The recognition of Rochester Medicine provides a brilliant and varied description ranging from the smallpox vaccine evaluation studies in Monroe County's designation as one of three national demonstration centers of basic research in diagnostic sensing

Convergence 2002 -- keynote address

It is a pleasure for me to return to my alma mater on this auspicious occasion and to participate in a conference that could not possibly be more relevant to the serious and ugly new threat of bioterrorism. You at the Medical Center are assuming a leadership role in the nation's preparedness. That is welcome. As in no other field of medicine is there a need to bring together the very best of science from academia, the private sector and industry. That joining of effort has, as yet, scarcely begun. There are major problems to address and they will not go away. The genie is out of the bottle. Presently, I can identify little in prospect that is likely to significantly diminish those threats we face.

It is generally agreed that the 21st century brings with it a new era in the biological sciences with advances in molecular biology and biotechnology that promise longer, healthier lives and the effective control, perhaps elimination of a host of acute and chronic diseases. The prospects are bright but there is a dark side -- the possibility that infectious agents might be developed and produced as offensive weapons; that new or emergent infections, like HIV/AIDS, might overwhelm available preventive and therapeutic measures or that laboratory scientists, perhaps inadvertently, might create and release a new and lethal agent. These concerns are as relevant to Europe, to Africa, to Asia as they are to America. In today's world of rapid travel and large migrant populations, epidemic disease, wherever it occurs and of whatever origin, threatens the security of all nations. We are, today, ill-prepared to deal with these challenges.

Nothing in the realm of natural catastrophes or man-made disasters rivals the complex problems of response that would follow a bioweapons attack against a civilian population. The consequence of such an attack would be an epidemic and, in this country, we have had little experience in coping with epidemics. In fact, no city has had to deal with a truly serious epidemic accompanied by large numbers of cases and deaths since the 1918 influenza epidemic, more than two generations ago.

Senators Hart and Rudman, chairs of the United States Commission on National Security in the Twenty-first Century, singled out bioweapons as perhaps the greatest threat that the U.S. might face in the next century. Admiral Stansfield Turner pointed out that, besides nuclear weapons, the only other weapons with the capacity to take the nation past the "point of non-recovery" are the biological ones.

The Dark Winter scenario dramatizes the catastrophic potential of smallpox as a weapon. It is, of course, not the only possible organism that might be used. In 1993, the Office of Technology Assessment estimated that 100 grams of anthrax released upwind of a large American city - the model being Washington, DC - could cause between 130,000 and 3 million deaths, depending on the weather and other variables. This degree of carnage is in the same range as that forecast for a hydrogen bomb. Although there is legitimate concern about the possible use of chemical weapons, they are far less effective pound for pound and extremely difficult to deploy over large areas. One hundred grams of anthrax can produce as many casualties as a ton of a chemical nerve agent and we now know what 10 grams can do when sent through the mails.

The insidious manner by which a biological attack would unfold is itself alarming. The fact of an attack using an explosive or chemical weapon would be recognized immediately and resources summoned quickly to deal with the consequences and to begin to remediate the situation. A biological agent would, in all probability, be released clandestinely as an aerosol spray, odorless and invisible, which would drift slowly throughout a building or across a city. Not until days to weeks later would people begin to fall ill; new cases would continue to occur over a period of one to several weeks. Some of those exposed, in all likelihood, would be hundreds of miles away when they develop symptoms -- in other cities, in other countries. Thus, the consequence of the attack would extend well beyond the immediate area of release.

Why have biological weapons not been used. It is not because it was believed they would not work.

As Gradon Carter has pointed out, the utility of bioweapons has been demonstrated by all possible means short of war. By the 1960s, the U.S. knew how to grow and process many microorganisms in a form usable for mass casualty biological weapons. Trials that modeled dispersion of simulant agents as aerosols were conducted in many cities and scores of tests with live biological agents using animals as targets were performed at the Johnson Atoll from 1963 to 1969. There is now no doubt and there was then no doubt, of the capacity of these weapons to cause widespread casualties. A World Health Organization (WHO) analysis, now 30 years old, supported the belief that biological weapons are strategic, population-destroying weapons. Since then, the technology needed to create and disperse these weapons has advanced significantly.

The year 1972 was a significant one in the history of bioweapons. That year, the Biological Weapons Convention was agreed upon, calling for all signatory countries to cease research on biological weapons and to destroy existing stocks. The Soviet Union and Iraq were both parties to the Convention. The Soviet Union, however, began immediately to greatly expand and modernize its existing biological weapons program, and to develop genetically engineered pathogens and other organisms that could serve as strategic weapons. A new organization was created called Biopreparat. Ostensibly a civilian operation, it recruited some of the most capable of Russian biologists. At its peak, it employed over 60,000 persons. There was also a military program of at least 15,000 people and an agricultural program making crop pathogens that employed 10,000 people. The overall complement of staff was equivalent in size to that of its nuclear program. Biopreparat's agenda included the manipulation of viruses and micro-organisms to render them capable of surviving delivery on missile warheads; the development of particularly virulent strains of organisms that are resistant to vaccines and antibiotics; the creation of peptides that could alter moods and heart biorhythms; and the manufacture of tons of anthrax, as well as smallpox virus and antibiotic-resistant strains of plague.

Although the Soviet program was of prodigious size and sophistication, the infrastructure that is actually necessary to make a biological weapon is, in fact, comparatively simple and inexpensive, especially compared to that required to make a nuclear weapon. To make one kilogram of plutonium requires 100 tons of uranium ore; a substantial quantity of specialized equipment; and an enormous facility readily visible from the air.

biological weapon can be produced with the same equipment one uses to produce an ordinary vaccine; it can be readily housed in a building the size of a two-car garage; nothing on the exterior would identify its use. Moreover, the room and the equipment could be sufficiently cleansed within 24 hours so that no one, on inspection, would be able to determine whether it had been used to make vaccines or biological weapons.

The intelligence agencies have estimated that at least a dozen states possess or are actively seeking an offensive biological weapons capacity. ~~Most of these states are those named by the State Department as sponsors of terrorism~~. Expertise for operating these facilities is readily available from now poorly funded laboratories of the Russian biological weapons complex. ~~For these countries,~~ biological weapons have a special appeal. They are inexpensive, they occupy little volume, they are readily transportable from place to place and they are capable of being disseminated covertly so that attribution may be impossible.

It is also important to appreciate that the technologies needed to build biological weapons are available in the open literature and on the Internet. This is not knowledge that is limited to a few hundred scientists isolated in a laboratory in the western desert. ~~There are many scientists who have this knowledge and are capable of putting together a biological weapon~~

A key reason for being concerned about biological weapons is the remarkable progress now being made in biotechnology and genomics research.

~~Indeed, it is generally acknowledged that the life sciences will be the most important technology of this century.~~

But, as the understanding of molecular biology increases and as we develop the ability to manipulate cellular processes, we are also creating the tools and knowledge for building more powerful and more diverse weapons. When we discover why a particular virus or bacteria is especially virulent or why it has become resistant to antibiotics, we create an opening for building a new drug or a new vaccine. At the same time, we facilitate the creation of tools needed to build more virulent weapons.

It is difficult to imagine how the public might respond in today's world to a fast-moving lethal epidemic. In recent decades, there have been few such epidemics in industrialized cities. One of the more recent occurred in India in 1994. Plague broke out in the diamond-polishing district of Surat. It was reported by the media as a deadly, mysterious fever, possibly plague. Within hours, panic reigned. People began streaming from the city. Many in the medical community were among the first to leave. Eventually half a million fled, leaving the city a ghost town. It is estimated that India lost some two billion dollars in lost trade, embargoes, and production as a consequence of this outbreak. How many actually died of plague is still not clear but the total was not more than 50.

Epidemics have the potential to spread internationally as we have observed with the HIV/AIDS epidemic. The disease is contagious but it is not easily transmitted from one person to another. Nevertheless, it spread across the globe and is changing the population demographics in some African countries to a degree comparable to that caused by the Black Death of the 1300s, which killed a third of the European population.

Addressing the Threat

Beginning in 1995, when the first Presidential Decision Directive was issued, preparations to respond to terrorism focussed almost exclusively on training and equipping "first response" teams to counter the effects of a nuclear or conventional explosive device or a chemical attack. Training programs in 120 cities were targeted to include police, fire and emergency rescue personnel in a "lights and sirens" type of response and special full-time units of the National Guard were constituted whose function is not clear but certainly have little to do with bioterrorism.

Not for several years was there a beginning comprehension that the consequences of use of a biological weapon would be an epidemic and that those first detecting its presence and those primarily responsible for controlling the disease would be public health personnel and physicians. Accordingly, in most cities, public health, medical and hospital personnel were not included either in planning or training. Finally, in FY99, ~~significant~~ funds began to be made available to the Department of Health and Human Services, ~~primarily the Centers for Disease Control (CDC),~~ whose traditional responsibility, with state and local health departments, has been the surveillance and control of infectious diseases. Some ~~two~~ three years ago an Office dealing with Bioterrorism was established at CDC; modest funds began to be made available to the states for development of programs

On January 10, this year, funds for a major new initiative were appropriated by the Congress -- in all some $3 billion for the Department of Health and Human Services, a ten fold increase over the amount made available only one year before. The funds ~~had~~ were ~~been~~ identified by the Congress for a variety of different initiatives by the different Agencies and Centers of the Department. Secretary Thompson was concerned both about coordination of activities as well as the likely duplication of effort. Indeed, even after 3 years of comparatively modest funding, a host of programs had already sprung up. You should know that in a bureaucracy, whenever funds are appropriated for a new program, many existing offices and programs discover that they have a role to play that is vitally important to the new initiative and who are deeply concerned that they receive additional funds to discharge that responsibility. Thus, there was interest and appeals by special offices concerned with women's health, minority health, Indian affairs, alcoholism, drug abuse, ingrown toenails, sports medicine and who knows what others. The Secretary ~~Thus, he~~ decided to create a new Office of Public Health Preparedness and prevailed upon me to be its first Director. He assigned to the Office the full $3 billion with instructions to release the funds only when we were satisfied that there was direction, coordination and accountability. I can only say that since January 10, we have been extremely busy.

Concern about the "second shoe" – need to be better prepared.

Decision to distribute $1 billion to states
Normally 3 – 4 months → 3 weeks. Use 20% Want plans by 15 Apr
Broad authority for planning and use of funds.

Items: State and local
1) Strengthen state and local public health management and infra-structure. 24/7 response
2) Link to Emergency rooms.
3) Build out laboratory capacity – 100 labs able to diagnose the principal agents
4) Regional planning for hospitals – surge capacity of 50 beds.
5) Plan for rapid immunization – mass distribution of antibiotics or smallpox vaccine

Vaccines and antibiotics –

Two organisms of greatest concern – smallpox, anthrax.

Smallpox vaccine – 91 000 doses on Sept. 15
Now an emergency reserve of 150 million doses.
Now T.C. vaccine – 210 million by end December
Antibiotics – 12 push packs
Enough to Rx 20 million x ten days.

Educational initiatives

Research

Most important is the need to mount a robust research and development program. This will be my primary area of responsibility as Principal Adviser to the Secretary. We must engage the genius of the universities, the pharmaceutical firms and the biotechnology companies in meaningful research efforts -- and I underline the word meaningful.. Unfortunately, there are a great many research and development projects that have failed to identify actual needs. Thus, we are steadily bombarded with prototypes and proposals for any number of "solutions" for supposed needs that really are not. What many have not appreciated is that the bioscience community has no substantial history of engagement with defense projects and, by and large, they have not been eager to work with government in this field. Expertise in the academic world is singularly deficient as the diseases of greatest concern are unknown or virtually so in this country and present public health staff have almost no experience in dealing with epidemics.

The budget this year provides only limited funds for research in the area of bioterrorism but the President's budget for next year calls for an increase of $1.5 billion. The National Institute of Allergy and Infectious Diseases will administer most of this money. In the course of a meeting last February , they laid out a research agenda as follows:

1. Better Understanding of the Biology of the Microbe --to better understand the microbial components that define the pathogen's life cycle and the processes critical to initiating infection or influencing disease severity. Comparative genomics will be a particularly important part of the effort.

2. Studies of host responses to define pathogen-triggered protective and deleterious immune responses; to develop new immuno-stimulatory agents; to better understand pathogen-specific immuno-regulation.

3. New and improved vaccines especially for anthrax and smallpox

4. A broader, more robust arsenal of anti-infective agents, including monoclonal antibodies against critical virulence factors

5. Diagnostics that can more rapidly and accurately identify the key organisms with a special emphasis on micro-chip based platforms.

6. Expansion of research resources, both physical and professional, in part, through the development of regional Centers of Excellence with capacity for BSL 3/4 capaability.

This is an inadequate summary for all that is planned and I would suggest that you contact the NIAID for a copy of their report should you have further interest.

Meanwhile, we will be convening this summer a National Advisory Committee on Biopreparedness and that Committee will have specific components dedicated to dealing with research initiatives and policy -- basically, to ascertain what more needs to be done to obtain the cooperative participation of government, industry and academia.

There is much to be done. An interesting perspective on all of this was offered during conversation I had with a high level government official while travelling on Air Force 1.