

DoD Global Emerging Infections System



Armed Forces Institute of Pathology

Military Infectious Disease Research Program

Uniformed Services University of the Health Sciences

United States Army

United States Navy

United States Air Force

*Office of the Asst. Secretary of Defense
(Health Affairs)*

US Regional Unified Commands

DoD Overseas Laboratories

US Centers for Disease Control & Prevention

United States Department of State

Pan American Health Organization

World Health Organization

Partnering in the Fight Against Emerging Infections

Annual Report
Fiscal Year 2002



EXECUTIVE SUMMARY

The events of and following September 11, 2001 brought into focus timely global surveillance for emerging infections as a cornerstone of national and global security. It became clear that public health infrastructure could no longer be a secondary consideration in national and local budgets, but that it is part of the foundation of our individual and collective well-being. The anthrax events of 2001 may have only harmed a small number of people in the United States but worldwide, even in developing countries that regularly cope with major naturally occurring outbreaks of infectious diseases, countries woke up with a start to the threat of bioterrorism. The emergence in China of SARS in late 2002 not only highlighted a new and serious threat in its own right but also reinforced that emerging infections that may emerge in one part of the world can rapidly cause devastating problems elsewhere. These events have all shown as prophetic those experts and government leaders who called for the establishment of DoD-GEIS in the early 1990s.

Fiscal year 2002 was DoD-GEIS's sixth year of funded operations. The DoD-GEIS central management hub coordinated activities with a core budget of \$9 million. This was leveraged through an extensive network of partnerships within the DoD, with other US government agencies, and with many foreign governments and international agencies. These partnerships supported both domestic and foreign programs of surveillance, response, capacity building, and training. Many of these programs provided direct benefits to the global war on terrorism.

A particular leadership role played by DoD-GEIS in the global war on terrorism has been the fostering of two automated syndromic surveillance systems, ESSENCE (Electronic Surveillance System for the Early Notification of Community-based Epidemics) and EWORS (Early Warning Outbreak Recognition System). ESSENCE, which was established as a pilot project in 1999 to provide rapid "syndromic" morbidity monitoring for 100 DoD clinics in the Washington, DC region, scaled up to encompass more than 300 medical treatment facilities around the world within days of 11 September 2001. As a pioneer in automated syndromic surveillance, ESSENCE is

helping to develop the standards for this new method of surveillance. Its global coverage and the diversity of the geographic foci under surveillance make it a key test-bed in evaluating methodologies for data capture, synthesis, analysis, and presentation. EWORS employs a methodological approach more appropriate for use in countries that have a rudimentary informatics infrastructure. Its potential, though, is no less appreciated and demand for it has spread beyond the five Asian countries now using it to other continents.

Fiscal year 2002 brought other exciting DoD-GEIS systems to a new state of operations. One of these is the near real-time global mortality surveillance conducted by the Armed Forces Institute of Pathology. New automated approaches to antibiotic resistance surveillance were successfully established at several DoD medical treatment facilities through a partnership with Focus Technologies, Inc. The rapid expansion of West Nile virus infection across the US in 2002 was another startling example of the potential of emerging infections to invade the US. West Nile virus went from being absent from the US prior to 1999 to causing at least 241 deaths across the country in 2002; surveillance conducted in 122 DoD and other federal installations this year documented that 36% had evidence of West Nile virus infection in animals or mosquitoes.

Laboratory capacity is the foundation of a public health system that can respond to the unexpected emergence of new threats such as West Nile virus, anthrax, or SARS. Since many new infections at first have symptoms similar to those of influenza, DoD-GEIS continues to invest extensively in capability for respiratory disease studies at the Air Force Institute for Occupational Health and the Naval Health Research Center. Other laboratories, such as the US Army Medical Research Institute of Infectious Diseases and the Naval Medical Research Center, have also been supported to ensure that quality diagnostic reagents for less common agents are on the shelf. The infrastructures of these organizations must be ready to respond to unexpected events.

The five overseas medical research units of DoD located in Egypt, Kenya, Thailand, Indonesia, and Peru

continue to be central to DoD-GEIS being, as the Institute of Medicine has stated, “a critical and unique resource of the United States in the context of global affairs.” The quality and productivity of each laboratory’s DoD-GEIS program continues to grow as expertise is strengthened and partnerships expanded. This year DoD-GEIS, largely through the overseas laboratories, had substantial collaborations in over 50 countries around the world. DoD-GEIS is contributing to active surveillance for new strains of influenza in the Far East, the Middle East, Africa, and Latin America. Global knowledge of anti-malarial resistance patterns is expanding not only as a result of studies conducted by DoD-GEIS, but also through successful efforts to provide training and transfer equipment to host-country investigators. Similarly, knowledge of antibiotic resistance in bacteria associated with diarrhea is growing through solid, high-quality DoD-GEIS surveillance in many parts of the world. Surveillance for the causes of fevers is also producing unexpected findings. These observations are enabling clinicians to alter treatments so they are more on target and effective.

In 2000, about midway through execution of the first DoD-GEIS five-year strategic plan, DoD-GEIS engaged the Institute of Medicine to evaluate the program. Their conclusions were published in September 2001 and reported on in the 2001 DoD-GEIS annual report. Positive responses to the report’s recommendations were evident in the work of FY 2002. Each overseas laboratory DoD-GEIS program is now led by at least one fully trained epidemiologist with experience in public health practice. Support staff have grown at both the Central Hub and at many of the field operating elements. Epidemiologic, laboratory, and informatics training have received stronger emphasis, especially at the overseas laboratories. Over the last few years, hundreds of DoD and host-country professionals have received training under the auspices of DoD-GEIS. A particularly gratifying outcome of this training is that many of the host-country partners who have been trained are now trainers for others in their own and neighboring countries. DoD-GEIS has, as recommended by the IOM, emphasized partnerships.

Recognizing the centrality of the World Health Organization (WHO) in the global system of emerging infections surveillance and response, DoD-

GEIS continues to actively support the WHO through funding of several DoD-based WHO collaborating centers, co-sponsoring courses, supporting a DoD officer’s assignment to WHO headquarters, and participating in the WHO Global Outbreak Alert and Response Network. DoD-GEIS has been a beneficiary of superb support from the CDC. This has included assignment of CDC personnel to overseas DoD-GEIS programs, support with informatics training projects (eg, support on surveillance efforts for influenza), and close coordination to ensure that DoD’s efforts are complementary and supportive of Health and Human Services initiatives.

As DoD-GEIS prepares for its next five years, inspiration can be taken from the March 2003 Institute of Medicine (IOM) report entitled *Microbial Threats to Health: Emergence, Detection, and Response*. In this new report, antimicrobial resistance is a focus, along with vector-borne infections, zoonotic infections, and infections associated with chronic diseases. Reflecting the post-September 11 reality, intentional use of biological agents is given serious consideration. The IOM offers 21 recommendations, including many for the DoD. The DoD is encouraged to continue enhancing global response capacity, especially focusing on threats in the developing world. The report states, “DoD should expand and increase in number its DoD-GEIS overseas program sites” and that DoD should foster diagnostics development, reagent distribution, and technology transfer. It recommends that all federal overseas surveillance activities, including DoD’s, should be coordinated by a single agency such as the Centers for Disease Control and Prevention. It calls for implementation of automated laboratory-based reporting of notifiable infections. ESSENCE is mentioned multiple times, and research on syndromic surveillance and geographic information systems is advised. DoD is encouraged to develop and expand intramural and extramural training in applied epidemiology, field-based research, and control of vector-borne and zoonotic diseases. Federal agencies are reminded of the need for a flexible research agenda to permit rapid assessment of new and emerging threats.

DoD-GEIS is a leader in a new and evolving national security construct. Pioneering innovations and broad outreach within the military health system and in the international setting have been central to success

during its first five-year plan. Vibrant cross-service teamwork has produced beneficial outcomes for service members, their families, other Americans, strategically important partner nations, and the global community in general. Despite these successes, public health capacity in military and civilian sectors is not yet optimal; the global human, microbiological, and ecological factors behind infectious disease emergence continue to gain strength. As DoD-GEIS anticipates its second five-year plan, the bioterrorism events of FY

2002 and the emergence of SARS in early FY 2003 only reinforce as prophetic the words of Wilbur Sawyer in his 1944 Presidential Address to the American Society of Tropical Medicine and Hygiene:

“No country can live to itself in disease prevention ... Failure of one is a failure of all.”

CONSOLIDATED FY02 DoD-GEIS REPORT

In 1992 the National Academy of Sciences published a landmark report entitled *Emerging Infections: Microbial Threats to Health in the United States*. Though that prophetic document was primarily concerned about naturally occurring disease emergencies such as HIV, Legionnaire’s disease, toxic shock syndrome, antibiotic resistance, West Nile virus infection, and Lyme disease, the domestic and international public health weaknesses it outlined are of even more concern as we struggle to deal with the potential use of biological agents for terrorism. Despite the fact that most nations have committed themselves to the Biological Weapons Convention, multiple international actors are still thought to possess biological weapons. Appreciation of this threat emphasizes the need to see emerging infections surveillance not only in the traditional public health context but also as an essential contributor to our national security. As was written in the November 2002 National Geographic, “...whenever weapons of mass death are unleashed, all humanity is downwind.”

The 2001 Institute of Medicine program review of the DoD-Global Emerging Infections Surveillance and Response System (DoD-GEIS) stated that DoD-GEIS is “the only U.S. entity that is devoted to infectious diseases globally and that has broad-based laboratory capacities in overseas settings.” As noted by the IOM, the “rare, sometimes unique, diagnostic capabilities” found in the DoD overseas medical units represent critical international “medical research, public health, and diplomatic resources to the benefit of not only the U.S. military but also U.S. civilian and global interests alike.” The events of FY 2002, including the anthrax incidents with their domestic and international rami-

fications and the expanding war on terrorism, only strengthen these statements.

The genesis of DoD-GEIS is found in the 1996 Presidential Decision Directive on Emerging Infections. This directive, recognizing DoD’s unique assets for international public health surveillance, states:

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

Fiscal year 2002 was DoD-GEIS’s sixth year of funded operations. The DoD-GEIS central management hub coordinated activities with a core budget of \$9 million. This continued to be leveraged through an extensive network of partnerships within the DoD, with other US government agencies, and with many foreign governments and international agencies.

DoD-GEIS programs are divided into two main groups: (1) activities conducted with international partners, especially out of the five tropical DoD overseas medical research units, and (2) activities through initiatives within the Military Health System (MHS). The MHS program, which receives about a third of the DoD-GEIS budget, is focused on improving MHS capabilities across a wide range of emerging infections issues. The foci of MHS activities are relatively stable

from year to year and are chosen 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 timely public health actions
- Responsiveness to critical operational theater needs
- Accessibility of nonfiscal resources needed for execution
- Quality of the science
- Area not covered by an existing core MHS public health program
- Consistency with DoD-GEIS five-year strategic plan

The second primary setting for DoD-GEIS work is an expanding network of collaborative international partnerships. Within the network, the overseas medical research units manage on a regional basis

state-of-the-art syndromic and disease-specific surveillance, training, response, and capacity building initiatives. These laboratories, which are located in Peru, Indonesia, Thailand, Egypt, and Kenya, are multidisciplinary and employ largely host-country nationals under the leadership of US scientists. They are stable and productive entities, each having been established at least 20 years ago. Their partnerships with host governments and regional World Health Organization offices are central to their success in contributing to regional health and stability.

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

IMPLEMENTING ACTIONS OF PRESIDENTIAL DECISION DIRECTIVE NSTC-7

The Presidential Decision Directive mandate for DoD-GEIS is organized around several focal points of action that are to be coordinated, where relevant, with PDD 39 on U.S. counterterrorism policy. The key implementation action called for is:

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

ACTIVITIES BASED IN THE MILITARY HEALTH SYSTEM Health Indicator Surveillance (ESSENCE)

A challenge to surveillance for emerging infections is that, by definition, these conditions are either clinically ill-defined or unexpected. This brings out a weakness in traditional approaches to surveillance which rely on laboratory confirmation of conditions described by well-established case definitions. The phenomenon of bioterrorism with unusual agents highlights this challenge particularly well. In 1999 DoD-GEIS, inspired by innovative surveillance projects in New York City, established a pilot “health indicator” or “syndromic” surveillance system for the Washington, DC, area called the Electronic

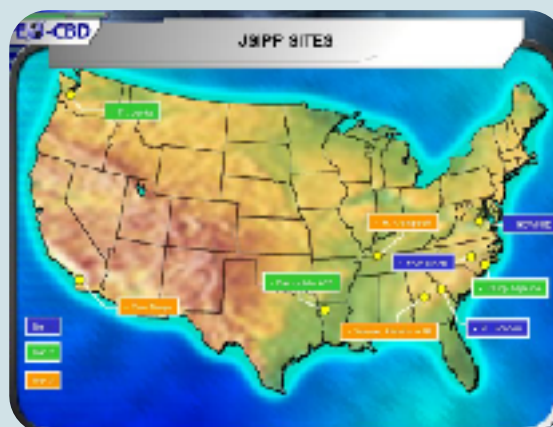
Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE). Following the September 2001 terrorist attacks, ESSENCE, though still in development, was rapidly scaled up to provide increasingly real-time surveillance for more than 300 DoD installations around the world. ESSENCE has focused on daily tracking of diagnoses generated in ambulatory primary care clinics. Each day’s morbidity experience for a given location is compared with historic data to evaluate statistically the deviation from expected ranges.

Essence and the Joint Service Installation Pilot Project

The Joint Service Installation Pilot Project (JSIPP), a Department of Defense program managed by the Defense Threat Reduction Agency, is designed to upgrade nine military installations—three each from the Army, Navy, and Air Force—to be model sites for biological and chemical safety. The sites will be provided with equipment and training to enhance protection, detection and emergency response. Chemical and biological sensor data will be integrated with medical surveillance, although the primary recipients and users of the medical data will be the public health and medical personnel, and the sensor data will be analyzed by the emergency operations center. The Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE) has been selected to participate in this pilot project to help with biomedical surveillance.

ESSENCE, a tool for surveillance of infectious disease clusters, is currently accessible via the web by all DoD medical treatment facilities. ESSENCE staff will train epidemiologists and infectious disease specialists at each of the nine JSIPP sites on the use and operational advantages of ESSENCE to enhance medical surveillance on their respective

installations. An enhanced version of ESSENCE is being developed for use at the JSIPP sites. This version will include several new components: a geographic information system component for both mapping disease distribution and detecting unusual spatial clusters, military pharmaceutical data, and new analytic methods for detecting disease alerts.



The installations selected to be the first participants in the JSIPP are Camp Lejeune, NC; Fort Campbell, KY; Pope Air Force Base (AFB), NC; Barksdale AFB, LA; Fort Lewis, WA; Navy Region Southwest San Diego, CA; Fort Gordon, GA; Robins AFB, GA; and Naval Surface Warfare Center Dahlgren, VA.

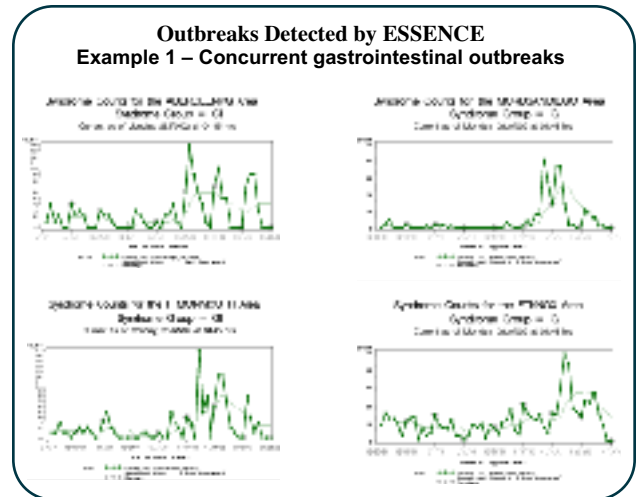
In FY 2002, the highly productive ESSENCE partnership with the Johns Hopkins Applied Physics Lab (JHU/APL) continued to grow, largely due to supplementary funding from the Defense Advanced Research Projects Agency (DARPA). One of the outcomes has been a redesigned, secure ESSENCE website to provide expanded information to approved users around the world. This included graphs for ICD-9 sub-groupings, age groups, clinic types, and line listings of patient data stripped of identifiers. A tri-service meeting began the process of decentralizing interpretation and response activities to the service level. This is critical because a system such as ESSENCE is actually a system of local surveillance systems, each with its own unique population and performance characteristics.

Ambulatory data represent only one health indicator among several during the natural history of an outbreak, so in FY 2002 ESSENCE evaluated data

from the DoD Pharmacy Data Transaction Service (PDTS) to see if this source could serve as an leading indicator of an evolving health pattern. Negotiations to acquire DoD nurse hotline data and animal data were also pursued. Studies were conducted at basic training posts to validate ESSENCE against on-the-ground, active surveillance. The value of tracking non-specific ICD-9 codes was also evaluated, and a validation study was done comparing ICD-9 codes reported electronically to ESSENCE with the actual findings documented in the medical records. Considerable advances were made with JHU/APL in the development of new temporal and spatial detection networks with which to analyze various data sources. The Defense Threat Reduction Agency (DTRA) provided supplementary funding to evaluate ESSENCE in Albuquerque, NM, and develop improved geographic information system (GIS) interfaces. An interesting development in ESSENCE methodology has been the exploratory use of

ESSENCE to track mental health diagnoses at the community level in association with stressful events such as the September 2001 attacks.

A powerful advantage of ESSENCE, as compared to similar systems in development, is its sheer volume of cases processed daily from a highly heterogeneous collection of communities around the world. This throughput has allowed regular detection of naturally occurring outbreaks and assessment of system performance in a variety of settings. One of the most interesting phenomena detected was the nearly simultaneous occurrence of gastrointestinal outbreaks in DoD training settings around the country in January of 2002. The largest of these, at the Marine Corps Recruit Depot in San Diego, involved more than 130 trainees yet its full magnitude was not appreciated until ESSENCE provided the “big picture.” An



investigation at the Depot by ESSENCE staff confirmed this outbreak to have been caused by a Norwalk-like virus.

Mortality Surveillance

Prior to a DoD-GEIS initiative, DoD lacked an organized mortality surveillance program. With DoD-GEIS funding, a program of daily mortality surveillance has now been established in the Office of the Armed Forces Medical Examiner (AFME) at the

Armed Forces Institute of Pathology. The AFME is now involved in all active duty deaths, sometimes to the point of transferring the body from a civilian facility to a military one for autopsy. The mortality surveillance program continues to grow stronger; DoD-GEIS interest is primarily in tracking deaths in real time for infectious or potentially infectious etiologies. Since January 2002, daily reporting has been underway for all four services. Weekly, electronic, graphical reporting to the service medical chiefs has been established. The registry at the conclusion of FY 2002 had approximately 4,700 records dating back to January 1998. Reports of 230 illness-related deaths were investigated in FY 2002. Of these, 14 were due to infections, two listed co-morbid infections, and two were still under review. In-depth investigations occurred in several cases, including the death of an airman from multi-system organ failure shortly after receiving a vaccine, a malaria death that identified a cluster of cases in a single unit, and a West Point cadet who died of meningococemia. Tissue from a fatal case of epiglottitis was archived for future evaluation after viral and bacterial cultures and PCR for known agents came up negative.

Figure 1 shows the number of cases by disease.

Fig 1: Armed Forces Infectious Deaths for Federal Fiscal Year 2002

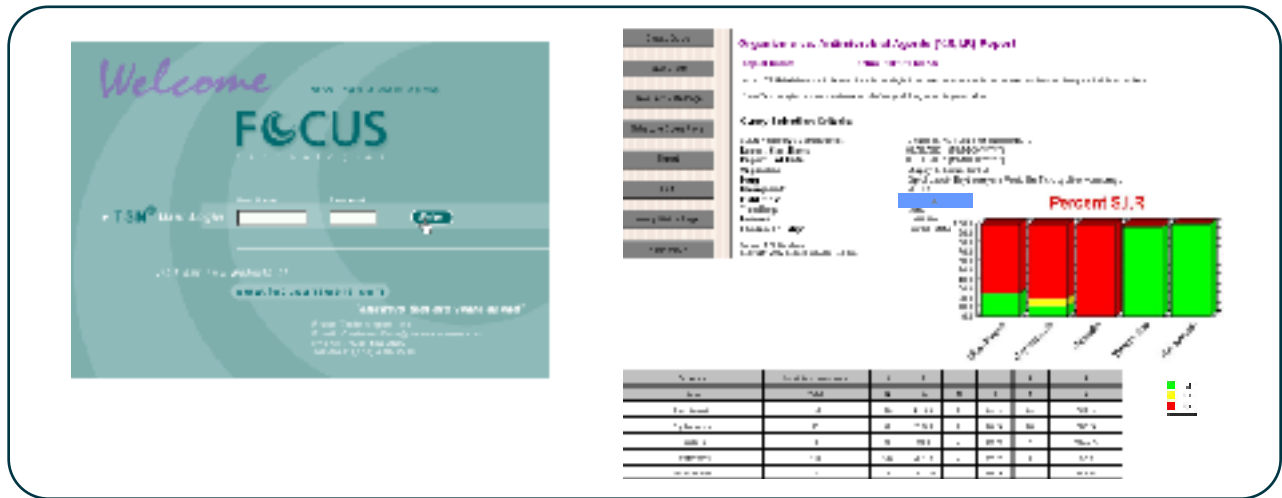
Cause of Death	Cases
Pneumonia, organism unspecified	4
Adult Respiratory Distress Syndrome, pneumonia secondary	1
Myocarditis	1
Meningitis, neisseria & pneumococcal	2
Hepatitis C	2
Septicemia, streptococcus, group A	1
HIV disease, Pneumocystis carinii pneumonia	1
Malaria, falciparum	1
Epiglottitis	1
Co-morbid Conditions	
Myocarditis (secondary to heat stroke)	1
Pneumonia (secondary to acute intermittent porphyria)	1
Under Review	
Fulminant hepatitis	1
Liver cirrhosis, non-alcohol related	1
Total Cases	18

Surveillance and Response for Antibiotic Resistance and Sexually Transmitted Diseases

Antibiotic resistance is a growing global problem. The federal government's lead agents for addressing this problem are the Centers for Disease Control (CDC), the National Institute of Health, and the Food and Drug Administration, but the DoD, as a federal entity in charge of one of the largest health care systems in the nation, has a unique role. DoD-GEIS represented DoD on the Federal Antibiotic Resistance Task Force. The task force focused initially on a strategic plan for addressing the problem domestically, but during FY 2002, it focused on writing a report to address the international dimension of antibiotic resistance. With DoD personnel serving around the world and with extensive microbiological capabilities at the overseas medical research units, DoD participation in the Task Force was useful and valued.

A key DoD-GEIS partnership with Focus Technologies, Inc., has been established through a Cooperative Research and Development Agreement. Focus has developed a real-time hospital-based

surveillance for antibiotic resistance. This system, which is called TSN®, involves daily downloads of microbiology laboratory data without identifiers. Key MHS participants in this effort have been Wilford Hall Medical Center, Tripler Army Medical Center, and Keesler Medical Center. DoD-GEIS is trying to increase the number of medical treatment facilities, which Focus is supporting by implementing a DoD-specific web interface for on-line data analysis. With TSN, it is possible for hospital microbiology departments to create antibiograms rapidly and post them on their intranet sites. For example, antibiograms that previously took Wilford Hall technicians more than 40 hours to create can be done in minutes with TSN. TSN has proven valuable to both clinicians needing to know sensitivity patterns and to infection control staff needing to evaluate the impact of antimicrobial interventions on susceptibility trends before and after the intervention. TSN enables DoD facilities to compare their data to other DoD medical treatment facilities (MTFs) and to comparable regional and national institutions.



Another antibiotic resistance focal point of DoD-GEIS this past year has been to support the CDC Gonococcal Isolate Surveillance Program (GISP). Extensive use of modern molecular diagnostic methods has made it harder to get antibiotic sensitivity patterns based on testing isolates. The DoD-GEIS GISP has concentrated on Hawaii, where in 2001 28% of all gonococcal infections reported were from military facilities. The dramatic rise of

ciprofloxacin-resistant gonococci in Hawaii (<1.5% before 1997 vs. 20.7% in 2001) was attributed by some to US troop importations following redeployment from Asia. The 16 military gonococcal isolates from Hawaii studied in 2002 were, interestingly, all susceptible to ciprofloxacin, a finding that countered the prior opinion that military personnel were a significant source of resistant gonorrhea.

Within the DoD, DoD-GEIS has been an active supporter of the work of the DoD Sexually Transmitted Disease Prevention Committee. The committee has highlighted the fact that although STDs cause significant morbidity in the services, screening, case finding, diagnosis, treatment, reporting, contact tracing, and prevention activities are neither standardized nor rigorously evaluated. In October 2001 DoD-GEIS co-sponsored with the US Medicine Institute for Health Studies a forum entitled "STDs: Regaining Lost Ground, Improving the Future." In partnership with

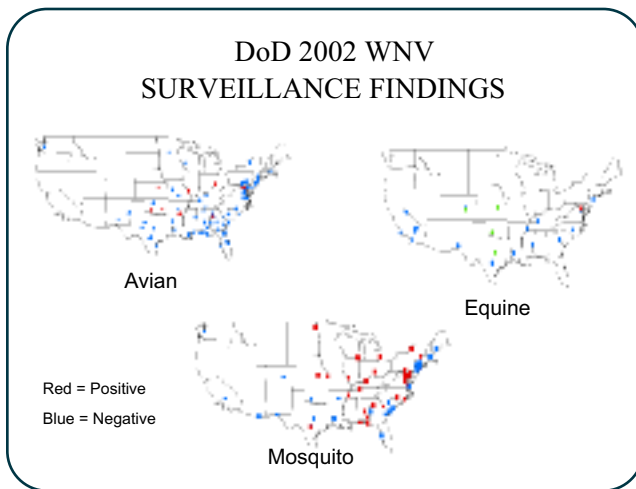
the US Army Center for Health Promotion and Preventive Medicine (CHPPM), objectives for a DoD STD center were developed, including standardizing and improving reporting; standardizing screening, diagnostic testing, and case management; monitoring antibiotic susceptibility; and developing and evaluating educational materials. In February 2002, CHPPM and DoD-GEIS hosted a tri-service conference to advance the concept of a DoD STD Center supported by DoD-GEIS.

West Nile Fever

During FY 2002, the West Nile virus (WNV) continued its westward spread, ultimately causing 3,858 human cases in 2002 and at least 241 deaths. One hundred twenty-two DoD installations and federal government sites participated in DoD WNV surveillance. Forty-four (36%) of these had surveillance findings indicative of WNV, and 11 that had positive mosquito findings also had avian or mammalian findings suggestive of viral transmission risk. No reports were received of active duty personnel having acquired WNV (though one reservist was a confirmed case). Thirteen active duty

personnel were admitted to DoD MTFs for possible WNV infection, but laboratory studies ruled out WNV in each case. At least 121 persons were tested for WNV at DoD facilities.

Two hundred eighty-four mosquito pools from 15 DoD installations were found positive for WNV. Seventy-nine percent of the positive pools were from seven installations around Washington, DC. Ninety percent of the positive pools were composed of Culex mosquitoes. At least 106 sick or dead birds at 40 sites were found positive for WNV. Sentinel chicken flocks at Fort Polk, LA, and Langley Air Force Base, VA, seroconverted during 2002 surveillance. Interestingly, both of these conversions came in the absence of other positive WNV surveillance findings at those locations. DoD also conducted WNV in government-owned equines during 2002. There was one definite seroconversion noted in a horse at Fort Myer, VA. A second horse at Fort Riley, KS, seroconverted but the immunization history made it unclear whether this was due to viral infection or immunization. Other horses have had mild antibody responses, which are also awaiting clarification. None had clinical illness. Civilian veterinarians diagnosed six civilian-owned horses (five stabled on post and one next to an installation) as having acquired WNV.



General Public Health Laboratory Improvement

In 1999 DoD-GEIS sponsored a Military Public Health Laboratory Symposium and Workshop. Subsequently, a memorandum of agreement was developed with the Armed Forces Institute of Pathology to develop an online directory of DoD public health laboratory services

so that access to state-of-the-art diagnostics could be facilitated and laboratory-based surveillance information could be more completely captured. Progress reported during 2002 included the creation of a prototype using current, industry-standard software and

advanced search routines. The database was populated with information on 150 infectious agents and 25 government laboratories. After demonstrating the system, access was given to participating laboratories so that DoD users could update their respective capabilities before opening the directory to general access.

Essential to DoD-GEIS efforts to strengthen DoD laboratory capacity is the US Army Research Institute of Infectious Diseases (USAMRIID), with its extensive BSL-3 and BSL-4 facilities. The goal of DoD-GEIS support is to maintain readiness to diagnose emerging and re-emerging infectious diseases. This capability includes producing, testing, and stockpiling reagents for use in special assays. USAMRIID has a particular role in serving as a DoD reference center and WHO Collaborating Center for the isolation of, identification of, diagnosis of, and consultation on unusual, rare, or emerging infectious diseases. Training is another key USAMRIID function.

During FY 2002, USAMRIID performed 2,244 assays for viruses (eg, Hantaan, West Nile, Powassan, orthopox, dengue, and Venezuelan equine encephalitis). Reagents were produced and stockpiled for West Nile, Crimean-Congo hemorrhagic fever, Ebola-Zaire, Ebola-Reston, and Ebola-Ivory Coast, Marburg, Lassa, Rift Valley fever, dengue, various equine encephalitis viruses, plague, anthrax, and various toxins. Diagnostic kits were provided to DoD, as well as national and international collaborators. This included USAMRIID's support of the Theater Area Medical Lab, WNV surveillance of military horses, the 121st Evacuation Hospital-Korea, USACHPPM-South, and US SOUTHCOM exercises in Central America. It also provided support to DoD and federal agencies in the investigation of the ongoing WNV outbreak in the US. It also supported an investigation of anthrax and brucella in bison in Canada.

Respiratory Disease Surveillance and Capacity Building

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

The DoD influenza surveillance program does etiology-based and population-based surveillance. The Air Force Institute for Environment, Safety, and Occupational Health Risk Analysis (AFIERA) conducts the etiology-based surveillance, and the Naval Health Research Center in San Diego focuses on surveillance of high-risk populations such as recruits at basic training centers.

The DoD Influenza Surveillance Program, which is supported by DoD-GEIS, continues to provide key data to the annual Food and Drug Administration meeting that selects components for the influenza vaccine. The 2002-2003 season influenza vaccine contained the H3N2 Panama strain that was obtained



through the DoD surveillance program. Annually, the DoD Influenza Surveillance Working Group meets to review program operations from the prior year and plan improvements for the following year. One valuable improvement has been AFIERA's increasing emphasis on rapid, standardized dissemination of data throughout the network during the influenza season by providing twice-weekly internet reports for sites contributing specimens. Web-based GIS tools have also been used to display current worldwide DoD influenza activity on the website.

During the 2001-2002 Northern Hemisphere influenza surveillance season, 20 sentinel sites and 45 nonsentinel sites submitted 3,119 throat swabs. These were supplemented by 324 specimens from DoD-GEIS overseas surveillance in non-DoD settings in Nepal, Thailand, South America, and Uganda. Of the 3,119 specimens, 18% were positive for influenza viruses (90% type A, 10% type B). Of the type A influenza isolates, 94% were H3N2 and 6% H1N1. The H3N2 strains were typed as A/Panama/2007/99-like, a component of both the 2000-2001 and 2001-2002 vaccines. The H1N1 strains were typed as A/New Caledonia/20/99-like, also a component of those two vaccines. Of 1,118 swabs yielding a positive viral isolate, 50% grew influenza and 29% grew adenoviruses.

During FY 2002, AFIERA established a nucleic acid sequencing facility for analysis of influenza isolates, a major move forward for DoD in global influenza surveillance. Specimens with a high likelihood of significant antigenic alterations that otherwise would not have been subtyped have been reported to CDC. (More than 70 influenza isolates and sequences were shared with CDC during the fiscal year.) AFIERA now is only one of a handful of laboratories in the US that can do surveillance on both the hemagglutinin and neuraminidase antigens of the influenza virus. In collaboration with USAMRIID, AFIERA also evaluated influenza primers and probes for PCR. This is a model of a tri-service surveillance effort; public health personnel from both the domestic and international sides of the DoD-GEIS network benefited from training provided by AFIERA staff.

The Naval Health Research Center (NHRC) conducted tri-service, population-based surveillance for febrile respiratory illness (FRI) among basic trainees at eight centers. During FY 2002, adenovirus remained the leading cause of FRI among recruits, with 979 of 1,662 (59%) of specimens positive. Of these, 98% were adenovirus serotype 4. Adenovirus outbreaks were documented at Fort Benning (July 2002) and NTC Great Lakes (September 2002). Like AFIERA, NHRC emphasized rapid dissemination of findings via the web, and it recorded more than 10,000 user sessions on the website in FY 2002. This surveillance provided compelling data to support the decision to re-acquire adenovirus vaccine. Some of the respiratory disease surveillance infrastructure at NHRC funded by DoD-

GEIS has been instrumental in a double-blind controlled clinical trial of 23-valent pneumococcal vaccine in recruits. At the close of the fiscal year, 127,775 recruits had been enrolled and 520 pneumonia cases reported.

To explore a potentially more effective method for influenza and adenovirus surveillance, DoD-GEIS collaborators at NHRC and the Armed Forces Institute of Pathology studied two PCR methods for evaluation of fixed, room-temperature samples at Fort Jackson, SC. One hundred ninety-five recruits were enrolled and yielded 27 influenza specimens and 62 adenovirus specimens. Compared with viral culture, sensitivity and specificity of the influenza PCR was 89% and 85% respectively. Sensitivity and specificity for the adenoviral PCR was 94% and 75% respectively. Among culture-negative samples, 25 were PCR-positive for influenza and 33 for adenovirus. These PCR methods hold promise for augmenting viral culture, especially in settings where maintaining the cold chain is impractical.

NHRC also tracked invasive *Streptococcus pneumoniae* at seven MTFs. To date, 350 specimens with invasive strains have been studied. Antibiotic resistance was widespread (35% to penicillin, 24% to erythromycin, 14% to ceftriaxone, and 37% to trimethoprim/sulfamethoxazole; 23% were resistant to three or more antibiotics). Antibiotic resistance of invasive serotypes does not seem to be increasing, and most of the invasive types from the US are in the current 23-valent vaccine. In addition to surveillance of strains from DoD MTFs, the NHRC DoD-GEIS program has also been supporting *S. pneumoniae* surveillance by the NAMRU-3 (Cairo, Egypt) DoD-GEIS program. In contrast to the US strains, the majority of the NAMRU-3 strains were not represented in the pneumococcal vaccine. One servicemember was investigated who died of an emerging non-vaccine pneumococcal strain, serotype 38.

Surveillance of *Staphylococcus pyogenes* is also done using isolates from clinical laboratories at nine recruit training centers. Among 942 specimens tested, 100% were susceptible to penicillin, levofloxacin, and vancomycin. Overall low levels of antibiotic resistance (< 6%) were documented against erythromycin, tetracycline, and clindamycin, but Lackland Air Force Base

stood out has having more erythromycin resistance. NHRC also has conducted *Bordetella pertussis* surveillance at four recruit centers. This has included evalua-

tion of a PCR-based beacon probe. Of 147 specimen sets studied, only one was positive by culture, but 9 were positive for *B. pertussis* by PCR.

Malaria and Other Public Health Threats in the Republic of Korea

The 18th Medical Command, considering the density of U.S. troops in South Korea and the range of infectious disease threats there, is a critical DoD-GEIS partner. The re-emergence of vivax malaria in South Korea in 1993 and its impact on troops is prototypical of the global problem of emerging infections. During the period of 1998 to 2000, the reported number of malaria cases ranged from 3,621 to 4,142 cases in Korean soldiers and civilians. During 2001, the number of reported cases decreased to 2,537. By 26 December 2002, fewer than 1,800 cases had been reported, but there is some reporting lag. Increased use of chemoprophylaxis by the Republic of Korea Army may have contributed to this decline. In contrast to the ROK trends, trends in US Force-Korea showed an increase in reported cases from 29 in CY 2001 to 41 in CY 2002. Transmission is attributed to

exposures during exercises near the Demilitarized Zone. This year, risk was attributed particularly to being near the Munsan and Paju training sites and installations. Surveillance data are being used to target chemoprophylaxis recommendations for U.S. forces.

Human case surveillance was supplemented by EIA or PCR analysis of trapped mosquitoes for evidence of malaria infection. Although about 12,000 mosquitoes collected during 2001 were studied (4,000 from the Western Corridor), none were positive. Future testing will be expanded to include training sites thought to be at higher risk. Another complementary element of the program was surveys of soldier knowledge, attitude, and behavior concerning malaria prevention. Based on approximately 1,200 surveys, a number of misconceptions and compliance issues were identified and troops will get targeted re-education to improve their acceptance and use of personal protective measures.

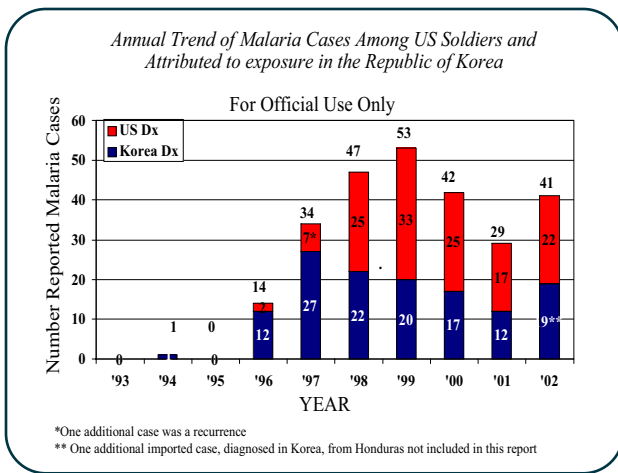


Figure 3. Annual trend of vivax malaria among USFK soldiers and Korean Augmentees (KATUSAs) attributed to exposure in the ROK and diagnosed in the ROK and US (Preventive Services Directorate).

DoD-GEIS continues to support surveillance of mosquitoes for Japanese encephalitis (JE) virus. The JE virus is circulating in at least two widely dispersed sites (Kunsan Air Base-South and CP Greaves-North). US troops could be developing asymptomatic or mild infections. JE immunization coverage in the Korean population is very high. Studies of rodents continue to show evidence for circulation at various times and places in Korea of hantavirus infection, scrub typhus, murine typhus, leptospirosis, and *Ehrlichia* and/or *Anaplasma* infection. Although Korean hemorrhagic fever has been increasingly reported in South Korean civilians (311 cases in CY 2002), no cases of KHF were recognized in US forces this year.

ACTIVITIES CONDUCTED BY THE DoD OVERSEAS MEDICAL RESEARCH UNITS

Sixty-five percent of the core DoD-GEIS budget supports initiatives conducted by the five tropical overseas medical research units of the Walter Reed Army Institute of Research and the Naval Medical

Research Center. In FY 2002, this amounted to approximately \$5.85 million. Each laboratory has a broad-based program focused on surveillance, response, training, and capacity building. In many

cases this was supplemented with additional funding from sources such as USAID and humanitarian assistance funds from the DoD Combatant Commands. The overseas medical research units put a strong emphasis on building regional partnerships. NAMRU-2 and NAMRU-3 have been designated as WHO Collaborating Centers for Emerging and Reemerging Infections. Several other DoD-GEIS laboratories are pursuing the multi-year process to obtain this key designation.

Governments and organizations in the following locations had substantive FY 2002 collaborations with the DoD-GEIS international program:

Antigua	Brunei	Ecuador
Argentina	Cambodia	Egypt
Austria	Canada	El Salvador
Bahamas	China	France
Barbados	Colombia	Grenada
Barbuda	Costa Rica	Guatemala
Belize	Dominica	Guyana
Bangladesh	Dominican Republic	Haiti
Bolivia		Honduras

India	Oman	Singapore
Indonesia	Pakistan	Sudan
Jamaica	Panama	Syria
Jordan	Paraguay	Thailand
Kazakhstan	Peru	Trinidad and Tobago
Japan	Philippines	Ukraine
Laos	Russia	Uzbekistan
Malaysia	Saint Kitts and Nevis	Vanuatu
Maldives	Saint Lucia	Vietnam
Mexico	Saint Vincent and the Grenadines	Yemen
Myanmar		
Nepal		
Nicaragua		

The overseas laboratory DoD-GEIS program emphasizes several core surveillance efforts: influenza, drug-resistant malaria, antibiotic-resistant enteric organisms, fevers of undetermined etiology, and syndromic surveillance. In response to local needs or opportunities, additional programs have also been implemented at the laboratories. The most important programmatic highlights and findings follow.

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

The AFRIMS laboratory has a remarkable history extending back to its founding following the 1956-8 cholera pandemic. Today that institution employs several hundred staff working in Bangkok and over 40 field sites in Thailand, Nepal, Cambodia, Vietnam, Laos, and Bangladesh. Its research focus is broad and encompasses important regional, military, and civilian threats including malaria, diarrhea/dysentery, dengue fever, HIV, hepatitis, influenza, and scrub typhus. It was characterized by the Institute of Medicine in 2001 as “probably the most sophisticated diagnostic and research laboratory in all of Southeast Asia.”

AFRIMS has a robust enteric illness program motivated by the historic importance of diarrheal diseases in military and civilian public health. The DoD-GEIS enterics surveillance program at AFRIMS involves prospective evaluation of patients (host-national adults and children, soldiers, or expatriates) at six sites with acute diarrhea. These include clinical centers in Thailand, Nepal, and Vietnam, plus the multinational Cobra Gold military exercise in Thailand. The program evaluated specimens from 1,032 cases and

837 controls during FY 2002. *Campylobacter* spp. accounted for 21% of pathogens isolated in Cobra Gold, 14% in travelers in Thailand, and 16% in travelers in Nepal. Interestingly, among Thai children in Kanchanaburi, *Campylobacter* was isolated among 21% of diarrhea cases and 24% of controls. Similarly at several sites in Thailand, *Salmonella* was detected at approximately the same frequency in cases and controls. *Salmonella* was the leading cause of diarrhea in deployed troops (29%), although control data were not available. *Shigella* and ETEC were noted in variable frequency across the sites. Twelve percent of traveler’s diarrhea in Nepal was attributed to *Giardia lamblia*. Ten percent of the Nepalese isolates were *Cyclospora* and 11% rotavirus. Rotavirus was found to be the main cause of acute diarrhea in Vietnamese children under five years of age (39%).

Antibiotic resistance noted at these enteric surveillance sites was noteworthy. For example, *Campylobacter* spp. isolate resistance to nalidixic acid and ciprofloxacin ranged from 87% for Cobra Gold to 36% in Vietnam. Last year the resistance in Vietnam

was 0%. Meanwhile, resistance to macrolide antibiotics, erythromycin, and azithromycin, was detected in 6% of Thai isolates but in none of the isolates from Nepal and Vietnam. *Salmonella* and ETEC isolates were generally sensitive to ciprofloxacin, although resistant *Salmonella* was isolated from three foreigners at a Bangkok hospital. In conjunction with the surveillance, training of technicians and clinicians in the region was provided and ranged from basic skills in specimen processing and enteric isolation to antibiotic susceptibility screening, database use, PCR, and DNA hybridization.

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

AFRIMS continues to monitor anti-malarial drug susceptibility patterns in vitro and in vivo and to make the data available for national policy planning. For the first time, this has provided solid antimalarial drug susceptibility data for sentinel sites in Vietnam (Bao Loc), Myanmar (Than Dwe), and western Thailand (Sangkhlaburi). Contrary to other reports, AFRIMS detected neither improvement of mefloquine resistance in Vietnam nor along the western border of Thailand. As a result of observation by the Thai Malaria Control Program and a preliminary report from AFRIMS on the poor efficacy of mefloquine monotherapy (76% late failure rate) in the region of Sangkhlaburi and adjacent areas, the Thai Ministry of Public Health changed treatment policy for that region in June 2002 to a combination of artesunate and mefloquine for first-line treatment of uncomplicated falciparum malaria. Bangladesh is also an emerging antimalarial multidrug resistant area. In vitro mefloquine resistance is common in Bangladesh, but the degree of resistance is below that of the Thai-Myanmar border. No artemisinin-resistant *Plasmodium falciparum* isolates have been found among the wild isolates from this region collected by AFRIMS.

With DoD-GEIS support, the AFRIMS program is distributing free of charge (via the internet: <http://malaria.farch.net>) a new method and software to apply enzymatic methods for assessing parasite

growth for in vitro antimalaria drug susceptibility testing. Because this method is easier and uses available reagents, it will be of benefit to public health laboratories in the developing world. Several substantial forms of training were provided, including courses for microscopists and collaborators involved with malaria epidemiology field studies in Nepal. In November 2002, personnel from Thailand, Vietnam, Indonesia, and Japan were also trained in a technique developed at AFRIMS to assay for antimalarial drug sensitivity by detection of HRP2 using ELISA.

For several years, the AFRIMS DoD-GEIS program has conducted community- and hospital-based surveillance of febrile illnesses among migrants and local residents in Sangkhlaburi, Thailand, near the border with Myanmar. This work has documented that leptospirosis is a common but underrecognized cause of year-round morbidity and mortality. Changes in the approach to empiric therapy will likely save lives. Serologic assessment of patients with respiratory complaints shows that prior infection with melioidosis (*Burkholderia pseudomallei*), not felt to be present in this region, is in fact quite common. AFRIMS also documented the first case of acute hepatitis E in the Sangkhlaburi area and, in cooperation with non-governmental organizations involved with refugee care, is keeping alert for febrile cases with jaundice. So far two cases of hepatitis E have been confirmed. Spotted fever group (SFG) rickettsioses have also been demonstrated in this region. *Rickettsia felis* was found responsible for SFG rickettsiosis for the first time in Asia. Extensive tick and flea surveys in the community and the forest fringes demonstrated the presence of 13 bacteria of the *Rickettsia*, *Anaplasma*, *Ehrlichia*, and *Bartonella* genera. These include human and animal pathogens. Flavivirus serologies are suggesting the possibility that another flavivirus, besides those that cause dengue and Japanese encephalitis, is circulating in the community.

A febrile surveillance program is also conducted to identify causes of icteric and hemorrhagic illnesses and encephalitis in Kathmandu and the Terai district of Nepal. Among 130 cases with febrile jaundice, 46% were confirmed to have hepatitis E. Other hepatitides were rare. Similarly, hospital-based surveillance is conducted in Kamphaeng Phet, Thailand. In this location, about 1,200 cases have

AFRIMS Scientists Determine the Cause of a Fever Epidemic in Nepal

In June 2002, at the request of the Thai Government, Ministry of Health, Department of Health Services, a team of medical researchers from the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, Thailand, the CIWEC Travel Medicine Clinic, and the Nepalese National Public Health Laboratory assisted the investigation of a large number of patients with high fever in the Bharatpur district of Nepal.

In conjunction with the Bharatpur District Hospital and the College of Medical Sciences, the team was able to obtain specimens to identify and characterize the organism causing the outbreak, assess the size and number of people affected by the outbreak, and, most importantly, make recommendations as to what medicines to use to treat affected patients.

Blood was drawn from 98 febrile patients attending the District Hospital on 26-27 June for blood cultures and malaria smear. Of 98 blood cultures, 33 were confirmed as *Salmonella typhi* and one as *S. paratyphi*; one stool culture was positive for *S. typhi*. All of the smears (97 in total) were negative for malaria parasites. Isolates from earlier in the outbreak and from before the outbreak were obtained from the College of Medical Sciences in Bharatpur and the National Public Health Laboratory in Kathmandu. Water samples were obtained from Bharatpur municipal and ground water sources. Many of these isolates were also positive for *S. typhi*, including one water sample.

At AFRIMS, complete antimicrobial susceptibility testing was performed using NCLLS standard disk diffusion methods. The majority of the isolates were resistant to nalidixic acid, ampicillin, tetracycline, trimethoprim/sulfamethoxazole, chloram-

phenicol, streptomycin, and sulfazoxidole. The isolates all appeared to be sensitive to ciprofloxacin and ceftriaxone in vitro even though there were reports of clinical failure. Using the “E Test” strip method for minimal



inhibitory concentration (MIC) to ofloxacin, ciprofloxacin, and ceftriaxone revealed an overall decrease in susceptibility as compared to what has been reported in the literature.

Pulsed field gel electrophoresis showed that all 34 isolates obtained from the District Hospital, all 7 isolates obtained from Bharatpur by the NPHL, all 21 isolates obtained from the College of Medical Sciences, and the water sample taken from the municipal water supply had an analytical similarity of 97% to 100%.

The multi-drug resistant typhoid epidemic in Bharatpur affected more than 6,000 patients in a 4- to 5-week period and was from a single source—the municipal water supply. This was a large increase above the area’s normal endemic level of typhoid/enteric fever. The data show multiple isolate resistance patterns before the outbreak and from around the country, but isolates collected from the time and place of the outbreak have a consistent resistance and PFGE pattern. There appears to be a decrease in the sensitivity by MIC compared to what is reported in the literature for ciprofloxacin, ofloxacin, and ceftriaxone. We conclude that this outbreak represents further movement along the continuum towards complete fluoroquinolone and ceftriaxone resistance in *S. typhi*.

presented with one of the specified clinical syndromes. Samples have been found positive for leptospirosis, scrub typhus, hepatitis A, and hepatitis B. Of 1,048 samples tested for anti-dengue IgM/IgG, 638 (60.9%) were positive. Of 17 tested for anti-JE IgM/IgG, 6 (35.5%) were positive.

The AFRIMS DoD-GEIS program expanded its influenza surveillance this year and submitted 150 specimens to AFIERA from sites including the US embassy-Bangkok, Sangkhlaburi, the CIWEC clinic in Nepal, Kamphaeng Phet, and the Maldives. These results are included in the presentation AFIERA makes annually to the CDC and FDA.

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

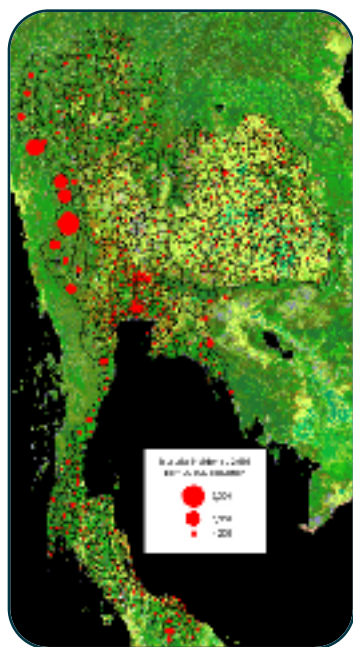


Figure 1. Malaria incidence in Thailand by district for year 2001. Malaria incidence is shown per 100,000 population of each district. Malaria incidence and district boundary data are displayed over a composite NOAA/NDVI image. This image has been given false colors to show areas with high green leaf biomass as dark green color. In general when moving from green to light green to yellow to brown colors indicate decreasing vegetation. Brown indicates no vegetation. Water is shown as black.

A collaboration with the Thai Ministry of Public Health and Thai Ministry of Agriculture and Cooperatives is developing a pilot information technology project to improve communications between the public health and livestock health communities in enhanced reporting, analysis, and investigation of zoonotic diseases. Surveillance for zoonotic and vector-borne diseases with the potential to cause epidemic outbreaks has also involved a systematic collection of small mammals through Thailand. During FY 2002, 2,300 small mammals representing 16 species were collected. Rodents were found positive for *Orientia tsutsugamushi* and *Bartonella*. Sera from rodents will be tested for Hantaan and arena viruses.

In the realm of information management, AFRIMS is collaborating with the Royal Thai Army to create an Oracle-based medical information management system that will greatly advance the ability to monitor

disease incidence across the country. Another tool with great potential for emerging infections surveillance is the HIV screening serum bank repository, containing specimens of excess sera from Thai Army personnel. Approximately 65% of accessions are tested annually. The AFRIMS DoD-GEIS program now manages this repository and related databases. Similarly, the DoD-GEIS program is instituting at AFRIMS CDC software for tracking laboratory information, LITS+, that will, among other things, help document archival specimen collections to maximize the potential for future use. Already AFRIMS banks an estimated 5,000,000 samples.

Training and capacity building are necessary investments of the DoD-GEIS program in order to augment limited DoD resources with the capabilities of host-country public health professionals. This extends the “reach” of the DoD-GEIS program and establishes professional relationships. AFRIMS has supported regional specialized disease surveillance infrastructure by providing diagnostic kits for agents such as hepatitis A, B, C, and E; leptospirosis; and scrub typhus. Field visits have been dedicated to training and assistance with quality assurance. Training at AFRIMS in ELISA, PCR, neutralization, tissue culture, and sequencing was provided to 10 scientists from the Institute of Virology in Tashkent, Uzbekistan. More than 50 other persons from Thailand and Vietnam were also trained.

Response is an increasingly important element of the AFRIMS DoD-GEIS program. These responses have ranged from an outbreak with ten scrub typhus cases in one infantry battalion of the Royal Thai Army near Bangkok to a large typhoid fever outbreak among the local population in rural southern Nepal. The multidrug resistant typhoid epidemic in Bharatpur, Nepal, affected over 6,000 patients in a 4- to 5-week period and came from the municipal water supply, as was shown by the antibiotic resistance and pulse gel electrophoresis (PFGE) patterns in the isolates. In July 2002, AFRIMS also supported the diagnosis of malaria in an outbreak of falciparum among Nepalese troops returning from a UN mission in Sierra Leone. In June 2002, AFRIMS was involved with coordinating laboratory support for the Republic of Maldives during an investigation of more than 4,000 cases of influenza A and B. AFIERA supported AFRIMS by providing

more advanced characterization of the influenza isolates. AFRIMS also provided onsite and Bangkok laboratory support to the Maldives during the first recognition in 50 years of human scrub typhus in those islands. The Ministry of Health on Gadhdhoo Island had recorded about 30 suspected cases with seven deaths. As the Maldives had no scrub

typhus diagnostic capacity, AFRIMS provided the laboratory confirmation. DoD-GEIS field epidemiologists attributed the reemergence to an increase in rodent populations secondary to a cat die-off caused by a feline pan-leukopenia virus and an environmental clear-up campaign that disturbed rodent habitats.

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

NAMRU-2's acclaimed emerging disease program, re-designated in FY 2001 for another four-year term as a WHO Collaborating Center for Emerging and Re-emerging Infections, has focused on establishing regional networks through cooperative host-national institutional affiliations to strengthen outbreak response and recognition capabilities. This approach embodies the concept of leveraging to extend the laboratory's finite resources. Leveraging of partners is achieved through technology transfer of diagnostics to foreign laboratories, through sponsorship of outbreak response training workshops, through direct and indirect support of outbreak investigations, through the implementation of the Early Warning Outbreak Recognition System (EWORS), and through the implementation of the website at ASEAN-Disease-Surveillance.net.

Working with the NAMRU-2 enterics program, the emerging infections program has helped establish an expanded enteric illness surveillance network in Indonesia.



Similarly, a network to profile causes of hemorrhagic illness other than dengue was put into operation. For example, a network of six hospitals in Cambodia gath-

ered information on the relative importance of *Orientia tsutsugamushi* and leptospirosis in acute, hospital-recognized hemorrhagic fever episodes. NAMRU-2 has also transferred technologies for diagnosing dengue to Laos and for diagnosing leptospirosis and hemorrhagic fevers to Vietnam.

During the fall of 2002, NAMRU-2 conducted its eighth Outbreak Response Training Workshop in Nias in North Sumatra. Over 10 days, 36 participants learned through presentations and hands-on exercises about outbreak-tailored surveillance. Topics included early warning systems, specimen collection and laboratory testing, field equipment and supplies, preparation of data collection instruments, the design of field studies, data management and analysis using EPI INFO, reporting, regional diseases of epidemic potential, and potential interventions.

Like AFRIMS, NAMRU-2 is extensively involved in outbreak investigations, such as dengue hemorrhagic fever in Laos, leptospirosis and cholera after flooding in Jakarta, Chikungunya in Java, rotavirus infection in West Timor, and cholera in Vietnam.

EWORS syndromic surveillance networks continued to grow stronger during FY 2002. EWORS recognized eight outbreaks, including major cholera and leptospirosis outbreaks in Jakarta after the January 2002 flooding. The early recognition of cholera in Jakarta and dengue in Bali prompted rapid, life-saving responses.

By the end of the fiscal year, at least 15 sites in Indonesia, Vietnam, Laos, and Cambodia were using EWORS for outbreak detection. Over three million infectious disease cases have been registered by EWORS in Vietnam, Indonesia, and Cambodia, providing the first standardized regional database of

Transitioning Navy Medical R&D Technology Products for Operational Function: EWORS in Korea

EWORS is capable of detecting suspicious rises of clustered signs and symptoms suggestive of outbreak occurrence. EWORS relies on instant relay of disease data using new information technologies and provides for instant and meaningful interpretation of data through graphic presentations. Additionally, EWORS' mapping features allow for geographical case clustering in making investigation and/or intervention more efficient. This approach is particularly appropriate for outbreak detection, in that laboratory supportive capabilities in developing areas are generally lacking, and any delay in results from the time of initial case presentation is contradictory to the notion of "early recognition." The spectrum of possible diagnostic etiologies is limited to available laboratory resources.

EWORS, developed at NAMRU-2 in Jakarta in collaboration with the Indonesian Ministry of Health, is currently being used by the public health sectors of Indonesia, Cambodia, Vietnam, and Lao PDR. The technology recently secured preliminary patent approval in the United States, awarded jointly to the US Navy and the Indonesian Ministry of Health.

Military Application in the Republic of Korea

Early Warning Outbreak Recognition System (EWORS) is a software-driven surveillance tool that enables operators to input and analyze the signs and symptoms of patients reporting to medical treatment facilities with suspected infectious diseases. Until recently, EWORS has not been applied in a military operational setting. However, in 2001 NAMRU-2 and the Republic of Korea Army (ROKA) began working on an initiative to install EWORS technology in a pilot program at two field medical units and at the ROKA headquarters in Daejeon. Initial discussions and an agreement for the NAMRU-2 supported pilot program led to the translation of EWORS display language, originally in Indonesian, to Korean characters during the visit of two ROKA medical officers to NAMRU-2 in early 2002. As geographic mapping

is also a feature of EWORS, NAMRU-2 and Korean programmers also installed appropriate geographical representations of the pilot sites. In September 2002, NAMRU-2 personnel visited the Republic of Korea to make final revisions to the EWORS software, train Korean personnel in EWORS use, and test the newly installed pilot network. The final phase of the pilot project implementation will begin at the pilot sites in October 2002.

Currently little disease surveillance is done within the ROKA. US Army medical personnel, who work closely with their counterparts in the ROKA on preventative medicine and disease surveillance issues, use a surveillance system which relies upon analysis of daily reports of ICD coding among US Army medical units. This system is fruitful for the US Army, but not appropriate for the ROKA as the latter service does not routinely collect ICD data and has limited diagnostic capability in most of its medical units. However, EWORS' syndromic approach may enable the ROKA – which operates with far fewer medical resources than does the US Army – to conduct sound, thorough disease surveillance and to initiate the early investigation of suspicious infectious signs and symptoms.

Pilot Project Sites and Objectives

The soldiers served by these medical units include infantry and artillery personnel deployed up to the border of the Korean Demilitarized Zone (DMZ).



NAMRU-2 personnel and representatives from ROK Army HQ medical department train LTC Kim, Commander of 3rd Division medical unit, 3rd ROK Army on EWORS utilization at his Command.

Transitioning Navy Medical R&D Technology Products for Operational Function: EWORS in Korea



Personnel from NAMRU-2, the ROK Army, and the US Army Korea meet with the Surgeon General of the ROK Army, Brigadier General Hyunjae Ra (first row, third from right).

Detection of troop exposure to biological and chemical agents is a concern, but also multiple infectious diseases including malaria and hemorrhagic fever due to Hantaan virus infection. (The Hanta'an River itself, the namesake of the virus, flows through this region.) Medical personnel at the 3rd and 6th Division medical units will daily

input the signs and symptoms from soldiers reporting with suspected infectious diseases. (These soldiers are often referred to the Division medical units from Battalion-level medical officers but may seek care directly from the Division facilities.) As with any EWORS system, the field sites will have the ability to analyze both temporally and geographically the multiple constellations of signs and symptoms displayed by soldiers reporting to their treatment facilities. All data will also be sent, via an internal ROKA email system, to the host server at ROK medical headquarters, where regular analysis of data will also take place. The host server will have the capability of analyzing data from both field sites to make assessments of findings within each Division's area of responsibility, in addition to analyzing data across division boundaries.

The pilot project will proceed for six months, after which the ROKA will evaluate the system for future use and expansion within the ROKA.

reliable syndromic data for trend analyses. The Minister of Health in Laos has requested expansion from the four sentinel sites to each of the country's 20 provinces. The EWORS methodology has achieved recognition outside of Southeast Asia; NAMRU-2 has also been requested to assist with implementations in Kenya and Poland. The NAMRU-2 EWORS team also hosted a group of Republic of Korea military officers to work on translating EWORS for use along the Demilitarized Zone in South Korea, and EWORS was implemented. An Agreement of Understanding was signed with the governor of East Java to form an EWORS network of 14 community health centers and seven district hospitals. Reflecting EWORS's perceived value to the host government, the Regional Government of East Java will itself be funding the training, equipment purchases, and general operational costs.

The implementation of the ASEAN-NET is another innovative DoD-GEIS information technology exchange project. This initiative seeks to rapidly disseminate outbreak information in the region; provide a mechanism for secure, confidential data

sharing; and catalogue relevant regional expertise, diagnostic resources, and regional training opportunities. The 10 members of ASEAN (Association of Southeast Asian Nations) accepted the concept proposed by the Government of Indonesia at the Senior Officials Meeting on Health held in Vietnam in October 2001. ASEAN formally adopted the concept in March 2002, and NAMRU-2 finalized a prototype in April 2002. A technical working group with 70 representatives provided significant advice on the web interface design, content, and organization of the product that has been officially named ASEAN-Disease-Surveillance.net. Implementation is planned for January 2003.

As is the case in most of the overseas laboratory DoD-GEIS programs, NAMRU-2 is involved with surveillance for antimalarial drug resistance. During FY 2002, in vivo testing for resistance to chloroquine in *P. falciparum* and *P. vivax* was carried out in Pulau Sembilan, an island in the Makassar Strait. Resistance studies were also conducted in Central Java. In Pulau Sembilan, 26% of 700 screened were shown to have malaria. Among 48 subjects enrolled in the in vivo

study, 40% were at risk of therapeutic failure of chloroquine with falciparum malaria, and confirmed resistance to chloroquine with vivax malaria was noted in three subjects. In a study of 118 subjects in Central Java, combination chloroquine and pyrimethamine/sulfadoxine provided greater than 92% efficacy against falciparum malaria. The studies generated useful scientific findings, and the many Indonesian investigators that were trained can now replicate this methodology in other regions. Another valuable example of leveraging in FY 2002 was the signing of a four-year agreement with USAID that will provide NAMRU-2 with \$1 million a year to help Indonesia build capacity for malaria control. This was done through the establishment of a non-profit organization, the Indonesia Anti-Malaria Initiative, which obtains access to technical expertise and Ministry of Health relationships through the resources of the DoD-GEIS-funded malaria surveillance program.

The NAMRU-2 DoD-GEIS malaria program also supported other population screening activities, a longitudinal malaria vector bionomic study, a review of records to document deterioration of the malaria situation in Java, the development of GIS methods for study of malaria reemergence, and genotyping of the chloroquine-resistance gene across the islands.

The enteric disease program at NAMRU-2 is a major DoD-GEIS contributor to understanding the distribution of antibiotic-resistant enteric organisms in the region. NAMRU-2 trained 80 Indonesian professionals from the Ministry of Health in Medan, Makassar, Jakarta, Pontianak, Padang, Bali, and Batam in techniques of routine bacterial isolation. Staffs at

collaborating hospitals were also trained in antimicrobial susceptibility methods. To strengthen the network, relevant laboratory equipment was also provided. Outcomes included the discovery that *Campylobacter jejuni* has shown increased multiple resistance to ceftriaxon, norfloxacin, and ciprofloxacin. In a recent surveillance study involving 6,760 patients reporting with diarrhea, the proportions of enteric bacteria found were *Shigella flexneri* 39%, *Salmonella* spp. 26%, *Vibrio* spp. 17%, *Shigella sonnei* 7%, *Campylobacter jejuni* 4.4%, *Salmonella typhi* 3%, and *Shigella dysenteriae* 2.3%.

The viral disease DoD-GEIS program at NAMRU-2 expanded and reorganized the influenza surveillance program in FY 2002. There are now six influenza surveillance sites around the archipelago, including a sports shoe factory in Jakarta, clinics at Sanglah Hospital in Bali, and clinics at Labuang Bajo Hospital in South Sulawesi. Training and reagents were provided to the Indonesian national laboratory. Personnel at outlying sites were trained in specimen collection and in use of rapid influenza detection assays. During FY 2002, 896 specimens from 449 participants were received, and 59 viral isolates were sent to the regional WHO influenza collaborating center in Australia for confirmation.

Three Chikungunya projects were supported by DoD-GEIS in FY 2002. Transmission of Chikungunya was identified in five regions of Indonesia and several coinfections of Chikungunya and dengue were noted. A follow-up serosurvey of 627 initially seronegative persons identified 26 seroconversions.

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

The largest and oldest overseas laboratory in the DoD-GEIS network is the NAMRU-3 laboratory located in Cairo, Egypt. It is a WHO Collaborating Center for Emerging and Re-emerging Infections and works closely with the Eastern Mediterranean Office of the WHO (EMRO) also located in Cairo. Consistent with the DoD-GEIS philosophy of partnership in the fight against emerging infections, NAMRU-3 is pursuing a five-year plan that includes input from the local Field Epidemiology Training Program, USAID, the Egyptian

Ministry of Health and Population, the CDC, the WHO, and the U.S. State Department. Through a joint effort, standardized case definitions have been developed, standardized laboratory methods have been identified, and standardized report forms and critical software inspired by CDC's National Electronic Disease Surveillance System (NEDSS) have been acquired. Valuable tools that can be shared have been developed to assess existing capabilities in laboratories and for surveillance.

The NAMRU-3 DoD-GEIS program has constructed over the last five years a network of infectious disease hospitals in Egypt that serves as the platform for enhanced surveillance for a variety of priority diseases including meningitis, acute febrile illness, dysentery, and hepatitis. Currently surveillance is being conducted in 12 sites in 10 governorates. This surveillance project has resulted in numerous public health applications over the last four years. Data on meningitis surveillance has been used to develop cost-effectiveness models for the inclusion of the *Haemophilus influenzae* vaccine into the Expanded Programme on Immunization. Key findings in the acute febrile illness surveillance include the emergence of brucellosis as a cause of acute fever in Egypt. The data are providing the Ministry of Health with important information on community-acquired infections and are serving as a model to upgrade laboratory capacity in other parts of the country. Due to the success of this surveillance activity, NAMRU-3 has been asked to assist in the development of a surveillance network and strategies in Central Asia, Sudan, and Jordan, as well as to conduct inter-country conferences and training for meningitis and disease surveillance in collaboration with WHO's training center in Lyon, France, and EMRO.

Hospital-based surveillance findings led NAMRU-3 to develop a program for population-based surveillance for patients with bloodstream infections. This will help establish the burden of disease associated with community-acquired infections, such as typhoid fever and brucellosis. In 2001, a population-based study in Fayoum Governate enrolled 1,796 patients. Blood cultures yielded 95 (5.3%) isolates with *Salmonella typhi* and 41 (2.3%) with *Brucella*. The estimated incidence thus was calculated as 52/100,000/year for typhoid fever and 57/100,000/year for brucellosis. In the majority (57%) of patients with brucellosis, the clinical diagnosis made by the provider had been typhoid fever, thus the patients received antimicrobial therapy that was not tailored to the cause of their disease. This information will be used to develop intervention and prevention strategies for these high-priority diseases.

In acute febrile illness surveillance, 1,704 serum samples from patients in eight fever hospitals in different parts of Egypt and showing negative bacterial blood cultures were analyzed for IgG antibodies

against *Rickettsia typhi* and *R. conorii*. A total of 694 (40.7%) were reactive against *R. typhi* antigens and 497 (29.2%) against *R. conorii* antigens.

Recently NAMRU-3 acquired capability to conduct pulse field gel electrophoresis (PFGE) through training at the University of Iowa. This new capacity has been instrumental in confirming the epidemiology of outbreaks of *Klebsiella* infection in Egypt. This included an outbreak associated with contaminated intravenous fluids used in neonatal intensive care units.

Important new information came from an investigation of unexplained hepatitis. Overall, 44% of patients with a clinical diagnosis of acute viral hepatitis from selected hospitals in Egypt had no serologic evidence of infection with the viruses that cause hepatitis A, hepatitis B, or hepatitis C. Serologic testing was conducted on serum samples from 459 non-ABC hepatitis patients using an ELISA for IgM antibody to leptospirosis. Overall, 82 (17.9%) patients tested positive for leptospirosis, and 64 (14%) patients had serologic results with intermediate findings on an EIA. Leptospirosis appears to be a common cause of acute hepatitis in Egypt. This has implications for treatment because specific antibiotic therapy that would not be indicated for viral hepatitis can be life saving in the case of leptospirosis.

Outside of Egypt, NAMRU-3's DoD-GEIS program continues involvement with surveillance for selected diseases in various countries of the Middle East, Africa, Eastern Europe, and South West Asia. Influenza surveillance efforts include not only Egypt but also Oman, Syria, Kazakhstan, and Ukraine. As participating countries develop capability to isolate influenza virus, additional countries will be invited to participate. Isolated and typed influenza viruses from these countries are sent to the WHO Collaborating Center on Influenza Viruses at the CDC for further characterization and potential incorporation into the next season's influenza vaccine.

In October 2001, NAMRU-3 was asked to provide assistance to the Ministry of Health in Uzbekistan to strengthen surveillance for multi-drug resistant typhoid fever. NAMRU-3 provided training in July 2002 to a network of six infectious disease hospitals in Samarkand and Dzhizak Oblasts. Over the first four months of the project, 231 patients were evaluated,

including 58 (25%) who had culture-confirmed typhoid fever. Antimicrobial resistance patterns revealed 25% of 28 isolates tested were multidrug resistant. Strengthening surveillance for patients with meningitis is a high priority of the Ministry of Health in Uzbekistan. Surveillance has been established there and in Oman and Jordan to identify pathogens causing bacterial meningitis, including *Streptococcus pneumoniae*, *Haemophilus influenzae* serotype B, and *Neisseria meningitidis*. Cerebrospinal fluid samples negative for bacterial agents are further evaluated for viral causes, including West Nile fever virus, enteroviruses, and coxsackieviruses.

In July 2002, NAMRU-3 provided training to a network of three hospitals for this purpose, one in Samarkand and two in Tashkent Oblast. Training included standardized clinical and laboratory procedures to evaluate patients who met clinical case definitions. At least 88 surveillance samples have begun analysis.

NAMRU-3 has several DoD-GEIS activities in direct support of US operational forces. In association with the Bright Star Exercise in Egypt, 3,000 post-deployment surveys were collected for analysis of disease incidence. Despite highly restricted troop movements due to proximity to September 11 and the consumption by almost all deployed personnel of mostly MREs, 128 enteric illnesses were evaluated to identify the relative importance of pathogenic organisms in diarrheal disease. Of 201 samples collected, 78 (39%) were positive for ETEC, 9 were positive for *Campylobacter*, and 2 for *Shigella*. NAMRU-3 also investigated high rates of acute gastroenteritis

among troops participating in Operation Northern Watch in Turkey.

Like the other laboratories, NAMRU-3 sees training of host-country partners as a critical method of expanding available resources and promoting good will. NAMRU-3 staff worked closely with the WHO training center in Lyon, France, to develop and teach an international course on surveillance and outbreak response in March and April 2002. NAMRU-3 also sponsored with WHO an intercountry meeting on surveillance for emerging diseases. Another co-sponsored conference and workshop was on pediatric bacterial meningitis. NAMRU-3 staff supported WHO and CDC in teaching an epidemiology course in Moscow in September 2002. Late in FY 2002, NAMRU-3 staff begun an in-depth evaluation of infection control in facilities of all levels in diverse regions of Sudan. A national implementation plan for infection control was an outcome of this consultancy.

NAMRU-3, along with the other DoD overseas medical research units, handles thousands of research and surveillance specimens per year (18,973 at NAMRU-3 in FY 2002). Many of these hold potential value for future studies of as yet unrecognized emerging infection problems. To facilitate data management for integrated accessioning, analysis, reporting, and storage of specimens, DoD-GEIS has contributed support to the CDC in the development of the Laboratory Information Tracking System Plus (LITS+) software program. NAMRU-3 has begun implementing LITS+ as a centralized system. Care is being taken to ensure that the needs of each NAMRU-3 program are met by the new system.

U.S. Army Medical Research Unit- Kenya Nairobi, Kenya

Fiscal year 2002 has seen considerable expansion of USAMRU-K's DoD-GEIS operations, with the formation of an eight-hospital infectious disease surveillance network, the completion of a new facility near Kisumu, and the planning of a new laboratory facility in Kericho. USAMRU-K is the smallest DoD overseas medical research unit in the DoD-GEIS network, so staff growth has been critical to creating a strong program. This year USAMRU-K added to its staff two

active duty infectious disease physicians, a molecular microbiologist, and, perhaps most critically, a military physician-epidemiologist to serve as DoD-GEIS director for the laboratory. With the new director in place, it has been possible to implement an integrated approach to infectious disease surveillance that brings the skills of a variety of scientists in entomology, malaria, enterics, and viral illnesses together into a consolidated program.

The new eight-hospital network spans Kenya. Each site is equipped and staffed with a clinician and laboratory technician providing capabilities for case identification and sample processing at each site. Three new protocols have been developed for surveillance of malaria resistance, enteric pathogen etiology and resistance, and viral/rickettsial etiologies of severe febrile illnesses.

Clinical officers and laboratory technicians at the network hospitals all received training in outbreak investigation and control techniques. This expertise came in handy when the Malindi site was extensively involved in the identification and testing of possible cases of viral hemorrhagic fever, sending 16 samples to the WHO reference laboratory in Nairobi. Further planning is underway to improve each site's communications capabilities, to include internet access. This will also involve basic computer instruction for network staff. Each network laboratorian will also receive the same laboratory training as employees at USAMRU-K, in compliance with Good Clinical Practices standards.

Sub-Saharan Africa is an area of traditional concern with respect to viral illnesses including viral hemorrhagic fevers. The WHO Reference Center located in the Kenya Medical Research Institute (KEMRI), the host institution for USAMRU-K, is a collaborative effort between KEMRI, USAMRU-K, and CDC. The DoD-GEIS program contributes resources to help support its role as a regional diagnostic reference center for suspected viral hemorrhagic and other viral illnesses. Currently it can employ ELISA, PCR, and RFLP-PCR methodologies. Isolations can also be done from various cell cultures. Alpha viruses, bunyaviruses, and flaviviruses identified by the presence of cytopathic effects in culture or IFA using NIH Arbovirus Pooled Grouping Serum are then inoculated into mice.

The current viral illness surveillance protocol seeks at least 4,160 samples per year, 10 per surveillance site per week from each of the eight network hospitals. Specimens are managed by algorithm once they reach the reference lab in Nairobi, with all being evaluated for agents such as alphaviruses, bunyaviruses, flaviviruses, hepatitis B virus, rickettsia, and leptospire. Depending on whether cases meet a yellow fever case definition or yield findings of cytopathic effect on cell culture, additional methodologies are pursued. Capabilities have been acquired specifi-

cally to diagnose hemorrhagic fevers (eg, Ebola, Marburg, Crimean-Congo, and Lassa). Prior to implementation of the full surveillance protocol, this fiscal year the WHO reference laboratory tested samples from 45 patients suspected of having viral hemorrhagic fever from across Kenya. None were positive.

Surveillance of enteric illnesses continues to be a core DoD-GEIS program in Kenya. A goal of studying 1,600 network patients with diarrhea per year has been set, and a wide variety of capabilities for parasites, bacteria, viruses, and antibiotic resistance testing have been established. In preparation for the implementation of this protocol, DoD-GEIS employed and trained two new assistant research officers for the USAMRU-K enterics division. Similarly USAMRU-K has established a new protocol for in vitro surveillance of drug resistant malaria using 16 pharmaceuticals. The director of the Kenyan National Malaria Control Program is a principle investigator. The surveillance will involve PCR for molecular markers of anti-malarial resistance in dihydrofolate reductase and dihydropteroate synthase and for the *pfmdr1* and *pfcr* markers of chloroquine resistance.

A malaria surveillance study was conducted during the fiscal year to discover if malaria transmission was occurring in Nairobi. In July 2002, 257 adults in the Korogocho slum of Nairobi presented to a clinic and were evaluated for malaria and epidemiologic factors. Of six patients positive by culture, all had traveled outside of Nairobi in the prior eight weeks. Of six positive by smear at the slum site, only one reported no travel history. Of the 13 positive by smear read by a KEMRI technician, only two had no travel history in the prior eight weeks. Whether this indicates a low rate of malaria transmission in Nairobi remains an open question. Ironically while it is clear that the overall prevalence of parasitemia is actually low, providers in Nairobi apparently believe otherwise and put 116 (45%) of the subjects on malaria treatment despite negative smears. USAMRU-K's entomologist continues to explore the issue of malaria transmission within Nairobi.

USAMRU-K participated in six outbreak investigations during FY 2002 and at the request of WHO, USAMRU-K DoD-GEIS personnel responded to two outbreaks in southern Sudan. The first outbreak investigated was in response to a report of viral hemorrhagic fever-like illness in southern Sudan on

Opening of the Malindi District Hospital Clinical Research Centre in Kenya



The new facility

The Malindi District Hospital Clinical Research Centre is collaboration between the Malindi District Ministry of Health, the Malindi District Hospital, the Kenya Medical Research Institute (KEMRI), the US Army Medical Research Unit-Kenya (USAMRU-K), and the U.S. DoD Global Emerging Infections Surveillance and Response System.

The creation of this clinic, which opened in mid-January 2003, was a project that included the rehabilitation of a former staff residential building into the research centre, which includes an examination room, an office, and a storage area. A patient waiting area was created, and guard service is provided. In 2003, the laboratory will be self-

contained and fully equipped to perform surveillance protocols. The office will be internet-linked early in 2003, allowing for real-time transmission of data. The project also rehabilitated a portion of the pediatric ward.

In attendance at the opening ceremony were the Deputy Director of KEMRI, the acting Malindi District Medical Officer of Health, the hospital Medical Superintendent; the commander of USAMRU-K; the hospital Matron; the Director of KEMRI's coastal Centre; and representatives of all USAMRU-K programs. This was a tangible sign of the international cooperation that brought about this improvement in local infrastructure in rural Kenya. It will be a boon to the local population and to the research institutions that support it.



27 February 2002. A second case was reported on 5 March 02. A USAMRU-K technician was deployed. Patients were isolated, safe nursing methods were taught, contacts were traced, and samples sent to KEMRI for evaluation. Both samples were ultimately negative for viral hemorrhagic fever. The second outbreak in southern Sudan involved an outbreak of tropical ulcer in July 02 involving almost 3% of the population of a refugee camp. The probable cause was mycobacterial. This knowledge allowed the WHO to plan effective medical and surgical intervention for the ulcers.

At the request of the Kenyan Ministry of Health, USAMRU-K investigated three outbreaks in Kenya. The first involved several sudden deaths among children living at a home for HIV orphans. All of these

children were HIV positive. All viral testing was negative, but after the water was chlorinated on USAMRU-K's recommendation, the illness disappeared in the children. The second outbreak involved 11 suspected cases of measles at a girls' school in Baringo District. Those with rash were positive for measles IgM and the Ministry was able to immediately respond with measles immunization for all children in the district. The third outbreak supported by USAMRU-K involved what appeared to be hepatitis in two prisons in Meru District. Following the anthrax scare of late 2001, the DoD-GEIS coordinator also supported the Ministry with technical advice and assistance in establishing a local anthrax testing facility.

Working in Kenya poses more challenging infrastructure problems that at many of the other DoD-GEIS

overseas sites. For this reason, DoD-GEIS has supported VSAT and MIMCOM systems, allowing for very reliable internet connections and communication among staff and collaborators. The largest communication accomplishment in FY 2002, however, was the redesign of the USAMRU-K website, found at <http://www.usamrukenya.org>. This is expected to become a primary means of data and information dissemination. Dissemination of knowledge has also been strengthened through the teaching of courses. In

June of 2002, USAMRU-K in partnership with collaborators at the Uniformed Services University of the Health Sciences conducted a two-day course in Nairobi on outbreak investigation. Participants included 57 persons from 13 governmental and other institutional entities around Kenya. Similarly, in May 25 participants attended a course for front-line public health workers from across Africa in the epidemiologic characterization, identification, and control of viral hemorrhagic fevers.

U.S. Naval Medical Research Center Detachment Lima, Peru

The sole US DoD overseas medical research unit in the Western Hemisphere is the US Naval Medical Research Center Detachment in Lima, Peru. One of its model programs contributes significantly to influenza surveillance in the South America. In FY 2002, specimens on 227 cases of respiratory illness in Colombia, Ecuador, and Peru were studied. By the end of the fiscal year, 13 sites were participating in Colombia (1), Ecuador (3), Peru (7), Bolivia (1), and Argentina (1). Among the 227 cases, specific pathogens were identified in 57 (25.1%). These included influenza A, influenza B, adenoviruses, parainfluenza, herpes simplex, and enteroviruses. Compared to prior years, influenza activity in FY 2002 declined in the participating countries.

An officer detailed from CDC to NMRCDD led a robust antimalarial drug resistance program. During the last 10 to 15 years, malaria has emerged as a major public health problem in the Amazon basin of South America. Migration, settlement, extension of the geographic range of the major vector, *Anopheles darlingi*, and increasing resistance are all likely contributors. The Amazon basin is now the second most drug-resistant area of the world. Due to lack of data, many countries do not have up-to-date national treatment protocols that reflect regional variation in resistance patterns. The primary methodologies are the standardized 14-day and 28-day in vivo trial methods recommended by WHO and PAHO. DoD-GEIS is seeking to transfer expertise to do these in vivo evaluations of resistance to host countries in the region. Peruvian investigators trained in these techniques by NMRCDD have participated in the subsequent training of colleagues in Bolivia and Ecuador. The NMRCDD DoD-GEIS program is playing a key role in a USAID-funded effort to revitalize malaria control

in the Amazon region. The emphases are on technical assistance with protocol design and conduct and on policy formulation in response to the findings.

Many specific antimalarial drug resistance projects were carried out in FY 2002. A 14-day study in Ushpayacu (western Amazon region of Peru) compared chloroquine and sulfa-pyrimethamine for treatment of *P. falciparum* infection in 59 patients with uncomplicated disease. This study confirmed high levels of resistance to chloroquine but only low levels to sulfapyrimethamine, a pattern that differs from other Amazon areas where neither drug is efficacious. A study near Iquitos, Peru, of chloroquine against *P. vivax* showed recrudescence of parasitemia at 28 days follow-up in five of 120 patients enrolled. A study was initiated to map the geographic distribution of *P. falciparum* mutations associated with drug resistance along the Peruvian borders of Ecuador, Colombia, and Brazil. For logistic and epidemiologic reasons, it has not been feasible to do in vivo trials in these areas, so drug-resistance data largely do not exist. More than 150 filter paper blood spots for PCR testing have been obtained. Another interesting evaluation involved the use of a rapid malaria test that would allow treatment of positives to begin quickly rather than waiting for a slide to be sent to the nearest government laboratory and then read. Workers using the rapid test saw significantly more febrile patients per month and treatment delays were significantly shortened compared to the traditional system.

Malaria work was also supported in Bolivia. Based on FY 2001 studies, the Bolivian Ministry of Health decided to change their first-line treatment for uncomplicated *P. falciparum* malaria to mefloquine plus artesunate in the Bolivian Amazon region. In

Suriname a study of safety and efficacy of mefloquine and mefloquine-artesunate in uncomplicated *P. falciparum* infection is being carried out. In Ecuador, two studies of chloroquine and sulfapyrimethamine for treatment of *P. falciparum* infection were carried out at coastal sites. Results indicate a pattern similar to the Pacific Coast of Peru, namely high levels of resistance to chloroquine and only low levels of resistance to sulfapyrimethamine. Further studies to address great gaps in resistance data in Guyana, Venezuela, and Colombia are under discussion.

Surveillance for antibiotic-resistant enteric organisms was conducted in FY 2002 at six sentinel sites in four cities in Peru and two sites in each of two cities in Bolivia. A total of 1,593 enteric bacterial isolates were studied. *Shigella* constituted 48.5% of the strains identified, but in Cuzco, Peru, and Santa Cruz, Bolivia, *Salmonella* was the most common bacterium isolated, at 47.5% and 37.5% respectively. Overall the proportion of *Salmonella* was only 8.9%. *Campylobacter* accounted for 17%, with a range among the six cities of 0 to 21.5%. With the exception of *Campylobacter*, very few enteric isolates were resistant to ciprofloxacin. There was notable variation by site in the resistance of *Campylobacter* to ciprofloxacin and azithromycin, the second-line drug. Since most of this effort is decentralized, NMRCDC conducts much of the training of collaborating scientists. Sixteen foreign collaborators were trained in enteric laboratory methods at NMRCDC for periods of up to six months.

NMRCDC's DoD-GEIS program also featured a syndromic surveillance project established at six locations in Peru, two in Ecuador, and one in Bolivia. Acute and convalescent blood specimens were collected from persons falling into various syndromic categories. Blood smears for malaria and toxoplasma were performed on-site and sera studied with assays for dengue, Mayaro, Orapouche, yellow fever, Venezuelan equine encephalomyelitis, and Group C viruses performed at regional Peruvian Ministry of Health laboratories and NMRCDC. Virus isolations were performed at NMRCDC. Assays for brucellosis, leptospirosis, Q fever, and rickettsial spotted fever were also performed at NMRCDC. The Instituto Nacional de Salud in Lima did influenza testing.

In this syndromic surveillance effort, Peru enrolled 1,684 cases, Ecuador 84, and Bolivia 41. The success rate for collection of convalescent specimens averaged

69%. In Peru, viruses were isolated from 248 acute specimens and included dengue-1 (85), dengue-2 (8), and dengue-3 (151). A single isolate of Mayaro virus was documented, as well as three of Venezuela equine encephalitis. In Bolivia, five Mayaro virus isolates were noted. In Ecuador, two patients were confirmed by virus isolation to have dengue fever, one in the Amazon town of Shell and the other in coastal Guayaquil. These were the first reported cases of dengue fever in the participating jungle region, and their recognition has markedly changed the approach of local health care providers to febrile illness among their populations.



Surveillance for tick-borne diseases also was a focus of the NMRCDC DoD-GEIS program in FY 2002. Samples came from the Febrile Syndromic Surveillance protocol and originated in three parts of Peru: Junin, Piura, and Cuzco. Serum samples were evaluated for the presence of antibodies to *Rickettsia rickettsii*, *R. typhi*, *Coxiella burnetii*, *Ehrlichia* spp., and *Borellia burgdorferi*. Of 368 samples studied by Dip-S-Ticks assay, 124 were positive for *R. rickettsii* and 16 for antibodies against *B. burgdorferi*. IFA results provided the first evidence of a spotted fever group *Rickettsia* infecting human patients within Peru. To expand entomologic capabilities to assay field collected ticks for *Rickettsia* and *Borrelia* using PCR procedures, a workshop for personnel from the NMRCDC and the Peruvian Ministry of Health was conducted in Lima by an investigator from the CDC.

As part of the DoD-GEIS response mission, NMRCDC also participates in outbreak investigations. During June and July of 2002, two males about 100 to 250 km north of Santa Cruz, Bolivia, developed a severe febrile illness compatible with hantavirus pulmonary syndrome; one died. Laboratory testing confirmed hantavirus infections. Several additional unconfirmed cases in the area prompted a request for outside assistance. The multinational response included personnel

from NMRCDC, CDC, and Argentina. NMRCDC contributions included laboratory support and rodent trapping in the affected areas. A capacity for human and rodent EIA assays for Sin Nombre and Laguna Negra viruses was fielded. NMRCDC also provided molecular analysis of suspected hantaviruses by PCR and sequence analyses. Training and technology transfer were also facilitated with CENETROP, the national reference laboratory in Santa Cruz. This training covered both ecologic and laboratory studies.

A total of 497 human and 225 rodent blood samples were processed. No samples were drawn from patients with known acute hantavirus pulmonary syndrome. Hantavirus IgG antibody prevalences in humans were 7% to 10% in the Mineros area and 10% near Concepción, both in Santa Cruz Department. Four IgM and eight IgG antibody-positive individuals were detected among 79 tested from Concepción. Molecular studies associated viruses from humans or rodents in the Concepción area with Laguna Negra virus, in the Mineros area with Rio Mamoré virus, and in the Tarija (southern Bolivia) with the Oran (Andes North) virus.

NMRCDC continues to support considerable training of US DoD and host-national scientists. The virology program conducted training workshops for DNA extraction from clinical specimens for colleagues at the Instituto Nacional de Salud. Thirty visiting scientists and technicians received training in laboratory techniques for periods of up to 5 months. NMRCDC also has taken a leadership role in the teaching of outbreak investigation short courses based on a CDC course. In FY 2002, these courses were conducted in Sucre, Bolivia, and Lima, Peru. Bolivia's course has three components: outbreak investigation (four days) followed by either a one-day workshop on anthrax diagnosis or a one-day symposium on antibiotic resistance. Eighty-five persons participated in Bolivia and 48 in Peru. Although more than a third of the participants in Peru led epidemiology units at the Ministry of Health, most had not been trained in outbreak investigation. The NMRCDC DoD-GEIS program also supported the field portion of the Military Tropical Medicine Course. Seventeen DoD physicians participated in a training experience in remote Amazon villages as part of their field experience. During the year, other trainees included residents and medical students from the US and Canada.

During FY 2002 the DoD-GEIS Central Hub continued a partnership with NMRCDC and the Instituto Nacional de Salud to implement in Peru a laboratory-based surveillance network based on the CDC's PHLIS (Public Health Laboratory Information System) software. The Overseas Humanitarian Disaster and Civic Aid program of the US Southern Command provided the funds for this project. The support has included the donation of computers for regional laboratories in every department of Peru and the conduct of regional training courses to enable laboratorians to implement hierarchical reporting with PHLIS. As the implementation phase closed in 2002, this system had been established in every department of Peru and serves at the backbone for government public health laboratory informatics throughout the nation. During FY 2002, five regional PHLIS training courses were taught, four in Peru (Tacna, Tumbes, Pucallpa and Lima), and one introductory course in Santa Cruz, Bolivia, for personnel from Bolivia, Ecuador, and Paraguay. These five-day, computer-based, hands-on courses were organized and taught by Peruvian Ministry of Health personnel and exemplify the degree to which this technology has been successfully transferred. Training was provided for 13 Ministry of Health personnel in Tacna, 16 in Tumbes, 10 in Pucallpa, and 16 in Lima. Personnel from the Peruvian Ministry of Health have become so expert in the PHLIS system and its implementation that a senior epidemiologist from the Instituto Nacional de Salud was retained by DoD-GEIS to support related training courses held in Washington, DC, in December 2001 and in Panama City, Panama, in October 2002 for establishment of a Central America PHLIS network.

An exciting and related information technology innovation piloted by NMRCDC during FY 2002 was a new telephony-based methodology for rapid reporting of surveillance data developed by a US-Peruvian company named Voxiva, Inc. This initiative was stimulated by a long unrecognized and deadly malaria outbreak among Peruvian Navy personnel assigned to a remote site along the Peruvian-Colombian border. The technology allows for touch pad-driven transfer of surveillance data by telephone to a secure internet database. It is particularly useful for automated surveillance from places with an otherwise very limited information technology infrastructure. Three Peruvian naval regions (Tumbes, Ventanilla, and Loreto) were selected for initial implementation.

DoD-GEIS Provides Training in the Caribbean and South America to Support an Electronic Public Health Network

Following the invitation of, DoD-GEIS has been involved in developing a hierarchical public health laboratory surveillance network with the Caribbean Epidemiology Centre (CAREC) of the Pan American Health Organization. This effort was supported by Atlantic Command (and later SOUTHCOM), under the Overseas Humanitarian, Disaster, and Civic Aid (OHDACA) program to promote projects relevant to Caribbean regional needs. The network to strengthen surveillance within countries and better link them to CAREC is based on the US Centers for Disease Control and Prevention Public Health Laboratory Information System (PHLIS) software. In the US, PHLIS links state public health labs to the CDC.

In past years DoD-GEIS provided training and equipment 11 Caribbean countries at 32 sites. Evaluations in 2001 revealed that while national sites were routinely entering data into their databases and reporting to CAREC, many were not validating data or analyzing data locally. Hence, a 3-day workshop was conducted in Trinidad from 11 to 13 September 2002 in Port-of-Spain, Trinidad, to deliver the needed training.

Participants were required to bring a copy of their national PHLIS database to the workshop. Objectives included enabling participants to conduct data validation, enabling participants to analyze PHLIS data, and introducing revised disease-specific modules. Thirty-three participants from 11 countries attended. By the end of the workshop, participants had cleaned and validated their individual PHLIS databases and acquired the skills necessary to run routine analyses in support of national public health decision making. It was a challenging workshop because of the variety of

datasets and problems, but the collaborative atmosphere and having several trainers available from CAREC and CDC helped to address all issues and problems.

The program was so successful in the Caribbean, it was expanded to South America. Peru, because it hosts the DoD-GEIS program at the Naval Medical Research Center Detachment in Lima, was the first country to receive equipment and training. The NMRCDC GEIS Program then coordinated a training course on the use of PHLIS in Santa Cruz, Bolivia, for students from other countries. The course was conducted at the Centro Nacional de Enfermedades Tropicales (CENETROP), from 30 July to 3 August 2002. Dr. Javier Vargas and Mr. David Campos, both of the Instituto Nacional de Salud in Peru, were the course instructors. Both gentlemen gained extensive experience with the program during its introduction in Peru and are sterling examples of the success of GEIS's dedication to train-the-trainer methods.

Course participants were invited from Paraguay, Ecuador, and Bolivia and included top-level representatives from each country's laboratory, surveillance, and informatics programs. Of the fifteen participants, ten were from Bolivia, two from Ecuador, and three from Paraguay.



Diseases reported included malaria, dengue fever, hepatitis B, asthma, acute respiratory disease, and gastroenteric illness. Telephone reports are posted within minutes and computer reports within seconds. Three training courses and a needs assessment were held for each area. A total of 119 personnel from 11 health centers were trained. Three surveillance levels were developed: operational (case reporting), interme-

diated (consolidation, analysis, monitoring, coordination), and directive (intervention, decision-making). The implementation to date has been smooth, and the benefits of near real-time monitoring is maintaining a strong incentive for continuation. It is hoped that this methodology can be eventually transferred to other DoD-GEIS sites around the world.

DoD-GLOBAL EMERGING INFECTIONS SURVEILLANCE AND RESPONSE SYSTEM: CLOSING OUT THE FIRST FIVE YEARS

The specific rationale for the DoD's role in global emerging infections surveillance and response was first articulated in the landmark 1992 IOM report entitled *Emerging Infections: Microbial Threats to Health in the United States*. Following specific authorization for the DoD-GEIS mission in the 1996 Presidential Decision Directive on Emerging Infections (NSTC-7), DoD assets were mobilized both domestically and internationally. The strategy for DoD's mobilization was published in November 1998 in a five-year plan entitled *Addressing Emerging Infectious Disease Threats: a Strategic Plan for the Department of Defense*. The DoD plan, which took inspiration from CDC's 1994 plan entitled *Addressing Emerging Infectious Disease Threats: a Prevention Strategy for the United States*, is now nearing the end of its term. It is thus appropriate to reflect on how far the program has come and how it might chart its future course.

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

In the area of surveillance, DoD-GEIS has set a specific programmatic vision for the overseas laboratories and allowed those laboratories to adapt their approach to local opportunities and resources. The five tropical overseas laboratories are now active contributors to the global influenza surveillance network and are, along with CDC, primary sources of surveillance data presented each year to the FDA committee that recommends the annual influenza vaccine composition. In multiple instances, DoD's contributions helped determine the components in the vaccine that protects tens of millions of Americans each year. The expertise of the DoD overseas laboratories in surveillance for drug-resistant malaria has generated data that have altered national malaria treatment recommendations. A particularly noteworthy aspect of this is how DoD-GEIS training efforts have enabled Ministries of Health to eventually conduct

these studies themselves. Inexorable increases in drug resistance among common enteric organisms have been documented, making it possible for providers in the military and elsewhere to know with more confidence how to treat diarrheal diseases most effectively. There have been many instances where DoD-GEIS febrile surveillance studies have identified the previously unappreciated endemicity of certain agents. These new recognitions have changed empiric treatments such that lives are likely being saved.

DoD-GEIS has also pioneered enhanced informatics systems that are laboratory based and advanced but still technologically appropriate. Laboratory-based enhancements to respiratory disease surveillance at NHRC and AFIERA have been particularly important to tracking respiratory disease etiologies during a time when lack of the adenovirus vaccine allowed the explosive return of adenovirus to basic training camps. This infrastructure foundation also has made possible critical research studies on respiratory disease prevention. DoD-GEIS has been the major funder of a formal, near real-time DoD mortality surveillance system based at the AFIP. The 1990-1991 Gulf War highlighted the critical deficiency and threat to credibility that existed because DoD's systems could not epidemiologically describe disease and non-battle injury mortality in the force in a timely manner.

Some of DoD-GEIS's most novel contributions have been in the area of informatics. The ESSENCE system is one of the world's most sophisticated entries into the new field of automated syndromic surveillance. In many ways it is a national pace setter, especially as a result of the DARPA-supported ESSENCE II partnership with the Johns Hopkins Applied Physics Laboratory and other academic and corporate partners. Recognizing, though, that each area of the world has its unique challenges, a valuable and innovative contribution to the field of automated syndromic surveillance for developing countries with a minimal existing informatics infrastructure arose from NAMRU-2's partnership with the Indonesian Ministry of Health. The EWORS project that grew out of this partnership has extended from a single hospital network in the Indonesian archipelago to parallel

networks in Cambodia, Laos, Vietnam, and the South Korean military. Through another public-private partnership (this time with Voxiva, Inc. and the Peruvian Navy), the NMRCDC has expanded the reach of informatics to the other side of the digital divide by supporting the implementation of Voxiva's Alerta™ System in the naval clinics along the Peruvian Amazon. This system allows electronic capture and reporting of data in places without any computer resources. Through partnerships with the Pan American Health Organization, the Caribbean Epidemiology Center, and the Peruvian Ministry of Health, DoD-GEIS, with US Southern Command humanitarian funds, has created electronic networks for laboratory-based surveillance using the CDC's PHLIS software. All of these informatics efforts have sought to foster more timely and standardized collection and analysis of surveillance data, and all are serving to some degree as models for elements of the global "system of systems" we need to encourage.

Response has primarily been focused on using the unique capabilities of the overseas laboratories to support regional outbreak investigations. These responses have encompassed problems in Asia, Africa, and South America. The products of these efforts have been not only routine epidemiologic insights but also the joint development by NASA and DoD-GEIS of a satellite remote sensing methodology for predictive modeling of Rift Valley fever epidemics in Africa.

A humbling conclusion nearly five years into the first strategic plan is that the human, microbial, and environmental conditions needed for infections to emerge are getting more common and complex. The amount of global human expertise is still falling short of the challenge. As a result, DoD-GEIS has placed increasing emphasis on training of both DoD and host-country personnel as a means to replace and leverage current assets. This training has taken many forms, including outbreak investigation courses at the overseas laboratories. It is only through vastly increasing the capacity of public health systems around the world that the challenge of emerging infections can be met.

About midway through the first five-year plan, DoD-GEIS engaged the Institute of Medicine to evaluate the program. Their conclusions were published in September 2001 and reported on in the 2001 DoD-GEIS annual report. The report's recommendations

have been taken very seriously at both the system level and by each of DoD-GEIS's components. As encouraged by the report, fiscal and other resources have continued to grow. Each overseas laboratory DoD-GEIS program is now led by at least one fully trained epidemiologist with experience in public health practice. Support staff have grown at both the Central Hub and at many of the field operating elements. Epidemiologic, laboratory, and informatics training has become a strong emphasis, especially at the overseas laboratories. Hundreds of DoD and host-country professionals have received training under the auspices of DoD-GEIS over the last few years. DoD-GEIS is particularly proud that many of the host-country partners who have been trained are now trainers for others in their own and neighboring countries. DoD-GEIS has, as recommended by the IOM, emphasized partnerships. Partners are currently to be found in over 50 countries and numerous US institutions. DoD-GEIS has actively supported the WHO through funding of several WHO collaborating centers, co-sponsoring courses, supporting a DoD officer's assignment to WHO headquarters, and participating in the WHO Global Outbreak Alert and Response Network. In a deep spirit of partnership, DoD-GEIS has been a beneficiary of superb support from the CDC. This has included the detail of CDC personnel to overseas DoD-GEIS programs, support with informatics training projects, support on specific surveillance efforts such as that for influenza, and a valuable dialogue to ensure that DoD's efforts are complementary and supportive of HHS initiatives.

A key recommendation of the IOM evaluation committee was to further timely dissemination of data and information for action. Most DoD-GEIS elements have embraced this notion, ever-conscious of the particular customers for their data. DoD-GEIS has presented its findings in numerous fora and has energetically participated in the biennial International Emerging Infections Conferences organized by the CDC. Websites or newsletters have been launched by most DoD-GEIS participants. At the Central Hub, internet methodologies have been established to move critical emerging infections data in a timely method to critical DoD consumers. ESSENCE is probably the quintessential example of increasingly timely dissemination, with syndromic surveillance analyses of morbidity at over 300 sites around the world currently updated every eight hours and made available through a secure website. DoD-GEIS

elements have been key in establishing, supporting, and strengthening intra-country and regional networks in many parts of the world. Tools have been put in place to measure and monitor the performance of the communication program.

So with the first five years behind DoD-GEIS, what should be its direction for the future? Inspiration for that can be taken from the March 2003 IOM report entitled *Microbial Threats to Health: Emergence, Detection, and Response*. This follows up the 1992 IOM report *Emerging Infections: Microbial Threats to the United States*, which was the stimulus for DoD-GEIS.

Many US government partners contributed to the support of this study. DoD provided \$100,000, \$50,000 from DoD-GEIS and \$50,000 from the Military Infectious Disease Research Program. The report emphasizes the national security dimension of the global emerging infections threat. Since the 1992 report was released, the world has seen an extension of the HIV/AIDS crisis with a pronounced societal dimension to add to the individual tragedies. The US has experienced the emergence of hantavirus pulmonary syndrome and West Nile virus infection. In this period, Malaysia saw the emergence of the deadly Nipah virus. The United Kingdom and other countries have suffered greatly from the combined effects of “mad cow disease” and its human counterpart, new variant Creutzfeldt-Jakob disease. Although all infectious disease epidemiologists are apprehensively awaiting the next influenza pandemic, as this final report goes to press the deadly and economically devastating SARS epidemic arising out of China reinforces that the new IOM report is not founded on conjecture.

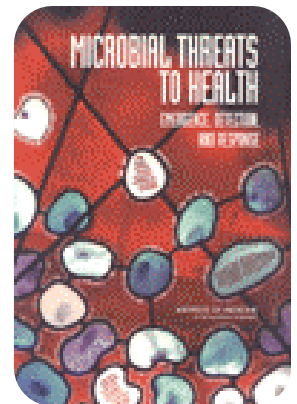
In the new report, antimicrobial resistance is a focus along with vector-borne infections, zoonotic infections, and infections associated with chronic diseases. Factors such as poverty, climate, war, and political will are highlighted as critical contributors to the global threat. And reflecting the post-September 11 reality, intentional use of biological agents is given a sobering treatment.

Twenty-one recommendations are offered, including many for DoD. DoD is encouraged to continue enhancing global response capacity, especially focusing on threats in the developing world. The report states “DoD should expand and increase in number its DoD-

GEIS overseas program sites” and that DoD should foster diagnostics development, reagent distribution, and technology transfer. It recommends that all federal overseas surveillance activities, including DoD’s, should be coordinated by a single agency such as the Centers for Disease Control and Prevention. It calls for implementation of automated laboratory-based reporting of notifiable infections. ESSENCE is mentioned multiple times and research on syndromic surveillance and geographic information systems is advised. DoD is encouraged to develop and expand intramural and extramural training in applied epidemiology, field-based research, and control of vector-borne and zoonotic diseases. Federal agencies are reminded of the need for a flexible research agenda to permit rapid assessment of new and emerging threats.

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

a transcendent moment nears upon the world for a microbial perfect storm. Unlike the meteorological perfect storm – happening just once in a century—the microbial perfect storm will be a recurrent event....Whereas the angry sea dissipates to an eventual calm, leaving few witnesses to a meteorological perfect storm, the factors creating a microbial perfect storm can perpetuate and even accelerate its effects – leaving multitudes of people to bear witness and fall victim to its destructive forces.



Microbial Threats to Health: Emergence, Detection, and Response, p. 21-22

DoD-GEIS has made critical progress in organizing DoD’s assets to identify that “microbial perfect storm.” The world is a large place, though, and many additional spotters and more far-reaching radars are needed to provide timelier alerts. As we have learned with HIV and are learning with SARS, national and global security are imperiled when those on watch are not alert or prepared when the epidemic winds start to blow.

ACRONYMS

AFIERA	Air Force Institute for Environmental, Safety and Occupational Health Risk Analysis
AFME	Armed Forces Medical Examiner
AFRIMS	Armed Forces Research Institute for Medical Science
APL	Applied Physics Lab
ASEAN	Association of Southeast Asia Nations
CAREC	Caribbean Epidemiology Centre
CDC	Centers for Disease Control and Prevention
CENETROP	Centro Nacional de Enfermedades Tropicales
DARPA	Defense Advanced Research Projects Agency
DoD	Department of Defense
DTRA	Defense Threat Reduction Agency
EMRO	Eastern Mediterranean Regional Office of WHO
ESSENCE	Early Notification of Community-based Epidemics
EWORS	Early Warning Outbreak Recognition System
FDA	Food and Drug Administration
FRI	Febrile Respiratory Illness
FY	Fiscal Year
GEIS	Global Emerging Infections System
GIS	Geographic Information System
GISP	Gonoccal Isolate Surveillance Project
HIV	Human Immunodeficiency Virus
IOM	Institute of Medicine
JE	Japanese Encephalitis
JHU	Johns Hopkins University
JSIPP	Joint Installation Pilot Project
LITS	Laboratory Information Tracking System
KEMRI	Kenyan Medical Research Institute
MHS	Military Health System
MIC	Minimal Inhibitory Concentrations

MTF	Military Treatment Facilities
NAMRU	Naval Medical Research Unit
NASA	National Aeronautics and Space Administration
NCCLS	National Committee for Clinical Laboratory Standards
NEDSS	National Egyptian Disease Surveillance System
NHRC	Naval Health Research Center
NMRC	Naval Medical Research Center
NMRCDD	Naval Medical Research Center Detachment
NPHL	National Public Health Lab
OAFME	Office of the Armed Forces Medical Examiner
OHDACA	Overseas Humanitarian, Disaster, and Civic Aid
PAHO	Pan American Health Organization
PCR	Polymerase Chain Reaction
PDD	Presidential Decision Directive
PDTS	Pharmacy Data Transaction Service
PFGE	Pulse Gel Electrophoresis
PHLIS	Public Health Laboratory Information System
ROK	Republic of Korea
ROKA	Republic of Korea Army
SARS	Severe Acute Respiratory Syndrome
STD	Sexually Transmitted Disease
USACHPPM	United States Army Center for Health Promotion and Preventive Medicine
USAID	United States Agency for International Development
USAMRIID	United States Army Medical Research Institute for Infectious Disease
USAMRU-K	United States Army Medical Research Unit - Kenya
WHO	World Health Organization
WNV	West Nile Virus

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