The CDC Prevention Strategy

The mission of CDC is to promote health and quality of life by preventing and controlling disease, injury, and disability. As the nation's prevention agency, CDC accomplishes its mission by working with partners throughout the nation and the world to monitor health, formulate prevention strategies, develop sound public health policies, implement prevention strategies, promote healthy behaviors, and foster safe and healthful environments. In keeping with this mission, CDC has strategic plans that address certain specific infectious disease threats, including HIV/AIDS, TB, STDs, and selected vaccine-preventable diseases. The concept of disease emergence has important implications for each of these.

Opportunistic infections in HIV-infected persons require cost-effective prevention strategies; drug resistance has become a barrier to TB control; STDs have been implicated as factors in chronic diseases (e.g., human papillomavirus and cervical cancer); and emerging diseases necessitate the ongoing assessment of vaccine development priorities (e.g., pneumococcal disease in children, respiratory syncytial virus [RSV] pneumonia, malaria). Strengthened efforts in the prevention and control of emerging infectious diseases will complement and improve the effectiveness of current efforts in HIV/AIDS, TB, STDs, and immunizations as well as other important infectious diseases.

To provide the vigilance and rapid response required to effectively address emerging infectious diseases, significant improvements in public health policy, program design, and infrastructure are needed. A far-reaching and comprehensive strategy, carefully integrated with broader plans for health care reform, is required. The CDC plan described below contains four critical goals that address specific IOM recommendations in the context of a broader vision for revitalizing our nation's ability to detect, contain, and most importantly, prevent the emerging infectious diseases that threaten populations both here and abroad.

This plan reflects the commitment of CDC to work with its partners in health departments, clinical practice, academia, private industry, and international health to meet the challenge of important emerging public health problems. It also embodies CDC's mission to prevent and control infectious disease, and addresses high priority infectious diseases in disadvantaged populations and underserved minorities, women, and children. Implementation of this plan with emphasis on extramural programs will strengthen the public health infrastructure in the United States at the local, state, and federal levels, and contribute to strengthening global surveillance networks. Most importantly, implementation of this plan will help the public health system identify, control, and prevent new, emerging, and drug-resistant diseases before they cause widespread epidemics, thereby reducing the cost of infectious diseases and improving the health and welfare of all Americans.

Goals and Objectives

Goal I ***Detect, promptly investigate, and monitor emerging pathogens, the diseases they cause, and the factors influencing their emergence.***

Objective I-A. *Expand and coordinate surveillance systems for the early detection, tracking, and evaluation of emerging infections in the United States.*

Surveillance serves several purposes: it characterizes disease patterns by time, place, and person; detects epidemics; suggests hypotheses and themes for epidemiologic investigation; evaluates prevention and control programs; and projects future health care needs.[67,68] In addition to monitoring and identifying needed public health responses for known infectious diseases, a well-functioning surveillance system maintains vigilance for emerging infectious diseases. The ability to detect what is new or emerging depends on the capacity to identify and track the routine as well as the unusual. National surveillance requires adequate infrastructure, including trained personnel, within the states and local communities and timely communications among state and local health departments, public and private laboratories, health care providers, and CDC.

Activities

i. *Improve surveillance for reportable infectious diseases by reevaluating current reporting mechanisms and requirements and providing technical and financial assistance to state health departments.*

National infectious disease surveillance systems form the foundation of our ability to know and track the routine. Certain infectious diseases—such as multidrug-resistant (MDR) TB, meningococcal meningitis, and botulism—warrant prompt detection of all cases because they cause substantial morbidity and mortality, require specific public health interventions, or may signal a potential outbreak. State and local public health authorities, other infectious disease experts, and CDC will reexamine currently reportable diseases, establish criteria for making a disease reportable, and explore ways to enhance rapid reporting of cases from clinical laboratories and health care practitioners. States must also examine the need to develop statutory requirements for clinical laboratories to

submit isolates of designated organisms of public health importance to the state laboratory. National infectious disease surveillance must be flexible enough to include newer problems, such as *E. coli* O157:H7-associated HUS, multidrug resistance in common pathogens (e.g., *S. pneumoniae*, *Mycobacterium tuberculosis*), and hantavirus pulmonary syndrome, and to reexamine the benefit of including currently reportable conditions, such as aseptic meningitis.

National notifiable disease surveillance is organized around state by state reporting systems for which states have ample legal authority. However, limited resources have left many state and local health departments with inadequate capacity to conduct surveillance for most infectious diseases. CDC could help ensure better capacity through cooperative agreements that provide financial and technical assistance, including training, to health departments.

ii. *Expand the use of Sentinel Surveillance Networks to complement other surveillance methods for detecting and monitoring emerging infections.*

The use of sentinel events to enhance surveillance is an effective public health tool that has proven useful in the monitoring of many diseases. Sentinel networks, linking groups of participating individuals or organizations to a central data receiving and processing center, have been particularly helpful in monitoring specific infections or designated classes of infections. Examples of such networks currently in use at CDC are the NNIS system (see Box),[69] the domestic influenza surveillance network (see Box), the National Respiratory and Enteric Virus Surveillance System, and the Pediatric and Adult/Adolescent Spectrum of HIV Disease Projects.

The National Nosocomial Infection Surveillance System

The NNIS system is an ongoing collaborative surveillance system among U.S. hospitals and the only national source of nosocomial infections data in the United States. This system is used to identify changing patterns in nosocomial infection characteristics, such as risk factors, patient infection sites, drug resistance, and emerging pathogens. Data are collected prospectively, using standardized surveillance components and nosocomial infection definitions.

Increasing the number of NNIS system hospitals allows for a more accurate estimate of the distribution and rates of various types of nosocomial infections while enhancing our ability to detect emerging pathogens.

In 1993, 163 hospitals voluntarily participated in the NNIS system. With adequate support, the system will continue to find more effective and efficient ways to characterize nosocomial infections and to assess the potential influences of patient risk factors, changes in hospital-based health care delivery, and modifications of infection control practices on the emergence of infectious diseases in the hospital setting.

Priority issues for future NNIS efforts include the following: surveillance of occupationally acquired infections in health care workers; broadening the scope of data collection to recognize nosocomial infections resulting in illness after patients are discharged from the hospital or other health care settings, such as out-patient surgical facilities; and detecting and monitoring selected community-acquired syndromes in hospitalized patients.

Sentinel Surveillance for Influenza

Domestic

The influenza sentinel physician surveillance network was established through the American Academy of Family Physicians and includes approximately 150 primary care physicians located throughout the United States. These physicians submit weekly reports of the number of patients seen with influenza-like illness by age group per number of patient visits, as well as the number of hospitalizations among patients with influenza-like illness. A subgroup (approximately 75 physicians) also collects nasopharyngeal specimens that are sent to a central laboratory for influenza virus identification. This system provides direct community influenza morbidity data that are otherwise unavailable.

International

An international network of collaborating laboratories was established in 1947 to monitor the emergence and spread of new epidemic and pandemic strains of influenza. This network now includes three World Health Organization (WHO) Collaborating Centers and approximately 120 WHO National Collaborating Laboratories. The primary purpose of this network is to detect, through laboratory surveillance, the emergence and spread of antigenic variants of influenza that may signal a need to update the strains contained in the influenza vaccine. To augment the WHO network, CDC supports a surveillance system for year-round influenza isolation in six sites in China, where many pandemic and epidemic strains have first appeared. The importance of these surveillance programs is underscored by the fact that viruses from the China surveillance system have been recommended for inclusion in the U.S. vaccine for the past 5 years.

Expanded use of the sentinel network concept, including strengthening existing systems, will improve our ability to detect and monitor emerging infections. With the cooperation of state and local health departments, CDC proposes to establish a series of electronically linked Sentinel Surveillance Networks, organized according to information source, that will use novel as well as traditional data sources important to the assessment of emerging infections (Table 3).

Table 3. Proposed Sentinel Surveillance Networks

- Blood Banks
- Clinical Microbiology Laboratories
- Emergency Rooms
- Family Practitioners
- Gynecologists
- Infectious Disease Specialists
- Internists
- Medical Examiners
- Pediatricians
- Travel and Tropical Medicine Clinics

Networks among selected physicians' groups, for example, could provide early warning of emerging syndromes of uncertain but possibly infectious origin, such as febrile diarrheal illnesses, meningitis, or encephalitis. Clinician- or laboratory-based networks also provide a mechanism for rapid interaction/consultation among members when unusual syndromes, such as unexplained adult respiratory distress syndrome (ARDS), idiopathic CD4 lymphopenia, or eosinophilia-myalgia syndrome, or when new or unusual laboratory isolates are detected. Such networks may also provide a more effective means for monitoring occupationally acquired infections in hospital and laboratory personnel.

Other networks could focus on the emergence of drug-resistant pathogens (e.g., clinical microbiology laboratories) or changes in seroprevalence of known diseases (e.g., blood banks). Special consideration will also be given to the formation of veterinary networks to monitor established zoonotic diseases (e.g., brucellosis, salmonellosis, cryptosporidiosis) or the increasing incidence of animal infections with zoonotic potential (e.g., bovine TB, bovine spongiform encephalopathy). An initial priority will be to establish a network of physicians (in cooperation with professional societies), to monitor such conditions as unexplained ARDS, meningoencephalitis of unknown etiology, and multidrug-resistant pneumococcal disease, or to investigate the increasing occurrence of rabies post-exposure prophylaxis.

iii. *Create population-based Emerging Infections Epidemiology and Prevention Centers to complement and support local, regional, and national surveillance and research efforts.*

The proposed centers will be developed through cooperative agreements with local and state health departments, in collaboration with local academic institutions and other governmental or private-sector organizations, and will be strategically located in sites across the country that offer access to various population groups. Wherever possible, centers will build upon existing capacities and partnerships. In contrast to the Sentinel Surveillance Networks, the centers' purpose will be to forge strong links with local medical, public health, and community representatives in order to establish ongoing sources for population-based data as a foundation for a variety of surveillance and prevention research projects relevant to emerging infections (Figure 7). These centers will also provide excellent opportunities for training public health professionals through cooperative arrangements between health departments, academic centers, and joint CDC/NIH training programs in infectious disease epidemiology.

In addition to providing population-based information, they will allow access to special populations including the rural and inner-city poor; underserved women and children; the homeless; immigrants/refugees; and persons infected with HIV. Although their presence may facilitate the reporting of new infections or rare syndromes recognized by health professionals in the area, these centers are not expected to significantly improve our ability to actually detect previously unknown or unrecognized infectious diseases. Rather, they are designed to assess the public health impact of emerging infections and to evaluate methods for their diagnosis, prevention, and control.

These population-based centers will provide a powerful tool for integrating information from many different places and sources, and about different emerging diseases. At the same time, national trends can be evaluated by combining information from the same project conducted at several centers across the country. Centers will maintain the flexibility to accommodate changes in specific projects as the need for information changes. Some projects will be conducted at all centers, while others might be carried out in only a few (Figure 7).

Priority activities will include the following:

1) Conducting active population-based surveillance projects to obtain detailed information about selected diseases for which adequate information is unavailable, such as foodborne infections (See boxes, pages 18, 19).

Figure 7. Potential Projects for Emerging Infections Epidemiology and Prevention Centers, United States

Potential Center Locations	Center Projects					
	Unexplained deaths of possible infectious etiology in young adults (e.g., ARDS)	Foodborne disease surveillance and prevention (e.g., *E. coli* O157:H7)	Opportunistic infections in HIV-infected inner city populations (e.g., crypto-sporidiosis)	Drug resistance in nursing homes and child care facilities (e.g., MDR pneumococcal disease)	Febrile and diarrheal illness in migrant farm workers (e.g., malaria, typhoid)	Etiologic agents in community-acquired pneumonia (e.g., *Mycoplasma*)
Northeast	X	X	X			
Mid-Atlantic	X	X	X	X		X
Southeast	X	X	X		X	
South	X	X	X		X	X
Midwest	X	X		X	X	
Southwest	X	X		X		X
West	X	X	X	X	X	
Northwest	X	X		X	X	X
U.S. Pacific Isles	X	X				X
U.S. Caribbean Isles	X	X	X			

Hepatitis Sentinel Counties

Although CDC conducts nationwide surveillance for acute viral hepatitis, underreporting and incomplete serologic testing and epidemiologic evaluation of all reported cases make it difficult to accurately assess changes in incidence of disease and risk factors associated with transmission.

To complement data collected nationally, a program of intensive surveillance for acute viral hepatitis was begun in Sentinel Counties in September 1979; since October 1981, it has been focused on four counties. These Sentinel Counties have provided precise data on the significant sources of viral hepatitis infection in the United States and the contribution of these sources to disease incidence.

In recent years, major changes have occurred in the incidence and epidemiology of the different types of viral hepatitis in the United States. Many of these changes were first recognized in the Sentinel Counties. The incidence of hepatitis A increased after a decade of decline, and drug users became an important source of communitywide outbreaks; more recently there has been an increase in hepatitis A associated with male homosexual activity, suggesting unsafe sexual practices. For hepatitis B, the disease transmission patterns in the Sentinel Counties showed that the immunization strategy that focused on adults at high risk had no impact on the incidence of disease. These data provided the rationale for a nationwide recommendation for universal infant hepatitis B vaccination (Advisory Committee on Immunization Practices [ACIP], 1991).

Testing of stored sera from acute and chronic non-A, non-B (NANB) hepatitis cases identified in the Sentinel Counties was used to show that the recently discovered hepatitis C virus was responsible for most NANB hepatitis in the United States. These counties have been the primary source for data describing the epidemiology and natural history of community acquired hepatitis C, and its importance as a cause of acute and chronic liver disease in the United States.[17] Although national data remain important for hepatitis surveillance, more detailed data, including behavioral risk factor data, are needed to plan and evaluate prevention programs.

2) Conducting special projects, such as evaluation of new diagnostic tests for Lyme disease; evaluation of illnesses often not specifically diagnosed but whose trends and etiologic information are important (e.g., diarrhea, community-acquired pneumonia); and investigation of the relationships between infections and chronic diseases (e.g., hantavirus infections and hypertension, hepatitis C and chronic liver disease, and respiratory virus infections and asthma attacks).

3) Conducting behavioral surveillance projects designed to assess trends in behaviors that either increase or decrease risks for infectious disease (e.g., in food consumption, sexual behavior, travel, or exposure to animals).

4) Examining infectious diseases in the context of populations at risk, recognizing that the incidence of many emerging diseases will be highest among underserved populations.

5) Implementing and evaluating pilot prevention/intervention projects for emerging infectious diseases that focus on safe food preparation in the home, handwashing in child care settings, appropriate use of antibiotics in clinical settings and in the community, and personal protection devices for clinical and laboratory personnel potentially exposed to infectious agents.

6) Providing technical assistance; epidemiologic, behavioral science, and laboratory expertise; and training to other agencies, institutions, or organizations in a center's area.

iv. *Expand field investigative and epidemic response capabilities.*

To address emerging infectious disease threats more effectively, CDC must build upon one of its essential strengths—the ability to conduct "shoe leather" epidemiologic field investigations. These field activities are essential to the rapid application of epidemiologic and laboratory expertise to prevent outbreaks from developing into broader public health crises.

CDC resources, including those that provide field training experiences for epidemiologists-in-training (Epidemic Intelligence Service [EIS] Officers conducting "Epidemic Aids") are not sufficient to provide all necessary support for outbreak investigations of emerging infectious diseases, which often require the presence of laboratorians, senior staff epidemiologists, and others in the field. The need to provide such additional support arose frequently in 1993 when CDC and state and local health department resources were severely strained in efforts to investigate and contain emergent disease threats, such as hantavirus pulmonary syndrome in the southwestern United States, cryptosporidiosis in Milwaukee, and *E. coli* O157:H7 disease in western states.

The availability of personnel to support field investigations is critical (See section IV-A below). To rapidly and effectively address the outbreak of HPS, professional and support staff were reassigned for several months from other high priority programs (e.g., drug-resistant pneumococcal disease, rabies). The availability of contingency funds for field investigations and the maintenance of adequate depth in personnel infrastructure at CDC would help prevent such situations.

Rapid and efficient mobilization of funds and personnel requires well-established mechanisms that lessen the usual administrative restraints inherent to any bureaucracy. For example, international response capability could be improved by development of a well-standardized system for foreign health officials to notify CDC and obtain assistance on short notice. Once the need for a field investigation is recognized, a mechanism is needed to rapidly allocate funds, personnel, equipment, and supplies.

Population-based Active Surveillance Project

CDC, together with state and local health departments and university-based investigators, conducts population-based active surveillance for bacterial, mycobacterial, and fungal diseases.

This project uses common infrastructures in population-based study sites to conduct surveillance, collect epidemiologic information, and gather isolates for laboratory study.

Active population-based surveillance, integrated with epidemiologic studies and laboratory study of surveillance isolates, has been a powerful way to study bacterial and mycotic diseases. Examples have included studies of listeriosis that led to dietary recommendations to reduce the risk for this disease; evaluation of the efficacy of new vaccines for *Haemophilus influenzae* type b (Hib) disease; documentation of increased risk for invasive Hib disease in HIV-infected men; evaluation of risk factors for neonatal group B streptococcal disease and of invasive group B streptococcal disease in adults; descriptive epidemiology and evaluation of risk factors for cryptococcal disease; and assessment of the efficacy of pneumococcal vaccine in HIV-infected persons.

Using a common infrastructure provides economies of scale in conducting studies as well as several other advantages. The impact of several diseases can be compared directly when they are studied in the same population during the same periods. For a given disease, temporal trends can be evaluated reliably, and monitoring of the impact of prevention plans can be facilitated.

To respond to emerging infectious disease threats, a designated administrative system is proposed to maintain and manage contingency funds, develop guidelines for notifying CDC and requesting assistance, and create mechanisms for the prompt allocation of resources (including equipment, products, and personnel) for surveillance and epidemiologic investigations.

v. *Assess and apply innovative tools (computer and communications technology) to facilitate collection, analysis, and dissemination of infectious disease surveillance information.*

Infectious disease surveillance in the United States should utilize modern computing and communications technologies to transform data into usable information quickly and effectively. Accurate, efficient data transfer with rapid notification of key partners and constituents is critical to effectively addressing emerging infectious disease threats. However, existing systems at CDC and at state and local health departments require upgrading and modification to minimize future data incompatibilities and to enhance rapid communications between federal and state/local health agencies by using common data standards and application protocols. In addition, the systematic evaluation of new and innovative tools for the collection and analysis of epidemiologic and laboratory data will enhance the speed with which technological, mathematical, and statistical advances are brought into use in efforts to better understand emerging infections. Included in this process will be the appropriate evaluation and utilization of

1) *Secure networks for the transmission of sensitive information.*
   These are essential and should take advantage of the national communications infrastructure for information dissemination and networking (Internet) being developed through the proposed High Performance Computing and High Speed Networking Applications Act of 1993.

2) *Automatic and direct reporting from physicians' offices, hospitals, and private and public laboratories.*
   Comprehensive health insurance and universal access to health care has the potential to facilitate this process and improve surveillance. Reporting would be received by state health departments as soon as cases are suspected or identified.

3) *Computer-based patient record technology.*
   CDC participation in the development of this capability is important to ensure that these systems are potentially compatible with automated public health surveillance systems and maintain patient confidentiality.

4) *Strategies to integrate existing and planned information systems.*
   Internet can provide the physical framework for improved information exchange and the establishment of "information superhighways" for public health. Internet application standards for information dissemination should be integrated into plans for existing (CDC WONDER) and planned (CDC INPHO network) systems. Existing CDC surveillance systems (e.g., NETSS, PHLIS) will need modifying, so that common standards and protocols are used and, therefore, data are stored in compatible formats and can be retrieved by easy-to-use interfaces.

5) *Field applications of computer technology.*
   Examples include the use of electronic forms that recognize information hand-written with an electronic pen. Such devices could potentially reduce data entry efforts and errors, and are already in use by commercial shippers and police departments. These computers can also use cellular transmission links for real-time connections between field staff and central data processing operations, reducing the need to return to the office to download data.

6) *Geographic information systems (GISs) and satellite imagery.*
   GISs allow geographically oriented information about disease distribution and occurrence to be visually and analytically linked to images of the environment. These images and data can include satellite-generated images, housing or other location data obtained from hand-held Global Positioning Systems (accurate to less than a meter), digitized street maps, and census data. The potential application of this technology to monitoring environmental changes that could affect the emergence of infectious diseases will be assessed.[70,71]

7) *New statistical and mathematical modeling methods.*
   New methods for analyzing time-space clustering, GIS data, and data from longitudinal studies need critical assessment for potential applications to the problems of emerging infections. Newer mathematical models can be used in both hypothesis generating and confirmatory analyses, and may provide excellent opportunities for the actual anticipation or forecasting of changes in the incidence or distribution of emerging or reemerging diseases. Mathematical models are also useful for predicting the relative success of alternative prevention strategies (e.g., oral animal rabies vaccine).

Objective I-B. *Develop more effective international surveillance networks for the anticipation, recognition, control, and prevention of emerging infectious diseases.*

Although infectious disease threats often emerge in regions remote to the United States and are readily

transported here,[12,51-58,65,72] practical mechanisms for the early detection of such threats, such as international infectious disease surveillance systems, are rudimentary and limited to a few specific diseases. Effective approaches to surveillance on an international scale should include early detection capability and the capacity—national, regional, or international—to generate public health responses.[72] However, public health infrastructure and infectious disease expertise vary widely from country to country. Even in industrialized nations, more timely and effective information exchange about emerging infectious disease problems is clearly needed.[73,74] For many developing countries, where this task will be the most difficult, established infrastructures, such as those in place for polio and Guinea worm eradication efforts, and existing resources, such as those available from ministries of health; WHO, the U.S. Agency for International Development, DOD, NIH, and CDC regional laboratories or offices; universities; and non-governmental organizations can assist in efforts to improve international cooperation in detecting and evaluating emerging infectious disease threats.

Activities

i. *Establish mechanisms for timely and systematic information exchange between public health agencies of different countries about emerging infectious diseases.*

Improved links among public health officials in different countries are needed to facilitate information exchange regarding trends in disease emergence and antimicrobial resistance.[73,74] CDC will work with ministries of health and international agencies to encourage exchange of surveillance information, adoption of compatible surveillance formats, and implementation of electronic data reporting and dissemination. The Internet international computer network system could facilitate efficient exchange of information. An international infectious disease database will be developed along the lines of the proposed U.S. Infectious Diseases Database described below (See Objective III-A, v).

ii. *Establish a global consortium of closely linked epidemiology/biomedical research programs/centers to promote the detection, monitoring, and investigation of emerging infections.*

The proposed global consortium will be established in close collaboration with local ministries of health and international agencies. The consortium will operate under the direction of an international steering committee, possibly chaired by WHO, with representatives from CDC and other national and international organizations. A central office will coordinate operations of the consortium and will begin by reviewing the current and potential capabilities of existing research facilities and surveillance networks.

The committee will assign priorities and select sites for the proposed consortium. Areas of expertise considered critical to the consortium goals of improved detection, monitoring, and investigation of emerging infections include epidemiology, clinical and veterinary sciences, field ecology (e.g., mammalogy, entomology), behavioral science, laboratory microbiology, and

Table 4. Examples of Potential Members of a Global Consortium of Epidemiology/ Biomedical Research Programs/ Centers

Existing Networks

- CDC Field Epidemiology Training Programs
- PAHO Polio Eradication Surveillance System
- International Clinical Epidemiology Network
- International Office of Epizootics Worldwide Information System
- WHO Arbovirus and Hemorrhagic Fever Collaborating Centers
- WHO Global Influenza Surveillance Network

Existing Research Facilities

- Caribbean Epidemiology Centre, Trinidad
- CDC: National Center for Infectious Diseases Field Stations (Côte d'Ivoire, Guatemala, Puerto Rico, Kenya, Sierra Leone, Thailand)
- DOD: U.S. Army Research Facilities (Brazil, Kenya, Thailand) and U.S. Naval Research Facilities (Egypt, Indonesia, Peru, Philippines)
- Food and Agriculture Organization Reference Centers (Argentina, Brazil, Colombia, Czech Republic, France, Germany, Hungary, Kenya, Panama, Senegal, Spain, Sri Lanka, Thailand, UK, Uruguay, USA)
- French Scientific Research Institute (e.g., Senegal, Congo, Côte d'Ivoire)
- Instituto de Nutriciòn para Centro America y Panama, Guatemala
- International Center for Diarrhoeal Disease Research, Bangladesh
- NIH, National Institute of Allergy and Infectious Diseases Supported Facilities (e.g., Brazil, Colombia, Israel, Mali, Mexico, Philippines, Sudan, Uganda, Venezuela, Zimbabwe)
- Pasteur Institutes (e.g., Algeria, Central African Republic, French Guiana, Iran, Madagascar, Morocco, New Caledonia, Senegal, Vietnam)

related disciplines. To minimize startup costs and avoid lengthy delays, highest priority for initial inclusion in the consortium would be given to facilities that currently maintain expertise in several of these disciplines (Table 4).

Consortium members will provide training and support to local and regional scientists and public health officials, assist in the formulation of public health policies, and aid outbreak investigations in the region. The facilities and expertise of the consortium would also enhance the likelihood of recognizing biological warfare events, an area of increasing international concern.[75] In addition to equipping consortium members with the ability to conduct certain critical tests under field laboratory conditions, laboratory and epidemiology back-up will be available from CDC and other collaborating organizations.

Objective I-C. *Improve surveillance and rapid laboratory identification to ensure early detection of antimicrobial resistance.*

Organisms resistant to antimicrobial agents pose a special threat to public health. In addition to the significant economic impact of antimicrobial resistance, evolution toward a "post-antibiotic era," when many antibiotics are ineffective, is rapidly becoming possible.[76,77] Even drugs used in the treatment of common bacterial infections are becoming increasingly ineffective, resulting in prolonged illness and higher mortality rates. With the number of antimicrobial agents under development decreasing, alternative therapies for pathogens such as vancomycin-resistant enterococci may not be available (Figure 5, page 13).[59,77] For example, FDA approved only five new antimicrobial agents in 1991 and two in 1990, and no new class of antimicrobial drugs is likely to be available in the present decade.[59] Managing pathogens that are already resistant and preventing the development of antimicrobial resistance in others will require a concerted, multidisciplinary effort.

Moreover, the problem of antibiotic resistance is global. Resistance can emerge rapidly and spread from one geographic area to another and from one organism to another. Recent examples include the international spread of multidrug-resistant *Salmonella typhi* and the introduction by travelers of drug-resistant *Shigella* to the United States.[59,78,79]

Activities

i. *Monitor trends in antimicrobial resistance patterns associated with both hospital- and community-acquired infections.*

The development of antimicrobial resistance is a dynamic process requiring continual surveillance of organism susceptibility over time. The surveillance of drug resistance depends upon the development of standard procedures for organism detection and in vitro susceptibility testing, and the establishment of a system for regular reporting of resistance data to local, state, and national surveillance programs.

Internationally, the management of resistance problems will require extensive cooperation. A high priority for the global consortium of Epidemiology/Biomedical Research Centers noted above (See Objective I-B, ii) will be to initiate a system for the international monitoring and reporting of antimicrobial susceptibility data.

Rapid compilation and analysis of national and international data are critical in providing timely guidelines to health care providers about antimicrobial therapy and in setting vaccine development priorities (See Objectives III-A, iv; III-B, i). For example, as antimicrobial resistance in *S. pneumoniae* emerges, practical information about the extent and distribution of this problem, in addition to modified treatment recommendations, is needed for clinicians to effectively care for patients with such common infections as pneumococcal pneumonia and otitis media.

ii. *Develop and evaluate tools for the reliable and rapid detection of antimicrobial resistance.*

Rapid screening procedures for antimicrobial resistance will become increasingly important for preventing the spread of disease and for limiting illness and death from drug-resistant pathogens. For example, the rapid identification of rifampin resistance, a marker for MDR *M. tuberculosis*, would permit earlier initiation of appropriate antimycobacterial therapy in individual patients, thereby decreasing their risk for serious disease and shortening the time during which infection could be spread to others.[80] The wider availability of such new techniques and their broader application to problems such as methicillin-resistant *S. aureus,* vancomycin-resistant enterococci, and aminoglycoside or third generation cephalosporin-resistant Gram-negative bacilli will depend on continued development, standardization, and validation of these techniques.

iii. *Determine risk factors for emergence of resistance through applied epidemiologic research.*

Risk factor analyses through appropriately designed epidemiologic studies are urgently needed to evaluate important aspects of antimicrobial resistance, such as the relationships between child care facilities and multidrug-resistant *S. pneumoniae*;[60] the use of antibiotics in livestock feed and resistant *Salmonella;*[81] and predisposing clinical conditions or antibiotic use and vancomycin-resistant enterococci.[77]

Antimicrobial usage patterns in clinical practice and animal husbandry may significantly impact the

emergence of resistant organisms through selective pressure, but further studies are needed to better characterize this impact and develop effective interventions. Molecular epidemiologic techniques, for example, have been useful in Sweden in tracing the potential spread to a human host of a trimethoprim-resistance gene in *E. coli* from antibiotic-fed swine.[82]

Objective I-D. *Strengthen and integrate programs to monitor and prevent emerging infections associated with food/water, new technology, and environmental sources.*

Potential sources of human infections change as society evolves. For example, microbiologically safe food and potable water, once considered standard amenities in most industrialized countries, are threatened by various emerging pathogens, even in the United States. As trade and economic developments such as the North American Free Trade Agreement take place, the globalization of food supplies is likely to have an increasing impact on foodborne illnesses. In addition, technologic changes, such as new (invasive) medical devices, may increase the risk of nosocomial infections, and changing human behavior and demographics may increase exposure to environmental sources of infectious agents, such as soil and surface water. These potential sources of emerging infections are diverse and cross the lines of various scientific disciplines and government agency responsibilities. Coordination between CDC and regulatory agencies, such as FDA, the U.S. Department of Agriculture (USDA), and the Environmental Protection Agency (EPA), is essential because surveillance and investigation of human disease can identify the need for new regulations as well as evaluate the effectiveness of existing ones.

Activities

i. *Evaluate technologic aspects of food processing and water treatment that may promote infectious disease emergence.*

Priority areas for increased epidemiologic evaluation and applied research will include 1) assessing the impact of technologic changes in food production, including pasteurizing eggs, treating chicken carcasses with disinfectant, and using automated cooking machinery in restaurants, on foodborne disease; 2) determining the risk of meat contamination related to various slaughter practices, such as using "distressed animals," slaughtering animals on a horizontal surface instead of hanging vertically, or perfusing carcasses with cold saline to chill them; 3) assessing the safety of drinking water, determining the etiologic agents and impact of waterborne gastroenteritis outbreaks, and evaluating the effectiveness of measures, such as reverse osmosis filters, to reduce waterborne illness; and 4) developing new tools for the rapid and reliable detection of microbial contamination in food and water.

In addition, because foodborne and waterborne infections that emerge abroad can affect U.S. as well as foreign populations, international efforts are also warranted. Improving the microbiologic safety of drinking water and food production in developing countries is critical to decreasing morbidity and mortality there, particularly in children, and is further needed to ensure the safety of the increasing amounts of food imported to the United States from these areas. In this regard, additional priorities will be 1) developing simple and sustainable measures to improve the safety of drinking water in developing countries with techniques such as narrow-necked water vessels or point-of-use filtering and disinfection, and 2) improving the hygienic standards of restaurants, street vendors, and food wholesalers.

ii. *Assess the impact of modern medical devices on the emergence and prevention of nosocomial infections.*

Use of invasive medical devices, such as indwelling catheters, often carries a risk for infection. Understanding the pathogenesis of these infections, evaluating new medical devices, and developing innovative prevention methods will be crucial in limiting infections in patients and protecting health care workers who use new devices. Applied research in the pathogenesis of intravascular catheter infections has already led to the production of a silver-ion coated catheter that may reduce infection rates. CDC must work closely with FDA and others to identify and evaluate problems associated with new medical devices.

iii. *Investigate environmental sources of infection and formulate effective control measures.*

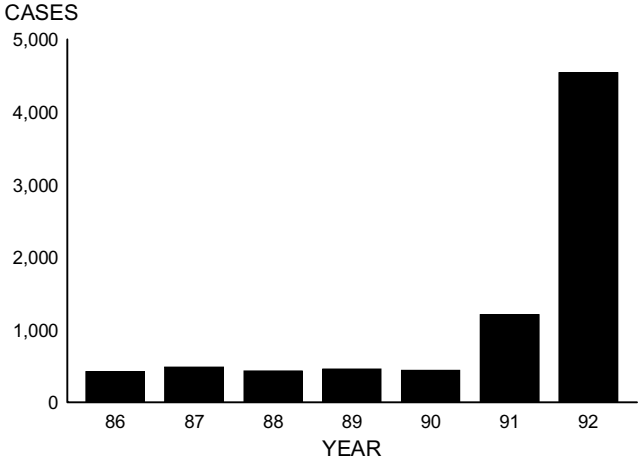
Many diseases, such as coccidioidomycosis, histoplasmosis, botulism, legionellosis, intestinal helminthiasis, and primary amoebic encephalitis, are caused by organisms that reside primarily in the soil or water. The environmental and climatic phenomena that influence the emergence or reemergence of such diseases have not been systematically evaluated. Expanded research is needed to better understand these events and enhance our ability to predict and control these infections. For example, existing technology, such as aerial photography and satellite imaging techniques, has been applied to the detection of root lice (grape phylloxera) that is attacking vineyards in central California; similar applications are needed for human infections.

The careful assessment of meteorologic events, such as prolonged droughts in California (see Box)[83] or extensive flooding in the midwestern United States, may

Coccidioidomycosis in California

Since 1991, California has experienced large increases in the number of reported cases of coccidioidomycosis (valley fever). Symptomatic coccidioidomycosis has a wide clinical spectrum, ranging from mild influenza-like illness to serious pulmonary disease to widespread dissemination. Among persons who become infected, blacks, Filipinos and other Asians, Hispanics, and women who acquire the primary infection during the later stages of pregnancy are at increased risk for disseminated disease. The recent outbreak may have been associated with weather conditions, especially a protracted drought followed by occasional heavy rains. The magnitude of the outbreak may be partially explained by recent migration of persons previously unexposed to *Coccidioides immitis* into areas of California where coccidioidomycosis is endemic. This outbreak illustrates how factors such as weather and demographic changes can affect the emergence of public health problems from infectious diseases.

Figure. Reported cases of coccidioidomycosis, by year—California, 1986-1992



provide valuable clues about the emergence of infectious disease. In situations such as widespread flooding, the ability to rapidly mobilize field teams to establish effective surveillance for emerging infections can be critical to early recognition and intervention.

In coordination with other groups, CDC will use available data about infectious disease threats caused by environmental changes to formulate intervention plans. Interventions might include evaluating or modifying a planned project, such as a new dam or irrigation project, to reduce the risk of altering the environment in a way that might promote emergence of infectious diseases. Although environmental impact statements are usually required before governmental approval of such projects, the panels that review proposals generally do not have infectious disease expertise. Participation in this review process by appropriate infectious disease experts would help ensure that a project's potential to foster the emergence of infectious diseases is considered.

Objective I-E. *Strengthen and integrate programs to monitor, control, and prevent emerging vector-borne and zoonotic diseases.*

Emerging pathogens maintained in animal reservoirs and transmitted to humans through food, arthropod vectors, or other means or are maintained in human reservoirs and transmitted from person to person by arthropod vectors pose ongoing threats to public health.[84] However, effective programs to monitor and control these threats are limited or nonexistent. Vector-borne and zoonotic diseases overlap extensively, and effective prevention and control of infections in both categories require well-integrated, multidisciplinary programs and a thorough understanding of the complex ecologic relationship between humans, insects, and animals.

Activities

i. *Monitor the distribution of animal reservoirs and vectors associated with human disease.*

Surveillance systems for important infectious disease vectors and animal infections that threaten human health, including studies of the prevalence of potential human pathogens in animal populations, are a key component of efforts to address emerging vector-borne and zoonotic diseases. The surveillance infrastructures discussed previously (Objective IA) may be used for this purpose. Priorities for surveillance include potential rodent reservoirs of hantavirus; rabies in raccoon populations (Figure 6, page 14); *Cryptosporidium* in cattle and wild ruminants such as deer; *Echinococcus multilocularis* in dogs and other canids; the distribution of tick vectors of Lyme disease and Rocky Mountain spotted fever; the distribution of mosquito vectors of arboviral encephalitides, dengue, and yellow fever (YF) (see Box, page 25); and the occurrence in humans, ticks, and potential animal reservoirs of emerging agents such as *Ehrlichia chaffeensis* (see Box, page 25). The potential use of satellite imagery or similar technology to anticipate changes in vectors, animals, and the environment that would directly affect the incidence of infectious diseases will be assessed.

In a cooperative project by CDC, USDA, DOD, the University of Florida, and other Florida state agencies, GISs and satellite imagery are being used to develop models to predict regions of high risk and periods of unusually high encephalitis virus activity.

Monitoring Yellow Fever in Kenya, East Africa

YF is a mosquito-borne viral disease that produces human mortality rates as high as 80%. In Africa and South America, many non-human primates maintain the infection in so-called sylvatic (jungle) transmission cycles. Humans contract the disease when bitten by mosquitoes that have been infected by primates. Many human deaths occurred in a 1992-93 outbreak in western Kenya. This outbreak was the first documentation of extensive YF transmission in that country. Although an emergency vaccination campaign protected close to 1 million people, a much larger population, living within 150 km of this region, will be at risk if transmission continues its apparent southward movement. The situation is particularly serious because common household mosquitoes like *Aedes aegypti* can transmit YF and cause massive urban epidemics if infected persons are bitten by domestic mosquitoes.

Urban epidemics could occur throughout Kenya and adjacent countries if infected persons or mosquitoes are transported to other areas. Therefore, ecologic conditions that favor increased sylvatic transmission in eastern Africa must be identified. An intensive entomologic/epidemiologic survey conducted in March 1993 demonstrated a clear association between YF transmission and well-defined vegetational zones. Techniques such as GIS analysis would be ideal tools for mapping these vegetational zones and predicting shifts in sylvatic transmission patterns, thereby helping target areas for vaccination campaigns.

These models may provide health officials with timely information for implementing early prevention and control strategies (personal communication; PB Ladd, Centers for Epidemiology and Animal Health, USDA).

ii. *Expand applied research on vector competence, distribution of infectious agents among known reservoirs and potential hosts, and ecologic factors contributing to the maintenance of vector-borne and zoonotic diseases in nature.*

Better understanding of animal reservoirs and vectors of infectious agents is important in anticipating and controlling emerging infections. For example, research to improve understanding of competence and life cycles of tick species that harbor *Borrelia burgdorferi* could lead to control strategies for Lyme disease. Similarly, research on *Aedes albopictus*, which was recently introduced into the United States and is a potential vector for the virus that causes eastern equine encephalitis, could identify other pathogens that use this mosquito as host. In addition, researchers could discover vectors for diseases not yet known to be vector-borne. For example, research is needed to determine whether arthropod vectors exist for cat scratch disease, bacillary angiomatosis, and septicemic disease caused by *Rochalimaea* species and to better define the role of microcrustacean copepods in the environmental persistence and transmission of waterborne cholera.

Human Ehrlichiosis, 1985–1992

Human ehrlichiosis is a newly recognized rickettsial disease. The etiologic agent, *Ehrlichia chaffeensis*, was isolated at CDC in 1990. From 1985 through 1992, 297 infected persons were identified in 27 states. Most patients experience fever, rigors, malaise, arthralgias, and nausea. Seven deaths have been associated with this disease, including one in a 6-year-old child. Complications, which are more likely in persons more than 60 years of age, include disseminated intravascular coagulation, renal dysfunction or failure, cardiomegaly, seizures, and coma.

Because this emerging disease is not familiar to most clinicians and no system for national surveillance exists, its impact on public health both here and abroad is probably underestimated. In an active surveillance study in Brunswick, Ga., conducted in partnership with the Georgia Department of Human Resources and Glynn Brunswick Memorial Hospital, the rate of ehrlichiosis (5.3/100,000 population) exceeded by more than sixfold the rate of Rocky Mountain spotted fever during the same time period. This high rate in conjunction with potentially severe clinical outcome suggests that better surveillance for this important and emerging tick-borne infection is urgently needed.

Goal II *Integrate laboratory science and epidemiology to optimize public health practice.*

Objective II-A. *Expand epidemiologic and prevention effectiveness research.*

To effectively address the threats of emerging infections, CDC and its partners must build upon traditional strengths in outbreak investigation and increase emphasis on development, implementation, and evaluation of prevention measures for emerging infectious diseases. These efforts will include behavioral risk factor studies, economic analyses of the impact of infectious diseases, and evaluations of the cost-effectiveness of new interventions and new diagnostic techniques.

Activities

i. *Determine which behaviors prevent or foster emerging infections and how to promote or discourage these behaviors.*

Human behavior is often a key determinant in the emergence of new diseases, and changing human behavior is often the most cost-effective (and sometimes the only practical) prevention strategy. Often, critical behaviors that put people at risk are initially unknown. Prompt field investigation of outbreaks can identify these critical behaviors and lead to effective emergency and long-term control measures for the infection. Knowing which behaviors will modify risk is a crucial first step in understanding disease transmission; however, implementing and sustaining effective behavioral changes may be a more difficult challenge. Efforts should focus on determining what message to disseminate, how best to communicate the message, and how to effect and sustain behavioral changes, recognizing that the approach may vary depending on the particular behavior and target group in question (Table 5). Messages are often most effective before unsafe behaviors develop; thus, particular attention should be given to educational efforts targeted at children and adolescents.

Table 5. Behaviors Shown to Reduce the Risk of Emerging Infections

1) Cooking hamburger thoroughly to prevent *E. coli* O157:H7 infections.
2) Using narrow-necked water containers to reduce the risk of cholera in homes without running water in cholera-endemic areas.
3) Practicing good hygiene with diapered children in child care facilities to reduce transmission of rotavirus, *Shigella*, *Giardia*, *Cryptosporidium, E. coli* O157:H7, and other agents of diarrheal disease.
4) Practicing safer sex to prevent the transmission of HIV and other sexually transmitted infections.
5) Eliminating artificial water containers around homes to limit urban habitats of dengue-carrying mosquitoes.

ii. *Characterize the impact of well-established and emerging infectious diseases on public health in the United States.*

Information on length of disability, physician visits, hospitalizations, late sequelae, and deaths due to infectious diseases is extremely limited. Moreover, current illness classifications underestimate the impact of infectious diseases; for example, while ICD-9 classifies injuries together, it distributes infectious diseases among several categories, obscuring their public health impact. Existing databases of hospital discharge records, outpatient visits, and pharmacy records should be analyzed to develop a comprehensive general assessment of the impact of infectious diseases. This assessment will include critical evaluations of the economic impact of emerging and other infections that will allow realistic intervention strategies to be developed, on the basis of both health and economic indicators.

iii. *Evaluate effectiveness and economic benefit of strategies to prevent emerging infectious diseases.*

After prevention strategies are formulated and implemented, they must be evaluated for effectiveness. For example, studies should assess the extent of the implementation and the impact of guidelines issued to prevent infections in child care facilities. Further, implementing prevention measures on a broad scale requires economic information. Some preventive strategies and vaccines are not used because of a perceived lack of cost-effectiveness. However, because formal cost-benefit analyses have not been performed for most of these options, some effective and available public health options may have been overlooked.

iv. *Through an extramural program for emerging infectious disease surveillance, epidemiology, and prevention, enhance public health partnerships between CDC, health departments, academic centers, and community groups.*

In 1973, the CDC extramural infectious disease research program was discontinued. Currently, extramural funding is available only for a few targeted areas of research, such as HIV/AIDS and Lyme disease. As noted in the 1992 IOM report, reestablishing this program would fill gaps in existing support for epidemiologic and prevention effectiveness research. Such a program would also enhance ties between CDC and the public health community; promote career paths; foster alliances among academia, public health, and private industry; and establish a national resource for responding to emerging infectious diseases.

Objective II-B. *Improve laboratory and epidemiologic techniques for the rapid identification of new pathogens and syndromes.*

Both nationally and internationally, CDC is often relied upon to characterize new infectious disease syndromes, identify etiologic agents, and train others to perform these tasks. For example, in recent years,

CDC was instrumental in finding the causes of Legionnaires' disease, TSS, and HPS and in describing the epidemiology of Lassa fever.[23,47-50,85,86] CDC's unique capability to rapidly apply laboratory and epidemiologic expertise to the identification of new or previously unrecognized pathogens is a critical public health resource.

Activities

i. *Establish the means for early, systematic evaluation of newly recognized pathogens or syndromes of probable infectious etiology.*

Improved information exchange among CDC, state and local health departments, and health care providers outlined in Objectives I-A and III-A will increase the likelihood that new infectious diseases will be recognized earlier. The Sentinel Surveillance Networks and population-based Emerging Infections Epidemiology and Prevention Centers, as well as special studies and outbreak investigations, can systematically look for evidence of emerging diseases. Because of recent experiences with hantavirus, for example, an early priority will be to apply newly developed diagnostic techniques in the assessment (through active surveillance and focused clinical evaluations) of unexplained ARDS.[49,50]

ii. *Improve laboratory capabilities to identify and characterize emerging pathogens.*

Essential laboratory activities include histopathologic evaluation of specimens, isolation of etiologic agents in culture, and use of modern molecular tools to identify agents that cannot be easily cultivated (e.g., amplification of 16S ribosomal RNA sequences to identify the etiologic agents of Whipples disease and bacillary angiomatosis).[87] Also part of this process is the ongoing accumulation and maintenance of specimen banks (e.g., serum, tissue, and pathogen isolates) which are critical to the comparative analyses that must take place to identify and characterize new pathogens (See also Objective IV-B, iii).

iii. *Refine and expand the epidemiologic applications of new techniques for typing/subtyping emerging pathogens.*

Accurate typing (or subtyping) of infectious agents is critical to many modern epidemiologic investigations. Phenotypic techniques (e.g., biotyping, serotyping, immunoblotting, electrophoretic typing), in addition to the newer molecular (genotypic) tools, are becoming increasingly important in tracing the spread of disease-causing strains, linking specific strains to point sources during outbreaks, and determining the virulence characteristics and pathogenesis of agents of emerging infectious diseases.[28,88] The molecular tools (e.g., restriction endonuclease analysis, pulsed-field gel electrophoresis, polymerase chain reaction) are particularly helpful in elucidating the clinical and epidemiologic characteristics of uncultured microbial pathogens.[87] The ability to understand the transmission of infectious diseases and the virulence characteristics of disease-causing strains is strongly enhanced when epidemiologic investigations are complemented by effective subtyping of infectious agents.[88] For example, molecular epidemiology was instrumental in documenting the transmission of HIV in a dentist's practice in Florida.[89] Typing/subtyping has been used as an epidemiologic tool to address many other infectious disease problems, including the relationship between foods and listeriosis [90] and the international spread of an epidemic-causing clone of group A *N. meningitidis*.[91,92]

The various techniques derived from immunology, biochemistry, and genetics for typing or subtyping pathogens are often referred to collectively as *molecular epidemiology*.[88] For a typing or subtyping method to improve understanding of epidemiologic phenomena, it must be reproducible and sufficiently discriminating to discern important epidemiologic relationships among different strains of the same species. For example, development of effective typing systems for *Aspergillus* might help identify environmental sources of outbreaks of invasive aspergillosis among hospitalized patients. New methods must be carefully evaluated according to the criteria of cost and ease of application. Subtyping can be a cost-effective public health tool when used to detect epidemics quickly and prevent their spread. (see Boxes, page 28) These techniques were critical in identifying Brazilian purpuric fever (BPF) as a new disease. After epidemiologic studies showed that BPF was more likely to occur in children with a recent history of conjunctivitis, molecular epidemiologic techniques (plasmid profiles, multilocus enzyme electrophoresis and ribotyping) demonstrated that the common noninvasive bacterial pathogen, *H. influenzae* biogroup aegyptius, had developed new virulence properties resulting in severe and often fatal systemic disease. Some of these techniques, such as plasmid profiles, also provide a basis for direct identification and description of newly acquired virulence factors.

iv. *Reestablish a core program in human and animal infectious disease pathology.*

CDC activities in the evaluation and control of emerging infectious diseases require pathology support to identify new or previously unrecognized infectious agents as well as to better characterize the pathophysiology and anatomic distribution of known agents in humans and in animal models. CDC needs to strengthen its capability in human and veterinary infectious disease pathology through replenishing expertise at CDC and through enhancing partnerships with academic pathologists, offices of medical examiners, and others. Infectious disease pathologists have

Diagnostic Assays and Reagents for Detecting Measles Virus

Between 1989 and 1991, more than 50,000 cases of measles, with 11,000 hospitalizations and 100 measles-associated deaths occurred in the United States. This resurgence of measles disease underscored the need for new assays to characterize measles virus infections. CDC investigators have developed serologic and antigen detection assays to diagnose acute infection and demonstrate prior immunity and have used genomic studies to characterize the infecting virus. These assays have distinguished measles from outbreaks of other rash illnesses, such as rubella or human parvovirus B19; identified vaccine-driven antigenic changes in wild measles viruses; demonstrated that mild and asymptomatic measles infections may be common in vaccinated populations; and distinguished wild-virus disease from vaccine-induced disease. These assays are essential to understanding the epidemiology of measles in vaccinated populations.

Pulsed-field Gel Electrophoresis of *E. coli* O157:H7

E. coli O157:H7 strains are difficult to distinguish by classic methods. Pulsed-field gel electrophoresis, a newer subtyping method adapted for *E. coli* O157:H7 by CDC investigators, was used during the fast-food restaurant hamburger outbreak in western states in January 1993. Using this method, CDC investigators demonstrated that strains from patients in four states and from the suspect hamburger patties were indistinguishable from each other and different from the more than 100 strains in CDC's collection.

Multilocus Enzyme Electrophoresis of Group C *N. meningitidis*

In the past several years, an increasing number of serogroup C meningococcal outbreaks have been reported in the United States. Multilocus enzyme electrophoresis, which further differentiates among organisms of the same serogroup, has aided in the early identification of outbreaks by establishing that isolates from outbreak-associated cases were identical, in contrast to cases of sporadic disease, which are usually caused by a variety of strains. This information is critical to the formulation of optimal vaccination strategies in affected communities.

been crucial in elucidating emerging infections such as cat scratch disease and bacillary angiomatosis, ocular and systemic microsporidiosis, and HPS.

An active program in infectious disease pathology also forms an important avenue of communication between CDC scientists and practicing clinical pathologists who submit specimens for diagnostic evaluation from patients with suspected infectious diseases. These specimens may provide sentinel indicators of new pathogens and emerging diseases. Finally, CDC will consider establishing cooperative training programs with universities in infectious disease pathology, analogous to those under consideration for clinical infectious diseases.

Objective II-C. *Ensure timely development, appropriate use, and availability of diagnostic tests and reagents.*

Efforts will focus on providing well-standardized, economical, high performance tests for diseases whose earlier diagnosis would enhance treatment and decrease spread, especially diseases for which private industry or other institutions are not likely to develop diagnostic tests and reagents.

Activities

i. *Develop and evaluate new diagnostic tools for emerging infections.*

Improved tools to diagnose important emerging infections, such as Lyme disease, would facilitate earlier treatment, thereby decreasing disability and medical costs. Developing, evaluating, and applying tools to diagnose infectious diseases that are considered rare or exotic are also needed, as are better diagnostic tools capable of distinguishing acute from prior infections.

Since commercially developed diagnostic tools may have uncertain sensitivity and specificity, evaluating diagnostic tests is an important public service to be carried out by CDC and its partners.

ii. *Maintain diagnostic and reference reagents for the identification of emerging pathogens.*

CDC proposes to renew its commitment to maintaining diagnostic and reference reagents to support outbreak investigations; to provide backup for state, local, and clinical laboratories; and to distinguish known infectious diseases from new and emerging ones. Partnerships with universities and private industry will be helpful in maintaining this capability.

Objective II-D. *Augment rapid response capabilities for vaccine delivery and expand evaluation of vaccine efficacy and the cost effectiveness of vaccination programs.*

The National Vaccine Program (NVP) coordinates the nation's efforts in the development, administration, and evaluation of vaccines. CDC will continue to contribute both its laboratory and epidemiologic expertise to this effort, including support of the President's Childhood Immunization Initiative.

Activities:

i. *Improve rapid response capability and coordinated contingency plans for the emergence of new strains of known pathogens, particularly influenza, that threaten to cause pandemic disease.*

CDC, FDA, NIH, NVP, private industry, and others must work together to address new, and possibly more dangerous, strains of known pathogens. Influenza A viruses, for example, have undergone major antigenic shifts at unpredictable intervals, causing pandemics with high morbidity and mortality. During this century, influenza pandemics occurred in 1918, 1957, 1968, and 1977. The pandemic of 1918 was the largest in recent history, causing an estimated 500,000 deaths in the United States and 20 million worldwide. New strains of influenza have often emerged in Asia, making virus surveillance on an international scale critically important to detecting and monitoring the emergence, spread, and impact of new strains (see Box, page 16). To lessen the impact of the next pandemic, contingency plans developed in 1977, and modified a decade ago, will be updated by CDC and others in cooperation with NVP. Implementation of these plans will help ensure that the recognition of new influenza strains capable of causing pandemic disease is followed by prompt reformulation of vaccines and development of recommendations for administering vaccines and antiviral drugs.

ii. *Expand the use of CDC specimen banks and diagnostic test development in the identification of prospective vaccine components.*

CDC is well positioned to identify promising protective antigens for use in vaccines because its broad-based surveillance systems and development of diagnostic tests have resulted in representative collections of etiologic agents and candidate antigens. Once potential antigens are identified by state-of-the-art molecular techniques, they can be evaluated in animal models, and the most promising ones can be selected for vaccine development. Diseases for which new or improved vaccines are needed include Lyme disease, meningococcal disease, pneumococcal disease, hepatitis E, RSV, and malaria.

iii. *Evaluate vaccine efficacy and the costs and benefits of vaccination programs for emerging infections.*

Evaluating the efficacy of and the immunologic response to vaccines against diseases such as those caused by *S. pneumoniae*, *H. influenzae* type b, and *N. meningitidis*; hepatitis A, hepatitis B, group A rotavirus, and influenza viruses; and *Plasmodium* is a critical step in vaccine development. As new vaccines for emerging pathogens are developed, CDC and its partners will need to focus on their evaluation, particularly of postlicensure performance.

In addition, available information about vaccine efficacy and duration of protection, as well as surveillance information, will be used to develop appropriately targeted and cost-effective vaccination strategies (see Box, page 30). Economic analyses will be an important part of this process.

Goal III *Enhance communication of public health information about emerging diseases and ensure prompt implementation of prevention strategies.*

Objective III-A. *Use diverse communication methods for wider and more effective delivery of critical public health messages.*

Surveillance data, results of epidemiologic outbreak investigations, recommendations developed from risk factor analyses, and other forms of public health information relevant to emerging infections are of little value unless they reach the appropriate audiences (e.g., public health policy makers, health care professionals, the public) in the form of effective public health messages. To effectively deliver important public health information, CDC and its partners must expand and diversify the mechanisms used to inform constituencies. An important first step in this process will be to inventory existing informational materials at CDC and elsewhere and to set up a clearinghouse for their distribution.

Activities

i. *Develop and distribute educational materials about CDC's emerging infections prevention programs to health care professionals.*

These materials will include videos for commercial, public, and cable TV programs; video and printed

Vaccination Strategies for Meningococcal Disease

Between 1981 and 1990, 10 outbreaks of group C meningococcal disease were identified in the United States.[93] In contrast, between 1991 and 1993, eight such outbreaks have been reported. Since the disease has a mortality rate of about 15% and survivors may have severe complications, including limb amputation and neurologic deficits, even small numbers of cases frequently create intense public concern and require a rapid response by local and state public health authorities. The only effective means of controlling outbreaks of this disease are mass vaccination campaigns. However, the decision to vaccinate a large population for group C meningococcal disease is difficult.

Current work at CDC to develop specific guidelines for management of group C meningococcal disease outbreaks will require analysis of available surveillance data to facilitate early detection and cost-benefit analyses of potential prevention and control strategies. Long-term management of group C outbreaks will require enhanced nationwide surveillance of this disease.

materials for use in public health clinics; and slide sets or other training materials (e.g., for cholera, HIV/AIDS and other STDs, neonatal group B streptococcal infections, hepatitis B, and occupationally acquired infections) for use by health care professionals and others, who could help expand the dissemination of such information through lectures, workshops, and other educational activities. Educational efforts should also be directed toward medical schools to ensure that physicians-in-training understand the importance of surveillance and their responsibility for proper notification of public health authorities.

ii. *Enhance media awareness and understanding of CDC's scientific publications on emerging infections.*

CDC currently produces informational materials that address many important public health problems. Media packages for soon-to-be-released publications about emerging infections are needed to ensure that the correct messages about these new threats are communicated effectively. For example, brief video segments will be developed to accompany the distribution of important *Morbidity and Mortality Weekly Reports* (*MMWR*s) that appeared in the recently introduced series, "Emerging Infectious Diseases."

CDC staff should be prepared to respond to media or public inquiries, particularly during field investigations that command national attention (e.g., the recent outbreaks of rodentborne HPS and waterborne cryptosporidiosis). Effectively responding to such inquiries will require identifying the appropriate individuals for interviews, distributing press packets and pamphlets, and providing technical information specialists who can respond to public inquiries from segments of society with differing levels of medical sophistication.

iii. *Expand distribution of* MMWR *and other important public health information sources.*

MMWR is CDC's primary mechanism for rapidly disseminating important public health information to a wide range of national and international constituents. Because of resource restraints, distribution of free copies of *MMWR* to medical students, general health care practitioners, and others ceased in 1981. Although coordination with other medical publications has greatly assisted with the dissemination of information contained in *MMWR*, further broadening the distribution of *MMWR*, in electronic as well as printed format, would substantially enhance CDC's ability to provide health professionals with critical updates on infectious (and other) diseases.

iv. *Disseminate laboratory information to private and public health laboratories, hospitals, and practicing physicians about emerging infectious diseases and antimicrobial drug resistance.*

The scope of *MMWR* should be broadened, or a new publication should be created to report on important laboratory developments in public health. Regarding resistance to antimicrobial drugs, CDC, in coordination with state and local health departments, will assist in ensuring that physicians receive better and more timely information about which drugs should be used as first-line therapy in their locale and which are likely to fail. Also needed to slow the pace of development of antimicrobial drug-resistance are more detailed guidelines regarding the use of first-line drugs for uncomplicated infections.

v. *Create an accessible and comprehensive U.S. Infectious Disease Database that increases awareness of infectious diseases, facilitates their prompt recognition, and promotes public health action.*

The Infectious Disease Database will synthesize information from the many surveillance activities and contain updated information on 1) antimicrobial resistance, 2) foodborne infectious diseases, 3) outbreaks of infectious diseases, 4) synopses of diseases and syndromes, 5) travelers' health, 6) trends in the incidence of infectious diseases, 7) vaccine and antimicrobial drug availability, and 8) vaccine guidelines. The database will provide information in print and on computer networks and will conform to the guidelines and standards established in the CDC Comprehensive Plan for Public Health Surveillance (1992 Status Report).

Raccoon Rabies

Canine rabies was all but eliminated throughout the United States in the 1950s through the use of effective veterinary vaccines; in the 1960s and 1970s, wildlife rabies predominated in the approximately 3,000–4,000 diagnoses annually. During 1990, 1991, and 1992, 4,881, 6,975, and 8,645 cases of animal rabies were reported, respectively. Increases were due primarily to the epizootic spread of raccoon rabies from the mid-Atlantic region into the northeastern United States. Unprecedented numbers are now being reported from portions of New England, once largely free from terrestrial rabies. Because of their distribution and abundance, particularly in urban areas, raccoons are expected to play a major role in the spread of this epizootic to new areas for years to come. Although no raccoon-associated cases of human rabies have yet been reported, already scarce public health resources are being reallocated to prevent this eventuality. Included in this reallocation are increased funds for specimen collection, submission, and diagnosis; animal control activities; companion animal vaccination; public education; and human treatment for suspected rabies exposures. Increasing expenditures for postexposure prophylaxis are critically straining existing resources.

New approaches need to be developed to contain this epizootic and prevent human infections. Until recently, long-term, cost-effective methods to control rabies in free-ranging animals were not available. However, recently, new animal rabies vaccines have been introduced that can be incorporated into edible baits. Such techniques have already been used to successfully control fox rabies in Ontario, Canada, and in 12 European countries and should be evaluated for controlling racoon rabies in the United States.

Objective III-B. *Establish the mechanisms and partnerships needed to ensure the rapid and effective development and implementation of prevention measures.*

In addition to information dissemination, implementation of prevention measures includes developing and ensuring the correct use of guidelines, providing critical prevention materials to constituencies, and working with agencies that have regulatory authority, such as FDA, to remove dangerous products from the consumer market (as occurred with certain tampons implicated in TSS) or with EPA and USDA/FDA to help ensure microbiologically safe water and food, respectively.

Activities

i. *Develop, evaluate, and assist in the implementation of guidelines for preventing emerging infectious diseases.*

CDC guidelines, such as the Guidelines for Treatment of Sexually Transmitted Diseases and Guidelines for Prevention and Control of Nosocomial Infections, provide direction for health care professionals who take care of patients or develop local regulations. CDC will continue this important activity to review available data and develop future guidelines in cooperation with advisory groups such as ACIP and the Hospital Infection Control Practices Advisory Committee.

In addition, guidelines analogous to those for preventing nosocomial infections will be developed to prevent infections in other institutional settings, including nursing homes, prisons, and child care centers. For example, CDC has collaborated with FDA to produce videotapes for safe food handling in nursing homes, where foodborne infections are most likely to have serious, or even fatal, results. Similar efforts are needed to promote the appropriate use of antimicrobial drugs and infection control procedures in nursing homes.

FDA and CDC have also collaborated to produce guidelines for the prevention of foodborne infections in persons with immunosuppression. This video, entitled "Eating Defensively: Food Safety Advice for AIDS Patients," is available through the National AIDS Clearinghouse, which has already distributed more than 10,000 copies. In addition, the formation of community-based health action groups—made up of state and local health officials, clinicians, and others—would increase support for recommendations.[94]

Coordination and ongoing communication with professional organizations that issue guidelines or practice parameters to their members (such as the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, the American College of Physicians, the American College of Emergency Physicians, and the American Academy of Family Physicians) will maximize the consistency of guidelines for health care professionals.

ii. *Establish the programs and mechanisms to provide critical prevention materials to state and local health departments and other partners and constituents.*

Providing prevention materials to state health departments will ensure that target groups have ready access to such materials. Examples of these materials include brochures about food safety, prevention of infectious diseases in child care centers, and travelers' health information; vaccines and other biologics; in-

structions for emergency water treatment; point-of-use water treatment devices; and pesticides for emergency vector control. Provision of these materials often involves interagency cooperation, such as CDC working with EPA to facilitate pesticide approval or waiver processes during public health emergencies. This type of cooperation is also needed during periods of increased threat from reemerging zoonotic diseases, such as raccoon rabies, when innovative means for vaccine delivery may be helpful (see Box, page 31).

iii. *Establish a coordinated approach for responding to increased demand for (as well as shortages and inappropriate use of) drugs and biologics.*

A network of specialists, including representatives from FDA, DOD, USDA, NIH, and industry, who would systematically exchange information about problems related to the availability and use of drugs and biologics is needed. This group would evaluate current or anticipated shortages of and increased demand for drugs, biologics, or related medical devices. Recruitment of professionals with expertise in pharmacoepidemiology would be particularly helpful. This group would also initiate necessary actions related to the

Investigation of Hantavirus Pulmonary Syndrome in the United States, 1993[47-50]

The importance of and need for core public health functions are demonstrated by the outbreak of disease in 1993 that was first detected in the Southwest when a physician there observed an unusual cluster of fatal cases of adult respiratory distress syndrome (ARDS) in young adults.

Subsequent investigations involved the cooperative efforts of clinicians, laboratorians, ecologists, epidemiologists, and others, representing several organizations and agencies including the Navajo Nation Division of Health; the Indian Health Service; the New Mexico Department of Health and the Office of Medical Investigations; the University of New Mexico School of Medicine; state health departments in Arizona, Colorado, and Utah; DOD; and CDC.

Testing done at CDC on specimens collected during these investigations included screening for various infectious agents. The diseases and agents considered in the differential diagnosis included bacteria (plague, tularemia, anthrax, legionellosis, leptospirosis, *Mycoplasma*, *Chlamydia*), viruses and rickettsia (influenza, parainfluenza, respiratory syncytial virus, adenoviruses, cytomegalovirus, arenaviruses, hantaviruses, filoviruses, Q fever), fungi (coccidioidomycosis, cryptococcosis, histoplasmosis), and protozoa (*Pneumocystis*). This intensive investigative process revealed infection by a previously unrecognized hantavirus. The efforts involved in identifying this agent demonstrated the need for maintaining professional expertise concerning a broad array of infectious agents, some of which are not necessarily considered to be of high public health priority today.

Clinicians have since diagnosed and reported more than 50 cases of HPS (more than half fatal) in persons from 15 states: Arizona, California, Colorado, Idaho, Indiana, Kansas, Louisiana, Minnesota, Montana, New Mexico, North Dakota, Nevada, Oregon, South Dakota, and Texas. Illnesses in more than 70 persons with ARDS reported from many other state health departments also are being investigated by CDC.

Because hantavirus infections have been transmitted in laboratory settings and because disease associated with this new strain has been fatal in most cases and has no known effective antiviral treatment, much of the laboratory work must be carried out in high-level biocontainment facilities.

This is a newly recognized virus and a newly recognized disease. No one yet knows the extent of the disease, its geographic and temporal trends, its clinical spectrum, or the ecology of the infectious agent in rodent reservoirs. Also needed are specific diagnostic tests that can be used by public health and clinical laboratories, optimal treatment strategies, and public and professional educational programs.

Working with state and local health departments, other federal agencies, private health care providers academia, private industry, community organizations, and other appropriate groups, CDC is undertaking the following activities to address the problem:

- National surveillance
- Determination of the ecology of hantaviruses in rodents
- Expansion of diagnostic capabilities
- Definition of pathogenetic mechanisms and immunologic responses to hantavirus infections
- Assessment of therapeutic regimens in confirmed and suspected cases
- Development and evaluation of public and professional educational materials and programs
- Development and evaluation of rodent control and risk reduction strategies

availability of drugs and biologics; such actions include procuring needed materials, establishing reserve supplies, identifying target populations, and expediting distribution. The provision of primaquine for malaria, sulfadiazine for toxoplasmosis, and antitoxin for botulism are recent examples of how CDC has responded to such challenges.

Another critical component of this activity will be to address the use of antimicrobial drugs by clinicians and their patients. The current crisis in antimicrobial resistance cannot be adequately managed without dramatic changes in current patterns of antimicrobial drug usage. Clear, readily available guidelines for the appropriate use of antibacterial, antiviral, antifungal, and antiparasitic medications must be developed and kept current.

Goal IV *Strengthen local, state, and federal public health infrastructures to support surveillance and implement prevention and control programs.*

Objective IV-A. *Ensure the ready availability of the professional expertise and support personnel needed to better understand, monitor, and control emerging infections*

The results of a recent CSTE survey (June 1993) illustrate the inadequacy of personnel resources in state health departments available to detect and to respond to emerging infectious diseases in this country.[6] Similarly, a task force report from the Association of State and Territorial Public Health Laboratory Directors (ASTPHLD) voices concerns about the future of public health laboratories.[95] Rebuilding an infrastructure capable of efficiently managing emerging infectious disease threats requires improved support for personnel and training at local, state, and federal levels.

The considerable efforts recently applied in investigating HPS are a timely reminder of the extensive personnel resources, equipment, supplies, economic resources, multidisciplinary coordination, and cooperation among state and federal agencies, health care providers, and academia required to rapidly link a previously unrecognized human pathogen with a severe illness (see Objective I-C). However, this outbreak also illustrates the burden that such mobilization places on an infrastructure that has limited surge capacity (see Box, page 32).

Activities

i. *Ensure that expertise in rare or unusual, but potentially important, infectious diseases is maintained.*

CDC is frequently called upon to provide reliable information about the diagnosis, clinical management, and control of rare or unusual infectious diseases (e.g., botulism; amoebic meningoencephalitis; neurocysticercosis; plague; leptospirosis; and Ebola, Marburg, and Lassa viral hemorrhagic fevers). To meet this public obligation, CDC must maintain expertise for such diseases in the event of their possible reemergence or introduction into new niches in the United States and elsewhere. Maintenance of this expertise requires an ongoing commitment of resources because the necessary knowledge and skills are difficult to acquire and even more difficult (and costly) to replace if lost. Such expertise is frequently required at CDC, but can, and often is, supplemented by experts at other governmental or academic facilities. Innovative "retainer" arrangements would aid access to outside expertise, particularly in emergency situations.

ii. *Reestablish a CDC program for state-of-the-art training in diagnostic evaluation and testing for emerging infectious diseases.*

CDC should ensure that state and selected local health department personnel, as well as appropriate public health and university hospital laboratory personnel, receive training to support the diagnosis and surveillance of selected infectious diseases. The training, which should involve regional laboratories, should also address computer and laboratory skills, as well as quality assurance and biosafety in laboratories supporting prevention and surveillance activities. Such a program would not only serve the purpose of training, but also strengthen liaison between public health agencies and clinical laboratory personnel to facilitate rapid communication regarding the occurrence of unusual syndromes or infectious diseases of unknown cause.

iii. *Establish a public health laboratory fellowship in infectious diseases.*

This program, analogous to the EIS for epidemiology training, is needed to recruit and retain medical microbiologists for intramural programs and to train such persons for employment at, or assignment to, state health and other laboratories. CDC has a unique approach to reference diagnostic work, molecular epidemiology, and research; a combination of these skills, knowledge, and experience will be required to respond to the laboratory challenges posed by new

agents of infectious diseases, increased virulence of known pathogens, increased resistance of pathogens to antimicrobial therapies, and the changing susceptibility in human populations.

Objective IV-B. *Make available state-of-the-art physical resources (laboratory space, training facilities, equipment) needed to safely and effectively support the preceding goals and objectives.*

In addition to personnel resources, reference laboratory facilities and services are critical to the effective management of emerging infectious disease threats. For instance, the Laboratory Initiatives for the Year 2000, a joint venture between ASTPHLD and CDC, has documented the need to enhance the diagnostic and analytical capability/capacity of state public health laboratories in order to ensure that the *Healthy People 2000* objectives are met. Expanded physical resources will be required to attain the goals and fulfill the objectives of this plan.

Activities

i. *Equip public health facilities to meet anticipated computer and laboratory training needs.*

Health departments as well as CDC need improved training facilities and equipment. Because many training activities have been phased out over the past several years, little physical infrastructure exists for on-site training or newer systems for remote teaching, such as teleconferencing. Laboratory training emphasizing the identification of emerging pathogens will require access to sophisticated equipment and laboratory facilities with appropriate levels of biocontainment.

ii. *Ensure that the laboratory space, equipment, and supplies needed to address emerging infectious diseases are available.*

Improvement and expansion of local and state health department and CDC laboratory facilities will be critical to addressing emerging infections. Setting priorities for such improvements will require careful evaluation of space and equipment needs. Moreover, laboratory capabilities must be maintained in a manner that optimizes flexibility and "surge capacity" so that unanticipated needs (e.g., responding to new outbreaks such as HPS) can be adequately and efficiently addressed. Immediate priorities should include improving facilities to deal with infectious agents that require high level microbiological safety precautions.

iii. *Expand existing facilities or build new facilities that can adequately and safely maintain a specimen bank of etiologic agents and clinical specimens.*

A well-maintained and well-catalogued bank of etiologic agents and clinical specimens provides an invaluable resource for addressing emerging infectious diseases. Well-defined clinical specimens can also be used to evaluate the performance characteristics of diagnostic tests under development for emerging infectious diseases.

iv. *Upgrade and expand animal care facilities and insectary space.*

Animal care facilities must be expanded to meet the increased demand for animal models used to elucidate the pathogenesis of emerging pathogens or to test new vaccines for emerging or reemerging infectious diseases. Insectaries need to be expanded to provide the containment necessary to conduct applied research on emerging arboviruses, such as Rift Valley fever virus and Congo Crimean hemorrhagic fever virus, and other important vector-borne infectious agents.

v. *Furnish the equipment and facilities needed to provide reference diagnostic services for emerging infections.*

Timely detection of emerging infectious diseases depends on the existence of an adequate laboratory diagnostic base, which in turn requires standardized reagents (i.e., antisera, antigens, cultures, and epidemiologically well-characterized control samples). These reagents, as well as reference procedures for specialized diagnostic and molecular epidemiologic approaches, are usually not produced commercially. CDC should ensure that such reagents are made available to all state public health laboratories—either directly or through extramural contacts and cooperative agreements. In a recent survey of state laboratories conducted by ASTPHLD, state laboratory directors endorsed the need for CDC to enhance its capability to provide reagents and reference materials/procedures to state public health laboratories to help them fulfill their mission as the primary reference microbiology center in their respective states.