Addressing Emerging Infectious Disease Threats

A Strategic Plan for the Department of Defense

GLOBAL
EMERGING
INFECTIONS
SYSTEM

Department of Defense Global Emerging Infections Surveillance and Response System.
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Executive Summary

Historians in the next millenium may find that the 20th century's greatest fallacy was the belief that infectious diseases were nearing elimination. The resultant complacency has actually increased the threat. Both naturally occurring and bioterrorist infectious disease agents hold an increasing potential to destabilize international security. Failure to recognize and accept this concept will lead to disaster.

Globally, infectious diseases remain the leading cause of death. The ability of microbes to adapt and breach our traditional defenses coupled with changes in society, technology, and the environment sustain the likelihood that regional and global epidemics reminiscent of the worst in history will recur. In addition, terrorists with some expertise in molecular biology and modest financing can now wage biological warfare on cities, regions, and even the entire planet. A responsible assessment indicates that national and global security requires a robust "early warning system" for emerging infections.

In the early 1990s public health experts at the National Academy of Sciences, CDC, NIH, and WHO developed plans for addressing and mitigating the threat of emerging infections. The DoD, owing to its wide-ranging assets for disease control, was prominent in their recommendations. These recommendations culminated in Presidential Decision Directive NSTC-7 in June 1996 that formally expanded the mission of DoD to support global surveillance, training, research, and response to emerging infectious disease threats. President Clinton directed a centrally coordinated program that improved DoD epidemiological capabilities and involved both US military treatment facilities and military medical research units in the United States and abroad. Leveraging US capabilities through training foreign technicians and epidemiologists was also encouraged.

The DoD Global Emerging Infections Surveillance and Response System (DoD-GEIS) has developed a five-year strategic plan that parallels the five-year plan developed by the CDC. The four goals of the DoD strategic plan follow.

Goal I: Surveillance

Detect and monitor emerging pathogens, the diseases they cause, and the factors influencing their emergence to protect military readiness, the health of DoD beneficiary populations, and other national interests.

Goal II: Systems Research, Development, and Integration

Integrate public health practices and improve capabilities in clinical medicine, military medicine, laboratory science, epidemiology, public health, and military medical research to facilitate rapid identification and response to emerging infections.

Goal III: Response

Enhance the prompt implementation of all prevention and control strategies for emerging infections to include improving communication of information about emerging agents.

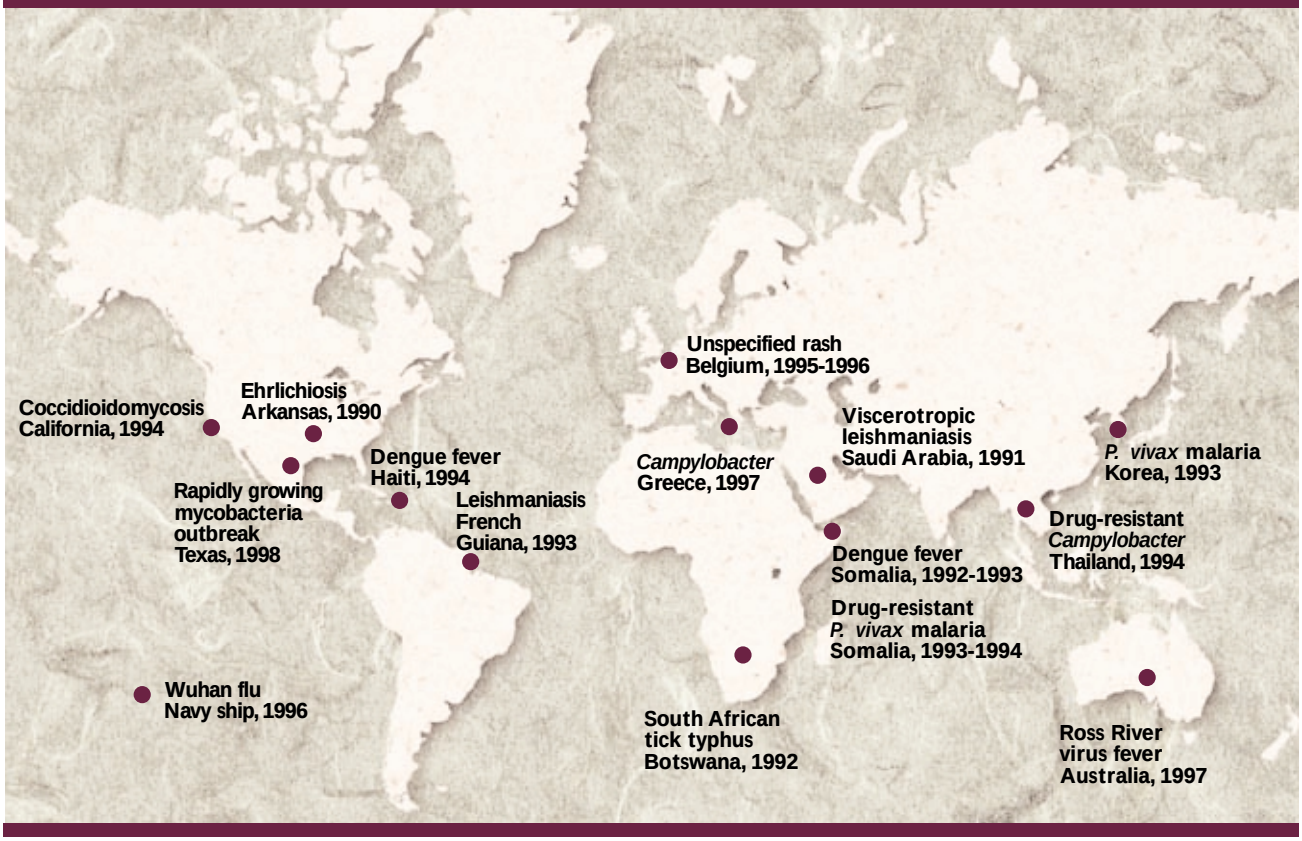
Goal IV: Training and Capacity Building

Leverage DoD and international public health infrastructures through training, networking, and other forms of assistance to support surveillance, assessment, response, and prevention of emerging infections.

The Threat of Emerging Infections

Emerging infectious diseases are due to infections that have increased in frequency within the past two decades or threaten to increase in the near future (Institute of Medicine 1992). Emergence or reemergence may be local, regional, or global. Some of these infections include malaria along the Korean demilitarized zone, Lyme disease, coccidioidomycosis, acute respiratory diseases caused by adenoviruses, H5:N1 influenza in Hong Kong, Hantavirus infections, dengue in Central America, and cholera in Latin America.

Examples of US Military Emerging and Resurgent Infections in the 1990s



Courtesy of J. Brundage, Henry M. Jackson Foundation for the Advancement of Military Medicine, Rockville, Maryland.

Recently it has become common to view diseases resulting from biowarfare/bioterrorism as different from the above emerging infections only with respect to their unnatural origin. In addition, although HIV infection is not a "battle stopper," the societal destabilization associated with 20+% prevalences in parts of Africa may well cause battles. Similarly there are many emerging infections (eg, Rift Valley fever in East Africa) that affect economically important animals or crops and can indirectly result in serious security problems.

Factors that have changed to make the late 20th century a time of increasing risk for emerging infections include environmental alterations such as the growth in densely populated cities in underdeveloped countries; deforestation or reforestation, which increases human exposures to disease vectors; the occurrence of antibiotic resistance that outpaces the development of new drugs; changes in sexual and other behaviors; increased international travel and agricultural trade; and breakdowns in public health measures. Clearly US military personnel, because of the exigencies of military life, have an elevated likelihood of exposure to emerging infections occurring both naturally and from bioterrorism. For example, during operations other than war deployed US military personnel (medical and others) frequently come in close contact with members of the local populace, displaced persons, and coalition force military personnel from around the world. During Operation Uphold Democracy, deployed medical units treated peacekeepers of many different nationalities. Multinational operations greatly increase the potential for exposures to infectious agents, especially among immunologically naive populations.

There is broad consensus that the public health infrastructure in the United States is poorly prepared to confront emerging infections. The military is in some ways significantly less prepared than many civilian public health agencies. Military medical surveillance is fragmentary and largely dependent on information sources not designed for epidemiologic

purposes. New practice patterns associated with managed care have made hospitalization data much less useful for surveillance purposes. Not only are military public health laboratories and laboratory-based surveillance procedures less robust than those found in the average state, they are far less than what is needed to address the threat. In addition, surveillance for unexplained deaths is neither systematic nor standardized. As with more traditional military threats, timely recognition of emerging infections necessitates a robust early warning system. Such a system would allow a response to be undertaken before epidemics harm readiness. This is especially true with rapidly moving agents such as pandemic influenza or with biological warfare agents that may surface insidiously.

To distinguish the unusual from the usual, emerging infections surveillance must be routine and systematic so that trends in typical incidence and distribution can be understood. Investigations of the type usually undertaken only in public health laboratories are necessary to detect strain patterns that may not be relevant to the therapy of individuals but are central to the detection of diffuse epidemics.

DoD Emerging Infections Prevention Strategy

The DoD strategy for addressing the threat of natural and bioterrorist emerging infectious disease threats reflects a comprehensive, interagency systems approach. The strategy serves not only DoD but also brings some of the unique assets of DoD into partnership with other federal, private, and international organizations. Only through such leveraging will it be feasible to deal productively with this global issue. Just as emerging infections do not respect international borders, they do not respect agency boundaries. An effective prevention and control strategy requires an almost unprecedented spirit of teamwork.

The four goals of the DoD emerging infections strategic plan are the foundation of DoD-GEIS and are explained below.

Goal I: Surveillance

Surveillance is the routine, standardized, systematic collection of health information necessary for taking timely public health action. Quality information must be generated on emerging and reemerging infections, and that information must be shared effectively with those who can act upon it. The scope must be both foreign and domestic. This sharing will necessitate coordinated and complementary activities among the services and the DoD overseas medical research units.

Within the DoD military health system, laboratory-based surveillance will be strengthened with particular emphasis on influenza and other respiratory pathogens. Mechanisms to track the emergence of antibiotic resistance patterns and to share that information broadly will be implemented. A standardized approach to the surveillance of unexplained deaths in active duty personnel and other beneficiaries will also be established. At the overseas medical research units, the focus will be on standardized sentinel surveillance of indigenous and expatriate populations for drug-resistant enteric organisms, drug-resistant malaria, influenza, and other serious fevers including dengue. The establishment of catalogued specimen archives at the overseas labs will be key to the rapid investigation of new infections when they are first recognized. Innovative methods of surveillance such as those involving remote sensing and geographic information system technologies will also be supported. Partnerships with other federal and international agencies will be actively sought.

Goal II: Systems Research, Development, and Integration

The processes needed to successfully operate a comprehensive DoD emerging infections system, improve elements that are found inadequate, and integrate various elements must be understood so that a strong, action-oriented system can function successfully. The first element is

to properly identify expertise. Personnel requirements will be defined so that DoD has sufficient expertise across a range of disciplines to address this multifaceted threat. Second, to generate necessary information will require an enhanced DoD public health laboratory capability. DoD-GEIS will define an appropriate scope of public health laboratory capabilities, develop a cost-effective "virtual" public health laboratory through integrating various DoD, other federal, state, academic, and commercial capabilities, and coordinate the development and implementation of a system to track specimens and results.

DoD-GEIS will provide active leadership on DoD, federal, and international committees dedicated to building a global emerging infections system. Medical informatics is the backbone of gathering and communicating surveillance data. DoD-GEIS will be an active advocate for fostering necessary improvements in DoD systems to capture laboratory-based surveillance data and for developing international standards for surveillance systems. Expertise in quantitative public health decision making will be used to foster the economic evaluation of competing approaches to disease control issues.

Examples of Emerging and Reemerging Infectious Diseases

Inside the United States

1997	*Staphylococcus aureus* infection with reduced sensitivity to vancomycin
1996	Pertussis (whooping cough)
1995	Multidrug-resistant *Salmonella typhimurium* DT104 infection
1995	Fluoroquinolone-resistant gonorrhea
1995	Strain of highly transmissible tuberculosis
1995–1997	Cyclosporiasis
1993	Multidrug-resistant pneumococcal disease

Outside the United States

1997–1998	Rift Valley fever in East Africa
1997	Ross River virus fever in Australia
1997	Influenza H5:N1 in Hong Kong
1997	Hantavirus pulmonary syndrome in Argentina
1997	*Staphylococcus aureus* infection with reduced sensitivity to vancomycin in Japan
1996	Variant Creutzfeldt-Jakob disease in United Kingdom
1996	*Escherichia coli* O157:H7 infection in Japan
1995–1997	Epidemic serogroup A meningococcal meningitis in West Africa
1995	Yellow fever in Peru
1995	Leptospirosis in Nicaragua
1995	Japanese encephalitis in Australia
1995	Ebola hemorrhagic fever in Democratic Republic of Congo (then Zaire)
1994	Plague in India
1994	Pertussis (whooping cough) in the Netherlands
1994	Epidemic dengue in Costa Rica and Panama
1994	Dengue hemorrhagic fever in Saudi Arabia

Adapted from CDC. 1998. *Addressing Emerging Infectious Disease Threats II: Entering the 21st Century.* Atlanta: Centers for Disease Control and Prevention.

Goal III: Response

Response refers to any action to reduce morbidity or mortality or the threat of morbidity or mortality. Response to an emerging infection can involve a wide range of activities. At one end the response may be as basic as enhanced public and professional education. Response may also include expanded surveillance, a new policy, outbreak investigation, targeted research, the stockpiling of drugs and biologics, and the initiation of large-scale immunization programs.

To be effective DoD-GEIS must be responsive to a wide range of people who need information: health care beneficiaries, policy makers and resource managers, clinicians and laboratory personnel including those in training, commanders and the National Command Authority, the scientific community, and many other national and international interests. A wide range of communications efforts will be initiated, including a web site with multitiered communications forums and an emerging infections publication for DoD personnel. DoD scientists will be actively supported to participate in relevant international scientific meetings. The assets (expertise, products, and logistics) that DoD can bring to a response will be catalogued, and mechanisms to rapidly deploy those assets to serve the needs of both DoD personnel and others will be established. Deficiencies will be identified and corrected. This will include appropriate memoranda of agreement with organizations such as the CDC, Department of State, and WHO.

Goal IV: Training and Capacity Building

Those personnel and physical resources needed for a global emerging infections system will be determined. Within DoD such a system will require maintaining a robust level of epidemiologic and infectious disease clinical and laboratory expertise to cope with rare or unusual infectious diseases in a timely fashion. The DoD overseas medical research units, owing to their being "forward-deployed," have a unique role as platforms to support the education and training of foreign technicians and epidemiologists. A goal of DoD-GEIS is to have each overseas medical research unit serve as a model for regional surveillance efforts and thus leverage DoD's capabilities through mentoring relationships. Regional commanders-in-chief of the unified commands have a keen interest in emerging infections control and have mobilized significant humanitarian assistance funds to strengthen surveillance systems in developing countries. It is a goal of DoD-GEIS to continue these highly beneficial multilateral activities.

This strategic plan reflects the commitment of DoD to join with other federal agencies to implement Presidential Decision Directive NSTC-7 on emerging infections. There is a sense of urgency in working toward these four goals. Not only are naturally occurring infections emerging at an inexorable pace, but the perceived threat of bioterrorist events has grown significantly in recent years for various reasons. As noted in 1952 by Alexander Langmuir, the founder of the CDC's renowned Epidemic Intelligence Service (EIS),

> The detection and control of saboteurs are the responsibilities of the FBI, but the recognition of epidemics caused by sabotage is peculiarly an epidemiologic function. . . . Therefore, any plan of defense against biological warfare sabotage requires trained epidemiologists, alert to all possibilities and available for call at a moment's notice anywhere in the country.
> (Langmuir and Andrews 1952)

The goals in this strategic plan are consistent with those of the CDC and with the recommendations of the Institute of Medicine. Some of the specific activities detailed under "DoD Emerging Infections

Prevention Strategy" are already being implemented. Many will require further planning and coordination. Although the plan is ambitious and will need additional funding and the acquisition of additional trained personnel, the mandate is clear. Readiness, our first obligation, demands these most basic investments.

High Priorities for DoD-GEIS Implementation, 1998–2002

Goal 1: Surveillance

- Conduct malaria, enteric infection, influenza, and fever surveillance at six OCONUS laboratories
- Implement laboratory-based surveillance within DoD
- Enhance influenza surveillance in DoD populations
- Institute unexplained mortality surveillance in DoD populations

Goal 2: Systems Research, Development, and Integration

- Develop a DoD "virtual" public health laboratory network
- Establish appropriate specimen archiving and information gathering systems

Goal 3: Response

- Develop mechanisms for communicating surveillance data to those who need to know to include a web site and the DoD-GEIS Emerging Infections Report
- Establish appropriate interagency agreements with CDC and the Department of State
- Address product availability and influenza pandemic planning issues

Goal 4: Training and Capacity Building

- Continue humanitarian assistance projects funded by regional unified command CINCs to leverage global resources for surveillance in developing countries

The Problem

Throughout human history, infectious disease epidemics and pandemics have affected not only the health of individuals but also the success of military operations and even the stability of societies. Despite tremendous public health progress during the 20th century, numerous infectious conditions have grown harder to control, and some new infectious diseases have emerged. It has become clear to public health leaders that optimism or indifference displayed toward infectious diseases poses a threat to society. This is equally true, if not more so, in the military because of the demands of military readiness and the particular environments in which military personnel train and deploy.

The term "emerging infectious diseases" is applied to those conditions in which the incidence in humans has increased within the past two decades or threatens to increase in the near future. Emerging infectious diseases have taken a major toll on the US military. Beyond the obvious scourge associated

Outbreak of a New Antigenic Strain of Influenza among Vaccinated Sailors Forces Ship to Port

Background

In February 1996 an outbreak of influenza A (H3N2) occurred on board the USS *Arkansas* even though 498 of the 526 crewmembers had received a trivalent influenza vaccine in early December. The outbreak forced the ship into port for 2 days.

A subset of the affected crew was examined. Pharyngeal cultures were obtained, and sick call records were reviewed. A self-administered survey was given to the crew during and after the outbreak.

USS *Arkansas.*

Results of the Examinations and Surveys

A case was defined by symptoms of sore throat, headache, cough, fever, or myalgias that occurred between February 1 and 23. The ship sailed on February 1. The outbreak first occurred on February 3 and peaked on February 5. It then tapered off, with the last case occurring on February 20. During the 3 weeks, 217 crewmembers had an illness similar to influenza. The attack rate (41%) was the same for vaccinated and unvaccinated crewmembers; 45 crewmembers were confined to quarters, and one was hospitalized.

Another ship received the same lot of vaccine and shared messing facilities with the outbreak ship up to the day of deployment but experienced no outbreak. Antigenic analysis characterized the strain as A/Wuhan/359/95-like. Once influenza A was isolated, amantadine was flown to the ship. Amantadine was offered to new cases and as prophylaxis for unvaccinated personnel who were symptomatic of influenza. Of the eight unvaccinated crewmembers who elected to take amantadine, none had symptoms of influenza.

Statement

This outbreak demonstrates the potential for rapid spread of influenza through a confined population. The high attack rate was due to a significant antigenic drift and occurred despite appropriate vaccination. This subtype, first isolated in Wuhan, China, in 1995, has only recently been isolated in the United States. Although this outbreak occurred in a young and immunized population, it still resulted in significant morbidity, with a dramatic impact on military readiness.

WHO and FDA recommended that A/Wuhan/359/95 be included in the 1997 influenza vaccine.

Courtesy of K. Earhart, M. Pruts, H. Regnery, L. Miller, M. Wallace, Department of Internal Medicine, Division of Infectious Diseases, Naval Medical Center, San Diego, California; E. Ledbetter, C. Beadle, Navy Environmental and Preventive Medicine Unit No. 5, San Diego, California; A. Hawksworth, G. Gray, Naval Health Research Center, San Diego, California.

with several thousand HIV infections, emerging infections have plagued our service personnel during both training and operational deployment. Some of the operationally significant emerging infections problems affecting our troops have included an outbreak of primaquine-tolerant vivax malaria after operations in Somalia, dengue after operations in Somalia and Haiti, and the resurgence of malaria along the demilitarized zone in Korea.

The Wuhan strain of influenza A, which emerged and recently circulated around the world, was first recognized outside of China in a US Air Force health care beneficiary. This emerging strain was considered so important a threat that the WHO recommended its inclusion in influenza vaccines used worldwide during the last two years. The threat of emerging strains of influenza to military populations is not new. The US military was affected early during the infamous 1918–1919 influenza pandemic that killed more than 20 million people worldwide including more than 43,000 US military personnel. Some historians credit this epidemic with contributing to the end of World War I. The memory of this catastrophic pandemic mobilized the United States in 1976 after a fatal swine influenza infection occurred in a recruit at Fort Dix, New Jersey.

Militarily relevant emerging infections include not only previously unrecognized agents such as those causing HIV, Lyme disease, human ehrlichiosis, or new influenza strains but also better established infectious agents that have become resistant to antibiotic therapy. For example, large numbers of US military personnel deploying to Thailand and Greece have experienced gastrointestinal infections with ciprofloxacin-resistant *Campylobacter.* In much of the developing world, use of antibiotics is not regulated well. This and inappropriate use of antibiotics in the industrialized world have favored the development of antibiotic resistance in bacteria that cause illnesses including pneumonia, sexually transmitted diseases, and diarrhea. In some instances infections with malaria and tuberculosis have become almost impossible to treat successfully.

Physicians and medical scientists in recent years have become increasingly aware that many infections can have long-term consequences. Some of these are quite militarily relevant. Many infections caused by agents such as hepatitis B virus and *Helicobacter pylori* have been acquired by US service personnel working overseas. These and other infections have the potential for chronicity and may lead to conditions such as liver cirrhosis and peptic ulcers. The Hantavirus responsible for Korean hemorrhagic fever has been associated with hypertension decades later in personnel who survived the initial infection (LeDuc et al. 1992). There is even evidence implicating the common respiratory infection *Chlamydia pneumoniae* in the pathogenesis of atherosclerotic heart disease. *C. pneumoniae* has been recognized as a frequent cause of acute respiratory disease in military people (Berdal 1992, Gray 1994, Kleemola 1998).

As the US military downsizes yet continues to become more active around the world, it becomes even more critical to swiftly recognize emerging infections that compromise military readiness and national security. DoD medical surveillance systems must be significantly improved to meet this challenge. Existing systems to detect and track emerging infections domestically and internationally are inadequate. Unlike every state in this country, the DoD health care system does not have a program for laboratory-based reporting of infectious disease surveillance data. This is especially needed because provider-based reporting is generally far from complete and impractical to enforce. Ironically, although DoD medical laboratories are required to report certain laboratory findings to civilian jurisdictions, they are not required to report those same

Chronic Diseases Associated with Infections in Military Personnel

- Stomach ulcers and *Helicobacter pylori*
- Hypertension and Hantavirus
- Liver cancer and hepatitis C virus
- Atherosclerosis and *Chlamydia pneumoniae*
- Cancer and Epstein-Barr virus
- Cervical cancer and human papillomavirus
- Infertility and *C. trachomatis*

Major Deficiencies in DoD Emerging Infections Surveillance

No program of laboratory-based reporting of surveillance data

- Is essential to identify and track antibiotic resistance patterns
- Could couple with geographic information system for timely recognition of bioterrorism
- Would help address nonspecific inpatient and outpatient diagnoses
- Would address significant clinician-based underreporting
- Would raise DoD to the surveillance standard of practice followed by the 50 states in mandating reporting of laboratory data to the CDC

No timely epidemiologically focused mortality surveillance system

Lack of at least a "virtual" DoD public health laboratory system

- Military public health questions must be addressed in addition to patient care issues (eg, serotyping to recognize outbreaks)
- Resources are not coordinated and diagnostic gaps exist
- Resources often are not institutionalized and are "personality dependent"

findings to military public health authorities. Both in the civilian sector and in the military, laboratory-based surveillance systems are needed for the early detection of microbes that could enter circulation naturally or as a result of bioterrorism.

In addition to laboratory-based reporting, the DoD needs a timely, epidemiologically focused mortality surveillance system. Current casualty data suffer significant inaccuracies that limit their value for epidemiologic purposes. Even those data that do exist are not analyzed from a population perspective to identify clusters and important common factors that may suggest an emerging infectious disease problem.

The DoD also lacks a coordinated public health laboratory system. A “virtual” DoD public health laboratory system would help detect patterns in individual test results that could have public health implications. Important outbreaks that are manifest by a geographically diffuse case distribution may be best detected through laboratory efforts. Diffuse outbreaks, such as those that could follow redeployment to multiple sites after a training exercise, are important to detect. A “virtual” DoD public health laboratory system would help coordinate resources, plug important diagnostic gaps, and identify quality sources of laboratory work. Such a system would help DoD manage special public health issues such as the recent problems with acute respiratory diseases caused by adenoviruses in military basic training camps. A coordinated DoD public health laboratory system, coupled with a geographic information system, would assist in the timely recognition of bioterrorist events.

The Concept of Emergence

Disease emergence reflects the contribution of many factors. Genetic changes may be responsible for the emergence of new infectious diseases from existing organisms (eg, influenza). Known diseases may spread to new geographic areas and populations as has been observed with raccoon rabies in the northeastern United States. Previously unknown infections may occur when humans enter certain environments that increase exposure to insect vectors, and other reservoirs, or environmental sources of new agents. Activity in once remote tropical rainforests is an example of how humans might come into contact with previously unknown infectious agents. Breakdowns in public health measures for previously controlled infections have also contributed to the spread of more well-known illnesses such as cholera and pertussis.

Factors in Emergence

Societal disruption (eg, urban decay, refugee migration, or economic impoverishment) may lead to the emergence or reemergence of infectious diseases. Such disruption may explain the reemergence of malaria on the Korean peninsula.

Advances in health care also contribute to the development of emerging infections. In addition to the effects of drugs causing immunosuppression, the widespread and unrestricted availability of antibiotics in much of the world is an important consideration. The concern is not only the acquisition by US forces of antibiotic resistant organisms while receiving health care during operations overseas but also the importation of these infections to US health care facilities.

As even a casual visit to a US supermarket will indicate, Americans consume food that is grown, processed, or packaged throughout the world. Processing and packaging associated with a global food supply have increased the occurrence and spread of emerging infections.

Over the last several decades Americans have greatly increased their international travel and changed their sexual behavior patterns. These and other changes in human behavior (eg, increased use of child care facilities and certain recreational pursuits) increase the risk of acquiring emerging infections. American service personnel reflect these behavioral factors.

Global warming, deforestation, floods, drought, famine, and other ecological factors also affect the emergence of infectious disease. Decay in public health infrastructure is another contributor. Communicable disease surveillance systems are inadequate in this country and almost nonexistent in some parts of the world. Better surveillance may have allowed HIV infection to be recognized earlier.

Reemergence of *Plasmodium vivax* Malaria in Korea

Vivax malaria reemerged in South Korea in 1993 after a 20-year absence. Although the reasons for this reemergence are unclear, the initial appearance immediately south of the border suggests that transmission began in North Korea.

Malaria was documented in Korea as early as 1913, but the problem became much worse during the war in the early 1950s. A successful program to eradicate malaria was sponsored by the WHO in the late 1960s and culminated in complete elimination by 1973. This program included vector control, case detection, and treatment.

The 1993 outbreak began with only two cases but quickly grew to 39 cases in 1994, 118 in 1995, 367 in 1996, and 1642 in 1997. Most patients have been South Korean soldiers stationed near the northern border. Cases have occurred in US Army soldiers, but the number of patients was limited to 27 in 1997 thanks to aggressive vector control measures at American installations. Increases in the number of Korean civilian cases (461 in 1997) suggest that local foci of transmission have become established, so the epidemic is likely to spread geographically.

Malaria in Korea is unstable because conditions for transmission probably exist for only a few months each year and the vector, *Anopheles sinensis*, prefers to feed on cattle. Relatively mild vector control and case detection efforts can therefore block transmission, although these measures are not currently in place. The strain of *Plasmodium vivax* found in this part of Asia is known for its long incubation, which regularly extends from summer to the next spring before signs of illness appear. This aspect of vivax malaria in Korea complicates the problem of thoroughly treating the human reservoir. The long incubation also favors geographic spread, both by Korean soldiers returning to their homes throughout the peninsula and by American soldiers returning to the United States.

Courtesy of Stephen C. Craig and Brian H. Feighner, USACHPPM, Aberdeen Proving Ground, Maryland.

Factors in Disease Emergence

Categories	Factors
Social change	Economic impoverishment; war or civil conflict; population growth and migration; urban decay
Health care	New medical devices; organ or tissue transplantation; drugs causing immunosuppression; widespread inappropriate use of antibiotics
Food	Globalization of food supplies; changes in food processing and packaging
Human behavior	Sex; drug use; travel; diet; outdoor recreation; child care facilities
Environment	Deforestation/reforestation; changes in water ecosystems; flood/drought; famine; global warming
Public health infrastructure	Curtailed or reduced prevention programs; inadequate communicable disease surveillance; lack of trained personnel (epidemiologists, laboratory scientists, vector and rodent control specialists)
Microbial adaptation	Changes in virulence and toxin production; development of drug resistance; microbes as cofactors in chronic disease

Adapted from CDC. 1998a. *Addressing Emerging Infectious Disease Threats II: Entering the 21st Century*. Atlanta: Centers for Disease Control and Prevention.

There is a lack of trained public health personnel throughout the world. The US military is not immune from the shortage. For example, in the US Army, the modeled objective force for preventive medicine physicians as of September 1997 called for 112 active duty officers, yet only 60 were on active duty. Similar shortfalls are faced in the other services. With respect to infectious disease physicians, the deficit is almost as bad: the modeled objective force required 64 officers, yet only 40 were on active duty in September 1997. To control emerging infections additional epidemiologists, infectious disease specialists, laboratory scientists, and vector and rodent control specialists must be trained.

Of course microbes themselves have an uncanny ability to adapt. Thus even without the other factors humanity will likely never be spared the need to respond to the challenge of emerging infections.

A Call to Action

The National Academy of Sciences concluded in the late 1980s that the ability of the US public health system to deal with emerging infectious diseases was jeopardized. The academy noted in a 1987 report entitled "The US Capacity to Address Tropical Infectious Disease Problems" that this country was in a poor state of readiness with respect to our ability to recognize, treat, and control tropical infectious disease threats, many of which have obvious relevance to the military (Institute of Medicine 1987).

In 1988 the National Academy of Sciences published another report entitled "The Future of Public Health," which concluded that the US public health system was in disarray and that our approach to problems has too often been crisis driven or reactive rather than proactive (Institute of Medicine 1988). Some of the same criticisms could be levied against the US military public health infrastructure, as was evident as the Persian Gulf illnesses issue surfaced. Although some of these deficiencies have been corrected, more work remains.

In 1992 the National Academy of Sciences published still another report entitled "Emerging Infections: Microbial Threats to Health in the United States." To break the complacency regarding infectious disease control that had stalled

government planners, the report provided specific recommendations for the CDC, NIH, FDA, DoD, and other agencies (Institute of Medicine 1992).

In 1994 the CDC, the National Institute of Allergy and Infectious Diseases, and the WHO each published strategic planning documents on emerging infections. Interestingly, in each of these seminal reports, the DoD was noted to be in a position to contribute to the worldwide effort against emerging infectious diseases, particularly because of its unique network of overseas medical research units. No other US federal agency has an overseas medical research presence that compares with the DoD overseas laboratories.

In June 1996 President Clinton issued Presidential Decision Directive NSTC-7. In this document he directed federal agencies to take action in four key areas: developing a global surveillance network; enhancing research and training; engaging our international partners; and strengthening public outreach. Part of the directive follows:

> The mission of the DoD will be expanded to include support of global surveillance, training, research, and response to emerging infectious disease threats. DoD will strengthen its global disease reduction efforts through: centralized coordination; improved preventive health programs and epidemiologic capabilities; and enhanced involvement with military treatment facilities and United States and overseas laboratories. (President 1996)

The presidential directive lays out six specific objectives:

- Expand missions and authority of US agencies
- Collaborate to establish a global surveillance network based on regional hubs linked by modern communications
- Ensure availability of drugs, vaccines, and assays
- Strengthen domestic infectious disease surveillance and response
- Strengthen research into diagnostics, treatment, and prevention
- Promote public awareness

Clearly, the DoD network of overseas medical research units can contribute to meeting the objective set by President Clinton to establish regional hubs linked by modern communications. In addition, the US Army Medical Research and Materiel Command has historically made available for humanitarian purposes certain drugs, vaccines, and diagnostic assays that are generally unavailable from other agencies or commercial entities. Because US military personnel travel extensively overseas they may often be among the first Americans to acquire emerging infections. Thus enhanced surveillance of US military personnel will benefit not only the US military but also domestic infectious disease surveillance and response. The Air Force's Project Gargle has demonstrated this larger benefit to the nation by isolating important emerging strains of influenza that were subsequently incorporated into annual vaccine recommendations.

The concept that some infectious diseases are "domestic" as distinct from "international" is outdated. In an era in which business and recreational travel, environmental change, and population migrations are occurring on a global scale, it is unrealistic to think that national borders can secure the United States from infectious disease threats. On many levels the DoD must be active in this national security issue. The international importance of emerging infections has been reflected in the appearance of this issue in discussions involving the world's most senior leaders including the G7, the United States-European Union New Transatlantic Agenda, the Gore-Chernomyrdin Commission, and the Gore-Mbeki Commission. At the 1997 Denver summit the United States presented a major infectious disease initiative that included a commitment from the heads of state to develop a global surveillance system.

To implement Presidential Decision Directive NSTC-7, the National Science and Technology Council formed a task force on emerging infectious diseases that is cochaired by representatives from the CDC and the White House Office of Science and Technology Policy. The executive summary of the first annual report of this task force prominently noted "the creation of a DoD Surveillance and Response System for Infectious Diseases; the

These Soldiers Have Malaria

Military troops deploy around the globe. Diseases acquired in one part of the world may become apparent only after the troops have left that area. Operation Restore Hope provides an example.

During 1992–1993 more than 30,000 US troops deployed to Somalia as part of a humanitarian relief effort called Operation Restore Hope. Malaria was recognized as a substantial medical threat, and preventive measures were taken. Only 48 cases of malaria occurred among US troops in Somalia. However, a few months after the troops returned to their permanent duty stations outside Somalia, several hundred malaria cases were diagnosed throughout the United States and Europe. The malaria was caused by *Plasmodium vivax*, a parasite that can live for months in the body without causing illness.

The frequency of vivax malaria exposure had not been expected because of insufficient surveillance data; hence the appropriate terminal prophylaxis drug, primaquine, was not initially used. Eventually a standard dosing regimen of primaquine, a drug that kills this type of parasite, was prescribed to those US troops who had served in Somalia, but malaria cases continued.

A team of military medical scientists from the WRAIR was sent to Fort Drum, New York, to investigate. Because the 10th Mountain Division at Fort Drum had sent the largest contingent of Army troops, it had the most malaria cases in one location. Studying 79 cases in detail, the scientists showed that the vivax malaria acquired in Somalia was relatively tolerant to primaquine and recommended that the usual dose of primaquine be doubled.

These events highlight an important aspect of military medicine: diseases have no geographical boundaries for today's armed forces.

Courtesy of Bonnie Smoak, United States Army Medical Research Unit—Kenya.

establishment of a DoD Internet-based Central Communications Hub; and the expansion of DoD's overseas laboratory capabilities and epidemiology training" (CISET 1997).

The primary mission of DoD is to defend the United States against military enemies. Inherent in accomplishing this mission is the acquisition and training of a healthy force followed by its employment under the protection of a broad array of preventive medicine interventions. This force protection mission is accomplished through the integrated efforts of commanders and their subordinates, physicians, epidemiologists, environmental health professionals and other health care providers, researchers, and specialists in threat assessment.

Emerging infections pose well-documented challenges to protecting our forces. Whether it be pandemic influenza, untreatable forms of malaria, or the anxiety associated with potentially infectious, ill-defined "postwar syndromes," a proactive, anticipatory strategy is indicated. The problem of emerging infections is a global issue and one that reaches beyond the resources of any military organization or any single nation. Partnerships among military organizations, federal and state agencies, and national and international groups are integral to a proactive strategy because they leverage limited resources and provide access to information needed for force protection.

DoD Emerging Infections Prevention Strategy

To meet the challenge of emerging infections and respond to Presidential Decision Directive NSTC-7, DoD-GEIS has a prevention strategy that addresses surveillance, research, response and training and capacity building. Strengthened efforts in these areas will pay dividends that go beyond emerging infections in that other areas of public health will simultaneously benefit. This will facilitate our ability to respond to biological warfare threats, "postwar syndromes," and many routine military public health problems.

Beyond benefits to DoD, the application of DoD leadership and expertise in this area will provide direct benefits to the nation and enhance global health. This vision is clearly reflected in the formal expansion of the DoD mission in Presidential Decision Directive NSTC-7 on emerging infections. Using DoD resources and expertise to enhance global health is also consistent with President Clinton's foreign policy vision of "engagement and enlargement" and with former Secretary of Defense Perry's Doctrine of Preventive Defense (Perry 1996).

The DoD prevention strategy described below addresses four critical goals. These goals are intended to plug major gaps in the DoD public health infrastructure and to address specific recommendations of the Institute of Medicine, the CDC, Presidential Decision Directive NSTC-7, and the White House Committee on International Science, Engineering, and Technology (CISET). The plan reflects the commitment of DoD to combine its unique assets with those of other federal and international agencies. Most importantly, implementation of this prevention strategy will help DoD protect its forces by improving the ability to identify, control, and prevent new, emerging, drug-resistant, or human-engineered infectious agents before they disrupt training, readiness, or combat operations or produce long-lasting effects.

Some Emerging Infectious Diseases That Are Military Threats

- Agents of biological terrorism
- Influenza A (Sydney strain)
- Acute respiratory disease caused by adenoviruses
- Vivax malaria in Korea
- Dengue fever in the Caribbean
- Drug-resistant scrub typhus in Asia
- Cholera in Latin America
- Falciparum malaria in Peru
- Rift Valley fever in East Africa
- Drug-resistant *Campylobacter*

Goal I: Surveillance

Detect and monitor emerging pathogens, the diseases they cause, and the factors influencing their emergence to protect military readiness, the health of DoD beneficiary populations, and other national interests.

Objective I-A

Within the DoD health care system, coordinate and improve surveillance systems for the early detection, tracking, and evaluation of emerging infections that occur in or could spread to areas where military members and other DoD beneficiaries may be affected.

Public health surveillance is the sustained, routine, standardized, systematic, and timely collection, quality assurance, analysis, interpretation, and dissemination of health and other related data. It is conducted so that specific prevention and control actions can be taken. Surveillance data characterize the incidence of health conditions with respect to person, place, and time. The data prompt hypotheses into factors that may be affecting incidence and allow the effect of interventions to be evaluated. By documenting routine disease incidence, an effective surveillance infrastructure will improve the likelihood of an unusual or emerging condition being recognized promptly. The necessary infrastructure includes trained personnel, thoughtfully designed medical informatics systems, the capacity to conduct laboratory investigations of unusual agents, and reliable systems for communicating information to those who can act on it.

Multinational Forces Bring Hepatitis E Virus to Haiti

Infection with hepatitis E virus is the most common form of acute viral hepatitis among young adults in the developing world. In the fall of 1995, within a month of deployment in support of the United Nations Mission in Haiti (UNMIH) for peacekeeping duty, four Bangladeshi soldiers developed acute icteric hepatitis. Hepatitis E was found to be the etiologic agent. Testing revealed high genomic identity with Asian strains of hepatitis E rather than the Mexican strain, which strongly suggested that the causative strain had indeed been imported. The soldiers probably acquired their infection while living in a cantonment area outside Dhaka, Bangladesh, for one month before deployment.

A follow-up serologic survey was conducted to determine the prevalence of hepatitis E infection among other UNMIH peacekeepers and Haitian civilians. Of the 981 participants in the survey, 876 were soldiers from eight UNMIH-participating countries representing Asia, Africa, and the Americas, and 105 were Haitian civilians.

Prevalence of Hepatitis E Infection among UNMIH Peacekeepers and Haitian Civilians (from Highest to Lowest)

Country	Prevalence
Pakistan	62%
India	37%
Nepal	37%
Bangladesh	27%
Djibouti	13%
Honduras	6%
Guatemala	5%
Haiti	3%
United States	2%

United Nations peacekeeping soldiers in Haiti.

Over 90% of those surveyed from Guatemala, Haiti, and Honduras, where prevalence data have been scarce, appeared susceptible to hepatitis E infection. The cluster of imported cases and serologic survey results demonstrate the importation of an important infectious disease in a multinational peacekeeping force and the potential high susceptibility of host country nationals and other peacekeepers to infection.

Courtesy of J. Gambel, Division of Preventive Medicine, Walter Reed Army Institute of Research, Washington, DC.

The focus of this effort is emerging infections. Emerging infections are those infectious agents that have either increased recently in their prevalence in a particular locality or threaten to do so for biologic or ecologic reasons. Emerging infections include agents not previously recognized (eg, HIV in 1982; *Escherichia coli* O157:H7), agents not previously recognized in a given locality (eg, Sin Nombre virus in the US southwest), agents returning to a given locality (eg, vivax malaria in South Korea in the 1990s), agents that threaten to return to a locality (eg, dengue type 3 in the eastern Caribbean), or agents developing new antigenic types, antibiotic sensitivity patterns, or virulence patterns (eg, periodic influenza drifts or shifts).

Activity i

Develop and maintain coordination and communications systems among clinicians, pathologists, laboratory personnel, preventive medicine personnel, researchers, DoD medical executives, other DoD parties, and external agencies to achieve an integrated DoD-GEIS.

The front line of emerging infections surveillance includes primary care providers, emergency responders, intensive care staff, and clinical laboratory scientists. Many emerging infections may first present to these individuals as ill-defined syndromes, unexplained deaths, or novel laboratory findings. Newly emergent infections may not be specifically reportable in routine, established reportable disease surveillance systems based on standard case definitions. Similarly, many unexplained deaths will not fit neatly into specific, established, international classification categories. Front line personnel must have a sense for the possible emerging infection significance of unanticipated presentations or findings. This sense requires an awareness of emerging infections in general, of those scenarios that should prompt an aggressive public health investigation, and of the mechanisms to invoke such an investigation. DoD-GEIS has a clear role in developing such awareness for these front line personnel.

Unexplained mortality surveillance is an explicit focus of the CDC national emerging infection plan. Establishing such a program is also an objective of DoD-GEIS. Syndromic surveillance is increasingly recognized in military deployment surveillance and as part of the WHO efforts to identify internationally significant outbreaks. Syndromic surveillance may also be key to rapidly identifying bioterrorist events. Within DoD the development of model real-time systems that optimally integrate the capabilities of clinicians, laboratory personnel, public health professionals, and others will be supported by DoD-GEIS. Such systems may integrate geographic information systems, surveillance of emergency room diagnoses, and community antibiotic consumption patterns.

Some Important Emerging Infectious Diseases That Have Presented as Unexplained Severe Disease or Death

- Legionnaire's disease
- Toxic shock syndrome
- Acquired immunodeficiency syndrome
- *Escherichia coli* O157:H7
- Hantavirus pulmonary syndrome
- Ebola hemorrhagic fever
- New variant Creutzfeldt-Jakob disease
- H5N1 influenza
- Falciparum malaria
- Yellow fever
- Rabies

Activity ii

Evaluate and assess current surveillance mechanisms and requirements, identify areas where deficiencies exist or enhancements are needed, and assist DoD and the services in improving surveillance systems.

The services have as their basis of public health surveillance several types of data including provider reported infectious diseases and other significant conditions; specialized surveillance systems for conditions such as HIV and respiratory infections in basic training; and administrative health care databases. Unfortunately provider-based reporting in both the military and civilian setting has historically been weak; typically less than 25% of reportable infections have been reported. Even hospitalized cases of reportable diseases are usually not reported by providers because of ignorance of the requirement, ignorance of the mechanism to report, or lack of incentive. It is now the standard in all 50 states to require reporting from licensed clinical laboratories. Ironically, although DoD labs are not required to report reportable infections to DoD authorities, they report to civilian public health authorities. For example, in the case of the Walter Reed Hospital laboratory, 21 different infection-related laboratory results are reported to civilian public health authorities. Institution of such a mechanism of rapid laboratory-based reporting through CHCS will allow not only tracking the incidence of important infections but also the tracking of trends in the emergence of antibiotic resistance. The goal is the prompt detection of all cases that warrant a public health response.

DoD-GEIS will also periodically monitor the list of DoD reportable infections to ensure that the list is current given the identification of new infectious agents. Consideration will also be given to developing requirements for isolates of designated organisms of public health importance to be submitted to a "virtual" DoD public health laboratory network.

Another DoD-based surveillance program planned for establishment is a system to epidemiologically track mortality among DoD personnel. Many emerging infections manifest as unexplained deaths (eg, Hantavirus pulmonary syndrome). There is no formal surveillance system for epidemiologically characterizing deaths owing to any cause in DoD. The needed system would capture not only complete physician-determined death certificate data but also terminal event medical records and autopsy records. This deficiency was recognized by the Armed Forces Epidemiology Board in December 1997 and resulted in a formal recommendation to institute a surveillance system.

When indicated, DoD-GEIS may also organize conferences and other forms of training to enhance DoD infectious disease surveillance. A prototype of such a conference was the one-week 1997 WRAIR-CHPPM sponsored Army Preventive Medicine Symposium entitled "Surveillance: The Key to Public Health Practice."

Activity iii

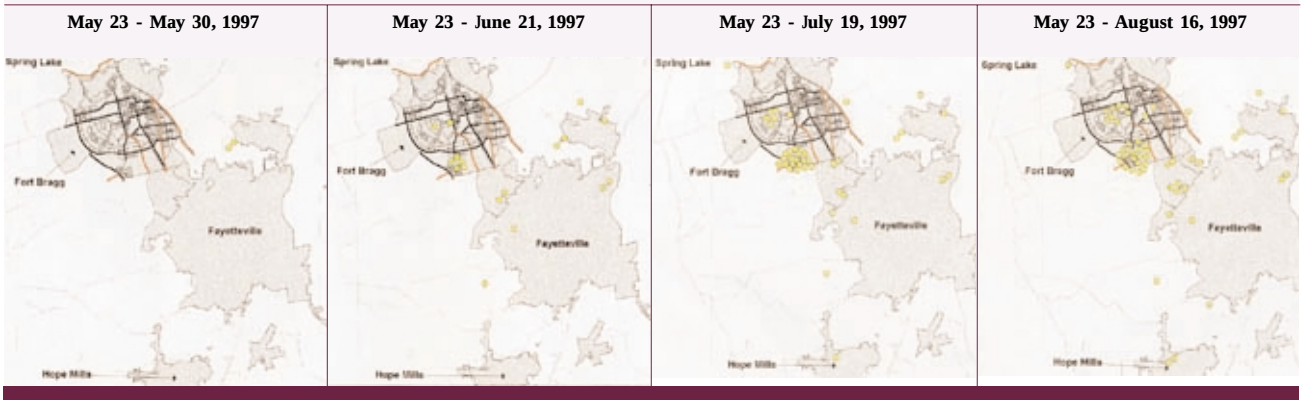
Ensure that DoD surveillance systems complement and support local, regional, national, and international surveillance efforts.

Since 1976 the Air Force has operated a sentinel influenza surveillance network known as Project Gargle. This network has served not only the needs of the Air Force but has also contributed on a global scale to the tracking of emerging flu strains. For example, the Wuhan strain of influenza that was incorporated in 1996–1997 into the WHO-recommended composition of influenza vaccine strains was first isolated outside of China through Project Gargle. Unfortunately the Army's efforts in respiratory virus surveillance were greatly curtailed several years ago with closure of the Letterman Army Institute of Research and the termination of an established contract with the University of Colorado.

Since 1947 one of the best organized international emerging infections surveillance efforts has been in the area of influenza surveillance, yet some major nations contribute few or no isolates to this critical monitoring network. Because the rapid spread of a virulent influenza pandemic is probably the most worrisome naturally occurring military infectious disease threat, a focused surveillance effort is indicated to ensure that emerging strains are detected

Application of a Geographic Information System

Progression of a 1997 outbreak of *Shigella sonnei* among military health care beneficiaries at Fort Bragg, North Carolina. This geographic information system application allowed for identification and real-time tracking of outbreak clusters (*yellow dots*) at Fort Bragg and in the surrounding civilian community and facilitated targeted interventions to control further spread of disease. Geographic information system applications could become invaluable in understanding outbreaks caused by emerging infectious agents, including those spread by terrorists.



Courtesy of Kelly T. McKee, Preventive Medicine, Fort Bragg, North Carolina.

early. The 1997 avian influenza outbreak in Hong Kong, although only affecting 18 persons, indicated through the 33% case-fatality rate that even sophisticated health care systems can be challenged when a pathogenic strain emerges. Months are generally required to produce an influenza vaccine, and the influenza virus has the capacity to develop resistance to the usually employed antiviral drug, amantidine.

The CDC influenza branch has recognized that DoD can make a unique contribution in the area of influenza surveillance. It is the objective of DoD-GEIS to better define the needs of the services with respect to respiratory virus surveillance, define a program of etiologic and population-based surveillance for these viruses in DoD populations, and build capacity within DoD to execute such a plan. The DoD overseas labs will initiate or contribute to surveillance in their regions by establishing sentinel influenza networks when possible. A particular effort will be made to unite selected foreign military health care establishments in the Asia-Pacific region into such a network. Influenza viruses often first emerge in Asia for ecologic reasons. Monitoring military populations is logical and desirable because they have been historically important in past emergences, because military barracks facilitate transmission, and because military health care systems facilitate standardized protocols and capture of incidence data.

The forwarding of isolates of selected infectious agents to appropriate DoD or contract labs for public health purposes will be fostered. For example, for many years isolates from all Army beneficiaries infected with *Neisseria meningitides* were forwarded to the Department of Bacterial Diseases at WRAIR for grouping and typing. This program unfortunately dissolved over time. The characterization of isolates of various bacteria, although not necessarily needed for the treatment of individuals, is valuable from a public health perspective to identify epidemics, transmission patterns, and other information needed for control.

The CISET subcommittee on quarantine and containment stated in its recommendations that surveillance data on military populations should be exchanged with relevant state health authorities to ensure that disease importations are properly managed not only within the DoD but also with respect to affected civilian populations. DoD reporting systems must be evaluated to ensure that necessary information is exchanged with other health agencies.

DoD Proposed List of Reportable Infectious Diseases, 1998

- Amebiasis
- Anthrax
- Biological warfare agent exposure
- Botulism
- Brucellosis
- *Campylobacter* infection
- *Chlamydia trachomatis*, genital infections
- Cholera
- Coccidioidomycosis
- Cryptosporidiosis
- *Cyclospora* infection
- Dengue
- Diphtheria
- Ehrlichiosis
- Encephalitis
- *Escherichia coli* O157:H7
- Fever
  - Acute
  - Hemorrhagic
  - Q
  - Relapsing
  - Rheumatic
  - Rift Valley
  - Rocky Mountain spotted
  - Typhoid
  - Yellow
- Filariasis
- Giardiasis
- Gonorrhea
- *Haemophilus influenza* (invasive disease)
- Hantavirus disease
- Hepatitis A, B (acute), and C (acute)
- Influenza
- Legionellosis
- Leishmaniasis
- Leprosy
- Leptospirosis
- Listeriosis
- Lyme disease
- Malaria (all)
- Measles
- Meningococcal disease
- Mumps
- Pertussis
- Plague
- Pneumococcal pneumonia
- Poliomyelitis
- Rabies (human)
- Rubella
- Salmonellosis
- Schistosomiasis
- Shigellosis
- Smallpox
- Streptococcus (group A, invasive)
- Syphilis
- Tetanus
- Toxic shock syndrome
- Trichinosis
- Trypanosomiasis
- Tuberculosis (pulmonary)
- Tularemia
- Typhus
- Urethritis (nongonococcal)
- Varicella

Activity iv

Assess and apply innovative tools (eg, communications technology and geographic information systems) to facilitate collection, analysis, and dissemination of information and to improve disease-reporting mechanisms.

The Internet, the CHCS, and global imaging systems are all underexploited resources that can enhance the capability to conduct emerging infections surveillance and response. The Internet provides timely access to information on many emerging infections through systems such as ProMed and the WHO outbreak rumor list. Many other agencies disseminate information that is relevant to DoD disease control efforts. Global imaging systems are now allowing disease prediction models to be developed.

This may help assess the temporal risk of militarily relevant conditions such as malaria, coccidioidomycosis, Hantavirus infection, and adenovirus infection. Capture of these images and their association with validated, user-friendly models should eventually allow better threat assessments.

Objective I-B

Help develop more effective international surveillance networks for the anticipation, recognition, control, and prevention of emerging infectious diseases.

As noted in the CDC's *Addressing Emerging Infectious Disease Threats* (CDC 1998a), practical mechanisms for the early detection of emerging infections that arise in many international settings are rudimentary and limited to a few specific diseases. As a result emerging infections can, before effective recognition, spread to such an extent that they are difficult to contain or control. Effective means are needed both to identify these infections and to generate public health responses. Public health infrastructure and levels of expertise vary widely among countries, especially in the underdeveloped world. It will only be through multilateral cooperation that an effective system of international surveillance and response can be achieved.

The DoD is key for several reasons. First, in much of the developing world, the best clinical laboratories are those found in military health care facilities. The WHO has recognized this and is placing a clear focus on working with many national defense medical labs to build a network for emerging infections surveillance. It is natural that the DoD, as the

DoD Medical Research Units

most sophisticated military medical establishment in the world, should lead among the nations participating in this military surveillance network. Second, the DoD network of six tropical overseas medical research units is unique. They are important epidemiologic assets to not only the six host nations in which they are located but also to all the 31 nations in which they work. They provide state-of-the-art laboratory, epidemiologic, and clinical consultation and training in underdeveloped localities where recognition of emerging infections should not be delayed. These labs are commonly seen by their host nations as important collaborators in addressing unusual health events in their region. As a result of these activities both formal and informal surveillance networks are created.

Activity i

Establish mechanisms for timely and systematic exchange of information and laboratory specimens among public health agencies of different countries, the CDC, WHO, and DoD.

The DoD 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. Initial efforts along these lines have included a project supported by Atlantic Command (ACOM) and Southern Command (SOUTHCOM) to establish a network of medical surveillance in the Caribbean. During 1997-1998, using approximately $350,000 of humanitarian assistance funding from ACOM and SOUTHCOM, DoD-GEIS donated 71 desktop computer systems to 15 Caribbean nations for use in developing a public health surveillance network linked via the Internet with PAHO's Caribbean Epidemiology Centre (CAREC). In addition DoD-GEIS personnel trained approximately 160 public health personnel from these countries to use this equipment and standardized surveillance software developed by the CDC. With DoD support, CAREC is developing a web site for acquisition of data from member states and for dissemination of surveillance results.

Surveillance Modules Being Implemented at DoD Overseas Medical Research Units

- Antibiotic-resistant diarrhea
- Drug-resistant malaria
- Influenza
- Hemorrhagic fevers including dengue

DoD Partners in Global Surveillance

- US Department of State
- Other federal agencies: CDC, NIH, USAID, NASA, FDA, USDA, NOAA
- International agencies: WHO, UNAIDS, PAHO, CAREC
- Ministries of health
- Public and private universities
- Industry

Future plans include proliferating this model of hierarchical, standardized, Internet-facilitated surveillance focused on centralized reporting sites to other areas of the world. DoD will continue to work with CDC and WHO to facilitate the adoption of compatible surveillance formats and standardized means of electronic data reporting. DoD will also undertake projects to improve the laboratory capabilities of overseas partners by improving their capacities to make specific bacteriologic, virologic, and serologic diagnoses. DoD has a natural role in this arena because it leads in the development and testing of simple yet high quality field diagnostics that can be used effectively in underdeveloped nations. In light of readiness requirements, the DoD policy of "engagement," and the Doctrine of Preventive Defense, such activities are also consistent with the assistance activities supported by each regional commander-in-chief.

Activity ii

Enhance the surveillance activities of DoD/host nation laboratory activities for influenza, drug-resistant enteric organisms, drug-resistant malaria, and febrile illnesses, including dengue.

Because emerging infections will often appear first in non-DoD overseas populations and because the President explicitly saw DoD-GEIS as contributing on an international scale, the six DoD tropical overseas medical research units have been given explicit surveillance responsibilities. These labs employ nearly 700 persons and are based in Thailand, Indonesia, Kenya, Egypt, Brazil, and Peru and operate in more than 30 countries overall. These labs are usually located alongside medical agencies of the host country. Their role in emerging infections surveillance is clearly aligned with the second major objective of the presidential directive: to establish a global communications network built around regional hubs. No other US agency has a comparable network of multidisciplinary overseas medical research units. Each lab will, within resource constraints, establish coordinated regional sentinel surveillance programs for influenza, drug-resistant malaria, drug-resistant enteric organisms, and hemorrhagic fevers including dengue. These efforts will be guided by standard DoD protocols as much as possible.

Historically the most recurrent serious infectious disease threats to US military operational effectiveness have been malaria and enteric infections. These infections are also the major threats to civilian health in much of the developing world. The inexorable rise of drug resistance heightens this threat, especially as the number of effective drugs for prophylaxis and treatment decreases. Febrile illnesses including dengue have always been important, and hundreds of these illnesses occurred in association with recent deployments to Somalia and Haiti.

Influenza is often dismissed as a self-limited, easily controlled infection, but this sweeping characterization is a delusion. This is partly because its most severe epidemiologic manifestations are sporadic and difficult to predict. No single naturally occurring infection poses more of a military threat than influenza. More than 43,000 US service personnel died of the flu in 1918–1919. Furthermore, the fatality rate was more than 80% for the 17- to 60-year-olds who developed the Hong Kong avian influenza in 1997 (CDC 1998b).

DoD Influenza Surveillance

Worldwide surveillance for influenza is vital to avoid pandemics such as that which occurred in 1918–1919. One-fifth of the world's population was infected, resulting in 20 million deaths including 550,000 in the United States.

DoD resources are well-positioned to augment the existing WHO global influenza surveillance network. This network includes approximately 110 collaborating laboratories in 80 countries with central coordinating laboratories in Australia, Japan, the United Kingdom, and the United States. Because active duty military personnel receive annual influenza vaccinations, surveillance for influenza in this population is a unique and valuable means to monitor vaccine effectiveness and to detect newly emerging strains. In addition, the isolation and identification of influenza among family members in the United States and overseas provide useful information about locally circulating influenza viruses.

For more than 20 years, the US Air Force's Project Gargle has used this model to conduct laboratory-based influenza surveillance at many of its air bases throughout the world. Data from Project Gargle have helped determine the components of the upcoming year's influenza vaccine. Under DoD-GEIS all services will be joining Project Gargle.

A unique asset of the DoD is its six overseas medical research laboratories. In fact, the US Army Medical Component-Armed Forces Research Institute for Medical Sciences located in Bangkok, Thailand, joined with a clinic serving expatriates in Kathmandu to initiate influenza surveillance in Nepal in 1997. Plans are soon to be implemented to include local military and nonmilitary Nepalese in influenza surveillance activities. Collaborations between the DoD and other militaries in Asia offer additional opportunities to augment the WHO global influenza surveillance network.

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DoD Influenza Surveillance – *continued*

Worldwide influenza surveillance sites for Project Gargle, US Air Force (1997–1998). At the start of the 1997–1998 influenza season the US Air Force was the only service conducting laboratory-based influenza surveillance. Project Gargle was initiated in 1976 to survey Air Force active duty members and other beneficiaries at selected sites worldwide. Modeled after Project Gargle, the DoD global laboratory-based influenza surveillance effort will sample members from all military services, other beneficiaries, and foreign nationals in collaboration with DoD overseas research units.

The hope is that these programs will become model sentinel surveillance efforts that can be expanded and cloned by partners so more of the world's population can be placed under effective public health surveillance. It is believed that as infrastructure and expertise are built to deal with highly defined core surveillance programs, the capacity to confront less defined newly emerging infections will incidentally grow.

Activity iii

Actively support and participate in an international global consortium of closely linked epidemiology/biomedical research programs/centers to promote the detection, monitoring, and investigation of emerging infections.

Because of the global scope of emerging infections and the limited capabilities of any organization, the only realistic means to address this challenge is through effective, well coordinated partnerships. A global consortium has been proposed that would involve existing CDC and WHO programs and surveillance systems plus other international research and public health agencies.

DoD-GEIS is an important member of this consortium because of its historic leadership in infectious disease control and its unique assets. According to the CDC the following areas of expertise are critical to this consortium: epidemiology, clinical and veterinary sciences, field ecology, behavioral science, laboratory microbiology, and related disciplines. DoD already has thousands of scientists and other

Influenza Pandemic of 1918–1919

As World War I labored to a close, a new and deadly influenza virus attacked humans in the trenches and around the globe with violent swiftness. Civilian and military casualties from influenza were 20 to 49 million in less than one year; these numbers are more than twice the number of fatalities during the whole four years of World War I.

The 1918 influenza was unlike any flu seen since or before. It worked brutally, and rather than affecting only the infirm, children, or the aged, it killed young, fit adults. Patients presented with purple blisters on the skin and barely able to breathe through hacking gasps. Within 11 hours of the first symptoms, they would die. An Army doctor at Fort Devens, Massachusetts, describes conditions at the base hospital in a letter to a colleague dated September 29, 1918:

> These men start with what appears to be an ordinary attack of La Grippe or Influenza, and when brought to the Hosp. they very rapidly develop the most viscous type of Pneumonia that has ever been seen. Two hours after admission they have the Mahogany spots over the cheek bones, and a few hours later you can begin to see the Cyanosis extending from their ears and spreading all over the face. . . . It is only a matter of a few hours then until death comes, and it is simply a struggle for air until they suffocate. It is horrible . . . . We have been averaging about 100 deaths per day, and still keeping it up. There is no doubt in my mind that there is a new mixed infection here but what I don't [sic] know. . . (Stanford University 1998)

Influenza killed more than 43,000 US military personnel; in the US Army nearly 80% of the war casualties during World War I were caused by influenza.

Military and Political Consequences

Germany's General Erich von Ludendorff wrote, "It was a grievous business to listen every morning to the Chief of Staff's recital of the number of influenza cases and their complaints about the weakness of their troops." Ludendorff noted that in June 1918 more than 2000 men in each division had influenza and "blamed the failure of his July offensive, which came so close to winning the war for Germany, on the poor morale and diminished strength of his armies, which he attributed in part to flu" (Crosby 1976).

Similarly, some historians blame President Woodrow Wilson's ineffective negotiating at the Treaty of Versailles on the influenza he contracted in Paris in 1919.

Modern Analysis

Organs of flu victims preserved by Army doctors in 1918 have provided modern researchers with samples of the actual virus. Specimens from the lungs of one Army private were used by the Armed Forces Institute of Pathology to establish in 1997 that the virus originated in American pigs. Nine fragments of viral RNA were sequenced and are consistent with a novel H1N1 influenza A virus that belongs to the subgroup of strains that infect humans and swine (not the avian subgroup).

The influenza emerged in US military camps, spread to the European battlefields, and swept around the world. Total mortality is unknown because much of the world's population (especially Asia and Africa) was not tracked. Some 20 million deaths were reported worldwide. According to Stanford University, 20% of the entire world's population was infected, and in the United States one of every four persons was infected.

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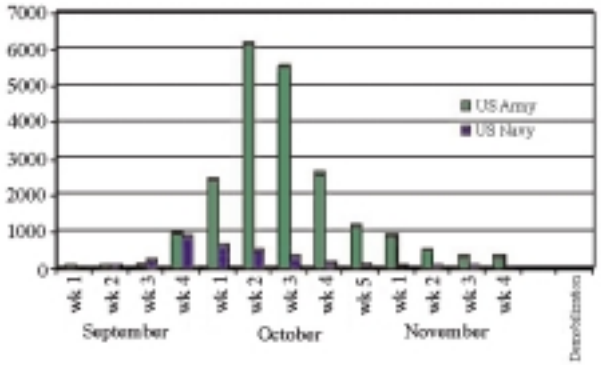
Influenza Pandemic of 1918-1919 – *continued*



US Army and Navy deaths caused by influenza and pneumonia: fall 1918. Values are shown for each week from September to November.

health professionals with expertise in these areas distributed around the globe. DoD-GEIS is well-positioned to leverage this experience by training and supporting local and regional scientists and public health officials and assisting in responding to emerging infections problems as they arise. Such training would also help recognition of and response to biological warfare/terrorism. DoD could also arrange laboratory and epidemiology back-up in collaboration with other consortium partners.

Objective I-C

Improve surveillance for rapid laboratory identification of antimicrobial resistance.

Antimicrobial resistance is a growing problem that will likely evade a permanent solution until a highly effective vaccine is in place for every infection. Many antibiotics are becoming ineffective, and some malaria and tuberculosis infections are becoming almost untreatable. To slow the development of resistance will require a strong international effort, especially because lax antibiotic usage patterns in one geographic area can foster the emergence of resistant strains that then can spread globally. Travelers, including military personnel, have brought back to the United States drug-resistant enteric organisms including *Salmonella typhi* and *Shigella*. Clearly a parochial approach to these issues is insufficient.

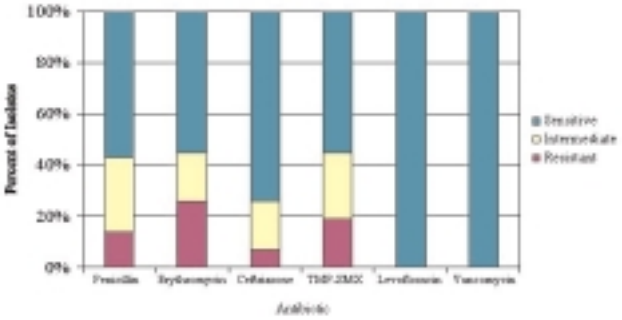
Activity i

Monitor trends in antimicrobial resistance patterns associated with both hospital and community acquired infections in the DoD population of active duty members and other beneficiaries.

DoD health care facilities provide care for a population that is particularly important for antibiotic resistance surveillance because our personnel travel extensively to overseas areas where antimicrobial resistance is a great problem. To know how to effectively treat service members, it is useful to understand resistance patterns where the infection was acquired, not necessarily where it is ultimately diagnosed. A highly deployable force necessitates an appreciation for what constitutes appropriate antibiotic treatment not only at home but also abroad in areas where we deploy or may deploy. A wound infection acquired in the Middle East, a sexually transmitted disease acquired in southeast Asia, and pneumonia acquired in Central America may all be due to organisms with different antibiotic resistance patterns than those acquired in the continental United States.

DoD-GEIS plans to facilitate the acquisition of standardized antibiotic resistance data from DoD medical treatment facilities both CONUS and OCONUS where troop disembarkation is common.

Antibiotic Resistance of *Streptococcus pneumoniae* Isolates Infecting US Military Health Care Beneficiaries



Between October 1997 and March 1998, 42 isolates were collected. TMP-SMX, trimethoprim-sulfamethoxazole.

Courtesy of Naval Health Research Center, San Diego, California.

HIV Surveillance in the Military

The US military HIV surveillance program was instituted in 1985. Its mandate is to track prevalence and incidence of HIV infection in the various components of the DoD services (eg, active duty, reserves, National Guard, and military entrance processing station populations).

Through routine HIV testing of active duty personnel, the incidence of new infections has been closely monitored. From 1985 to 1997, 1160 new cases of HIV-1 infection have been reported among previously negative active duty Army personnel. From 1990 to 1997, new cases in the Navy, Air Force, and Marine Corps have numbered 1139, 343, and 246, respectively. Over the 12 years, the rate of new infections occurring in the Army is 0.2 new cases per 1000 person-years of follow-up. Although relatively stable for the past seven years, this rate continues to represent approximately 70–100 new cases of HIV-1 infection in the Army annually.

DoD's involvement in worldwide HIV surveillance has led to increased activities concerned with detection and characterization of HIV genetic subtypes and deployment-related HIV exposure and transmission. This work also supports development of preventive HIV-1 vaccines. The advancement of laboratory techniques in molecular biology has enabled researchers to study the emergence of primate lentiviruses such as HIV-1, HIV-2, and SIV with unprecedented clarity.

Despite uncertainties surrounding the emergence of HIV-1, it is a global pandemic. Given the difficulties in tracking the global epidemiology of HIV-1, researchers are using molecular biological techniques to track the spread of genetic variants or subtypes and to trace the sources of new epidemics. For example, the prevailing assumption early during the HIV epidemic in Thailand was that there was one emergence of HIV-1 among injecting drug users that then spread to commercial sex workers. Molecular methods have shown that two parallel emergences of HIV-1 occurred in Thailand in the middle to late 1980s, resulting in the epidemic currently raging there.

The US Military HIV Research Program conducts ongoing surveillance of genetic subtypes of HIV-1 throughout the world, particularly in regions where the military may deploy.

The rapid detection of emerging viral subtypes is essential in the characterization of risk to US military personnel around the world as well as in the development of global HIV-1 vaccines.

Courtesy of P. Renzullo, Division of Retrovirology, Walter Reed Army Institute of Research, Washington, DC; J. Carr and F. McCutchan, Henry M. Jackson Foundation for the Advancement of Military Medicine, Rockville, Maryland.

Eventually all DoD facilities should participate in standardized antibiotic resistance monitoring and rapid reporting. DoD overseas labs can contribute significantly by monitoring antibiotic resistance in their regions and by facilitating efforts of local partners. Industrial partners can also help improve DoD access to global and domestic antibiotic resistance data necessary for patient care, policy development, and pharmacology research. These findings will be accessible through the DoD-GEIS web site to facilitate their use for patient care, clinical planning, policy development, and prioritizing vaccine development efforts. They will also be shared and combined with the findings of appropriate partners such as WHO, CDC, and industry.

Activity ii

Evaluate tools and systems for reliable and rapid detection and reporting of antimicrobial resistance and develop new tools where needed.

The development of rapid screening procedures for antimicrobial resistance is being emphasized so that the spread of resistant infections and associated morbidity and mortality can be limited. DoD overseas researchers are often in a unique position to validate diagnostics of this type because of their location and because the quality of DoD overseas labs permits both experimental and "gold standard" methodologies to be employed.

Activity iii

Determine risk factors for the introduction of resistant microbes into the global network of US military medical facilities.

Because of the exigencies of combat casualty care and the routine air evacuation of critically ill DoD health care beneficiaries, the CONUS-based DoD health care system may be particularly vulnerable to nosocomial spread from wound infections and overseas hospital-acquired infections from agents that are uncommon in the United States. Risk factor analyses through appropriately designed epidemiologic studies are indicated to better characterize this risk and motivate appropriate interventions.

Objective I-D

Strengthen and integrate programs to monitor and prevent emerging infections associated with food, water, new technology, and environmental resources.

Military service frequently brings about exposure to locally procured foods, specially processed and handled foods, potentially contaminated water sources, and exposure to desert, tropical, aquatic, or other environments under less than desirable conditions. This can lead to infections such as shigellosis, campylobacteriosis, legionellosis, coccidioidomycosis, and histoplasmosis. Unfortunately, a growing worry is the threat of unnaturally occurring infections owing to bioterrorism.

Activity i

Assess military food procurement policies and militarily unique food processing and water treatment modalities that may promote infectious disease emergence.

Despite considerable DoD resources in the areas of food procurement and water treatment, outbreaks still occur. The ability to rapidly and reliably detect microbial contamination of food and water is less than optimal. Policies should be reviewed, behavioral and other impediments to hygiene and other risk factors studied, and the current technology for determining food and water safety assessed.

Some Possible Bioterrorism Agents

Many bacteria, viruses, and toxins that have been identified as potential biological warfare agents can also be used for bioterrorism. Those mentioned traditionally include *Bacillus anthracis*, *Yersinia pestis*, Venezuelan equine encephalomyelitis virus, botulin toxin, staphylococcal enterotoxin B, and Ricin. In addition, many other agents can be adapted for this purpose.

Bacteria

- *Bacillus anthracis* (anthrax)
- *Vibrio cholerai* (cholera)
- *Yersinia pestis* (plague)
- *Francisella tularensis* (tularemia)
- *Coxiella burnetii* (Q fever)

Viruses

- Variola (smallpox)
- Venezuelan equine encephalomyelitis virus
- Hemorrhagic fever viruses (eg, Ebola)

Toxins

- Botulin
- Staphylococcal enterotoxin B
- Ricin
- T-2 mycotoxins

Activity ii

Identify environmental sources of infection, develop means for assessing and communicating risk, and formulate effective control measures.

Organisms that reside in the environment are a particular hazard to military personnel. Some of these risks are easier to anticipate than others. Some seem to be associated with climatic phenomena such as El Niño. For example, the 1998 outbreak of Rift Valley fever in East Africa seems to

have been directly related to unseasonally heavy rains in that area associated with El Niño. Satellite imaging techniques can easily show the effect of this climatological phenomena on the regional ecology. Similarly remote sensing data seem to suggest that cholera outbreaks can be correlated with changes in ocean color, which reflects the growth of certain organisms.

The careful correlation of remotely sensed meteorologic events with disease incidence may help predict episodes such as militarily relevant outbreaks of respiratory infections in basic training camps, coccidioidomycosis at Fort Irwin, malaria in Korea, Hantavirus in the US Southwest, and dengue in the Caribbean. The development of predictive models can help strengthen the hand of commanders by improving the accuracy of infectious disease threat assessments. Because infectious disease risk is dynamic and varies in a given location over time, factors that vary temporally must be appreciated in assessing a threat. Surveillance data obtained or generated by DoD-GEIS should be shared with partners from NASA and the National Oceanic and Atmospheric Administration to develop valid models of this type. For some localities around the world DoD scientists are in the best position to collect or validate the accuracy of available disease incidence data.

Objective I-E

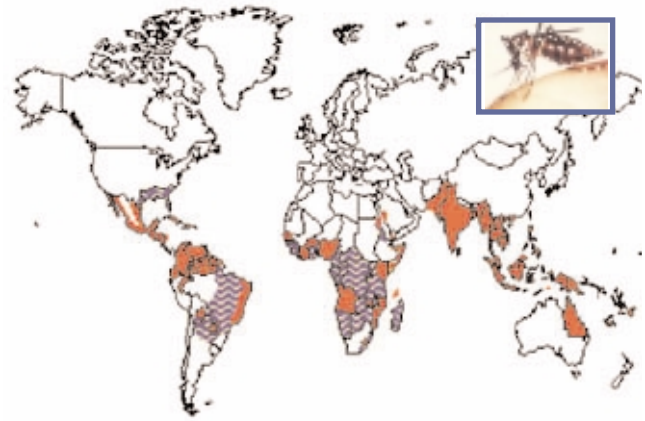
Strengthen and integrate programs to monitor, control, and prevent emerging vector-borne and zoonotic diseases.

Several newly recognized militarily relevant emerging infections have been associated with rodents and insects. These include Lyme disease, human ehrlichiosis, Hantavirus pulmonary syndrome, various hemorrhagic fevers, Rift Valley fever in East Africa, and malaria along the Korean demilitarized zone.

Activity

Monitor the distribution of animal reservoirs and vectors associated with human disease in areas of military importance and use these data to develop predictive models.

World Distribution of Mosquitoes Capable of Transmitting Dengue, 1997



Blue,* areas infested with *Aedes aegypti*; *red,* areas with *Aedes aegypti* and dengue epidemic activity. *Inset, Aedes aegypti.

Courtesy of Division of Vector-Borne Infectious Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado.

Effective programs to monitor animal reservoirs and arthropod vectors of emerging infections are limited. These infections are well-recognized threats to US forces on virtually every overseas deployment, even to temperate climates such as those found in Bosnia and Korea. Effective disease control requires integrated multidisciplinary programs led by experts in the complex ecologic settings into which our forces are sent. Remote sensing research already involving DoD personnel may extend our ability to anticipate how environmental and climatic changes can affect human risk. This may help not only with readiness but by averting destabilizing political and human crises associated with poor harvests, low animal survival, and certain human epidemics such as mosquito-borne forms of encephalitis.

Goal II: Systems Research, Development, and Integration

Integrate public health practices and improve capabilities in clinical medicine, military medicine, laboratory science, epidemiology, public health, and military medical research to facilitate rapid identification and response to emerging infections.

Objective II-A

Develop the information management tools for clinicians, laboratorians, pathologists, epidemiologists, and preventive medicine/public health practitioners to address the unique aspects and concepts of emerging infectious disease detection and prevention.

Traditional clinical practice is focused on the individual patient, but emerging infections have clearly underscored the necessity of a "big picture" public health focus. The threat of weaponized infectious agents further highlights the need for a population-based component to disease control that goes well beyond determining the best therapy for a particular patient. Information must be disseminated that will allow the public, the health care system, and governmental agencies to detect emerging infections as early as possible, respond to them at the individual, community, national, and global level, and prevent them in the future.

Activity i

Establish and maintain effective communication and coordination and a means for sharing data and information.

DoD-GEIS recognizes the wide range of information that must be disseminated to a wide range of customers to facilitate an effective global surveillance and response system. An effective system is a timely system, and a timely system means that consciousness of the issue of emerging infections must be high in the minds of those who may encounter these problems early. DoD-GEIS plans to work toward this global system through not only internal DoD activities but also by providing leadership at the national and international levels.

Some communication modalities planned include the DoD-GEIS web site that will provide information about surveillance findings, response capabilities, training programs, and relevant research. The web site will also facilitate Internet-networked communications with internal DoD partners, DoD executives, DoD health care providers, the general public, and other legitimate external collaborators. In addition DoD-GEIS will publish an emerging infections newsletter to regularly raise the consciousness of DoD health care personnel to emerging infections issues. A newsletter is necessary because a web site will not regularly attract all who must know about this issue. DoD personnel will be supported to participate in national and international scientific and policy forums relating to emerging infections.

Activity ii

Assess current electronic data systems and links and foster enhancements or develop and implement new systems and links.

Medical informatics is a rapidly growing field. Unfortunately the functional requirements for medical informatics systems often reflect almost exclusively managed care and individual patient care needs, making the vast amounts of information relatively inaccessible or inappropriate for public health surveillance purposes. As the DoD's medical informatics systems migrate and improve, opportunities arise for incorporating the functionality necessary to support emerging infections surveillance. DoD-GEIS plans to help identify those capabilities (eg, the need for laboratory-based surveillance) that should be incorporated into system upgrades.

The DoD overseas medical research units pose a different challenge. Because of their role primarily as model surveillance platforms and training sites focusing on non-DoD beneficiary populations, their medical informatics needs are somewhat separate. DoD-GEIS is already leading the implementation at the DoD overseas labs of a customized version of the CDC's Laboratory Information Tracking System (LITS). Among other features this implementation will foster the standardized collection of surveillance data on specimens processed by the labs. It will also facilitate the archiving of specimens so that they can be easily retrieved years in the future for retrospective studies to address certain emergence-related issues. Another CDC software program, the Public Health Laboratory Information System (PHLIS), is also being studied for the hierarchical reporting of surveillance data. This program, which now links the 50 states with the CDC, is being implemented

successfully in DoD sponsored surveillance training programs. DoD-GEIS plans to collaborate with CISET and the WHO to try to advance development of a global surveillance software standard to ensure compatibility as many systems develop simultaneously.

Activity iii

Evaluate the effectiveness and economic benefit of existing and proposed strategies to detect and prevent emerging infections.

Prevention strategies, even if once proven effective, must be continuously revisited, especially in the military, where readiness depends on an assessment of the threats of today and tomorrow, not yesterday. Antibiotic resistance is constantly emerging in bacteria that infect our forces. Malaria resistance is likewise dynamic and seems to occur faster than prophylactic drugs can be developed. Even annual updates of the influenza vaccine are in some years insufficient to contain a rapidly spreading new strain. For example, in 1998 the influenza A Sydney strain caused military epidemics because the trivalent vaccine designed in early 1997 did not cover that virus.

Clearly ongoing comprehensive surveillance is necessary to monitor the effectiveness of existing DoD disease control and treatment policies. Because of economic trends, the fiscal implications of prevention decisions are more significant than they were in some cases in the past. For example, to replace the DoD's ability to procure adenovirus vaccines, an up-front commitment of at least $10 million may be necessary. The ability to balance the cost of preventive interventions against the cost of disease must be well established because delays in acquiring this information may lead to costly morbidity and reductions in readiness.

Activity iv

Enhance public health partnerships among the Joint Staff, the Joint Commands, and the three services and among the DoD and Department of State , WHO, CDC, health departments, academic centers, and community groups.

The role of the military epidemiologist and public health professional is growing, and many needs are not filled.

New Tick Typhus in Botswana

New infectious diseases are sometimes first recognized in military personnel. Military medical authorities are often the first to detect an unexpected number of previously healthy individuals becoming ill at the same time and/or place. Investigations commence to identify the cause so that preventive measures can be initiated to prevent more casualties. Sometimes unknown or poorly described pathogens are discovered. Historical examples are the outbreaks of scrub typhus in World War II and Korean hemorrhagic fever during the Korean War. The modern warrior is not exempt from this phenomenon.

Physical examination of soldier who has tick typhus (rash on abdomen).

In 1992 after a 2-week training exercise in Botswana, over 30% of the 169 deployed soldiers sought medical attention. Symptoms included fever, headaches, regional lymphadenitis, and skin lesions. Military medical epidemiologists and scientists found that 23% of the soldiers had been infected by a spotted fever *Rickettsia* transmitted by ticks. The likely causal agent, *Rickettsia africae*, has been proposed as a new species.

The outbreak established the potential of this infectious agent to infect many soldiers in a short time when deployed to Africa and reinforced the need for preventive measures to protect against diseases that are transmitted by arthropods.

Courtesy of Bonnie Smoak, United States Army Medical Research Unit—Kenya.

To build the type of partnership network needed for global emerging infections surveillance (and to meet many other military public health needs), a significant growth in relevant military specialties to include preventive medicine, infectious disease, entomology, public health laboratory medicine, veterinary public health, and information management is needed. With such assets it will be possible to move toward a proactive approach to the threats of naturally and unnaturally occurring emerging infections. Training positions must be increased to fill the gaps between what is on the personnel rosters and the well-recognized need for more military personnel with epidemiologic and public health expertise.

Objective II-B

Improve laboratory infrastructure for rapid identification of new pathogens and syndromes.

Activity i

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

The public health laboratory is an essential dimension of any infectious disease surveillance and response program. DoD currently lacks an organized public health laboratory that can address the unique issues that go beyond what is needed to guide individual patient care. Many relevant techniques are grouped under the heading of molecular epidemiology. These techniques often have as their objective characterizing strains of viruses and bacteria to detect outbreak-related patterns or unusual virulence patterns. A laboratory that did not provide or arrange services of this sort could, for example, miss small-scale bioterrorist experiments if epidemiologically significant but clinically less relevant strain patterns were not detected.

It is probably not necessary for DoD to have a single public health lab with a capability comparable with one of the better state labs. The necessary capabilities can be patched together from various DoD clinical and research laboratories and through partnerships with CDC and high quality state labs. What is necessary is a "virtual" public health laboratory

Clinical versus Public Health Laboratories

Clinical microbiology laboratories at military medical facilities directly support primary health care providers in the diagnosis and management of infectious diseases. This is accomplished by agent isolation and identification, serologic tests, and determinations of antibiotic sensitivities. Clinical microbiology laboratories are designed to deal with the microorganisms reasonably expected to occur in the patients supported by the laboratory. Therefore they possess no resources to handle unusual pathogens. Additionally, clinical laboratories generally use algorithms or standard procedures in processing specimens and have limited capabilities for conducting exploratory bench work in the event an organism cannot be definitively identified or even isolated. Clinical laboratories also plan for workloads based on the routine inpatient and outpatient census.

Military clinical laboratories will be funded on a capitation basis. This will likely result in little flexibility to pursue unknowns or to deviate from established work practices for other reasons. Clinical laboratories usually cannot support an epidemiological investigation because of the volume of specimens collected and/or nonavailability of the needed tests. Historically, these limitations of clinical microbiology laboratories in the United States were the reasons why a public health laboratory system was maintained.

In the civilian sector this system consisted of many robust state health laboratories and the CDC, both of which contained great depth and breadth in microbiological capabilities. Within the US military, public health laboratory functions were performed by the 406th Medical Laboratory (Camp Zama, Japan), the 10th Medical Laboratory (Landstuhl, Germany), other service laboratories, and medical research and development laboratories that were permitted the latitude and flexibility to perform both research and public health service.

Clinical versus Public Health Laboratories – *continued*

With the eradication of smallpox and impressive control of other infectious diseases (eg, tuberculosis) an attitude developed in the US medical community in the 1970s that all infectious diseases had been or were nearly eliminated. With a marked shift in focus toward cutting costs and maintaining only core laboratory competency in the clinical medicine community and a shift from infectious diseases to health promotion and protection from environmental chemical hazards in the public health community, the civilian and military systems were reduced in numbers of laboratories and services available.

Features of a Public Health Laboratory

Broad Capabilities

- Performs unusual tests unavailable in clinical labs
- Is part of a larger system of public health and academic laboratories
- Acts as a referral and reference laboratory and is supported by more sophisticated labs in the larger system
- Stays abreast of state-of-the-art tests
- Understands molecular epidemiology and is sensitive to the needs of physicians doing outbreak investigation and population medicine
- Archives unknown and unusual specimens for later study
- Is closely linked with epidemiologists responsible for surveillance

Flexibility

- Has protocols and procedures for the systematic evaluation of unknowns but also has the resources to deviate from protocols
- Is innovative and can developmentally test new procedures or create special procedures
- Can adjust resources quickly to support public health threats

Objectives of the DoD Public Health Laboratory Initiative

- Identify and describe public health laboratory capabilities within DoD and available to DoD personnel
- Produce a DoD directory that defines public health laboratory services currently within DoD or available to DoD personnel and describe access to these services
- Develop a concept of a DoD public health laboratory system that will result in maximum benefit from available resources with no or minimal duplication of effort
- Identify needed improvements with priorities to guide the distribution of funds
- Construct algorithms so that important specimens may be expeditiously processed and sent to reference or support laboratories
- Develop a plan for data capture management, analysis, and dissemination.

system that catalogues the capabilities of DoD and partner labs and facilitates the testing and tracking of specimens referred to those labs. A central coordination point for lab data of public health relevance is also desirable and should be an objective of DoD-GEIS. Such a central focal point would facilitate recognition of patterns indicative of emerging infections and thus facilitate a timely response.

Activity ii

Identify requirements for new or improved laboratory capabilities to improve detection and epidemiologic evaluation of emerging infections.

DoD has a well established program for the development of rapid diagnostic assays to support troops in the field. This program needs active support to ensure that all appropriate techniques for rapid diagnosis can be brought to bear and that a wider range of agents is covered.

Another requirement is continuing to organize and catalogue the DoD's vast collections of biological specimens at the overseas medical research labs, at the Armed Forces Institute of Pathology, and at the Tri-Service Serum Repository. These banks are invaluable for comparative analyses to define emerging pathogens. For example, the Armed Forces Institute of Pathology used rare specimens in its collection to characterize the deadly influenza virus that circulated in 1918–1919. WRAIR and CDC used Army banked sera to retrospectively identify an outbreak of human ehrlichiosis that occurred before the first human case was reported in the literature. These banked sera helped define the typical clinical spectrum of this new emerging disease much better than case reports, which tended to reflect only unusually severe and dramatic presentations.

Objective II-C

Ensure timely development, appropriate use, and availability of diagnostic tests and reagents.

The DoD is a recognized leader in developing well standardized, sensitive, specific, and simple diagnostic assays for infectious diseases. Because of their simplicity many of these tests have applications both in forward deployed settings and in clinical labs found in the underdeveloped world.

Activity i

Identify points of contact within DoD for special or unusual laboratory tests for emerging infections and distribute a directory of the points of contact.

There are various entities involved with developing diagnostic tests within DoD. Although the prime focal point is the research program funded by the DoD Military Infectious Disease Research Program, considerable work is undertaken outside of this program through cooperative research and development agreements, small business initiative research grants, and other means. A central listing of these activities and their status and a listing of opportunities for licensure of assays should be developed.

Activity ii

Identify and/or develop and evaluate new diagnostic tools for emerging infections.

Because the appearance of new emerging infections seems to be inevitable and relentless, the need for diagnostic tests will likely be ongoing. DoD-GEIS will review these conditions as they surface and evaluate the need for appropriate military diagnostics. DoD-GEIS attempts to foster military-industrial partnerships to develop, validate, commercialize, or license new assays such as those for dengue, leptospirosis, and tuberculosis.

Activity iii

Maintain adequate stocks of diagnostic and reference reagents for use by DoD laboratories for the identification of emerging pathogens.

The DoD overseas laboratories are in many ways viewed as regional reference centers because of the depth of diagnostic laboratory capacity they possess. DoD-GEIS will develop a central listing of their capabilities and explore the utility of designating all six tropical DoD overseas labs as WHO reference centers for emerging infections, a status that has been achieved by the Navy Medical Research Unit-2 in Jakarta, Indonesia. A review of current

Diarrhea Outbreaks Must Be Taken Seriously in the Global Village

Citizen soldiers acquired drug-resistant diarrhea in Greece and brought it back to the United States when they returned home.

Background

On October 24, 1997, the Minnesota Department of Health was notified of an outbreak of diarrhea among Minnesota Army National Guard troops who had returned from a training exercise in Greece during October 4–18, 1997. *Campylobacter* reportedly had been isolated from the stool of at least one ill soldier.

Soldiers who participated in the exercise were interviewed regarding illness, food and water consumption during the last week in Greece, and antibiotics received. A case-control study was conducted to identify risk factors.

Campylobacter isolates from Guard personnel who had sought health care were submitted to the Minnesota Public Health Laboratory where they were identified to species, tested for antibiotic resistance, and assigned molecular subtypes (ie, DNA "fingerprints") by restriction fragment length polymorphism of the flagellar gene.

Results of Interviews and Laboratory Testing

Of the 350 soldiers who were in Greece, 203 were interviewed: 106 met the case definition, and 29 of these cases were confirmed by isolation of *Campylobacter* from their stool.

Cases had diarrhea for a median of 7 days (range 3–63 days): 23 cases had diarrhea for at least 2 weeks, and nine had diarrhea for at least 3 weeks. Of 104 cases, 81 reported stomach cramps; 75 reported fever and/or chills; 21 reported blood in their stools; and 16 reported vomiting. Three cases were hospitalized, each reportedly for three nights.

The 29 *Campylobacter* isolates from ill troops were *C. jejuni*. All isolates were resistant to ciprofloxacin and tetracycline and sensitive to erythromycin; 25 of 25 typeable isolates were identical by molecular subtype analysis, indicating a common source of infection.

Bottled water was a clear risk factor. Cases were 10.6 times more likely than controls to have drunk bottled water on October 14. Other risk factors included eating dinner at the military base on October 16 and drinking unpasteurized milk during the final week in Greece.

Fifty-nine of 106 cases were treated with an antibiotic. Treatment failures occurred among 13 of 39 cases who initially received a fluoroquinolone versus none of six cases who initially received an antibiotic other than a fluoroquinolone.

Statement

This event is likely a point source outbreak of ciprofloxacin-resistant *C. jejuni*. Water bottled in Greece is the most likely vehicle. This conclusion is based on the strength of association of drinking bottled water on October 14 with illness, the fact that bottled water could account for 98% of cases, and the observation that exposure on October 14 fits best with the classical 3- to 5-day incubation of *C. jejuni* infection in humans.

Increasing resistance to fluoroquinolones among *C. jejuni* isolates from humans has been reported from numerous countries in Europe and Asia since the late 1980s. Resistance rates of >80% have been reported among US military personnel deployed to Thailand.

Lessons Learned

- Overseas military operations can rapidly introduce emerging infections into US civilian settings
- Sophisticated public health laboratory support is invaluable in outbreak investigations
- Safety of all food and water (including bottled) sources must be questioned

Adapted from M. Osterholm et al. "Outbreak of *Campylobacter jejuni* Infections among Minnesota Army National Guard Personnel Returning from Greece, 1997." Minneapolis MN: Minnesota Department of Health.

diagnostic resources and a projection of desired capabilities will be undertaken.

Objective II-D

Augment rapid response capabilities for vaccine acquisition and expand evaluation of vaccine efficacy and the cost effectiveness of vaccination programs.

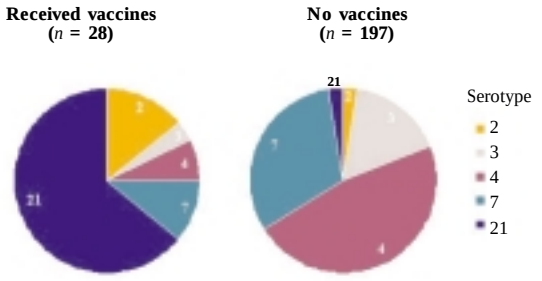
The DoD has significant expertise in the full range of vaccine design, animal testing, human testing, pilot lot manufacturing, and licensure and regulatory issues. The National Vaccine Program coordinates the nation's efforts in vaccine development, administration, and evaluation. DoD should continue to work closely with the National Vaccine Program and other federal partners to support the nation's needs for vaccines. In some cases, DoD can offer relatively uncommon facilities that can be of inestimable value in emergencies (eg, WRAIR vaccine pilot production facility, BSL-3 labs at the new WRAIR, and BSL-4 facilities at USAMRIID). Appropriate memoranda of agreement among DoD, CDC, NIH, FDA, and other federal agencies must be executed to ensure that when the need arises, necessary mechanisms for access and related issues have been anticipated.

Activity 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.

Only a well coordinated partnership among the United States and other nations can justify the hope that we can contain new and possibly dangerous pathogens such as a reemergence of the 1918 influenza. Interestingly, both the 1918 influenza pandemic and the 1976 swine flu cases were first recognized in US Army training camps. Since 1976 the Air Force has taken vital leadership in influenza surveillance through Project Gargle. That program must be expanded to tri-service coverage. Increased emphasis should be given to influenza surveillance in the Asia-Pacific theater. Traditionally new influenza strains have first been recognized in that region. Expanded surveillance

Adenovirus Serotypes by Vaccine Status



Adenovirus serotype distribution patterns among vaccinated and nonvaccinated trainees having positive adenovirus cultures. Vaccines were received against adenovirus types 4 and 7. These data suggest that vaccines for types 4 and 7 adenovirus are effective against those strains.

Courtesy of Emerging Illness Division, Naval Health Research Center, San Diego, California.

ideally could be conducted as military-to-military collaborations with other forces in the region. This is a well-recognized international health priority and could serve as a model of international military cooperation. In addition military personnel serve as ideal populations for influenza surveillance because they are young, live under conditions that foster transmission, and have access to health care in a fashion that allows epidemiologists to track rates of disease.

Better DoD surveillance will allow rapid recognition of outbreaks and prompt implementation of the DoD pandemic influenza response plan. This plan has recently been reviewed and should be reviewed annually to ensure that ongoing developments in surveillance, prophylaxis, treatment, and vaccine development are reflected.

Activity ii

Contribute to CDC specimen banks to identify prospective vaccine components. Seek reciprocal contributions to support DoD vaccine development efforts.

CDC and DoD are both well-positioned to identify antigens that may be effective in vaccine products. Collaborations should be fostered to ensure that CDC and DoD antigens are characterized and exchanged when they can facilitate new or improved vaccines for diseases such as meningococcal meningitis, hepatitis E, malaria, and influenza.

Activity iii

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

As new vaccines are developed, their ongoing evaluation, particularly after licensure, is indicated. DoD can be important in this effort owing to the structure of DoD populations, the DoD health care system, and the regimented military life. Tracking the efficacy and immune response associated with vaccine use under postmarketing conditions is a valuable contribution of DoD, as studies of meningococcal and Japanese encephalitis vaccines and their duration of protection have shown. For many years influenza vaccine responses and efficacy were tracked in young Air Force trainees, but this was curtailed several years ago because of funding cuts. Partnerships could help reinstate this valuable effort.

Goal III: Response

Enhance the prompt implementation of all prevention and control strategies for emerging infections to include improving communication of information about emerging agents.

Objective III-A

Use diverse communication methods for wider and more effective delivery of critical public health information, alert messages, and prevention and control recommendations.

Response refers to any action to reduce morbidity or mortality or the threat of morbidity or mortality. Response to emerging infections may be as basic as enhanced public and professional education. More complex responses include expanded surveillance, a new policy, outbreak investigations, targeted research, the stockpiling of drugs and biologics, and/or the initiation of large-scale immunization programs.

Emerging infections will often first come to clinical attention far from academic research centers and major public health organizations. For the many that emerge in the underdeveloped world, the time and distance between the event and scientific characterization will be even greater. Information on emerging infections (eg, epidemiologic trends, antibiotic resistance patterns, sources of diagnostic support, or policy guidance) must get to those who are closest to the source. It is imperative for military physicians to receive effective and timely education in diseases that are not normally seen in the United States but have the potential to be significant problems in deployment locations. Policymakers, troops, and family members must also be informed about emerging infections.

Activity i

Distribute educational materials about emerging infections prevention to health care professionals.

DoD-GEIS plans a comprehensive needs assessment to identify target populations and the most appropriate educational mechanisms for each population. Some of these will be mechanisms unique to DoD, and some will be borrowed from the civilian sector. Some information will be distributed through the DoD-GEIS web site. A goal is to address the vast majority of DoD primary care providers through a more accessible regular newsletter addressing relevant surveillance, therapeutic, and disease control policy issues. Education on the importance of surveillance will be emphasized to medical students and DoD clinicians.

Activity ii

Disseminate aggregate laboratory information about emerging infections and antimicrobial resistance obtained from DoD medical facilities worldwide to all DoD laboratories, hospitals, and practicing physicians.

Antimicrobial surveillance is a major focus of DoD-GEIS. This information is useful not only for guiding individual patient care but for also setting local and DoD antibiotic use policies. Because the DoD overseas labs can produce high quality antibiotic resistance work, their contribution to the global efforts in this regard are significant. Partnerships with commercial groups and the provision of leadership in the multinational

consortium of military clinical labs being assembled by the WHO emerging infections office are two important roles for DoD-GEIS. DoD-GEIS resistance data will be fully shared through its web site and through partner organizations.

Activity iii

Create accessible and comprehensive infectious disease databases that increase awareness of infectious diseases, facilitate their prompt recognition, and promote preventive action.

The DoD possesses vast information pertinent to disease control both internally and externally. Some of these data are not commonly or easily available outside of DoD. Some are distributed over numerous DoD web sites. The DoD-GEIS web site will capture much of this information to include DoD disease control policies and information pertinent to bioterrorism and civil preparedness through either links or direct entries.

Objective III-B

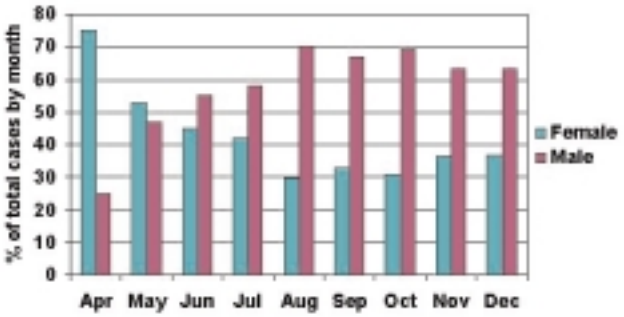
Establish mechanisms and partnerships needed to ensure rapid and effective development and implementation of assessment, response, and prevention measures.

The problem of emerging infections is more than any single agency can address. DoD-GEIS will lead in helping to define a common agenda with commercial, international, and US entities and execute at the appropriate level relevant agreements. These agreements could cover access to training, diagnostic support, containment facilities, and personnel. Agreements are contemplated with other agencies including CDC, US Department of State, and US Department of Agriculture. In areas such as bioterrorism and pandemic planning, close collaborations with FDA will also be required to move necessary products to approval safely and rapidly. DoD will be an active member of CISET, which coordinates the emerging infections efforts for the executive branch.

Activity i

Identify existing response capabilities within the three services and areas where capabilities are lacking.

Reemergence of Adenovirus in Basic Training, 1997



The first reported outbreak of acute respiratory disease caused by adenoviruses in otherwise healthy young women occurred in soldiers in basic combat training at Fort Jackson, South Carolina, in 1997. This type 4 outbreak was sustained over several months and followed two events: combining men and women in one training program and disrupting the routine use of adenovirus vaccines against types 4 and 7 viruses. The vaccines had been used to successfully control respiratory disyeases in male trainees since 1971; *n* = 752 (31.9% women).

Courtesy of K. Mills McNeill, Dwight D. Eisenhower Medical Center, Fort Gordon, Georgia.

DoD-GEIS will capture this information through surveys, interviews, and use of mock scenarios to address plausible problems in executing a response.

Activity ii

Develop and successfully staff a DoD assessment and response plan for military medical treatment facilities and DoD beneficiary populations.

A DoD assessment and response plan will be developed for emerging infections events in a DoD population. It is anticipated that development of such a plan will highlight strengths and deficiencies in areas of personnel, training, diagnostics and other laboratory issues, prevention, treatment, logistics, information management, and infrastructure.

Activity iii

Develop and successfully staff a DoD assessment and response plan for a US military emerging infections response in a foreign country.

A successful response to a request for assistance from another country may bring many benefits. Most obvious is the hope that spread to our own

populations will be curtailed. Such spread could occur through the importation of foods or other products as well as human travel. As is well appreciated by the CINCs, disease control benefits are frequently the least controversial forms of foreign engagement. Such activities may also help preclude economic instability that would lead to costly humanitarian assistance requests and civil unrest. Any response must be closely integrated with the local US ambassador and US Department of State, the CDC, the WHO, the ministry of health, and various nongovernmental organizations. Within DoD, a multiservice response involving medical and logistic elements may be involved. Such a complex response activity would require considerable preplanning to be executed in a t imely fashion. DoD-GEIS will develop the full range of planning and coordination documents to ensure that validated requests for assistance can be handled appropriately.

Objective III-C

Establish mechanisms and partnerships needed to ensure adequacy of stocks and prompt availability of prophylactic drugs, vaccines, and seldom used therapeutic agents for treatment, prevention, and control of emerging infections.

DoD-GEIS should participate in the CISET emerging infections subcommittee on the availability and use of biologics and drugs. Issues relating to shortages and increased demand should be coordinated. This CISET committee will initiate necessary actions related to product availability. Militarily relevant issues of this type include the availability of primaquine for malaria, antitoxin for botulism, and ciprofloxacin for anthrax prophylaxis.

Activity i

Identify points of contact for procuring vaccines and drugs.

Activity ii

Establish a directory of points of contact for monitoring vaccines and drug stock levels.

Activity iii

Identify means for periodically reviewing and updating the directory of products that may be needed for prevention and control of emerging infections.

Goal IV: Training and Capacity Building

Leverage DoD and international public health infrastructures through training, networking, and other forms of assistance to support surveillance, assessment, response, and prevention of emerging infections.

Objective IV-A

Support programs and efforts, including residency training, to ensure the ready availability of the professional expertise and support personnel needed to better understand, monitor, control, and prevent emerging infections.

Emerging infections have brought to light a great need for training and capacity building. Within the United States, public health infrastructure has crumbled over the last several decades. For DoD to address similar internal problems, training must be increased. For example, the DoD's recent demand for epidemiologists to confront postwar syndrome issues, accession standards issues, a greatly increased deployment tempo, and biological/chemical warfare education in addition to DoD-GEIS has resulted in a shortage recognized by Army Personnel Command of roughly 50 preventive medicine physicians. In the overseas arena, although the DoD labs have highly expert scientists and lab capabilities, their number is grossly insufficient to have a regional impact unless training of local scientists is implemented as a form of leveraging.

Activity

Identify areas where professional expertise and support personnel are lacking, particularly those areas of a militarily unique nature.

Over the last several decades DoD has lost tremendous expertise in various infectious diseases laboratory areas. Most notable has been the drain on the DoD research community in the area of respiratory viruses; there is no longer active research ongoing. This has led to challenges in addressing the loss of the adenovirus vaccines. Many programs in the areas of hemorrhagic fevers and similarly lethal threats have shrunk. Currently there is no Army infectious disease physician available for assignment to the HIV research program nor to most WRAIR research programs in bacterial diseases. Expertise in laboratory diagnostic and research aspects of leptospirosis, plague, and influenza are well below previous levels.

Advocacy to raise these issues will be important to the ultimate success of DoD-GEIS. Even at the clinical level in DoD, the type of public health laboratory expertise once embodied in the 10th Medical Laboratory has mostly disappeared. Supporting the DoD tropical medicine course and the WRAIR preventive medicine residency is just one way that DoD-GEIS intends to support training.

Objective IV-B

Coordinate with and utilize the resources of the Department of State, CDC, Joint Staff, and Joint Commands to develop infrastructure in support of emerging infection detection, response, and prevention in foreign countries.

DoD-GEIS has worked effectively with ACOM and SOUTHCOM to provide humanitarian assistance to countries in their regions for the purpose of improving medical surveillance. These programs are usually well received and fit well with each CINC agenda to provide broad regional benefits. They also leverage DoD resources and provide access to emerging infections information through enhanced networks with other professionals.

Activity i

The missions, capabilities, roles, and priorities of all key organizations must be known and understood to accomplish effective, efficient communication and coordination. All key organizations must be in agreement to enable coordinated, timely, and appropriate responses to emerging infections.

Success in the control of emerging infection requires close coordination with other federal agencies, the WHO and its regional activities, and appropriate professional organizations. DoD-GEIS will support WHO in its objective of using multinational military clinical laboratories for global surveillance purposes, especially to track antibiotic resistance in the developing world.

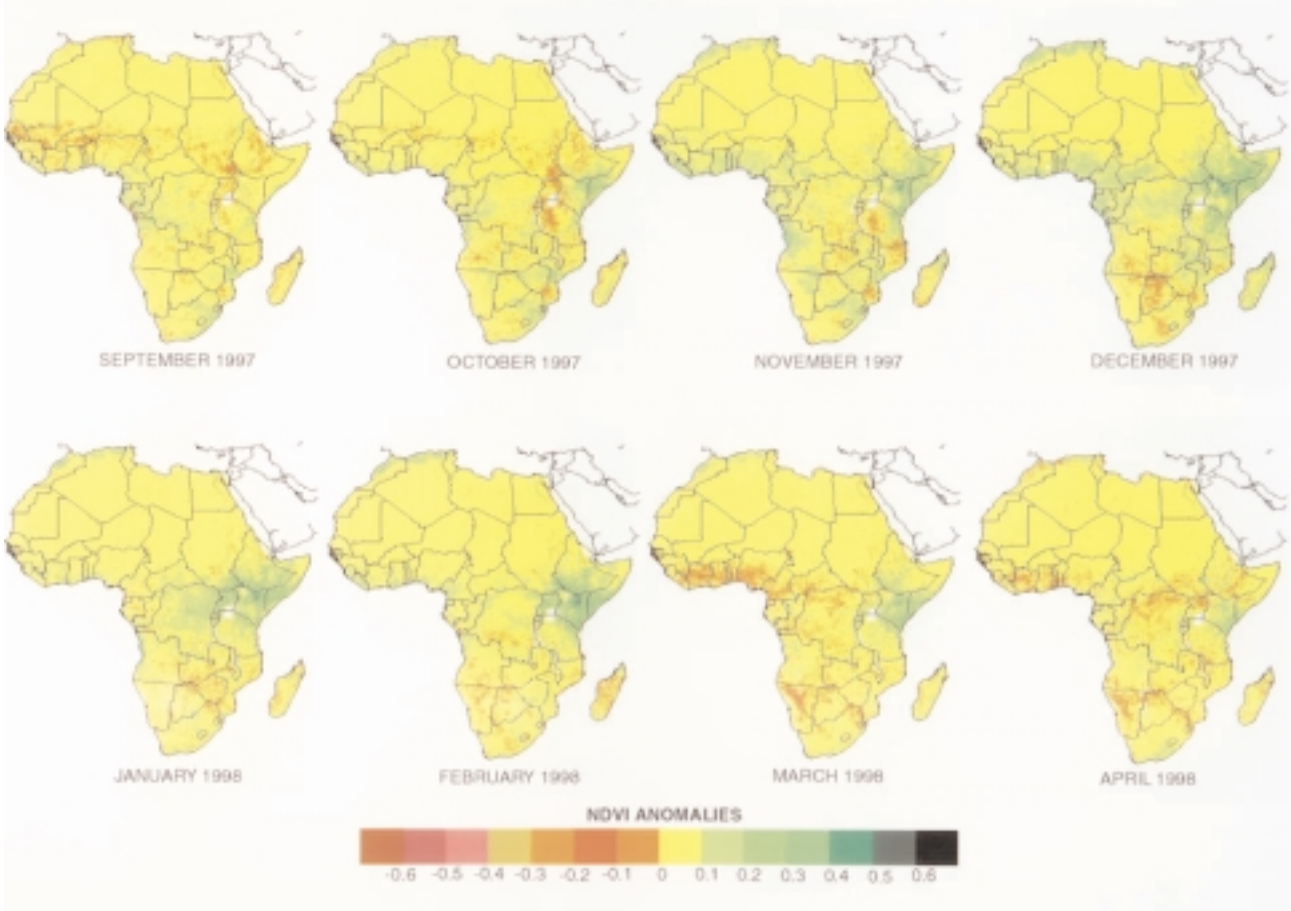
Activity ii

Conduct humanitarian assistance projects in conjunction with the CINC Overseas, Humanitarian, Disaster, and Civil Aid Program (OHDACA).

To help build a global network for emerging infections surveillance and response, DoD-GEIS activities have included consultations, training courses, and equipment donations to help foreign nations build disease control infrastuctures. This is consistent with current US foreign policy objectives of engagement to facilitate international stability and prevent the societal disruption that can accompany outbreaks of disease.

The outbreak of Rift Valley fever associated with El Niño in East Africa during the winter of 1997–1998 and its effects on that region illustrate the potential for disease to disrupt societies. Hundreds of people died a gruesome death, and the associated rains and flooding greatly affected these pastoral and nomadic peoples through high rates of fatal illness in livestock and significant crop destruction.

Increased Rainfall from El Niño Caused Outbreak of Rift Valley Fever in East Africa



The recent El Niño phenomenon significantly increased rainfall in East Africa between September 1997 and April 1998. These maps display composite normalized difference vegetation index (NDVI) data collected by the advanced very high resolution radiometer on NOAA satellites for Africa. Yellow and light green to dark green indicate increasing NDVI values. In East Africa NDVI values above 0.4 persisted through the normal short rainy period (October to December) and into the normal dry season (January to March). Previous predictive models have demonstrated that NDVI values above 0.4 that persist for extended periods will precipitate Rift Valley fever epidemics/epizootics.

Early in December significant levels of a fatal hemorrhagic illness were noted in livestock in East Africa. Disease soon spread to humans. Manifestations included acute high fever, severe headache, neck and back pain, abdominal cramps, joint/muscle pain, vomiting, and diarrhea. Sometimes frank gastrointestinal hemorrhage occurred followed by bleeding from the mouth and nose and death within 12–24 hours. At least 478 deaths (initially unexplained) were noted in Kenya. Ultimately at least 89,000 persons are estimated to have been afflicted.

Diagnostic testing in South Africa and by the CDC subsequently established many cases to be due to Rift Valley fever. (Other conditions facilitated by the rains included malaria, *Shigella* dysentery, and leptospirosis.) DoD-GEIS assisted with the epidemiologic investigation by contributing personnel from the US Army Medical Research Unit in Kenya, the Armed Forces Research Institute of Medical Science in Thailand, and the Navy Medical Research Unit-3 in Egypt. In Kenya, Navy Medical Research Unit-3 personnel established a capability to perform Rift Valley fever diagnostic assays, and USAMRIID supplied human Rift Valley fever vaccine for use under an investigational new drug application in at-risk laboratory workers.

Animal epidemics of Rift Valley fever occur periodically in parts of Africa after heavy rains promote hatching of the primary vector and reservoir, *Aedes* spp. mosquitoes. High levels of viremia in animals lead to infection of secondary arthropod species, virus amplification in livestock, and spread to humans through mosquito bites or contact with infectious fluids from viremic animals. The widespread Rift Valley fever transmission and the likelihood of repeated episodes in the future make it critical to improve remote sensing methodologies to enable better targeting of surveillance, prevention, and therapeutic activities.

Maps and NDVI data courtesy of Assaf Anyamba and C. J. Tucker, Goddard Space Flight Center, NASA, Greenbelt, Maryland

Assets of DoD for Emerging Infections Surveillance and Response

Unique network of facilities in the United States and overseas

- Overseas medical research units
- Service surveillance centers
- Modern laboratories with BSL-3 and BSL-4 facilities
- Vaccine production pilot plant
- Active infectious disease projects in more than 31 countries
- Established relationships with WHO and local health authorities

Multidisciplinary studies in bacterial, viral, and protozoal infections

- Basic science
- Epidemiology and entomologic field studies
- Vaccine and drug development (including clinical trials)
- Veterinary support

Extensive infectious disease expertise

- 700 persons stationed at DoD overseas laboratories
- 800 infectious disease scientists and support staff based inside the United States

Worldwide state-of-the-art communications

- Full Internet connectivity
- Satellite communications from field
- Telemedicine
- GEIS web site

Cutting-edge field diagnostic reagents

- Basic science
- Epidemiology and entomologic field studies
- Vaccine and drug development (including clinical trials)
- Veterinary support

Special drugs and vaccines

Globally deployed forces under medical surveillance

DoD Global Emerging Infections Surveillance and Response System

Partners

in the Fight Against Emerging Infectious Diseases

World Health Organization

Caribbean Epidemiology Centre

Armed Forces Institute of Pathology

US Regional Unified Commands

US Centers for Disease Control and Prevention

Pan American Health Organization

Uniformed Services University of the Health Sciences

US Department of State

Defense Medical Surveillance System

DoD Overseas Laboratories

Military Infectious Disease Research Program

US Air Force

US Navy

US Army

The Vision of DoD-GEIS: To Enhance Force Protection and Preven

Almost since the beginning of the US military medical departments in 1775, the military medical community has identified and provided solutions to many significant national and international problems in infectious diseases. Usually the work was directed toward a problem that was causing significant and costly morbidity and/or mortality in military personnel. Smallpox, typhoid fever, and acute respiratory diseases caused by adenoviruses produced great suffering and seriously interfered with the work of the military services before the implementation of effective vaccine interventions.

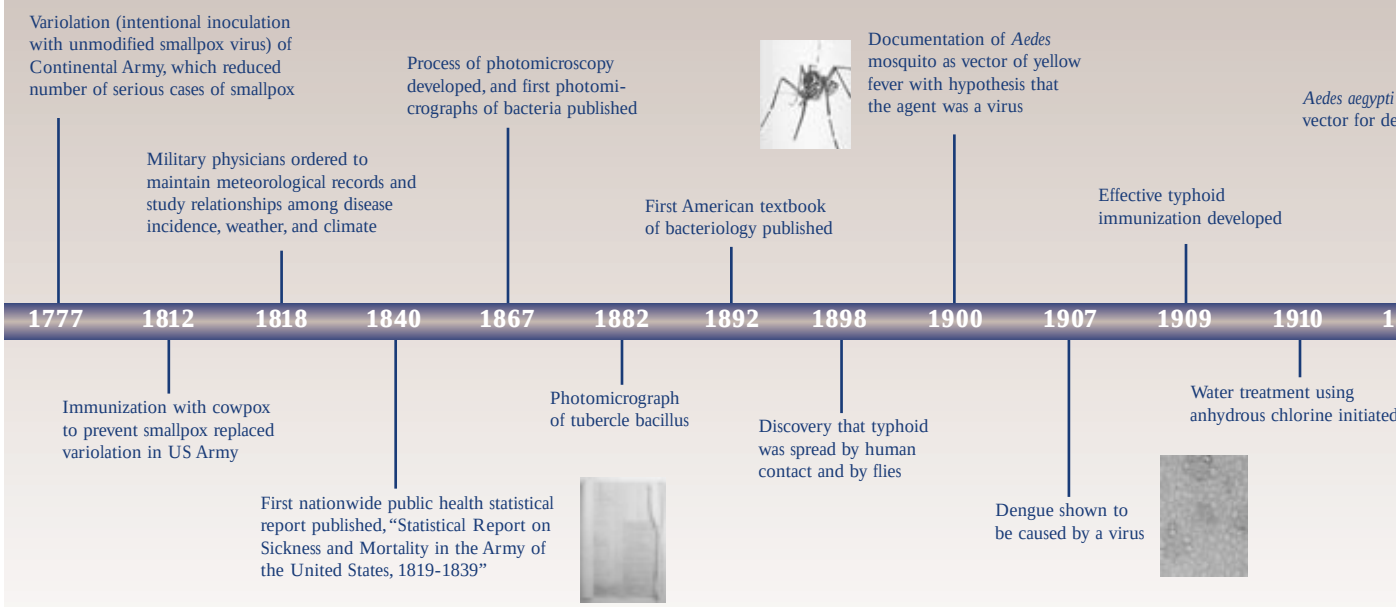
The military medical community often found itself executing government policy in remote areas and able to make significant contributions to civilians in great need. Most military medical accomplishments have provided at least some benefit to domestic and/or foreign civilian populations as illustrated by hookworm disease in Puerto Rico and yellow fever in Panama.

In 1899 Lieutenant Bailey K. Ashford, US Army Medical Corps, discovered that the New World type hookworm, *Necator americanus*, caused Puerto Rican anemia. His work on drug therapy, prevention, and control significantly reduced hookworm disease in Puerto Rico. He also contributed greatly to the Rockefeller Foundation's efforts to attack hookworm disease in the southern United States. Similarly, during construction of the Panama Canal, the US military worked successfully to prevent and control disease, particularly yellow fever. Eradicating yellow fever was essential to the completion of the canal and provided lasting improvements in the health of the local population.

Infectious diseases persist as menaces to the US military and the readiness of our forces. Acute respiratory diseases in military training camps and sexually transmitted diseases still threaten our uniformed people with great morbidity and perhaps even mortality. The complacency that resulted from an attitude that there were no longer important infectious diseases except for AIDS led to significant reductions in infrastructure and resources that have placed the United States at great risk.

DoD-GEIS is working to promote and enhance communication and coordination among the

Significant US Military Contributions in the Identification, Prevention, and Control of Infect

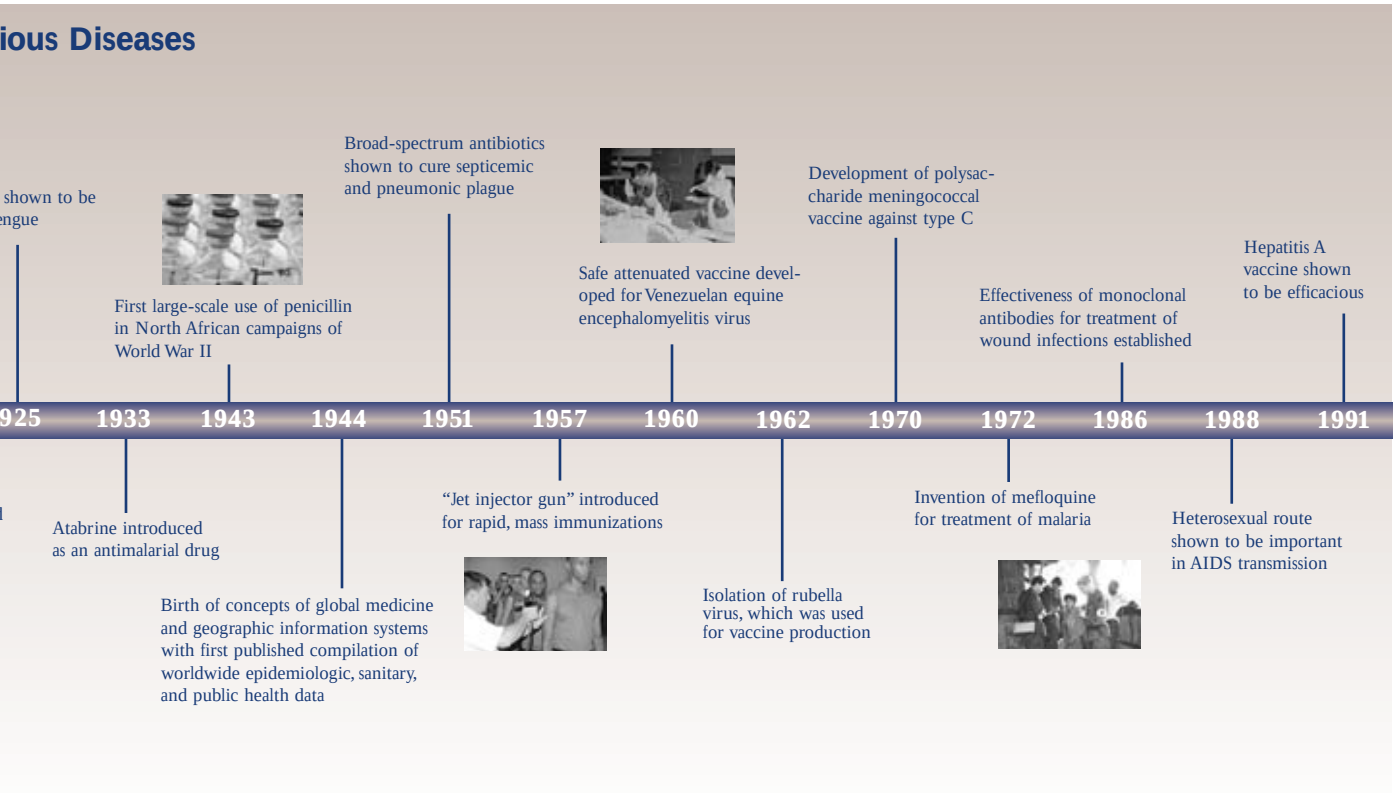


Adapted from *Military Medicine on the Threshold of Tomorrow.* 1998. Washington, DC: Walter Reed Army Institute of Research (brochure). See also Engelman and Joy 1975.

military services, the Armed Forces Institute of Pathology, Uniformed Services University of the Health Sciences, and other DoD programs and systems, such as the Defense Medical Surveillance System. The objectives of this effort are to identify and define significant threats and to prevent or control adverse impacts. These objectives will be met through effective surveillance for infectious diseases and responses to threats that may include educational campaigns, implementation of better diagnostic and treatment methods, or large-scale epidemiologic investigations dealing with severe disease syndromes caused by unknown agents. The pillars of this effort, in addition to surveillance and response, are education and training for medical and nonmedical people, research to ensure that appropriate drugs and laboratory tests are available when needed, and reestablishment of critical infrastructure. All are being addressed in coordination with the CDC and the national plan for emerging infections.

US forces are still widely scattered across the globe and face the unique risks of the region in which they are located. Although our overseas military commands and medical research laboratories work to assess risks to US personnel and to provide protective measures, the US military as always finds itself able to also provide significant medical assistance to the local populations. Working with the WHO, PAHO, Caribbean Epidemiology Centre, commanders-in-chief of the regional unified commands, and the Department of State, DoD-GEIS is attempting to assist in the identification of areas where needs and capabilities provide opportunities for the US military to contribute to the health of host nations. Influenza, drug-resistant malaria, drug-resistant enteric organisms, and febrile diseases like dengue offer opportunities for making significant contributions to the health of civilian and military people of many nations.

The vision of DoD-GEIS is that communication and coordination will occur smoothly and effectively among all involved groups. It is hoped that this will occur in a way that will result in the rapid identification and assessment of significant infectious disease threats and rapid, coordinated, and preplanned responses to these threats that will prevent or control morbidity and/or mortality.



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Abbreviations

ACOM	Atlantic Command
AIDS	acquired immunodeficiency syndrome
BSL	biosafety level
CAREC	Caribbean Epidemiology Centre
CDC	Centers for Disease Control and Prevention
CHCS	Composite Health Care System
CHPPM	Center for Health Promotion and Preventive Medicine
CINC	commander-in-chief
CISET	Committee on International Science, Engineering, and Technology
CONUS	continental United States
DoD	Department of Defense
EIS	Epidemic Intelligence Service
EU	European Union
FDA	Food and Drug Administration
HIV	human immunodeficiency virus
G7	Canada, France, Germany, Italy, Japan, United Kingdom, United States
GEIS	Global Emerging Infections Surveillance and Response System
LITS	Laboratory Information Tracking System
NASA	National Aeronautics and Space Administration
NDVI	normalized difference vegetation index
NHRC	Naval Health Research Center
NIH	National Institutes of Health
NMRC	Naval Medical Research Center
NOAA	National Oceanic and Atmospheric Administration
OCONUS	outside the continental United States
OHDACA	Overseas, Humanitarian, Disaster, and Civil Aid
PAHO	Pan American Health Organization
PHLIS	Public Health Laboratory Information System
SOUTHCOM	Southern Command
UNAIDS	United Nations AIDS program
UNMIH	United Nations Mission in Haiti
USAID	United States Agency for International Development
USAMRIID	United States Army Medical Research Institute of Infectious Diseases
USDA	United States Department of Agriculture
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research

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