

Conference addresses newly emerging and re-emerging infectious diseases

by John Grauerholz, MD

The following report, by a specialist correspondent, is presented as a contribution to the debate on how to deal with emerging diseases, and biological warfare.

On May 13-14, 1996 a conference on "Building a Global Network For Infectious Disease Prevention, Surveillance, and Interventions" occurred in Washington, D.C. Sponsored by GenCon, the National Consortium for Genomic Resources Management and Services, it assembled scientists, administrators, and technologists to discuss building a global network to combat infectious disease. Representatives of the White House National Technology and Science Council (NTSC), National Institutes of Health, U.S. Department of Agriculture, USDA Animal and Plant Inspection Service, USDA Agricultural Research Center, and the Federal Bureau of Investigation were present on the program. Other speakers included a former head of the Centers for Disease Control, the head of the Office of Emergency Preparedness of the U.S. Public Health Service, representatives of the Pan-American Health Organization, World Bank, U.S. Agency for International Development, the Institute for Genomic Research, Arms Control and Disarmament Agency, and several distinguished academic microbiologists and private sector biotechnology companies. Combining speakers and attendees, this event had the broadest spectrum of institutional representation at a meeting on a particular topic.

We need a 'concerted quick response system'

Opening the conference, Thomas W. Frazier, president of GenCon, described the principal challenge as "successful integration of organizational resources and missions into a concerted quick response system with a global reach. If that weren't difficult enough, global travel and the speeds at which microbial agents can spread internationally would require unprecedented levels of international cooperation in detection, analysis, and control efforts. Past multilateral cooperative efforts have left a lot to be desired with respect to speed and efficiency in meeting common social and medical needs."

Frazier noted that "detection and analysis technology still has a long way to go to be useful in a quick response context. Traditional analytic methods take far too long and are too

expensive for routine or priority screening purposes. DNA-based analytic technology shows promise here, but has been represented to be more fully developed than it really is. In any event, we need more sensitive, less expensive, and more quickly performed screening tests. This requires intensive attention and coverage of promising alternative lines of research by both military and civilian research organizations.

"The motivation for creating a global network for responding to microbial threats comes from two developments: 1) New and re-emerging lethal diseases are cropping up in disturbing numbers around the world; and 2) biological and chemical weapons are now seen as the principal military threats now that nuclear missile threats have diminished. The concern about 'loose nukes' (small nuclear devices that can be fashioned from pirated material and then transported by land to the target site) is low because only small amounts of fissionable materials are unaccounted for. Since BW and CW threats come from both nation-states and terrorist organizations, compensatory activities must be developed on the part of law enforcement, intelligence, and defense organizations alike, hopefully in a cooperative manner.

"While the BW and CW threats are of greater apparent concern to the Congress, they cannot easily be distinguished from natural exposures to disabling or lethal microbes. For example, anthrax is one agent that nations with BW programs have in inventory. It has an unusually large physical reach and can induce very high casualty rates in comparison with other BW agents. Anthrax is also a naturally occurring disease that can continue to infect animals as well as humans for years, once established in a given location. So there can be a problem detecting where the pathogen originated and how it arrived at the location involved. If these determinations are successful, then there is the problem of determining an appropriate course of action, whether or not the pathogen was introduced deliberately or through natural occurrence. From whatever origin, the treatment plan may still have to be the same, assuming that treatment is possible.

"There is a reluctance in official quarters to divulge how vulnerable we really are to terrorist uses of CW and BW agents. One concern is that public discussions will precipitate amateur terrorist ambitions and events. There are concerns

that disclosures of animal diseases, such as the Mad Cow disease, will adversely affect a production industry, as recently happened in Britain. So, there is much reluctance in official government quarters to divulge such information. On the other hand, if a deadly epidemic does occur, such as a 'Super Flu,' the public should not be just ignorant victims. Front line health and rescue workers would need specific advance training to be really helpful and not just carriers of the infectious disease.

"Terrorist handbooks already exist for downloading from the Internet, as Senator Biden illustrated recently on the Senate floor. Government efforts to deny existing threats often backfire, as illustrated in the British Mad Cow disease affair. And it is difficult to administer large interagency programs in a secure way or in a way that classifies parts of the program but not other parts.

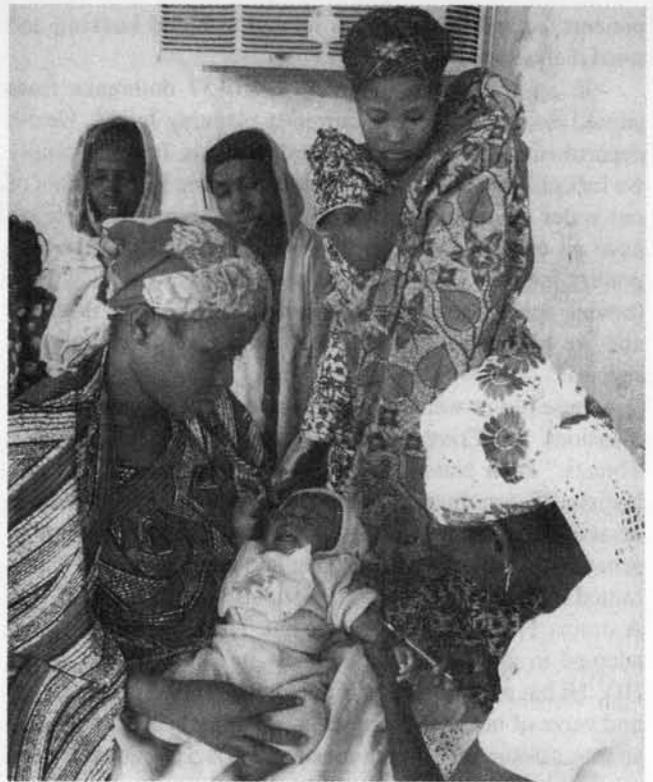
"Therefore, it makes sense to me to err on the side of excessive public disclosure of actual threat potential and impending threats. The public concern that results could then be useful in motivating useful public health education and in building public support for a truly effective networking program. In fact, I can see public health education channels on TV and an international infectious diseases information clearinghouse for public use through the Internet, as well as a parallel information clearinghouse for medical professionals. How these information resources might become a part of an official intergovernmental global network remains to be seen.

"In any event, it is important to take these concerns seriously and personally. We all need to think what we might be able to do to support a comprehensive networking development effort. As for GenCon, I think we could expand the GenCon network into a larger consortium that could function analogously to Sematech but in the infectious diseases area. At the least, we could create another study committee on infectious diseases that would review developments and provide advisory support to government on a continuing basis."

National security implications

Dr. Frazier then introduced Dr. Laura Efras of the White House Office of Science and Technology Policy (OSTP). The Committee on International Science, Engineering, and Technology (CISSET) of OSTP had produced a report on "Emerging and Re-Emerging Infectious Diseases," which called for a global disease surveillance network. Dr. Efras, a senior policy analyst in the Division of National Security and International Affairs, is responsible for coordinating White House initiatives on emerging infectious diseases. In her talk, "NTSC Perspectives on a Global Network," Dr. Efras discussed national security and international affairs as related in the CISSET report and a 1995 NTSC report. Having paid lip service to the importance of the problem and the need for cooperation, she got to the point: There is no new funding, and agencies are supposed to cooperate using existing funds.

Following this, came an "Overview on Emerging and Re-



Immunization of children in Niger. Experts agree that we are ill prepared to deal with the spread of infectious diseases, due to a lack of resources and poor coordination of the resources we have.

Emerging Infectious Diseases" by Frederick A. Murphy, DVM. He is the dean of the School of Veterinary Medicine at the University of California at Davis, and a former head of CDC. It is not a pretty picture. "We will have 100 million AIDS cases by the year 2000. Virulent strains of Venezuelan equine encephalitis are proliferating along with mosquito vectors. Ecologic factors include new strains from unique and isolated environments that are released by deforestation and population inroads into these areas. Primitive irrigation, without arthropod control, leads to increasing vector populations. Uncontrolled urbanization clusters large numbers of susceptible individuals in areas where they are subject to new agents. Resurgence of dengue represents a failure of vector control. Malaria is becoming drug resistant. Tick-borne diseases, such as Lyme, are becoming prevalent. There is a problem of zoonotic diseases, such as raccoon rabies and Ebola. Services such as PROMED (an Internet site for reporting on newly emerging diseases) are helpful, but we need front line people, clinicians and pathologists, who are aware of these problems and alert to new diseases such as hantaviral syndrome. There is a personnel problem in entomology and mammology. There are no young people in the loop. Behavioral problems enhance the spread of infectious diseases. Daycare centers are disseminators of infectious diseases. Then we have iatrogenic diseases; immunosuppressed transplantation and chemotherapy

patients, as well as problems related to blood banking and renal dialysis.

"In agriculture we have *E. coli* 0157 outbreaks from tainted meat (the epidemic currently plaguing Japan). Health departments lack personnel to deal with this. In water supply we lack ability to deal with cryptosporidium. Fifty percent of our water treatment plants can't cut it. Among animals we have an epidemic of avian influenza hitting our high-tech poultry industry. There are the prion diseases, such as BSE [bovine spongiform encephalopathy, or Mad Cow disease], and we have emerging diseases among some endangered species."

These topics were expanded on in the first panel on "Dimensions of Contemporary Human Infectious Disease Threats." Peter Nara of the Frederick Cancer R&D Center, National Cancer Institute, noted that the problem is infectious disease departments are viewed as a cost. There is complacency in the blood banks. In Thailand the parenterally transmitted B strain of HIV has been superseded by the E, C, and A strains. HIV 1B infections are flat. The E strain, which has adapted to genital transmission, is in a log growth phase. HIV 1E has a transmission efficiency of 1/10. There is a second wave of heterosexual transmission by genitally adapted strains, associated with pre-existing STDs. He said oral transmission is not out of the question due to genetic recombination. HIV spawns primary and secondary opportunistic infections. We need well-trained people to set up a sort of DEW line for emerging diseases. Nara laid strong stress on training new clinicians and researchers.

Bioweapons and terrorism

Kathleen Bailey of Lawrence Livermore Laboratory, who works on arms control for the National Security Agency, spoke on bioweapons and terrorism. Bioweapons are possessed by Russia and Iraq, among others, she said. Among terrorists, they pose the greatest threat and greatest probability of use of weapons of mass destruction. The Iraqi sites were discovered in August 1995 on the basis of information from defectors, after three years of searching couldn't find them. The Iraqis were working on anthrax, botulism, aflatoxin, wheat smut, and camel pox. So, they were contemplating attacks on crops and animals, as well as people. Russia had weaponized smallpox. It has had a long-standing program comprising six institutes and five production plants, employing 15,000 people, with a high surge capacity. They were developing tularemia and plague resistant to antibiotics.

Terrorist actions include a 1984 use of salmonella in Oregon by the Bhagwan cult. The Japanese Aum Shin Rikyo worked on biological agents and tried to obtain Ebola. They apparently had access to remote-controlled aircraft. In May 1995 an individual ordered plague from a type collection. There was an episode of ricin production. Mechanisms of control exist under the biowarfare convention of arms control agreements. Export controls are necessary. The Biological

Anti-Terror Act of 1989 is supposed to deal with these problems. Given the problem, military budgets for dealing with biowarfare have been cut 50%. The most likely delivery of mass bioweapons is by air, e.g., cruise missiles or drone aircraft with sprayers.

Dr. Bailey is well aware of the problems of coordinating government agencies to respond to terrorist use of bioweapons (see book review, p. 12). This lack of coordination and cooperation emerged again and again as the major problem at this conference.

Edward McSweegen of the National Institute of Allergy and Infectious Diseases stressed the importance of research and training infrastructure, and the need to expand research.

Plant and animal diseases

The second panel covered Impacts of Plant and Animal Diseases on Productivity, Agricultural Economics, and Human Diseases. Thomas E. Walton, DVM, PhD, who is the director of the Ames, Iowa, USDA Agricultural Research Service National Animal Disease Center, stated that agriculture is a \$150-200 billion per year industry. One major problem is zoonotic pathogens, organisms that spread from animals to people. The veterinary community is a resource for training animal disease doctors. There are 26 veterinary medical schools in the United States. There is the Foreign Animal Disease Laboratory at Plum Island, New York, which is part of the Animal and Plant Health Inspection Service (APHIS) that is responsible for stopping the entry of new animal and plant pathogens into the country. There is need for additional labs and biocontainment facilities, but federal funding has been flat. Animal pathogens are important, as in the recent outbreak of leptospiral pneumonia in South America. The BSE hysteria indicates the level of fear of animal pathogens.

Linda Detweiler of the USDA Animal and Plant Health Inspection Service described the extent of the industry. New Jersey exports 12 million horses a year! Tuberculosis eradication among horses began in 1905. Three herds were infected by contact with deer. Pseudorabies is caused by a herpesvirus. Eradication began in late 1980s. Avian influenza, H5, H7, is the most devastating U.S. poultry disease. BSE was first seen in Great Britain in 1986, possibly related to scrapie in sheep. Cattle were fed sheep renderings that included brain and spinal cord material. Currently there are 60,000 cases in Great Britain, which represents 98% of all cases.

Roy Gingery of the Animal Research Center in Beltsville, Maryland spoke on plant health. There is a new strain of corn blight from Mexico. A major problem is Karnal Bunt of wheat, a disease that originated in the Indian state of Karnal. It is not a human toxin, but produces kernel discoloration. On March 8, 1996 it was found in some U.S. grain. The economic implications are immense. Forty countries prohibit import of grain with Karnal Bunt. For years the U.S. bragged that its grain was free of Karnal Bunt. Now there is a nationwide survey for Karnal Bunt. Several states are under quarantine.

Another problem is restraint of trade, using disease as a non-tariff trade barrier to bypass the General Agreement on Tariffs and Trade and the North American Free Trade Agreement. How do we coordinate all this? Will the Pentagon share information with the World Health Organization? What about the problem of info-terrorism?

Call for public health infrastructure

Panel three discussed "Functional Requirements For a Global Network For Prevention, Surveillance, and Control of Microbial Threats to Humans." Gail Cassell, PhD, a professor at the University of Alabama at Birmingham, presented the problems in setting up a global network. We need a public health infrastructure, she said. The elements exist, but we lack a clear chain of command and responsibility. She stressed yet again the need for better interagency coordination. There is no U.S. agency to respond to foreign outbreaks and no funding available.

James Shih of the National Institutes of Health Department of Transfusion Medicine related the problems of HIV and the varieties of transmissible hepatitis. Starting from hepatitis A and B, we are now up to hepatitis G.

Kyle Olson of the Arms Control and Proliferation Analysis Center of TASC, Inc., an Arlington, Virginia defense consulting firm, spoke on "The Challenge of Surveillance." He noted that biological agents represent a major new weapon in the terrorist arsenal, and that biowarfare has been weaponized for the battlefield and probably used. Industrialized societies are at great risk from both strategic and tactical uses of biological warfare. He said that taboos against use of weapons of mass destruction by terrorists that may once have existed, have been eroded or even erased. Noting that TASC predicted terrorist nerve gas attacks, he said the sarin gas attack in Tokyo's subway system represented the crossing of a line. He concluded that while the technology exists to tie together international health and security experts, the policy community is still unclear about how to act, and this failure is potentially fatal.

The final panel of the day was "Agricultural Considerations in Building a Global Network for U.S. Protection from Microbial Threats." Donald L. Plucknett, PhD, president of Agricultural Research and Development International, described the process of breeding plants for increased yield and disease resistance. He argued that, contrary to some environmentalist claims, substantial further gains in yields are possible and that today's crops are hardier and more disease resistant than their predecessors. These results are attained by the effective use of genetic resources. However, it takes 20 years from the first cross to the development of a crop plant, and it requires continuing research to maintain these yields. Because of this, it is essential to learn about potential pests before they get here.

Joan Lunney of the Agricultural Research Center in Beltsville, Md., discussed the role of sanitary and phytosanitary

agreements under the World Trade Organization. Alejandro Thiermann of the USDA Animal and Plant Inspection Service discussed the role of that agency in monitoring animal and plant diseases.

Perspectives for international cooperation

The following day, Stephen Morse, PhD, professor at Rockefeller University, chaired the panel on "Strengthening International Programs and Capabilities for Infectious Disease Prevention, Surveillance and Control." He stressed that there is a large untapped reservoir of viruses in the wild, and that current surveillance systems would not pick up human immunodeficiency virus (HIV) if it appeared today. This is because these systems lack coordination. The three components of an effective system are: 1) strategically located clinical facilities; 2) an effective laboratory system; and 3) epidemiologic capability. Citing ProMED (Program for Monitoring Emerging Diseases), which was started by the Federation of American Scientists in 1993, as an example of a network to address the problem, he stressed the need for global leadership, possibly under WHO. Francisco Pinhero of the Pan-American Health Organization discussed the situation in South America, which has recently experienced new and old disease outbreaks. Like the other physicians who spoke, he stressed the need for more research and training of clinicians. Francis Carr of the U.S. Agency for International Development, in the course of a litany about biodiversity loss, climate change, sustainable development, etc., again raised the issues of public health collapse and the need for cooperative efforts in view of the lack of funds.

The next panel discussed "Existing U.S. Programs and Capabilities for Infectious Disease Prevention, Surveillance and Control." The panel chairman, Rear Adm. Franklin Young, MD of the Office of Emergency Preparedness for the U.S. Public Health Service, described the National Disaster Medical System which has the capability to put an emergency team on the ground in the United States in one-half to three hours from notification of a medical emergency. He stressed the need for a cadre of general clinicians and first responders to deal with these problems. Randall S. Murch, director of the FBI Scientific Analysis Laboratory, spoke on surveillance of terrorism. The FBI is the lead agency for crisis management and would treat a chemical, biological, radiological (CBR) event as a crime scene. He described the Bureau's biggest problem as lack of access to surveillance data. Kelley Preston of APHIS discussed existing USDA programs, including the Foreign Animal Diseases program in the context of a terrorist agricultural bioattack. Stephen Hoffman of the U.S. Naval Medical Research Institute described the network of worldwide tropical disease laboratories run by the U.S. military, noting that all of the present antimalarial agents were developed by the U.S. military.

The third panel of the day discussed Microbial Detection and Analysis Technology. The chairman, Lt. Col. Victor

Weedn, MD, JD, of the Armed Forces Institute of Pathology, described advances in DNA technology which enable rapid and highly specific identification of biological material. Craig Venter of the Institute for Genomics Research then depicted the progress in sequencing and identifying the genetic material of numerous organisms, from the simple to the complex. Allen Northrup of Lawrence Livermore National Laboratory described progress in DNA diagnostics. Lennie Klevan of Life Technologies, one of the conference sponsors, discussed techniques of genetic amplification such as the polymerase chain reaction (PCR), which can increase the amount of available genetic material from a sample. Abel de la Rosa of Digene Diagnostics then described a technique of signal amplification which can detect minute traces of DNA without the need to use PCR.

The final panel attacked the question of "Network Building: Technology Integration, Coordination, Management and Training." Robert E. Shope, MD, professor of Pathology, Microbiology, and Immunology at the University of Texas Medical Center, Galveston, chaired this session. Dr. Shope, one of the giants of virology, and a foremost expert on insect-transmitted viruses, recapped the needs for research, training, and personnel. Eugene Boostrom, MD, of the World Bank then described a number of health monitoring programs run by the World Bank in the context of developing a surveillance network. Michael Snyder, an economist with the Fogarty International Center of the National Institutes of Health, closed with a discussion of economic impacts of infectious diseases and the savings a global surveillance network could realize.

Not if, but when

The impression of the conference was that we are ill prepared for a real problem, due to lack of resources and poor coordination of the resources we have. The need for an entity to coordinate diverse governmental and private capabilities is obvious. Recent events such as the Tokyo gas attack, the Oklahoma City bombing, and the crash of TWA flight 800 tell us a terrorist bioattack is a question of when and not if. Malcolm Dando, in *Biological Warfare in the 21st Century* (Brassey's, London: 1995), cites a series of studies that indicate biological agents have a mass casualty potential much closer to nuclear weapons than chemical agents. Kathleen Bailey estimates that only five people and \$100,000 would be needed to produce enough of a single agent to make a formidable biological weapon. When we consider the hundreds of thousands of dollars the Aum cult spent on research materials and facilities (according to testimony before the Senate Permanent Subcommittee on Investigations hearings on "Global Proliferation of Weapons of Mass Destruction"), the implications are not comforting. One ray of hope is that GenCon was able to assemble this diverse group to focus on the problem. On the other hand, there are indications that the FBI, counting on dissension within the Defense Department, is moving to consolidate any such network under its control.

Book Review

Fictional, but true account of bioterror

by John Grauerholz, MD

Death for Cause

by K.C. Bailey

Meerkat Publications, Livermore, Calif., 1995
284 pages, paperbound, \$12

The author, an expert on the proliferation of weapons of mass destruction, has worked in the U.S. Department of State, the U.S. Arms Control and Disarmament Agency, and Lawrence Livermore National Laboratory. The book, which could also be called "Mission All Too Possible," describes three young scientists infected with terminal environmentalism, who, to further their cause, devise a series of biological weapons which they deploy to force the U.S. government and the Vatican to adopt radical changes in environmental and birth control policies.

Who would do this sort of thing? A RAND Corp. study on "Terrorists and the Potential Use of Biological Weapons" reported:

"Therefore, it is virtually impossible to 'predict' which terrorist groups are most likely to embark upon biological terrorist attacks. However, we can identify some basic characteristics that would make certain types of groups more likely than others to experiment with these weapons.

"One important characteristic is a perception by the members of a group that biological weapons would not create a backlash among the group's supporters. Thus, nationalistic groups such as the IRA and E.T.A.—which at times have engaged in bombings and shootings that claimed the lives of innocent civilians—would most likely find the possible repercussions of biological weapons too risky. These types of groups depend upon the support—political, logistical, and financial—of significant segments of the population that may not necessarily approve of a group's violent tactics, even though they support its political and territorial objectives.

"Terrorist groups that could conceivably initiate an attack with biological weapons would thus probably exhibit