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EFFECTS OF SOCIAL, ENVIRONMENTAL AND ECONOMIC FACTORS ON CURRENT AND FUTURE PATTERNS OF INFECTIOUS DISEASES

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1. Introduction: Microbial Resilience

Social, environmental and economic factors, linked to a host of human activities, often accelerate and amplify the natural phenomena that modify infectious disease patterns in humans. They influence the ease at which microbes adapt to new environments and hosts, the rapidity with which they develop resistance to the antimicrobial agents used for treatment, and the limits to which they spread geographically. Social factors include the impact of urbanization on sanitation and the water supply; and behaviour – of health workers as they perform their routine functions – and of the general public as they strive to prevent and control the daily threat of infectious diseases. Environmental factors include naturally occurring variations in temperature and rainfall, and the impact of economic development on rivers, forests and agricultural lands; while economic factors include the level of investments in public health, and patterns in international trade and travel as globalization of commerce and markets continues to accelerate.

These factors in turn are influenced by the tools with which public health systems defend against the infectious disease threat – currently available vaccines and antibiotics that were ushered in through intensified research and development that began immediately following World War II; and technological advances in hygiene and sanitation. Industrialized countries have greatly benefited from these public health tools. Malaria, for example, endemic in many industrialized countries in both North America and Europe, disappeared with insecticides and antimalarial drugs. Tuberculosis hospitals in Europe and North America emptied as living conditions improved and effective drugs became available that could be used

to treat those with acute tuberculosis and prevent infection in their contacts. Influenza deaths could be prevented in industrialized countries by vaccinating elderly populations, and epidemics of diarrhoeal disease became rare events, limited to foodborne outbreaks when temporary breaches in sanitation occurred. And one infectious disease, smallpox, completely disappeared from industrialized countries through routine use of the smallpox vaccine, and then in the rest of the world after a global eradication effort [1, 2].

Progress has been more difficult and variable in developing countries, and has slowed as public health investments made by governments have decreased. At the same time, the microbes that cause infectious diseases remain complex, dynamic, and constantly evolving. They reproduce rapidly, mutate frequently, and adapt with relative ease to new environments and hosts; and they develop resistance to the drugs used to treat them. With increasing use of antimicrobial drugs, warning signs of microbial resilience began to appear. By the end of the 1940s resistance of hospital strains of staphylococcus to penicillin in the United Kingdom were as high as 14%, and by the end of the 1990s had risen to levels of 95% or greater [3]. In New York City in the 1990s multidrug-resistant strains of tuberculosis gained their hold in hospitals, prisons, and homeless populations [4]. At the same time multidrug-resistant tuberculosis merged in the Russian Federation and more than doubled in less than seven years, with over 20% of tuberculosis patients in prison settings infected with multidrug-resistant strains [5]. Antimicrobial drugs developed to treat AIDS and other sexually transmitted infections such as gonorrhoea likewise began to lose their efficacy because of the rapid development of resistance. During this same period, vaccine development lagged – with no effective vaccines to prevent infection of many of the major mortality causing infections such as tuberculosis, malaria, and AIDS. And newly emerging infectious diseases such as severe acute respiratory syndrome (SARS) and avian influenza (H5N1) have presented new global infectious disease challenges as they spread from country to country, and continent to continent [6].

2. Social and Behavioural Factors that Influence Infectious Diseases

The world's population more than doubled in the second half of the 20th century, accelerating most rapidly in the developing countries of the tropics and sub-tropics, where infectious diseases continued to have a hold

[7]. Rural-urban migration resulted in inadequacy of sanitation, crowded living conditions and other basic infrastructure associated with population growth. It thus contributed to the resurgence of many diseases, such as tuberculosis, cholera, typhoid, and plague, that are transmitted when living conditions and hygiene are sub-standard, and when overcrowding occurs. Cholera caused epidemics during the 1990s in parts of Latin America where it had previously been quiescent for over 100 years. By the 1980s crowded major urban areas in Africa and South America had experienced a dramatic re-emergence of yellow fever epidemics as the yellow fever virus was introduced by mosquitoes from rain forests into new and densely populated urban areas where bednets to protect from mosquito bites were no longer being used [8, 9].

Behaviours such as over or under-prescribing of antibiotics by health workers, and excessive demand for antibiotics by the general population, have had a remarkable impact on the selection and survival of resistant microbes, rapidly increasing levels of microbial resistance. Drug-resistant microbes have then spread from person to person and geographically, raising the prospect that common infectious diseases could become prohibitively expensive or impossible to treat [10]. The bacterial infections which contribute most to human disease are also those in which emerging resistance is of most concern: diarrhoeal diseases such as dysentery; respiratory tract infections, including pneumococcal pneumonia and multidrug-resistant tuberculosis; sexually transmitted infections such as gonorrhoea; and a host of hospital-acquired infections that are notoriously difficult and expensive to treat. Among the major infectious diseases, the development of resistance to drugs commonly used to treat malaria is of particular concern, as is the emerging resistance to anti-HIV drugs. Most alarming of all are microbes that have now accumulated resistance genes to virtually all currently available antimicrobial drugs, such as *Staphylococcus aureus* and *Salmonella typhi*, that now have the potential to cause untreatable infections.

Trends in tourism, with tourists penetrating deep into tropical forests, often without appropriate protection against insect bites or vaccination, result in importations of malaria and yellow fever to industrialized countries [11]. At the same time weak infection control procedures by health workers have caused the amplification of transmission in outbreaks such as Ebola to health workers and their contacts in sub-Saharan Africa, and hepatitis and SARS to health workers and those with whom they have contact in both developing and industrialized countries [12, 13].

3. Environmental Factors that Influence Infectious Diseases

Human disturbance and alternation of ecological zones throughout the world has increased the frequency with which microbes, usually confined to animals, cross the species barrier to infect humans. Deforestation disrupts natural habitats of animals, and can force animals, searching for food, into closer contact with humans. Outbreaks of Lassa fever in West Africa and of hantavirus in North America have been linked to such phenomena [14, 15]. In Latin America, Chagas disease emerged as an important human disease after deforestation caused the insect that transmits the infection to move from its wild natural hosts to involve humans and domestic animals in the transmission cycle, eventually transforming the disease into an urban infection that can be now also transmitted by blood transfusion [16].

Climate extremes, whether involving excessive rainfall or drought, can likewise displace animal species and bring them into closer contact with human settlements, or increase vector breeding sites. A 1998 outbreak of Japanese encephalitis in Papua New Guinea has been linked to extensive drought, which led to increased mosquito breeding as rivers dried into stagnant pools [17]. The Japanese encephalitis virus is now widespread in Papua New Guinea and threatening to move farther east.

An outbreak of Rift Valley Fever in Eastern Kenya resulted from flooding related to El Niño. Humans and cattle, forced to live in close proximity on islands of dry land surrounded by water, facilitated the transfer or the Rift Valley Fever virus from unvaccinated animals to humans by mosquitoes that had increased in numbers because of the abundance of pooled-water breeding sites [18].

Other examples of how insects that carry infectious diseases have exploited new opportunities created by environmental degradation and human behavioural change include epidemics of dengue and yellow fever that have been fuelled by the adoption of modern consumer habits in urban areas where discarded household appliances, tyres, plastic food containers and jars have created abundant artificial mosquito breeding sites. The *Aedes aegypti* mosquito is now well established in most, if not all, large African cities, increasing the risk of explosive urban outbreaks of Dengue [19]. Similar examples are occurring in Asia where Dengue and Dengue Haemorrhagic Fever have caused major outbreaks during 2004 in Indonesia and India [20]. In countries of the former Soviet Union, large amounts of stagnant water, created by ineffective irrigation schemes, provided mosquito breeding sites that permitted the re-emergence of malaria

in the most southern states, where a few incidental and probably imported cases in Tajikistan in the early 1990s multiplied to almost 20,000 reported cases in 1998 [21]. Such problems are compounded by the very small number of new cost-effective chemical pesticides, suitable for public health, that have been developed in recent years.

Though intensive research has failed to disclose the origins of Marburg and Ebola haemorrhagic fever outbreaks, microbes causing both diseases are also thought to be transmitted to humans as they encounter animal sources somewhere in the transmission cycle [22]. An outbreak of Ebola haemorrhagic fever in humans in 1995 was linked to a woodsman, who worked deep within the tropical rainforest making charcoal, and who is somehow thought to have become infected with the Ebola virus which he then carried back to his home village and family members, while a Swiss researcher is thought to have become infected with the Ebola virus while searching for the cause of a major die out of chimpanzees in a forest reserve in West Africa [23, 24].

The consequences of the environment and interspecies transmission of microbes are most clearly demonstrated in the case of the influenza virus. It is thought to be only matter of time until an animal influenza virus circulating in domestic animals, recombines with a human influenza virus, and causes the next highly lethal influenza pandemic [25]. Intensive farming practices have placed humans in Asia in close proximity to domestic animals in densely populated areas. In 1997 in the Hong Kong Special Administrative Region of China, crowded conditions, and live poultry markets adjacent to residential areas, facilitated the transmission of a new avian influenza A virus (subtype H5N1), previously thought confined to birds. At least 18 humans were infected and six died, raising considerable alarm [26]. Although human-to-human transmission of the virus was documented, it was found to be relatively inefficient and uncommon [27]. A re-emergence of this same virus throughout Asia in late 2003 and 2004 has resulted in 42 human infections with 30 deaths in Thailand and Vietnam by 1 October 2004, and the continued threat of a global human pandemic [28].

3.1. *Economic Factors that Influence Infectious Diseases*

With the control of infectious diseases in industrialized counties during the 20th century came great optimism that infectious diseases were no longer a health problem. As a result of this optimism financial resources once used to combat infectious diseases were shifted to non-communicable disease

problems, and there was decreased and insufficient investment during the last quarter of the 20th century to adapt and use newly developed technologies for detection, monitoring and responding to infectious diseases [29].

In parallel, investment in research and development for new vaccines and antimicrobial drugs for infectious diseases was shifted to non-communicable diseases, those that still affected industrialized countries and were related to lifestyle, aging and environmental hazard. The resultant 10/90 research gap, with less than 10% of public and private funds being placed into research for infectious diseases such as tuberculosis, diarrhoeal diseases, malaria and AIDS, created a slow down in the development of new antimicrobial drugs and vaccines [30].

With decreased investment came the resurgence of known infectious diseases in industrialized countries, such as tuberculosis and common sexually transmitted infections such as syphilis and gonorrhoea; and a host of new infectious diseases such as hepatitis C and AIDS that escaped detection until they were firmly implanted in human populations [31].

Developing countries, on the other hand, had never accomplished the same decrease in infectious diseases. In these countries infectious diseases continued to remain an important cause of sickness, disability and death throughout the 20th century because of a lack of access to vaccines and drugs with which to prevent and treat them, and because of weak health systems that failed to consistently reach populations in need. The resources that these countries were able to invest in infectious disease control in the first half of the 20th century, often with the assistance of the colonial powers, decreased as the millennium progressed, with some of the greatest decreases occurring in sub-Saharan Africa [32].

Common infectious diseases that are spread directly from person to person such as tuberculosis continued to cause significant suffering and death in developing countries because of inequitable distribution of and curative drugs within developing country health systems, and because of the continued lack of development of preventive vaccines [33]. Treatment with partial regimes of tuberculosis drugs because of inconsistent drug supply to developing country health systems caused an increase in drug-resistant strains that resulted in an increase in cost for treatment because of the need to use more expensive second line tuberculosis drugs [34].

Infections such as diarrhoeal diseases of children, caused by lack of adequate sanitation and safe water, increased as sanitation systems in major metropolitan areas failed with increases in urban populations, and those in rural areas failed to develop. Vaccine preventable diseases such as measles,

for which access to vaccines was likewise not sustained, remained major public health problems. Decreased investment in childhood immunization programmes in Russia and the Ukraine in the early 1990s resulted in epidemics of diphtheria in Russia and the Ukraine in the early 1990s [35].

With decreased financial investment in programmes to control infection-carrying mosquitoes, a resurgence of malaria, dengue and yellow fever occurred, and mosquitoes then spread to new geographic areas. Following the deterioration of *Aedes aegypti* control campaigns during the 1970s, dengue resurged dramatically, with unprecedented numbers of its haemorrhagic form [36]. Prior to 1970, only nine countries had experienced epidemics of dengue. By 1998 a dengue pandemic occurred in which 1.2 million cases were reported from 56 countries. Since then dengue has continued to cause major epidemics with the most recent epidemic in 2004 resulting in over 60,000 cases and 700 deaths in Indonesia alone [37].

Other infectious diseases such as African trypanosomiasis or sleeping sickness began to resurge in the 1980s with a decline of most surveillance and tsetse fly control activities [38]. By the late 1990s, approximately 26% of mortality in low income countries was directly caused by infectious diseases that continued to circulate among large urban and rural populations. These low-income countries today represent over 80% of the estimated 14 million deaths caused each year by infectious diseases [39].

Other economic factors are also playing a role in infectious disease patterns throughout the world. Globalization, with a phenomenal growth in international travel and trade since the 1950s, has greatly increased the speed with which microbes, incubating in unsuspecting humans, can cross continents and invade new geographic territories. At the same time microbes living in insects concealed in cargoes or in the luggage holds and cabins of jets; in animals traded internationally, or in improperly or non-processed food and food products can also travel across continents and internationally. As a result, the threat of epidemic diseases with origins in one country and spread to others has become a real and constant threat.

Nothing more clearly demonstrates this global threat than the spread of AIDS in humans throughout the world during the latter half of the 20th century. Spreading throughout the world and amplified by unsafe sexual behaviour, AIDS has had a negative impact on economic development and healthy population growth. In 1999, the lower figure in the world life expectancy range, which had seen a steady increase in previous decades, declined to 33.2 years, just above the 33 years seen in 1949, largely due to the emergence and spread of HIV [40]. In recent years, every continent has

experienced an unexpected outbreak of some infectious disease directly related to increased travel and trade, the most recent having been severe acute respiratory syndrome (SARS) [41].

Advances in food production and storage technology, coupled with the globalization of markets, have resulted in a food chain that is unprecedented in its length and complexity, thus creating an efficient vehicle for microbes to spread to new areas and susceptible hosts. Tracing the origin of all ingredients in a meal has become virtually impossible, constituting an enormous challenge for the control of foodborne diseases [42]. Medical advances in such areas as blood transfusion, organ transplantation and other sophisticated surgical procedures, and the development of intensive care units have likewise opened new opportunities for the microbial world, creating ideal conditions for in-hospital transmission of infectious agents to new, atypical hosts [43].

In the late 1990s infections such as West Nile fever, that arrived in North America through the introduction of a single virus, and Rift Valley fever that arrived in the Arabian peninsula in infected livestock, have become endemic in these new geographic areas, adding to the infectious disease burden [44,45,46]. Once established on new continents, emerging or re-emerging infectious diseases change the dynamics in local infectious disease patterns change.

The universal nature of the microbial threat, with agents of disease, including drug resistant forms, passing undetected across increasingly porous borders, has placed all nations on an equally vulnerable footing. Economic prosperity has produced a world that is interconnected in matters of economics and trade, with the result that health has become both a domestic issue, and an issue with foreign policy considerations as well [47].

4. Future Patterns of Infectious Diseases

Social, environmental and economic factors; the availability of antimicrobial drugs and vaccines; and the resilience and natural selection and evolution of the microbial world will continue to have an impact on future patterns of infectious diseases. Water and sanitation systems will be challenged as populations continue to move to urban areas in search of work and economic betterment, with continued endemic and epidemic transmission of intestinal infections and diarrhoeal disease. Behaviour of health workers and the general population will continue to play an important role

in transmission of infectious diseases, and in development of antimicrobial resistance. Continued lack of vaccines for many of the major infectious diseases will dampen progress in prevention, while continued alterations in temperature and rainfall, and human impact on agricultural lands, forests and rivers will in some instances increase the number of insect vectors and alter the geographic distribution of animal hosts, leading to the emergence of new human infections and/or re-emergence of those that are known.

Underlying all these factors is the current acceleration in globalization, increasing the risk that infections in one country spread internationally in humans, insects, animals or food – thus raising infectious diseases higher on the agenda of human security. And finally, with continued inequitable distribution of the vaccines, medicines and goods available now to prevent, treat and control infectious diseases, coupled with weak public health delivery systems in developing and low income countries a disproportionate burden of human suffering and death from infections diseases will continue to occur in developing countries.

Public-private partnerships are currently addressing some of the needs to modify these future patterns of infectious diseases. The global Alliance for Vaccines and Immunizations provides financial support to accelerate the development of new vaccines needed primarily in developing countries, and has strategic and financial mechanisms for ensuring that new vaccines, when available, are supplied to developing countries in the highest quality and at the lowest possible price. Another public-private partnership, the Global Fund to Fight AIDS, Tuberculosis and Malaria, helps countries address complex and pressing problems that include supplies of medicines and other goods, weak health infrastructure, poorly trained personnel and weak delivery systems. Other public/private partnerships are addressing diseases such as leprosy, lymphatic filariasis and polio, the latter a disease that is targeted for eradication sometime during 2005 [48].

At the same time, with the continued evolution of antimicrobial resistance, our armamentarium for infectious disease control requires continued and increased investment for new antimicrobial drugs and for vaccines. For new antimicrobial agents and vaccines, even if the pharmaceutical industry were to step up efforts to develop new drugs immediately, current trends suggest that some diseases may have very few and, in some instances, no effective therapies within the next ten years [49]. Moreover, if current trends continue, many important medical and surgical procedures, including cancer chemotherapy, bone marrow and organ transplantation, and hip and other joint replacements, could no longer be undertaken out of fear that the

associated compromise of immune function might place patients at risk of acquiring a difficult to treat and ultimately fatal infection. Opportunistic infections in AIDS patients would likewise become an especially difficult challenge, and the choice of antimicrobial drugs for most infectious diseases would be severely limited. In research for new drugs, as well as that for vaccines, the challenge is to apply the genomic information and knowledge that has become available to tailor make the medicines and vaccines needed.

To minimize the impact of emerging and re-emerging infectious diseases, increased investment in national pubic health infrastructure is required in order to detect early and rapidly respond to infectious diseases outbreaks, as well as long-term programmes to modify or remove the factors that facilitate emergence. Likewise there is a need for an international safety net of global surveillance with a response mechanism should diseases begin to travel internationally. Recently a global partnership, supported by several new mechanisms and a computer-driven tool for real time gathering of disease intelligence, has been developed to detect and respond to infectious diseases of international importance [50].

Related to the emerging and re-emerging infectious diseases is a new infectious disease threat that dominates public health thinking and policies in some industrialized countries – that of deliberately-caused infectious disease outbreaks. Following the deliberate dissemination of anthrax spores through the US postal system in 2001, questions concerning the deliberate use of biological or chemical weapons have been raised with great urgency. The prospect of introduction of an infectious disease to non-immune populations that could cause severe illness and death has now become a stark reality.

Infectious diseases have caused human suffering, illness and death since Biblical times, and before. The threats posed by infectious diseases are today being amplified by social, economic and environmental factors that accelerate the natural phenomena that modify infectious disease patterns. Global recognition and partnership are required to keep them at bay.

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WHO Web Addresses for Further Information

World Health Organization: www.who.int
Disease outbreak news: www.who.int/disease-outbreak-news/
Weekly Epidemiological Record: www.who.int/wer/
Infectious diseases: www.who.int/health-topics/idindex.htm
Communicable disease surveillance and response: www.who.int/emc/index.html
WHO training office in Lyon, France: www.who.int/emc/lyon/ index.html
HealthMap: www.who.int/emc/healthmap/healthmap.html