Congressional Briefing

Infectious Disease Threats
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Infectious diseases are the leading cause of death worldwide and the third leading cause of death in the United States. As the new century begins we are challenged by newly emerging infections and the decreasing effectiveness of our antibiotic arsenal. On June 21, 1999 the American Society for Microbiology held a special briefing in the Senate Hart Office Building. The briefing included presentations by some of the nation’s most eminent researchers. They discussed threats from infectious diseases and biological terrorism as well as research and strategies to detect, treat and control the resurgence of infectious diseases.

SPEAKERS:

Joshua Lederberg, Ph.D.
Nobel Laureate
Rockefeller University
The Bugs vs. the People: the Evolutionary Race

Stuart Levy, M.D.
Director, Center for Adaptation Genetics and Drug Resistance
Tufts University
Antibiotic Resistance: Microbes on the Defense

Gail Cassell, Ph.D.
Vice President, Infectious Diseases, Drug Discovery Research and Clinical Investigation
Lilly Research Laboratories
Causal Links of Infectious Agents in Cancer, Arthritis and Other Chronic Diseases

Anthony Fauci, M.D.
Director, National Institute for Allergy and Infectious Diseases
National Institutes of Health
The Importance of Global Health Research

James Hughes, M.D.
Director, National Center for Infectious Diseases
Centers for Disease Control and Prevention
Public Health Strategies for Addressing Emerging Infections
Introduction

The outlook for infectious diseases has changed remarkably during the twentieth century. Much of this period was marked by steady progress in preventing and controlling a wide range of troubling, many of them deadly, diseases. Increasingly effective public health measures, broadened use of a growing number of vaccines, and the judicious application of powerful and ever more sophisticated antimicrobial drugs have contributed in a major way to curbing the toll in human lives and suffering that infectious diseases can exact.

Put simply, there is no more smallpox or polio to worry about, little anymore in the way of measles and rubella, and many other infectious diseases that can give rise to such life-threatening conditions as meningitis or bouts of pneumonia can be satisfactorily treated with effective antibiotics.

Yet, despite this remarkable progress, infectious diseases remain the leading cause of death worldwide and the third leading cause of death in the United States. Moreover, the past few decades have brought new challenges in this arena, including new and reemerging diseases, such as AIDS, tuberculosis, malaria, Legionnaires’ disease, and deadly infections caused by a rodent-borne Hantavirus; the appearance and spread of antibiotic resistance; and the growing realization that microorganisms seem to be at least partly responsible for causing a surprising number of chronic diseases.

These are but a few of the unsolved problems that microorganisms continue to pose for public health officials, physicians, and microbiologists as they look ahead to the next century. With such challenges in mind, the American Society for Microbiology (ASM) convened a special briefing for Congress, staff members, and Administration officials on June 21, 1999, “Infectious Disease Threats as We Enter the New Century: What Can We Do?”

During the briefing, five scientific experts from both the public and private sectors outlined a number of the key infectious disease issues we are facing and suggested some of the critical steps that will be required to deal with those challenges during the century that lies ahead.
Nobel Laureate Joshua Lederberg predicted that, even though the world is better equipped to deal with it, a major pandemic will occur sometime during the next century. Although the most likely source of that pandemic remains influenza, he said that monitoring for both it and other infectious diseases is an essential component of efforts to guard against a deadly, worldwide outbreak.

Dr. Lederberg points out that an important hallmark of pandemics and, indeed, of many smaller-scale emerging infectious diseases is that they are zoonoses—that is, they involve microorganisms that can move from one species to another. The influenza virus appears to move among humans, pigs, and avian species, including chickens and ducks. During these excursions, the genes of several kinds of influenza sometimes mix and reassort, occasionally leading to highly contagious or more deadly forms. Public health officials throughout the world closely monitor influenza outbreaks for signs of just such changes. Investigative teams are in place to analyze the viruses and to prepare new vaccines to counteract them as needed.

The genetic inconstancy of influenza viruses typifies the hereditary dynamism of microorganisms. That flux is especially pronounced in the invisible occupants of the microbial kingdom. Indeed, according to Lederberg, microorganisms are frankly “promiscuous”—freely exchanging genetic materials as they adapt to changing conditions that they encounter.

This genetic promiscuity seemingly equips them to overcome the defenses of the hosts they infect. Yet, Dr. Lederberg pointed out, they do not wipe out their hosts, whether humans, animals, or plants. This paradox reflects a coevolutionary force: parasitic microorganisms in general strike a balance between aggressive virulence, in which they threaten and sometimes irreversibly damage their hosts, and a milder state of parasitic growth, in which the parasite and host gingerly coexist.

Dr. Lederberg said that even after decades of research, microbiologists understand this balancing act rather poorly. Exploring this mystery may prove critical for developing new drugs and discovering new treatments against infectious diseases.

Germs as weapons represent another critical—and certainly far darker—side to this balancing act between human hosts and the microbes that threaten them, according to Dr. Lederberg. Whether developed for use by national governments or by independently acting terrorist groups, the threat of biological weapons raises a special set of public health concerns for experts who are charged with protecting the health and safety of military forces and civilian populations.

Much of the concern over biological weapons now focuses on their potential use by terrorist groups against unsuspecting civilian populations. Dr. Lederberg said that rogue states or smaller groups of fanatics are considered the likely source of a biological weapons-based attack.

He also pointed out that the burden of dealing with the immediate consequences of such an attack falls primarily on infectious disease specialists and other medical and public health experts—those who are charged with identifying the source of an epidemic disease, diagnosing the specific infectious agent that
was used, and treating the victims. In addition, law enforcement and national security officials will also be part of the overall response to such an incident. They are also deeply involved in efforts to prevent such attacks from occurring in the first place. Importantly, close cooperation among all these officials is a vital part of the overall defense against biological weapons.

Several bacteria and viruses head the list of potential biological warfare agents, including the pathogens responsible for causing anthrax and smallpox. After a massive vaccination program eradicated smallpox as a natural disease threat by the late 1970s, the global vaccination program was phased out. Moreover, the vaccine that protects against anthrax remains in relatively short supply and in limited use because anthrax is such an uncommon disease. Thus, the general population is particularly vulnerable to smallpox and anthrax, both of which can be deadly when weaponized.

Such circumstances are leading microbiologists, infectious disease specialists, public health experts, and law enforcement officials to develop a broad-based, coordinated strategy for dealing effectively with the threat of bioterrorism, according to Dr. Lederberg. This strategy includes anticipating how smallpox, anthrax, and the other agents might be used for such purposes; planning for diagnosis and consequence management at the local level; adopting measures to prevent panic among the general populace; and conducting the basic and applied research that is needed to address these complex issues.
Antibiotic Resistance: Microbes on the Defense
As many pathogens develop antibiotic resistance, medical practices and agricultural policies need reconsideration

Dr. Stuart Levy likes to remind people that microorganisms are survivors. No matter what we assault them with in terms of antibiotics, microorganisms can adapt and find ways to resist the effects of those antibiotics. It's in their nature.

Moreover, we help microorganisms in this effort by making sure they are constantly exposed to antibiotics. United States manufacturers produce some 50 million pounds of such drugs every year, about half for human consumption through therapeutic treatments and the other half for non-human use, mostly in agriculture.

In fact, perhaps 35 percent of all antibiotics being produced in the United States are used in agriculture as feed supplements. Other uses of antibiotics in agriculture include treatment of infected animals and spraying of fruit trees to treat certain blights. Such uses tend to distribute antibiotics widely throughout the environment, exposing bacteria in soils, waterways, and elsewhere to these drugs. Thus, it's no wonder microorganisms learn to adapt to and overcome the usual effects of these erstwhile wonder drugs.

For fifty years, antibiotics also have been used pretty freely—and sometimes, all too carelessly—in human medicine. For instance, antibiotics are prescribed when they are not needed, and sometimes patients do not take these drugs according to directions. Whatever the reason, resistance to these drugs has dramatically increased and continues to rise. Problems are being seen in hospitals, where antibiotic resistance can be commonplace, but also in communities, where treatment of individuals can be even more challenging because they are so difficult to observe or supervise.

Dr. Levy said that probably the most threatening problem in the near term is multidrug resistant Staphylococcus aureus, often referred to as MRSA. More and more often, physicians come up against pathogens that have acquired resistance to virtually all known drugs. For instance, some forms of multidrug resistant Staphylococcus aureus are proving life-threatening to patients following what was supposed to be routine orthopedic surgery. Removing the prostheses proved the only reliable strategy for saving one group of such patients who repeatedly failed antibiotic therapies. Nor are problems with MRSA confined to hospital settings. This form of antibiotic resistance is now well established in several geographically dispersed communities, including in Dallas, Texas, and in parts of Australia and New Zealand.

Because this situation is growing ever more serious, Dr. Levy said that it is time to take positive steps. He thus recommends several measures such as prescribing shorter courses of antibiotic therapy, cycling usage of common drugs, better educating consumers about the proper use of antibiotics and steps they may follow to reduce the spread of resistance, and encouraging research to develop new classes of antimicrobial products. Also worrisome are marketing efforts to coax consumers to use a range of antiseptic products throughout their homes, which Dr. Levy suggests could make matters worse rather than better. Instead of remaining at siege against commonplace microorganisms, he said that it would be wiser to “come to the peace table.”
Dr. Gail Cassell pointed out that physicians and public health experts are coming to appreciate that microorganisms play more of a role in chronic diseases than anyone thought. Chronic diseases, including heart disease, cancer, arthritis, diabetes, and asthma, cause a great deal of suffering and deaths and, each year, also cost a huge amount in terms of dollars spent on medical care and in lost productivity.

Heart disease is the number one killer in the United States, and the combined costs for heart disease and stroke amount to billions of dollars. For the past several years, several groups of investigators have been actively studying whether microorganisms may play a central role in causing atherosclerosis disease, a condition that often leads to acute heart attacks. Some studies indicate that microorganisms not only are found in lesions along arteries that feed the heart muscle, but antibiotic treatments to eliminate those microbes may actually reduce the risk of heart attacks. Studies in rabbits and mice lend support to this hypothesis, which has not been conclusively proved. Nonetheless, results suggest that microbial pathogens may play an important role in this debilitating disease.

Even sounder evidence indicates that microbial pathogens are involved in causing other chronic diseases, including peptic ulcers, several types of conditions affecting the lungs, chronic arthritis and several forms of cancer. Many members of the medical community were surprised to learn that a bacterium known as Helicobacter pylori can persist in the acid conditions of the stomach, where it can cause ulcers. This discovery is changing how physicians go about treating such ulcers. Infectious agents also may be responsible for causing a serious, sometimes fatal condition known as chronic obstructive lung disease that is common among prematurely born infants. Similarly, microorganisms are implicated as causing other chronic lung diseases, including certain forms of asthma.

Much of the research to uncover the connections between these chronic diseases and microorganisms is at an early stage. But it is forcing investigators to reconsider many time-honored beliefs and to rethink very carefully how microbes may play a part in diseases in which no one suspected them to be involved. In fact, there are a good many different ways in which microorganisms might participate in such disease processes besides directly causing them. For instance, microbes might serve as cofactors, or they might trigger immune responses, including autoimmunity, as well as inflammatory responses and consequent damage.

Coming to better understand these indirect, often subtle ways in which microorganisms contribute to human disease will not be easy, according to Dr. Cassell.
Indeed, she urges researchers and policy makers to begin thinking about new ways to study complex diseases—in part, by putting together teams of investigators whose specialized training comes in different disciplines. Such teams may need to work for extended periods, ranging to full decades, before they can determine precisely how microorganisms and host responses develop into certain disease syndromes. To be sure, such research efforts will be more expensive to support. But in the long run, developing a deeper understanding of chronic diseases is likely to be the most effective way to reduce the human suffering these diseases now cause.

Recent data suggest a role for one or more infectious agents in the following chronic diseases: chronic lung diseases (including asthma), cardiovascular disease, and cancer. Many of the agents implicated are commonly transmissible and are either treatable with existing antibiotics or are potentially treatable with antiviral drugs. Thus, proof of causality in any one of these diseases would have enormous implications for public health, treatment, and prevention. Few areas of research hold greater promise of contributing to our understanding of infectious diseases and the eventual relief of human suffering.

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Dr. Anthony Fauci, said that it is essential for NIH to think globally when planning the infectious disease research agenda. Infectious disease agents do not respect geographic or political boundaries. The virus that infects a poor villager in India or a young child in Africa can also cause havoc among residents in New York or Iowa. Researchers and physicians in the United States share a humanitarian duty to improve the health of everyone, no matter where they live. Sound health contributes to economic well being and political stability.

Dr. Fauci said that it is a mistake “to think of global epidemics as something that happens infrequently.” His elderly father, for example, has witnessed both the 1918 influenza pandemic and the ongoing AIDS epidemic caused by the human immunodeficiency virus (HIV). Thus, he pointed out, “to think that there won’t be another pandemic [affecting] our children... is naive.”

The AIDS epidemic is the pivotal infectious disease epidemic of the late twentieth century. The epidemic was first recognized in 1981 and its annual death toll has climbed steadily through the 1990s. A heroic research campaign, one waged in both the public and private sectors, has paid off with a series of new, potent antiviral drugs which used in combination, can retard the progress of HIV and reduce its deadly effects. However, these drugs are far from ideal. They cause a range of side effects, HIV develops resistance to them, and they are expensive—indeed, too expensive to have much impact except among industrialized nations.

Globally, more than 33 million people are infected with HIV. In countries throughout Sub-Saharan Africa, in Asia, and elsewhere, this virus is insidiously damaging not only the health of millions of young adults and children, but is also undermining local economies and threatening political stability.

Thus the need for a safe and effective vaccine to prevent further spread of HIV is paramount. In 1999 NIH allocated more than $194 million toward this effort, and it is involved in an international, cooperative effort to develop and test such a vaccine over the next decade. While those development efforts continue, the infrastructure is being built to clinically test and evaluate that vaccine.

On a similar global scale, NIH is stepping up its efforts to combat other worldwide killers, including tuberculosis and malaria. Both of these diseases are resurgent, in part because the agents that cause them have developed resistance to the drugs used for treating these infections. Recent research efforts have focused on the genetics of these microorganisms, with large-scale projects to identify new targets for developing more effective drugs and vaccines. Similar projects are under way, many of them nearly complete, to determine the full DNA sequences of a range of important human pathogens as a way of developing better diagnostic tests, vaccines, and drugs.
Dr. James Hughes described recent efforts by public health officials to strengthen programs for identifying, preventing, and, where necessary, combating infectious diseases. Recognizing that efforts to deal with infectious diseases are needed on many fronts, CDC officials have been forging ties with various domestic and international partners for this purpose.

Some of these watchdog programs involve partnerships between CDC and local or state agencies. For instance, CDC now works with state and local officials at eight separate sites throughout the United States monitoring for emerging infectious agents. These population-based efforts entail and focus on foodborne disease, invasive bacterial diseases, and instances of unexplained deaths or serious illnesses of possible infectious cause. A more modest effort of 28 states and two large cities aims at strengthening the capacity to conduct surveillance and epidemiological and laboratory investigations. Yet other collaborative projects call on emergency departments, infectious disease clinicians, and specialists who are likely to see international travelers—including those who move between the United States and Mexico—to serve as sentinels, watching for unusual instances of infectious disease.

Foodborne disease outbreaks over the past decade or more, some of them severe and a few of them deadly, have led CDC, in collaboration with the Food and Drug Administration and the U.S. Department of Agriculture to focus considerable attention on this source of infectious disease concerns. For instance, public health experts in over 30 states are now involved in the CDC PulseNet program, which enables them to rapidly identify the microbial culprits responsible for an outbreak through modern molecular fingerprinting technologies. Such outbreaks can spread rapidly over wide geographic areas unless contaminated foods are identified and promptly removed from the distribution chain. Because the health and economic consequences of such outbreaks can be substantial, public health officials are giving high priority to broadening this system as a way of ensuring the earliest possible detection of a problem for its quick remediation.

CDC officials initially formulated a comprehensive plan for combating emerging infectious diseases in 1994 and have revised and expanded it in 1998, according to
Dr. Hughes. Some changes reflect a renewed emphasis on rebuilding the public health infrastructure throughout the United States, while others address important global issues as well as heightened interest in the role of microorganisms in chronic diseases. And in practical terms, efforts are now underway to train young investigators in the epidemiologic and laboratory specialized techniques necessary for recognizing infectious agents quickly.

Beyond that, perhaps the most important message is for public health officials at CDC and elsewhere and for microbiologists who are concerned about emerging and reemerging infectious diseases is that they should expect and be prepared to deal with the unexpected.
The American Society for Microbiology (ASM) is the largest single life science society in the world with more than 42,000 members representing a broad spectrum of subspecialties, including microbiologists who work in biomedical, clinical, public health, and industrial laboratories. The mission of ASM is to enhance the science of microbiology to better understand basic life processes and to promote the application of this knowledge for improved health and for economic and environmental well-being.

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