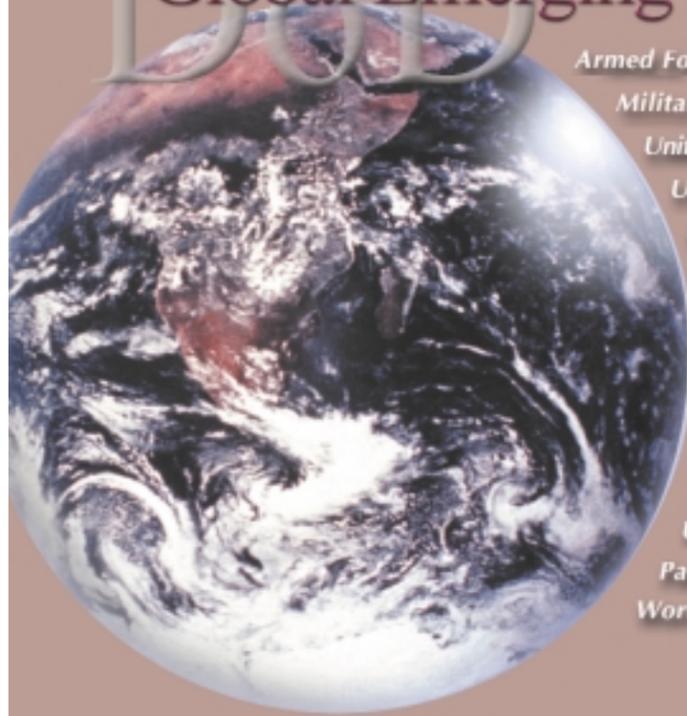


DoD Global Emerging Infections System

*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 2000



DoD Joins Growing Global Effort to Track Antibiotic Resistance in *Neisseria Gonorrhoeae*

In April 2000 the Hawaii Department of Health issued an alert advising that fluoroquinolones no longer be used to treat gonorrhea. Resistance in *Neisseria gonorrhoeae* had increased in Hawaii from 1.4% of isolates in 1997 to 9.5% in 1999. *N. gonorrhoeae* largely reaches Hawaii from the western Pacific, where fluoroquinolone resistance is established. Data indicate that resistance is becoming endemic in Hawaii.

Although military cases accounted for 33% (166/507) of all cases of gonorrhea reported in Hawaii during 1998, resistance data to date have come entirely from civilian clinical laboratories because the local military lab uses a non-culture based nucleic acid test for routine diagnosis of gonorrhea. With Hawaii serving the military as a principal gateway to the western Pacific, characterization of resistance within the military community is essential.

Gonorrhea remains a significant sexually transmitted disease around the world. In the United States and specifically in the DoD, it is the second most frequently reported communicable disease. Although gonorrhea rates in the United States have decreased almost every year since 1975, the case rate in 1998 was 1.32/1,000 (355,642 cases), an 8.9% increase over the preceding year. On a global scale, the case rate in 1999 was estimated to be 10.3/1,000 (62 million cases); about half of these were in the western Pacific and Southeast Asia, where the DoD has a sizable presence.

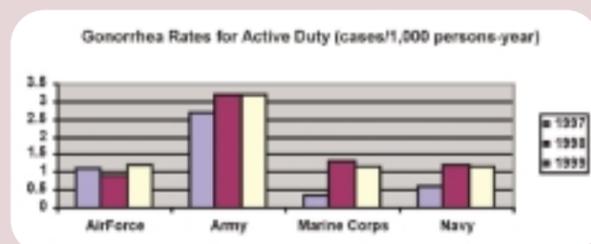
Effective gonorrheal disease control is a public health priority. Evolving gonococcal resistance to antibiotics is driving the need for surveillance of antibiotic susceptibilities. The CDC started the gonococcal isolate surveillance project (GISP) in 1987 to monitor resistance in *N. gonorrhoeae* in the United States. Many countries are engaged in resistance surveillance of gonorrhea, and WHO sponsors the gonococcal antimicrobial surveillance program (GASP) to encourage coordination of surveillance activities. For example, a long-term continuous surveillance in 19 countries of the western Pacific has tracked significant resistance in *N. gonorrhoeae* to the quinolones and penicillins since 1992. Currently the WHO and CDC are

working to increase collaboration among countries to standardize and share surveillance data and to identify additional areas to study.

The DoD is concerned with the potential military impact of the growing global threat of resistance in *N. gonorrhoeae*. Military personnel and their families are stationed in areas, such as Hawaii and the western Pacific, where fluoroquinolone-resistant gonorrhea is developing or established. They are stationed in or deployed in Europe, Africa, and South America where little information is available about gonorrhea susceptibility. The mobility of military personnel and their families through areas with resistance places them at risk of transmitting resistant disease to regions with little or no resistance, such as the United States.

DoD-GEIS is committed to working with the CDC, WHO, and other countries on the globalization of surveillance for *N. gonorrhoeae* resistance and is establishing a GISP to interface with the CDC project. By focusing on military populations in areas with known or suspected resistance in the civilian sector or areas where data in the civilian sector are lacking, DoD-GEIS can then determine if military resistance patterns reflect those seen in the civilian sector and recommend treatment for military populations. Priority sites include military treatment facilities in Hawaii, Korea, and Japan, where fluoroquinolone resistance is a concern among civilians; in Germany, where little is known of resistance patterns in civilians; and in highly mobile military concentration sites in the United States. To date, Tripler Army Medical Center in Hawaii has formally established a GISP site, and military treatment facilities in Japan and Korea are considering participation as sentinel sites.

DoD-GEIS is exploring the feasibility of surveillance of military personnel during deployments to areas of high or unknown resistance and partnership with foreign ministries of health to establish surveillance of civilian sex workers in areas hosting military personnel during such deployments.



Courtesy of Major Janette Goodman, Chief, Global Surveillance, Force Health Protection and Surveillance Branch, DoD-GEIS Air Force hub, Brooks AFB, Texas; Defense Medical Epidemiologic Database, Defense Medical Surveillance System, Army Medical Surveillance Activity, Washington, DC; Dr. Bob Morrow, Epidemiologist, Navy Environmental Health Center, Norfolk, Virginia.

previously isolated from military specimens were identified. These genotypes will undergo molecular sequencing to better understand the nature of the genetic changes and any implications of these changes on future adenovirus vaccine development.



Another respiratory disease tracked by the DoD-GEIS NHRC program was invasive *Streptococcus pneumoniae*. Clinical laboratories at seven U.S. military medical centers forward invasive *S. pneumoniae* isolates to NHRC to be tested for antibiotic resistance, serotyped, and subtyped. Of 231

isolates collected between August 1997 and September 2000, full or partial penicillin resistance was found in 77 (33.3%). Resistance to three or more antibiotics was noted in 54 (23.4%) of the isolates. An NHRC surveillance program at the U.S. Naval Academy in Annapolis, Maryland, also produced important findings for stimulating approaches to prevention. Of 85 midshipmen evaluated for acute respiratory disease, *S. pneumoniae* was found in 7.3%, *Mycoplasma pneumoniae* in 33.3%, *Chlamydia pneumoniae* in 52.6%, adenovirus in 1.2%, and influenza in 14.2%.

NHRC also established active surveillance programs for *Bordetella pertussis* at four military recruit training centers in light of the recognition that this infection is on the rise in adolescents and adults within confined populations. Preliminary results indicate that pertussis is present at DoD training camps. To evaluate whether respiratory syncytial virus is also an emerging pathogen in military camps, a joint protocol was developed and approved in FY00 to conduct respiratory syncytial virus surveillance at Fort Benning and at the Royal Navy recruit camp in the United Kingdom. Specimen collection is planned for October 2000 through April 2001.

The presence of a state-of-the-art public health laboratory for respiratory diseases at NHRC results in a

steady stream of specimens that can be used to evaluate new, rapid diagnostic tools that may be of use in military settings, especially for the rapid characterization of outbreaks. During FY00 NHRC evaluated a rapid diagnostic test for adenovirus against standard culture. The adenovirus assay had a sensitivity of 65%, a specificity of 60%, and a positive predictive value of 92%. Rapid tests for influenza were tested at three training centers. Final results are pending.

In addition to the evaluating diagnostics, the militarily unique respiratory laboratory infrastructure at NHRC funded by DoD-GEIS also allows NHRC to undertake respiratory disease clinical trials at a relatively small marginal cost. In FY00 these trials included a clinical trial at the underwater demolition school to determine whether oral azithromycin would be a useful prophylactic drug against cellulitis, acute respiratory disease, and pneumonia. Similarly, NHRC's respiratory lab capabilities allowed it to undertake the largest military clinical trial ever conducted, an effectiveness trial of 23-valent pneumococcal vaccine in 191,808 basic trainees at four Army and Navy installations. Enrollment and follow-up were slated to begin late in CY2000.

The contributions to surveillance made this year by the Air Force IERA respiratory disease laboratory had an impact that went far beyond the military. Their world-renowned influenza surveillance program grew to encompass 19 global sentinel sites, 49 nonsentinel sites, and three DoD overseas medical research laboratories. During the 1999-2000 influenza season, IERA received 3,825 throat swabs, which represents a 51% increase in specimen submission. Much of the increase reflected the explosive reemergence of febrile respiratory infections in trainees at Lackland and Sheppard Air Force bases. Throat swabs are tested for six viral agents (adenovirus, enterovirus, influenza A, influenza B, herpes simplex virus, and parainfluenza). Of 1,553 positive isolates, 23% were influenza A, 2% were influenza B, and 70% were adenovirus. To more effectively disseminate surveillance findings, IERA implemented weekly influenza activity reports for sentinel as well as nonsentinel sites and made them available on their website.

During FY00 the DoD-GEIS central hub also coordinated with the CDC to add additional DoD sites to the CDC gonococcal isolate surveillance project. The first site was Tripler Army Medical Center in Hawaii because of a recent increase in resistant gonococcal organisms in Hawaii. Specialized gonococcal antibiotic-resistance surveillance programs are also needed because nucleic acid testing has replaced the traditional culture methods at most military installations. Without such surveillance, treatment protocols used by DoD providers may not reflect local epidemiologic patterns of resistance.

In addition to gonococcal drug-resistance surveillance, DoD-GEIS also established a Cooperative Research and Development Agreement with MRL,

Inc. during FY00. MRL's automated approaches will be used for broader antibiotic resistance surveillance in several DoD health care facilities. It is anticipated that during FY01, Tripler Army Medical Center and Keesler AFB will be added to Wilford Hall in using the MRL program for antibiotic resistance surveillance.

The attention of DoD-GEIS to the broader issue of antibiotic resistance surveillance was also reflected in its active participation throughout the year in the federal task force on antibiotic resistance. A federal action plan was staffed, published for public comment, revised, and set for final publication early in FY01. This action plan highlights specific roles for the DoD as a large federal provider of health care.

DoD Surveillance Contributes Three Ways to 2000-2001 Influenza Vaccine

Three components of the 2000-2001 influenza vaccine were influenced by information gleaned through surveillance sponsored by DoD-GEIS. The DoD global influenza surveillance network comprises 19 sentinel sites and 49 ad hoc collection sites that every year provide data to the Food and Drug Administration and WHO for determination of the annual influenza vaccine.

In July 1999 the CDC became aware of an outbreak of influenza-like illness in Panama and contacted the DoD-GEIS central hub. At that time, the CDC had no isolates of the suspected influenza virus available for analysis. Through coordination by the DoD-GEIS Air Force hub at Brooks AFB, personnel at Howard AFB in Panama (now closed) collected and shipped 27 throat cultures to the Brooks AFB virology laboratory. Within only 2 weeks of the original call, influenza A had been isolated, antigenically subtyped, and sent to CDC for further studies. In addition, molecular sequencing was accomplished on a subset of these samples. Testing at the CDC indicated these viruses were antigenically similar to an H3N2 variant already identified from Moscow. That virus was not growing well in tissue culture, so the original specimen

from the Panama outbreak (A/Panama/2007/H3N2) became the seed virus for the H3N2 component of the 2000-2001 vaccine used throughout the United States.

The Brooks AFB lab also contributed to the selection of the H1N1 vaccine component of the 2000-2001 vaccine. During the 1998-1999 flu season a variant H1N1 virus was recovered from samples collected in Lima, Peru, by the DoD-GEIS program at the NMRC laboratory in Lima. These samples were then forwarded to Brooks AFB. The variant, not previously seen in Latin America, was identical to the H1N1 virus identified in New Caledonia in the South Pacific. Finding this variant in Peru supported the decision to change the H1N1 component for the 2000-2001 vaccine.

The influenza B component of the 2000-2001 vaccine remained unchanged, and DoD-GEIS influenced that decision. All type B isolates from the DoD surveillance program were the same as the previously isolated vaccine strain. This was true of isolates from other contributing laboratories. The confidence in a "no change" decision is increased when the body of evidence is both global and consistent.



Health Indicator Surveillance

Emerging infections, including bioterrorism, must be recognized as promptly as possible. A consensus has emerged that health indicator surveillance, including surveillance for syndromes in addition to laboratory-confirmed diagnoses, may help detect problems that surface in an insidious manner. The DoD-GEIS central hub, recognizing the great need for developing and evaluating methodologies for health indicator surveillance, took a major leadership role in this arena.

Focusing on the critical National Capital Region, the central hub continued developing the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE) as a tool for the daily monitoring of morbidity at more than 100 DoD primary care clinics. ESSENCE is based on ambulatory data routinely documented by DoD health care providers. During FY00 major progress was made in mathematical methods for using historical data to set adjusted norms against which to compare current data and in developing improved methods for displaying daily analyses. A key contribution to the development of ESSENCE has been the geographic information system contributions from the Army CHPPM. Realizing that a system with optimal sensitivity to detect events in the National Capital Region must be supplemented by non-DoD information sources, extensive and ongoing collaborations were pursued with other local entities including local universities and the Washington Metropolitan Council of Government's subcommittee on public health.

Health indicator surveillance is an innovative, ambitious, epidemiologically complex, and rather untested approach to public health surveillance. Recognizing that there is little precedent to consult for guidance and that many entities were independently trying to advance the relevant science, DoD-GEIS sponsored the "Conference and Workshop on Syndromic and Other Surveillance Methods for Emerging Infections, Including Bioterrorism" in May 2000. About 60 carefully selected invitees who represented a wide range of institutions and specialties with an interest in health indicator surveillance



came to this 3-day meeting. The meeting provided the first-ever forum to share work on the feasibility and utility of health indicator surveillance and to develop a consensus on a general approach to designing and implementing an effective, efficient, and integrated "system of systems" methodology, primarily for the homeland scenario. Proceedings of the conference and workshop are being prepared for publication.

In addition to these health indicator activities, the Navy Environmental Health Center used DoD-GEIS funds to improve syndromic and other surveillance capabilities for its shipboard deployed forces. The Navy Environmental Health Center and the Space and Naval Warfare Systems Command (SPAWAR) merged the desktop Shipboard Nontactical ADP Automated Medical Systems (SAMS) with the Naval Disease Reporting System. Specifically the medical event report, disease and nonbattle injury report, vaccine adverse event report, and tuberculosis screening modules were incorporated into SAMS. This integration extends to the shipboard setting an integrated surveillance and clinical data collection function similar to the same program that is deployed to all other medical settings within the Navy and Marine Corps. Release to the fleet is expected in early FY01. Additional testing, refinement, and training will follow. The expectation is that for the first time the Navy Environmental Health Center will have direct and smooth acquisition of shipboard surveillance data.

During FY00 the DoD-GEIS Air Force element also implemented a record validation program for reportable communicable diseases, designed a layout for web-based interactive surveillance reports using geographic information system utilities, and converted influenza reporting from routine to urgent.

Streptococcus Pneumoniae: An Emerging Pathogen of Military Importance

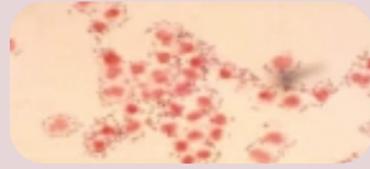
Problem:

1. Streptococcus pneumoniae causes an estimated 500,000 cases of pneumonia, 3,000 cases of meningitis, 50,000 cases of bacteremia, and 7,000,000 cases of otitis media annually in the United States.
2. Resistance in S. pneumoniae to antibiotics has risen dramatically.
3. S. pneumoniae has been responsible for outbreaks of pneumonia in military members.
4. Historical data suggest S. pneumoniae caused at least 12% of military hospitalizations for pneumonia in Navy personnel between 1981 and 1991.

Response:

Through DoD-GEIS funding and competitive grants, the DoD-GEIS Navy hub (Center for Deployment Health Research, NHRC, San Diego) has acquired the following unique capabilities to support surveillance, outbreak investigations, and special studies:

- Culture and sensitivity testing,
- Pneumolysin testing by PCR/enzyme immunoassay,
- Serotyping,
- DNA fingerprinting.



The NHRC respiratory disease laboratory accomplished the following in FY00.

1. Continued surveillance of invasive isolates from military medical centers that began in 1997. Of 231 isolates tested since 1997, 33.3% had full or partial resistance to penicillin, and 23.4% showed resistance to three or more antibiotics.
2. Initiation of an effectiveness trial of the 23-valent pneumococcal vaccine in 191,800 basic trainees at four different training sites with collaboration from military and civilian academic institutions.
3. Confirmation of S. pneumoniae as the etiologic agent for an outbreak of pneumonia that developed in about 5% of a large Marine training unit at Camp Pendleton in late 2000. The outbreak investigation was completed through collaboration with the Naval Medical Center and Naval Environmental and Preventive Medicine Unit Number 5 in San Diego.

West Nile Fever

The emergence of an Israeli strain of West Nile fever along the East Coast of the United States and its rapid spread from upper New England and New York to North Carolina illustrates the need for emerging infections systems to be able to recognize and respond to the unexpected. Although the surveillance and response to West Nile are primarily a civilian problem executed at the state level, the extensive presence of DoD installations in the affected area required coordinated DoD participation.

The DoD-GEIS central hub was asked to coordinate the reporting of DoD human, bird, and mosquito surveillance data and to represent DoD in weekly conference calls with the CDC and state West Nile

coordinators. Extensive mosquito surveillance was conducted by CHPPM along the East Coast. Of 2,805 mosquito pools collected, one positive *Culex pipiens* mosquito pool was found in Fort Hamilton, New York. The Walter Reed Health Army Medical Center's human surveillance in the North Atlantic Region detected no human cases. The North Atlantic Regional Veterinary Command coordinated bird testing, which confirmed four positive birds at West Point and one at Fort Hamilton. The Air Force also reported extensive mosquito trapping data. It is anticipated that in FY01 an even more robust DoD surveillance will be required because it is thought that West Nile will spread more extensively throughout the southeastern United States.

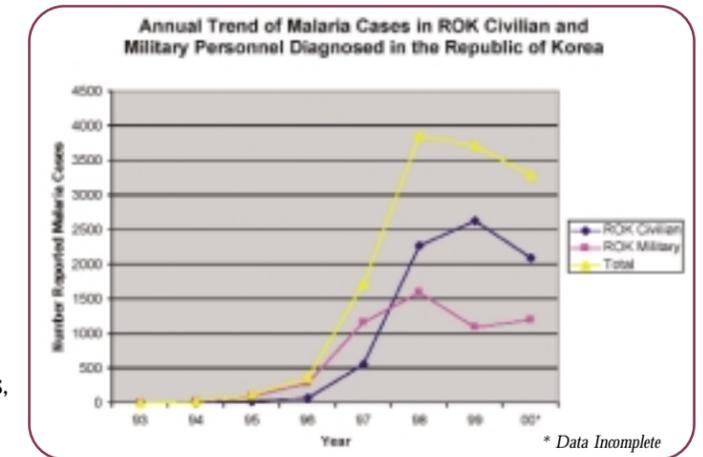
Malaria and Other Public Health Threats in the Republic of Korea

In consideration of the large U.S. troop presence in South Korea, the ongoing threat of malaria, Japanese encephalitis, and Hantaviruses in that country and the historic impact of these and other agents on morbidity and mortality, DoD-GEIS has focused on supporting improved field nonhuman surveillance capabilities in the 18th Medical Command. The recent reemergence of malaria in South Korea and ongoing morbidity in both Koreans and U.S. troops provide particular motivation for this support.

With support from the Army component of AFRIMS in Thailand, more than 25,000 trapped *Anopheles* mosquitoes are being tested by enzyme-linked immunosorbent assay to enable production of malaria risk maps. New methods of mosquito surveillance were also compared and evaluated. A comprehensive mosquito surveillance program using geographic information systems, satellite imagery, and larval collections was also supported at several key installations, and this has allowed a better appreciation of potential abatement sites under DoD control. Many other sites are on nearby private lands though which makes complete control more difficult. To better understand the use of anti-malaria personal protection measures by soldiers, another element during calendar year 2000 was to survey troops through a questionnaire.

Preliminary data are consistent with past information that the current system of education in the use of these effective means of protection is ineffective.

Japanese encephalitis is another concern for U.S. forces, although the widespread use of immunization in the Korean population tends to reduce the risk in host nationals. During FY00 mosquito surveillance for Japanese encephalitis in collaboration with USAMRIID identified several arboviruses. Final results are pending. Rodent-borne disease surveillance has also been instituted. Early results from surveys near one training site indicated the presence of rodents infected with both Hantaan virus and scrub typhus. Work is ongoing.



Activities Conducted by DoD Overseas Medical Research Units

The overseas medical research units of the Naval Medical Research Center and the WRAIR receive 65% of the core DoD-GEIS budget, which amounted to approximately \$4.6 million in FY00. Most of these funds are directed toward collaborative surveillance relevant to both the DoD and the host countries. Some of these collaborations reflect the regional roles of NAMRU-2 and NAMRU-3 as WHO Collaborating Centres for Emerging and Reemerging Infectious Diseases.

Institutions in the following locations had significant DoD-GEIS collaborations in FY00:

Argentina	Dominica	Indonesia
Bangladesh	Ecuador	Japan
Bahamas	Egypt	Jordan
Bolivia	Ghana	Kenya
Cambodia	Grenada	Korea
Czech Republic	Guyana	Laos
Djibouti	Hungary	Nepal

Conference to Integrate Surveillance Systems Breaks New Ground

Over the last 30 years considerable morbidity and mortality have resulted from disease outbreaks that probably could have been detected and responded to more promptly. Detection mechanisms for emerging infections, which tend to be inherently challenging to identify, are not sufficiently flexible when the condition is not reportable or diagnosable with readily available laboratory methods. Improving public health capabilities to handle disease emergencies, including those from bioterrorism, necessitates the consideration of how surveillance systems can be made more timely, flexible, and sensitive without compromising quality.

Motivated in part by the possibility of bioterrorist activities, many agencies and municipalities have recently explored novel and innovative approaches to surveillance. Although some have been implemented and many are being considered, lessons learned have not been widely disseminated. These include surveillance of Emergency Medical System calls, over the counter pharmaceutical sales volumes, and clinical laboratory assay requests. To avoid costly

mistakes and to foster efficient progress, DoD-GEIS sponsored the "Conference and Workshop on Syndromic and Other Surveillance Methods for Emerging Infections, Including Bioterrorism" in May 2000 in Gaithersburg, Maryland.

About 60 carefully selected invitees from federal, state, and local government agencies, the U.K. Ministry of Defence, and various academic and corporate entities with experience, expertise, or an interest in syndromic surveillance attended. The conference and workshop had two fundamental goals.

The first goal was to demonstrate the feasibility and utility of current and emerging surveillance methods for rapidly detecting and confirming disease outbreaks. This goal was unique because although virtually all forums on bioterrorism defense have recommended improvements in public health surveillance, no formal interagency meeting had ever been convened to discuss the special methodological approaches required.

The second goal was to bring together developers, managers, and users to reach consensus on a general approach to designing and implementing effective, efficient, and integrated surveillance systems. The conference and workshop helped create a necessary professional network dedicated to advancing these new public health methodologies.

The resulting recommendations are being prepared for submission to a major peer-reviewed journal. In addition, the recommendations are being shared with many organizations - government, academic, professional associations and commercial - that can and should be key in the rapid detection and confirmation of emerging outbreaks.



Pakistan	St. Vincent	Trinidad
Palestinian Authority		Uganda
Peru	Singapore	Ukraine
Philippines	Suriname	United Kingdom
Qatar	Syria	Vietnam
St. Kitts & Nevis	Thailand	Yemen

The overseas laboratory program of DoD-GEIS

supports several core surveillance efforts: influenza, drug-resistant malaria, antibiotic-resistant enteric organisms, fevers of undetermined etiology and syndromic surveillance. Some labs have added additional modules reflective of local needs or special opportunities. The most important programmatic highlights and findings of DoD-GEIS at each lab follow.

Naval Medical Research Center Detachment (NMRCDD)-Lima, Peru



As noted under "Respiratory Disease Surveillance and Capacity Building," surveillance by NMRCDD in partnership with the IERA influenza laboratory

had a worldwide impact by identifying isolates that contributed to decisions for the 2000-2001 influenza vaccine. The isolation of the New Caledonia H1N1 influenza A virus supported the conclusion that this new virus was spreading geographically. NMRCDD conducts surveillance of respiratory agents at eight sites: three in Ecuador, four in Peru, and one in Argentina. In FY00, 225 cases were studied. Influenza A and B viruses were isolated from Ecuador and coastal Peru, although it appeared that overall there was a decrease in influenza activity in FY00. A significant incidence of enteroviruses as a cause of illness among children in Buenos Aires was another important observation.

Surveillance for antimalarial drug resistance involved partners in Peru, Bolivia, and Suriname and was conducted largely under the supervision of a CDC officer assigned to NMRCDD. Surveillance in the Amazon basin, the second most drug-resistant area of the world, is a serious challenge. To ensure true capacity building, a major focus of DoD-GEIS is training of host country staff to conduct this surveillance using standardized WHO/PAHO 14- or 28-day *in vivo* drug protocols. *In vitro* parallel testing is also performed when possible. Results indicate widespread, intense resistance of *Plasmodium falciparum* to chloroquine but not to sulfadoxine-pyrimethamine on the north coast of Peru. In the

Amazon basin, resistance to both chloroquine and sulfadoxine-pyrimethamine is noted in the central Amazon region and along the northern and eastern borders with Columbia and Brazil. Resistance to chloroquine but not to sulfadoxine-pyrimethamine is noted in the western Amazon. The combinations of sulfadoxine-pyrimethamine plus artesunate and mefloquine plus artesunate proved more than 98% efficacious on the north coast and in the Amazon region, respectively. As a result of this work, Peru now has better and more up-to-date information on antimalarial drug resistance than any other country in the Americas.

These and other surveillance studies funded by DoD-GEIS prompted a decision to change treatment policy in early 1999 to quinine plus tetracycline in the Peruvian Amazon. Additional changes are expected in FY00 based on evaluations of combination therapy. Training of malaria control staff from Bolivia and Suriname, which was funded by USAID and PAHO as part of DoD-GEIS FY00 testing in Peru, has given Bolivia and Suriname the capacity to do this work with only minimal technical support from NMRCDD.

Surveillance for antibiotic-resistant enteric organisms generated 671 specimens from eight sites in Peru and Bolivia. Substantial progress was also made in enabling the Peru Ministry of Health to establish a network of 14 regional reference labs to perform surveillance of this type. FY00 surveillance indicated continuing high levels of resistance in both Peru and Bolivia. For example, 62.5% of *Campylobacter* were resistant to ciprofloxacin, although only 1.4% appeared resistant to azithromycin. More than 60% of *Shigella*, *Salmonella*, and *Campylobacter* were resistant to trimethoprim-sulfamethoxazole. Fewer than

West Nile Virus Spreads Along East Coast of United States

In the summer of 1999, an outbreak of fatal encephalitis occurred in the greater New York City area. Ultimately, 55 cases and seven deaths were attributed to the West Nile virus. This outbreak is the first known occurrence of West Nile virus in the western hemisphere.

West Nile virus, which has caused disease outbreaks in Mediterranean countries, Europe, Africa, and central and western Asia, is transmitted by mosquitoes and uses birds as its primary reservoir. The presence of viral RNA in over-wintering mosquitoes in New York City and the possibility that migrating birds could reintroduce the virus to the United States prompted federal and state health officials to prepare response plans in case the virus reappeared. Surveillance for the reemergence of the virus in mosquitoes and birds as well as humans in 2000 was a key component.

With DoD-GEIS coordination, commanders and medical personnel at DoD installations along the eastern seaboard were educated about the risk of disease caused by West Nile virus. Clinical, entomological, preventive, and laboratory information was prepared and distributed.

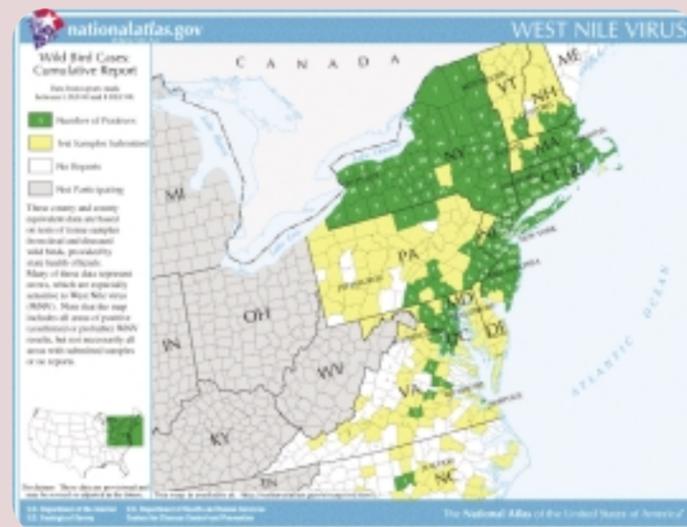
The capability to test mosquitoes for the presence of the virus was developed by the Entomological Sciences Division at CHPPM in Fort Meade, Maryland. CHPPM also assisted many installations with trapping and testing the insects and identifying and controlling mosquito breeding sites. Testing for potential human cases was offered at USAMRIID, to which all installations were encouraged to send any suspect specimens for analysis.

The 2000 season revealed not only a return but an apparently greater spread of West Nile. It was isolated from mosquitoes, birds, horses, and a range of other mammals between

New Hampshire and North Carolina. However, despite the increase in the geographic range, fewer human cases were reported: 14 from New York, six from New Jersey, and one from Connecticut. There were two deaths.

CHPPM tested 2,805 pools of mosquitoes. Only one pool containing three *Culex* mosquitoes, collected at Fort Hamilton in New York on 23 August, tested positive for West Nile virus. The pools submitted for West Nile virus testing this year contained 22,678 female mosquitoes collected from 17 Army and three Air Force installations in the North Atlantic region.

Five dead birds from DoD installations submitted for West Nile virus testing at the U.S. Geological Survey laboratory in Madison, Wisconsin, were positive. Four of the positive dead birds (one house sparrow, two cedar waxwings, and one hummingbird) were collected at West Point, New York, and the fifth positive dead bird (a crow) was collected at Fort Hamilton. USAMRIID tested 18 military beneficiaries for the presence of West Nile virus, and all were negative. Military surveillance data were collected and consolidated by DoD-GEIS before being transmitted to the CDC's national tracking system each week.



3% of *Shigella*, *Salmonella*, and ETEC isolates were resistant to ciprofloxacin.

Surveillance for mosquitos carrying arboviruses took place in four Peruvian Amazon basin sites with BSL-3 laboratory support provided by USAMRIID and additional assistance from the University of Texas, Galveston. Incidental field and lab training was provided to collaborators from the Ministry of Health. More than 57,000 mosquitos representing more than 100 species were collected. A total of 32 virus isolates were obtained and identified as eastern equine encephalomyelitis, Venezuelan equine encephalomyelitis, and at least four distinct Bunyaviruses.

Highly collaborative laboratory-supported syndromic surveillance for acute febrile illnesses in tropical, semi-tropical, and coastal regions of Peru and Bolivia was also conducted at eight health care facilities. Training of host country collaborators was again integral. As of October 2000, 297 patients had been enrolled. Patients fell into one of six syndromic categories (e.g., undifferentiated febrile syndrome without rash). Associated outbreak investigations were conducted in a large outbreak of dengue in northern coastal regions of Peru in which all four dengue serotypes were being transmitted, including both the American and Asian genotype of dengue type II. To share data among the many collaborating institutions, work is rapidly moving forward on a virtual data exchange site.

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



This year NAMRU-2 expanded its portfolio of core and innovative new surveillance and capacity building efforts. One critical regional gap filled by

NAMRU-2 is the establishment of ongoing influenza surveillance in Indonesia. During FY00, 730 specimens were collected, and 41 were positive for influenza A by either isolation or PCR. By hemagglutination inhibition, the strains were closely related to the H3N2 Sydney strain. Another new program headed by a CDC officer on loan to NAMRU-2 is sentinel surveillance for hemorrhagic fevers in Southeast Asia. During FY00 three sites were brought on line in Cambodia, and specimens from 164 patients have been obtained. Most (106) cases had dengue hemorrhagic fever. Others had leptospirosis (19) or scrub typhus (3). Personnel trained as part of this effort included nine laboratorians from the National Institute of Public Health and the Royal Cambodian Army.

The NAMRU-2 Early Warning Outbreak Recognition System (EWORS) is a computer-based sentinel syndromic surveillance system designed to provide early warning of possible outbreak conditions. EWORS grew to involve

eight sites throughout Indonesia plus three more in Cambodia. Five of these were new for FY00. A palm pilot version is being explored in a memorandum of understanding with the Singapore Ministry of Defence for use in refugee situations. EWORS was responsible for the recognition of cholera and dengue outbreaks in Indonesia. To provide an appropriate response to these warnings, NAMRU-2 also continued to teach its intensive 10-day outbreak investigation course to public health professionals. To date, eight of these courses have been conducted in Indonesia, Cambodia, and Laos. NAMRU-2 used its outbreak response skills while assisting with outbreaks in Indonesia (malaria, hepatitis, and dengue), Laos (pertussis), and Cambodia (typhoid, cholera, and malaria).

Preemptive Nipah virus surveillance indicated no evidence of Nipah virus in those Indonesian areas closest to Malaysia. These findings contributed to the lifting of importation restrictions on Indonesian pork products by the rest of the region.

With CINCPAC funds NAMRU-2 sponsored the "Regional Action Conference for Surveillance and Response to Infectious Disease Outbreaks in Southeast Asia." APEC, CDC, and other bodies co-sponsored this conference held September 2000 on Bali. More than 120 participants from 16 countries attended and produced a framework on which to

base regional surveillance and response efforts. As a first step in implementing this framework, NAMRU-2 has partnered with the Singapore Quarantine and Epidemiology Department, Ministry of the Environment, to establish a regional website to share emerging infections information across international borders.

As with NMRC, DoD-GEIS has a major investment with NAMRU-2 in surveillance for *in vivo* antimalaria drug resistance. Therapeutic response to chloroquine or Fansidar® was tracked in 161 patients in central Java. Another 120 patients were followed in South Sumatra. The Central Java follow-ups were ongoing as FY00 closed. In the South Sumatra surveillance NAMRU-2 found the first demonstration of clinical resistance to chloroquine by *P. malariae* anywhere in the world and the first demonstration of resistance to chloroquine by *P. vivax* on the main island of Sumatra. This information benefits the Indonesian malaria control program and travelers to these regions. A 5-day training and certification course in malaria microscopic diagnosis was given to 65 students in five locations in

Indonesia. A 2-week malaria vector entomology training course was also provided to technicians in Java. Malaria-related training and capacity building projects were also conducted in the Philippines with CINCPAC humanitarian assistance funds.

The work of NAMRU-2 on antibiotic-resistant enterics in FY00 involved nine sites in Indonesia. Most of the effort has focused on enhancing infrastructure at participating sites and in training local technicians. From January 1999 to June 2000, 3,535 rectal swab samples were processed. *Campylobacter* demonstrated a high level of resistance to almost all antibiotics including ciprofloxacin (32%), excluding chloramphenicol (5%). NAMRU-2 documented *Shigella dysenteriae* as resurgent after an absence of 15 years.

NAMRU-2 has also been a major innovator in implementing the CDC Laboratory Information Tracking System (LITS) for management of its specimen processing in Jakarta and Cambodia. To date more than 300,000 specimens have been catalogued and tracked in this system.

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



As the largest DoD overseas laboratory, NAMRU-3 fielded a particularly robust DoD-GEIS program in FY00. In addition, the benefit of having

a CDC officer on a long-term assignment to DoD-GEIS at NAMRU-3 was a tremendous asset.

Reflecting local needs, surveillance for meningitis and encephalitis is a primary focus of the DoD-GEIS NAMRU-3 program. By using a network of 12 Egyptian fever hospitals, a total of 2,152 suspected cases of acute meningitis were studied in FY00. A bacterial pathogen was diagnosed in 12% of cases. These included *S. pneumoniae* (38%), *Haemophilus influenzae* (17%), *Neisseria meningitidis* (34%), and tuberculosis (6%). Most other cases remain unexplained, and many are presumably viral. Serologic studies are underway to explore these cases further.

Based on more than 4,500 separate serologic assays to date, some viral meningitis cases caused by West Nile, Rift Valley, and sandfly fever (Naples) have been identified. Cerebrospinal fluid viral isolations have shown Sindbis, *Phlebovirus*, and enteroviruses. PCR studies are underway. In Egypt arboviruses appear to cause relatively few cases (about 1%) of diseases of the central nervous system. Special adjunct studies also documented important bacterial antibiotic resistance findings that may change therapeutic drug choices. The findings also prompted CDC to conduct a cost-benefit study on the potential role of *H. influenzae* immunization in Egypt. Incidental to this surveillance, local laboratory diagnostic and epidemiologic capacities have been greatly enhanced.

The network of Egyptian fever hospitals also served as a source of 1,473 cases for surveillance of acute febrile illnesses. Of these cases, 72 (5%) have positive blood cultures for *Salmonella typhi*, and 314 (21%) had probable typhoid fever based on Widal's

NAMRU-2 Cultivates Communication in Southeast Asia

Facilitating an emerging infections surveillance and response network in southeast Asia was a goal set in 1999 by the Emerging Infections Surveillance Subcommittee of the White House-led Committee on International Science, Engineering, and Technology. The importance of the Pacific Rim countries to the United States as stable trading partners and the regular emergence there of new and economically disruptive infections such as H5N1 influenza, foot-and-mouth disease, and the Nipah virus were compelling motivating factors. Consequently a joint CDC/DoD-GEIS project was accepted by APEC at its 17th International Science and Technology Working Group meeting in August 1999. Among its objectives, the project called for the United States to sponsor a meeting of regional stakeholders to develop a framework for infrastructure improvements to enhance infectious disease outbreak detection and response.

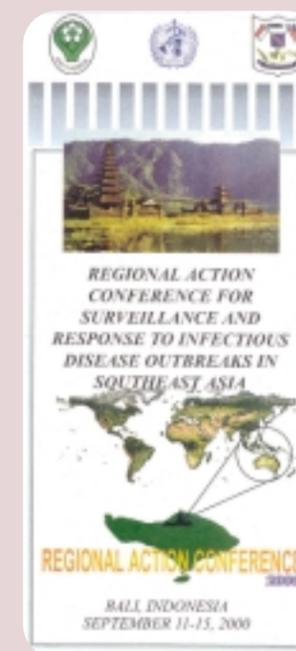
On 11-15 September 2000, the DoD-GEIS program at NAMRU-2 and the Indonesian Ministry Of Health hosted the "Regional Action Conference for Surveillance and Response to Infectious Disease Outbreaks in Southeast Asia" on Bali. APEC was a cosponsor. In light of the high priority the Pacific Command CINC gives DoD-GEIS efforts in the regional engagement plan, Pacific Command provided the necessary civic assistance funding. 120 delegates to the meeting represented 16 countries and included officials from Ministries Of Health, agriculture, defense, and tourism in addition to experts from academia, WHO, World Bank, Asia Development Bank, AFRIMS, CDC, UNICEF, JICA, AusAID,

and USAID. The Pacific Command surgeon and the Indonesian Minister Of Health also attended. Through lectures and workshops, a consensus framework document was developed.

The framework addresses the essential characteristics and development of laboratory and field surveillance, training programs, communications, and financial support. Two months later in November at the APEC Leaders' Summit in

Brunei, President Clinton communicated enthusiasm for efforts in this direction, and the closing declaration by the APEC leaders reflected the President's thoughts: "...new information and communication technology also enable important networks to be developed to extend health and medical services to the wider community and to address basic health issues. We commend the progress already made in strengthening disease information networks. We commit to fighting HIV/AIDS and other infectious diseases and call on relevant authorities to report in the next year on a strategy which can be used in APEC to more effectively meet these disease challenges."

Another element being developed by the DoD-GEIS program at NAMRU-2 is the South East Asian Infectious Disease Outbreak Surveillance Network (SEANET). This system of regional networks builds on existing networks to create Internet mechanisms to rapidly and securely share information about emerging outbreaks. SEANET is being led by NAMRU-2 in partnership with the Ministry of Health in Singapore. A focal point for coordination is a website created by NAMRU-2 that will be hosted by the government of Singapore.



reaction. Brucellosis was diagnosed by culture or serology in 155 (11%). Multidrug resistance among *S. typhi* was shown to have dropped at Abbassia Fever Hospital from about 60% in 1990 to <20% in 1999. Other fever cases were attributed to Rift Valley fever and sandfly fever (Sicilian).

Surveillance and associated training were also conducted at multiple sentinel sites for pathogens associated with severe diarrhea in Egypt. More than 500 children were systematically sampled and diagnosed with *Shigella*, *Campylobacter*, or ETEC. Additional studies for other bacteria, viruses, and parasites are underway on stored samples from these cases. Antibiotic resistance was common; however, ciprofloxacin was effective against all *Shigella* strains. Erythromycin was effective against all *Campylobacter* strains. Additional village-based surveillance was performed for diarrhea cases identified through more than 1,500 home visits per month. ETEC was

Armed Forces Research Institute of the Medical Sciences-Bangkok, Thailand



AFRIMS, the Army's largest overseas medical research unit, conducted the full range of core DoD-GEIS surveillance activities in its region

during FY00. Surveillance for antimicrobial resistance patterns was conducted in six different populations: U.S. soldiers during Operation Cobra Gold, adult travelers presenting to a clinic in Nepal, children younger than age 5 at a hospital in north-eastern Thailand near Laos, children younger than age 5 at a hospital in southern Thailand, children younger than 49 months in a village in central Vietnam, and children up to age 12 at two hospitals in the Bangkok area. In all, 2,571 human cases and 488 human controls were studied.

Among the nonimmune U.S. soldiers on Cobra Gold, nearly 70% of the diarrhea was caused by *Campylobacter*. Among *Campylobacter* isolates, resistance to nalidixic acid ranged from 90% for Cobra Gold to 8% in the central Vietnamese village. Ciprofloxacin resistance ranged from 90% in Bangkok to 7% in central Vietnam. Notably, 100%

the most common pathogen followed by *Campylobacter*. *Shigella* was uncommon. Again, high degrees of resistance were found. *Campylobacter* now routinely demonstrates resistance to quinolones.

During FY00 surveillance was also begun for multidrug-resistant tuberculosis using specimens from 13 chest and fever hospitals. CDC has been providing laboratory support. Results and analysis were pending at the conclusion of FY00.

NAMRU-3 also conducted influenza surveillance in Egypt and Syria. Inclusion of Djibouti was delayed until early FY01 because it was necessary to arrange a source of liquid nitrogen and other logistics. In Syria 96 cases were studied, yielding 19 cases of H3N2 influenza A, 16 cases of influenza B, and four enteroviruses. In Egypt 2,850 clinical samples were evaluated. Over 40% of the isolates were influenza, with about half influenza A and half influenza B.

(42/42) of the broiler chickens in Thailand cultured for *Campylobacter* had ciprofloxacin-resistant organisms. *Shigella* isolates were almost universally susceptible to ciprofloxacin and azithromycin (except 8% were resistant in central Vietnam). Most *Shigella* was resistant to trimethoprim-sulfamethoxazole.

Southeast Asia is known as the world's epicenter of drug-resistant malaria. About 137 *in vitro* *P. falciparum* resistance studies from FY00 are pending. These specimens were drawn from sentinel sites along the international border of Thailand, Lam Dong Province in Vietnam, and Chitagong, Bangladesh. Through collaboration with Nagoya University School of Medicine, specimens from Myanmar are also being evaluated. Specimens collected in FY99 document that multidrug-resistant malaria is prevalent along the Thai-Myanmar border. Mefloquine resistance has not improved since 1994. Areas with the highest degree of mefloquine and quinine resistance are on the central part of the Thai-Myanmar border near Maesod and in the Myanmar town of Mawlamyine. *P. falciparum* isolates from this region are still highly sensitive to artemisinin compounds. Other areas in Myanmar show intermediate mefloquine resistance, and

Bangladesh shows the lowest. Results have been presented to the malaria division of the Thai Ministry of Health for use in national policy formulation.

Febrile disease surveillance was undertaken in Sangkhlaburi, Thailand; Kathmandu, Nepal; and Kamphaeng Phet, Thailand. Sangkhlaburi district is a rural area located in the rainforests of western Thailand. Patients with nonspecific syndromes consistent with various case definitions have a range of assays performed. From July 1999 through September 2000, 326 persons were evaluated. Of these, 84% had acute and convalescent serologies. Results have been completed in 200 of these persons.

The biggest surprise was the prevalence and severity of leptospirosis, which had never been reported from the surrounding mountainous area. Leptospirosis affected 17.6% of the adults presenting with fever, the second most common diagnosis after malaria (21%). Leptospirosis was responsible for 60% of the revisits (most were not treated with antibiotics initially), 15% of the hospitalizations, and two of the three deaths. A seasonality was not noted.

Human granulocytic ehrlichiosis was also noted (a 6% prevalence among symptomatic persons). Monocytic ehrlichiosis was found too. Rickettsial disease was diagnosed. More detailed analyses are in progress. These findings have had an immediate local impact on medical practice, especially with respect to prompt institution of potentially lifesaving treatment for leptospirosis. Collaborators in this surveillance included the Harvard School of Public Health and the Uniformed Services University of the Health Sciences.

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



USAMRU-K is located at the Kenya Medical Research Institute

Although USAMRU-K is the smallest of the DoD overseas medical research labs, it is located in a region plagued with many emerging infections problems and many challenges to accom-

The AFRIMS febrile illness surveillance program in Nepal has also collaborated by supplying technology transfer and training to establish diagnostic capabilities at the Vector-borne Disease Research and Training Center in Hetauda, Nepal. AFRIMS continues to provide confirmatory diagnostics and a quality assurance function for Hetauda. Through the AFRIMS field station in Nepal, fever surveillance is focused on three hospitals in Kathmandu. More than 90 samples were screened for dengue and Japanese encephalitis, of which 31 were positive for Japanese encephalitis. The AFRIMS hospital-based febrile disease surveillance in Kamphaeng Phet identified patients who presented with one of several syndromes. A total of 683 cases were assessed serologically: 23 cases of leptospirosis and nine cases of scrub typhus were confirmed. No cases appeared to have an acute spotted-fever infection by serology.

Influenza surveillance was another focus with 39 specimens sent to the Air Force IERA influenza lab from suspect cases at the U.S. embassy in Bangkok, at the hospital in Sangkhlaburi, and at the CIWEC Clinic in Kathmandu. All isolates were either A/Sydney/H3N2 or B/Beijing.

A unique opportunity available to AFRIMS through its core DoD-GEIS program is a zoonotic disease surveillance module. An AFRIMS team worked with veterinarians and technicians from the Thai Ministry of Agriculture to collect specimens from domestic and wild animals in Sangkhlaburi district. Samples were collected from animals in the immediate vicinity of humans participating in a seroepidemiologic survey for leptospirosis. A total of 721 animals were sampled, and results were pending at the end of the fiscal year.

plishing quality surveillance. Despite a small staff and the difficulties of working in Africa, accomplishments were notable.

USAMRU-K endeavored during FY00 to establish the first *in vitro* malaria drug sensitivity facility in equatorial Africa and to begin a systematic evaluation of resistance patterns. The facility became operational in the middle of FY00. Initial data show

DoD Helps WHO Respond to Rift Valley Fever Outbreak in Yemen

On 21 September 2000, the Navy's research laboratory in Cairo (NAMRU-3) received an urgent request for assistance from WHO. Four days earlier health and agriculture officials in Yemen had received reports of Rift Valley fever in the El Zuhrah district of the Hodeidah governorate in Yemen. These reports followed by one week a confirmed outbreak of the disease in neighboring Saudi Arabia.

Through DoD-GEIS funding, NAMRU-3, which was approved just last year as a WHO Collaborating Centre, helps WHO respond to disease outbreaks in the Middle East. NAMRU-3 quickly assembled an investigative team that reached Yemen on 25 September and arrived in the outbreak area the next day. The team consisted of experts from the lab's virology, vector biology, and disease surveillance programs and three members of the Egyptian Field Epidemiology Training Program.

The first task was to confirm the cause of the outbreak, and on 28 September the team made a serologic diagnosis of Rift Valley fever in the affected region. For nearly 2 months the team continued to assist Yemen health and agricultural authorities by conducting epidemiologic and serologic surveys to characterize the evolution and extent of the outbreak and to help evaluate disease and vector control measures.

In the midst of this assistance, on 12 October, a terrorist bomb blew a hole in the hull of the USS Cole during refueling at Aden, Yemen, about 200 miles southeast of Hodeidah. Although the team was concerned for its safety, it maintained its schedule of grueling 18-hour days. As an indication of the humanitarian role of the military that DoD-



"Rift Valley Fever taking a toll on both people and economically important livestock."

GEIS fosters, a team member noted that they never felt threatened, saying, "[We] did not experience any anti-American sentiment. It was well-known that we were associated with the U.S. military - however, the work was perceived as a public health/humanitarian assistance response."

In addition to on-site assistance, DoD-GEIS supplied Rift Valley fever vaccine for investigators through USAMRIID. Through its partnership with NASA, the DoD-GEIS central hub provided satellite imagery to the NAMRU-3 team to better understand possible predictive environmental correlates.

Rift Valley fever is a mosquito-borne zoonotic viral disease predominantly causing abortion and deaths of young animals (e.g., sheep and goats). Epizootic and epidemic transmission is associated with periodic heavy rainfall. Human infection is usually not apparent or is associated with a brief self-limited febrile illness. However, complications such as retinitis, hemorrhagic fever, or encephalitis can occur. Transmission is primarily by contact with infected animal body fluids and mosquito bites. Person-to-person transmission has not been reported.

From 7 August to 7 November, 1,087 suspected human cases were identified in Yemen, including 121 deaths. Most cases were associated with contact with infected animals.

NAMRU-3 also provided technical assistance to the Saudi Arabia Ministry of Health to evaluate their response to the epidemic. The epidemics in Saudi Arabia and Yemen were the first known outbreaks of Rift Valley fever outside East Africa.

widespread and significant resistance. In the first tests in the new facility, 83 specimens from multiple sites in Kenya were evaluated. The mean chloroquine IC₅₀ values were 3.3 times higher than the standard chloroquine-resistant strain (W2). The mean mefloquine IC₅₀ was 2.6 times lower than D6, the mefloquine-resistant clone, and comparable with the mefloquine-susceptible W2 strain. The mean IC₅₀ values for quinine were 3.2 times higher than the quinine-sensitive D6 strain. Overall, 94.4% of isolates were resistant to quinine, and 81% were resistant to chloroquine, although mefloquine resistance was only 9.6%. No resistance to halofantrine was documented. PCR methods to check for drug-resistant genes are also being explored.

USAMRU-K worked to strengthen and derive additional benefit from the recently rejuvenated yellow fever network for Kenya, which is operated by the WHO reference center for hemorrhagic viruses that is co-located at the Kenya Medical Research Institute with USAMRU-K. The network consists of 24 clinics distributed widely in Kenya. In partnership with CDC, USAMRU-K provided two technicians to the WHO reference lab and supported the supply and travel budget. More than 1,200 blood specimens were screened during FY00 along with nearly 6,000 arthropod specimens. Screening by DNA or RNA amplification was performed for *Flavivirus*, *Alphavirus*, and *Bunyavirus*. This project confirmed dengue type II in Kilifi District Hospital on the coast of the Indian Ocean, the first confirmation of dengue in that area in 19 years. More than 8% of pediatric admissions for undiagnosed fever had positive immunoglobulin G or M titers to dengue, suggesting endemic transmission.

Congo-Crimean hemorrhagic fever was isolated at Misiko mission and West Nile near the border with Tanzania. Ticks positive for Tgoto virus, an often fatal virus for humans, were collected at a Nairobi abattoir. A fatal case of tick typhus, never before formally reported from Kenya, was found at Kijabe Mission Station. Preliminary data from a survey of cases of fever of unidentified origin in coastal and central Kenya found 0.7% immunoglobulin M (IgM) and 10.3% immunoglobulin G (IgG) positive for Hantavirus, which has never been proven present before in sub-Saharan Africa.

Studies on enteric illness antibiotic sensitivity were undertaken by USAMRU-K in collaboration with the African Medical and Research Foundation, the hub of a large regional network of hospitals and clinics. To support expansion of the work, USAMRU-K has expanded its enteric capabilities with an agreement with the Center for Microbiological Research. Enterics surveillance in FY00 centered at Entasopia, an area near the Tanzanian border; Machakos, north of Nairobi; and Marsabit. The surveillance identified three cases of *S. dysenteriae* type 12 at Machakos and Marsabit, the first found in Africa. Five cases of *Escherichia coli* O157:H7 were isolated in children in Entasopia, constituting the first epidemic with this agent documented in Africa. Resistance to three or more antibiotics was found in 76% of *Shigella*; 67% of enterohemorrhagic *E. coli* were resistant to multiple drugs.

Presidential Decision Directive NSTC-7 calls for the establishment of regional hubs linked by modern communications. Reliable communications are not easy in East Africa. In the spirit of the directive and reflecting USAMRU-K's shared location with many key emerging infections partners at the Kenya Medical Research Institute (CDC, WHO Viral Reference Centre, Japanese International Cooperation Agency, and Wellcome/Oxford), USAMRU-K erected a VSAT satellite dish and hired a full-time Internet supervisor-webmaster. The efficiency of scientific and public health communications has consequently been greatly improved for these agencies.

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

DoD-GEIS is primarily organized and funded as a public health surveillance and capacity building program. Most emerging infections research conducted by the DoD is managed and funded separately by the Military Infectious Disease Research Program (MIDRP). Nevertheless, DoD-GEIS has been in the position to facilitate the research agendas of MIDRP and other partners. In many cases this stems from the added value of using

Courtesy of LTC Kenneth Linthicum, U.S. Army, Walter Reed Army Institute of Research

surveillance specimens for additional research purposes such as the evaluation of new diagnostics. As noted under “Respiratory Disease Surveillance and Capacity Building,” DoD-GEIS assets have leveraged diagnostics development both domestically and internationally. The DoD-GEIS surveillance program is well positioned to recognize research questions that must be answered pertaining to the epidemiology and control of emerging agents. Sharing of infrastructure (e.g., the VSAT satellite at USAMRU-K) and various fixed costs at the overseas labs has augmented the output of both the MIDRP and DoD-GEIS programs at those institutions.

An operationally oriented research area of DoD-GEIS has been the development of new tools specifically for surveillance. For example, ESSENCE, the GEIS syndromic surveillance program for emerging infections including bioterrorism, is geared to test and evaluate new and innovative approaches to conducting surveillance.

Another unique operationally oriented research area of DoD-GEIS has been the application of satellite remote sensing to predict the occurrence of Rift Valley fever in East Africa. As one product of an interagency agreement between DoD-GEIS and NASA’s Goddard Space Flight Center, a monthly Rift Valley fever prediction map for Africa is made and posted on the DoD-GEIS website (www.geis.ha.osd.mil/riftvalleyfever/index.htm). When Rift Valley fever broke out in 2000 in Saudi Arabia and Yemen, appropriate remote sensing data were made available to ground investigators from NAMRU-3 to assist in determining whether predictive models could be extended to that area. Similar work was also conducted to develop methods to predict dengue hemorrhagic fever in Southeast Asia and *Filovirus* infections in Africa.

Behavioral issues, although not a major emphasis of DoD-GEIS, have received attention in various contexts such as the knowledge, attitude, and behavior surveys of U.S. soldiers in Korea concerning their use of the DoD personal protection system for the avoidance of malaria-transmitting mosquitos.

“3. Expand formal training and outreach to health care providers.”

Virtually all elements of DoD-GEIS are involved with training DoD personnel, collaborating foreign scientists, and public health workers. Many training efforts are formal courses such as the outbreak investigation course taught by NAMRU-2 in Laos in FY00. Other efforts include more informal yet still substantive training of laboratorians and other collaborators at hospitals, clinics, and other sites that serve the regional DoD-GEIS networks.

In addition the CINCs support humanitarian assistance projects such as the efforts funded by Southern Command that are directed toward building electronic laboratory-based emerging infections networks in the Caribbean and in Peru. For example, under these Southern Command projects, during FY00 DoD-GEIS and its partner, the Caribbean Epidemiology Centre, trained more than 60 public health professionals in the Bahamas, Guyana, St. Kitts, Grenada, and Peru in the use of computers for public health surveillance.

Perhaps the most significant for the DoD is the DoD-GEIS overseas medical research laboratory orientation training program. Arguably the greatest challenge to DoD in addressing the problem of emerging infectious diseases is maintaining a cadre of well-trained and enthusiastic uniformed professionals able to work both CONUS and OCONUS on these challenges. Economic opportunities and retirements have taken their toll on the pool of military tropical disease experts. The overseas lab orientation training program is targeted toward recruiting young military professionals from various relevant disciplines to a career involving international infectious disease surveillance, prevention, and research. This year 15 candidates were competitively selected for a mentored field experience at one of the five DoD overseas labs. The trainees spent on average of about 5 weeks at the laboratory and its field sites. Initial feedback has been excellent, and early indications are that some of these trainees are heading toward careers in this arena.

Another major venue for outreach was the “Second International Conference on Emerging Disease” organized by the CDC with financial assistance from many groups including DoD-GEIS. Researchers and public health professionals from the

DoD made 38 presentations over the 3-day meeting in July 2000 in Atlanta that was attended by nearly 1,800 members of the public health and scientific communities and the media. Additional publications and presentations are documented under “Consolidated DoD-GEIS Publications and Abstracts/Presentations.”

Another focus of outreach is the DoD-GEIS website that aspires to be a one-stop focal point for linking DoD and external parties to information relevant to DoD infectious disease control. During FY00 the site was redesigned to ease use, and more up-to-date content was made available. An electronic “GEISWeb User Survey” was incorporated to help GEIS understand and meet the needs of visitors from the DoD and general public.

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

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

Although controlling the migration of infected travelers is primarily the responsibility of the Quarantine Division of the CDC, the cooperation of DoD is essential, especially in light of the rapid movement of large numbers of DoD personnel in and out of the country. Fortunately, during FY00 large exposure-prone deployments were not as significant as in recent years. However, lines of communication must be regularly exercised and expanded to ensure improvement. Internal to DoD, GEIS hopes to more effectively disseminate travel-related health information through the proactive use of “push” technologies on its website. In addition, during FY00 DoD-GEIS participated in the organizing meeting of the WHO Global Outbreak and Alert Response Network and continues to share information, as appropriate, with DoD health authorities.

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

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



DoD-GEIS has been a leader in helping other nations move emerging infections higher on their agendas. A particularly vivid example is the leadership of NAMRU-2 in organizing a 1-week conference on Bali in September to establish a Southeast Asian emerging infections network. Attendees included representatives of WHO, 16 countries of the region, and the international banking community. DoD-GEIS endeavored to also support WHO through the Global Outbreak and Alert Response Network and by continuing to arrange for the detail of a U.S. Navy physician to WHO headquarters in Geneva in FY01. Plans are for this individual to serve for 2 years as the civil-military liaison officer at the WHO. WHO has an interest in fostering military emerging infections networks. In pursuit of that theme, DoD-GEIS was a major contributor at the 10th Annual Asia-Pacific Military Medical Conference held in Singapore in May 2000. More than 400 delegates from 28 nations participated. Over one-third of the infectious disease papers at the 5-day conference (14 of 41) were from programs supported by DoD-GEIS.

During the year NAMRU-3 was formally approved as a WHO Collaborating Centre for Emerging Infections and in that capacity led the WHO response to the outbreak of Rift Valley fever in Yemen.

DoD-GEIS participated in the PAHO Emerging Infections Task Force Meeting. DoD-GEIS also arranged using funding from the Southern Command Humanitarian Assistance Program for a four-person team, led by the U.S. Army Health Facilities Planning Agency, to perform a 1-week on-site consultation in Trinidad to help PAHO's Caribbean Epidemiology Centre plan a major infectious disease laboratory renovation.

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

In FY00 DoD-GEIS, through partnerships with other federal agencies, responded to numerous endemic and epidemic situations that could affect U.S. interests. An increase in resources this fiscal year made more robust contributions possible. Diverse nations have accepted the offer of DoD-GEIS public health assistance in the best spirit of international cooperation. Old ties have been strengthened, and new ties have been established. Common ground has been found where previously there was little collaboration. DoD-GEIS has supported other federal agencies in moving the problem of emerging infections beyond the health agenda into economic and global security forums, thus expanding and strengthening the emerging infections control mandate. The availability of experienced personnel continues to be the greatest limiting factor in supporting the U.S. agenda through this valuable form of engagement.

The Future

DoD-GEIS has established itself as a key international asset for dealing with the full range of emerging infections problems. It continues to execute its domestic and international programs in accordance with the 5-year strategic plan approved and published in 1998.

To ensure that its programs are scientifically sound, fiscally reasonable, and responsive to the needs of the taxpayer and to the nation's service-members, DoD-GEIS contracted with the Institute of Medicine of the National Academy of Sciences in FY00 to have a committee of eight internationally recognized public health experts perform a thorough review of all aspects of the program. This review, which includes site visits to each overseas lab and various CONUS elements, was begun in April 2000 and will be completed in late FY01. It is expected that the committee's

recommendations will help refine DoD-GEIS plans, although emphases are expected to still include improving MHS surveillance and response capabilities, addressing product availability issues, developing needed human resources, and using the DoD overseas lab as robust forward-deployed platforms from which to conduct emerging infectious disease work in the interest of U.S. national security. DoD-GEIS expects to continue to play to the historic strength of the overseas laboratories in the areas of field epidemiology, malaria, enteric diseases, viral diseases, entomology, and veterinary science. A strong continuing effort to leverage DoD capabilities through the training of collaborators will also remain a focus along with assisting other federal agencies in providing international leadership in scientific, public health, and diplomatic settings.

DoD-GEIS Trains Scientists for the Future

Deployed U.S. troops can find themselves slogging through rice patties in Southeast Asia, sleeping on the African savanna, or training in South American jungles. While these environments challenge the armed forces, they also nurture emerging infectious diseases.

To combat these unique threats, the Army and Navy operate five tropical research and surveillance centers in Egypt, Indonesia, Kenya, Peru, and Thailand. All are staffed with active duty and U.S. civilian scientists along with local researchers and support personnel. Maintaining a cadre of skilled scientists who seek the challenge and opportunity to work at the overseas labs is essential to their continued success.

For the past 2 years DoD has sponsored short training rotations at the labs for early and mid-career scientists who are interested in assignment at one of the facilities. Many want first-hand knowledge of the programs and the local living and working conditions before committing to a career in military tropical medicine research.

The first trainee was selected in late 1999, and by the end of FY00, 15 individuals had spent an average of 39 days at the DoD overseas labs. Five more were selected for training in early 2001. Trainees have come from Uniformed Services University of the Health Sciences, residency training programs, and fellowships.

Major Michael Lewis was a preventive medicine resident at WRAIR in 1999 when he was

awarded a 3-week rotation to study febrile illness in Nepal under the mentorship of an established AFRIMS scientist in Bangkok. Lewis is now assigned to the AFRIMS lab.

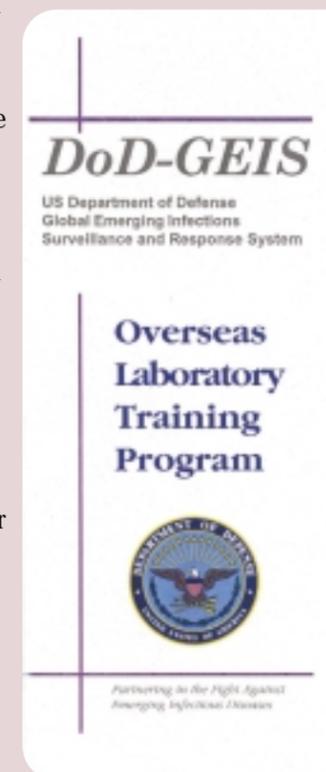
"Although I had a pretty good idea that I wanted to go to Thailand," says Lewis, "having the opportunity to spend time on the ground,

seeing the quality of the work, the outstanding quality of the people, and the overall enthusiasm of everyone I met, solidified my decision." Lewis also had a 2-year-old and an infant and says, "Having the opportunity to check out the family situation was probably the biggest thing...in giving my family the comfort to pick up and move."

Postrotation surveys consistently commend the projects and mentors at the labs. So far, Thailand has been the most popular training site, but opportunities are plentiful at all labs both for training and assignment.

The training program offers career choices that young physicians and scientists may not

otherwise consider because many have limited knowledge of the depth and breadth of the DoD research and development program. Exposure to the overseas labs can be a powerful and unique enticement for individuals to pursue a career in tropical infectious diseases. Information about the program, including eligibility requirements and application guidelines, is available on the DoD-GEIS website.



Acronyms

ADP	Automatic Data Processing
AFB	Air Force base
AFRIMS	Armed Forces Research Institute of Medical Sciences (Thailand)
AIDS	Acquired Immunodeficiency Syndrome
APEC	Asia-Pacific Economic Cooperation
AusAID	Australian Agency for International Development
BSL	Biosafety Level
CDC	Centers for Disease Control and Prevention
CHPPM	Center for Health Promotion and Preventive Medicine
CINC	Commander-in-Chief
CINCPAC	Commander-in-Chief, Pacific Command
CIWEC	Canadian International Water and Energy Consultants
CONUS	Continental United States
DoD	Department of Defense
ESSENCE	Electronic Surveillance System for Early Notification of Community-based Epidemics
ETEC	Enterotoxigenic Escherichia coli
EWORS	Early Warning Outbreak Recognition System
FY	Fiscal Year
GASP	Gonococcal Antimicrobial Surveillance Program (WHO)
GEIS	Global Emerging Infections Surveillance and Response System
GISP	Gonococcal Isolate Surveillance Project (CDC)
HIV	Human Immunodeficiency Virus
IC50	Inhibitory Concentration 50
IERA	Institute for Environment, Safety, and Occupational Health Risk Analysis
JICA	Japan International Cooperation Agency
MHS	Military Health System
MIDRP	Military Infectious Disease Research Program
NAMRU-2	Naval Medical Research Unit Number 2 (Indonesia)
NAMRU-3	Naval Medical Research Unit Number 3 (Egypt)
NASA	National Aeronautics and Space Administration
NHRC	Naval Health Research Center
NMRCD	Naval Medical Research Center Detachment (Peru)
NSTC	National Science and Technology Council
OCONUS	Outside the Continental United States
PAHO	Pan American Health Organization
PCR	Polymerase Chain Reaction
SAMS	Shipboard Nontactical ADP Automated Medical System
SEANET	South East Asian Infectious Disease Outbreak Surveillance Network
SPAWAR	Space and Naval Warfare Systems Command
UNICEF	United Nations Children's Fund (originally United Nations International Children's Emergency Fund)
USAID	U.S. Agency for International Development
USAMRIID	U.S. Army Medical Research Institute of Infectious Disease
USAMRU-K	U.S. Army Research Unit-Kenya
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research

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- Pavlin J. "The DoD Global Emerging Infections Surveillance and Response System" AFMIC Medical Intelligence Course. November 1999.
- Pavlin J. "Emerging Global Infectious Diseases: Threats & DoD's Strategic Plan" CME lecture at NSA. 17 November 1999.
- Pavlin J. "Surveillance: Uses and Evaluation." Kazakhstan School of Public Health. 21 January 2000.
- Pavlin J. "Potential DOD-GEIS projects in CENTCOM AOR." CENTCOM HQ, Tampa, FL. 16 February 2000.
- Pavlin J. "Preventive Medicine and Emerging Infections - Making an Impact on Worldwide Surveillance." PM interest group at USUHS. 24 April 2000.
- Pavlin J. "Vaccines Against Agents of BW/BT." Given to grad students at USUHS. 25 April 2000.
- Pavlin J. "DOD-GEIS and ESSENCE" BT subcommittee of the DC COG. 26 April 2000
- Pavlin J. "Syndromic Surveillance for Bioterrorism and other Emerging Infections" by invitation at the American Academy of Medical Administrators Conference, Bethesda, MD. 27 April 2000.
- Pavlin J. "ESSENCE" presented to a group at the USDA. 10 May 2000.
- Pavlin J. "ESSENCE" Conference and Workshop on Syndromic and Other Surveillance Methods for Emerging Infections Including Bioterrorism. 23 May 2000.
- Pavlin J. "Overseas Lab Participation in Influenza Surveillance" DoD Influenza Surveillance Working Meeting, San Antonio, TX. 8 June 2000.
- Pavlin J. "Surveillance for Bioterrorism" as Member of Marcel Faber Roundtable at the Annual Meeting of the Society for Industrial Microbiology, San Diego, CA. 27 July 2000.
- Pavlin J. "DoD-GEIS" - at the Central Region Medical Symposium, Tampa, FL. 8 August 2000.
- Pavlin J. "ESSENCE" at the DARPA ENCOMPASS PI meeting. 23 August 2000.
- Pavlin J. Member of panel at Mitretek meeting on infectious disease modeling. 12-13 September 2000.
- Pavlin J. BW Syndromic Surveillance - Report of a DOD-GEIS Workshop.-Armed Forces Epidemiology Board meeting. 12 September 2000.
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- Pavlin J. "Surveillance Methods for Detection of Bioterrorism" Part of live satellite broadcast Biological Warfare and Terrorism - Medical Issues and Response. 28 September 2000.
- Ryan MAK. "Respiratory Infections of Military Importance." Part of Military Tropical Medicine Course. Uniformed Services University of the Health Sciences. July 2000.
- Poddar SK, Le CT, Gray GC. "Fluorometric detection of B. pertussis by polymerase chain reaction and molecular beacon probe." International Conference on Emerging Infectious Diseases 2000, 16 July -19 July 2000, Atlanta, GA.
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