DoD GEIS

Annual Report

Fiscal Year 2001

DoD GEIS | Global Emerging Infections System

Executive Summary

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Completing its fourth year of operations during 2001, the DoD Global Emerging Infections System (DoD-GEIS) was hailed in an extensive formal program review by the Institute of Medicine of the National Academy of Sciences as:

"a critical and unique resource of the United States in the context of global affairs. It is the only U.S. entity that is devoted to infectious diseases globally and that has broad-based laboratory capacities in overseas settings."

The powerful capabilities of DoD-GEIS should be seen as much more than enhancing military health and readiness or even the health of Americans in general. As highlighted in the recent National Intelligence Estimate, "The Global Infectious Disease Threat and its Implications for the United States," emerging infectious diseases are a global security issue. They have the capability to harm U.S. interests abroad through destabilizing key institutions, obstructing trade and human migration, slowing or reversing economic growth, fomenting social unrest, and complicating our response to refugee situations by increasing the demand for humanitarian intervention. They also have a potential association with biological terrorism and warfare.

DoD-GEIS activities, which are performed under a mandate to DoD contained in the Presidential Decision Directive on Emerging Infections (NTSC-7), occur in three primary settings: the Military Health System (MHS); the DoD overseas medical research units in Peru (NMRCD), Egypt (NAMRU-3), Kenya (USAMRU-K), Thailand (AFRIMS), and Indonesia (NAMRU-2); and various training, leadership, and capacity building partnerships with regional military commands and other governmental and international agencies.

The Presidential Decision Directive called for implementation actions in several areas:

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

Within the MHS, DoD-GEIS has focused most of its resources on facilitating general improvements of the military public health laboratory system, establishing laboratory-based surveillance for respiratory diseases and antibiotic resistance, and fielding for the National Capitol Region a near-real-time prototype syndromic surveillance system for emerging infections to include bioterrorism. After 11 September 2001, this system, the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE), was expanded from a pilot project to encompass more than 300 tri-service Medical

Treatment Facilities around the world. GEIS recognized that an ideal system to detect the full spectrum of emerging infections outbreaks would be a system of systems integrating other potentially useful civilian and military data from nurse hotlines, intensive care units, pharmacies, laboratories, and veterinary surveillance sources. To this end early in FY 2001 the GEIS group at WRAIR partnered with the Johns Hopkins Applied Physics Lab and several other institutions and obtained a grant of more than $10 million from the Defense Advance Research Projects Agency (DARPA) to develop a prototype integrated civil-military health indicator surveillance system for the NCA called ESSENCE II.

A key step taken during FY 2001 to reconstitute and unify the DoD network of laboratories providing public health laboratory services was directed towards developing an on-line DoD Directory of Military Public Health Laboratory Services. This directory, to be managed by Armed Forces Institute of Pathology, would include public health services that have been provided by a highly competent but uncoordinated and in some cases generally unknown collection of DoD clinical, research, and veterinary laboratories around the world.

Surveillance and respiratory diseases continue to be an important focus of the DoD-GEIS program. A highlighted effort is the ongoing operation and expansion of the tri-service DoD Influenza Surveillance System under the leadership of the Air Force Institute for Environmental, Safety, and Occupational Health Risk (AFIERA). Seventeen sentinel sites, 49 non-sentinel sites, and multiple DoD overseas labs submitted 3702 specimens for analysis during FY 2001. The impact of the DoD influenza surveillance program continued in that one of its viral isolates from Panama was chosen as one of three strains included in the 2000/2001 vaccine, 70 million doses of which are distributed to Americans. The Naval Health Research Center (NHRC) in San Diego provided an outstanding complement to the AFIERA efforts through application of a variety of specialized laboratory capabilities to conduct rigorous, in-depth respiratory disease surveillance at military training centers.

Timely, comprehensive, and consolidated clinical and epidemiologic characterization of deaths in military personnel is a core public health function that did not exist before investments made by DoD-GEIS. Emerging infectious diseases, such as hantavirus pulmonary syndrome, new strains of influenza, Legionnaires disease, and even rare cases of adenovirus infection in recruits, may present as rapidly progressive and unexplained fatal illnesses. While DoD-GEIS has supported mortality surveillance for several years, in FY 2001 significant advances were made to resource and systematize the effort, including the assignment of a dedicated active duty epidemiologist to the Office of the Armed Forces Medical Examiner at the AFIP.

Due to the size of the U.S. military presence on the Korean peninsula, the need for maximal military readiness, and the spectrum of disease threats there, DoD-GEIS has made a specific commitment to provide 18th MEDCOM with resources to support activities that go beyond the standard military medical surveillance program. During FY 2001, initiatives focused on development of an integrated malaria and Japanese encephalitis vector surveillance system, rodent-borne disease surveillance for areas of high-risk, and tick-borne disease surveillance to support risk analysis and identify potential human threats. Close collaborations with the South Korean government and academic institutions have been cultivated over the last several years and are helping obtain valuable current incidence data on South Korean military and civilian populations.

Internationally, DoD-GEIS, largely through the overseas medical research laboratories, conducted substantial collaborations with institutions in 34 countries around the world. The work focused on surveillance for drug-resistant malaria, antibiotic-resistant enteric organisms, influenza, and unexplained febrile illness. A variety of innovative tools for surveillance have been implemented, such as the Early Warning Outbreak

Recognition System (EWORS) developed by NAMRU-2 and the Indonesian Ministry of Health. Surveillance findings from the overseas labs have changed therapeutic policies and practices in several areas of the world. Skills for performing surveillance of drug-resistant malaria are being actively shared with partner countries. A number of new agents have been recognized and are being further defined. Some of the changes in treatment policy resulting from surveillance on malaria and other febrile diseases probably are saving lives. The overseas laboratories, with CINC support, have been providing training opportunities for local scientists and public health technicians and have been providing key regional leadership.

"Enhance biomedical and behavioral research efforts on emerging infectious diseases."

Although the primary DoD-GEIS mandate is not research, DoD-GEIS has facilitated the research agendas of the Military Infectious Disease Research Program and other partners. In many cases this is from the added value of a steady stream of surveillance specimens for use in the evaluation of diagnostics. In other cases, surveillance data, such as that for antimalaria drug resistance, helps guide the malaria drug development program. A particular research emphasis of DoD-GEIS has been the development of innovative methods for surveillance such as ESSENCE, EWORS, and the joint DoD-GEIS/NASA Rift Valley Fever predictive model based on information from satellite remote sensing.

"Expand formal training and outreach to health care providers"

A major focus of DoD-GEIS during FY 2001 was training. The IOM evaluation of DoD-GEIS strongly recommended this emphasis as a way to build up much needed local capacity and also expand DoD's own internal resources. All five tropical overseas medical research units supported various training initiatives. These included not only laboratory and epidemiology training for internal staff but also outreach to host-nation partners. Several of the greatest success stories have been the ongoing 10-day courses on the conduct of outbreak investigations that NAMRU-2 has been offering in Southeast Asia and NMRCD's training of host-nation personnel to conduct in vivo antimalarial drug-resistance studies. Another highlight of FY 2001 was that with strong support from Southern Command's Humanitarian Assistance Program, DoD-GEIS was also able to establish three pilot regions in Peru for a laboratory-based surveillance initiative. Like a similar SOUTHCOM-funded GEIS initiative in the Caribbean, this training project has been focused on the creation of computerized networks for hierarchical reporting. The backbone of the effort is the CDC-developed Public Health Laboratory Information System (PHLIS) software.

"Encourage other nations and international organizations to assign higher priority to emerging infectious diseases."

"Support the WHO and other bodies in playing a stronger role in the surveillance, prevention, and response to emerging infectious diseases."

As noted by the IOM, DoD-GEIS continues to be a unique asset of the U.S. government in advancing the response to emerging infections around the world. Government-to-government public health surveillance collaborations are taking place in more than 30 countries throughout the world. Elements of DoD-GEIS work closely with the World Health Organization and many of its regional offices. DoD-GEIS has been a regular supporter of the U.S. government's efforts under the Asia Pacific Economic Cooperation and helped craft documents that led in November 2000 to the APEC Summit's Leaders Declaration on emerging infections.

A notable step forward in supporting the DoD-GEIS mission globally was the placement this fiscal year of a U.S. Navy preventive medicine officer in the Communicable Disease Surveillance and Response directorate at the WHO Headquarters in Geneva. With partial programmatic funding from DoD-GEIS,

this officer is heading up a civil-military liaison section that should further expand international capabilities for emerging infections surveillance by improved coordination of relevant military capabilities. This officer's assignment to the key focal point for international public health surveillance information has also already proven invaluable in understanding threats to U.S. forces such as the 2001 outbreak of Crimean-Congo hemorrhagic fever in Kosovo.

In summary, DoD-GEIS is making considerable progress in improving the capabilities of the military health care system essential to meet the special requirements of service families. The program evaluation by the Institute of Medicine will greatly facilitate the interactive process of refining the program and improving its effectiveness. This effectiveness is measured not only though effects on force protection and the public health of other beneficiaries, but it is also measured through benefits that inevitably accrue to the health of the general American population. Likewise, diverse nations continue to partner with DoD-GEIS in the best spirit of international cooperation and are thus also benefited. Old partnerships have been strengthened and new ones continue to bloom. In many places, the universal value that public health represents has served as a focal point for progress across a spectrum of health, economic, and diplomatic interests where previously there was little collaboration.

Consolidated FY01 DoD-GEIS Report

Completing its fourth year of operations during 2001, the DoD Global Emerging Infections System (DoD-GEIS) was hailed in an extensive formal program review by the Institute of Medicine of the National Academy of Sciences as:

"..a critical and unique resource of the United States in the context of global affairs. It is the only U.S. entity that is devoted to infectious diseases globally and that has broad-based laboratory capacities in overseas settings."

The powerful capabilities of DoD-GEIS should be seen as much more than solely enhancing military health and readiness or even the health of Americans in general. As highlighted in the recent National Intelligence Estimate on Emerging Infections, emerging infectious diseases are a global security issue. They have the capability to harm U.S. interests abroad through destabilizing key institutions, obstructing trade and human migration, slowing or reversing economic growth, fomenting social unrest, and complicating our response to refugee situations by increasing the demand for humanitarian intervention. They also have a potential association with biological terrorism and warfare.

The Presidential Decision Directive (PDD) on Emerging Infections (National Science and Technology Council-7, 1996) formally expanded DoD's mission in recognition of the fact that emerging infections were an internal health care and readiness challenge for DoD, but also because DoD was in a unique position to contribute to the national agenda. The PDD emphasized that:

"…the national and international system of infectious disease surveillance, prevention, and response is inadequate to protect the health of United States citizens from emerging infectious diseases."

It specifically tasked DoD to undertake a global effort that was characterized by:

"…centralized coordination; improved preventive health programs and epidemiological capabilities; and enhanced involvement with military treatment facilities and United States and overseas laboratories."

The mandate emphasized using the DoD overseas medical research units as foundation stones for the U.S. government's international outreach efforts. DoD was specifically tasked to:

"… ensure the availability of diagnostic capabilities at its three domestic and six overseas* [medical research] *laboratories … DoD will make available its overseas laboratory facilities, as appropriate, to serve as focal points for the training of foreign technicians and epidemiologists."

To execute this mandate in fiscal year 2001 DoD-GEIS received core funding of $8,000,000 from the Defense Health Program. The provision of the basic programmatic infrastructure that this budget allowed put many DoD recipients of DoD-GEIS funds into a position to create strong sources of leverage and enter into collaborations with other organizations that in turn provided funding or other sources of "hard" support that directly benefited the DoD-GEIS mission. Other entities that contributed resources during FY 2001 to synergize with the core DoD-GEIS investment include the Defense Advanced Research Projects Agency (DARPA), the Centers for Disease Control and Prevention (CDC), the U.S. Agency for International Development (USAID), the DoD Overseas, Humanitarian, Disaster and Civic Aid Program (OHDACA), the Military Infectious Disease Research Program (MIDRP), the World Health Organization (WHO) and its subordinate offices, foreign ministries of health, and industrial partners

interested in the development of diagnostics, vaccines, and antibiotic resistance data. The Institute of Medicine recognized aspects of these synergies in their report on DoD-GEIS by stating:

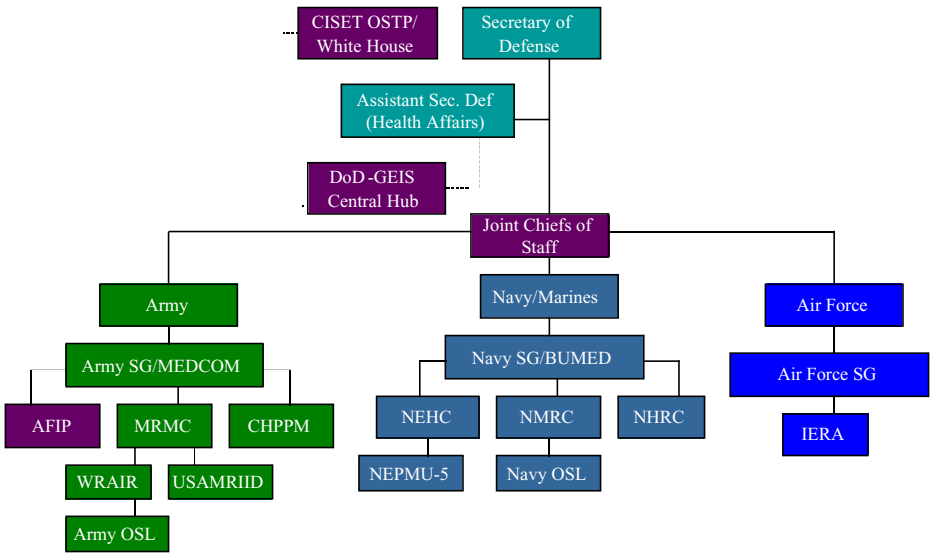
"GEIS has also done an astounding job of leveraging minimal resources to implement capacity-building projects in support of its public health partners overseas."

DoD-GEIS supports activities in three primary settings. The first focuses on the Military Health System (MHS). In the MHS each service pursues programs and projects directed against emerging infectious disease manifestations in DoD personnel. Activities are chosen for support and reviewed annually based on several factors:

- Potential to fill a critical gap in MHS public health programs
- Likelihood of tri-service or service-wide benefits
- Facilitation of more timely public health actions
- Responsiveness to critical operational theater needs
- Accessibility of the non-fiscal resources needed for execution
- Scientific quality
- Other than an existing core MHS public health program
- Consistency with the DoD-GEIS five-year strategic plan

The second major setting for DoD-GEIS work is the five DoD tropical overseas medical research units in Egypt (NAMRU-3), Kenya (USAMRU-K), Thailand (AFRIMS), Indonesia (NAMRU-2), and Peru (NMRCD). The overseas lab program emphasizes use of DoD expertise to improve regional capacity to recognize, track, and respond to emerging illnesses of interest. Timely, sensitive, specific, laboratory-based sentinel surveillance programs are a key activity and their particular foci reflect DoD overseas lab strengths and the needs of the Department of Defense, the U.S. government, the host country, and the international community as articulated by the World Health Organization.

The U.S. Unified Commands (headed by the Commanders in Chief or CINCs) support the third major dimension of DoD-GEIS coordinated activities: training and external relations. As part of their theater engagement plans, the CINCs have increasingly seen the value of public health initiatives such as those promoted by DoD-GEIS. Since DoD-GEIS grew out of a national response to an international problem, its activities are highly cross-disciplinary and collaborative.



The Eight Implementing Actions of Presidential Decision Directive NSTC-7

Eight key areas of action were laid out in the Presidential Decision Directive. DoD-GEIS has used these as a framework for organizing its approach to the problem of global emerging infectious diseases. This annual report will highlight for each of the PDD's implementing actions relevant accomplishments in FY 2001.

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

Activities Based in the Military Health System

General Public Health Laboratory Improvement and Laboratory-Based Surveillance

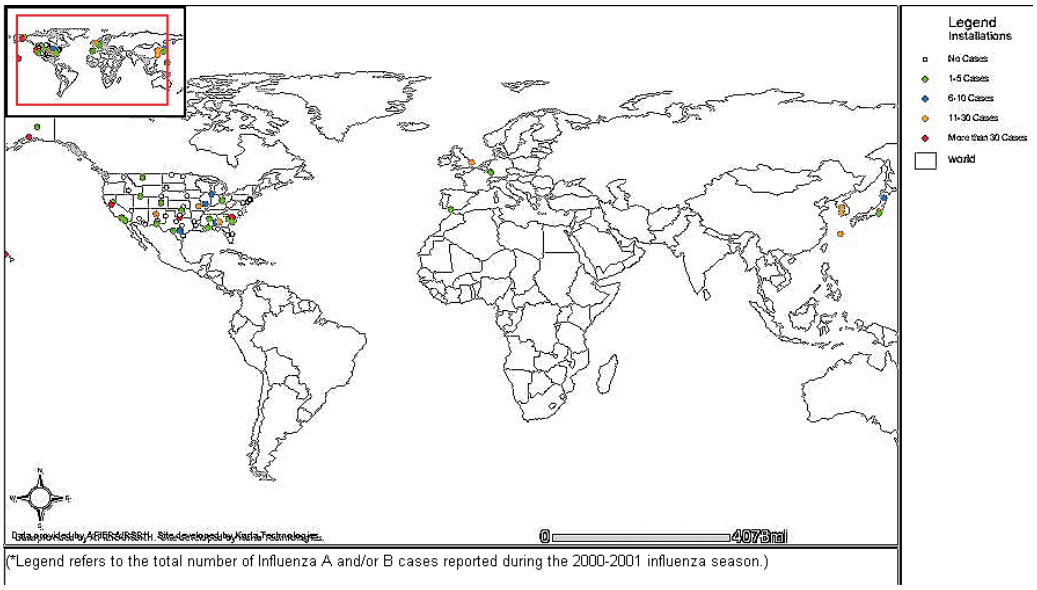
Core to any public health program involved with infectious diseases are laboratory capabilities. As was highlighted at the DoD-GEIS sponsored Military Public Health Laboratory Symposium and Workshop held in September of 1999, these capabilities differ in significant ways from those established for routine patient care. Public health laboratories must focus on surveillance and outbreak detection, specialized and reference laboratory testing, population-based data integration, formal coordination and information exchange with regional and national networks, flexibility and capacity to meet emergency needs, and applied research (Wilcke BW Jr, The state of public health laboratories, *Mil Med*, 2000;165(Suppl 2): 8-11). In recent decades, restructuring of civilian and military health care and changes in the practice of medicine inadvertently created challenges to the delivery of critical, high-quality public health laboratory services. The Military Public Health Laboratory Symposium highlighted these and made specific recommendations that were endorsed by the Armed Forces Epidemiological Board.

A key step taken during FY 2001 to reconstitute and unify the DoD network of laboratories providing public health laboratory services was directed towards developing an on-line DoD Directory of Military Public Health Laboratory Services. These would include public health services provided by a highly competent but uncoordinated and in some cases generally unknown collection of DoD clinical, research, and veterinary laboratories around the world. These are or should come under the oversight of the Armed Forces Institute of Pathology (AFIP) office that manages the DoD implementation of the Clinical Laboratory Improvement Program and which will manage the on-line directory. The IOM characterized this initiative as "making good organizational sense" and noted the potential of this tool to make DoD's assets "more accessible … and [for] encouraging collaboration and use of the full spectrum of DoD laboratory capabilities in the conduct of GEIS projects."

To this end during FY 2001 a Memorandum of Agreement (MOA) was developed between the DoD-GEIS Central Hub and the AFIP, and start-up funding was provided. A web-based prototype developed in-house by the DoD-GEIS Central Hub was reviewed by the AFIP, hardware to support this system was purchased, installed, and tested, and the necessary

DoD Influenza Surveillance Program Develops Capabilities to Address Vaccine Shortages

The 2000-2001 influenza season began under the cloud of a developing crisis. In July 2000, the Centers for Disease Control and Prevention announced that there would be a delay in delivering vaccine and a possible shortage. With little time before the influenza season began, the Brooks Virology Laboratory (BVL) at Brooks Air Force Base, TX, quickly took a number of actions to minimize the delay's effects. BVL influenza data were extracted twice a week, and the DoD Influenza Surveillance website was updated with the current influenza results to improve the timeliness of information dissemination. The development of a mapping function that shows current influenza activity around the globe was another major step. Using a world map (as opposed to the US alone) created some challenges but a product was developed. The timeliness of the information made available a number of opportunities for decision-making, such as the reallocation of influenza vaccine to areas at highest risk if the vaccine delay or shortage was affecting distribution. The map represents cumulative influenza activity during FY01.



(*Legend refers to the total number of Influenza A and/or B cases reported during the 2000-2001 influenza season.)

Fortunately, the FY01 influenza season started out slowly and was relatively mild. One of the challenges of influenza is the unknown severity, in advance, of each influenza season. Had there been a greater disease burden, it is likely that vaccine distribution would have been altered to meet the needs of the areas most affected. The world map of DoD influenza activity would have played a key role in identifying those areas at highest risk and would have aided the redistribution plan.

The DoD Influenza Surveillance Program continues to evolve to meet the challenges of the disease and the military population it serves. Collaboration with national and international health organizations enhances its abilities, as well as its reputation, as a vital resource.

personnel have been hired. The AFIP also procured freezers for the long-term centralized storage of specimens of public health importance (e.g., specimens associated with significant clinical or epidemiologic outcomes but which are universally negative to tests for known agents). Implementation of the directory is expected in the Spring of 2002. The U.S. Army Medical Research Institute of Infectious Disease (USAMRIID) has unique public health laboratory capabilities. DoD-GEIS has helped USAMRIID leverage its renowned research capabilities so as to maintain the capacity to provide DoD and the nation with specialized public health services. These services usually are related to agents that must be handled at the BSL-3 or BSL-4 level. DoD-GEIS support helped USAMRIID continue as a WHO reference center for the hemorrhagic fever viruses and other arthropod-borne viruses and helped USAMRIID support diagnostic confirmation for lower level labs, evaluation of diagnostic assays, transfer of diagnostic technology to U.S. military medical laboratories and other U.S. and international public health laboratories, production and stockpiling of a wide variety of reagents, and outbreak response. During FY 2001, over 1,500 assays were completed for patients and animals being evaluated for infections with agents such as hantaviruses, West Nile virus, and the pathogens that cause anthrax, plague, ebola, and Venezuelan equine encephalitis. Because none of these assays has a sufficient commercial market to encourage the expense of FDA approval, USAMRIID follows special testing requirements and reporting procedures under the Clinical Laboratory Improvement Act. Related training was coordinated for both in-house personnel and the Theater Area Medical Laboratory. Outbreak investigations of West Nile infection and anthrax were supported also.

Respiratory Disease Surveillance and Capacity Building

Surveillance and respiratory diseases continue to be an important focus of the DoD-GEIS program. A highlighted effort in this regard is the ongoing operation and expansion of the DoD Influenza Surveillance System under the leadership of the Air Force Institute for Environmental, Safety, and Occupational Health Risk (AFIERA). Operations are guided by a plan developed at an annual meeting of the DoD Influenza Surveillance Working Group. It is now a fully tri-service effort that also includes Army and Navy overseas labs as sources of specimens.

Seventeen sentinel sites, 49 non-sentinel sites, and multiple DoD overseas labs submitted 3,702 specimens for analysis during FY 2001. Prominent observations were that influenza B was almost equal in incidence to influenza A and that the circulating strains were well matched to the 2000-2001 vaccine. Once again, in FY 2001 this program was only one of two efforts invited to present surveillance data to the FDA advisory committee that makes recommendations concerning the composition of the annual influenza vaccine. This input supported the FDA and WHO decisions to continue to recommend inclusion of the AFIERA-isolated H3N2 Panama strain influenza virus in the 2001-2002 vaccine. AFIERA made significant advances also in the dissemination of their surveillance data via the World Wide Web. Reporting of global DoD surveillance data on the web was increased from monthly to twice weekly (https://pestilence.brooks.af.mil/Influenza) and an improved presentation format with geographic information system (GIS) drill-down capability for assessments of world-wide DoD influenza activity was introduced. This may help direct scarce vaccine supplies to areas with the highest disease activity. Through a DoD-GEIS collaboration with the Uganda Virus Research Institute, arrangements were also made to have AFIERA become, starting in FY 2002, one of the few recipients in the world of influenza surveillance specimens from sub-Saharan Africa.

Hantavirus Disease at Mountain Home Air Force Base, Idaho

An emerging condition of growing importance, hantavirus pulmonary syndrome (HPS) was first recognized in the Four Corners region of the southwestern United States in 1993. In January 2001, a case of HPS was diagnosed in a 21-year-old active-duty male living on Mountain Home Air Force Base in Idaho. The airman's case became unusually severe but after a month's coma and the amputation of his hands and feet, he did survive. The outcome of this case of HPS is a sobering reminder of the risk HPS poses to military personnel. This disease is caused by any one of a number of viruses in the family Bunyaviridae. Deer mice are the reservoir for Sin Nombre virus, the cause of this case, and an infection is acquired when a person inhales virus in aerosolized rodent feces or urine.

A program of education and increased rodent trapping was instituted on base to reduce the risk of additional infections, and a professional cleanup company was hired to clean one rodent-contaminated building. Realizing that the rodents and the contamination likely would be a continuing problem, representatives from the US Army Center for Health Promotion and Preventive Medicine–West and the USAF Institute for Environment, Safety and Occupational Health Risk Analysis were asked to make an on-site evaluation of the problem and make recommendations for short-term and long-term risk reduction. In early April 2001, a number of environments on the main base and Saylor Creek Range were examined. Contamination in those areas ranged from none to scattered droppings in base housing to the floors of storage vans covered in mouse and rat droppings (Figure). Large, plastic boxes of deployment equipment kept outdoors were severely infested, and live mice and nests were observed in the boxes. In several instances, debris close to buildings provided harborage for mice, and poor construction (e.g., gaps around doors, poorly fitting siding) allowed mice easy entry into buildings.

Recommendations for personnel protection and cleanup were tailored for the different situations. For minor contamination, which could be easily disinfected without generating aerosols, recommendations included spraying with a disinfectant, wiping up with a paper towel, and discarding the towel in a sealed bag. Personal protective equipment in this situation could be limited to rubber gloves. Heavily contaminated buildings in which cleanup would generate dusts or aerosols require extensive use of personal protective gear, such as face mask with P-100 (HEPA) filters, tyvec coveralls, and rubber boots. Some situations, such as crawl spaces under buildings and infrequently-visited storage facilities, pose particular problems. In these areas, disinfection is difficult, cleanup is extremely labor intensive, and reinfestation and recontamination occur rapidly. If access to these areas is limited, both in frequency and duration, disinfection and cleanup may be inefficient. In these situations, the most reasonable approach is to use a mask with P-100 filters, coveralls, gloves and boots while in the environment, and decontaminate the equipment and anything removed from the area.

The rodent infestation at this Air Force installation is not unique, and many DoD facilities, particularly those in the western United States, are at risk of hantavirus. The recommendations made for risk reduction at this particular base also are appropriate for those installations and are being included in DoD pest management guidance.

Mouse and rat feces on floor of storage van.

AFIERA is also unusual in its capability to sequence the hemagglutinin gene of influenza. In a phenomenal accomplishment that will enhance surveillance for strain evolution, this year AFIERA became one of the few labs (and the only DoD lab) capable of neuraminidase characterization. They also made great advances in the use of PCR techniques for real-time detection of influenza viruses, keeping DoD on the cutting edge of surveillance for what caused more deaths (over 40,000) among military personnel during the last century than any other infectious disease. Such real-time capabilities can help rapidly distinguish between influenza and more worrisome causes of influenza-like illnesses, such as anthrax. DoD-GEIS funding provided to AFIERA is also helping to conduct an influenza vaccine effectiveness study in young health care personnel at Misawa Air Base in Japan. This is designed to help define levels of vaccine breakthrough, risk factors for vaccine failure, ideal immunization frequency, and cost-effectiveness issues in the active duty setting.

The Naval Health Research Center (NHRC) in San Diego provided an outstanding complement to the AFIERA efforts. NHRC used its specialized laboratory capabilities to conduct rigorous in-depth respiratory disease surveillance at military training centers. The impact of NHRC's College of American Pathologists certified lab was felt during FY 2001 through work involving 17 collaborating military commands in the U.S. Many of the respiratory bacteria and virus laboratory capabilities that DoD-GEIS supports at NHRC are unique within DoD and are providing insight into potentially preventable, previously uncharacterized causes of morbidity. NHRC has also completed the application for status as a WHO Collaborating Center.

Active surveillance for febrile respiratory illnesses (FRI) was conducted at 8 tri-service basic training centers with weekly rates reported and specimens sent to San Diego for laboratory testing. Data are rapidly made available via the NHRC web site (www.nhrc.navy.mil/geis). Among 7,888 specimens evaluated this fiscal year, 61% were adenovirus-positive. The laboratory found adenovirus in pathologic specimens from two military recruits who died following an episode of acute respiratory illness. This provided further impetus for DoD to find a manufacturing partner willing to begin production of the adenovirus vaccine again. Molecular characterization of adenovirus surveillance strains isolated from recruits is also ongoing and may help identify significant differences from vaccine strains.

Recognizing the emergence of antibiotic-resistant *Streptococcus pyogenes* in recruits, NHRC has also continued surveillance for this pathogen. Between February 1998 and September 2001, 622 isolates from training centers have been studied, with resistance documented at 8% for erythromycin (an important second-line drug for penicillin-allergic recruits during the common recruit center epidemics). Testing for invasive *S. pneumoniae* in 282 isolates from seven military medical centers also documented resistance. Full or partial penicillin resistance was documented in 34% of these specimens and 22% had resistance to three or more antibiotics. Pertussis is an increasingly recognized problem for young adults, and recruits seem to be no exception. NHRC has established surveillance for *Bordetella pertussis* at four basic training centers and have enrolled more than 150 recruits. Using culture, serology, and PCR, 34 of 65 (52%) recruits were positive on at least one test for pertussis. Using cell culture, PCR, and serology, respiratory syncytial virus (RSV) was also documented as a concern through surveillance at Fort Benning, GA, the Marine Corps Recruit Depot in San Diego, and at the Royal Navy Recruit camp in the United Kingdom. Three hundred and ten recruits meeting the "suspect" case definition submitted specimens, with rates for RSV ranging from 11.5% to 15.3% by training center.

NHRC has used and expanded on GEIS-supported infrastructure in many ways. It has enabled them to embark on many valuable projects, such as the evaluation of rapid tests for influenza and a collaboration with the AFIP to develop a PCR test for influenza and adenovirus that can be used on specimens shipped at

Unexplained Deaths May Herald a New Disease

The newly established Mortality Surveillance Division in the Office of the Armed Forces Medical Examiner is a joint effort of the DoD-GEIS and the Armed Forces Institute of Pathology. It was created to obtain baseline mortality data on military personnel and monitor in near real-time cause-specific mortality among service personnel, an objective that is facilitated by the Division's location at the AFIP. A specific goal is to immediately investigate deaths without a clear explanation so they can be evaluated for a possible infectious cause. The division begins to collect data within hours of an active duty member's death being reported to casualty offices. Supplementary sources of mortality information include death certificates, medical records, autopsy reports, AFIP consultations, toxicology studies, and investigative reports from legal agencies. Many emerging infectious diseases, such as Legionnaire's disease, hantavirus pulmonary syndrome, and H5N1 influenza, were first recognized when they caused unexpected deaths.

In a recent example, a Special Forces soldier died of malaria after returning from duty in Nigeria. The Division was notified and began an investigation to determine if the death was caused by a new drug-resistant strain of malaria, which would be important news for those preparing military personnel for travel to Africa. After a thorough investigation, the Division found that the problem was not drug resistance but the inadequate use of personal protective measures. With this information, medical personnel could advise commanders on the proper actions to prevent this situation from recurring.

The infrastructure supported by DoD-GEIS provides capabilities that go beyond detection of emerging infections, however. The Mortality Surveillance Division was called into action after the September 11th attacks. The effort to identify the remains of the victims was staffed by many specialists from the AFIP. One of those, MAJ Lisa Pearse, is the chief of the Mortality Surveillance Division. She created an electronic database to track victim identification information for those who died in the attack on the Pentagon. This is the first time that the Office of the Armed Forces Medical Examiner has used an electronic tracking database to supplement paper records. This made the reports coming from the field team more accurate and timely. Dr. Pearse described the tracking system is this way: "The database tracked demographic information on the missing [and]….as identifications were made, we utilized the database to keep track of who had been identified and by what method (dental, fingerprint, or DNA)." The Division is analyzing the data to evaluate casualty identification methods and injury patterns and is assisting Pentagon engineers in identifying structural issues in the building that might have influenced survival patterns.

Integrating the insights of epidemiologists, pathologists, clinicians, and legal investigators gives the Division a unique perspective from which to identify emerging infectious diseases of public health significance.

A dead service member is more than just an individual tragedy; the death may be a harbinger of disease and death to come. Investigations into unexplained deaths, which are relatively rare events in the military, may reveal critical, population-based insights that can be used to focus prevention efforts. This coffin at the Dover AFB Port Mortuary holds recently identified remains of a victim of the September 11th attack on the Pentagon.

ambient temperature. Such tools would greatly facilitate global influenza surveillance. Another example of leveraging is that the NHRC DoD-GEIS laboratory has been able to take on, with supplementary funding and support from other sources, the conduct of the largest clinical trial (about 190,000 volunteers planned) ever done within the DoD. This is a double-blind/placebo controlled clinical effectiveness trial of the 23-valent pneumococcal vaccine.

Mortality Surveillance

Timely, comprehensive, and consolidated clinical and epidemiologic characterization of deaths in military personnel is a core public health function that did not exist before investments made by DoD-GEIS. Emerging infectious diseases, such as hantavirus pulmonary syndrome, new strains of influenza, Legionnaires' disease, and rare cases of adenovirus infection in recruits, may present as rapidly progressive and unexplained fatal illnesses. Prompt centralized recognition of these events is important to ensure a proper and timely public health response. While DoD-GEIS has supported mortality surveillance for several years, significant advances were made to resource and systematize the effort during FY 2001. A MOA was signed with the AFIP highlighting the functional characteristics of the system that will be managed by the Office of the Armed Forces Medical Examiner. The AFIP identified a military authorization and a very capable Army active duty physician-epidemiologist was assigned to fill the position of mortality surveillance officer. Mechanisms were exercised to rapidly disseminate information about suspicious deaths. The development of syndrome-based protocols for specimen collection and analysis are underway, along with expansion of the rapid alert mechanisms to capture Navy and Air Force deaths.

Surveillance and Response for Sexually Transmitted Diseases and Antibiotic Resistance

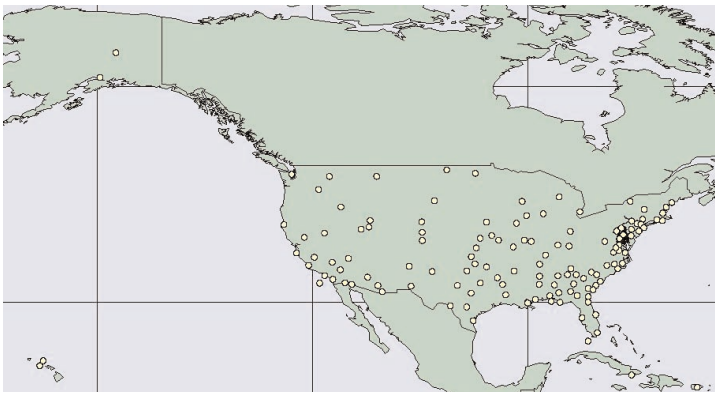
Though often not thought of as dramatic causes of morbidity and mortality, both the acute and the insidious, chronic effects of sexually transmitted diseases can disrupt military readiness, lead to evacuations from the field for problems such as pelvic inflammatory disease, and cause significant long-term health care costs and suffering. This year the DoD-GEIS Central Hub addressed STDs in the military in several ways. DoD-GEIS provided sustained epidemiologic expertise to help the DoD Sexually Transmitted Diseases Prevention Committee (STDPC) characterize the extent of the DoD problem. Some of the epidemiologic issues defined were the inconsistent methods used by the services to conduct STD surveillance and the fact that data on viral STDs and antibiotic resistance are not being captured. On 2 October 2001 DoD-GEIS and the U.S. Medicine Institute for Health Studies (USMI) sponsored for about 85 policy and scientific experts an interactive forum on STDs at the Sumner Museum in Washington, DC. The meeting, entitled "STDs: Regaining Lost Ground & Preparing for the Future," was largely funded by industry and foundation sources. Attendees were drawn from the military disease control community, academia,

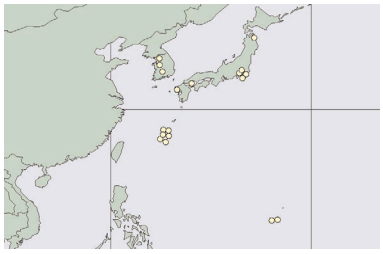
ESSENCE Expands in Response to Terrorist Threat

The Electronic Surveillance System for the Early Notification of Community Based Epidemics (ESSENCE) was developed by the DoD Global Emerging Infections Surveillance and Response System in response to its mandate under Presidential Decision Directive NSTC-7 on emerging infections. ESSENCE is a developmental program that began approximately two years ago with a goal of establishing a sensitive, specific, timely, standardized, and flexible health indicator surveillance system for the National Capital Region (NCR). ESSENCE has focused on the transparent acquisition, analysis, interpretation, and dissemination via secure web site of daily Ambulatory Data System syndromic data from over 100 Military Health System primary care clinics and emergency rooms in the NCR.

In the wake of 11 September 2001, the need to track the health of all military personnel and beneficiaries became apparent. Within 10 days, ESSENCE expanded to include the processing of daily data from 121 Army, 110 Navy, 80 Air Force, and 2 Coast Guard installations worldwide (see maps). To prioritize the more than 2,700 health status graphs now generated daily, an alert roster is produced linked to detailed graphs and maps. To further track the health of military communities worldwide, the ESSENCE vision has been expanded to include integration of civilian data (which is essential for optimal sensitivity and representativeness in many DoD communities), more advanced mathematical and alert methodologies, and the addition of other health indicators such as intensive care unit data, over-the-counter pharmacy data, school absenteeism, and laboratory test requests. ESSENCE II, as this expanded version of ESSENCE is called, is a project of a DARPA-funded consortium of Johns Hopkins University Applied Physics Lab and Bloomberg School of Public Health, DoD-GEIS, George Washington University School of Public Health, Carnegie Mellon University, IBM, and Cycorp.

Geographic Locations Participating in ESSENCE





industry, congressional staff, retired flag officers, and scientists from CDC and NIH. Challenges to implementing improvements in civilian and military STD control programs were identified and discussed, along with the role of cost-effective screening and the need for managed care priorities to be sensitive to public health priorities such as the conduct of cultures for antibiotic resistance. Other needs included communicating in a clear and concise way to legislators and civic leaders the nature and scope of this hidden problem. To further promote solutions within DoD to the problem of STD prevention and control, DoD-GEIS provided FY 2001 funding for the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) to sponsor a tri-service meeting to explore the concept of a DoD STD Control Office at USACHPPM. This office would serve as the dedicated staff of the STDPC to provide evidence-based epidemiologic support, help operationalize related policies, and share best practices. The meeting will take place during early FY 2002.

One aspect of STD prevention and control needing additional focus has been surveillance for antibiotic-resistant gonococci. While the DoD generally follows CDC guidelines for the management of STDs, those guidelines are not necessarily ideal for places where drug-resistance patterns differ from what is the current pattern on the U.S. mainland. DoD-GEIS has continued this year to support the participation of Fort Bragg, NC, and Tripler Army Medical Center, HI, in the CDC Gonococcal Isolate Surveillance Program (GISP). Additional DoD sites have been identified for enrollment, including a site in Korea.

For resistance of other organisms and to move the DoD forward on using automated laboratory-based surveillance as a key public health methodology, DoD-GEIS has entered into a Cooperative Research and Development Agreement with Focus Technologies, Inc., a company that has developed and manages an internationally respected network for antibiotic resistance surveillance, The Surveillance Network® (TSN®). During FY 2001 two key medical centers were enrolled in the TSN network, Tripler Army Medical Center and Wilford Hall Air Force Medical Center. Daily downloads of antibiotic resistance patterns from routine microbiology lab cultures were arranged. Arrangements have been made to have Keesler Air Force Medical Center join the network in 2002. Once five DoD sites are fully operational, a DoD network will be formed and a centralized DoD antibiotic resistance information sharing mechanism established. Participation in the TSN system facilitates daily, independent quality-assurance review and feedback to microbiology labs, the continuous updating of antibiograms, the comparison of one institution's experience with that of other similar military and civilian institutions, and access to data for MHS-wide and local policy making purposes.

During FY 2001 the U.S. Government published part 1 of the Federal Inter-Agency Antibiotic Resistance Task Force Action Plan. Part 1 focuses on delineating priorities for improving surveillance, prevention and control, product development, and research as they relate to antibiotic resistance within the U.S. Part 2 will focus on international initiatives that the government wishes to promote. The DoD has been an active contributor to this consensus process since, as the manager of one of the two large federal health care systems, it should serve as a model for non-federal entities trying to respond to Federal Task Force objectives. DoD-GEIS has been tracking DoD antibiotic resistance initiatives such as work of the DoD Pharmacoeconomic Center in preparation for the first Task Force progress report that will be published in 2002.

Development of Health Indicator and Other Innovative Surveillance Tools

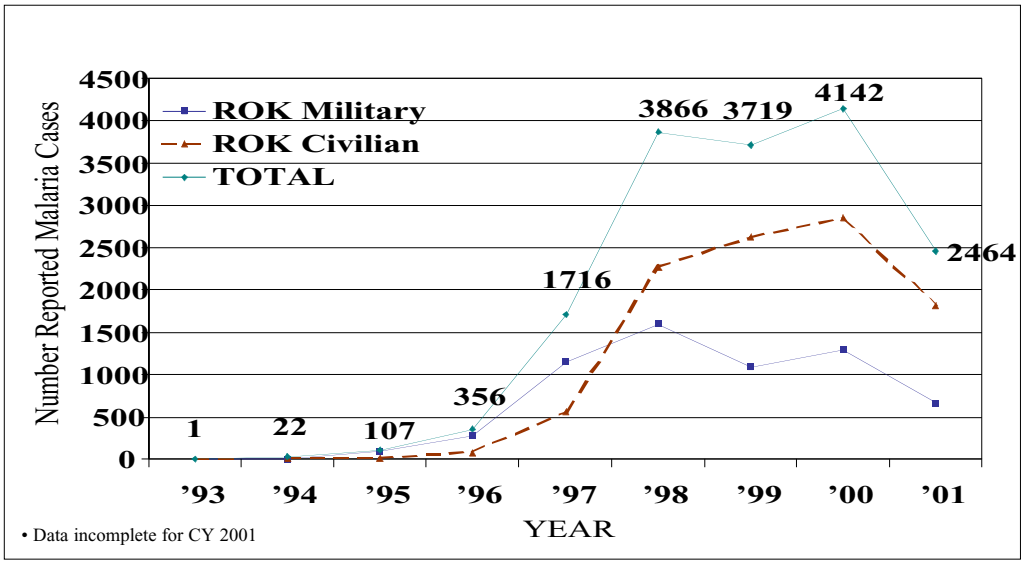
Emerging infections, to include bioterrorism, must be recognized as promptly as possible. A consensus has emerged that real-time health indicator surveillance, to include surveillance for syndromes in addition to laboratory-confirmed diagnoses, may promote earlier detection of outbreaks and important sentinel events, facilitate the evidence-based allocation of rapid response assets (e.g., drugs, vaccines, public health responders), and provide civic leaders with the information needed for credible risk communication to populations perceiving a risk.

DoD-GEIS has pioneered the development of ESSENCE, the Electronic Surveillance System for the Early Notification of Community-based Epidemics. Development, initially focused on daily surveillance of syndromes detected in DoD ambulatory care clinics in the National Capitol Area, began in 1999. DoD-GEIS recognized that an ideal system would be a system of systems integrating other potentially useful data from nurse hotlines, intensive care units, pharmacies, laboratories, and veterinary surveillance sources. To this end early in FY 2001 the DoD-GEIS Central Hub partnered with the Johns Hopkins Applied Physics Lab and several other institutions and obtained a grant of more than $10 million from the Defense Advance Research Projects Agency (DARPA) to develop a prototype integrated civil-military health indicator surveillance system for the NCA called ESSENCE II. Enhancement of the initial ESSENCE system was undertaken during the fiscal year through the development of new aberration detection models and methods to present geographic information system data. Access by military public personnel with a need to know was enhanced by placement of the daily surveillance data on a secure website. The events of September 11 prompted a rapid expansion of the ESSENCE system from the NCA to all DoD Medical Treatment Facilities worldwide (121 Army, 110 Navy, 80 Air Force, and 2 Coast Guard). This scale-up greatly increased the amount of data to be interpreted every day to approximately 3,000 syndrome-specific regional and subregional charts and necessitated the development of automated, mathematically based presentation techniques to prioritize the information for further investigation. The expanded, global scope of ESSENCE required work to begin on organizing across multiple chains of command the tri-service human elements needed to implement timely follow-up actions.

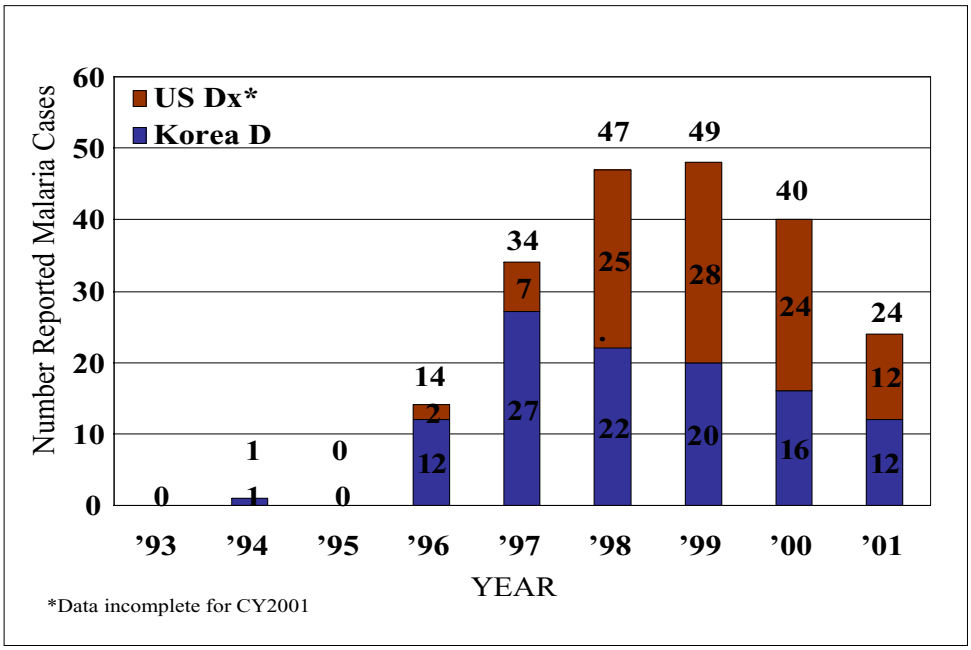
DoD-GEIS also supported at the Madigan Army Medical Center the development of an MHS-based approach to surveillance and focal outbreak detection based on linking Ambulatory Data System (ADS), MHS laboratory data, and Geographic Information System (GIS) information to enable the plotting of reportable disease information. The initial effort has been focused on using both ambulatory and laboratory data on syphilis, gonorrhea, and chlamydia. Progress during FY 2001 included achieving technical and legal access to the necessary data, acquisition of encryption software, and other procedural issues. The Bloomberg School of Public Health at Johns Hopkins University assisted with the development and evaluation of the GIS maps for the Madigan region. During FY 2002 the mapping software will be fully deployed and tested in anticipation of its use by other military treatment facilities.

DoD-GEIS also continued its fruitful collaboration with NASA in using satellite remote sensing data to predict outbreaks with environmental correlates. The initial focus has been Rift Valley Fever (RVF), a lethal disease of human and veterinary importance that has historically been a threat to pastoral populations in East Africa and more recently to the southern Arabian Peninsula. Using methods developed jointly by DoD-GEIS and NASA in prior years, during FY 2001 DoD-GEIS continued to post on its website monthly RVF predictive risk maps and related information. Processing of newer forms of satellite data (1-km Resolution SPOT vegetation data) was initiated that should support development of a broad spectrum of related surveillance activities for other diseases worldwide.

Annual Trend of Malaria Cases in Republic of Korea Civilians and Military Personnel Diagnosed in the Republic of Korea (as of 17 November 2001)



Annual Trend Of Vivax Malaria In U.S. Forces Korea Soldiers And Korean Augmentees (KATUSA) Diagnosed In The Republic Of Korea



Malaria and Other Public Health Threats in the Republic of Korea

Korea is a key operational theater for U.S. forces. The range of emerging or potentially emerging disease threats is wide and includes malaria, hantavirus infections, leptospirosis, Japanese encephalitis, scrub typhus, murine typhus, and sexually transmitted diseases. Due to the size of the U.S. military presence, the need for maximal military readiness, and this spectrum of disease threats, DoD-GEIS has made a specific commitment to provide the 18th MEDCOM with resources to support activities that go beyond the standard military medical surveillance program. During FY 2001 initiatives focused on development of an integrated malaria and Japanese encephalitis vector surveillance system, rodent-borne disease surveillance for areas of high risk, and tick-borne disease surveillance to support risk analysis and identify potential human threats. Close collaborations with Korean governmental and academic institutions have been cultivated over the last several years and are helping DoD-GEIS obtain valuable current incidence data on Korean military and civilian populations.

The explosive re-emergence of malaria in South Korea during the 1990s, especially along the DMZ where many U.S. forces rotate, has made the careful epidemiologic documentation of patterns in civilians, Korean military, and U.S. military important. GEIS-supported partners at the 18th MEDCOM have done this, documenting not only the continuing high rates but also the use of chemoprophylaxis, the characteristics of vector populations, and rainfall correlates. The Armed Forces Research Institute of Medical Sciences (AFRIMS) supported these efforts during FY 2001 by ELISA testing of more than 25,000 mosquito specimens for the presence of malaria, mostly from FY 2000 collections near Camp Greaves. Interestingly all the mosquitoes tested were negative for malaria. CHPPM-Japan is providing analysis for mosquitoes collected in FY 2001. The 18th MEDCOM has used the malaria surveillance data to decide that only persons residing north of the Imjin River will be placed on chemoprophylaxis, thereby limiting the use of chemoprophylaxis at a major cost-savings to the health care system. A traditional challenge to military malaria control has been failure to employ personal prevention measures (PPM) effectively. To document the current level of soldier knowledge, attitudes, and behavior concerning PPMs, a questionnaire was developed for the 2001 malaria season. Data analysis is pending, but it appears that troops continue to show deficiencies with regard to the use of PPMs.

With respect to environmental surveillance for the Japanese encephalitis threat, during FY 2001 4,300 *Culex tritaeniorhynchus* mosquitoes collected during 2000 were analyzed, and 12 (1/357) carried the Japanese encephalitis virus. This is of concern as the mosquitoes were collected within 0.5 km of Camp Greaves and less than 2 km from the Joint Security Area (Camp Bonifas). Considering the potentially devastating human effects of Japanese encephalitis, the implications of this for expanded vector surveillance, human serosurveillance, and possible immunization need to be defined further.

DoD-GEIS also helped to support the evaluation of rodents around military encampments for infection with hantaviruses and scrub typhus. Findings were quite variable by region but worthy of close attention. Two human cases of hemorrhagic fever with renal syndrome occurred in U.S. forces in 2000, one of these at Dagmar North and the other from Firing Point 131-A. The rodent surveillance showed that the hantavirus infection rate exceeded 60% at Dagmar North and that it was 25% at FP 131-A. During FY 2001, over 60% of *Apodemus agrarius* field mice collected at FP 131-A were positive for hantavirus infection. Further data collection is underway to permit trend analysis and predictions, but it appears that many training areas should be considered high-risk during at least part of the year. Other rodent surveillance studies are documenting notable rates of DNA positivity for the agents of human ehrlichiosis.

DoD-GEIS Surveillance Activities Conducted by DoD Overseas Medical Research Units

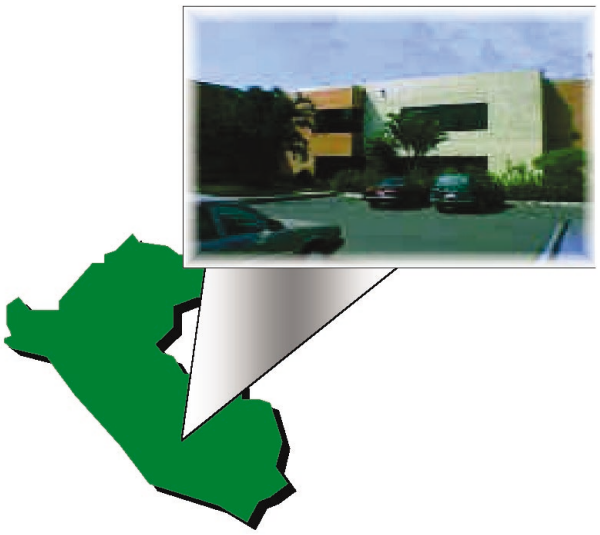
The overseas medical research units of the Naval Medical Research Center and the Walter Reed Army Institute of Research receive 65% of the core DoD-GEIS budget. In FY 2001 this amounted to approximately $4.55 million. Most of these funds are directed towards collaborative surveillance relevant to both the DoD and the host countries. Some of these collaborations reflect the roles of NAMRU-2 and NAMRU-3 as WHO Collaborating Centers for Emerging and Reemerging Infectious Diseases.

Institutions and governments in the following locations had substantive FY 2001 DoD-GEIS collaborations:

Argentina	Indonesia	Saudi Arabia
Bangladesh	Japan	Singapore
Brunei	Kenya	South Korea
Bolivia	Laos	Suriname
Cambodia	Malaysia	Syria
Canada	Mexico	Trinidad and Tobago
Djibouti	Myanmar	Thailand
Ecuador	Nepal	Uganda
Egypt	Oman	United Kingdom
France	Peru	Vietnam
Ghana	Philippines	Yemen

The overseas laboratory DoD-GEIS program has several core surveillance efforts that it supports: influenza, drug-resistant malaria, antibiotic-resistant enteric organisms, fevers of undetermined etiology, and syndromic surveillance. Some of the labs have added additional programs reflective of local needs or special opportunities. The most important programmatic highlights and findings follow.

Naval Medical Research Center Detachment (NMRCD) –Lima, Peru



As part of its highly collaborative work throughout South America, the Naval Medical Research Detachment (NMRCD) in Lima, Peru, continues an expanding program to fill regional gaps in the WHO regional influenza surveillance network. As with all other NMRCD programs, the underlying philosophy is to establish programs that are increasingly integrated into host-nation surveillance systems so that eventually NMRCD's role can become more advisory. The NMRCD influenza surveillance program, which during FY 2001 was conducted at 10 sites in Argentina, Ecuador, and Peru, focused on persons 2 to 55 years who met a specific case definition. Throat swabs from 482 cases were sent in FY 2001 to the Air Force influenza laboratory in Texas for isolations to be made. Acute respiratory disease pathogens have grown from about 30% of the specimens.

Interestingly this year in Peru influenza B was isolated more frequently than influenza A (44 type B isolations vs. 32 for type A).

A particularly strong element of the NMRCD program is surveillance for antimalarial drug resistance. Ensuring that this initiative is well integrated with host-country public health policy development has been greatly favored by the long-term presence of a Public Health Service physician from CDC. The Amazon Basin is the second most drug-resistant area of the world and up-to-date information on *Plasmodium falciparium* drug resistance in the nine countries making up the Amazon Basin is very limited. What data are available has often been difficult to interpret because methods have not been standardized. Chloroquine-resistant *P. vivax* is an even less defined issue. Again the long-term goal is to build capacity in the region so that ministries of health can monitor antimalarial drug resistance in a standardized manner and make evidence-based decisions. Evidence of the progress along these lines has been that Peruvian Ministry of Health staff with experience from earlier studies have helped with the training in Ecuador and Bolivia. The surveillance method used by the NMRCD-GEIS program is the standardized WHO/PAHO 14- or 28-day in vivo drug efficacy protocol. During FY 2001, a 28-day study in Iquitos, Peru, compared mefloquine (MQ) alone with MQ plus artesunate. Efficacy against *P. falciparium* was 100% with both regimens. In Sullana, on the north coast of Peru, a 28-day comparison of sulfa-pyrimethamine (SP) monotherapy with SP plus artesunate showed the combination was 99% effective while SP alone had an efficacy of 97%. As a result of these studies the Peruvian Ministry of Health officially instituted MQ-artesunate as the first-line treatment for uncomplicated *P. falciparium* in the Amazon Basin and SP-artesunate as the first line for uncomplicated *P. falciparium* on the north Pacific coast. It is now the first country in the world to use two different combination regimens in different regions of the country.

A 28-day study of chloroquine efficacy against *P. vivax* at two sites in the Amazon region of Peru and one on the north coast of Peru clearly suggested the presence of resistance. This is the first report of chloroquine-resistant *P. vivax* in Peru. Other innovative malaria resistance-related activities in Peru include initiation of *P. falciparium* resistance mutation mapping at about 20 sites where in vivo studies have not been feasible and the establishment of a formal surveillance system for adverse drug reactions to SP-artesunate along the north coast. As a result of these ongoing collaborations, Peru's antimalaria drug-resistance surveillance data is the most current and accurate in the Americas.

In the Bolivian Amazon, a 28-day study comparing MQ with MQ plus artesunate showed 100% efficacy with both regimens. The Bolivian Ministry of Health is planning to use these data to recommend a combination therapy policy. Surveillance in Suriname is affected by the fact that economic problems in that country preclude use of expensive drugs like MQ. An efficacy study of quinine for 5 days in cases of *P. falciparium* showed a 56% parasitemia recurrence rate. Also in Suriname, a 28-day study of a 3-day quinine-clindamycin regimen showed a 32% recurrence rate.

Surveillance for antibiotic resistant enteric agents in Peru continues to be justified based on the broad increases in resistance seen during the 1990s. Surveillance for antibiotic susceptibility was conducted during FY 2001 at four sites in Peru (including two new sites in Iquitos and Cuzco) and two in Bolivia; 1,018 enteric bacterial isolates were evaluated. Shigella species constituted almost 50% of the isolates. Of note has been a reported overall increase in the resistance of salmonella to a wide range of antibiotics. Among seven drugs (chloramphenicol, cephalothin, ciprofloxacin, erythromycin, gentamycin, tetracycline, trimethoprim-sulfa) for which there were substantial FY 2000 and FY 2001 data, salmonella resistance rates in FY 2001 for all surveillance sites were higher (resistance to erythromycin was 100% both years). Fortunately 99% of the isolates remained susceptible

to ciprofloxacin. Susceptibility to ciprofloxacin tended to hold for all bacteria tested, with the exception of *Campylobacter*. Ciprofloxacin resistance in *Campylobacter* appeared to vary considerably across locations, but fortunately 96% of *Campylobacter* isolates were susceptible to azithromycin. Broad resistance also appeared to be on the rise for enterotoxigenic *Escherichia coli*. To highlight the data from Bolivia, the Technologic Food Institute in Sucre sponsored a well-attended drug resistance symposium for the local medical community.

Mosquito surveillance in the Amazon is an ongoing NMRCD program to document arboviral threats and develop insight into appropriate control. In FY 2001 over 37,000 mosquitoes of more than 80 species were collected (when the surveillance started in 1996, only 25 species were known in the region of Iquitos). Viral isolations done with the support of USAMRIID and the University of Texas have so far yielded 16 different viruses, including eastern equine encephalitis virus. Fortunately despite the fact that this potentially deadly virus makes up the majority of isolates isolated from mosquitoes, analyses of human sera indicate that eastern equine encephalitis virus is not the most likely cause of febrile illness of unknown origin. Substantial differences in mosquito species distributions and densities were documented in different Amazon ecologies. Tests on paired sera from febrile humans identified cases of infection with Caraparu and Venezuelan equine encephalitis viruses (VEE).

The problem of acute febrile syndromes of undetermined etiology has made standardized, lab-based etiologic surveillance for these conditions a key NMRCD DoD-GEIS program. During FY 2001 such surveillance was conducted at six sites in Peru, two in Ecuador, and one in Bolivia. Acute and convalescent sera for antibody testing and agent isolations were collected from patients meeting various case definitions. Among 79 samples from Ecuador, dengue type 1, 2, and 3 viruses and VEE virus were isolated. Among 779 samples from six sites in Peru, 29 dengue and 5 VEE isolations were made. Two seroconversions to Oropouche were also noted. Seven of 60 Peruvian samples showed seroconversion to *Rickettsia rickettsii*. Other screening serological studies suggested evidence of infections with *R. typhi, Coxiella burnetii,* and *Borrelia burgdorferi*. Among 117 paired specimens from febrile patients in Bolivia, no viruses could be isolated nor was evidence of seroconversion noted. Clearly there are still many causes of acute febrile syndromes yet to be determined.

Naval Medical Research Unit Number 2 (NAMRU-2) – Jakarta, Indonesia

Indicative of NAMRU-2's outstanding contributions to global emerging infections surveillance and response, during FY 2001 it was redesignated for another prestigious four-year term as a World Health Organization Collaborating Center for Emerging and Re-emerging Diseases. NAMRU-2's DoD-GEIS program has featured technology transfer of diagnostic capabilities to regional partners as central to leveraging its finite resources. For example, enteric diagnostic capabilities in various parts of Indonesia were expanded beyond cholera to include campylobacter, shigella, and enterotoxigenic *Escherichia coli*. Testing capacities for dengue, leptospirosis, and

rickettsia were established at the National Laboratory and Epidemology Center in Laos. Similarly capacity for bacterial, viral, and rickettsial testing was established at the joint National Institute of Public Health/NAMRU-2 lab in Cambodia, and leptospirosis diagnostics were strengthened at the Pasteur Institute in Vietnam. All of this technology transfer was done in the context of protocol-driven surveillance collaborations.

NAMRU-2 has continued to offer popular regional outbreak response training workshops and assisted with outbreak investigations in Cambodia (malaria), Laos (dengue), and Indonesia (dengue and hepatitis A). In August 2001, 30 students from Vietnam attended one of these 10-day workshops conducted collaboratively with the Ministry of Health. In response to a call by the November 2000 Asia-Pacific Economic Cooperation (APEC) Leaders Summit for a regional emerging infections plan, this course was conducted as part of the U.S. government response and under the official sponsorship of the APEC. Previous workshops have been held in Indonesia, Laos, and Cambodia. NAMRU-2's innovations in electronic public health surveillance, headlined by the expanding syndromic, near-realtime Early Warning Outbreak Recognition System (EWORS) and by the design and implementation of the web-based ASEAN-Net for sharing outbreak information, continue to be seen as international models. These accomplishments point directly to the contributions of DoD-GEIS to the second objective of the PDD which states that U.S. agencies will

" work with other nations and international organizations to establish a global disease surveillance and response system, based on regional hubs and linked by modern communications."

During the fiscal year NAMRU-2, in partnership with the Indonesian Ministry of Health, received provisional approval for a U.S. patent for EWORS. It also upgraded the EWORS software. EWORS surveillance was expanded to seven hospitals in Vietnam through a partnership with the Pasteur Institute and arrangements, including necessary translation, were made to expand EWORS to Laos. By the end of the fiscal year, over 500,000 EWORS entries, often from some of the most remote and economically depressed parts of the region, were available for instant syndromic trend analysis. This tool has facilitated the recognition and characterization of four large outbreaks in Indonesia. It has been credited with providing early detection of an incipient problem with dengue hemorrhagic fever in Bali, allowing for timely procurement of essential blood products with consequent reductions in mor-

NAMRU-2 GEIS program conducts an Outbreak Response Training Workshop in Vietnam in response to APEC's call for action against emerging infections.

bidity. EWORS surveillance data from Cambodia also helped preclude costly but off-target disease responses to severe flooding.

ASEAN-Net, a direct outgrowth of the joint NAMRU-2/Indonesian Ministry of Health September 2000 regional action conference on emerging infections surveillance and response funded by U.S. Pacific Command reported in last year's annual report, aims to facilitate rapid yet confidential dissemination of outbreak information within the region, catalogue regional expertise and laboratory capabilities, and disseminate information on training opportunities. ASEAN-Net was officially adopted as part of the ASEAN Health Initiative at the ASEAN Health and Development Secretariat Meeting held in October of 2001.

NAMRU-2 supported during FY 2001 targeted surveillance into important causes of enteric and hemorrhagic diseases. Based on surveillance work done in Indonesia, Laos, Vietnam, and Cambodia, leptospirosis appears to be one of the more important causes of febrile disease. NAMRU-2 supported surveillance of U.S. troops involved with humanitarian and Joint Task Force Full Accounting operations in Laos, Cambodia, and Vietnam. Personnel are screened in Hawaii before deployment and in Thailand after exposure. In prior years, important early findings were published suggestive of in-vivo drug resistance associated with *Orientia tsutsugamushi*. Final results are pending. Serologic surveillance of Gurkha troops and their families based in Singapore before and after their six-month home leave to Nepal is also ongoing.

During FYs 2000 and 2001 surveillance of 6,760 hospitalized children and adults with several diarrheal diseases yielded isolations of *Shigella flexneri* (39%), *Salmonella* spp. (26%), *Vibrio* spp. (17%), *Shigella sonnei* (7%), *Campylobacter jejuni* (4.4%), *Salmonella typhi* (3%), and *Shigella dysenteriae* (2.3%). *S. dysenteriae* reemergence was noted in Bali, Kalimantan, Batam, and Jakarta after an apparent absence of 15 years. All bacterial isolates were susceptible to quinolones, with the exception of *C. jejuni* and S*almonella* spp., which were resistant to ciprofloxacin, norfloxacin, and nalidixic acid. These findings highlight the decline of *V. cholerae*, the rise of *S. flexneri*, and the reemergence of *S. dysenteriae* in Indonesia.

A Successful Year for EWORS

EWORS (Early Warning Outbreak Recognition System), a disease outbreak detection and surveillance system, was developed by NAMRU-2 in Jakarta, Indonesia, to fill a gap in regional surveillance capabilities. The software is now being used in Indonesia, Cambodia, Vietnam, and Laos. EWORS is intended to identify suspected clusterings of like, syndromic cases and possible disease outbreaks. EWORS's emphasis on establishing baseline measures for trend analysis to differentiate outbreaks from non-outbreak disease is unique. The system provides for timely and accurate dissemination of information that can then lead to effective intervention measures such as investigative and containment activities. One advantage of EWORS is that users do not need analytical training, which is lacking in many rural areas in southeast Asia, for recognizing a potential outbreak. Whether such a finding warrants investigation or intervention is made at a higher level.

The Indonesia Ministry of Health, partners with NAMRU-2 in this project, has already benefited from using EWORS. During a diarrheal disease outbreak in 2001, Ministry of Health staff used EWORS to detect the outbreak, the information collected with EWORS allowed Ministry of Health officials to design and execute a comprehensive public health outbreak investigation, and the results of the outbreak investigation provided sufficient information so that effective intervention measures could be implemented. EWORS can be used by the Indonesian Ministry of Health as a national disease outbreak detection and surveillance system. Thus, EWORS meets a key aim of the DoD-GEIS program, which is to develop a program that is affordable, user-friendly, effective, and acceptable as an integral and permanent component of the national public health program.

Major EWORS successes in FY 01:

- Recognized four large outbreaks in Indonesia.
- Provided early detection of incipient dengue hemorrhagic fever outbreak cases in Bali, allowing for timely procurement of essential blood products and preventing possibly hundreds of cases.
- Contradicted rumors of a cholera epidemic during severe flooding in Cambodia, thus saving scarce resources for other interventions.
- Uses more than 500,000 case entries, from some of the most remote and economically depressed areas of southeast Asia, for instant inclusion into standardized trend analyses.
- Was awarded a provisional U.S. patent.

Important parasitic disease findings were also made by NAMRU-2 this year. For the first time throughout the world, resistance to chloroquine by *P. malariae* was documented as a result of surveillance in South Sumatra. A follow-up surveillance of chloroquine resistance in *P. falciparium* and *P. vivax* in Nias Island, north Sumatra, showed little change in therapeutic failure since the initial survey seven years ago. NAMRU-2 also performed extensive reviews of over 10 years of *P. falciparium* and *P. vivax* resistance to chloroquine in Indonesia. Following up on surveillance work done in a prior assignment, Dr. Baird from NAMRU-2's program reported a new species of malaria (the first new species reported since 1922) affecting humans in Guyana. An in vivo clinical trial of chloroquine plus sulfadoxine for therapy of uncomplicated *P. falciparium* in Purworejo, Central Java, demonstrated more than 95% efficacy. As in South America, national authorities are using these data to guide critical policy decisions. The centerpiece of the NAMRU-2 DoD-GEIS malaria program was the design of an intervention strategy to combat epidemic malaria in Central Java. To fund this strategy, which was adopted by the Indonesian Ministry of Health, NAMRU-2 obtained $500,000 from USAID. NAMRU-2 conducted for the MOH a randomized survey of malaria knowledge, attitudes, and practice that was essential to targeting the intervention. NAMRU-2's vector surveillance is also contributing to the formulation of targeted interventions. Analytic tools that support malaria work in Central Java are providing local health officers with a broader capability to do real-time collection and analysis of health data. After an apparent absence of malaria for 25 years, surveillance done by NAMRU-2 also confirmed its re-emergence in a coastal tourist area within a few miles of the 12 million people living in Jakarta.

NAMRU-2 expanded its DoD-GEIS program in FY 2001 to include influenza surveillance; this meant restarting an effort that had lapsed 7 years earlier. Surveillance at three sites (Jakarta, Bandung, and Tangerang) yielded 425 specimens. Isolates were shared with the Australian CDC for further analysis. Also during the FY, surveillance for Chikungunya was conducted and strongly supports the hypothesis that Yogyakarta, Java, Indonesia represents the first identified locus of endemic Chikungunya transmission.

Naval Medical Research Unit Number 3 (NAMRU-3) – Cairo, Egypt

The region of activity for NAMRU-3, the largest of the DoD overseas medical research units, extends from the Middle East to Eastern Europe, Western Asia, and North Africa. Benefiting from the long-term assignment of a Public Health Service officer detailed from the CDC, the NAMRU-3 DoD-GEIS program has developed strong ties with regional public health entities.

Since 1998 NAMRU-3 has conducted in Egypt, through a network of 14 infectious disease hospitals, enhanced surveillance for patients with meningitis, acute febrile illness, dysentery, and hepatitis. Using standard case definitions, NAMRU-3 trained personnel

at these hospitals have evaluated thousands of patients. Of 1,690 meningitis patients evaluated between October 2000 and August 2001, 8% had positive bacterial cultures including 46 for *Streptococcus pneumoniae*, 30 for *Haemophilus influenzae*, 29 for *Neisseria meningitides*, and 16 for *Mycobacterium tuberculosis*. Among children *H. influenzae* was the number one cause of meningitis. These data have been used to build a cost-effectiveness model for the introduction of the Hib vaccine into the Expanded Program on Immunization. Of 1,589 patients evaluated for acute febrile illnesses, 90 were classified with confirmed and 274 with probable typhoid fever. In addition, 42 were classified with confirmed and 188 with probable brucellosis. Consumption of dairy products (raw milk and soft cheese) appears to be a risk factor. Testing also suggested that murine typhus may be a common cause of acute fever in Egypt. Arboviral infections appeared to be generally uncommon though evidence for transmission of *Rickettsia typhi,* West Nile virus, and the viruses that cause Sinbis, Sandfly fevers (Naples and Sicilian), and Rift Valley fever was found. Dysentery surveillance was only recently implemented but *Shigella* spp. were the most commonly identified pathogens. In the course of hepatitis surveillance at four sites, evidence for hepatitis C virus infection was found in 24%, for hepatitis B virus in 17%, and for hepatitis A virus in 15%. The WHO has asked NAMRU-3's assistance in developing similar surveillance networks elsewhere in the region.

NAMRU-3 also conducted standardized population-based surveillance of 473,472 persons in the Bilbeis district. This included surveillance at the Bilbeis Fever Hospital, the private clinic of a fever specialist, and in the offices of selected primary care providers. Of 466 patients evaluated, 4.2% had positive blood cultures for *Salmonella typhi* and 3.1% were positive for *Brucella* spp. Brucellosis was the most common cause of febrile illness. Most brucellosis patients were initially misdiagnosed as having typhoid fever. Less than 33% of typhoid infections were seen in the fever hospital.

Standardized surveillance among young children for pathogens associated with severe diarrhea was conducted at two hospitals in Egypt: Benha Fever Hospital and Abu Homos District Hospital, both in the Nile Delta. Between May 2000 and September 2001, 980 children were studied, most of whom were under one year of age. ETEC was the most common pathogen (22%). *Giardia*, rotavirus, and *Cryptosporidium* were also important etiologies. *Campylobacter* and *Shigella* each accounted for only 2% of the episodes. No *Vibrio* were identified and only two *Aeromonas*. *Entamoeba histolytica* also seemed uncommon. *Shigella* and ETEC were sensitive to both naladixic acid and ciprofloxacin but inconsistently sensitive to other antibiotics. *Campylobacter* was sensitive to erythromycin but not to naladixic acid or ciprofloxacin.

Further antibiotic resistance characterization data were obtained on 2,879 *E. coli* and *Shigella* isolates collected between 1995 and 2000 in rural Egypt. Among ETEC strains, multiple antibiotic resistance was noted in 27.4% vs. 40.3% among non-ETEC strains though across time upward trends were not particularly evident. About 20% of *Shigella* spp. demonstrated multiple antibiotic resistance.

The NAMRU-3 DoD-GEIS program provided support to CENTCOM by conducting enteric disease surveillance of roughly 15,000 active duty U.S. military personnel during the Brightstar Exercise held in Egypt between 24 September 2001 and 7 November 2001. Over 200 stool samples on 128 troops were collected. *E. coli* was by far the most common organism isolated, accounting for 78 of the enrollees. Resistance to ciprofloxacin and naladixic acid was universal among the 9 *Campylobacter* isolates. Complete results are pending.

Surveillance for arboviruses, including West Nile virus, began in the Sinai through cross-sectional serosurveys of 877 Bedouins (254 families), monthly arthropod surveillance, and sentinel chicken surveillance. In the El-Arish area (on the north coast), West Nile antibody prevalence rates varied from about 5% in persons 4 to 10 years of age to about 20% for those

over age 70. In the Nuweiba area (on the eastern coast near Israel), West Nile prevalences were much lower, generally about 5% or less in most age strata. There was evidence in both regions of the Sinai for generally low rates of transmission with Sinbus and Sicilian sandfly fevers. The data suggested that Naples sandfly fever was a bit more common, though antibody prevalences remained less than 10% in most age groupings. Complete analysis of collected arthropods and sentinel chicken sera is pending.

NAMRU-3 has played an integral role in strengthening WHO influenza surveillance in the region. Training of laboratorians from partner countries has been central to this effort. Influenza isolates are sent to CDC influenza laboratory for detailed characterization as indicated. Other respiratory viruses isolated are being provided to the Enterovirus Section at CDC and to the GEIS-supported respiratory infections program at the Naval Health Research Center, San Diego. Since the surveillance began in 1998, over 5,120 samples have been obtained in Egypt. In 2000/2001 all subtyped influenza A viruses were A/New Caledonia/20/99-like H1N1s and all type Bs were B/Sichuan/379/99-like. Over the course of several years, 125 cases from Syria were studied. After overcoming significant liquid nitrogen availability problems and investigator illness, Djibouti provided from two sites 24 samples during the year, two of which were positive for viruses other than influenza. Using CENTCOM funds surveillance was initiated in Oman in the late summer of 2001. In just a few months, over 300 samples were collected and analysis is pending.

NAMRU-3 DoD-GEIS program. Serosurveys were undertaken in Djibouti and Yemen and hospital surveillance (both rural and urban) for dengue-like illness was established in Djibouti. Significant problems have arisen with respect to completing the assays due to security restrictions imposed on the shipping of dengue reference strains for the neutralization assays from the U.S. to Egypt. Among 46 nursing students in Djibouti, the West Nile IgG prevalence rate (as measured in a generic flavivirus IgG ELISA) was 88.5%, though proximity to a yellow fever immunization may have produced cross-reactions. Among two groups of police recruits totaling 266 persons, the overall prevalence was 6.8%. Dengue titers are pending. Dengue results from hospital surveillance are also pending though none of 59 patients had IgM to West Nile, Sinbis, sandfly fevers (Sicilian and Naples), and Rift Valley fever. The serosurveillance of over 800 university students in Yemen documented West Nile prevalences of between 4.2% and 6.9%.

Like all the other DoD overseas laboratories, NAMRU-3's DoD-GEIS program also conducts antimalarial drug resistance studies. Northern Ghana is the primary focus for these efforts. In August 2001, 497 children aged 6 to 20 months were enrolled in the Kassena-Nankana District. They will be followed for the occurrence of clinical malaria and the in vivo efficacy of chloroquine and Fansidar compared in mild cases.

NAMRU-3 also supported many regional outbreak investigations during FY 2001, including the first outbreak of Rift Valley Fever on the Arabian Peninsula, and outbreaks of salmonella and newborn sepsis in Egypt. The problem with newborn sepsis appeared related to contamination of IV fluids with several agents (mostly *Klebsiella pneumoniae*). As a result of the sepsis investigation, a project targeted towards 40 hospitals was jointly developed with the Egyptian government to evaluate laboratory capacity and initiate surveillance, to assess infection control practices and provide training, and to monitor laboratory improvement.

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

In their evaluation of the DoD-GEIS program, the Institute of Medicine committee described AFRIMS, the Army's largest overseas medical research unit, as "probably the most sophisticated diagnostic and research laboratory in all of Southeast Asia."

Building upon this reputation AFRIMS endeavors to strengthen its epidemiologic capabilities while still capitalizing on its reputation as a "center of excellence" in the area of diagnostics for flaviviruses, hepatitis, HIV, malaria, and enteric pathogens. In this capacity, AFRIMS has positioned itself as an important provider of laboratory training and capacity building support in the region. One notable contribution in this area was AFRIMS' collaboration with several Thai government departments and universities in the sponsorship of a major conference on leptospirosis diagnosis. AFRIMS is supporting the printing of a post-conference handbook entitled "The Handbook of Laboratory Methods for Leptospirosis Diagnosis." With the DoD-GEIS program, it has increasingly developed a public health role to complement its reputation as a leading research institution. This has included assisting the Royal Thai Army in developing its surveillance and preventive medicine capabilities.

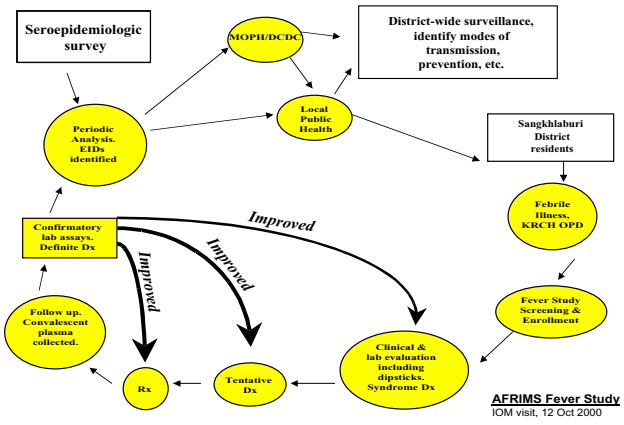
AFRIMS continues to conduct antimicrobial resistance surveillance in six sentinel populations in Thailand, Vietnam, and Nepal. Generally these are young children, tourists, or U.S. military personnel deployed to Operation Cobra Gold. This year AFRIMS reported enteric surveillance data from 744 cases and 539 non-cases. *Campylobacter* was the most common pathogen identified in the non-immunes with diarrhea (Cobra Gold, and travelers in Nepal and Bumrungrad Hospital, Bangkok) ranging from 14% to 36% but not frequently isolated from indigenous populations (Vietnamese children and Thai adults). *Shigella* prevalence is low in Thailand (Cobra Gold and Bumrungrad) but more common in Nepal (17%) and Vietnam (8%). *Salmonella* was detected in cases as well as healthy non-cases among foreigners and Thais seen at Bumrungrad Hospital (about 15%). ETEC is one of the common pathogens in Nepal, isolated from 12% of cases. ETEC was found in 7% of foreigners and Thais with diarrhea. Ciprofloxacin-resistance *Campylobacter* is common in Thailand: 96% in Cobra Gold cases and 82% in cases at Bumrungrad Hospital. In Nepal ciprofloxacin resistance in *Campylobacter* was lower (50%), and it was 0% among children in Vietnam. Macrolides are still effective for *Campylobacter* at every site. High resistance to nalidixic acid (96%) occurred among isolates from troops affected by *Campylobacter* during Cobra Gold. Ciprofloxacin is very effective for *Shigella* isolates, and it usually also covers salmonella and ETEC well. AFRIMS has started to participate in the WHO Global Salmonella Surveillance Program (Global Salm-Surv) by sending in isolates and participating in external quality assurance protocols.

AFRIMS also continues to support critical regional anti-malaria drug resistance studies. During FY 2001, 217 *P. falciparium* isolates from Vietnam, Myanmar (Shan State), Thailand (Sankhlaburi), and Nepal (Terai Region) were collected. AFRIMS in vitro data indicate no improvement in mefloquine resistance on the Thai-Myanmar border in recent

years. An in vivo evaluation of the field efficacy of mefloquine documented the spreading of mefloquine resistance to Sangkhlaburi along the Thai-Myanmar border, requiring urgent revision of Ministry of Health treatment protocols for the region. In contrast to reports from others, AFRIMS has also been unable to show a decrease in mefloquine resistance in Vietnam. Antimalarial multidrug resistance appears to be emerging in Bangladesh. However, no artemisinin-resistant *P. falciparium* isolates have been found among wild isolates from the region.

The Kwai River Christian Hospital along the Myanmar border in Thailand has proved to be a useful site to conduct surveillance for undifferentiated febrile illnesses and identify new pathogens. Based on completed evaluations of the first 300 patients (1999-2000), leptospirosis is now recognized to be a very common but previously under-appreciated cause of morbidity and mortality. Despite numerous Ixodid ticks, no evidence for *Borrelia burgdorferi* has been found. Another new surveillance finding is that melioidosis (*Burkholderia pseudomallei*) not only is now seen as occurring in the region but it is also recognized as being quite common. Typhoid fever outbreaks also have been documented and many cases seem to respond slowly to quinolones. This year AFRIMS documented the first recognized case of hepatitis E in Sangkhlaburi. Surveillance data also suggest the first reports in Southeast Asia of Spotted Fever Group rickettsioses identical or closely related to *Rickettsia helvetica* or *Riskettsia conorii* (Indian strain). Exposure to Ehrlichia spp. seems to occur along with murine typhus and a flavivirus other than Japanese encephalitis or dengue. Scrub typhus seems rare.

Feedback Loop from Data Generated at Fever Study in Sangkhlaburi, Thailand



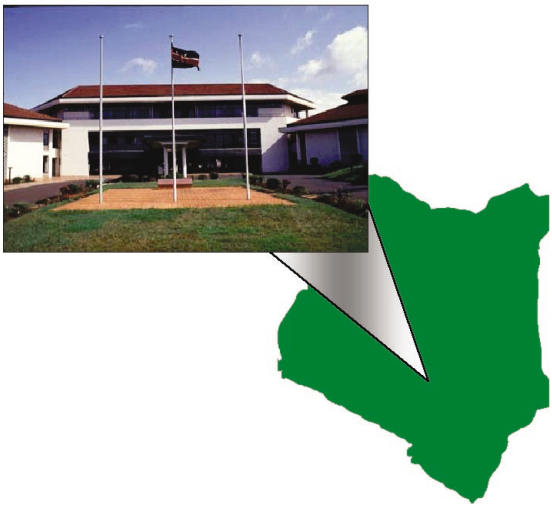
Related serosurveillance for fever has been conducted in the Terai district of Nepal, an area of tropical lowlands near the border with India and in the Kathmandu Valley. Preliminary Terai data based on HAI assays that are potentially cross-reactive with flaviviruses raise the possibility that in addition to Japanese encephalitis (9 “pure” positives), Chikungunya, West Nile encephalitis (30 “pure” positives), and Murray Valley encephalitis (19 “pure” positives) viruses may be focally present. The paucity of dengue results mitigate against this being a problem in the Terai. Before the surveillance in the Kathmandu Valley, there was no evidence to suggest that Japanese encephalitis was endemic there. Hepatitis E was noted to be the leading cause of acute hepatitis in Kathmandu (39%).

Hospital-based febrile syndromic surveillance continued this year in Kamphaeng Phet, Thailand. Findings included 58 cases of EIA-confirmed leptospirosis. Dip-S-Tick assays were also positive for *Ehrlichia*. One hundred and forty-four adult dengue cases were also serologically diagnosed, an unexpected finding since dengue is usually regarded as a pediatric illness. Another unexpected finding was seroconversion by five patients to a *Bartonella* spp. never before described in Thailand. AFRIMS continued to support the DoD Global Influenza Surveillance Program by collecting and forwarding 75 samples this FY from patients in Nepal and Thailand.

The strong veterinary medicine group at AFRIMS conducted adjunct surveillance efforts using sentinel animals. Eighty pigs and 100 chickens and ducks were used for sentinel surveillance for flaviviruses at 20 sites in Sangkhlaburi District. Rapid, almost immediate seroconversions indicated that pigs and ducks are sensitive indicators but chickens are not. AFRIMS has also begun leptospirosis surveillance in a range of domesticated animals and rodents in this region. Of 245 feral rodents studied, about 10% had pathogenic strains of *Leptospira* grow from kidney cultures.

The Royal Thai Army has a large medical care system consisting of 37 hospitals that not only care for military personnel but also many civilians. In fact, 80% of the patients are non-military. AFRIMS is supporting efforts of the Royal Thai Army to establish a hospital information system network to support surveillance. Also, for units in border regions without regular access to fixed hospitals, AFRIMS is helping to adapt other software for syndromic surveillance.

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



As noted by the IOM, "USAMRU-K is well positioned to meet the goals and objectives of DoD-GEIS and can substantially contribute to a global infectious disease surveillance and response network." However, FY 2001 was a major challenge to the DoD-GEIS program at USAMRU-K due to staff shortages, including lack of a dedicated physician-epidemiologist to manage the program, and due to the declining infrastructure in Kenya.

It was possible, though, for the staff to continue surveillance for diarrheal diseases in the Mathare slum of Nairobi and among the rural Masai. A total of 424 patients from Mathare met the case definition between February 2000 and October 2001. Diarrheal specimens were also evaluated for 165 Masai from March to November 2000. At the Mathare site, the overall isolation rates for diarrheal stools were 29% *Shigella* spp, 19% pathogenic *E. coli*, 17% *Campylobacter*, and 3% *Salmonella*. Among the Masai, *E. coli* species were the most common etiology, accounting for 21% of all cases, followed by *Shigella* (16%), *Campylobacter* (3%), and *Salmonella* (2%).

Of the *E. coli* isolates at the Mathare site, 100% were resistant to ampicillin and erythromycin, while more than 70% were resistant to tetracycline and sulfamethoxazole. No resistance to norfloxacin or

nalidixic acid was found. The *E. coli* isolated from the Masai site showed resistance to tetracycline (80%) and sulfamethoxazole (68%). Again no resistance to norfloxacin or nalidixic acid was found. At the Mathare site, 100% of *Shigella flexneri* isolates were resistant to erythromycin. Over 90% of these species were also resistant to tetracycline, ampicillin, and sulfamethoxazole. Significant resistance to first-line antibiotics was also seen in *Shigella dysenteriae, S. boydii,* and *S. sonnei*. No resistance was noted to nalidixic acid or norfloxacin. *Shigella* from the Masai site also showed resistance to tetracycline (63%) and sulfamethoxazole (44%). No resistance was noted to nalidixic acid or norfloxacin. The high rate of *Campylobacter* isolation in this study is noteworthy since *Campylobacter* has not been an etiology of interest in most diarrheal studies in Kenya.

During FY 2001, USAMRU-K began operation of the first in vitro anti-malaria drug testing facility in East Africa. Initial analyses focused on 400 frozen *P. falciparium* specimens from the previous two years. Results are pending.

USAMRU-K also provides extensive support, in partnership with the CDC, to the WHO Virus Reference Centre at the Kenya Medical Research Institute. The main work of this center is surveillance for yellow fever at 22 hospitals and clinics around Kenya. This infrastructure also facilitates surveillance for other hemorrhagic fevers. In October 2000, this Centre diagnosed the first confirmed case of human Crimean-Congo hemorrhagic fever in Kenya. Using RT-PCR, a diagnosis was made within 24 hours after receipt of the serum sample from one of the surveillance sites. Because ticks can transmit a wide range of pathogens, the Reference Center is currently investigating for viral pathogens 16,250 ticks collected at two Nairobi slaughterhouses. To date 39 viruses have been isolated and are being characterized.

The significant needs of Kenya and other countries in the region have necessitated notable investments in staff training and infrastructure. In the localities where the other four DoD tropical overseas medical research units are located, trained local laboratorians and epidemiologists and basic communications infrastructure are much more available. In Kenya, more emphasis has been required on employee training and on the acquisition of Internet services through purchase of a Very Small Aperture Terminal (VSAT) satellite antenna. A notable development related to communication this fiscal year was the launching of the USAMRU-K web site, http://www.usamrukenya.org.

"2. Enhance biomedical and behavioral research efforts on emerging infectious diseases."

The DoD-GEIS program is organized and funded as a public health surveillance, response, training, and capacity building program. Most emerging infections research conducted by the Department of Defense is managed and funded separately by the Military Infectious Disease Research Program (MIDRP) under the direction of the Commanding General of the Army Medical Research and Materiel Command (MRMC). Nevertheless, DoD-GEIS has been in the position to facilitate the research agendas of the MIDRP and other partners. As noted above, both domestically and internationally, DoD-GEIS assets have leveraged diagnostics development. The DoD-GEIS surveillance program is well positioned to recognize research questions that need to be answered pertaining to the epidemiology and control of emerging and re-emerging agents.

A particular research emphasis of DoD-GEIS has been to focus on the development of innovative methods for surveillance, such as ESSENCE, EWORS, and the joint DoD-GEIS/NASA Rift Valley Fever predictive model based on information from satellites. Recognition of the re-emergence of malaria in Korea has stimulated survey research into the knowledge, attitudes, and behaviors of soldiers toward personal protective measures such as military insect repellants. The collation of MIDRP projects and DoD-GEIS projects at field sites associated with the overseas research activities contributes to both scientific and fiscal efficiency.

"3. Expand formal training and outreach to health care providers."

A major focus of DoD-GEIS during Fiscal Year 2001 was training. The IOM evaluation of DoD-GEIS strongly recommended this emphasis as a way to build up much needed local capacity and thus extend DoD's own internal resources. All five tropical overseas medical research units supported various training initiatives. These included not only laboratory and epidemiology training for internal staff but also outreach efforts to host-nation partners. Two of the greatest success stories have been the ongoing 10-day sessions on conducting outbreak investigations that NAMRU-2 has been offering in Southeast Asia and NMRCD's training of host-nation personnel to conduct in vivo antimalarial drug-resistance studies. With strong support from Southern Command's Humanitarian Assistance Program, DoD-GEIS was also able to establish during FY 2001 three pilot regions in Peru for a laboratory-based surveillance initiative. This training project has focused on the creation of computerized networks for hierarchical reporting. The backbone of the effort is the CDC-developed Public Health Laboratory Information System (PHLIS) software. The project has included the donation of more than 50 computers to the Peruvian Ministry of Health and assistance with six informatics training courses provided to more than 80 public health workers from San Martin and Ayacucho departments and from around Lima. Southern Command also provided resources to continue a similar training initiative begun in the Caribbean four years ago and to start a project for all the countries in Central America.

Another primary training focus has been the DoD-GEIS Overseas Medical Research Laboratory Training Program. This program exposes junior military officers with a potential for service at the overseas research facilities to the scientific satisfactions and cultural issues associated with such service. It is a necessary investment to help recruit persons into the small cadre of physicians and scientists needed to

maintain strong DoD-GEIS and MIDRP programs. During FY 2001, 15 officers representing several disciplines spent approximately 30 days in the environs of one of the overseas labs working on various surveillance or research projects. The yield of the program since its inception several years ago has been excellent. Trainees generally return highly enthusiastic about the work performed at the overseas research activities and have resolved many of their apprehensions about life for an American family stationed in one of these locations. Four trainees from FY 2000 have already obtained permanent assignments at the overseas facilities.

Also in the vein of training, DoD-GEIS supported this year a number of major meetings. These included several sessions of the Institute of Medicine Emerging Infections Forum and two day-long conferences conducted in partnership with the U.S. Medicine Institute for Health Studies. One of these conferences, "Vaccine Availability – A Forum for Government Leaders," drew approximately 100 policy makers and scientists from the federal government, academia, and industry. The findings highlighted the nation's growing challenges in acquiring or maintaining stocks of a variety of critical vaccines. Many of these are "orphan" products with small (e.g., limited to the military) or no current markets (e.g., certain potential bioterrorism agents). Business disincentives and the

limitations of a free market approach to vaccine research and production were noted. This Forum concluded that the current problems with vaccine availability should be seen in the national security context and that Congress and the National Security Council should address fragmentation of oversight and the need for improved interagency communication.

"4. Review and update regulations, procedures, and resources for screening and quarantine at ports of entry into the United States."

"5. Make information about ill international travelers with communicable diseases more accessible to domestic health authorities."

Within the federal government, the lead for these objectives laid out in the Presidential Decision Directive is the Department of Health and Human Services. DoD also has key responsibilities in this arena. In recent years, the DoD Directive and DoD Instruction on deployment medical surveillance have set policy for a more systematic approach to assessing health before, during, and after deployment. Policies must sit on an infrastructure, though, to achieve their ends.

Many specific, and previously mentioned, DoD-GEIS funded efforts are working to make information about MHS beneficiaries with communicable diseases more accessible to public health authorities. These initiatives are wide ranging and include ESSENCE, the Virtual Public Health Laboratory, the DoD Mortality Surveillance Program, the DoD Influenza Surveillance Program, and DoD participation in the CDC's Gonococcal Isolate Surveillance Program. DoD-GEIS has also been funding laboratory-based surveillance initiatives that support deployments such as Cobra Gold, Bright Star, and the regular assignment cycle to and from South Korea. Troops involved with these assignments sometimes acquire infectious diseases that only manifest after their return to the U.S. Many of these infections have implications not only for the servicemember but also for public health in general. Through improving laboratory networks, improving communications tools, and sponsoring scholarly meetings, DoD-GEIS helps to improve the accessibility of important public health information.

"6. Encourage other nations and international organizations to assign higher priority to emerging infectious diseases."

"7. Support the World Health Organization and other bodies in playing a stronger role in the surveillance, prevention, and response to emerging infectious diseases."

As noted by the IOM, DoD-GEIS continues to be a unique asset of the U.S. government in advancing the response to emerging infections around the world. Elements of DoD-GEIS work closely with the WHO and many of its regional offices. Many of the accomplishments of DoD-GEIS in this arena have been noted above. In September 2001, NAMRU-3's DoD-GEIS program, in partnership with the Eastern Mediterranean Office of the WHO, conducted a regional major meeting in Egypt on the emergence in 2000 of Rift Valley Fever in Saudi Arabia and Yemen. DoD-GEIS has been a regular supporter of the U.S. government's efforts under the APEC and helped craft documents that led in November 2000 to the APEC Summit's Leaders Declaration on emerging infections.

Another notable achievement was the placement of a U.S. Navy preventive medicine officer in the Communicable Disease Surveillance and Response directorate at the WHO Headquarters in Geneva. With partial DoD-GEIS support, this Naval officer is head of the new civil-military liaison activity that aims to increase international emerging infections surveillance by improving WHO's coordination between host-nation civilian public heath and military organizations. This officer's placement has also already proven invaluable in understanding threats to

U.S. forces such as the 2001 outbreak of Crimean-Congo hemorrhagic fever in Kosovo. DoD-GEIS funding supported four laboratories that hold prestigious positions as WHO Collaborating Centers. These are NAMRU-2, NAMRU-3, USAMRIID, and the Division of Experimental Therapeutics at WRAIR. The DoD-GEIS-supported NHRC Respiratory Disease Laboratory has applied to become a collaborating center and other DoD-GEIS partners are in the process of doing so.

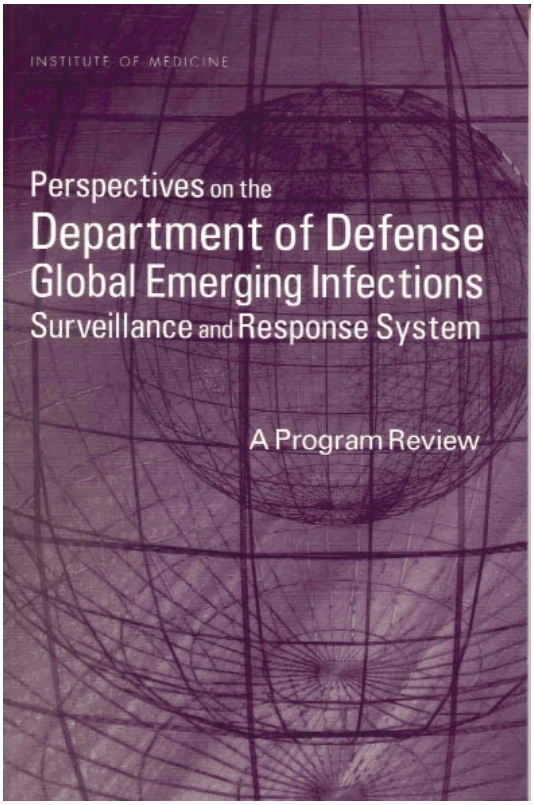
"8. Expand United States agency missions and mandates in order to ensure that responsible agencies are provided with the authority, emergency procurement powers, and resources to respond to worldwide disease outbreaks that have the potential to adversely affect the United States."

The events of September 11, 2001, and the subsequent anthrax episodes highlighted the way in which public health can be affected by previously underappreciated threats. Fortunately, though, the DoD-GEIS program had been organized and resourced such that it could respond to this emergency in a uniquely capable manner. Specifically, within ten days of the attacks, the ESSENCE program was scaled up to encompass more than 300 DoD medical treatment facilities around the world. It now constitutes the largest and most automated syndromic surveillance system for bioterrorism in the world. An increase in DoD-GEIS resources this fiscal year made many other international contributions possible. Diverse nations continue to enter into DoD-GEIS collaborations in the best spirit of international cooperation. Old partnerships have been strengthened and new ones continue to bloom in such areas as Central and Southeast Asia. The universal value placed on public health has served as a focal point where previously there was little collaboration. DoD-GEIS has continued to support its federal partners in moving the issue of emerging infections beyond the health agenda into economic and global security forums.

DoD-GEIS has been a regular supporter of the APEC (Asia-Pacific Economic Cooperation) strategy as President Bush is strongly committed to the global fight against infectious diseases. With U.S. leadership, APEC has developed over the past year a strategy that identifies how it can help combat infectious diseases throughout the region. APEC Leaders endorsed this strategy in October 2001, and called for its immediate implementation. Its key goals are (1) improving surveillance and monitoring of disease, (2) boosting national capacity to respond to outbreaks, and (3) training of health authorities.

The IOM Report and the Future of DoD-GEIS

In late September 2001, DoD-GEIS received from the IOM the results of an 18-month review of its program. The 190-page report was the work of eight world experts in the public health aspects of emerging infections, supplemented by a dedicated andinsightful IOM staff. The experts were drawn from a variety of settings, including academia (University of Washington, Johns Hopkins, and Emory), the Maine State Health Department, WHO offices in Geneva and the Caribbean, and Health Canada. Their report noted that, in spite of the relatively small investment made, DoD-GEIS had made substantial progress toward its goals. It also made many recommendations on how DoD-GEIS could reach and even exceed those goals. These recommendations in many ways serve DoD-GEIS as a road map for the future.



These recommendations were wide ranging, and implementation had already begun in cases. One key recommendation dealt with the need for a full-time and properly prepared DoD-GEIS program manager at each overseas research facility. This has recently been achieved. The recommendation highlighted the importance of various training programs for insuring a steady stream of epidemiologists, laboratorians, and field scientists to fill DoD-GEIS positions. The committee also emphasized the importance of training foreign public health workers who, in many cases, will remain engaged in surveillance and response in their countries and produce a positive return on that investment for years to come. The IOM encouraged greater emphasis on partnerships with other federal agencies. Currently Public Health Service personnel are assigned to three overseas research activities and to the DoD-GEIS Central Hub. Additional co-placements could be of mutual value and reduce the duplication of infrastructure.

A critical and ongoing emphasis of this program is the improvement of information dissemination. DoD-GEIS has pursued this through fostering up-to-date web sites; co-sponsoring general and focused meetings at the local, regional, national, and international levels; giving public presentations; and publishing papers in peer-review journals. There remain gaps, though, in this multi-pronged effort. Considering the volume of quality information produced, more emphasis needs to be placed on identifying key customers and on targeting delivery of this information to ensure timely public health action. This will require increasingly formalized reporting mechanisms tailored to the needs of specific end users.

The development of the DoD-GEIS program has been an iterative process. The 5-year strategic plan approved and published in 1998 has served DoD-GEIS well. However, conceptualizing and implementing an

unprecedented DoD global disease surveillance and response network primarily through existing personnel and organizations has required constant refinements. These refinements will continue as threats come and go and as programs are evaluated against specific metrics for return on investment. Flexibility to respond to new and sometimes unanticipated threats must be maintained. The results of DoD-GEIS initiatives, as they have since the program's inception in 1997, will continue to benefit not only the DoD but also broader national and global health and security interests. The future of DoD-GEIS will depend on seeking the best guidance possible from DoD and external sources. Resources permitting, there is also a clear need for DoD-GEIS to expand its initiatives to new areas of the world that are of interest to the United States. These efforts will likely include not only bold, innovative approaches to meet the challenges of today and tomorrow but also the less glamorous but fundamental training and capacity-building efforts that are necessary to achieving lasting value.

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ACRONYMS

AFIERA	Air Force Institute for Environment, Safety and Occupational Health Risk Analysis
AFIP	Armed Forces Institute of Pathology
AFRIMS	Armed Forces Research Institute of the Medical Sciences
APEC	Asia-Pacific Economic Cooperation
CDC	Centers for Disease Control and Prevention
CENTCOM	Central Command
CINC	Commanders in Chief
DARPA	Defense Advanced Research Projects Agency
DoD-GEIS	Department of Defense Global Emerging Infections System
ESSENCE	Electronic Surveillance System for the Emergency Notification of Community-based Epidemics
ETEC	Enterotoxigenic *Escherichia (E.) coli*
EWORS	Early Warning Outbreak Response System
FDA	Food and Drug Administration
FRI	Febrile Respiratory Illness
FY	Fiscal Year
GISP	Gonococcal Isolate Surveillance Project
IOM	Institute of Medicine
MEDCOM	Medical Command
MHS	Military Health System
MIDRP	Military Infectious Disease Research Program
MOA	Memorandum of Agreement
MQ	Mefloquine
MRMC	Medical Research & Materiel Command
NAMRU-2	Naval Medical Research Unit – 2
NAMRU-3	Naval Medical Research Unit – 3
NASA	National Aeronautics and Space Administration
NCA	National Capital Area

NHRC	Naval Health Research Center
NIH	National Institutes of Health
NMRCD	Naval Medical Research Center Detachment
PCR	Polymerase Chain Reaction
PDD	Presidential Decision Directive
PHLIS	Public Health Laboratory Information System
RVF	Rift Valley Fever
SOUTHCOM	Southern Command
STD	Sexually Transmitted Diseases
STDPC	Sexually Transmitted Disease Prevention Committee
TSN	The Surveillance Network
USACHPPM	U.S. Army Center for Health Promotion and Preventive Medicine
USAID	U.S. Agency for International Development
USMI	U.S. Medicine Institute for Health Studies
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USAMRU-K	U.S. Army Research Unit - Kenya
VEE	Venezuelan Equine Encephalitis
VSAT	Very Small Aperture Terminal
WHO	World Health Organization

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