DoD Global Emerging Infections System

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US Centers for Disease Control & Prevention
United States Department of State
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World Health Organization

Partnering in the Fight Against Emerging Infections

Annual Report
Fiscal Year 2003

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Abstract

DoD-GEIS is a network of DoD medical professionals in multiple partnerships focused on outbreak response preparation. This report presents background about DoD-GEIS within the context of infectious disease outbreaks affecting DoD, the United States, and the world. The assistance provided by DoD-GEIS to DoD in surveillance and response to disease emergencies is described along with DoD-GEIS activities through the five overseas military research laboratories that made substantial contributions to global outbreak detection and control and to public health capacity building and biosecurity. DoD-GEIS activities were described on 3 March 2004 when the office of the Assistant Secretary of Defense (Health Affairs) delivered an address to the Armed Forces Epidemiology Board subcommittee entitled "DoD Health Affairs Perspective." The following were highlighted as "significant contributions" made by DoD-GEIS to DoD (Health Affairs).

- ESSENCE, which served as a national and international model for the use of outpatient data to detect naturally occurring and/or intentional community outbreaks and which was used for tracking influenza-like illness in DoD beneficiaries during the influenza season.
- SARS response, which included deployment of DoD-GEIS liaison officers to the CDC Emergency Operations Center, deployment of a central hub staff member to Southeast Asia to assist international epidemiological response, and weekly SARS situation reports to DoD (Health Affairs).
- Influenza program that produced the weekly DoD influenza report and biweekly influenza situation reports to DoD (Health Affairs), provided input into CDC/WHO laboratory surveillance, contributed to FDA (VRBPAC) influenza strain selection, and served as the backbone of DoD SARS and influenza A/H5N1 surveillance in military treatment facilities.
- Surveillance for febrile respiratory illness within DoD, especially at recruit and basic trainee facilities, that contributed to the development of the new adenovirus vaccine.
- DoD mortality surveillance that identified possible disease clusters involving influenza, adenovirus, *Neisseria* species, *Streptococcus pyogenes*, and *S. pneumoniae.*
- DoD West Nile surveillance that provided direct staff support to DoD (Health Affairs) to coordinate vector and human surveillance, develop recommendations, and provide regular reports.

Executive Summary and Historical Context

DoD-GEIS was created in response to the June 1996 Presidential Decision Directive NSTC-7 which states that emerging infections threaten national and global security. The DoD mission was expanded to support surveillance and response to microbial threats through central coordination and enhanced support of overseas laboratories and through improved international cooperation and collaboration with civilian agencies.

FY03 was the seventh year of funded operations for DoD-GEIS. The central hub coordinated its activities with Defense Health Program dollars and U.S. Army executive agency management. The DoD-GEIS core program objective memorandum was leveraged through an extensive network of partnerships within DoD, with other U.S. government agencies, and with many foreign governments and international agencies. About two-thirds of the DoD-GEIS dedicated budget supported the overseas DoD laboratories. DoD-GEIS partnerships supported both domestic and foreign programs in surveillance, response, capacity building, and training. All these programs were consistent with the promotion of force health protection and with national-security-through-defense against microbial threats. Many DoD-GEIS programs provided direct benefit to the global war on terrorism.

In the aftermath of 11 September 2001, civilian public health systems were confronted with the challenge of deliberate infections from microbial agents as

demonstrated in several states by the letters containing anthrax that were delivered through the mail. Many agencies within DoD responded with clinical, epidemiological, academic, and laboratory services, providing expertise and medical information that helped determine the causative microbial agent, point-sources of exposure, and persons exposed. DoD also assisted CDC and other agencies in disease control activities and partnered with other government agencies in assisting criminal investigations.

In response to these events in 2001, DoD and civilian agencies reorganized bioterrorism defense using clinical medicine, public health systems, and academic institutions as basic infrastructures. DoD-GEIS continues to be an important partner in this transformation of the public health system. As stated in the DoD-GEIS 1998 five-year strategic plan:

> ***The DoD strategy for addressing the threat of natural and bioterrorist emerging infectious disease threats reflects a comprehensive, interagency systems approach....An effective prevention and control strategy requires an almost unprecedented spirit of teamwork.***

In keeping with the spirit of that five-year plan, DoD-GEIS emphasized the formation of productive cooperative partnerships within DoD medical elements and with external civilian medical agencies and organizations. Through these partnerships DoD-GEIS enables and supports medical and public health activities throughout DoD and indirectly supports other DoD activities even in the absence of formal arrangements. This annual report reflects the accomplishments of DoD-GEIS partnerships in FY03, which have continued to grow and mature.

The story of the DoD-GEIS professional network in FY03 can only be understood in the context of a comprehensive understanding of events affecting global and national public health systems and the entirety of DoD military medicine. International or national outbreak emergencies that could affect DoD generally evoke alerts and preparations among DoD-GEIS partners and more elaborate responses on behalf of DoD when appropriate. The "credit" for the accomplishments of DoD-GEIS partners must encompass all military medical leaders and the 80,000 military healthcare workers who provide medical information. DoD-GEIS partnerships incorporate the work of hundreds of people (including international collaborators) to produce medical knowledge and expertise for military stakeholders that have been leveraged into even broader DoD medical department successes and shared with the civilian community.

Throughout 2003, DoD assisted the Department of Health and Human Services and the CDC in improving state and local epidemiological and diagnostic capacities through bioterrorism training courses and through laboratory support at DoD-GEIS partner USAMRIID in Fort Detrick, Maryland.

The military vaccination (MILVAX) program (an activity sharing a professional relationship with but not receiving funds from DoD-GEIS) promptly shared its extensive experience in the 2003 military smallpox vaccination that was later expanded to civilian public health officials, clinicians, and emergency first-responders. There was special concern about direct-contact transmission from smallpox vaccine site wounds to other persons, severe rash illnesses from accidental inoculation of hosts with impaired immune systems, and transmission of vaccinia within healthcare settings. MILVAX employed methods that were consistent with CDC and FDA guidelines and safely vaccinated more than 400,000 active duty troops, developed systems to detect episodes of accidental vaccinia transmission, developed methods for intensive case investigations and contact tracing, and promoted use of appropriate infection control precautions to minimize transmission in healthcare settings. MILVAX provided information to CDC and other civilian agencies documenting that the Dryvax smallpox vaccine caused few episodes of accidental vaccinia transmission and no episodes of transmission in healthcare settings.

The CDC emergency operations center established in Atlanta in March 2003 was a significant advance in national and international epidemiological capacity that facilitated coordination of the international response to the SARS pandemic and the identification of the microbial agent as a novel coronavirus (SARS coronavirus). Senior DoD officials had significant concerns about the military and strategic implications of SARS because the pandemic was recognized only several days before the 2003 invasion of Iraq. The pandemic was associated with adult international

travelers, caused severe respiratory illness with high mortality, and was efficiently transmitted in health-care settings by droplets and direct contact. Case investigations and contact tracing bore some similarities to recent investigations with anthrax and vaccinia.

The entire DoD-GEIS network was asked to provide as much immediate medical information as possible about SARS illnesses in each partner's area of responsibility. Because of the wide global distribution and expertise of DoD-GEIS activities, the military medical leadership relied heavily on the central hub for daily reports, analysis, and synthesis of medical information relating to SARS, and CDC leadership requested DoD-GEIS personnel at their Atlanta emergency operations center during the SARS crisis. DoD-GEIS sent three military medical officers as liaisons for DoD-GEIS and DoD to staff the center for about 60 days. They assisted CDC as needed, learned about CDC methods for response coordination, and kept military leaders appropriately informed. DoD-GEIS also facilitated the development of DoD policy on SARS detection and management.

DoD-GEIS also supported a U.S. Navy preventive medicine physician on permanent assignment in Geneva at the WHO Global Alert and Outbreak Response Network office. This officer facilitated rapid communication and liaison among DoD and U.S. government officials and WHO. DoD-GEIS sent another public health officer to Cambodia on a cooperative mission with WHO Regional Office for the Western Pacific to assist Cambodia with its investigation of potential SARS cases; to prevent, detect, and manage any imported cases of SARS into Cambodia; and to improve national capacity to diagnose and manage SARS illnesses in that country and others within the WHO Western Pacific Region.

ESSENCE, the state-of-the-art syndromic surveillance project developed and supported by DoD-GEIS, provided ongoing information about respiratory illness disease clusters within the continental United States. These data facilitated outbreak investigations regionally and provided a centralized perspective on the outbreaks. North Carolina used ESSENCE to provide enhanced surveillance for SARS-like illnesses in communities surrounding imported SARS cases.

In addition, DoD-GEIS support of NAMRU-2 in Indonesia provided other timely syndromic surveillance information about respiratory illnesses from five southeast Asian countries using the Early Warning Outbreak Recognition System (EWORS). DoD-GEIS partners at WRAIR and NMRC coordinated with outside agencies and communicated among network elements and with the military leadership. In addition, diagnostic capabilities were optimized at the DoD research labs (USAMRIID, AFIP, NHRC, and AFIOH) and at MTFs, aiding clinical care support from USACHPPM. The flexible structure and funding capabilities of DoD-GEIS allowed forward deployment of expertise and delivery of excellent services and reliable medical information for DoD leadership. DoD-GEIS facilitated central coordination within DoD and promoted comprehensive preparedness for the detection and response to SARS as a collaborative effort with civilian agencies.

During the spring of 2003, civilian clinicians in the Midwest identified a cluster of ill patients with rash and fever caused by an orthopox virus. Public health officials and clinicians quickly eliminated a bioterrorism event from smallpox. The illnesses were found to be caused by monkeypox introduced by imported exotic pets. Prompt diagnosis, case finding, and contact tracing ensued with the use of smallpox vaccination for persons with monkeypox exposure (MMWR 2003;52(24):561–564). DoD-GEIS disseminated CDC guidelines about possible indications for use of cidofovir or vaccinia immunoglobulin in the event of severe monkeypox illnesses.

DoD-GEIS involvement in the monkeypox investigation included informing DoD leadership about the progress of this civilian epidemic, supporting special diagnostic testing capabilities at USAMRIID, and coordinating military veterinary officer responses. At least one military medical officer was directly involved in investigation and control measures for monkeypox in a cooperative arrangement with Missouri. That monkeypox investigation was facilitated by a CDC emergency operations center for coordination and the previous vaccination of public healthcare workers for smallpox earlier in 2003 for state health department biodefense purposes. The lessons learned from contact tracing from smallpox vaccination programs and SARS response, and the central coordination provided by the CDC emergency operations center in Atlanta and Missouri, clearly led to prompt control of the 2003 monkeypox epidemic. Such support and coordination are the by-products of the civilian public

health strengthening and military-civilian medical cooperation derived from the bioterrorism preparedness supported by DoD corporately and DoD-GEIS partners specifically over the last several years.

During the spring and summer of 2003, U.S. military medical officials responded to various medical problems related to combat operations in Iraq and Afghanistan. Some infections investigated among trauma casualties were due to antimicrobial-resistant organisms. In response, DoD-GEIS interacted with private industry, public health officials, clinicians, and policy makers regarding antimicrobial resistance. Antimicrobial-resistant organisms have presented special challenges to infection control programs within some MTFs, and DoD-GEIS provided a forum to share management and prevention ideas through networking with infection control activities and through electronic communications.

The reemergence of cutaneous leishmaniasis in 2003 was noted among military personnel deployed in Southwest Asia. Leishmaniasis clinical care was supported to a great extent by clinicians at Walter Reed Army Medical Center and Uniformed Services University of the Health Sciences (MMWR 2003;52(42):1009–1012). DoD-GEIS assisted by providing materials on its website and linking to other DoD sites such as http://www.pdhealth.mil/main.asp.

A large outbreak of malaria from troops deployed to Liberia in September 2003 required support of DoD-GEIS partner laboratories at WRAIR. The management of this outbreak by DoD was facilitated by DoD-GEIS encouragement to coordinate among the three services' respective medical departments and through confidential communication with CDC and state epidemiologists on Epi-X, the web-based secure epidemic network at CDC.

DoD-GEIS assisted USACHPPM in the investigation of a cluster of severe respiratory illnesses of unknown cause initially recognized by clinicians in Iraq and Landstuhl, Germany, in June 2003. DoD-GEIS deployed two epidemiologists to examine cases, obtained systematic clinical data from questionnaires, and supported laboratory diagnostics for a wide range of respiratory pathogens. Ultimately 19 military patients met the preliminary case definition of acute nontraumatic respiratory illnesses with respiratory failure (more than one per week) from U.S. servicemembers who had been in Southwest Asia since March 2003 and who required mechanical ventilation. Unfortunately two of these patients ultimately died (MMWR 2003;52(36):857–859), and ten had evidence of increased eosinophilia.

Although many challenges were posed by the conduct of a complex disease-cluster investigation in a war zone, and the fact that the etiology of the disease could have been a previously unknown emerging pathogen, the investigation was successful. First, because it determined that an association with an unexpectedly high frequency of severe illness in tobacco smokers was apparent. Second, although definitive etiological data are not yet available, the investigation caused a risk communication to be directed to soldiers in Iraq that strongly discouraged smoking in general, especially the smoking of locally procured products. DoD-GEIS provided extensive support to the lead investigators at USACHPPM and regular triservice coordination during this crisis that included formal and informal communication with CDC and with military medical expertise and leadership.

FY03 brought other innovative DoD-GEIS systems in support of force health protection and promotion of public health security. One of these is the near real-time global mortality surveillance conducted by AFIP, which assisted in the initially unexplained severe respiratory illness cluster in Iraq and in outbreaks of adenovirus and meningococcal illnesses in recruit camps and serious influenza outbreaks among military populations. An automated, triservice tool for antibiotic resistance surveillance was successfully piloted and developed to augment the TSN® system conducted under a Cooperative Research and Development Agreement with Focus Technologies, Inc. (Herndon, VA).

The rapid expansion of West Nile virus infection across the western United States in 2003 was another emerging infection requiring multidisciplinary surveillance and response from DoD-GEIS to mitigate exposure and disease among DoD populations. Ultimately, West Nile virus caused 9,862 illnesses across the country in 2003. The DoD-GEIS website provided nonsensitive information specific to DoD. Soon password-protected intranet sites, in cooperation with DoD (Health Affairs), will allow more

robust discussions of West Nile virus and other emerging infections in an appropriately secure environment for DoD healthcare providers.

Laboratory capacity is the foundation of a public health system that can respond to the unexpected emergence of new threats such as anthrax, SARS, and West Nile virus. Because many new infections first have symptoms similar to those of influenza, DoD-GEIS continues to invest extensively in capability for respiratory disease studies at AFIOH and NHRC. These laboratories were especially helpful in identifying influenza and adenovirus outbreaks as causes of serious illness in military populations in 2003. Other laboratories, such as USAMRIID and NMRC, were also supported by DoD-GEIS to ensure that quality diagnostic reagents for less common agents are on the shelf. Infrastructures of these organizations must be ready to respond to unexpected events.

The five DoD overseas medical research units in Thailand, Indonesia, Egypt, Kenya, and Peru continue to be a major focus of DoD-GEIS. The 2001 Institute of Medicine (IOM) program review calls these laboratories, "a critical and unique resource of the United States in the context of global affairs." The quality and productivity of each laboratory's DoD-GEIS program grow as resources and expertise are strengthened and partnerships expand.

This year the DoD-GEIS overseas laboratory network had substantial collaborations in more than 50 countries. Through the labs, DoD-GEIS provides WHO and CDC with active surveillance for new strains of influenza in the Far East, the Middle East, Africa, and Latin America that regularly influence immunization formulations. Antimalarial drug resistance surveillance conducted through DoD-GEIS has led to improved disease treatment algorithms for host countries. DoD-GEIS has improved core competencies and capacities in epidemiology and laboratory methods and clinical medicine, causing durable outbreak preparedness and capacity for coordinated emergency responses.

At the labs DoD-GEIS provides training and cooperative technology transfer to hundreds of host nation disease investigators and healthcare providers each year. Important surveillance information was provided by DoD overseas laboratory partners in antimicrobial-resistant enteric pathogens and in microbial agents that cause febrile illnesses such as dengue and Rift Valley fever.

After the SARS outbreak and response in 2003, the world recognized in a new way the importance and international influence of WHO in global emerging infections surveillance and response. The potential impact of a disease on international travel and global security was also appreciated. DoD-GEIS continues to support WHO through funding of several DoD-based WHO collaborating centers, cosponsored courses, and the Navy preventive medicine physician on permanent assignment in Geneva.

DoD-GEIS has worked collaboratively and cooperatively with CDC, including the assignment of CDC personnel to overseas DoD-GEIS programs, support with informatics training and influenza surveillance, and close coordination to ensure that DoD efforts complement and support initiatives of the Department of Health and Human Services.

The March 2003 IOM book entitled *Microbial Threats to Health: Emergence, Detection, and Response* focuses on bioterrorism agents, antimicrobial resistance, vector-borne infections, zoonotic infections, and infections associated with chronic diseases. Among the 21 recommendations of the IOM are many for the DoD, which is encouraged to continue enhancing global response capacity, especially focusing on threats in the developing world. The book states that, "DoD should expand and increase in number its Global Emerging Infections Surveillance overseas program sites" and that DoD should foster diagnostics development, reagent distribution, and technology transfer. Implementation of automated laboratory-based reporting of notifiable infections is recommended. ESSENCE is cited several times, and research on syndromic surveillance and geographic information systems is advised and promoted. IOM encourages DoD to develop and expand intramural and extramural training in applied epidemiology, field-based research, and control of vector-borne and zoonotic diseases. Federal agencies are reminded by IOM of the need for a flexible research agenda to permit rapid assessment of new and emerging threats.

DoD-GEIS is a leader and vital partner of many recently reorganized public health agencies that also detect and control microbial threats in support of

national security. DoD-GEIS provides ongoing support with the following capacities:

- Core competencies in epidemiology, diagnostic laboratory methods, research methods, public health, zoonoses, and clinical infectious disease medicine;
- Ongoing surveillance and rapid disease detection systems and processes focusing on diseases relevant to force protection that also provide a stream of useful medical information;
- Response capabilities linked to centralized coordination of surveillance systems that are augmented by training and public health systems research and an efficient communications network;
- Cooperation with civilian agencies and military officials to magnify the medical force and secure force protection and to support national and international security by combating microbial threats.

Multidisciplinary teamwork supported by DoD-GEIS benefited servicemembers, civilians, strategically important partner nations, and the global community. This achievement has positioned DoD-GEIS to influence and facilitate constructive transformation within DoD. Despite many successes, public health capacity in military and civilian sectors is not yet optimal; the global human, microbiological, and ecological factors behind infectious disease emergence continue to strengthen. As DoD-GEIS anticipates its second five-year plan, the bioterrorism events of 2001 and the emergence of SARS in early FY03 highlight recent improvements and continued vulnerabilities in military, national, and international public health systems.

Overview

The Institute of Medicine of the National Academy of Sciences published a landmark report in 1992 entitled *Emerging Infections: Microbial Threats to Health in the United States*. According to the IOM, naturally occurring emerging disease conditions such as HIV, Legionnaire disease, toxic shock syndrome, antibiotic resistance, West Nile virus, and Lyme disease are examples of weaknesses in the domestic and international public health systems. These ideas influenced the creation of Presidential Decision Directive NSTC-7 in June 1996 which directed the following:

The mission of 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 epidemiological capabilities; and enhanced involvement with military treatment facilities and United States and overseas laboratories.

Presidential Decision Directive NSTC-7 led to broad national investments in microbial threat preparedness that included the founding of DoD-GEIS and the CDC Emerging Infections Program. DoD (Health Affairs) health care program dollars supported DoD-GEIS as a program dedicated to surveillance, preparedness, and response for microbial threats. The 2001 IOM program review of DoD-GEIS states that DoD-GEIS is "the only U.S. entity that is devoted to infectious diseases globally and that has broad-based laboratory capacities in overseas settings." According to the IOM, the "rare, sometimes unique, diagnostic capabilities" found in the DoD overseas medical units represent critical international "medical research, public health, and diplomatic resources to the benefit of not only the U.S. military but also U.S. civilian and global interests alike."

The challenges to public health systems were highlighted when biological agents were deliberately used as agents of terrorism in the days immediately after 11 September 2001; these challenges were mitigated in part by DoD's longstanding core competencies and interest in biodefense and by an increased investment in emerging infections expertise at CDC and DoD that included DoD-GEIS.

DoD-GEIS was founded with the recognition that defense against microbial threats is a massive undertaking, that no one government or agency has control or responsibility for all expertise and technical capability needed to defend against microbes that do not recognize political borders, and that mechanisms of multinational medical, research, and public health

cooperation are essential. Emerging infections surveillance and response were necessarily expanded to include priority agents of bioterrorism, and the bioterrorism events of 2001 validated the view that public health capability and preparedness were important contributors to our national security.

DoD-GEIS efforts are divided into two fields of action: 1) actions through initiatives within the Military Health System (MHS) and 2) actions conducted out of the five tropical DoD overseas medical research units. The first field of action, which receives about one-third of the DoD-GEIS budget, focuses on improving MHS capabilities across a wide range of emerging infections issues. The foci of MHS activities are chosen and reviewed annually based on the following factors:

- Potential to fill a critical gap in MHS public health programs
- Likelihood of triservice or service-wide benefits
- Facilitation of timely public health actions
- Responsiveness to critical operational theater needs
- Accessibility of nonfiscal resources needed for execution
- Quality of the science
- Areas not covered by an existing core MHS public health program
- Consistency with DoD-GEIS five-year strategic plan

The second field of action is an expanding network of collaborative international partnerships. Within DoD-GEIS, the overseas medical research units manage state-of-the-art syndromic and disease-specific surveillance, training, response, and capacity building initiatives, all on a regional basis. These multidisciplinary laboratories, which are located in Thailand, Indonesia, Egypt, Kenya, and Peru, employ largely host country nationals in partnership with U.S. scientists. They are highly productive medical research laboratories that are platforms for public health preparedness and response, each having been established at least 20 years ago. Their partnerships with host governments and regional WHO offices are central to their success in contributing to regional health and stability.

The U.S. Combatant Commands have a long history of interest in the work of the overseas laboratories in their regions. The Commands have regularly supported the laboratories in various projects to strengthen regional relationships, improve the capacity of developing nations to mitigate destabilizing health threats, and understand medical threats that could affect U.S. personnel in these regions.

Implementing Actions of Presidential Decision Directive NSTC-7

The DoD-GEIS mandate from Presidential Decision Directive NSTC-7 is organized around eight implementing actions that are to be coordinated, where relevant, with Presidential Decision Directive 39 regarding U.S. counterterrorism policy. The key implementing action follows:

Enhance the surveillance and response components of our domestic and international public health infrastructure.

Activities Based in the Military Health System

Health Indicator Surveillance (ESSENCE)

A challenge to surveillance for emerging infections is that these conditions are either clinically ill-defined or unexpected. This challenge brings out a weakness in traditional approaches to surveillance that rely on laboratory confirmation of conditions described by well-established case definitions. In 1999 DoD-GEIS, inspired by innovative surveillance projects in New York City, established a pilot "health indicator" or

"syndromic" surveillance system for the Washington DC area called the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE). ESSENCE disseminates medical information along with syndromic surveillance analyses of morbidity from more than 300 sites around the world; data are updated every 8 hours and are made available through a secure website.

After the September 2001 terrorist attacks, ESSENCE, although still in development, was rapidly scaled up to provide increasingly real-time surveillance for more than 300 DoD installations around the world. ESSENCE has focused on daily tracking of diagnoses generated in ambulatory primary care clinics. Each day's morbidity experience for a given location is compared with historic data to evaluate the statistical deviation from expected ranges.

In FY03, the highly productive partnership between ESSENCE and the Johns Hopkins University Applied Physics Laboratory (JHU/APL) continued to grow. ESSENCE and JHU/APL were jointly awarded funds from the Defense Threat Reduction Agency to update ESSENCE and expand coverage to local civilian public health agencies at nine installations under the Joint Services Installation Pilot Project. ESSENCE staff worked with JHU/APL to incorporate pharmacy and current procedural terminology data; provide geographic information system maps; run new autoregressive, exponential weighted moving average and SaTScan algorithms; view disease and nonbattle injury and reportable disease cases; change viewing parameters; and extend available historical data from 2 months to 15 months.

ESSENCE also developed a comprehensive training package that includes documentation (slide sets and notebooks) for the Joint Services Installation Pilot Project. ESSENCE participated in an event sponsored by the Defense Advanced Research Projects Agency (DARPA) to test detection capabilities on real data. The algorithms developed by the JHU/APL and DoD-GEIS team performed the best of all those tested. ESSENCE established a classified syndromic surveillance system using joint medical workstation data from the CENTCOM theater. This system is up and running for disease and nonbattle injury and other special surveillance categories and is monitored by the Office of Deployment Health in DoD (Health Affairs).

A powerful advantage of ESSENCE, compared with similar systems in development, is its sheer volume of cases processed daily from a highly heterogeneous collection of communities around the world. This throughput has allowed regular detection of naturally occurring outbreaks and an assessment of system performance in various settings. ESSENCE assisted with multiple investigations through the provision of data about gastrointestinal disease outbreaks at Fort Carson (Colorado) and *Campylobacter* disease at Fort Leonard Wood (Missouri) and frequent influenza outbreaks at MCRD San Diego and Wright Patterson Air Force Base (Ohio).

For influenza, an influenza-like illness grouping was added. In contrast to clinical visit syndrome counts, which are compared with recent (and historical) counts for that syndromic group, influenza-like illness is a proportion; the numerator represents medical encounters with ICD-9 codes within the influenza-like illness group, and the denominator represents all encounters. This new feature was designed to facilitate comparison of ESSENCE with CDC influenza surveillance data. ESSENCE data and the influenza-like illness grouping became a regular part of the DoD global influenza surveillance weekly report and SARS surveillance in FY03. With the recent loss of DARPA funding, ESSENCE has made efforts to become part of DoD (Health Affairs) surveillance to secure sufficient funding to continue its mission.

Electronic Laboratory Reporting Mechanisms Research

DoD-GEIS began two projects in FY03 at the Navy Environmental Health Center to examine the means by which military laboratory data may be used to improve public health. These data are not standardized in the Composite Health Care System. MTFs performing the same tests may have different test names and results, making the use of these data for surveillance or other public health purposes difficult. Over time, several MTFs have developed their own mechanisms for using laboratory data. The goal of the first project is to document existing and potential initiatives in the military for facilitating electronic

laboratory-based reporting of notifiable events. In this project, the advantages and disadvantages of each initiative are explored. Those that can be replicated within the MHS are identified, and any modifications that must be made for implementation within the entire MHS are determined. The long-term hope is to develop electronic laboratory reporting capabilities throughout the MHS, which would not only improve and expand surveillance of medical events but also surveillance of antibiotic-resistant strains of particular diseases as well as timely monitoring of emerging infectious disease threats.

The second project explores the reliability of clinical datasets for medical surveillance. Electronic outpatient and inpatient ICD-9–coded records (SADR and SIDR, respectively) are available for patients visiting an MTF. These data are collected centrally in a timely manner and are used for conducting epidemiological studies and feeding several medical surveillance tools. Several anecdotal efforts to validate coding of SADR/SIDR records have shown conflicting results. This project was designed to compare ambulatory data records and inpatient data records with Composite Health Care System laboratory data to validate ICD-9–coded records and integrate laboratory data in medical surveillance. The intent is to use laboratory data with outpatient and inpatient data to create an enhanced, reliable, and more robust medical surveillance system.

Mortality Surveillance

DoD-GEIS initiated and continues to fund the DoD mortality surveillance program that monitors all active duty deaths for infectious or potentially infectious etiologies in real time, with notification to DoD-GEIS in the event of any clusters or unusual types of clinical presentations suggesting contagious infections. The program is part of the Mortality Surveillance Division in the office of the Armed Forces Medical Examiner at the AFIP, and DoD-GEIS funds the Alert Component of the division.

DoD-GEIS facilitates the obtainment of specimens, including pathological studies for more extensive testing and/or archiving whenever preliminary indications suggest that these procedures are clinically indicated or are needed for public health purposes. Reports of 358 illness-related deaths were investigated in FY03. Of these, 17 were due to infections.

In-depth investigations occurred in several cases, including the deaths of two active duty servicemembers who developed fatal eosinophilic pneumonia while serving in Iraq. Both cases were investigated as being possibly related to a larger apparent cluster of 19 seriously ill soldiers, all of whom required ventilatory support (MMWR 2003;52(36):857–859). The epidemiological investigation also reviewed records from other less seriously ill soldiers with clinically diagnosed pneumonia from Southwest Asia. Another pneumonia case that generated intense interest was a basic trainee who died from pneumonia who had tested positive for both adenovirus and *Neisseria meningitidis*. That case was also part of a larger outbreak of respiratory disease and raised important questions about the role of co-infections in disease severity.

Surveillance and Response for Antibiotic Resistance and Sexually Transmitted Diseases

Antibiotic resistance is a growing global problem. The federal government's lead agents for addressing antibiotic resistance are the CDC, the National Institutes of Health, and the FDA. As a federal entity in charge of one of the largest healthcare systems in the nation, DoD has a unique role. DoD-GEIS represents DoD on the annual federal antibiotic resistance task force. The task force first focused on a strategic plan for addressing antibiotic resistance domestically. Then during FY03, it began considering how DoD activities might be integrated with a national approach to antimicrobial resistance that would be compatible with the WHO strategic plan. With DoD personnel serving around the world and with extensive microbiological testing capabilities at the overseas medical research units, DoD participation in a global effort to combat antimicrobial resistance will be valuable to both military and civilian populations.

The key DoD-GEIS partnership with Focus Technologies (Herndon, VA), which was established through a Cooperative Research and Development Agreement, continued in FY03. Focus has developed a real-time hospital-based surveillance for antibiotic resistance. Called TSN®, the system involves daily downloads of microbiology laboratory data without personal identifiers. Data are then standardized and compiled for surveillance. Key MHS participants have been Wilford Hall Medical Center (Texas), Tripler Army Medical Center (Hawaii), and Keesler Medical Center (Mississippi). DoD-GEIS is increasing the number of participating MTFs. To encourage enrollment, DoD-GEIS has implemented a DoD-specific web interface for on-line data review and utilization. With TSN, hospital microbiology departments can create antibiograms rapidly and post them on their intranet sites, reducing the work involved in creating and maintaining antibiograms at MTFs. For example, antibiograms that previously took Wilford Hall technicians more than 40 hours to create can be performed in minutes with TSN. TSN has proven valuable both to clinicians needing to know sensitivity patterns and to infection control staff needing to evaluate the impact of antimicrobial interventions on susceptibility trends before and after the intervention. TSN enables DoD facilities to compare their data with other MTFs and with comparable regional and national institutions.

DoD-GEIS encouraged MTF participation in the CDC Gonococcal Isolate Surveillance Program. Extensive use of molecular diagnostic methods, which leads to fewer clinical isolates being obtained, has made it harder to obtain appropriate antibiotic sensitivity patterns based on testing isolates. DoD participation in the surveillance has focussed on Hawaii, where the threat posed by fluoroquinolone resistance is highest based on its geographic spread.

West Nile Virus Surveillance and Response

During FY03, the West Nile virus reached the West Coast of the United States, ultimately infecting 9,862 humans nationwide and causing 211 deaths in all states but Washington, Oregon, Alaska, Hawaii, and Maine. At least 50 DoD and federal government sites reported surveillance findings indicative of West Nile virus presence (mosquito, bird, or mammal).

DoD-GEIS received reports of 37 possible cases of West Nile virus among DoD healthcare beneficiaries in FY03. Many of these were in Colorado, the epicenter of West Nile virus in 2003. USACHPPM tested at least 21,821 mosquito pools for West Nile virus and found 160 positives. By concentrating on CONUS Air Force bases, AFIOH contributed to the overall surveillance performed by USACHPPM, testing more than 1,509 pools of mosquitoes during the 2003 season, identifying positives from Delaware, Colorado, and Texas. These pools were principally composed of *Culex* mosquitoes, including *C. tarsalis*, a species recognized to be a competent vector for West Nile virus.

DoD-GEIS continues to strengthen triservice cooperation and coordination among the multidisciplinary professionals that are involved with West Nile virus surveillance and response and helped DoD prepare for the transmission of West Nile virus that was expected to heavily affect the western United States in 2004.

General Public Health Laboratory Improvement

In 1999 DoD-GEIS sponsored a Military Public Health Laboratory Symposium and Workshop. Subsequently, a memorandum of agreement was developed with the AFIP to develop an on-line directory of DoD public health laboratory services so that access to state-of-the-art diagnostics could be facilitated and laboratory-based surveillance information could be more completely captured.

Progress during 2003 facilitated by DoD-GEIS includes the creation of a prototype directory using current industry-standard software and advanced search routines. The database was populated with information on 160 infectious agents and 40 government laboratories. On 1 October 2002, participating laboratories were given access to the directory to modify and update their respective lists of tests. The

password-protected directory was made available for general use over the internet in June 2003, and it is linked to the DoD-GEIS and AFIP websites. Non-DoD users are allowed to view information about agents and diseases; only authorized DoD users have additional access to laboratory test information.

With its extensive BSL-3 and BSL-4 facilities, USAMRIID is essential to DoD-GEIS efforts to strengthen DoD laboratory capacity. The goal of DoD-GEIS support is to maintain readiness to diagnose emerging and reemerging infectious diseases. This capability includes producing, testing, and stockpiling reagents for use in special assays. USAMRIID has a particular role in serving as a DoD reference center for the isolation of, identification of, diagnosis of, and consultation on unusual, rare, or emerging infectious diseases. Training in these areas of expertise is another key USAMRIID function. USAMRIID serves as a WHO collaborating center for the hemorrhagic fever viruses.

With DoD-GEIS support during FY03, USAMRIID performed 19,212 assays for rare or unusual agents (e.g., agents that cause Hantaan virus, West Nile fever, smallpox, dengue, and Venezuelan equine encephalitis). Reagents were produced and stockpiled for SARS coronavirus, West Nile virus, Crimean-Congo hemorrhagic fever virus, Ebola virus Zaire, Ebola virus Reston, Ebola virus Côte-d'Ivoire, Lassa virus, and Rift Valley fever virus. Diagnostic kits were provided to DoD and national and international collaborators for West Nile fever, dengue, equine encephalitis, viral hemorrhagic fever viruses, and Hantaan virus. Supplying the kits was facilitated through USAMRIID and DoD-GEIS support of the U.S. Army Theater Area Medical Lab, the 121st Evacuation Hospital-Korea, USACHPPM-South exercises in Central America, and USAMRU-K.

Through DoD-GEIS, USAMRIID also supported DoD and federal agencies in the investigation of the SARS outbreak and assisted in poxvirus testing for civilian state health departments, CDC, and DoD during the civilian monkeypox investigations and the transmission of smallpox after the military vaccination in early 2003.

In FY03, the Naval Medical Research Center began a project to support surveillance efforts at the overseas laboratories for *Rickettsia* and *Rickettsia*-like diseases. The DoD overseas laboratories, supported in part by DoD-GEIS, are measuring the extent of rickettsial diseases, their threat to military operations, and the emergence of antibiotic resistance. The labs perform initial testing of sera with commercial antibody detection kits that have inherent limitations in sensitivity, specificity, and reproducibility. The need continues for a DoD reference laboratory to confirm antibody detection results, to assay for live organisms, and to standardize detection systems based on polymerase chain reaction (PCR). DoD-GEIS is ideally suited to support this function. The main DoD-GEIS tasks are to use the DoD overseas laboratories to discover, document, and report emerging and reemerging diseases and the drug resistance phenomenon. DoD-GEIS already supports work with the rickettsial diseases at NMRCD, NAMRU-2, and AFRIMS. This program made available both serological and molecular biological assays to overseas laboratories so that they could conduct outbreak and epidemiological investigations.

Emerging Drug–Resistant Malaria Surveillance and Detection

With support from DoD-GEIS, the Division of Experimental Therapeutics at WRAIR manages the project entitled Surveillance and Detection of Emerging Drug-Resistant Malaria at WRAIR, USAMRU-K, and the Australian Army. The Division of Experimental Therapeutics served as the hub for antimalarial drug resistance and assisted in outbreak investigations and in the training of personnel.

Through DoD-GEIS, the division also assists USAMRU-K in its antimalarial testing and works with the Australian Army malaria laboratory to continue to characterize the molecular basis of antimalarial drug resistance.

At the end of FY03, 40 Marines returned from Liberia with an undiagnosed febrile illness. The Division of Experimental Therapeutics investigated the in vitro antimalarial susceptibility of patient samples from the Marines hospitalized at Bethesda Naval Medical Center in Bethesda, Maryland, and Landstuhl Regional Medical Center in Landstuhl, Germany.

Results showed problems with both mefloquine resistance and compliance in taking the drug.

The reemergence of malaria in Panama was also investigated through DoD-GEIS. *Plasmodium falciparum* endemic transmission has been reestablished in Panama. A study was started in FY03 to rapidly detect, through the use of molecular techniques, the *P. falciparum* mutations associated with resistance to antimalarial drugs currently used in Panama. Results indicated high levels of mutations associated with resistance to chloroquine, pyrimethamine, and sulfadoxine. Although these preliminary results have important implications for immediate control of the disease, they must be further investigated to establish a rational national malaria drug treatment policy.

Respiratory Disease Surveillance and Capacity Building

A cornerstone of the DoD-GEIS MHS activities has always been surveillance for respiratory diseases. Historically, these are common causes of morbidity and mortality in military settings. Pandemic influenza probably is one of the most serious emerging infections threats globally and is a particular threat to the military given the mobility and crowding characteristics of military populations. The instability in the influenza vaccine supply, with its periodic shortages, has further raised the level of concern.

The DoD global influenza surveillance program, which is supported by DoD-GEIS, performs etiology-based and population-based surveillance. AFIOH conducts etiology-based surveillance, and NHRC San Diego focuses on surveillance of high-risk populations, principally recruits at basic training centers.

AFIOH

The AFIOH laboratory runs the DoD influenza and respiratory virus surveillance program, was designated a WHO collaborating laboratory in 2003, and continues to provide key data to the annual FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting that selects components for the influenza vaccine.

A DoD-GEIS global influenza surveillance program partner staff member from AFIOH cohosted the NATO-WHO workshop entitled "Strengthening Influenza Pandemic Preparedness through Civil-Military Cooperation," which was held in St. Petersburg, Russia, in May 2003.

During the 2002–2003 Northern Hemisphere influenza surveillance season, 20 sentinel sites and 42 nonsentinel sites submitted 3,190 throat swabs to AFIOH. Of the 2,003 processed specimens, 599 (19%) were positive for influenza viruses (49% type A, 51% type B). Of 229 selected influenza isolates subtyped by AFIOH, 43% were A/H3N2, 31% were A/H1N1, and 26% were B/Hong Kong. Of 1,280 specimens yielding a positive viral isolate, 47% were influenza and 42% were adenovirus. During the latter part of the influenza season, a different strain of A/H3N2, the Fujian strain, was detected in DoD, CDC, and WHO surveillance. Despite cooperative efforts of all surveillance activities, a suitable vaccine seed strain could not be identified from the isolates available to CDC or WHO by the deadline needed for the VRBPAC decision. VRBPAC wanted to include a Fujian-like strain as the A/H3N2 component in the U.S. vaccine (WHO had a similar concern about the component), but the 2002–2003 A/H3N2, the Panama strain, was included for 2003–2004.

A major event in the 2002–2003 influenza season was the international outbreak of SARS, which was recognized at the end of the season. The DoD global influenza surveillance program was the backbone of the DoD surveillance for SARS, and the AFIOH laboratory was heavily involved in the response. Newly deployed sentinel sites were added in the midst of the season to enhance respiratory surveillance in the CENTCOM area of responsibility. AFIOH added reports about SARS cases to its weekly DoD global influenza surveillance reporting, added DoD-wide features incorporating ESSENCE surveillance and the new ESSENCE influenza-like illness grouping, and generally enhanced laboratory support and information coordination and dissemination regarding both diseases. The molecular biology laboratory optimized available CDC primers and probes for use on any

Influenza Variant Detected and Spreads Around the World

Detecting newly emerging strains of the influenza virus is fundamental to the DoD global influenza surveillance program. The fear of a pandemic drives the program, but subtle amino acid substitutions can also threaten public health.

The 2002–2003 season was remarkable in large part because of the variety of influenza strains isolated. Generally, one strain will predominate, but during that season, both influenza A viruses (A/H3N2 and A/H1N1) and B/Hong Kong circulated. In the midst of this variety, a variant A/H3N2 was detected in samples collected from Korea in December 2002.

The molecular capabilities of the laboratory at Brooks City-Base (Texas) were enhanced during FY03, and the sequencing of selected viruses was expanded. The presence of two amino acid changes in the influenza hemagglutinin was unusual but did not necessarily indicate that these viruses were antigenically distinct. However, through consultation with the CDC, it was learned that CDC had also seen the same substitutions in some specimens from China and had determined there was decreased immunological protection from the A/Panama/H3N2 vaccine component.

The search for a seed virus suitable as a vaccine candidate for the 2003–2004 season was complicated because this virus did not grow optimally in eggs. Isolates grown in tissue culture are unacceptable as a seed virus for the vaccine. Thirty-two original specimens that had yielded isolates matching the variant were forwarded to the CDC so they could be inoculated into eggs. Unfortunately, none of these grew well enough to be considered as a seed virus.

The original variant was identified in Asia and was subsequently seen in the United Kingdom and then in South America and the United States. Because the H3N2 component of the influenza vaccine remains A/Panama/2007/99 for the 2003–2004 Northern Hemisphere season, DoD-GEIS anticipates the 2004–2005 season to be more virulent, with the possibility of increased morbidity and mortality. DoD-GEIS continues to collaborate with CDC to monitor the spread of influenza viruses and emerging variants.

respiratory specimen arriving from an area potentially affected by SARS. These probes were tested on specimens from a suspect case group with results completely confirmed by the CDC. The AFIOH laboratory has also been in the forefront of developing primers and probes to a host of respiratory agents, including a universal influenza set, and developed some reagents specific for avian influenza.

To analyze influenza isolates, AFIOH successfully established a DNA sequencing facility. During FY03, AFIOH analyzed more than 70 influenza isolates and forwarded the results to the CDC. Specimens with a high likelihood of significant antigenic alterations that otherwise would not have been subtyped have been reported to CDC. During December 2002, the DoD began isolating viruses from Korea and parts of Asia belonging to a new lineage of H3N2 influenza A viruses. AFIOH now is only one of a handful of laboratories in the United States that can perform surveillance on both the hemagglutinin and neuraminidase antigens of the influenza virus. In late 2003, AFIOH influenza surveillance and clinical isolates documented the Fujian variant influenza A/H3N2 early in the influenza season and provided evidence of suboptimal vaccine effectiveness. AFIOH also assisted USACHPPM on a multiservice investigation of several influenza outbreaks among U.S. Army trainees in 2003.

For the current 2003–2004 influenza season (which was not finished at the time this report was prepared), influenza activity peaked between weeks 40 and 53, then decreased rapidly; 27 sentinel sites and 44 nonsentinel sites submitted 3,308 throat swabs, and 1,006 were positive for influenza. Of those processed by week 17 (25 April–1 May), 99% were influenza A and 1% influenza B. Of 531 influenza isolates subtyped, 519 were A/H3N2, 2 were A/H1N1, 9 were B/Sichuan-like, and 1 was B/Hong Kong. Of the respiratory specimens causing a viral isolate, 73% were influenza and 19% were adenovirus. Note that AFIOH received 65 specimens from deployed sites in Qatar and Kyrgyzstan, 22 which were positive for influenza A.

The ability to monitor for influenza-like illness among deployed sites is a critical extension in the DoD-GEIS surveillance network and a significant accomplishment this year. According to VRBPAC assessment and selection of vaccine components for the 2004–2005 Northern Hemisphere vaccine, the match between circulating strains and the vaccine should be better than the match for the 2003–2003 vaccine. Current information is posted on http://www.geis.fhp.osd.mil/GEIS/Surveillance Activities/Influenza. Web-based geographic information system tools have been used to display current worldwide DoD influenza activity on the website.

NHRC San Diego

Through DoD-GEIS, NHRC San Diego conducted triservice, population-based surveillance for febrile respiratory illness among basic trainees at eight centers. During FY03, adenovirus remained the leading cause of febrile respiratory illness among recruits, with 1,897 of 2,537 (75%) of specimens testing positive. Adenovirus outbreaks were documented at MCRD San Diego, MCRD Parris Island (South Carolina), Great Lakes Naval Training Center (Illinois), and Fort Sill (Oklahoma). NHRC emphasized rapid dissemination of findings via the web, and it recorded more than 12,000 user sessions on the website in FY03. This surveillance continued to provide compelling data to support the decision to re-acquire the vaccine for adenovirus.

Three Recruit Deaths Associated with Adenovirus

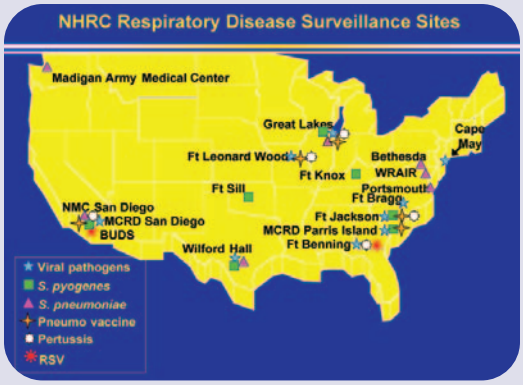
Within the military, adenovirus has long been recognized as a source of significant morbidity, with the potential to contribute to mortality. Recruits are particularly vulnerable and carry the greatest burden of adenoviral illness. In FY03 alone, 75% of specimens from recruits with febrile respiratory disease from all services tested positive for adenovirus.

During the 2003–2004 winter, the etiology of illness in four recruit deaths within the DoD was investigated through DoD-GEIS. Tissues available at autopsy from these cases were forwarded to the NHRC Respiratory Disease Laboratory for molecular and classic cell culture testing. Evidence of adenoviral infection or coinfection was found in three of the four cases. One of the three also had a positive lung culture for Neisseria meninginitis.

Deaths within our young, healthy, military population are a tragedy. Adenoviral-associated deaths are more troubling because they are potentially preventable by vaccine. All recruit deaths possibly related to infectious illness should be extensively investigated using advanced laboratory diagnostics, as was quickly facilitated through DoD-GEIS and NHRC in these cases.

Surveillance for Febrile Respiratory Illness Established among Basic Trainees

Military populations are prone to outbreaks of respiratory illness because respiratory infections can spread swiftly through close quarters, especially in basic training camps.



Within its respiratory disease surveillance program supported by DoD-GEIS, NHRC established population- and laboratory-based surveillance for febrile respiratory conditions at eight U.S. basic training centers that represent all military branches.

During FY03, NHRC identified high rates of adenovirus at all eight sites, including one outbreak at MCRD San Diego in which more than 100 trainees were hospitalized. An influenza B outbreak was identified in February 2003 at Fort Leonard Wood (Missouri), and several influenza A (H3N2/Fujian-like) cases were identified in November 2003 before immunizations were widely used. This active surveillance in recruits remains vital to military public health and readiness.

Shipboard Surveillance for Febrile Respiratory Illness Detects and Prepares for Emerging Pathogens

Outbreaks of respiratory illness occur frequently aboard ships, although the etiology is seldom determined. Ships from the Pacific Fleet are of particular interest because they deploy to areas of the world where emerging viral pathogens often originate.

During FY03, outbreaks of influenza A were identified aboard two ships that had recently made port stops. The first outbreak occurred in March 2003 after a stop in Pearl Harbor, Hawaii, and the second occurred in July 2003 after a stop in Sydney, Australia. The July outbreak was caused by the 2003 Southern Hemisphere influenza strain (A/Fujian/411/2002-like), which became the predominant strain during the 2003–2004 influenza season in the Northern Hemisphere.

Although neither outbreak prevented the ships from performing duties, each incident illustrates the capacity for sailors to contract illness and transmit pathogens around the world. Shipboard surveillance will continue to provide timely data on global disease threats, as demonstrated by the early detection of influenza strains in this surveillance.

Influenza surveillance among recruits was also a priority for DoD-GEIS. Recruits are highly vaccinated, so cases of recruit influenza would indicate drift of the circulating strain and poor protection by the vaccine. The public health implications are wide because no other highly vaccinated population is under more stringent active surveillance.

In FY03, DoD-GEIS piloted a new effort to conduct surveillance for respiratory illness aboard U.S. Navy ships and submarines. Five ships began participation in early 2003. This project allows NHRC to conduct surveillance for febrile respiratory illness among military populations deployed throughout the world and has provided remarkable geographic diversity of influenza isolates on an ongoing basis that is of great value to CDC and WHO (e.g., the isolation of Southern Hemisphere influenza A that was among the first specimens tested).

Respiratory illness surveillance was also performed by NHRC during the 2003 annual Cobra Gold exercise in Thailand and helped alleviate concerns over introduction of active SARS transmission in that country. Specimens were collected from individuals presenting with fever and respiratory symptoms. No suspect cases of SARS were identified, but laboratory processing of acquired samples showed transmission of influenza A/H3N2/Fujian variant before the onset of the influenza season in the United States, which was dominated by this H3N2 variant. The coronavirus OC43 (not SARS), respiratory syncytial virus, and rhinovirus were other identified pathogens from febrile individuals during this short exercise. Diagnostic capabilities for adenovirus and influenza A and B were also optimized for use on original patient specimens with the LightCycler (Idaho Falls, ID). These capabilities were implemented on an aircraft carrier and provided to a forward-deployable preventive medicine unit in Iraq.

With DoD-GEIS support, NHRC also studied the burden of disease caused by the human metapneumovirus (a newly recognized pathogen first described in 2001) in high-risk military personnel. Of 218 samples that had previously tested negative on the NHRC viral panel when the pathogen was unknown, 22 samples (10.1%) were positive for human metapneumovirus. Local transmission at recruit camps was demonstrated with sequencing and phylogenetic analysis. This is the first time that human metapneumovirus has been identified in a U.S. military recruit training population. This preliminary result represents significant morbidity in the recruit population. Coronavirus (OC43 and 229E) was also identified in 4% of these samples. NHRC continues to expand its molecular identification capabilities, uses sequencing analysis for validation of molecular results, and is dedicated to exploring newer diagnostic methodologies that will assist in rapid, accurate diagnosis of respiratory illness etiologies.

To explore a potentially more effective method for influenza and adenovirus surveillance in regions where maintaining a cold chain is not feasible, DoD-GEIS collaborators at NHRC and AFIP have studied PCR methods for evaluation of fixed, room-temperature samples at Fort Jackson (South Carolina) for the past 2 years. One hundred ninety-eight duplicate nasal swab specimens were collected and then tested with both viral culture methods and PCR methods from room temperature samples. Compared with viral culture, sensitivity and specificity of the PCR were 73% and 98%, respectively, for influenza A and 86% and 99%, respectively, for influenza B. Sensitivity and specificity for the adenoviral PCR were 95% and 40%, respectively. PCR testing detected more positives using room temperature specimens than it did using frozen viral media specimens. This 2-year ongoing project demonstrated the ability to accurately detect viral pathogens, particularly influenza, in room temperature specimens using PCR methods. These PCR methods hold promise for augmenting viral culture, especially in settings where maintaining the cold chain is impractical. The technique will undergo further refinement and optimization in FY04.

Through DoD-GEIS, NHRC also assisted in an outbreak response involving group A streptococcal pneumonia among U.S. Marine recruits in late 2002 that involved close cooperation with clinicians at the local San Diego military hospital and coordinated advanced laboratory support (MMWR 2003;52(6):106–109). Later in 2003, another special investigation in the recruit setting suggested possible coinfection with *Neisseria meningitidis* and adenovirus.

NHRC also tracked invasive *Streptococcus pneumoniae* at seven MTFs. To date, 381 specimens with invasive strains have been studied. Antibiotic resistance was widespread (34% to penicillin, 24% to erythromycin, 13% to ceftriaxone, and 38% to trimethoprim/sulfamethoxazole; 22% were resistant to three or more antibiotics). Antibiotic resistance of invasive serotypes does not seem to be increasing, and most of the invasive types from the United States are covered in the current 23-valent vaccine.

Viral Gastroenteritis Surveillance and Diagnosis Aboard U.S. Navy Vessels

Outbreaks of viral gastroenteritis have been a significant problem in the military for many years. Of the few outbreaks that have been studied, most were caused by human caliciviruses, the original and most famous strain of these is Norwalk virus and its relatives, together called Norovirus (formerly Norwalk-like viruses). Although the illness is neither life-threatening nor of long duration, the outbreaks can affect and incapacitate huge numbers of personnel in the unit. Deployed ships in particular were hit hard by Norovirus outbreaks in FY03, and ground units were also affected. No specific treatment exists, but there is potential for an oral vaccine to be developed.

The year 2003 was extremely active for Norovirus outbreaks, both for ships afloat and for land forces in combat during Operation Iraqi Freedom. Through DoD-GEIS, NHRC investigated several outbreaks of gastroenteritis, and Norovirus was confirmed from every outbreak in which stool specimens were collected. Linkage was seen between some outbreak strains in the same area, and the idea of Marines bringing Norovirus aboard an amphibious assault ship was given credence for a few outbreaks. NHRC, with DoD-GEIS, now supports outbreak investigation on all big deck carrier ships all the time, rather than following one or two deployed ships.

Norovirus Outbreaks during FY03

In Units Ashore

Unit	Location	Date of outbreak	No. of cases	Confirmed
MCRD	San Diego CA	October 2002	288	Yes
Area 31	Camp Pendleton CA	February 2003	40	Yes
MCRD	Parris Island SC	February 2003	232	Yes
1MEF	Iraq	April–May 2003	>100	Yes

On Big Deck Carriers

Ship	Date of outbreak	Previous port	No. of cases	Confirmed	Postoutbreak work
Lincoln	Sep–Oct 2002	Singapore	378	No stools	No
Belleau Wood	Sep–Oct 2002	Singapore, Phuket	82	No stools	Yes
Washington	Oct 2002	?Med	*	No stools	No
Theodore Roosevelt	Dec 2002	Norfolk	520	Yes	No
Constellation	Dec 2002	Singapore	747	Yes	Yes
Enterprise	Feb 2003	Norfolk	96	Yes	No
Vinson	Feb 2003	Hawaii	107	Yes	Yes
Boxer	May 2003	Persian Gulf	99	No stools	No

* Data unavailable.

A goal for DoD-GEIS was to gain laboratory diagnostic assays that could be used in the field or at sea during wartime. This goal was met by the development of assays to confirm Norovirus as a major cause of morbidity in Marines fighting in Iraq. These research assays were validated in combat conditions and provided timely information to the medical staff for the 50,000 Marines and Army personnel in 1MEF. Without this tool, the cause of the large gastroenteritis outbreaks in Iraq after the fall of Baghdad may never have been determined, and the use of bioweapons might have been mistakenly suspected.

Tracking Malaria and Other Threats to Public Health in the Republic of Korea

Based in South Korea, the Army's 18th Medical Command is a critical partner for DoD-GEIS. The reemergence of vivax malaria on the Korean peninsula in 1993 and its impact on troops are prototypical of the global problem of emerging infections. Since 1993, the annual incidence of vivax malaria in Korea increased, with a cumulative total of nearly 20,000 cases among Koreans reported by the end of October 2003. For the second year since its reintroduction, malaria rates decreased among Koreans, and the number of malaria cases decreased to 23 vivax cases among U.S. troops in Korea in 2003 (MSMR 2004;10:6–8), due, in part, to increased use of chemoprophylaxis by the Republic of Korea Army and lower *Anopheles* mosquito populations resulting from adverse weather conditions.

The reemergence of vivax malaria has drawn much attention because 1) it had been eradicated from South Korea, 2) its reemergence may have been caused by an introduction from North Korea (temperate zone strain), 3) its impact on unit readiness, 4) it is imported into the United States by returning soldiers and may affect soldiers deployed to other areas of the world (e.g., Afghanistan and Iraq), and 5) it continues to spread throughout South Korea even though cases there have decreased over the past 3 years.

Trapped mosquitoes were analyzed through DoD-GEIS support for evidence of malaria infection. Although more than 14,000 mosquitoes collected during 2002 were studied, none were positive. Another element of the DoD-GEIS program was to survey soldier knowledge, attitude, and behavior concerning malaria and methods of prevention. Malaria awareness was lower than in past years, perhaps because emphasis on malaria was reduced after the SARS pandemic.

DoD-GEIS continues to support surveillance of arthropods that carry other diseases. Through this surveillance in FY03, DoD-GEIS learned that the Japanese B encephalitis virus is circulating in at least two sites in Korea. This virus can infect U.S. troops stationed there, who could be developing asymptomatic or mild infections. Six cases of Japanese B encephalitis were seen in southern Korea in FY03. (Japanese B encephalitis immunization coverage in the southern Korean population is high.) DoD-GEIS also supports preliminary studies on pesticides and application methods intended to improve malaria control efforts.

Actions Conducted by the DoD Overseas Medical Research Units

In FY03, 65% of the DoD-GEIS budget supported initiatives conducted by the five DoD tropical overseas medical research units of WRAIR and NMRC:

- Armed Forces Research Institute of the Medical Sciences (AFRIMS), Bangkok, Thailand
- U.S. Navy Medical Research Unit No. 2 (NAMRU-2), Jakarta, Indonesia
- U.S. Navy Medical Research Unit No. 3 (NAMRU-3), Cairo, Egypt
- U.S. Army Medical Research Unit–Kenya (USAMRU-K), Nairobi, Kenya
- Naval Medical Research Center Detachment (NMRCD), Lima, Peru

DoD and Korean Health Officials Collaborate to Enhance Military and Civilian Health Protection in South Korea

To combat the threat of infectious disease to U.S. troops deployed on the Korean peninsula, DoD-GEIS facilitated cooperation between 18th MEDCOM and local public health officials. This cooperation led to broader dissemination of disease data, evaluation of a pesticide application method, and assessment of rodent- and tick-borne pathogens. Health protection of both the U.S. military and the Korean civilian and military populations was enhanced.

Mutual Reporting Disseminates Disease Incidence and Distribution Data

The office of the Deputy Chief of Staff, Force Health Protection, 18th MEDCOM, and Korea Center for Disease Control and Prevention report cases of disease among U.S. Forces Korea (USFK) and Korean populations. These data give the Deputy Chief of Staff a critical overview of disease incidence, which enhances the effectiveness of 18th MEDCOM in reporting health hazards and risk to the USFK commanders.

Simultaneously, these data help Korean officials to formulate suitable public health policy. The incidence and geographical distribution of malaria, Japanese encephalitis, scrub typhus, Hantavirus, and leptospirosis, and, more recently, the epidemiology of avian influenza in Korea were reported in FY03.

Ultra Low Volume Fogging and Biting Propensity of Mosquitoes Evaluated

Mosquito control throughout USFK installations and training sites is the responsibility of the Pest Control Section, Department of Public Works, Korean Regional Office. Evidence suggested that of the methods used, ultra low volume (ULV) fogging was largely ineffective.

Therefore, the office of the Deputy Chief of Staff, Force Health Protection, 18th MEDCOM, in collaboration with the Korean Army 5th Medical Detachment and Korea National Institute of Health conducted preliminary evaluations of ULV fogging operations at Camp Greaves, near the demilitarized zone, during a 6-day evaluation. These preliminary data suggest that ULV fogging had little effect on reducing populations of biting mosquitos. Although it appears that the ULV fogging greatly reduced the mosquito population, this same reduction was observed at the control site where fogging was not conducted. A more comprehensive survey is scheduled for 2004 to evaluate ULV fogging at both installations and training sites.

Risk Analysis of Rodent- and Tick-borne Diseases Improves

The Deputy Chief of Staff, Force Health Protection, 18th MEDCOM, collaborated with personnel from Korea and Chonbuk Universities, the Korea National Institute of Health, and the Korean Army 5th Medical Detachment to conduct surveillance for rodent- and tick-borne disease at selected USFK training sites as part of health risk assessment.

The deadly Hantavirus, which is transmitted to humans through direct or respiratory contact with rodent saliva, urine, and/or feces, surfaced at rates that, although variable, were >40% at some training sites. At sites where rates of Hantavirus exceeded 30%, USFK training was moved to other sites of lower risk, when possible.

Tall grass was the greatest indicator of high rodent populations and corresponding scrub typhus infections. Scrub typhus rates among rodents, which were also variable, were often >80%.

Each laboratory has established an extensive broad-based DoD-GEIS program focused on microbial threat surveillance, outbreak response, laboratory and public health training, and host nation capacity building in support of U.S. force health protection and U.S. national security. In many cases, DoD-GEIS activities supplemented USAID and humanitarian assistance projects from the DoD Combatant Commands. The overseas laboratories build regional partnerships with host nation ministries of health, national scientific

research facilities, and academic institutions. The U.S. Navy medical research laboratories in Cairo and Jakarta are designated as WHO Collaborating Centres for Emerging and Reemerging Infections. The other three overseas DoD laboratories are pursuing the multiyear process to obtain this prestigious designation.

The DoD-GEIS program at the overseas laboratories emphasizes the following five pillar conditions that remain significant issues for U.S. force health protection:

- Influenza
- Drug-resistant malaria
- Antibiotic-resistant enteric pathogens
- Fevers of undetermined etiology
- Syndromic surveillance

In response to local needs or opportunities, additional programs have also been implemented at the laboratories. DoD-GEIS programmatic highlights and findings follow.

Armed Forces Research Institute of the Medical Sciences (AFRIMS) Bangkok, Thailand

AFRIMS has a remarkable history extending from its founding after the 1956–1958 cholera pandemic. Today AFRIMS employs several hundred staff working in Bangkok and more than 40 field sites in Thailand, Nepal, Cambodia, Vietnam, Laos, and Bangladesh. Its research focus is broad and encompasses U.S. military, regional, and host nation threats including malaria, diarrhea/dysentery, dengue fever, HIV, hepatitis, influenza, and scrub typhus. In 2001 AFRIMS was characterized by the IOM as "probably the most sophisticated diagnostic and research laboratory in all of Southeast Asia."

The robust enteric illness surveillance program at AFRIMS is motivated by the historic importance of diarrheal diseases in the U.S. military and civilian public health in the region. DoD-GEIS surveillance for enterics involves prospective evaluation of patients (host national adults and children, soldiers, or expatriates) with acute diarrhea at six sites including clinical centers in Thailand, Nepal, and the multinational Cobra Gold military exercise in Thailand. *Campylobacter* spp. accounted for 38% of pathogens isolated in Cobra Gold, 1% in travelers in Thailand, and 17% in travelers in Nepal. Similarly, *Salmonella* was detected at approximately the same frequency in cases and controls at several sites in Thailand. *Salmonella* has been the leading cause of diarrhea in deployed troops from previous Cobra Gold exercises but was identified in only 8% this year. *Shigella* and enterotoxigenic *Escherichia coli* (ETEC) were noted in variable frequency across the sites. Twelve percent of traveler's diarrhea in Nepal was attributed to *Giardia lamblia*. Eight percent of the Nepalese isolates were *Cyclospora* and 11% rotavirus.

Enteric organism antibiotic resistance was noteworthy at these surveillance sites. *Shigella* spp. isolates from all sites were generally resistant to trimethoprim/sulfamethoxazole and sensitive to ciprofloxacin. *Campylobacter* resistance to nalidixic acid and ciprofloxacin was high for Cobra Gold participants (100% and 90%, respectively) and Thai adults in Nepal (78% and 71%, respectively). Conversely, resistance to macrolide antibiotics (erythromycin and azithromycin) was low for isolates from Thai children (5%) and tourists in Bangkok (9%) and absent for isolates from upcountry, Cobra Gold, and Nepal. *Salmonella* and ETEC isolates are generally sensitive to ciprofloxacin, although ciprofloxacin-resistant *Salmonella* was isolated from three foreigners in Bumrungrad Hospital in Bangkok and one case at the Children's Hospital in Bangkok.

AFRIMS participates in the WHO Global Salm-Surv *Salmonella* surveillance network by supplying data and isolates and also serves as a reference laboratory for the International Vaccine Institute *Shigella* surveillance and epidemiology sites in Pakistan, Bangladesh, and China.

Through DoD-GEIS, AFRIMS continues to monitor antimalarial drug susceptibility patterns in vitro and in vivo, which provides data for national policy planning. In vitro data collected by AFRIMS indicate no recent improvement of mefloquine resistance on the Thai-Myanmar border, and in vivo studies have actually documented spreading resistance along the northern Thai-Myanmar border south of Mae Sot, Thailand. This resistance has required the implementation of a new treatment regimen (artesunate-

mefloquine combination was introduced in 2002) for uncomplicated *P. falciparum* malaria in this border area that is the world's hotspot for multidrug-resistant malaria.

In contrast to other reports, AFRIMS detects no improvement of mefloquine resistance in Vietnam. AFRIMS has identified Bangladesh as a region of emerging resistance to multiple antimalarial drugs. In vitro mefloquine resistance is common in Bangladesh, but the degree of resistance is below that of the Thai-Myanmar border. No artemisinin-resistant P. falciparum isolates have been found among the wild isolates from Bangladesh collected by AFRIMS.

A new in vitro assay technique for assessing antimalarial drug sensitivity developed by AFRIMS through DoD-GEIS (HRP2 by ELISA) has been found to be field-expedient, semiautomated, and nonisotopic. The assay has the potential to replace existing techniques that are time-consuming, difficult to standardize, and/or require radioisotopes.

For several years, the AFRIMS DoD-GEIS program has conducted community- and hospital-based surveillance of febrile illnesses among migrants and local residents in Sangkhlaburi, Thailand, near the Myanmar border. Fever with respiratory symptoms and nonspecific findings are the most commonly encountered syndromes in the test area. In the absence of sophisticated laboratory testing capability, antimicrobial therapy remains largely empiric. Malaria is a common cause for fever in patients presenting with fever. By syndrome, malaria most commonly presents either with a fever without specific symptoms or fever with splenomegaly.

Surveillance for febrile illness is also conducted to identify causes of icteric and hemorrhagic illnesses and encephalitis in Kathmandu and the Terai region of Nepal. Among 42 cases with febrile jaundice, 33% were confirmed to have hepatitis E. Similarly, hospital-based surveillance is conducted in the Kamphaeng Phet province of Thailand. In Kamphaeng Phet, about 1,200 cases have presented with one of the specified clinical syndromes. Positive samples have been found for leptospirosis and scrub typhus. Of 360 samples tested for anti–dengue IgM/IgG, 214 (59.4%) were positive. Of 21 tested for anti–Japanese B encephalitis IgM/IgG, six (28.5%) were positive.

Through DoD-GEIS, AFRIMS and the Thai Ministry of Public Health have established a pilot web-based zoonotic disease surveillance program that will facilitate the reporting of human and animal disease between officials of the public health and livestock communities. A national level working group established during FY03 selected the zoonotic diseases to be monitored. The group also 1) selected one province in northeastern Thailand (near Kohn Kaen, Thailand) for a 1-year pilot study to demonstrate the feasibility and usefulness of the program; 2) assessed the needs of the province; and 3) contracted with a programmer to develop a web-based software program and homepage. The program will expand in FY04 to at least one more province in a different geographic region of Thailand.

The AFRIMS DoD-GEIS influenza surveillance program was suspended during the 2003 SARS crisis. In the past, AFRIMS had submitted specimens to the Air Force Institute for Environmental, Safety and Occupational Risk Assessment (now AFIOH) from sites including the U.S. Embassy in Bangkok, CIWEC clinic in Nepal, Sangkhlaburi and Kamphaeng Phet in Thailand, and the Maldives. Normally, these results are included in the presentation AFIOH makes annually to the CDC and FDA. AFRIMS will resume influenza reporting in 2004.

DoD-GEIS encourages the development of innovative technologies for surveillance. AFRIMS is pursuing a DoD-GEIS–funded geographic information system based on remote sensing to predict malaria transmission risk in villages in northwestern Thailand. Substantial progress has been made in the construction of maps, the processing of relevant satellite data, and the collection of entomologic data on insect biting and larval distribution patterns.

The development of an infectious disease surveillance and outbreak response system in the Royal Thai Army is both an important step in the development of an overall preventive medicine capability and an achievable goal. Through DoD-GEIS the Unit-Based Information System software has been developed for inputting and analyzing syndromic and diagnostic data. Software has been programmed to allow the units to conduct simple analysis and to automatically generate the reports required for forwarding to headquarters. The Unit-Based Information System is

expanding to additional commands this year and is providing data about the health status of border units along the Cambodian (and soon the Myanmar) border.

Training and host nation capacity building are necessary investments of DoD-GEIS to augment limited DoD resources with the capabilities of host country public health professionals. This capacity building extends the reach of DoD-GEIS and establishes beneficial professional relationships. AFRIMS has supported regional specialized disease surveillance infrastructure by providing diagnostic kits for agents such as hepatitis A, B, C, and E; leptospirosis; and scrub typhus. Field visits have been dedicated to training with the kits and for assistance with quality assurance. Training is provided at AFRIMS in ELISA, PCR, neutralization, tissue culture, and sequencing.

Outbreak response is a significant element of the AFRIMS DoD-GEIS program. To combat one of the region's most visible and explosive epidemics in years, AFRIMS provided verified, on-the-ground data about the status of SARS in Bangkok. AFRIMS maintained daily contact with the Thai Ministry of Public Health Bureau of Epidemiology and the CEO of Bumrungrad Hospital in Bangkok, a large hospital oriented to ex-patriots. AFRIMS also facilitated the transport of SARS specimens through the region onward to the CDC in Atlanta. Acting in this coordinating capacity permitted the timely receipt of specimens by U.S. scientists for the accurate identification of the virus causing SARS. Several AFRIMS researchers were key advisors to the public health ministries in Thailand and the Maldives and served on ad hoc committees and as technical experts to emergency conferences such as the WHO SARS meeting held 17–18 June 2003 in Kuala Lumpur, Malaysia, and the South Asian Association for Regional Cooperation emergency meeting for health ministers on SARS held 29 April 2003 in the Maldives.

AFRIMS collected potential SARS specimens from U.S. troops deployed to Thailand for Operation Cobra Gold 2003 and facilitated the implementation of the NHRC protocol to collect specimens, provided the supplies and liquid nitrogen for the storage of specimens in Pattaya, hosted and transported the lead NHRC researcher during her visit to Thailand, collected specimens from suspected cases in Pran Buri, collated the demographic results, and shipped all specimens to NHRC at the conclusion of Cobra Gold.

Surveillance Preceding Cobra Gold Eases Fears of SARS Transmission

NHRC was challenged with conducting laboratory-based surveillance for respiratory pathogens, including SARS, at the May 2003 Cobra Gold military exercise in Thailand. At that time, SARS was a threat in Thailand, and there was concern that exercise participants could be exposed and return to another country with the disease. Through DoD-GEIS, surveillance was initiated, and servicemembers who met the case definition during the exercise were evaluated at one of two appointed medical care units.

Geographic exposure history was determined to screen for potential SARS suspect cases, and throat swabs were taken. No one met the case definition for suspect SARS during the surveillance, but 16 individuals met the case definition for febrile respiratory illness. Of sampled participants, 44% (7/16) tested positive for influenza A, 13% (2/16) for coronavirus, 13% (2/16) for respiratory syncytial virus, 6% (1/16) for rhinovirus, and 25% (4/16) were negative.

Important information on respiratory infections during Cobra Gold was collected, and concerns about SARS transmission eased after surveillance was established.

Naval Medical Research Unit No. 2 (NAMRU–2) Jakarta, Indonesia

NAMRU-2 is a WHO Collaborating Centre for Emerging and Reemerging Infections and focuses on establishing regional networks through cooperative host national institutional affiliations to strengthen outbreak response and recognition capabilities. These networks are achieved through technology transfer of diagnostics to foreign laboratories, sponsorship of outbreak response training workshops, direct and indirect support of outbreak investigations, and design and implementation of EWORS and the ASEAN surveillance website (http://www.asean-disease-surveillance.net).

During the worldwide SARS outbreak, the Indonesian National Institute of Health Research and Development requested assistance from NAMRU-2. Personnel from NAMRU-2 assisted in formulating regional strategy to control the SARS pandemic, coordinated the Indonesian Ministry of Health SARS testing, including liaison with the CDC, and were recognized by the Vietnamese government as having contributed to Vietnam's successful and early containment of SARS through the workshops in outbreak response training conducted by NAMRU-2.

Through DoD-GEIS, NAMRU-2 hosted a guest scientist from Emory University/CDC who provided seminars and trained laboratory staff and scientists from Indonesia, Laos, Cambodia, and Vietnam in diagnostic techniques for SARS. NAMRU-2 acquired SARS coronavirus serological testing capability from CDC, implemented standard operating procedures for containment (requiring BSL-2 capacity or higher) and in-house testing, and provided oversight for the testing, data analysis, and reporting of approximately 80 specimens received from 39 suspect cases between 31 March and 7 June 2003. With DoD-GEIS support, NAMRU-2 conceived, developed, and sponsored the ASEAN surveillance website that became operational in June 2003. ASEAN identified the website as the official forum for disseminating SARS information to its ten member nations.

The enterics and emerging infections programs at NAMRU-2 have established an expanded enteric illness surveillance network in Indonesia in collaboration with the Indonesian ministry of health that represents the only archipelago network of cholera surveillance. The DoD-GEIS enteric disease program is also a major contributor to understanding the distribution of antibiotic-resistant enteric organisms in the region. Of 2,535 rectal swab specimens, *Shigella* spp. was the predominant bacterial pathogen (4.07%) isolated followed by *Salmonella* spp. (2.52%) and *Campylobacter* spp.(1.3%). Most *S. flexneri* isolates were resistant to ampicillin, trimethoprim-sulfamethoxazole, chloramphenicol, tetracycline, and cephalothin and were sensitive to nalidixic acid, ceftriaxone, and ciprofloxacin. *C. jejuni* was still sensitive (100%) to erythromycin; however, in past studies, 35% of *C. jejuni* were found to be resistant to ciprofloxacin. *S. typhi* and *Vibrio cholerae* O1 are still sensitive to all antibiotics. Other enteric pathogens showed varied patterns of susceptibility and/or resistance.

NAMRU-2 trained Indonesian professionals from the ministry of health in Medan and Padang on Sumatra, Makassar on Sulawesi, Pontianak on Borneo, Denpasar on Bali, and the island of Batam to identify noncholera *Vibrio* bacteria. In September 2003, NAMRU-2 held a workshop in Cambodia that trained laboratory staff from the Cambodian ministry of health in laboratory methods of medical preparation, sample collection, handling, processing, isolation, and identification of enteric pathogens. Like the other OCONUS labs, NAMRU-2 is extensively involved in outbreak investigations, such as hepatitis A in east Java and south Sumatra, dengue in Indonesia and Laos, cholera in Vietnam, and chikungunya virus in various locations throughout Indonesia.

EWORS syndromic surveillance networks, which continued to strengthen during FY03, facilitated recognition of the first case of SARS in Laos and was formally adopted into national surveillance strategies in Laos, Cambodia, Vietnam, and Indonesia. Operational funding for EWORS in Indonesia has transitioned from NAMRU-2 and DoD-GEIS to the Indonesian ministry of health. More than 5 million infectious disease cases have been registered by EWORS in Vietnam, Indonesia, and Cambodia, uniquely providing the first standardized regional database of reliable syndromic data available for trend analyses.

During FY03, NAMRU-2 DoD-GEIS programs were severely restricted because of the departure of all U.S. Navy investigators from October 2002 through April 2003 ordered by the State Department. Despite this absence, more than 6,000 civilians were screened for parasitic diseases and more than 70 persons were trained to increase host country capacity for control and surveillance of malaria and other parasitic diseases.

Malaria remains a significant force health protection issue for the United States because military deployments to worldwide regions highly endemic for malaria continue to cause human malaria cases. NAMRU-2 personnel were the first to describe the epidemiology of malaria outbreaks in west Java and north Sumatra and provided control measure recommendations to host country health officials. Critical malariometric data were provided to the Indonesian ministry of health in support of planned antimalarial drug resistance surveillance activities in the Lampung province of Sumatra and to provincial health officials in central Java to assess the impact of malaria control efforts over the preceding 2 years. NAMRU-2 also co-developed a tool to predict sulfadoxine-pyrimethamine resistance by *P. vivax* in an epidemiological setting and started a collaborative project to identify a gene-based tool to predict chloroquine resistance in *P. vivax*. NAMRU-2 remains engaged in host country capacity building through training programs in malaria diagnosis, filariasis diagnosis and control, geographic information systems, and molecular epidemiology.

The NAMRU-2 DoD-GEIS influenza surveillance program in Indonesia continues to serve as the primary resource for regional laboratory-based influenza expertise. From October 2002 to September 2003, 1,407 specimens were collected from 710 participants presenting with influenza-like illness at six sentinel sites in Indonesia. From tissue culture, 114 influenza viruses were isolated and 169 cases are pending complete analysis. The predominant circulating serotype was influenza A/H3N2, mostly Moscow- or Fujian-like. A substantial increase (from 6 to 29) in the circulating influenza B viruses was noted (predominantly Hong Kong-like). Forty-seven isolates were sent to the WHO collaborating center for influenza in Melbourne for confirmation.

In FY03, NAMRU-2 provided laboratory support for large-scale outbreaks of acute fever and severe joint pains suggestive of chikungunya virus infection in several locations in Indonesia. Between October 2002 and September 2003, NAMRU-2 received 1,145 samples from 16 districts throughout Indonesia. Chikungunya isolates were found in 8.3% of the samples tested. In addition, NAMRU-2 completed the first ever prospective serosurvey study observing active chikungunya virus transmission in the region around Yogyakarta on the island of Java, which showed a baseline seropositivity rate of 18.4%, with 4.9% of the seronegatives converting 1 year later.

Naval Medical Research Unit No. 3 (NAMRU–3) Cairo, Egypt

The largest and oldest of the five overseas laboratories in the DoD-GEIS network is NAMRU-3 in Cairo, Egypt. The laboratory is a WHO Collaborating Centre for Emerging and Reemerging Infections and works closely with the Eastern Mediterranean Regional Office of WHO, which is also in Cairo. Consistent with the DoD-GEIS philosophy of partnership in the fight against emerging infections, NAMRU-3 is pursuing a second DoD-GEIS 5-year plan that includes input from the local field epidemiology training program, USAID, the Egyptian Ministry of Health and Population, CDC, WHO, and the U.S. State Department. Through a joint effort, standardized case definitions have been developed, standardized laboratory methods have been identified, and standardized report forms and critical software inspired by the National Electronic Disease Surveillance System at CDC have been acquired. Additional tools have been developed to assess existing capabilities in laboratories and to conduct surveillance.

Over the first 5-years of DoD-GEIS, NAMRU-3 has engaged a network of infectious disease hospitals in Egypt that serves as the platform for enhanced surveillance for various priority diseases of military and host nation significance including dysentery, hepatitis, acute febrile illness, and meningitis. Surveillance is being conducted in seven sites throughout Egypt, causing numerous public health applications.

After FY03, surveillance for meningitis, hepatitis, and acute febrile illness will be integrated through DoD-GEIS into a system (which will be modified from the National Electronic Disease Surveillance System at CDC) that will use standard reporting forms and reporting by local health staff trained in the use of the system. The system is being implemented progressively by NAMRU-3 in collaboration with the Egyptian Ministry of Health and Population, CDC, USAID, and WHO. Implementation in all districts in all governorates will be completed by the end of FY04.

This surveillance has had numerous public health applications over the past 5 years. Acute febrile illness surveillance data were used to develop novel models to measure the burden of disease for the most common causes of community-acquired bloodstream infections. Data on antimicrobial resistance are being used to refine recommendations for the treatment of patients with typhoid fever, bacterial meningitis, and acute dysentery.

The sentinel site surveillance network established in Egypt through DoD-GEIS funding is a model for initiating sentinel site surveillance programs in other countries or regions in collaboration with local and regional health officials. Specifically, pilot networks for infectious disease surveillance and reporting were established in six districts in Samarkand oblast in Uzbekistan (bacterial acute febrile illness) and six districts in Zakarpatska oblast in west Ukraine (viral acute febrile illness and meningitis). Meningitis surveillance has been newly established in Uzbekistan and is being planned for eight other countries in the Eastern Mediterranean Regional Office of WHO.

Hospital-based surveillance findings led NAMRU-3 to develop a program for population-based surveillance for patients with bloodstream infections. This surveillance will help establish the burden of disease associated with community-acquired infections, such as typhoid fever and brucellosis. To date, a population-based study in the Fayoum Governorate has enrolled 2,670 patients. Blood cultures yielded 6.3% of isolates with *S. typhi* and 3% with *Brucella*, giving an annual estimated incidence of 134/100,000/year for typhoid fever and 82/100,000/year for brucellosis. The FY03 incidence rates for typhoid and brucellosis in the Fayoum are greatly increased over the FY02 rates (typhoid: 57 /100,000/year; brucellosis: 58/100,000/year), and efforts are underway to determine the factors responsible for these increases. A conference and workshop on typhoid and brucellosis were conducted by the Egyptian Ministry of Health and Population to determine how best to use this new epidemiological information and to develop a national strategy for the prevention and control of typhoid fever and brucellosis.

The NAMRU-3 DoD-GEIS program continues surveillance for selected diseases that cause viral febrile illness and meningitis/encephalitis syndromes in various countries of the Middle East, Africa, Eastern Europe, and Southwest Asia, targeting West Nile virus and other emerging zoonotic infections.

NAMRU-3 processed 852 human serum samples from patients presenting with acute febrile illness at ten fever hospitals in several governorates of Egypt. All sera were tested for IgM antibodies against Rift Valley fever, sandfly fever Naples, sandfly fever Sicilian, West Nile virus, and Sindbis fever.

A cohort study to determine the prevalence and incidence of West Nile virus throughout Egypt revealed the following seroprevalence rates:

Upper Egypt	35%
Middle Egypt	27%
Lower Egypt	14%
Northern Sinai	1%
Southern Sinai	7%

Seroconversion rates of West Nile virus antibodies were 18%, 17%, and 7% in upper, middle, and lower Egypt, respectively; positive samples were confirmed by PRNT. At all sites, seroconversion was age-related and peaked in individuals aged 60 years or older. No clinical cases that required hospitalization were reported during the study. Sentinel chickens showed seroconversion to West Nile virus in all study sites all year round. West Nile virus was isolated from sentinel chickens in upper and lower Egypt and from mosquitoes (mainly *Culex pipiens* and *C. perexiguus*) in upper, middle, and lower Egypt during the summer. In addition, human samples were collected for arbovirus testing from Djibouti, Yemen, and Jordan.

A network of infectious disease hospitals was established in the Transcarpathian mountains of western

Ukraine, an area highly endemic for both hemorrhagic fever with renal syndrome and tick-borne encephalitis, and enrollment is scheduled to begin in early FY04. DoD-GEIS sponsored training in arboviral diagnostics for ministry of health staff from various countries in Cairo.

Capacity building and surveillance for respiratory diseases are DoD-GEIS priorities at NAMRU-3. Geographic areas that lack representation in global influenza surveillance are targeted. During FY03, influenza surveillance was conducted in Egypt, Oman, Kazakhstan, and Ukraine. Ministry of health staff from each country underwent training both in Cairo and in their own labs. As participating countries develop capacity to isolate influenza viruses, DoD-GEIS will invite additional countries to join.

NAMRU-3 processed 2,733 samples from outpatient clinics in Alexandria and Cairo. The isolated viruses were influenza A (n = 54) and B (n = 183), adenoviruses (n =156), enteroviruses (n = 28), and numerous other viruses that have not yet been identified. During the season, 140 samples were collected from Oman and 97 from Kazakhstan, the first year of reporting from each country.

Staff members from the National Influenza Center in Kiev, Ukraine, were trained and are prepared to initiate influenza surveillance during the FY04 season. Isolated and typed influenza viruses from Ukraine and the surrounding countries are sent to the WHO Collaborating Centre on Influenza Viruses at the CDC for further characterization and potential incorporation into the next season's influenza vaccine.

A joint surveillance bulletin (Egyptian ministry of health and the virology research program) was published and distributed to the WHO and hospitals throughout Egypt. Adenoviruses are sent to NHRC San Diego for further characterization. In FY04, surveillance for cross-species transmission of influenza will begin in Egypt. Influenza viruses transmitted directly from birds to humans can be lethal, and the pig is a well-known source of recombinant viruses. Therefore, NAMRU-3 and DoD-GEIS have initiated surveillance in migratory and domestic birds and pigs in Egypt. Diagnostic capacity was established at NAMRU-3 for SARS and avian influenza and is a regional asset for both WHO and the DoD for outbreak response.

For military and political reasons, the Central Asian republics have become increasingly important for the United States. In October 2001, NAMRU-3 was asked by Uzbekistan to provide assistance to the ministry of health in Uzbekistan to strengthen surveillance for multidrug-resistant typhoid fever.

Through DoD-GEIS, NAMRU-3 trained staff at a network of six infectious disease hospitals in Samarkand and Dzhizak oblasts in Uzbekistan in July 2002. Information and experience from this effort were used to support a recent WHO mission to assess surveillance for communicable diseases. Meningitis surveillance data are being used to help redefine and update Uzbekistan national guidelines on meningitis. Surveillance and laboratory analysis for acute febrile illness cases have provided practical information about antibiotic resistance of *S. typhi* in Uzbekistan, leading to important changes in national treatment regimens. This surveillance and analysis also identified *Brucella* infection as a significant cause of acute febrile illness and has triggered ongoing discussion among ministry of health, ministry of agriculture, and WHO officials on the regional problem of brucellosis.

Additionally, DoD-GEIS will support a workshop on typhoid fever and brucellosis, similar to that which was conducted in Egypt in FY03, that will be conducted in Tashkent, Uzbekistan, in FY04. It is anticipated that epidemiological and laboratory-based findings will be discussed, leading to decisions on prevention and control strategies. DoD-GEIS and NAMRU-3 sponsored a WHO mission to Uzbekistan to evaluate the public health reporting system by leading two teams of WHO, CDC, and NAMRU-3 staff in a comprehensive nationwide evaluation.

NAMRU-3 provides epidemiology and laboratory assistance to U.S. troops deployed in this region where there are unique and serious infectious disease threats to military populations including arbovirus, viral hepatitis, and enteric disease. These diseases can significantly degrade mission readiness and adversely affect force health protection. Thus it is critical to develop a capacity to study the local epidemiology of infectious agents and to develop active surveillance.

For example, at the request of the commanding officer at Incirlik Air Base in Turkey, NAMRU-3 investigated high rates of acute gastroenteritis among troops participating in Operation Northern Watch and

conducted syndromic surveillance in U.S. military and civilian personnel for common enteropathogens including *Salmonella, Shigella*, and acute respiratory illnesses.

With DoD-GEIS support NAMRU-3 recently completed a diarrhea surveillance study in U.S. troops supporting Operation Bright Star 2002. Nearly 15,000 servicemembers participated in the exercise. Although participants had limited access to local food sources, 201 samples were collected from 128 ill servicemembers: 39% were positive for ETEC, 4% were positive for *Campylobacter*, and 1% were positive for *Shigella*. These findings again demonstrate the high risk to troops from enteric infections and the relative importance of ETEC as a cause of diarrhea. Various enteric pathogens of public health importance, including *Shigella, Salmonella*, and parasites, require ongoing surveillance to provide accurate information regarding the risk for the region.

Through DoD-GEIS, NAMRU-3 continues arbovirus and vector surveillance in U.S. troops assigned to the Multinational Forces and Observers deployed in northern and southern Sinai.

NAMRU-3 and DoD-GEIS provided laboratory and technical support to the WHO for diagnosis of *Bordetella pertussis* infections from Afghanistan. Although *Bordetella* was cultured, no *B. pertussis* was isolated. As a result, standard operating procedures for sterile sample collection, as well as transport and archiving, were developed and shared.

In May 2003, DoD-GEIS and NAMRU-3 provided technical support for infectious disease surveillance during transition of the regional WHO office and participated in establishing general health surveillance in southern Iraq to precede the formal team. Laboratory supplies and diagnostics were provided to WHO in Basra to support a pertussis outbreak. In addition, DoD-GEIS and NAMRU-3 supported the Egyptian ministry of health and WHO with staff, supplies, technical assistance, and diagnostics for several outbreaks. Hundreds of animal, human, and mosquito pools were tested. NAMRU-3 and DoD-GEIS provided technical support for WHO missions on hepatitis, infection control, measles, and meningitis to the WHO Eastern Mediterranean Regional Office countries and cosponsored several regional public health workshops.

U.S. Army Medical Research Unit–Kenya (USAMRU–K)
Nairobi, Kenya

DoD-GEIS activities at USAMRU-K include infectious disease surveillance, outbreak response, research and surveillance platform development, infrastructure development, host nation human capacity development, and training of U.S. medical personnel. Surveillance covers febrile illness, malaria drug sensitivity, and diarrheal pathogen sensitivity and is performed out of a seven-site network in Kenya and Uganda, with planned expansion into another site in Kenya and a site in Cameroon, both within the next fiscal year. Outbreak response is conducted on a regional basis at the request of the WHO, host nation ministry of health, and/or nongovernmental organizations providing healthcare in the region. Recent outbreak responses include investigation of yellow fever in southern Sudan, hemorrhagic illness for MSF France, and influenza at a local boarding school.

Sub-Saharan Africa is an area of recurring concern with respect to viral illness, particularly viral hemorrhagic fevers. The WHO reference center located in the Kenya Medical Research Institute (the host institution for USAMRU-K) represents a collaboration among the institute, USAMRU-K, and CDC. DoD-GEIS contributes resources to help support its role as a regional diagnostic reference center for suspected viral hemorrhagic and other viral illnesses.

The seven surveillance sites in sub-Saharan Africa are ministry of health hospitals located in areas across East Africa that represent diverse populations and ecology. Clinical and laboratory personnel at each site are specially trained in outbreak identification and in sample collection and processing. Each site has basic laboratory equipment to allow safe processing and shipping of samples. The personnel and equipment give each site the organic ability to perform case identification and sample processing and to provide safe transport of specimens.

The current focus of USAMRU-K febrile illness surveillance is the epidemiology and etiology of acute febrile illnesses in Kenya. Malaria, viral hepatitis, arboviral fevers, viral hemorrhagic fevers, rickettsial illnesses, and leptospiral pathogens are identified in patients of all ages admitted to participating hospitals. The medical data produced and reported to the ministry of health assists in the formulation of public health policy and in early recognition and response to outbreaks of potentially devastating illnesses. Since the protocol began on 8 November 2002, 581 subjects have been enrolled. Of these 581 subjects, 32% had been treated for malaria in the past 6 weeks, approximately 60% had taken either Fansidar or quinine, and 63% had positive malaria smears on admission.

At all surveillance sites except Kijabe, Kenya (which is not in a malarious area), investigators perform semi-annual collection of 100 blood samples of patients with smear-positive malaria. Blood samples are then cultured for malaria parasites, and the parasites are tested against 15 commonly used antimalarials at the USAMRU-K laboratory in Nairobi to determine regional resistance patterns and to monitor for the emergence of new drug resistance. Testing for genetic mutations is also performed to develop more easily fielded tests for antimalarial resistance. Data are then provided to the National Malaria Control Program and used to formulate antimalarial drug policy on a national and a regional level. In FY03, 256 subjects were enrolled in the study, and results are pending.

In May 2003, the USAMRU-K/DoD-GEIS team responded to a request from WHO to send a technician to southern Sudan to assist in sample collection and processing during an investigation of a hemorrhagic fever outbreak. A member of the team successfully demonstrated yellow fever virus as the etiologic agent, allowing for a vaccination campaign to begin, thus saving many lives.

USAMRU-K investigated two other suspected hemorrhagic fever outbreaks (one in June and one in August of 2003) for which an etiologic agent could not be found. A monitoring system was established for the June outbreak. In September 2003, the DoD-GEIS team confirmed that influenza B was the cause of the August outbreak at a local boarding school that had affected 50% of their students within 1 week. Control measures were instituted that prevented further spread, particularly to the younger children and to the surrounding community.

DoD-GEIS supports many educational programs and activities designed to increase the scientific capacity of the host nation and the United States, including sponsoring two Kenyan scientists in their PhD studies and two others in their MS studies, training ministry of health personnel in outbreak investigations, and hosting four U.S. military physicians and medical students during rotations in Kenya. DoD-GEIS also began a program to train host nation laboratory technicians in emerging infectious disease surveillance during a 2-month traineeship that includes instruction in general epidemiology and outbreak recognition and control. The program emphasizes laboratory work and will include instruction in advanced laboratory techniques in partnering reference laboratories.

U.S. Naval Medical Research Center Detachment (NMRCD) Lima, Peru

NMRCD is the sole DoD overseas medical research unit in the Western Hemisphere. A key contribution of the NMRCD DoD-GEIS program has been revitalizing malaria control in the Amazon Basin.

During the last 10–15 years, malaria has emerged as a major public health problem in the Amazon region. In a combined effort with USAID, NMRCD and DoD-GEIS have provided technical assistance to ministries of health on protocol design and antimalarial drug resistance research, as well as policy formulation in response to the findings. Drug resistance in the Amazon Basin has been mapped, which helped Peru and Bolivia to enhance malaria treatment policies by using combination therapy and multiple region-specific regimes per country. During FY03, work continued in Peru, Ecuador, Guyana, and Suriname but was postponed in Colombia, Venezuela, and Bolivia given political unrest and violence. In vivo drug efficacy biological studies of chloroquine and sulfadoxine-pyrimethamine against *P. falciparum* in two sites in Ecuador, mefloquine versus

mefloquine-artesunate against *P. falciparum* in Suriname, and chloroquine against *P. vivax* were completed in Peru.

NMRCD and DoD-GEIS also contribute significantly to the DoD Global Influenza Surveillance Program. In past years, strains collected at NMRCD DoD-GEIS sites have been included in the formulation of the influenza vaccine for the Northern and Southern Hemispheres. In FY03, 589 cases were studied, of which 147 (35%) identified a specific pathogen, such as influenza A (37.4%), influenza B (22.6%), adenoviruses (9.7%), parainfluenza (10.3%), herpes simplex (9.7%), enteroviruses (4.5%), metapneumovirus (1.9%), and other viruses (4%). This identification of human metapneumovirus is among the first reports in South America of this newly described agent. Also, the virology component of NMRCD DoD-GEIS established a surveillance network and developed the core capabilities to recognize and respond to the SARS pandemic in collaboration with ministry of health officials in nine South American countries. NMRCD personnel trained healthcare professionals; personal protective materials for caregivers were stockpiled, and the procedures for the collection, handling, and shipping of specimens for laboratory testing at NMRCD were instituted.

Surveillance for antibiotic-resistant enteric organisms was conducted in FY03 at six sentinel sites in four cities in Peru and two sites in each of two cities in Bolivia. A total of 1,521 enteric bacterial isolates were studied. Over 55% of all isolates examined for antimicrobial susceptibility were *Shigella* spp., whereas *Campylobacter* spp. and ETEC constituted 16.7% and 15.3% of isolates for antimicrobial susceptibility testing. Except for *Campylobacter*, few enteric isolates were resistant to ciprofloxacin.

Of particular concern in FY03 was increased resistance of *Campylobacter* isolates to most of the antibiotics used. A significant increase was found in the percentage of *Campylobacter* isolates resistant to 11 of the 12 antibiotics for which there is comparable FY02 data. Over 50% of *Campylobacter* isolates were resistant to ciprofloxacin or nalidixic acid, a troubling finding because these two antimicrobials are commonly used alternatives to sulfamethoxazole/trimethoprim in developing countries. Increases in resistance levels to nalidixic acid were observed among all species and to ciprofloxacin among all species except ETEC. These results were presented to health officials in Peru, Bolivia, and Ecuador to discuss the current antibiotic recommendations to manage diarrheal disease. The Peruvian Army updated its treatment guidelines, replacing sulfamethoxazole/trimethoprim with ciprofloxacin for adults and either erythromycin or nalidixic acid for children.

In a new syndromic surveillance effort, Peru enrolled 1,669 cases, Ecuador 152, and Bolivia 49. The success rate for collection of convalescent specimens averaged 69%. In Peru, viruses were isolated from 257 acute specimens and included dengue-1 ($n = 13$) and dengue-3 ($n = 230$); this surveillance tracked the introduction of dengue-3 in Peru's Amazon Basin. Isolates of Mayaro virus ($n = 5$) were documented, as well as Venezuela equine encephalitis ($n = 5$). In Bolivia, six patients had dengue fever. In Ecuador, seven patients were confirmed by virus isolation to have dengue fever. In Peru and Ecuador, serological testing identified leptospirosis in 17–22% of febrile patients, Q fever in 13–14% of patients, and brucellosis in 2–3% of cases; two cases of spotted fever were reported in Peru.

During FY03, diagnostic assays were performed using a nested PCR for the flagellin gene of *B. burgdorferi* and PCR for the 16S gene found in ticks. Collaborators from the Immigration and Naturalization Service were provided with kits and training to perform Western blot analyses (Trinity Biotech, Carlsbad, CA) to confirm the presence of antibodies (IgG and IgM) against *B. burgdorferi* in samples that tested positive using the Dip-S-Ticks assays [PanBio (Columbia, Maryland) and GenBio (San Diego)]. Western blot was consistently used to confirm serologic exposure to *B. burgdorferi*.

During FY03, DoD-GEIS supported multiple outbreak investigations by NMRCD of deadly disease agents in South America among military and civilian populations. In Bolivia, an outbreak of Mayaro fever was studied in March 2003, and in August a combined NMRCD-CDC-Bolivian ministry of health team investigated the circulation of the Machupo virus near the Brazilian border in Beni province.

In Peru, outbreaks studied included cases of yellow fever in Cusco, dengue-3 affecting soldiers garrisoned in Piura, more than 150 cases of diarrheal disease at

the Peruvian Navy base in Callao, and more than 2,200 civilians affected by a viral conjunctivitis in Iquitos.

Surveillance not only detected novel agents and the emergence of drug resistance but also led to system development and integration. Since 2001, NMRCD DoD-GEIS has sponsored the implementation of validated, cost-effective surveillance models such as PHLIS for disease reporting and integration of laboratory and epidemiological data. New programs such as the Alerta DISAMAR surveillance system (Voxiva Inc., Washington DC) are being piloted on multiplatform technology that allows the integration of remote reporting units. By using radio relays, telephone, or the web, disease events occurring in 15 health facilities along the remote Peruvian Amazon are reported and accessed in real-time. Automated alerts and warnings are sent to the Peruvian Navy, and weekly preprogrammed reports are disseminated.

NMRCD continues to support considerable training of DoD and host national scientists. Twelve DoD physicians participated in applied clinical training in remote Amazon villages as part of the field portion of the military tropical medicine course. Another two military physicians completed 4-week rotations funded by DoD-GEIS at NMRCD project sites in Iquitos and Lima in addition to four civilian graduate students who each work in Peru for 2 months. An additional 47 students were trained in laboratory diagnostics over a total of 475 weeks.

After two courses in FY02, the outbreak investigation training consolidated during FY03. After two spinoff courses led by the Peruvian ministry of health, NMRCD organized its second course in Lima, training 68 participants from the ministry of health and Peruvian Navy. This course represented a successful validation of the training model, incorporating the laboratory capacities of the Peruvian National Institute of Health in the program, both as contributors and beneficiaries. The course was followed by another replicate course in May in Puerto Maldonado in which 40 physicians, nurses, and laboratory technicians were trained at the local level, and the first course in Argentina, in which 60 professionals from the Argentine ministry of health were trained. Future steps involve expansion of the training to other South and Central American countries and linking the training with the implementation of early warning disease surveillance systems.

Orientation for the Next 5 Years

In 1998 DoD set for itself four broad goals: 1) enhance surveillance for emerging pathogens that threaten one or more aspects of national security, 2) improve DoD public health systems through research, development, and integration, 3) enhance implementation of prevention and control strategies, and 4) leverage DoD and international structures through training, networking, and other forms of assistance.

DoD-GEIS supported surveillance at the five DoD overseas laboratories that allowed the laboratories flexibility to adapt their approach to local opportunities and resources while encouraging projects in five DoD-GEIS pillar conditions:

- Influenza
- Drug-resistant malaria
- Antimicrobial-resistant enteric pathogens
- Microbes that cause febrile illness including dengue and viral hemorrhagic fevers
- Syndromic surveillance

The overseas laboratories contribute to the global influenza surveillance network and are, along with CDC, primary sources of data for the annual VRBPAC decision about the influenza vaccine composition. DoD-GEIS support for influenza surveillance contributed components to the vaccine that protects tens of millions of servicemembers and civilians throughout the world each year.

The expertise of the DoD overseas laboratories in surveillance for drug-resistant malaria has generated data that have altered national malaria treatment recommendations for host countries and expanded capacity and expertise that enabled ministries of health to eventually conduct these studies themselves.

Steady increases in antimicrobial drug resistance among common enteric pathogens have been documented by the labs in specific countries and regions. This documentation enables military clinicians to treat diarrheal diseases effectively in areas where troops may serve. In many instances DoD-GEIS febrile illness surveillance has identified the previously unappreciated endemicity of conditions such as rickettsial illnesses and leptospirosis. These new recognitions have changed empiric treatments such that lives are likely being saved.

DoD-GEIS pioneers enhanced informatics systems that are laboratory-based and advanced but still technologically appropriate. Laboratory-based enhancements to respiratory disease surveillance at NHRC and AFIOH have been particularly important for tracking respiratory disease etiologies during a time when lack of the adenovirus vaccine allowed the explosive return of adenovirus to basic training camps.

The solid foundation in infrastructure has also fostered critical research on respiratory disease prevention. DoD-GEIS has been the major funding agency of formal, near real-time DoD mortality surveillance based at AFIP. The 1990–1991 Gulf War highlighted the critical deficiency and threat to credibility that existed because DoD systems then could not epidemiologically describe disease and nonbattle injury mortality in the force in a timely manner. DoD-GEIS will continue to find ways to get technology to forward-deployed units.

DoD-GEIS will continue to make novel contributions in public health systems research and informatics. ESSENCE is one of the world's most sophisticated systems of automated syndromic surveillance and is a partner with DARPA and JHU/APL and other academic and corporate institutions. Another automated syndromic surveillance supported by DoD-GEIS, EWORS, was developed from the NAMRU-2 partnership with the Indonesian Ministry of Health. EWORS was designed for developing countries with minimal existing informatics infrastructure and has extended from one hospital network in the Indonesian archipelago to parallel networks in Cambodia, Laos, Vietnam, and the South Korean military.

Through another private-public partnership supported by DoD-GEIS (between Voxiva and the Peruvian Navy), NMRCD expanded the reach of informatics to the other side of the digital divide by supporting the implementation of the Alerta DISAMAR surveillance system in the naval clinics along the remote Peruvian Amazon. Alerta allows electronic capture and reporting of data in places with only telephone access but no computer resources.

Through partnerships with the Pan American Health Organization, the Caribbean Epidemiology Centre, and the Peruvian Ministry of Health, DoD-GEIS and U.S. Southern Command humanitarian aid created electronic networks for laboratory-based surveillance using the PHLIS software from CDC.

These informatics efforts foster timely and standardized collection and analysis of surveillance data that can be useful despite being preliminary and unconfirmed from definitive laboratory diagnostic tests. Locating these programs within official public health offices and in areas with ready access to public health laboratory diagnostics is convenient because clusters of outbreaks identified by this preliminary syndromic surveillance can then be thoroughly investigated by laboratory professionals when appropriate.

Response has included the DoD overseas laboratories' legacy of support to regional outbreak investigations. These responses encompassed problems in Asia, Africa, and South America. The products of these efforts were not only routine epidemiological insights but also the joint development by the National Aeronautics and Space Administration and DoD-GEIS of a satellite remote sensing methodology for predictive modeling of Rift Valley fever epidemics in Africa.

As expressed in the 1992 IOM book entitled *Emerging Infections: Microbial Threats to the United States*, the human, microbial, and environmental conditions needed for infections to emerge are growing more common and complex. The global human expertise still falls short of the challenge. As a result, DoD-GEIS increasingly emphasizes training of both DoD and host country personnel as a means to magnify the medical forces that are needed to detect and respond to microbial threats throughout the world. This training has taken many forms, including outbreak investigation courses and information technology training at the overseas laboratories. It is only through vastly increasing the capacity of public health systems around the world that the challenge of emerging infections can be met.

Each overseas laboratory DoD-GEIS program has at least one fully trained epidemiologist with experience in public health practice. Support staff grew at many of the field operating elements. Epidemiologic, laboratory, and informatics training received increasing emphasis at the overseas laboratories. Hundreds of DoD and host country professionals received training under the auspices of DoD-GEIS over the last few years.

DoD-GEIS is particularly proud that many host country partners who have been trained are now training others in their own and neighboring countries. As recommended by the IOM, DoD-GEIS emphasizes networking and partnerships because these create a wealth of expertise available for queries about novel problems, serve as back-up and overflow systems when local epidemiological and laboratory capacity is exceeded, and provide surge capacity to detect microbial threats and respond in emergencies. Partners are located in more than 50 countries and numerous U.S. institutions.

DoD-GEIS has actively supported WHO through funding of several collaborating centers, cosponsored courses, and providing a military officer's assignment to WHO headquarters in Geneva.

DoD-GEIS has enjoyed support from the CDC, and CDC has benefited from information and other professional support from DoD-GEIS. Support of CDC has included the detail of CDC personnel to overseas DoD-GEIS programs, informatics training, specific surveillance efforts such as influenza, and a valuable dialogue to ensure that DoD efforts are complementary and supportive of initiatives from the Department of Health and Human Services. Additionally a military medical officer will soon be permanently assigned to CDC in Atlanta as a liaison to DoD (Health Affairs) who will work closely with DoD-GEIS.

The IOM program review of 2001 recommended timely dissemination of data. Many DoD-GEIS elements have embraced this recommendation, ever conscious of the particular customers for their data. DoD-GEIS has presented its findings in numerous forums and has energetically participated in the biennial International Emerging Infections Conferences organized by CDC. Websites and newsletters have been launched by many DoD-GEIS participants. At the central hub, internet methodologies such as ESSENCE have been established to promptly move critical emerging infections data to appropriate DoD consumers. DoD-GEIS participants have promoted establishing, supporting, and strengthening intra-country and regional networks with epidemiological, laboratory diagnostic, and outbreak response capacity in many parts of the world.

The March 2003 IOM book entitled *Microbial Threats to Health: Emergence, Detection, and Response*, which follows the 1992 IOM book, again emphasizes the effects on national security from global emerging infections. Since the 1992 IOM book was published, the worldwide HIV crisis markedly worsened, Hantavirus pulmonary syndrome and West Nile virus infection appeared in the United States, and the deadly Nipah virus appeared in Malaysia. The United Kingdom and other countries experienced epidemic bovine spongiform encephalopathy (mad cow disease) and its human counterpart, new variant Creutzfeldt-Jakob disease. Infectious disease epidemiologists are apprehensively awaiting the next influenza pandemic.

The IOM describes the historic phenomena behind emerging infections with a meteorological analogy:

> ***A transcendent moment nears upon the world for a microbial perfect storm. Unlike the meteorological perfect storm—happening just once in a century—the microbial perfect storm will be a recurrent event….Whereas the angry sea dissipates to an eventual calm, leaving few witnesses to a meteorological perfect storm, the factors creating a microbial perfect storm can perpetuate and even accelerate its effects—leaving multitudes of people to bear witness and fall victim to its destructive forces.***
>
> ***Microbial Threats to Health: Emergence, Detection, and Response, 2003, pp. 19–20***

DoD-GEIS made tangible progress during 2003 in organizing and networking with DoD assets to identify and defend against that "microbial perfect storm" and to coordinate with many partners to minimize disease and contagion.

Both DoD and the world are large and complex, though, and many additional willing partners, more trained observers and clinicians, and improved rapid diagnostic technologies are needed to provide timelier alerts, more accurate diagnoses, and more effective responses to microbial threats. A fundamental lesson from SARS was that coordinated and effective public health responses to international crises require both active investigation of the threat by highly trained professionals with epidemiologic, clinical medicine, and diagnostic laboratory expertise projected to remote locations and sufficient logistics and supportive policies from organizational and governmental leadership.

Acronyms

AFIOH	Air Force Institute for Operational Health
AFIP	Armed Forces Institute of Pathology
AFRIMS	Armed Forces Research Institute of the Medical Sciences (Thailand)
ASEAN	Association of Southeast Asian Nations
BSL	biosafety level
BUDS	Basic Underwater Demolition School
CDC	Centers for Disease Control and Prevention
CENTCOM	U.S. Central Command
CIWEC	Canadian International Water and Energy Consultants
CONUS	continental United States
DARPA	Defense Advanced Research Projects Agency
DoD	Department of Defense
ELISA	enzyme-linked immunosorbent assay
ESSENCE	Electronic Surveillance System for the Early Notification of Community-based Epidemics
ETEC	enterotoxigenic Escherichia coli
EWORS	Early Warning Outbreak Recognition System
FDA	Food and Drug Administration
FY	fiscal year
GEIS	Global Emerging Infections Surveillance and Response System
HIV	human immunodeficiency virus
Ig	immunoglobulin
IOM	Institute of Medicine
JHU/APL	Johns Hopkins University Applied Physics Laboratory
MCRD	Marine Corps Recruit Depot
MEDCOM	U.S. Army Medical Command

1MEF	First Marine Expeditionary Force
MHS	Military Health System
MILVAX	military vaccination program
MSF	Médecins sans Frontières
MTF	military treatment facility
NAMRU	Naval Medical Research Unit (Egypt and Indonesia)
NATO	North Atlantic Treaty Organization
NHRC	Naval Health Research Center
NMRC	Naval Medical Research Center
NMRCD	Naval Medical Research Center Detachment (Peru)
OCONUS	outside the continental United States
PCR	polymerase chain reaction
PHLIS	Public Health Laboratory Information System
PRNT	plaque reduction neutralization test
RSV	respiratory syncytial virus
SADR	standard ambulatory data record
SARS	severe acute respiratory syndrome
SIDR	standard inpatient data record
TSN®	The Surveillance Network®
ULV	ultra low volume
USACHPPM	United States Army Center for Health Promotion and Preventive Medicine
USAID	United States Agency for International Development
USAMRIID	United States Army Medical Research Institute for Infectious Disease
USAMRU-K	United States Army Medical Research Unit–Kenya
USFK	U.S. Forces Korea
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research

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