

Global Diseases in the 21st Century

Throughout the industrialized world over the past half century, there was a growing complacency that the infectious diseases were a plague of the past. Until well into the 90s, we in the industrialized world had become increasingly complacent about the infectious diseases. Beginning in the 1940s, an emerging cornucopia of antibiotics brought victory over much of the bacterial world and new technologies, including tissue cell culture, brought a host of vaccines, including those to counter some of the most serious viral illnesses. At the same time, nutrition and housing standards improved. Smallpox and polio cases decreased sharply and then vanished. Other formerly important infectious disease problems all but disappeared or, at least, could be treated –measles, tetanus, rubella, diphtheria, pneumococcal infections, tuberculosis and others. The confidence of the time was aptly summarized by Sir Macfarland Burnet, the Australian Nobel Laureate who wrote: “one can think of the middle of the 20th century as the end of one of the most important social revolutions in history, the virtual elimination of the infectious diseases as a significant factor in social life.” It was an amazing statement considering how little progress had been made in dealing with the prevalent diseases of the tropics. However, the United States Surgeon General reflected the prevalent mood when he urged scientist to turn their attention now to the new frontier of the chronic diseases. In the United States, a number of medical schools closed their departments of microbiology; state and local health departments became smaller, many, in fact, eventually winding up with no expertise at all for dealing with infectious diseases; and the CDC, the Communicable Disease Center, changed its name to the Center for Disease Control and shifted resources to deal with chronic diseases.

In June 1981, a cloud appeared on the horizon. That month, the first cases of AIDS were discovered and by February 1983, the first 1000 cases had been identified. The attitude of arrogant self-confidence was apparent in April 1984 when the Secretary of Health of the U.S. announced the discovery of the human immunodeficiency virus and proclaimed “the triumph of science over a dreadful disease”. On the advice of her science advisers, she announced that a vaccine would be ready for testing within 2 years. Now, 20 years later, there is as yet no vaccine and only a few drugs, which at enormous cost are able to suppress virus growth for months to a few years.

In 1989, a more humble group of scientist met in Washington to explore the uncomfortable question as to what the prospects might be for other serious disease epidemics to occur. One especially disturbing scenario was raised: specifically, what if HIV had acquired a gene which permitted transmission by aerosol, as influenza spreads, for example. If that were so, and, give the many years that may elapse between initial infection to emergence of disease, those initial cases of AIDS, first identified in June 1981, might well have been only the first symptomatic victims of a massive pandemic with hundreds of millions of persons already infected. It is only too apparent that our basic understanding of microbes and pathogenesis is still inadequate to develop quickly either drugs or vaccines in the face of an emergency. Time is required and this means that we need to have the earliest possible notification of a microbial threat. It is clear now that HIV/AIDS was circulating widely in Africa for upwards of a quarter century—totally unrecognized.

The microbial world with its countless species multiplies at astronomical rates, each species continually mutating, adapting, changing to assure its own survival. Thus, it is inevitable that, from time to time, there will arise mutant forms, some highly lethal to man and some with a capacity to grow and to spread readily. Of special concern are the viruses, given their need to become entangled with the substance of host cells in order to replicate.

Over the past two decades, unusually large numbers of new or emergent infections have continued to appear and some of these have been able to spread rapidly and widely throughout large populations and across national borders. Some of these, such as Ebola virus are associated with case-fatality rates of over 80%; some, such as prion infections resulting in Cruetzfeld-Jacob disease, the human derivative of “mad cow” disease, may behave like HIV, exhibiting a very long latent incubation period before becoming symptomatic and thereby detectable. Finally, there is one virus, just over the horizon at the moment, which could seriously threaten the survival of the civilized world as now we know it – the H5N1 Asian chicken flu which, thus far, has resulted in 34 cases of influenza pneumonia in humans, two-thirds of whom have died. One hates to imagine what this virus would do should it begin to spread from human to human like current

influenza strains. Note that the Swine flu global pandemic of 1918-19 killed between 20 and 40 million persons. Its death rate is estimated to have been only one to two percent.

What is to account for this phenomenon of new and emergent diseases. What factors have a significant bearing on new disease occurrence. I would cite 4 in particular. A most significant force is population growth. Rapid changes are occurring, especially in terms of urbanization. As recently as 1800, less than 2% of the world's population lived in urban settings. By 1950, the proportion had risen to 20%. That number will rise to two-thirds by the year 2020. Looking at this phenomenon another way, there were in 1950, only two cities with a population of 7 500 000 or more – New York and London. Today, there are 30 such cities and 7, in fact, have populations larger than 15 000 000. A number of these are in tropical or subtropical developing countries and there, crowding, malnutrition, poor sanitation and environmental pollution are present of a nature never before witnessed. This is fertile soil indeed for a mutant pathogen to become established.

The second major force is travel, both international and national. Jetliners accommodate large numbers of travelers and at diminishingly low cost. Ever more adventuresome tourists and entrepreneurs now regularly travel into previously isolated areas. And, throughout the world, road systems now penetrate into formerly pristine areas and with inexpensive bus, truck and train travel, entire families travel from rural to urban areas and back in unprecedented numbers. This has greatly heightened the probability of unusual microbes being acquired in remote habitats and transported within a day or two to other points in the country or the globe.

A third major adverse influence is the proliferation of hospitals, a comparatively recent phenomenon. In many parts of the world, hospital resources are limited; isolation facilities are often ineffective or non-existent; and most accommodate large numbers of visitors. Hospitals have and have been the primary site for epidemic transmission of measles, Lassa fever and Ebola virus disease, among others. Some spread by direct contact but for others, contaminated needles and syringes are the cause because many hospitals have few supplies and are ill-equipped for proper sterilization.

Finally, the industrialization and internationalization of food supplies is taking place in all countries. It is an unprecedented change. Once food was grown locally on small farms and preserved or prepared for commercial use in small establishments. If

contamination occurred at any point, few were afflicted. However, economies of large-scale production dictate ever larger farms and the capacity for processing food on an industrial scale. Contamination at any point in the food production chain now can result in massive epidemics extending across many countries. The spread of the highly infectious E.Coli strain O:157:H7 throughout the U.S. and to Europe and Asia is aptly illustrative.

The Bioweapons Threat

The geometric increase in factors conducive to the development and spread of microorganisms across the world is cause enough for a global reconsideration of both national and international priorities and strategies. Heightening the concern is the all too recent appreciation of the serious threat posed by biological weapons.

False confidence had been engendered by the 1973 Biological Weapons Convention which called for the destruction of all offensive biological weapons and cessation of research efforts in this field. It was signed by virtually all countries. No provisions were made for verification of compliance but, until the 1990s, it was thought that the Convention was being adhered to. However, some 15 years ago, defectors from the Soviet Union reported that a major program was extant in that country, and later it was discovered that the program, in size, rivaled the nuclear program in numbers of personnel and sophistication. The existence of the program was confirmed by President Yeltsin. It was also discovered that a program was in place in Iraq and that a Japanese religious cult was likewise developing biological weapons. How many other countries might be similarly engaged was difficult to know.

Establishing a biological weapons capacity is comparatively easy. Major advances have been made in techniques for growing and manipulating microorganisms. What once was limited to sophisticated laboratories with expensive equipment is now being conducted in high school biology classes. Needed equipment is applicable for a variety of legitimate purposes and is not unique to biological weapons development. Moreover, both knowledge about biological weapons and strains suitable for use became more readily available coincident with the dissolution of the Soviet Union and reductions in support to the biological weapons laboratories. Large numbers of Soviet scientists dispersed to other laboratories and other parts of the world.

Committees that have studied the threats posed by weapons of mass destruction, identify the threat of biological weapons as being at least as significant as that posed by nuclear weapons in terms of numbers of casualties that might be caused. However, their use is deemed more likely because of their low cost, their simplicity of production, their ease of dispersion and their potential, as expressed by one writer, to cause panic sufficient to threaten the integrity of the state.

In sum, given the potential of both man and Mother Nature to cause potentially catastrophic disease epidemics, it would seem prudent that all nations reconsider their degree of readiness to deal with such problems.

Thanks for invitation.

Opportunity to discuss with you what are extremely serious concerns which potentially pose problems of a magnitude we would prefer not to talk about

Zurich

Global Diseases

biological challenges of the 21st Century

D.A. Henderson, MD, MPH

Center for Biosecurity, U. of Pittsburgh Medical Center

Global Medical Forum
Zurich

24 March 2004

- Man's only competitors for the dominion of the planet are the viruses – and the ultimate outcome is not foreordained.

Joshua Lederberg

In brief...

- The new threats and challenges of infectious diseases in the 21st century have scarcely begun to be appreciated
- The sources of the threat:
 - Natural mutation; emergence from remote areas
 - Biological terrorism
- The threat is global

Solutions will require a far greater level of international cooperation and agreement than is now in place

"Conquest" of the infectious diseases 1950s-70s

- Dramatic changes post WW II
 - Vaccines
 - Antibiotics
 - Nutrition
 - Housing
 - Sanitation
- Demise of disease - industrialized countries
 - Smallpox, diphtheria, whooping cough, tetanus, polio, measles, *et alia*

1962

- *"One can think of the middle of the 20th century as the end of one of the most important social revolutions in history, the virtual elimination of the infectious diseases as a significant factor in social life"*

Sir Macfarland Burnet

The consequences ...

- In medical schools
 - Departments of microbiology
 - Research support
- In hospitals
 - Infectious disease training programs
- At state and local health departments
- Nationally
 - U.S. Communicable Disease Center becomes the Center for Disease Control

A cloud on the horizon

- June, 1981 – first cases of AIDS identified
- April, 1984 – HIV is identified
 - “the triumph of science over a dread disease”
 - “a vaccine will be available in 2 years”
- A world-wide pandemic in progress
 - No vaccine as of 2004
 - No curative drug as of 2004

HIV is not the only surprise

- 1989 Conference on Emerging Infections
- A short, partial list of a new inventory
 - Legionnaires disease
 - Lassa fever
 - Ebola and Marburg virus infection
 - BSE – “mad cow” disease
 - Creutzfeldt-Jakob disease (human BSE)
 - Monkeypox

Recent concerns in the Americas

- SARS – from Asia
- Monkeypox – from Africa
- West Nile encephalitis – from the Eastern Mediterranean
- Anthrax – from ?
- H5N1 – most alarming of all threats

Increasing numbers of emerging diseases Major causes

- Growth in urban populations
 - Population of cities
 - 1950 – 2 with more than 7,500,000
 - 2000 – 30 with more than 7,500,000
 - 7 with more than 15,000,000
- Urban areas
 - 20 % in 1950
 - 67 % in 2020

Increasing numbers of emerging diseases Major causes

- Growth in urban populations
- Travel
 - Volume
 - Increased proportion of children
 - Remote area destinations

Increasing numbers of emerging diseases Major causes

- Growth in urban populations
- Travel
- Proliferation of hospitals in endemic areas
 - Major sites for disease distribution
 - Problem of blood borne diseases

Increasing numbers of emerging diseases Major causes

- Growth in urban populations
- Travel
- Proliferation of hospitals in endemic areas
- Industrialization and internationalization of food supply

Biological Weapons

- A threat, largely ignored until 1995
 - Too difficult to grow organisms
 - Technologically difficult to disseminate
 - Seldom used because of an inherent moral barrier

1995 Watershed events USSR Bioweapons Program

- A secret program – unknown until the 1990s
- 1992 – Ken Alibek, Deputy Director of USSR bioweapons program, deserts
- Bioweapons program consisted of 60,000+ persons in 50 different labs.

"On May 8, 1980, WHO announced that smallpox had been eradicated..Soon after, smallpox was included in a list of biological weapons targeted for improvement in the 1981-85 Five -Year Plan..."

Where other governments saw a medical victory, the Kremlin perceived a military opportunity..the military command issued an order to maintain an annual stockpile of 20 tons (of smallpox virus)."

Alibek, 1998

1995 Watershed Events Aum Shinrikyo -- Japan

- Religious cult releases Sarin gas in Tokyo subway
 - Cult - previously unknown to intelligence
 - Thousands of members, well-funded
 - Tried to aerosolize anthrax and botulinum toxin throughout Tokyo at least 8 times
 - Organized team to go to Congo to obtain Ebola virus
- Concern -- unknown, non-state sponsored organization, acting without concern for moral deterrents

1995 Watershed events Iraq

- Hussein Kamal deserts
 - Research reports reveal a much more extensive and sophisticated program than UNSCOM had been able to uncover
- Concern: If so much activity could continue undiscovered despite UNSCOM and other intelligence, how many other countries might be similarly engaged?

Russia today

- More than half of the scientists are no longer working in the old biological weapons labs. Many have gone abroad
- The major production lab for smallpox virus, at Sergiyev Posad, remains a secret facility
- The major viral weapons research lab continues work on smallpox, Ebola, et al
- Former Vice-Minister of Health Burgasov admits (2002) aerosolized smallpox was released on Voz Island in 1971 for studies

New World Coming

"While conventional conflicts will still be possible, the most serious threat to our security may consist of unannounced attacks on American cities by sub-national groups using genetically engineered pathogens."

U.S. Commission on National Security/21st Century
15 September 1999

Biological Agents of Greatest Concern

- | | |
|------------|--|
| ■ Smallpox | ■ Tularemia |
| ■ Anthrax | ■ Botulinum Toxin |
| ■ Plague | ■ Hemorrhagic fevers
Ebola, Marburg, etc. |

Agents that, if used, could threaten the integrity of civil government

Acquisition

- Instructions for the weaponization of major agents were described on the internet until 24 months ago
- Anthrax was listed as available from 46 labs in many parts of the world (2002 survey)
- Scientists from the former Soviet Union with knowledge and perhaps strains of organisms

Basic elements in preparedness

- Detection
 - Health centers and hospitals prepared to report promptly a disease outbreak, esp.
 - Hemorrhagic disease
 - Disease with rash
 - Paralytic illness
 - Epidemic disease response unit at national/state level ready to investigate unusual outbreaks
 - New approaches in surveillance--unproven
e.g. syndromic surveillance, drug usage, etc

Basic elements in preparedness

- Diagnosis
 - National lab capability and/or established link with WHO collaborating lab
- Response
 - Notification to WHO as appropriate
 - Isolation of patients
 - Vaccination or antibiotics

Basic elements in preparedness

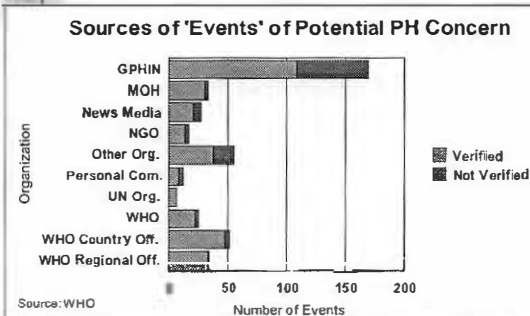
- International Health Regulations
- International -- WHO
 - Global Outbreak Alert and Response Network GOARN
 - 120 technical institutions participating
 - 2000-02 -- Responded to 34 events in 26 countries
 - Coordination of SARS and H5N1 threats
 - Global Public Health Information Network -- GPHIN

Daily Flow of GPHIN Information



Number of Reported Outbreaks by Source of Initial Reporting.

01 Jan 2001 to 31 Dec 2002. (n=439)



Barriers to global disease containment

- Lack of appreciation of the new threats posed by microbes in the 21st century
- Failure to recognize that the most critical problems are not national but international
- Provision of adequate resources
- Willingness to welcome joint participation in problems at the earliest possible date

Only the first few, tentative steps have been taken. Important as they are, there is a very long way to go before we can begin to feel confident about dealing with the microbial threats of the 21st century.

CATTS TROITE -
HANI

SARS