourage and assist countries in developing acceptable and efficient food control systems, while simultaneously indicating the minimum or basic parameters or requirements for such purpose.

**Travel to visit friends and relatives**

The visiting friends and relatives (VFR) market appears to be a widely-accepted form of tourism. It involves travel with the purpose of visiting friends and/or relatives. However, as might be the common perception, it does not necessarily mean that VFR travellers share the living accommodations of their friends and/or relatives. The term “VFRs” generally refers to immigrants from a developing country to an industrialized country who subsequently return to their home countries for the purpose of visiting friends and relatives.

According to the World Organization of Tourism, from the 800 million international journeys in 2005, 26% had as target VFR or pilgrimages.

In many countries immigrants now constitute more than 20% of the population. Immigrants increasingly travel to their place of origin to VFR, and VFR travel is now a major component of the 800 million international journeys that take place annually. VFRs are at increased risk of travel-related diseases, such as malaria, hepatitis A and B, typhoid fever, rabies, tuberculosis, and the diseases normally preventable by routine childhood immunization as compared with tourists to the same destinations. According to the surveillance data on returned travelers conducted by GeoSentinel (an international network of travel medicine provider), eight times more VFR travelers than tourists present with malaria and it is estimated that VFR account for more than half of the cases of imported malaria in Europe and North America (10). VFRs have a greater risk than other...
travelers related to a number of factors, including higher risk of exposure and insufficient protective measures.

These patients rarely seek medical advice or vaccination before traveling and are more likely to stay in rural areas, travel for a longer period of time, be in closer contact with the local population and consume local food and beverages, undertake last-minute travel (linked to deaths or other family emergencies) and make trips of greater duration. VFRs tend to perceive less risk related to travel because of their familiarity with their destination which is why they often don't seek pre-departure vaccination or malaria prophylaxis. Health insurance programmes often do not cover the cost of pre-travel consultation, so for VFRs, in particular those with large families the consultation may be onerous. In addition the access to travel medicine services may be hampered by cultural and linguistic limitations.

Another study carried out in one of the clinics of the GeoSentinel Surveillance Network in a hospital in Zurich evaluated various epidemiological factors in patients seeking medical attention for different diseases following international travels, during January 2004 and May 2005; the study compared travelers VFR with other groups of travelers (11) and analyzed 451 patients: 181 emigrants, 227 travelers, 25 foreign visitors, 18 others (expatriats, students, military staff). Their age ranged between 16-87 years (median 33), 48% were women. Immigrants were defined as persons born in another country, having permanent resident status in Switzerland and travelers who had not immigrated before were considered traditional travelers. All persons who traveled with the purpose of visiting their friends or relatives were called VFR. 671 diagnosis were registered: fever (43.0%), gastrointestinal diseases (42.7%), ORL diseases (25.2%), respiratory diseases (24.3%), musculoskeletal diseases (12.8%), cutaneous diseases (11.9%). When comparing travelers VFR with tourists and other travelers (121 vs. 217), they observed that for travelers VFR the spectrum of infectious diseases and the risks were different from those of traditional travelers: they had higher risk for malaria (OR 2.9, CI 1.2-7.3) or viral hepatitis (OR 3.1 CI 1.1-9) than traditional travelers, but sought medical attention before their trip less often than other travelers (20% vs 67% p<0.0001). Acute diarrhea rates were lower in travelers VFR compared to other travelers (173 vs 364 for 1.000 returned travelers). Malaria was most commonly acquired in sub-Saharan Africa.

In conclusion, improving the access of VFRs to pre-travel health counseling is of increasing public health importance.

- increase the awareness of both health-care providers and VFRs of travel-related health risks
- facilitate uptake of pre-travel health advice, vaccinations and, where indicated, malaria prophylaxis.

**Pilgrimages and mass gatherings**

Hajj, the annual Muslim pilgrimage to Mecca and Medina in Saudi Arabia is the greatest assembly of humankind on earth. In scale and international diversity, the Hajj is a unique religious pilgrimage. It is undertaken by Muslims as a once in a lifetime act of religious devotion during the days of the Hajj; The Umrah is a similar pilgrimage undertaken at other times of the year. During the Hajj, more than 2 million Muslims from all over the world congregate to perform their religious rituals. Today we can learn much from Hajj. Pilgrimage presents a unique opportunity to study health issues in a mobile population. Due to massive scale and singular focus on one city, Hajj affords insights no other migration can yet offer. Substantial hazards accompany such extraordinary congestion; both health hazards of performing Hajj and the public health concerns relating to the returning pilgrim. Health hazards could be infectious and noninfectious problems encountered during Hajj. The resulting overcrowding has led to stampedes, traffic accidents and fire injuries.

Cardiovascular disease is the most common cause of death. Heatstroke and severe dehydration are also frequent when the Hajj season falls during the summer months.

The congestion and the mass migration of the pilgrims bring a number of infectious processes to the fore. Meningococcal disease (MCD), respiratory tract infections, blood-borne, diarrheal and zoonotic diseases all are frequently encountered problems for the pilgrims, either during Hajj or following Hajj. Unique occupational infections affect the abattoir worker at the Hajj and the pilgrims from the barbers, areas that are now firmly addressed by the Saudi authorities. Most concerning are emerging infectious diseases (including SARS/avian influenza) and their devastating potential to spread. (10,12,13)
Each year, the date of Hajj is earlier than in previous year, by 10 or 11 days, since it is dictated by the Islamic lunar calendar. Thus different seasonal conditions prevail during the Hajj and may be favorable to different diseases, such as influenza or dengue fever.

Extensive outbreaks of meningococcal disease among pilgrims have prompted the Saudi Arabian health authorities to introduce mandatory vaccination. All pilgrims must now be given the quadrivalent meningococcal vaccine (protecting against serogroups A, C, Y and W135). The most frequently reported complaints among pilgrims are upper respiratory symptoms. Seasonal influenza vaccination has been reported to reduce influenza-like illness among pilgrims and should be a highly recommended vaccination for all those making the Hajj. In 2009, the ministry of health of Saudi Arabia recommended that individuals with certain chronic diseases (such as cardiac, renal, respiratory or neurological diseases and diabetes mellitus) and acquired or congenital immunodeficiency, pregnant women and extremely overweight individuals who are more likely to experience complicated forms of pandemic influenza A (H1N1) 2009 virus infection, defer from performing the Hajj. Deferring was also recommended to individuals aged less than 12 years or more than 65 years. Where seasonal influenza vaccine and pandemic H1N1 vaccine were available in countries of origin, proof of both vaccinations were required by competent authorities before issuing visas. Pneumococcal vaccination should also be recommended for those aged over 65 years and those who would benefit from it because of underlying medical conditions. Hajj-related outbreaks of cholera occurred in the past but not since 1989, following improvements to the water supply and sewage systems. Hepatitis A vaccination is recommended for non-immune pilgrims, and routine vaccinations (such as poliomyelitis, tetanus, diphtheria and hepatitis B) should be up to date. Yellow fever vaccine is a requirement for pilgrims coming from areas or countries with risk of transmission of yellow fever.

Since 2005, the Ministry of Health of Saudi Arabia has required that all travelers aged under 15 years from polio-affected countries show proof of vaccination with oral polio vaccine (OPV) 6 weeks before application for entry visa and all these individuals will receive OPV upon entry at border points. Since 2006, in addition to the above, all travellers from Afghanistan, India, Nigeria and Pakistan, regardless of age and previous immunization history, will also receive an additional dose of OPV upon arrival in Saudi Arabia.

According to "Domestic Tourism Study 2006, 80 million Indians travel each year for religious purposes. In India certain important sites are well known throughout the country attracting hundreds of thousands of pilgrims annually, Varanasi situated on the north bank of the Ganges, is probably the most significant, and it's one of the seven holy cities, representing a favored place for Hindus to die and be cremated in. This, according to their belief, ensures the liberation of the soul or moksha. It is also a sacred city to Buddhists and Jains and it's one of the oldest living cities with records that prove over 3000 years of continuous inhabitation Encircling the city is a sacred path of 50 miles touching 108 shrines called the Panchakroshi Parikrama and completing the circle is an essential part of the pilgrimage, although those who are unable to complete the path due to illness are able to do it symbolically by visiting the Panchakroshi temple that has the 108 wall reliefs of the temples. The river Ganges is revered as a goddess whose purity cleanses the sins of the faithful and through its 2510 km course it supports over half a billion people or one tenth of humanity. However, India's growing population imposes a growing burden on the river, which is now polluted with human and industrial waste, the majority being represented by organic waste (sewage, trash, food, animal and human remains).

City populations along the Ganges have grown at a tremendous rate, while waste-control infrastructure has remained relatively unchanged over the past century. The old sewagesystem channels add to this problem. Each day some 300 million gallons of waste pour into the river. Recent water samples collected in Varanasi reveal fecal-coliform counts of about 50,000 bacteria per 100 milliliters of water, approximately 10,000% higher than the government standards for safe river bathing. This pollution conduct to a large array of water-borne diseases including cholera, hepatitis, typhoid and amoebic dysentery. (13) The Pilgrimages of Christianity are safer in terms of infectious diseases, due to high standards of health system and infrastructure in European countries (Rome, Lourdes, Santiago de Compostella). However, respiratory transmitted diseases may occur as a result of overcrowding.
Lourdes represents an important destination for Christians, with 5 million visitors each year. The number of visitors increased to 8 million in 2008, at the celebration of 150 years from the appearance of the Virgin. Some Norovirus epidemics from 2002 and 2008 have been linked to the pilgrimage in Lourdes. (14, 15)

Holy water also poses many health risks, containing fecal-coliforms, staphylococci and fungi. Pilgrims who bathe in the holy water of the Gange river are not aware of health risks like pollution with arsenic and pesticides or human carbonized remains. In Thailand a study of holy water revealed that only 9 of the 76 probes met the WHO criteria for safe drinking water. In some western countries holy water brought in hospitals caused a series of epidemics. Hence, travelers should be aware of the elementary hygiene principles concerning food and water during their pilgrimages.

The world is constantly changing and what happens in one area may rapidly affect other areas at great distances, which means that a disease that is endemic in one area can rapidly become epidemic in another area through the movements of global travelers. Therefore, international travelers should seek competent advice on potential hazards and outbreaks in regions in which they will be visiting or from which they are returning.

**References**

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