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SARS AND THE GLOBAL RISK OF EMERGING INFECTIOUS DISEASES

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IN THE BEGINNING: THE "BIG BANG" OF SARS

On February 21, 2003, Dr. Liu Jianlun, a doctor from Guangdong in south China came to Hong Kong to attend a family wedding and stayed at the four star Metropole Hotel. Shortly after arriving in Hong Kong, he complained of a fever and respiratory difficulties, and was admitted to a local hospital. He warned his doctors to be careful. His colleagues in south China had been seeing a number of patients with an unusual severe pneumonia that appeared able to spread from person to person. He had recently treated such a patient himself and thought he must have caught the disease from him (Rosenthal 2003). Despite treatment, he died in the hospital.

During Dr. Liu's stay at the hotel, at least a dozen other guests contracted this odd pneumonia from him. These people then went their separate ways. One, a New York businessman, was on his way to Hanoi, Vietnam. Another guest went to Singapore. A 78-year-old woman from Toronto returned soon afterward to Canada. Two other guests fell ill while still in Hong Kong, went to hospitals there, and infected at least 99 health care workers who were unfamiliar with the disease and therefore did not take any of the special precautions used for transmissible infectious diseases. Unfortunately, it appears that the doctors who treated Dr. Liu did not pass along his warnings to doctors in other Hong Kong hospitals or the wider world.

AS SARS BEGINS TO SPREAD WORLDWIDE, THE WORLD HEALTH ORGANIZATION ACTS

The hotel connection was the "Big Bang" of the disease that would soon acquire worldwide fame as SARS ("Severe Acute Respiratory Syndrome") (Pottinger 2003). Shortly afterward, Hanoi reported an unusual pneumonia, brought in by a traveler from Hong Kong. Vietnam would eventually report 63 cases, including 37 hospital workers. Among the victims was Dr. Carlos Urbani, an Italian doctor working in Vietnam for the World Health Organization (WHO). Dr. Urbani reported the disease and his clinical observations before succumbing to the disease himself. Then, in early March 2003, a Toronto hospital reported several cases of an "atypical pneumonia". Brought to Canada by the woman who stayed at that same fateful hotel in Hong Kong, the disease rapidly spread throughout the hospital to health care providers. Belatedly, health authorities recognized that they were dealing with an unusual transmissible pneumonia. Local chains of transmission were ultimately reported in mainland China, Hong Kong, Taiwan, Hanoi, Singapore, and Toronto, as well as more limited transmission in the United Kingdom and the United States. New York City missed a serious case literally by one day. A physician from Singapore who came to New York for a medical meeting fell ill just before leaving to go back home. He was placed into isolation in Germany when his plane made a scheduled stopover there (WHO 2003; see "SARS Timeline" below, 15 March 2003). Several children in New York City who had just been adopted from China also were believed to have SARS, and there were other cases reported throughout the United States (Broder 2003). But, outside Asia, Toronto was the hardest hit by far, largely as a result of spread within hospitals. By the time the outbreak was over, in mid-summer 2003, there had been 251 cases in Toronto alone, and the World Health Organization (WHO) had issued an advisory that warned travelers to avoid Toronto, as well as several cities in Asia.

This was the Western world's first experience with the viral infection known as SARS. The disease had originated in Asia and spread worldwide in a matter of weeks. Altogether, by time the epidemic was eventually controlled, there were 8,098 known cases with 774 deaths worldwide, including the 251 confirmed cases with 38 deaths in Canada. SARS, new to western medicine, powerfully demonstrated the potential for a disease to spread far beyond its origins and to cause tremendous human and economic effects. Fortunately, there have been only a few sporadic cases since then (including some infections of laboratory workers), and no sustained transmission.

In many ways, SARS represented a significant watershed for the World Health Organization. WHO, a United Nations agency headquartered in Geneva, is the world's public health agency. During the SARS epidemic, for the first time WHO began to take a more proactive approach to an infectious disease epidemic, issuing travel advisories for areas known to have SARS and updating the warnings regularly. WHO may have been motivated in part by delays in reporting from some governments. For example, China had been experiencing outbreaks of SARS starting in November 2002 (if not earlier), but did not begin reporting the cases until February 2003 (see "Timeline"). By the time the Chinese government officially reported, they already listed over 300 cases.

As part of its proactive stance, WHO used modern technology to facilitate research and communications. WHO convened regular teleconferences to allow the numerous national public health agencies, such as CDC (the US Centers for Disease Control and Prevention), and collaborating laboratories to rapidly share information with each other on both the epidemiology and the basic science. As a result, by mid-April 2003 the responsible virus was identified and modern molecular biological techniques were used to develop candidate diagnostic tests.

ECONOMIC AND SOCIAL EFFECTS

The social disruption caused by SARS was also considerable and worldwide. Many hospitals were forced to make extra room and take extra precautions to protect workers and other patients. Toronto, its hospitals hard hit by SARS, introduced the idea of "work quarantine" in which hospital workers were allowed to go between home and their hospital but only if they did not have contact with anyone on the way (by driving alone in their own cars, for example). As a result of travel advisories and fear of contracting SARS, many meetings in Asia were cancelled. Airlines reported massive losses of revenue on trips involving destinations in Asia. Passengers boarding these flights were also subjected to screening. Hong Kong and Singapore, among others, used scanners to determine whether a boarding passenger had a fever (a test that was not very specific and had many false positives).

The disease was heavily reported in the media, probably increasing the level of anxiety among the public. (The H5N1 avian influenza is receiving similar media attention in 2005-2006.) As a result, effects were not limited to SARS-affected areas alone. The University of California at Berkeley cancelled the enrollment of about 500 summer students from China, Taiwan, Hong Kong, and Singapore because of concerns about SARS, while other universities and many corporations discouraged travel to affected areas (Murphy 2003). It has been estimated that SARS cost the world economy over US $40 billion including lost trade and tourism; this includes an estimated 2.6 per cent GDP loss to Hong Kong and 1.05 per cent GDP loss to mainland China (Lee and McKibben 2004).

WHAT CAN SARS TEACH US ABOUT EMERGING INFECTIONS?

Although public health agencies rose admirably to the occasion, the SARS outbreak exemplified many recent concerns about infectious diseases. Recent years have witnessed an increasing number of apparently novel infectious diseases in both animal species and humans. I had called these "emerging" infections (Morse 1991; Morse 1995). Infections can be defined as emerging if they have newly appeared, or are rapidly increasing in incidence (number of new cases) or geographic range. In addition to SARS, recent examples of emerging diseases in various parts of the world include HIV/AIDS; Rift Valley fever in Africa and the Mediterranean basin; hantavirus pulmonary syndrome, first recognized in an outbreak in the southwestern United States in 1993; and hemolytic uremic syndrome, a food- or waterborne infection caused by certain strains of the common bacterium Escherichia coli (in the United States, O157:H7). Influenza also remains a persistent concern, with worldwide epidemics (pandemics) of novel influenza varieties occurring, on average, several times a century. Avian influenza, of subtype H5N1 (the so-called "bird flu"), was not even known to cause human disease until an outbreak in Hong Kong in 1997, with 18 human cases and 4 deaths. Since then, H5N1 has continued to evolve in Asia. It's spread from infected poultry to humans has been documented in several countries, including Vietnam, Thailand, Indonesia, Cambodia, and China. By the end of 2005, confirmed human cases of H5N1, acquired from contact with infected poultry, totaled 142, with 74 deaths (WHO website: *www.who.int/*; accessed 30 December, 2005).

The occurrence of emerging infectious diseases may seem sudden and inexplicable, but factors responsible for their emergence can be identified in virtually all cases that have been carefully studied (Morse 1995). The most novel infectious diseases are often transfers from another species (e.g., rodents, as with hantavirus pulmonary syndrome, or bats, as with Ebola), where they have existed naturally for many years, even millennia. The process of pathogens crossing species has long occurred naturally, but modern conditions, with the increasing rate of environmental or ecological changes caused by humans (including, notably, agricultural practices), and greater global interconnectivity, provide ever greater opportunities. These occurrences suggest that the interface between humans and other animals is of great importance in the process of disease emergence. In the case of SARS, the direct link to humans was the weasel-like mammal known as the palm civet, Paguma larvata (Guan et al. 2003). Palm civets are prized as a food animal in south China. Many are farmed and brought to the cities, while others are caught in the wild. The initial cases of SARS, in mainland China, were in food handlers and some restaurant patrons who had eaten civet (although this was only recognized much later, when the cases in south China were reported and subsequently investigated). However, while a number of food handlers and animal slaughterers showed evidence of having been infected by the SARS virus, or a closely related virus (Guan et al. 2003), wild or farm-raised civets were rarely if ever found to be infected (Kan et al. 2005). The mystery was solved only in 2005, when it was shown that the ancestor of the SARS virus normally resides in bats (Li et al. 2005), but civets can become infected when they are brought to live animal markets in the cities (Kan et al. 2005) and presumably come in contact with infected bats. Molecular studies show that the SARS virus strains that infect civets are more easily transmitted to humans. This spread between animal species through the live animal markets is almost an exact repetition of the 1997 avian influenza outbreak in Hong Kong, in which the live animal markets were implicated in the spread of the disease. To control the 1997 avian influenza outbreak, Hong Kong authorities closed the live animal markets, and slaughtered all the local poultry (Lipatov et al. 2004).

Once an emerging infection enters the human population, it faces the hurdle of establishing itself in the human population and becoming transmitted from person to person. Most never do, infecting humans only accidentally and sometimes causing dramatic outbreaks in the process. Such has been the fate of ebola and monkeypox (a close relative of smallpox) in Africa, the hantavirus pulmonary syndrome, and other equally notorious examples. Some, however, whether through having the right biological properties, by undergoing further evolution, or by a combination of biology and circumstances, are successful at making the leap to establishment and transmission in humans. HIV/AIDS has been the most devastating of these recent emerging infections, but there have been several others such as E. coli O157:H7. It is rare for emerging infections to spread by the respiratory route, but infections that can spread by this route have been a special concern for many years. Some familiar infections that spread by the respiratory route, like influenza and measles, can spread with remarkable efficiency and speed. The 1918 influenza pandemic, the "Spanish flu", was everyone's nightmare scenario (Barry 2004; Crosby 1989). It infected virtually the entire world, leaving an estimated 25-50 million dead in its wake. Thus, when SARS appeared and was recognized, its ability to spread by the respiratory route galvanized public health action. Fortunately, SARS was not nearly as transmissible as influenza. With a few exceptions, most cases occurred under fairly close contact conditions, such as in hospitals.

GLOBALIZATION AND HUMAN DISPLACEMENTS PROVIDE OPPORTUNITIES FOR EMERGING INFECTIONS

Globalization has had a major effect on infectious disease emergence. An infection introduced anywhere in the world, no matter how remote, can come to our doorstep in mere days. SARS forcefully demonstrated how one case, in a strategic location, could lead to hundreds of others, in a widening spiral. And while Hong Kong is a hub, well connected to the outside world, so are many other cities. JFK Airport in New York handled over 17 million international passengers in 2004. It has become a cliché to say that microbes need no passports, and know no borders, but examples like SARS demonstrate the truth of that statement.

Internal displacements caused by war or economic necessity can also help to disseminate previously localized diseases. Although the exact origin of HIV-1 as a human infection is unknown, it was probably first introduced as a cross-species transfer in rural Africa, perhaps more than once. As people moved from rural areas into cities for economic reasons, HIV probably came along. After its likely first move from a rural area into a city, HIV-1 spread regionally along highways, then by long distance routes, including air travel, to more distant places.

As trade becomes increasingly globalized, other new opportunities are presented for once localized microbes. For example, the food trade has become truly international. In the United States and other affluent Western countries, in order to be able to enjoy fresh fruits and vegetables out of season, we import produce from all over the world. The 1996 US outbreak of Cyclospora (a one-celled parasite that causes severe cramps and diarrhea when ingested), on raspberries imported from Guatemala, is one obvious example. High-density agriculture, the high-tech equivalent of the live animal markets, also offers opportunities for once-limited infections to spread through the food chain. E. coli O157:H7, although related to bacteria that normally live in the human gut, probably originated in cattle. Once found only in cattle in a few isolated locations, the bacterium has spread through the gathering of cattle into high-density feedlots. Similarly, meat from a variety of farms or feedlots may be centrally processed, allowing a small amount of infected meat to contaminate several tons of final product.

THE IMPORTANCE OF EARLY WARNING

One important protection against emerging infections is early warning and response. It is clear that early warning might have prevented many of the subsequent SARS cases. Dr. Liu personally warned his health care providers in Hong Kong to be especially careful. Mainland China had noted some early cases of SARS in late 2002 (see "Timeline"), but follow-up had been limited. It is tempting to speculate that a clarion call to the world at either of those two critical points might have prevented much of the SARS epidemic. The same is very likely true for many other infectious diseases. Taking AIDS seriously at the outset might have helped to prevent its inexorable global spread.

Why wasn't this done? Several factors combine to limit global surveillance, beginning with lack of political will and incentives to report. It is well known that many governments are reluctant to report human or agricultural health information for fear of economic, political, or trade repercussions, or fear that it may make the government look ineffectual. Lifesaving as early warning may be, it is also easy for developing countries to question the motives of industrialized countries that advocate an early warning system, especially if it's an unfunded mandate. A health official in Asia made the following analogy: "You in the United States are like a castle. You want to put bells in all these other countries to give you early warning of infections, so that when one of these bells goes off, you can withdraw into your castle and put up the drawbridge. You don't really want to help us. Perhaps that's why we don't take the idea of early warning the same way you do" (Kenneth E. MacWilliams, personal communication, December 2005). Compounding the problem, there is no international structure that can compel early warning. WHO itself consists of 192 member states, essentially every country in the world. Like any international organization, WHO is dependent on the goodwill and cooperation of its members. In a major emergency, a member state can request assistance (and many have), but WHO can generally intervene only when asked. In the pre-SARS past, WHO has been accused of being too passive about announcing disease outbreaks and recommending action until the reporting member state has given WHO permission. Because of WHO's dependence on its member states, this has been such a carefully observed tradition that the rare past exceptions have become notable examples. Several decades ago, in one of those rare exceptions, WHO divulged that Egypt had an ongoing cholera outbreak even though the Egyptian government did not officially report it. That is one reason why the WHO'S rapid and active response to SARS was such a break with tradition. But it remains a work in progress. When SARS appeared in Toronto, the Canadian government was conscientious about reporting its cases, and as a result WHO promptly added Toronto to the travel advisories. Anecdotal reports from Toronto suggest that Canada felt punished, not rewarded, for honestly reporting their SARS cases, although, despite this, it is likely that Canada will continue to be as forthcoming as they have been in the past. Although many people debated the value of the travel advisories, it represented the first time that WHO took public action rapidly and on its own initiative, independent of the member states. WHO deserves commendation for its efforts to be proactive.

BARRIERS TO ACTION

Another problem is political. Despite its life-and-death nature, health does not generally have a high priority in most governments, and public health therefore rarely commands major resources. Even in those governments where health is accorded a full ministry, the Health Minister generally commands fewer resources, and has less access to the top decisionmakers, than the Economics or Internal Affairs ministries. Agriculture, because of its economic importance, is often in a better position, but still often inferior to the key political ministries. Other than educating policymakers, I see little that can be done to alleviate this situation. Because agricultural diseases can lead to starvation, as well as economic impacts, there have been attempts to link Agriculture and Health Ministers in certain spheres. An example is a Pan-American Health Organization program to combat foot-and-mouth disease (a major livestock problem), which requires the combined effort of several ministries in each South American country joining the program. But these solutions are difficult to apply universally.

In some cases, the interests of different government agencies may even be diametrically opposed. For example, many agriculture ministries might wish to increase the density of animals on commerical farms (to reduce production costs), while public health experts would point to avian influenza and SARS as reasons to be cautious of higher density agricultural settings. The situation for other intra-governmental alliances are even worse. Health and other powerful ministries may have even less in common. There are many examples of dam building or other development projects, for example, that lead to increased risks of vector-borne diseases or other negative health outcomes. One of the best known examples, from about two decades ago, is the Diama Dam in Mauritania, which led to a marked increase in cases of Rift Valley fever (a serious viral disease spread by mosquitoes, that can affect humans and several livestock species), but there are many other examples of development projects with serious health consequences.

It is clear that there are many perceived disincentives for reporting disease. Are there any incentives? The answer is, too few. After the SARS outbreak, some thought that the delayed and incomplete reporting by some governments undermined public faith in their credibility, and led to over-reaction: the tremendous impact on Asian travel, and the corresponding loss of revenue. It was therefore thought that these negative experiences would encourage governments to be more proactive in reporting diseases. But it is too soon to tell if this has had the desired effect. There have been major improvements in disease surveillance in China, but also suggestions that China may have delayed reporting some of their H5N1 influenza cases, despite their previous experience with SARS (Normile 2005). Such delays in reporting are all too frequent world-wide.

It must also be remembered that infectious disease surveillance, diagnosis, and control may be among the public health activities most evident to the public, but represent only a portion of the many functions carried out by public health authorities, from advising on safe water supplies, to providing maternal care and childhood immunizations, to recommendations on food and dental practices. Consequently, the priority accorded infectious disease activities varies tremendously between jurisdictions. In a federal system, like the United States, these differences are more obvious, but these issues become more pressing as countries or organizations (like WHO) face limited resources and must make priority decisions.

Another reason may be that the perception that developing truly effective global systems of early warning (or "health intelligence") is simply too hard to do. I believe that, while these problems can be daunting, they are not insurmountable. As an example, consider the following. One would think that it might be fairly simple to develop regional centers of excellence (based on existing facilities that already have many of the needed capabilities), whether through WHO or through regional inter-governmental organizations, to augment official systems and allow mutual cooperation (Henderson 1993). On the other hand, if diseases can emerge anywhere, how can one have eyes and ears literally everywhere? That seemed a formidable task, so we decided to try tackling the easier one first. In an attempt to fill what many experts (including this author) saw as the fragmentation of disease surveillance systems and the lack of global capacity, ProMED (the Program for Monitoring Emerging Diseases) was begun by a group of concerned scientists and public health officials as an international follow-up to a 1989 US National Institutes of Health meeting on emerging viruses and a 1992 Institute of Medicine Report. At meetings in Geneva and elsewhere, the Steering Committee (which I chaired) recommended developing a system of regional centers of excellence to identify and respond to unusual disease outbreaks (Morse et al., 1996). But it soon became apparent that the 60 or so Steering Committee members from around the globe had no consistent means of communication even just to use for convening regular meetings. As a result, in 1994, ProMED connected all its Steering Committee members by e-mail, at that time a fairly novel method of communication. Some of the members were in such remote places that satellite uplinks were required to provide them with simple e-mail connectivity (these links were provided through another nonprofit organization, SatelLife, in Boston). The system, originally designed as a direct scientist-to-scientist network, rapidly grew into a prototype system for outbreak reporting and discussion, especially after a 1995 Ebola outbreak in Africa. Now open to all, and edited (moderated) by a group of scientists and infectious disease experts, today ProMED-mail (as it is now known) has over 30,000 subscribers in at least 155 countries around the world. In fact, with the rapid growth of the Internet in the last decade, it is now possible to have reports contributed from much of the world. At the same time, there is still no global network of regional centers of the sort envisioned by D.A. Henderson (Henderson 1993) or by the original ProMED proposal (Morse et al. 1996), although improvements in recent years and greater activity by WHO have de facto brought the world somewhat closer to that goal.

The example of ProMED-mail also encouraged the development of several other systems. The Canadian government started a government-only system, GPHIN (Global Public Health Intelligence Network), a few years after ProMED-mail, using a "web crawler" (the precursor to search engines such as Google) to identify potentially relevant content in news reports from around the world. In recent years, as press reports have become more widely available on the Web, an increasing amount of the content on ProMED-mail and other systems is gleaned from press reports and other open sources.

As the above examples indicate, early warning and response are essential. Although there have been a number of experiments in automated data collection and extraction (generally referred to collectively as "syndromic surveillance"), the cornerstone of early warning at present is still the proverbial "astute clinician" or individual who reports an unusual case. This still remains the most important source of information. The crux, then, is how to provide incentives for reporting, and to empower the local clinician to diagnose (or at least recognize the unusual), and to report.

WHAT ELSE CAN WE DO TO PREVENT AND CONTROL EMERGING DISEASES?

While early warning is essential, it is useful only if followed up by appropriate action. There remains a shortage of qualified personnel available for epidemiological investigation and disease control, and resources are limited. There is a need for expanding laboratory capacity throughout the world, as well as research and development to add new tools to our armamentarium. All of these require financial commitment and well-trained personnel.

Another very important need is good public communication. The media can be valuable for keeping the public informed and reducing unnecessary anxiety. During the SARS epidemic, WHO and several governments made significant strides in keeping the media and public informed, but even more is needed. Health agencies and governments must learn how to garner credibility by providing the most reliable current information rapidly, even in the face of great uncertainty, recognizing that the situation may be rapidly changing. Providing context in which to understand the epidemic is often helpful in demystifying the outbreak and reducing fear.

It should also be clear by now that the occurrence of epidemic disease is indeed a global problem. The best place to stop the next major epidemic is at the source. A novel disease can arise anywhere and circumnavigate the world in mere days. In this increasingly globalized world, the inescapable conclusion is that we are all in this together, and it is in our own interest to help strengthen global health. But one commodity that has been in particularly short supply is political will. There has been a long history of good intentions undermined by policy failures and lack of funds (Henderson 1993; Garrett 2000). Good efforts are sometimes undertaken, with the best of motives, but are not sustained. This is a longstanding malady of public health in general. The example of the delays in taking AIDS seriously at the outset, which helped allow the disease to take hold worldwide, was mentioned earlier (Shilts 1985; Garrett 2005). Indeed, HIV/AIDS is still expanding. In 1995, a broad US government interagency group, the Committee on International Science, Engineering, and Technology Policy (CISET) at the White House Office of Science and Technology Policy (OSTP) discussed the problem of emerging and re-emerging diseases, and published a report which made a number of very sensible recommendations for improving surveillance and response (CISET 1995). Despite the excellent case made by the document, relatively few of the recommendations were implemented. The report ends with a "Final OMB/OSTP Caveat" added by the Office of Management and Budget after drafting, which states in part:

The Administration is committed to a broad range of high priority investments (including science and technology), to deficit reduction, and to a smaller, more efficient Federal government. These commitments have created a very challenging budget environment – requiring difficult decisions and a well thought-out strategy to ensure the best return for the nation's taxpayer. As part of this strategy, this document does not represent the final determinant in an overall Administration budget decision making process. The research programs presented in this report will have to compete for resources against many other high priority Federal programs. If these programs compete successfully, they will be reflected in future Administration budgets.

Former officials involved in the development of the report believe that the "OMB caveat" prevented anyone from taking the recommendations seriously. A decade later, in November 2005, President George W. Bush announced a new initiative for pandemic influenza, with a budget request of $7.1 billion (White House 2005). One can only hope that the sense of urgency has been increased by the recent history of SARS and other close calls.

CONCLUSIONS

- The SARS virus probably originated in bats, was spread in Asian live animal markets to civets (a small mammal prized for food), and infected food handlers or restaurant patrons who prepared infected civets or their meat.
- Once the SARS virus "jumped" to the human population, it continued to evolve, and spread by the respiratory route to others in close contact with patients (such as healthcare workers and family).
- There are many other currently unknown infectious diseases.
- Most are pathogens (viruses or bacteria) that exist in nature and get an opportunity to cross species.
- So, for example, a virus of another species may come in contact with people through agriculture or by contact with food animals that may be natural hosts for the infection.
- Many "new" infections are unable to transmit readily to others; but, if it can transmit, a novel infection can spread worldwide through population movements and global travel (e.g., HIV/AIDS), or even by one infected person in a large hub (SARS, from Hong Kong).
- Emerging infections will continue to occur, and possibly even increase, as opportunities increase for introduction and spread of novel pathogens.
- Early warning and appropriate public health actions (epidemiology, such as case investigation, understanding and interrupting transmission; and laboratory work identifying the infectious agent and developing diagnostic tests) are essential to recognition and control of emerging infections.
- Disease reporting is often delayed, sometimes for fear of political or economic repercussions. Given that early warning and recognition are of critical importance in containing an emerging infection such as SARS, should it be considered an ethical obligation to report

SARS TIMELINE

2002 (cases in southern mainland China)

November

6th: First case recognized, Foshan

27th: Guangdong Province, China: Non-official report of outbreak of respiratory illness with government recommending isolation of anyone with symptoms (GPHIN)

December

17th: First cases in Heyuan
- 11 cases recorded, 8 medical staff
- Index patient: Cook in a restaurant

26th: First cases in Zhongshan
- 28 cases clinically recognized (13 medical staff)

2003

January

21st: Guandong (China) provincial investigators report on "atypical pneumonia"

31st: First community SARS case in Guangzhou, China

February

10th: Report of "PNEUMONIA – CHINA (GUANGDONG)" posted on ProMED-mail (an e-mail listserv for reporting and discussion concerning emerging infectious diseases)

11th: Guangdong Province, China: report to WHO office Beijing of outbreak of atypical pneumonia (WHO)

14th: Guangdong Province, China: Official confirmation (to WHO) of an outbreak of atypical pneumonia with 305 cases and 5 deaths (China)

21th: SARS transmission at Metropole Hotel, Hong Kong

26th: Hanoi, Vietnam: Official report of 48 year-old businessman with high fever (> 38 degrees C), atypical pneumonia and respiratory failure, and with history of previous travel to China and Hong Kong

March

5th: Hanoi, Vietnam: Official report of 7 medical staff from French Hospital reported with atypical pneumonia

Early March:
- Hong Kong: Official report of 77 medical staff from Hospital reported with "atypical pneumonia"
- WHO teams arrive in Hong Kong and Hanoi, and confer with governments on investigation and containment activities

12th: First WHO global alert describing atypical pneumonia in Vietnam and Hong Kong

14th:
- Report of "ACUTE RESPIRATORY SYNDROME – CANADA (ONTARIO)" posted on ProMED-mail
- Four persons in Ontario, and three persons in Singapore, with severe atypical pneumonia reported to WHO

15th:
- Medical doctor with severe atypical pneumonia reported by Ministry of Health, Singapore on return flight from New York
- Second WHO global alert
- WHO issues travel advisories

28th: Details of earliest SARS cases from Chinese officials

30th: Outbreak of SARS in Amoy Gardens apartment complex (Hong Kong) announced

April

2nd: WHO travel advisory for Hong Kong and Guandong Province

16st: Virus identified

23rd: WHO issues travel advisory for Beijing, Shanxi Province, and Toronto

2003

January

5th: China and WHO confirm SARS case in Guangdong Province (no additional spread reported)

April

- Occasional sporadic cases in 2004 (some due to laboratory accidents)
- Last known cases, April 2004: 2 laboratory workers in Beijing (laboratory-acquired infection)

Source: Institute of Medicine (2004), WHO, and personal communications.
Note: Events before 10 February, 2003 are reconstructed from information made available later.

FACTORS IN INFECTIOUS DISEASE EMERGENCE:
(SOME EXAMPLES)

ECOLOGICAL CHANGES (including those due to economic development and land use)
Agriculture; dams, changes in water ecosystems; deforestation/reforestation; flood/drought; famine; climate change
Rift Valley fever (dams, irrigation); Argentine hemorrhagic fever (agriculture); Hantaan (Korean hemorrhagic fever) (agriculture); Hantavirus pulmonary syndrome, southwestern US, 1993 (weather anomalies)
HUMAN DEMOGRAPHICS, BEHAVIOR
Societal events: Population migration (movement from rural areas to cities); war or civil conflict; economic impoverishment; urban decay; factors in human behavior such as commercial sex trade, intravenous drug use; outdoor recreation; use of child-care facilities and other high-density settings
Spread of HIV and other sexually transmitted diseases; spread of dengue (urbanization)
INTERNATIONAL TRAVEL AND COMMERCE
Worldwide movement of goods and people; air travel
Dissemination of HIV; dissemination of mosquito vectors such as Aedes albopictus (Asian tiger mosquito); ratborne hantaviruses; introduction of cholera into South America, dissemination of O139 (non-O1) cholera bacteria (via ships)
TECHNOLOGY AND INDUSTRY
Food production and processing: Globalization of food supplies; changes in food processing and packaging. Health care: New medical devices; organ or tissue transplantation; drugs causing immunosuppression; widespread use of antibiotics
Food production processes: Hemolytic uremic syndrome (certain E. coli strains, from cattle, contaminating meat and other food products); Bovine spongiform encephalopathy; Nipah (pigs); avian influenza; SARS (probably)Health care and medical technology: Contaminated injection equipment (Ebola, HIV); opportunistic infections in immunosuppressed patients; Creutzfeldt-Jakob disease from contaminated batches of human growth hormone
MICROBIAL ADAPTATION AND CHANGE
Microbial evolution, response to selection in environment
"Antigenic drift" in influenza virus; possibly genetic changes in SARS coronavirus in humans; development of antimicrobial resistance (HIV, antibiotic resistance in numerous bacterial species, multi-drug resistant tuberculosis, chloroquine resistant malaria)

Caption:

FACTOR*

EXAMPLES OF SPECIFIC FACTORS

EXAMPLES OF DISEASE EMERGENCE

Source: Modified from Morse, 1995.
*Categories should not be considered mutually exclusive; several factors may contribute to the emergence of a particular disease.

ABOUT THE AUTHOR

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Most recently, Dr. Morse was Program Manager at the Defense Advanced Research Projects Agency (DARPA), Department of Defense, where he codirected the Pathogen Countermeasures program and subsequently directed the Advanced Diagnostics program. Before joining Columbia, he was Assistant Professor of Virology at the Rockefeller University in New York, where he remains an adjunct faculty member. Dr. Morse received his PhD from the University of Wisconsin-Madison.

Dr. Morse was the founding Chair of ProMED (the nonprofit international Program to Monitor Emerging Diseases) and was one of the originators of ProMED-mail, an international network inaugurated by ProMED in 1994 for outbreak reporting and disease monitoring using the Internet. He was also the Chair and principal organizer of the 1989 National Institute of Allergy and Infectious Diseases (NIAID)/National Institutes of Health (NIH) Conference on Emerging Viruses (for which he originated the term and concept of emerging viruses/infections).

He was a member of the Institute of Medicine-National Academy of Sciences' Committee on Emerging Microbial Threats to Health (and chaired its Task Force on Viruses) and was a contributor to its 1992 report Emerging Infections. He was also a member of the IOM's Committee on Xenograft Transplantation. He has been an adviser to the World Health Organization, the Pan-American Health Organization, US Federal Department of Agriculture, the US Centers for Disease Control, the US Department of Defense, and other agencies.

Dr. Morse is the editor of two books, *Emerging Viruses* (Oxford University Press, 1993; paperback, 1996), which was selected by "American Scientist" for its list of "100 Top Science Books of the 20th Century", and *The Evolutionary Biology of Viruses* (Raven Press, 1994). He currently serves as a Section Editor of the CDC journal *Emerging Infectious Diseases* and was formerly an Editor-in-Chief of the Pasteur Institute's journal *Research in Virology*. His professional interests include the epidemiology of emerging infections, international cooperation for infectious disease surveillance, and defense against bioterrorism.