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 Assistant 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

Annual Report Fiscal Year 2004

Partnering in the Fight Against Emerging Infections

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Executive Summary

The FY04 DoD-GEIS Consolidated Annual Report presents a description of GEIS-related activities during this, its eighth year of funded operations. Global surveillance for emerging infectious disease threats, timely recognition of and response to outbreaks, together with the key laboratory and communications infrastructure supporting public health are cornerstones of national and global security. Events of 2001 (September 11th, anthrax incidents) continue to resonate; strengthening public health systems to address naturally occurring threats and preparations for bioterrorism are underway in many nations, including the US, and in DoD. The importance of global partnerships in prevention is evident in the world's success in controlling the SARS outbreak. Originating in China in 2002, it spread globally with 8,098 probable cases directly affecting 28 countries before it came under control. The global economic impact was immense. Avian influenza currently threatens large areas of Asia and national leaders recognize that it may trigger the next influenza pandemic. The vision of DoD-GEIS in the 1998 strategic plan was "To Enhance Force Protection and Preventive Defense;" communication and coordination have been seen as key to this vision, leading to rapid identification and assessment of significant infectious disease threats with timely, coordinated and appropriate responses. DoD-GEIS continues to work with and through its network of partners in the military health system, five DoD OCONUS laboratories, geographic combatant commands, and with US and international partners to prepare for and address emerging infectious threats as they relate directly to DoD, the health of its beneficiaries and to the nation as a whole.

FY04 Consolidated Annual Report

The Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS) is a network of DoD medical professionals, *a system of systems*. As such it is focused on outbreak response preparation and enabled by multiple partnerships. As a Tri-service program, DoD-GEIS works through partners and programs within the military health system and five DoD overseas laboratories with coordination by the GEIS Central Hub. DoD-GEIS was created in response to the June 1996 Presidential Decision Directive (PDD) National Science and Technology Council -7 (NSTC-7) which states that emerging infections threaten national and global security. In this directive the mission of DoD was expanded to support surveillance and response to microbial threats. This was to be accomplished through central coordination, enhanced support of overseas laboratories, collaboration with host country governments and improved cooperation and collaboration nationally and internationally. A strategic plan was prepared in 1998, *Addressing Emerging Infectious Disease Threats: A Strategic Plan for the Department of Defense* (an outline is included in Appendix A). The plan contained four goals: 1) Surveillance; 2) Systems Research, Development, and Integration; 3) Response; 4) Training and Capacity Building, with four surveillance priorities focusing on influenza, drug resistant malaria, antibiotic resistant diarrhea and febrile illnesses including viral hemorrhagic fevers and dengue. A new draft five-year plan and strategic plan is currently under development. A draft DoD directive was also created in 2004 to help define DoD-GEIS' role in DoD. These documents are pending action by the military medical leadership. GEIS activities and resources in the central hub, MHS and overseas laboratories support this plan. This report and prior DoD-GEIS annual reports illustrate how this network of professionals, with global projects and programs, support DoD's expanded mission. The threat of pandemic influenza and recent outbreaks such as global SARS in 2003 and A/H5N1 avian influenza underscore the need for constant vigilance and preparation.

This fiscal year (FY) 2004 DoD-GEIS annual report presents results of funded projects and activities with additional information about infectious disease outbreaks that affected DoD. These provide examples

of the preparation, assistance, service, and expertise by the DoD-GEIS professional partners to identify and mitigate these emerging infectious threats. In this report, activities and projects are presented for the Central Hub, MHS and overseas laboratories. Emphasis is placed on operationally relevant and forward-deployed activities through the five overseas military research laboratories and their substantial contributions to global outbreak detection and control, biosecurity and public health capacity building. These discussions may also include some activities and events that were not specifically commissioned, directed, or funded by the DoD-GEIS Central Hub. All, however, were accomplished in a spirit of partnership with DoD-GEIS activities; resources and capabilities are intended to be flexible and easily adaptable to changing circumstances, magnifying other capabilities. DoD-GEIS activities in the overseas laboratories complement other DoD medical assets worldwide (e.g., military treatment facilities, Combatant Commanders, Services, the Office of Secretary of Defense, Health Affairs (OSD(HA)). The DoD-GEIS professional network is configured to inform and to be informed, being constantly engaged with military and civilian medical activities world-wide, and to provide alerts, coordinate surveillance and analysis and to support medical investigations. DoD-GEIS also cooperates with global civilian partners including CDC and WHO.

Among the notable events in FY04 affecting the nation and DoD were 1) influenza/ avian influenza outbreaks (Asia, especially South East Asia), 2) multi-drug resistant *Acinetobacter baumannii* infections affecting military members injured in Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF)), and 3) interagency progress (events and professional activities related to strengthening collaborations, interoperability, and leveraging among DoD-GEIS, CDC/HHS, Department of State and WHO activities).

Several influenza outbreaks occurred on military facilities in November 2003, with DoD-GEIS facilitating special investigations led by USACHPPM and AFIOH in partnership and involving consultation with CDC. This led to the earliest estimates of influenza vaccine efficacy during a year marked by a mismatch between influenza vaccine antigen components and circulating virus strains. Influenza A/Fujian strain was documented as an important cause of epidemics in CONUS during the early phase of the 2003-4 influenza season. Several respiratory illness mortalities among active duty members and beneficiaries were collaboratively investigated by AFIP with NEHC, NHRC and AFIOH, again stressing the importance of influenza among potential causes of morbidity and mortality. These interactions led to DoD-GEIS sponsoring bimonthly telephone conferences including USACHPPM, NEHC, AFIOH, NHRC, NORTHCOM, the CDC DoD-Liaison, OSD (HA) and (at times) Surgeons Generals advisors for Infectious Diseases to establish timely communication regarding emerging threats.

Since the emergence of avian influenza (AI) A/H5N1 in Asia, with a human case in 1997 in Hong Kong, concern has mounted about its potential for global spread and potentially triggering the next human influenza pandemic. In addition to weekly GEIS/AFIOH DoD global influenza surveillance reports, regular reports from GEIS were requested by OSD (HA) on this emerging zoonosis in South East Asia. DoD-GEIS called on its partners, AFRIMS and NAMRU2 OCONUS laboratories that already were providing important epidemiological support regionally, for situational analysis, technical expertise and communications. A GEIS Central Hub staff member supported WHO's regional outbreak response in Laos at the request of the WHO GOARN network. This built upon relationships established regionally through DoD overseas laboratories and international support to regions affected by outbreaks, similar to the response to SARS described in the previous DoD-GEIS annual report. The AFIOH-based DoD global influenza surveillance program provided 1064 influenza isolates (766 derived from CONUS, 298 OCONUS) from the DoD system in the 2003-2004 influenza season to the WHO/CDC, a relationship that provides for influenza vaccine candidates in addition to global surveillance. According to CDC, a total of 129 National Respiratory and Enteric Virus Surveillance System (NREVSS) and WHO Collaborating Laboratories produced 24,649 U.S. derived influenza isolates during the 2003-2004 influenza season, and the 766 CONUS-based isolates of 1064 AFIOH total represented the 8th largest U.S contributor of U.S. derived positive influenza isolates, and 3% of the U.S. influenza isolate total. Additionally the remaining 298 OCONUS derived AFIOH processed international isolates that included isolates from Nepal (AFRIMS) and NMRCD (Peru), and others from NAMRU3 Cairo (348 isolates) and NAMRU2 Jakarta

(approximately 100 isolates) provided directly to CDC and WHO, respectively. DoD surveillance collectively produced at least 1512 influenza isolates representing an estimated 3% of the world's total influenza surveillance isolates derived from at least 18 countries and 4 continents (Appendix B)

DoD's medical leadership in 2003 described GEIS' role: "the premiere program for coordinating the nation's response to international emergence of new infections, development of antibiotic resistance, and development of local medical capabilities to identify and respond to infectious threats." In FY04, DoD-GEIS worked with WHO, GOARN, CDC and the US State Department; some examples are worth mention. GEIS provided representation at a WHO Consultation on Integrated Disease Surveillance, a more standardized approach to infectious disease surveillance which integrates diagnostic and reporting infrastructure. DoD-GEIS' liaison to WHO's Global Outbreak Alert Response Network (GOARN, http://www.who.int/csr/outbreaknetwork/en/) in Geneva is involved daily with national and world health issues that potentially have impact on DoD personnel, such as avian influenza and SARS. GEIS presented more than 20 scientific presentations at the International Conference on Emerging Infectious Diseases reporting results of GEIS supported projects, participating also in a joint seminar with CDC's International Emerging Infections Program (IEIP), including a joint presentation with GOARN. CDC's Epidemic Information Exchange (Epi-X, http://www.cdc.gov/epix/) includes GEIS on its advisory board; GEIS has facilitated training of over 100 DoD healthcare professionals and epidemiologists in the use of Epi-X to strengthen secure communications about epidemics for DoD. During FY04 in North America, Canada and many states in the US developed and published influenza pandemic plans; GEIS central hub staff attended state-level tabletop simulations of pandemic influenza with Maryland state public health personnel, USUHS and other DoD health officials. GEIS regularly participates in DoD policy discussions about influenza vaccines and antiviral medications for use in respiratory disease epidemics and important countermeasures for pandemics. US State Department asked GEIS to provide several presentations in partnership with HHS, DoE, USDA, and CDC at the Biological Weapons Convention sessions in Geneva. CDC's Director requested that GEIS' Director jointly visit the IEIP laboratory in Nairobi, Kenya in conjunction with visits to DoD OCONUS labs at USAMRU-K in Nairobi and NAMRU-3 in Cairo; this led to significant direct involvement with CDC for cooperative projects for influenza and other emerging infections involving laboratories at NAMRU-2 and NAMRU-3.

DoD-GEIS has long been involved in professional strengthening activities regarding antimicrobial resistance. In FY04 DoD-GEIS identified that there was insufficient information about the magnitude and scope of *Acinetobacter baumannii* infections in OIF/OEF injured patients throughout the MHS. As a result, a multidisciplinary infection control meeting was hosted by video teleconference; represented were DoD-GEIS, CENTCOM and TRANSCOM Surgeon's offices, Services' SG representatives, Landstuhl Regional Medical Center and medical staff from the 14 largest DoD medical centers, AFEB, CDC and academic consultant experts. An Army Epidemiological Consultation Service (EPICON) investigation was initiated as a result, augmented by Army infection control and USUHS personnel with DoD-GEIS facilitation. An outbreak involving this organism was documented to be affecting MTF's in Iraq and multiple medical centers. As a result of the conference and investigation, a coherent public health response was initiated [MMWR 2004; 53(45):1063-1066]. As a result of DoD-GEIS leadership in certain matters related to this investigation, partnerships were developed with infectious disease specialty/infection control advisors and to the respective Services' Surgeons General, and partnerships with CDC were strengthened. The professional partnerships among Infectious Disease, Preventive Medicine and Public Health practitioners, laboratory practitioners and government agencies built upon recent experience with SARS and on long-term relationships and infrastructure fostered through GEIS activities.

In summary, the vision of DoD-GEIS in the 1998 strategic plan was "To Enhance Force Protection and Preventive Defense." Communication and coordination have been seen as key to this vision, leading to rapid identification and assessment of significant infectious disease threats with timely, coordinated and appropriate responses. Support for Force Health Protection and the relevance of DoD-GEIS information and services to DoD's 8,500,000 medical

beneficiaries and 90,000 healthcare workers is evident in the activities presented in this, the DoD-GEIS FY04 Annual Report, and in the work of many, dedicated partners, without whom this work could not be accomplished. The DoD-GEIS internet site is available at http://www.geis.fhp.osd.mil for further information.

Central Hub Activities

The Central Hub served in a coordinating and communicating role for the DoD-GEIS in FY04. In addition to providing guidance and direction to the overseas laboratories, service hubs and affiliate partners, it also engaged in a number of activities in support of the Military Health System and fostered collaboration with other federal agencies and international organizations.

Begun in 2002 and based on earlier GEIS supported work, the Influenza-Like-Illness (ILI) ESSENCE project was developed to improve military influenza surveillance and to permit validation through comparison with national influenza surveillance data. The U.S. Centers for Disease Control and Prevention (CDC) uses sentinel physicians to monitor influenza activity as a percentage of visits to the sentinel physicians; reporting results weekly from week 40 until week 20 of the following year. Using ILI data from visits at military treatment facilities, an analogous, but automatic, electronic surveillance system was created and incorporated into year-round DoD global influenza surveillance.

The emergence and spread of antimicrobial resistance (AR) in pathogenic organisms is a public health problem of global dimensions that requires a concerted multi-disciplinary approach to its containment and resolution. DoD-GEIS recognized the threat of AR to DoD health care beneficiaries measured by morbidity and mortality, as well as to DoD health care delivery costs and efficiency. In FY 2004 DoD-GEIS expanded its effort in surveillance of antimicrobial resistant bacterial infections in DoD patient populations through a partnership with Focus Technologies, The Surveillance Network (TSN)®, and to represent the DoD on the U.S. Interagency Task Force on Antimicrobial Resistance. In addition, GEIS supported DoD efforts to define, control and prevent the further development of multi-drug resistant *Acinetobacter baumannii* infections in U.S. and Coalition Force wounded in Iraq and Afghanistan. GEIS also initiated efforts to develop a coordinated DoD-wide framework for combating AR as a health care issue for the DoD health care system including networking with infection control activities in MTFs.

Respiratory diseases remain a major cause of morbidity and concern in the U.S. military. Respiratory diseases, especially influenza are the top surveillance priority of DoD-GEIS. The U.S. Air Force Institute for Operational Health (AFIOH) and the Naval Health Research Center (NHRC) are the primary DoD-GEIS supported centers dedicated to influenza and febrile respiratory diseases of military trainees. The GEIS Central Hub staff served as consultants and sources of information to support activities of military importance and to facilitate the exchange of information throughout the military medical community.

As one of the pillars of the DoD-GEIS, education and training in emerging infections remains an important priority of our program. The Central Hub staff provided mentoring to resident physicians, graduate students and medical students who had curriculum or projects dealing with emerging infections of military importance. As in previous years, the GEIS Overseas Training Program funded and provided professional support to twelve residents from various military commands and from three medical services to participate in 30 day rotations at one of the five overseas laboratories.

This year GEIS initiated weekly discussions of current emerging infectious disease issues and topics that are contributed to the weekly CHPPM Health Information Operations (HIO) Update (http://chppm-www.apgea.army.mil/Hioupdate/); readership includes DoD top medical leadership and preventive medicine/public health practitioners. The Central Hub staff regularly provides communications through collaborations with the three medical services and with OSD(HA); in FY04 avian influenza in Asia, severe pneumonia with eosinophilia and *Acinetobacter baumanii* infections in deployed forces were topics of key interest. Central Hub staff in FY04 began bimonthly teleconference calls with GEIS partners and Service's epidemiology centers involved in outbreak preparation and response to

exchange timely information and to coordinate preparations for outbreaks. The Central Hub participates in the Joint Preventive Medicine Policy Group, allowing communication and consultation to key military medical policy makers concerned with population health and force health protection.

The DoD-GEIS provided professional assistance and material support to partners for various workshops, national and international meetings, symposia and the subsequent publication of proceedings of meetings (Appendix C) and other publications and presentations by DoD-GEIS activities are listed in Appendix D.

Outbreak Response: Assistance to WHO (World Health Organization)/WPRO(Western Pacific Regional Office) on A/H5N1 Avian Influenza through GOARN Coordination

Background: DoD-GEIS is a partner in the World Health Organization's Global Outbreak Alert and Response Network (GOARN) (http://www.who.int/csr/outbreaknetwork/en/). GOARN is an international vehicle for facilitating collaboration and coordination among governmental, professional, and institutional assets. It pools resources that can rapidly identify, confirm and respond to infectious disease outbreaks of international importance. GOARN is constantly vigilant and ready to respond to outbreak threats by maintaining a framework for immediately enlisting international expertise for real-time emerging infectious disease responses.

Methods: In response to the A/(H5N1) outbreak DoD-GEIS sent a Central Hub staff veterinarian with international experience to cooperatively serve as a member of the WHO GOARN Team in Laos per request coordinated through the DoD-GEIS liaison to WHO/GOARN in Geneva. The focus of this work was to assist Laos assess it's influenza A/(H5N1) risk and undertake measures to detect, control and prevent cases of infection in poultry and humans in Laos. This DoD-GEIS officer encouraged timely and accurate surveillance in poultry as early sentinels of human A/(H5N1) exposure risk. This included conducting training workshops in detecting and diagnosing avian cases. Workshops included demonstrations of safe practices including biosecurity for the at-risk animals, the humans working with them, and for health care providers. The officer also promoted surveillance, reporting and investigation of possible human cases. This included hospital record and patient registry reviews, and discussions with health care providers on influenza differentials and case findings. Where available, it also included the use of EWORS, a syndromic outbreak detection system developed by NAMRU-2, to facilitate the identification of influenza-like illness cases.

The DoD-GEIS response also included sending a US Navy microbiologist from NAMRU-2 to the Institute Pasteur in Ho Chi Minh City, Vietnam to provide training in rapid diagnostic test methodology. Through the US Air Force Institute for Occupational Health's influenza reference laboratory, DoD-GEIS supported A/(H5N1) diagnostic testing. In total, the DoD-GEIS system provided timely and relevant public health information to DoD officials to assist national and international decision making, including weekly reports to ASD(HA).

Accomplishments/results: As of October 2004, the A/(H5N1) avian influenza outbreak continues to smolder in several areas of Asia. It threatens the potential emergence of a global influenza pandemic. By working cooperatively within the WHO GOARN system, DoD GEIS provided a source of information to DoD leadership on ongoing outbreak events and thereby fostered preparedness in future outbreak management for Force Health Protection in the region and globally. By partnering with GOARN in its emerging infections surveillance and response activities, DoD-GEIS serves as a valued member of the global public health community and developed additional expertise to prepare both DoD and WHO organizations for possible future emergencies. It strengthened the U.S. military capability to meet the challenge and reduce the adverse impact of pandemic influenza on military force health and readiness.

Armed Forces Institute of Pathology

The Armed Forces Institute of Pathology (AFIP) is a DoD-GEIS partner that provides the Directory of Public Health Laboratory Services and the Alert Component of the DoD Medical Mortality Registry.

Initiated in 2000, the objective of the Directory of Public Health Laboratory Services was to establish an on-line DoD Directory of Military Public Health Lab Services where users could access information regarding infectious agents and their associated diseases. The Directory now contains over 170 infectious agents capable of being identified in more than 40 government laboratories. Participating laboratories update their listings regularly to keep their information current. The online directory is password protected and laboratory information is available only to appropriate government users. The Directory has been valuable for improving readiness and response as seen during military epidemiological investigations for diseases caused by salmonella and hepatitis C in 2004.

Also sponsored by GEIS is the Mortality Surveillance Division (MSD) of the Armed Forces Medical Examiner System. Specifically, GEIS funds the "Alert Component" of the Mortality Division, which includes the monitoring of all active duty deaths in real-time for infectious or potentially infectious etiologies, notification of DoD-GEIS and availability for prompt consultation in the event of any clusters or unusual types of infections or presentations, and obtaining specimens for more extensive testing and archiving. To date, the MSD is the only centralized agency in DoD with the mission and authority to investigate the medical cause of death for all active duty personnel. Other DoD agencies are service specific and have information on only a portion of the active duty deaths. Also, since MSD functions within the Office of the Armed Forces Medical Examiner, it is the only DoD agency with the authority, experience and capability to accurately track the medical cause of death, as determined by autopsy results, in a mass casualty event. Reports of 323 "illness" or "determination pending" deaths were received in FY04. All of these cases were expeditiously reviewed for a possible infectious cause. Of these cases, 283 were classified as "Illness" (Table 1), 45 met criteria for a more in-depth review, and 15 were determined to have an infectious cause of death with no predisposing condition. The majority of those 15 were classified as Respiratory, Myocarditis, Meningitis/Encephalitis, and Blood borne.

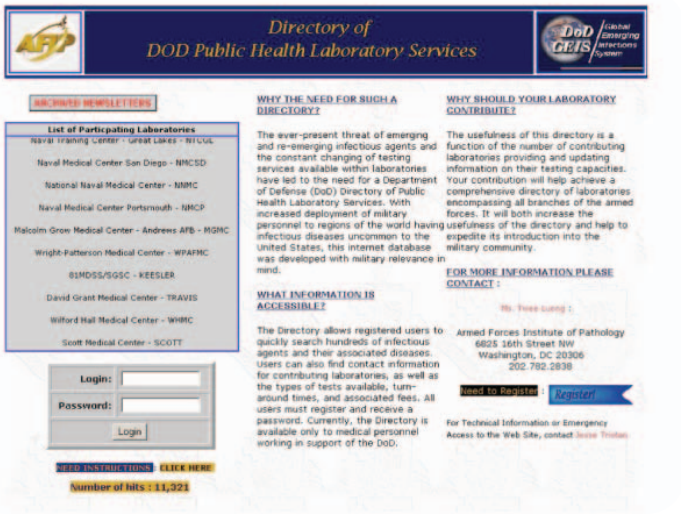


Table 1: Active duty and reserve component deaths by manner, FY 2004.

Branch	Accident	Combat	Pending	Homicide	Illness	Suicide	Undetermined	Total
Army	277	444	10	24	139	67	5	966
Air Force	104	3	4	7	61	54	1	234
USMC	99	159	8	10	15	26	1	318
Navy	109	12	18	12	68	43	1	263
Total	589	618	40	53	283	190	8	1781

U.S. Army Medical Research Institute of Infectious Diseases

USAMRIID is a DoD-GEIS partner that is a national resource for the isolation and identification of infectious disease agents that require handling at Biosafety Level (BSL) 3 and 4. In this capacity, USAMRIID serves as a WHO reference center for the hemorrhagic fever viruses and other arthropod-borne viruses. USAMRIID provides confirmatory diagnostic support for many overseas and domestic military medical laboratories. Development and fielding of new diagnostic assays, technology transfer to other government and civilian organizations, production and stockpiling critical reagents, and an ability to respond rapidly to outbreaks of emerging and re-emerging diseases have all been important components of the USAMRIID program. DoD-GEIS continues to serve as the primary source of funds to maintain these capabilities within USAMRIID. The ability of USAMRIID to continue to support overseas laboratories and the maintenance and improvement of current capabilities is, therefore, dependent on continued support from GEIS.

Diagnostic testing for many arthropod-borne and other hazardous biological agents is not available in most clinical laboratories. In fact, many of these biological agents are considered "orphan" diseases since frequency of disease in human populations is often so low as to make commercial production of diagnostic assays unprofitable and therefore unrealistic. Therefore, it is impossible for most civilian and military clinical laboratories to even acquire many of these reagents and assays to conduct clinical testing when the need arises. Although the frequency of these infectious diseases is quite low in the general world population, the impact of these diseases in endemic areas can be significant. Many of these endemic areas include rural and urban sites in developing countries, which suggest that military troops deployed to these areas may be at higher risk than is the general public.

The Applied Diagnostics Branch, Diagnostic Systems Division, USAMRIID serves a central role in providing diagnostic support for military and civilian medical requirements. It focuses on diagnostics of disease caused by the arthropod-borne viruses, hemorrhagic fever viruses, and diseases caused by other agents commonly associated with bioweapons and bioterrorism. This support is provided on an as needed basis such as in response to outbreaks or disease cluster investigations. In addition, USAMRIID provides consultation services to organizations requiring specialized training or reagents to established specialized diagnostic capabilities in remote or on-site locations. USAMRIID also provides consultation services on issues pertaining to disease control and prevention in endemic areas and during epidemic situations. Examples of this support are provided in the Table below.

In FY04, USAMRIID produced antigens for 12 viruses, to include many of the alphaviruses and filoviruses and produced antibodies to SARS, CCHF, and the filoviruses for use in rapid diagnostic assays. The laboratory developed an Electro-chemoluminescence (ECL) for rapid detection of West Nile virus and more than 1222 rapid diagnostic assays for various arthropod-borne and hemorrhagic viruses in support of DoD personnel and facilities; and 294 plaque reduction neutralization tests were performed by USAMRIID in FY04 in support of epidemiological studies of GEIS interest in Nepal, Cameroon, and the United States. In support of force health protection, USAMRIID assembled an immunodiagnostic "Iraq Panel" for testing sera of deployed troops presenting with undiagnosed disease from that region and have used it to test samples submitted by the United States, Japan, and Canadian forces. In addition, USAMRIID supported Hantavirus testing in Korea and alphavirus testing for DoD facilities in the United States. USAMRIID has also provided diagnostic support to Iraq Coalition forces and to other GEIS partners to support overseas and domestic outbreak investigations, surveillance projects and clinical care of military medical beneficiaries and to other GEIS partners for studies of GEIS interests.

Table 1

Laboratory Capacity Support	**Syndromic Based Outbreak Detection Projects Supported**
Antigens produced for diagnostic assays:	Developed West Nile Virus ECL Detection assay
Rift Valley Fever Virus	Produced and Characterized Anti-SARS Virus Monoclonal Antibodies
SARS Virus	**Epidemiology Capacity Supported**
Venezuelan Equine Encephalitis Virus – Trinidad Donkey	Nepal – Surveillance for West Nile Virus Antibody in Humans – 80 PRNT
Venezuelan Equine Encephalitis Virus – TC83	Nepal – Surveillance for Japanese Encephalitis Virus Antibody in Humans – 80 PRNT
Eastern Equine Encephalitis Virus – PE6	Cameroon – Surveillance for Vaccinia Virus Antibody in Humans – 50 PRNT
Western Equine Encephalitis Virus – CBA87	Cameroon – Surveillance for Rift Valley Fever Virus Antibody in Humans – 42 PRNT
Highlands J Virus	Cameroon – Surveillance for Crimean-Congo Hemorrhagic Fever Virus Antibody in Humans – 21 sera, pending development of a reliable PRNT test
Ebola Virus-Zaire, Sudan, Reston, Ivory Coast	United States - Surveillance for St. Louis Virus Antibody in Pheasant and Swine – 21 PRNT
Ebola Virus – Sudan	United States – Surveillance for West Nile Virus Antibody in Pheasants and Swine – 21 PRNT
Ebola Virus – Reston	**Force Health Protection Supported**
Marburg Virus – Musoke	Developed immunodiagnostic Iraq Panel for testing sera of deployed troops presenting with undiagnosed disease. Samples tested submitted by the United States, Japan, and Canada
Antibodies Produced for Diagnostic Assays:	Hantavirus testing for troops deployed to Korea
Rabbit anti-SARS polyclonal antibody	Arthropod-borne Virus testing for samples received from WRAIR, Fort Gordon, and Fort Meade
Anti-Crimean-Congo hemorrhagic fever mouse monoclonal antibody	**Other Cooperative Activities**
Anti-Ebola virus mouse monoclonal antibody	*Japanese Self Defense Force*
Anti-Marburg virus mouse monoclonal antibody	West Nile Virus Diagnostics – 8 assays completed
Rapid Diagnostics Support	Sandfly Fever Virus Diagnostics – 16 assays completed
West Nile Virus Diagnostics – 94 assays completed	Crimean-Congo hemorrhagic fever virus diagnostics – 8 assays completed
Japanese Encephalitis Virus Diagnostics – 74 assays completed	Miscellaneous arbovirus diagnostics – 12 assays completed
Tick-borne Encephalitis Diagnostics – 4 assays completed	*Egypt, NAMRU3: Provided assay support for surveillance of:*
Hantaan Virus Diagnostics – 732 assays completed	Tick borne encephalitis virus, Hantann virus, Puumala virus, Crimean-Congo hemorrhagic fever virus, Brucella, Q fever
Sandfly Fever Virus Diagnostics – 48 assays completed	*Kenya, Nairobi: Provided assay reagent support for surveillance of:*
Rift Valley Fever Virus Diagnostics – 64 assays completed	Dengue virus, Sindbis virus, Rift Valley Fever Virus, Crimean-Congo Hemorrhagic Fever Virus, Yellow Fever Virus, Chikungunya Virus, West Nile Virus
Crimean-Congo Hemorrhagic Fever Virus Diagnostics – 64 assays completed	
Venezuelan Equine Encephalitis Virus Diagnostics – 2 assays completed	
Lassa Virus Diagnostics – 58 assays completed	
Miscellaneous Arbovirus Diagnostics – 16 assays completed	
Miscellaneous Hemorrhagic Diagnostics – 66 assays completed	

18th Medcom Korea

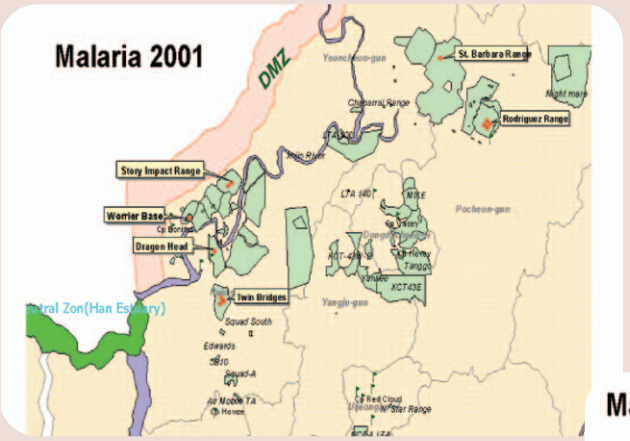
The Preventive Services Directorate, 18th Medical Command is a partner that was supported by the DoD-GEIS for the "Clinical and Vector Integrated Malaria and Japanese Encephalitis Surveillance Program, Republic of Korea" for fiscal year 2004. The objectives were to develop an integrated malaria and Japanese encephalitis vector surveillance and disease control system. This was done through 1) Analysis of historical and current malaria surveillance and other mosquito-borne disease data to develop disease trends, 2) Identification of infected mosquitoes to determine areas of transmission, 3) Survey of soldiers using questionnaires that identified knowledge of malaria and other mosquito-borne diseases and shortcomings in Personal Protective Measures (PPM), 4) Adult mosquito surveillance to determine season population trends and implementation of pest control strategies, 5) Evaluation of vector control to effectively reduce malaria infected mosquitoes, 6) Identification of mosquito species distribution and larval breeding habitats as part of disease threat/risk analysis and mosquito reduction strategies, 7) Taxonomy-Identification of vectors and their distribution, 8) Analysis of historical and current Japanese encephalitis and reservoir surveillance, and 9) Surveillance of JE virus and other arborviruses in mosquitoes.

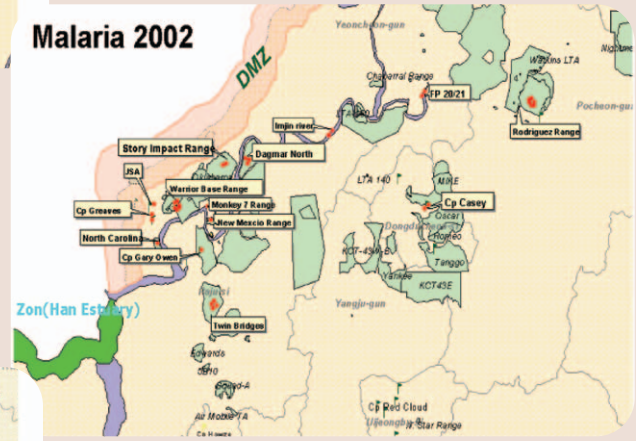
Vector-borne diseases continue to be a health threat to the United States Forces Korea (USFK). Vivax malaria, transmitted by the *Anopheles* mosquito, is just one of several diseases that historically impacted on military operations and major conflicts throughout history. Since *P. vivax* reemergence in 1993, malaria and other vector-borne diseases impact USFK personnel during training, as well as on military readiness and in preparation for hostilities. Readiness is a key issue for USFK personnel deployed to the ROK. *Anopheles spp*. populations were higher in 2004 compared to previous years and accounted for 38.7% of all mosquitoes collected. High populations of *Cx. Tritaeniorhynchus* during the late summer resulted in >44,500 specimens collected, which accounted for nearly 50% of all specimens collected. *Aedes vexans* populations were <50% of numbers of specimens collected the previous year.

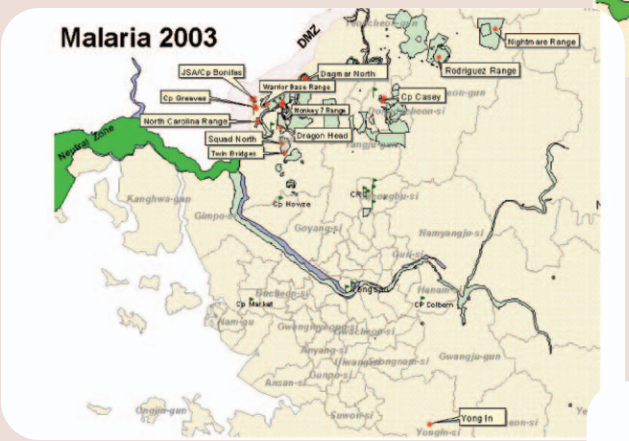
The topography of the Republic of Korea (ROK) is comprised of approximately 70% mountains. Wetland rice farming is the predominant agriculture among the scattered fertile valleys, and is to a large part, responsible for large mosquito populations. The mountainous topography and semi-isolated valleys result in the potential for focal malaria transmission. Human populations, including agriculture, are centered around villages, towns and cities unlike many of the tropical regions of the world where families reside on the land that they farm. Military bases are often associated with clustered civilian populations. This creates areas of dense populations and potential for magnification of focal transmission. Travel outside these areas of concentrated populations' compromises containment of focal transmission of disease, leading to further dissemination of malaria and other diseases throughout the ROK.

Surveillance systems provide USFK the capability to collect and assess data associated with anticipated exposures and to rapidly deploy and implement appropriate countermeasures. Results from military malaria patients indicated while 93% perceived that they received numerous bites from mosquitoes, only 20% had permethrin treated BDUs and only 40% used DEET insect repellent (commercial or military). During 2001-2004, except for one case, all malaria cases in US soldiers diagnosed in Korea are suspected to have been infected at training sites near Munsan (Western Corridor) and Dongducheon areas, less than 20 Km from the DMZ. Areas of malaria transmission to USFK are presented in Maps A-D. Efficient detection and interventions are needed to block the transmission of infectious agents. History has shown that the lack of detection capability and integration of appropriate interventions greatly affected casualty figures, both in mortality and morbidity, during the Korean War. Thus, effective and efficient surveillance systems that not only include the human component, but also the vector/reservoir components are required for the greatest predictive values in reducing DNBI with disease prevention strategies and determining the potential for morbidity and mortality.

Location of Suspected Malaria Transmission: U.S. Soldiers Diagnosed in Korea or Attributed to Exposure in Korea 2001–2004







Experimental Therapeutics

The methodology and approach required to describe antimalarial drug resistance demands well-documented clinical studies with adequate follow-up (time dependent upon the drug used), confirmation that adequate drug levels pharmacokinetics, and demonstration of anti-parasitic drug resistance in vitro and by using molecular markers.)

Investigations continued from the 2003 outbreak where 80 of 220 Marines contracted falciparum malaria in a deployment to Liberia, Africa. Blood level analyses verified that adherence to weekly mefloquine prophylaxis was suboptimal for many of these patients. Four patients with sub-therapeutic or non-detectable levels of Lariam developed severe and complicated malaria and requiring ICU intensive care unit treatment. *In vitro* susceptibility testing was performed on these and other samples. Patients without severe malaria were treated with oral Malarone® and all isolated parasites were susceptible to both atovaquone and proguanil. Three distinct resistance phenotypes were identified, including resistance to chloroquine, pyrimethamine and intermediate "resistance" to Lariam. There was no correlation between artesunate and mefloquine susceptibility. Parasites were susceptible to quinine and quinidine. Artesunate was up to fifty-fold more active than quinidine and artesunate was the most active of all artemisinin drug tested. Enhanced capability in FY04 included a new robotics system to automate susceptibility testing, used in surveillance and outbreak investigations such as that described above.

Aside from characterizing samples for mefloquine resistance, these samples were important for evaluating artemisinin drugs. In collaboration with the Medicines for Malaria Venture, WRAIR is developing an intravenous formulation of sodium artesunate (AS) to replace quinidine gluconate (QG) for the treatment of severe and complicated malaria. Emerging resistance to quinine, limited availability of QG, and requirements for ICU cardiac monitoring when QG is used are factors contributing to the unmet medical need for a safer, faster acting drug to rapidly diminish the level of parasitemia.

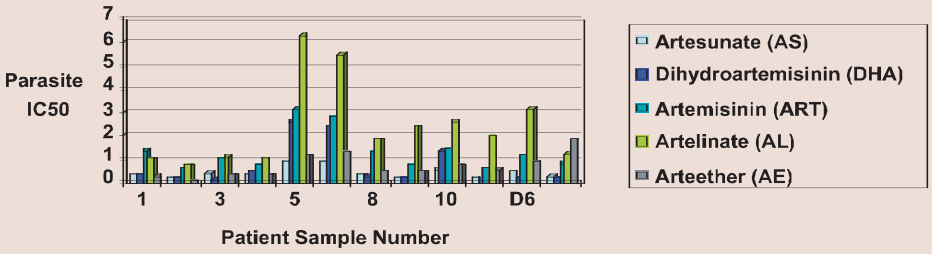
Given the potential for neuropsychiatric side effects with Lariam, it has been proposed that the isomers of mefloquine may be good replacement compounds for the commercially available *erythro* formulation if a superior therapeutic index could be demonstrated. Mefloquine contains two asymmetric carbon atoms, yielding four optical isomers and has one major carboxy metabolite *in vivo*. Dr. Geoffrey Dow has investigated the neurotoxicity and antimalarial activity of these four isomers and the metabolite using established in house screens. Significant differences were observed amongst the isomers in terms of neurotoxicity. The *threo* isomers, not present in the commercial formulation, were significantly less toxic to neurons in an *in vitro* neurocytotoxicity assay. The *threo* isomers were approximately 3-6 folds less neurotoxic than the *erythro* (Lariam) isomers. These findings merit further investigation with the malaria isolates from the Marines which have varying levels of susceptibility to mefloquine.

During FY04 ET monitored drug resistance throughout East Africa with an emphasis on Kenya where there are varying degrees of malaria drug resistance depending on the geographical location from where the parasites were isolated. ET screened isolated parasites against a battery of anti-malarial drugs to determine drug resistance profiles and performed genotyping analysis to determine the extent of genetic lesions leading to drug resistance. ET documented a direct correlation between Fansidar drug resistance and mutations in the DHFR and DHPS genes. ET concluded that numerous genetic alterations may be involved in chloroquine resistance which suggest that new molecular markers should be evaluated for malaria drug surveillance. The FY04 data will be used in subsequent years to determine a rate of drug resistance in Kenya. The initial data will establish a baseline for drug resistance that can be compared with an increase or decrease in resistance levels/markers over an extended period time. Since drug usage policies are currently being modified throughout East Africa, it will be important to capture the changes in drug resistance.

Data from the GEIS hub have been pivotal to elucidating global emerging drug resistance. Other studies are planned for antimalarial drug development process. ET/GEIS efforts have put DoD in a unique and advantageous position that will allow concurrent

data collection during national drug policy change. This is the first large scale malaria drug resistance project that can actually feed important data to the respective ministries of health to redirect drug treatment policies. There is also a high payoff or reward for DoD since Kenya serves as one of the major test sites for the U.S. Army malaria drug program. The drug resistance and susceptibility data collected in FY04 will be used to plan and guide malaria drug clinical trials.

In Vitro Activity of Artemisnin Drugs Against Falciparum Malaria Parasites from Marine Patients Samples



Naval Health Research Center

During FY04, the DoD-GEIS partner, Naval Health Research Center (NHRC) located in San Diego, California supported investigations of Respiratory Illnesses in the military. Military populations have historically been susceptible to outbreaks of viral febrile respiratory illness (FRI). Training populations, in particular, have been vulnerable to outbreaks caused by influenza and adenovirus. These epidemics disrupt training schedules, place a heavy burden on the military medical system, and ultimately, greatly impact troop readiness. NHRC conducts population-based surveillance for viral pathogens among basic trainees at 8 U.S. training centers. A systematic sample of trainees presenting for medical care with FRI symptoms are asked to permit a throat swab specimen and collection of clinical data. During FY04, 2,727 specimens were tested and more than 67% were positive for adenovirus. In order to estimate the impact of novel viral pathogens (pathogens that are not currently included in surveillance protocols), PCR testing has been developed and used to measure the rates of infection with rhinovirus, human metapneumovirus (HMPV) and two coronaviruses (CoV) among military recruits with FRI. During the first half of 2004, 320 throat-swab specimens were tested. Of these, two were positive for HMPV, five were positive for coronavirus, and 29 were positive for rhinovirus. These results showed a very significant spatial concentration of rhinovirus at the Marine Corps Recruit Depot (MCRD). Approximately 40% of these recruits with FRI test positive for rhinovirus. The rhinovirus positives were neither positively nor negatively correlated with adenovirus infection, the most common cause of FRI. These positives were spread evenly over the year, and rhinovirus was very rare elsewhere in the other seven centers.

No laboratory based surveillance for respiratory pathogens currently exists aboard ships or in the Pacific Rim, although viral illness outbreaks have occurred in these settings. During deployment, individuals presenting to the medical sick call of each ship with symptoms meeting the case definition of FRI were asked to permit a throat swab specimen and answer some symptom questions. These specimens were then transported periodically to NHRC for viral culture testing. Approximately 200 specimens have been collected from the nine currently participating ships. Of the 160 specimens that have been tested to date, clusters of Fujian-like Influenza A (A3N2) were documented aboard three different ships after port stops in Pearl Harbor, Singapore, and Sydney.

S. Pneumoniae is a leading cause of morbidity in the U.S. Similarly, it causes significant morbidity among populations served by U.S. military medical centers.

Antibiotic resistance has risen dramatically over the last decade, with varying levels of resistance found in different regions of the country. Currently, 7 U.S. military medical centers save all invasive *S. pneumoniae* isolates and refer them along with limited demographic data to NHRC where they are tested for antibiotic resistance and strain identification. To date, 401 *S. Pneumoniae* isolates have been received. One hundred thirty-one (32.7%) have shown resistance to penicillin, 92 (22.9%) to erythromycin, 50 (12.5%) to cefriaxone, and 147 (36.7%) to trimethoprim/sulfamethoxazole. Eighty-six (21.4%) isolates were resistant to 3 or more antibiotics. There were no significant variations in penicillin resistance patterns by age, gender, or geographic location. No discernable trend in resistance levels over time has been observed.

Streptococcus pyogenes (Group A strep or GAS) infections are common in young adults, and may manifest as pharynigitis, scarlet fever, pneumonia or other invasive disease. Acute *S. pyogenes* infections continue to be susceptible to penicillin treatment, but resistance to macrolide antibiotics has increased in recent years. As antibiotics are frequently used for prophylaxis of recruits against infection, vigilance is warranted to follow the characterization of *S. pyogenes* in such populations. A systematic sample of already-existing clinical *S. pyogenes* isolates are sent from clinical laboratories at 9 recruit training commands to the Respiratory Disease Laboratory at NHRC. Isolates are re-cultured and tested for antibiotic resistance, and a selected sample of isolates is also tested for emm-gene type to determine clonal relatedness.

Among the 1,789 specimens tested to date (148 in FY04), GAS maintains 100% susceptibility to the antibiotics penicillin and vancomycin. Two hundred sixty-five (14.8%) of the isolates exhibited full or partial resistance to erythromycin, 88 (4.9%) to tetracycline, 36 (2.0%) to clindamycin, and 21 (1.2%) to levofloxacin. Twenty-eight (1.6%) of the isolates were resistant to both erythromycin and tetracycline. Lackland AFB and Ft. Leonard Wood have shown a significantly higher level of erythromycin resistance. Temporal trends demonstrate no discernible patterns to date.

To date, 693 GAS specimens have been emm-gene typed. Among these, the most common emm-gene types were 29 (16.2%), 6 (13.7%), 3 (13.1%), 44/61 (9.7%), 2 (6.9%), 75 (6.3%), 1 (6.2%), and 12 (4.5%). These eight emm-gene types made up more than 76% of all the typed isolates. Erythromycin resistance varied by emm-gene type, with Type 75 exhibiting the most erythromycin resistance (64% fully resistant). Seventy-five percent of type 75 isolates came from referenced recruits at Lackland AFB.

Navy Environment Health Center

The Navy Environmental Health Center (NEHC) is the service surveillance hub for Navy Medicine. NEHC analyzes the Navy medical events reports and provides monthly feedback to Navy and Marine Corps TYCOMS and COCOMS, and forwards information to the Army Medical Surveillance Activity (AMSA)/Defense Medical Surveillance System (DMSS). NEHC coordinates four subordinate commands with specified areas of responsibility thus providing medical surveillance for Navy and Marine corps around the globe. Currently, NEHC is conducting a study to assess the validity of existing Military Health System (MHS) data sources and evaluate their use for surveillance and outbreak detection. It measures the agreement between three data sets: SADR (Standard Ambulatory Data Record), CHCS lab results, and Reportable Medical Events (RME) reports for the diseases *Chlamydia trachomatis* and *Neisseria gonorrhea*. Preliminary results show that agreement between RME and SADR records was very low for both diseases. In general, the level of agreement was higher for Chlamydia versus gonorrhea records. However, a large proportion of reported RMEs (59.3% of gonorrhea and 90.1% of Chlamydia) and a large portion of SADR records (59.2% gonorrhea and 80.0% Chlamydia) had supporting confirmatory lab results. Furthermore, a large number of positive lab results were not reported in either database. There is little agreement between IDC-9 coded records and RME reports although each has a high number of supporting lab results suggesting that a combination of the two might present a more complete epidemiologic picture of these diseases. Clearly none of these databases are sufficiently robust

when used in isolation for sexually transmitted illness (STI) surveillance.

The ongoing surveillance of medical events is essential to identifying and controlling outbreaks and emerging disease threats. As diagnosis of such diseases may heavily rely on the laboratory, centralized Electronic Laboratory Reporting (ELR) has been suggested to improve epidemiology and surveillance capacity in the MHS. Therefore, NEHC assessed the data in three repositories (CHCS-II, Air Force Project, Health Level 7 HL7 project) for their usefulness in medical surveillance. Each was evaluated for their timeliness, completeness, analysis capabilities, and accessibility. To date, they have found that the CHCSII project has the potential to provide more reliable and complete data for ELR in the future, but not in the next several years. Laboratory results data from the Air Force project is extremely limited and would be of little use. The HL7 project currently collects laboratory results data from most, if not all, Military Treatment Facilities and in addition, the data is available now for use. Recently, this technology provided useful information in support of investigations about *Acinetobacter baumanii* infection in patients from OIF/OEF. (MMWR 2004; 53(45):1063-1066.)

Navy Environmental Preventive Medicine Unit 6

The Navy Environmental Preventive Medicine Unit 6 (NEPMU-6) located in Pearl Harbor; Hawaii is a partner that provided support to the DoD-GEIS in 2004. One project studies the incidence, epidemiology and detection of Viral Gastroenteritis aboard U.S. Navy vessels and in other DoD Units. Viral gastroenteritis (VGE), especially caused by Norovirus (NV) is the most common causes of food-borne illness in the military and the U.S. in general. NEPMU-6 has served as a reference lab/clearinghouse for all military units for the past three years, but has actively monitored 25 U.S. Navy "Big Decks" such as aircraft carriers and troop carrying ships since 1999 for illnesses causing gastrointestinal illnesses. As such, they provide participating ships with specimen collection supplies prior to deployment. The data and the specimens are collected after an outbreak of gastroenteritis begins and they are sent to collaborators for confirmation and characterization. Eight VGE outbreaks were detected in FY04 plus a new one from 2003, however, only one provided samples of stools (NV was detected in that outbreak). A lack of onboard freezer space was a major limitation but soon will be rectified in 2005. Another NEPMU-6 project is the enhanced influenza surveillance in the Western Pacific. The objectives of this project were to improve surveillance for Influenza and other febrile respiratory pathogens throughout the Western Pacific by adding surveillance sites in key locations and through providing on-site educational products covering the diseases of interest and current methods of surveillance. Shore-based or shipboard facilities having either no surveillance activities or incomplete surveillance programs were first identified and then asked to participate. New sites were added at the U.S. Consulate; Hong Kong; the U.S. Naval Hospital, Guam; U.S. Navy Branch Clinic, Sasebo, Japan; and aboard the USS Kitty Hawk. An existing surveillance site at USNH Yokosuka was also visited to improve surveillance results. This initial year's project has improved awareness about existing influenza surveillance programs and has enhanced the geographic coverage of DoD's influenza surveillance effort.

Naval Medical Research Center

In a continued effort of collaboration, the DoD-GEIS is a partner with the Naval Medical Research Center Rickettsial Disease Department (RDD) located in Silver Spring, Maryland. Rickettsial diseases, including epidemic typhus, murine typhus, Rocky Mountain Spotted Fever, Mediterranean spotted fever, scrub typhus, ehrlichiosis, trench fever and others are endemic or re-emerging diseases in much of the developing world. In addition, antibiotic resistance and prophylaxis breakthroughs have been reported with *Oriential tsutsugamushi*, the agent of scrub typhus. The DoD overseas laboratories, also supported by GEIS, are measuring the extent of rickettsial diseases, their threat to military operations, and the emergence of antibiotic resistance. They perform initial testing of specimens with reagents provided by

the Division of Rickettsial Diseases. In addition, the Department provides training to perform the assays as well as act as a reference laboratory to perform confirmatory tests. There continues to be a need for a DoD reference laboratory to confirm antibody detection results, assay for live organisms, and standardize polymerase chain reaction (PCR) based detection systems.

The RDD is ideally suited to performing, training others to perform and developing diagnostic assays. They have personnel training in performing serological assays (ELISA, IFA, RFD), molecular biology assays (PCR, quantitative real-time PCR, micro arrays) and isolation techniques (yolk sacs, tissue culture). In addition they have a rickettsiae dedicated BSL-3 laboratory. To date, they have developed FDA-certified tests for typhus, spotted fever, and scrub typhus.

Rickettsial diseases are found throughout the world and are a risk to endemic and visiting populations. Little is known of the extent of the risk for these acute febrile diseases that may be life threatening and are often debilitating. Providing reagents and know how to detect these diseases is a benefit to both the U.S. military as well as the host countries. The RDD program provided ongoing expertise and consultation as needed through FY04 about molecular based microbial detection and rapid diagnostics for febrile diseases. NMRC collaborated with each of the 5 OCONUS labs, USAMRIID, WRAIR, and CHPPM-W in Central America on outbreak investigations involving febrile illnesses throughout the world.

Reagents and assays made for diagnosing/detecting the following diseases/agents:

DISEASES	AGENTS	SEROLOGIES	PCR ASSAYS
Scrub Typhus Group			
Scrub typhus	*O. tsutsugamushi*	IFA, ELISA, WB	PCR; quantitative real-time PCR
Typhus Group			
Epidemic typhus	*R. prowazeckii*	IFA, ELISA, WB	PCR; quantitative real-time PCR
Murine typhus	*R. typhi*	IFA, ELISA, WB	PCR; quantitative real-time PCR
Spotted Fever Group			
Rocky Mountain spotted fever	*R. rickettsii*	IFA, ELISA, WB	PCR; quantitative real-time PCR
Boutonneuse fever	*R. conorii*	IFA, ELISA, WB	PCR
African Tick Bite Fever	*R. africae*	IFA, ELISA, WB	PCR
Cat flea typhus	*R. felis*	ELISA	PCR; quantitative real-time PCR
Unknown	*R. montanensis*	ELISA	PCR; quantitative real-time PCR
Ehrlichiosis & Anaplasmosis			
Human Monocytic Ehrlichiosis	*E. chaffeensis*	IFA,	PCR; quantitative real-time PCR
Human Granulocytic Anaplasmosis	*A. phagocytophilum*	ELISA, WB	PCR
Bartonella Group			
Bartonelliosis	*B. bacilliformis*	Under development	PCR
Trench fever	*B. quintana*	IFA	PCR
Borrelia			
Relapsing fever	*B. recurrentis*		PCR; quantitative realtimePCR
Lyme disease	*B. burgdorferi*	commercial assays	PCR

Air Force Institute of Operational Health

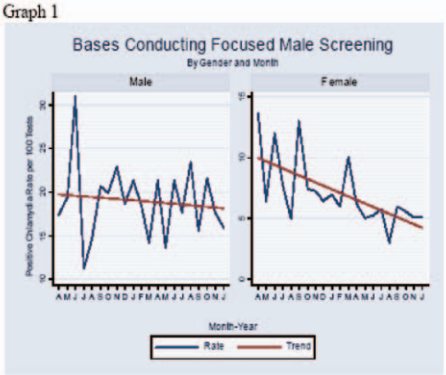
The DoD-GEIS in 2004 supported DoD's premiere influenza surveillance program operated by the Air Force Institute of Operational Health (AFIOH). During the 2003-2004 influenza season (October 2003 to June 2004), 3,693 throat swab specimens were sent to AFIOH yielding 1064 influenza viral isolates (1009 influenza A isolates and 55 influenza B) that were shared with CDC and WHO. This compares with 24,649 isolates reported for this period by WHO so that DoD's influenza program at AFIOH alone represented approximately 3% of the worlds lab capacity that is shared with WHO influenza program Approximately 99% of those were A/H3N2 and the remainder was influenza B/Sichuan influenza B/Hong Kong, and influenza A/H1N2. This program provides respiratory virus surveillance both within the continental U.S. and

overseas, including bases, research facilities in Asia, a region where novel influenza strains have historically emerged, and deployed sites in Central Asia and the Middle East, areas of critical strategic importance. Information from DoD influenza virus sequencing and surveillance is used annually to help determine components for the next year's vaccine.

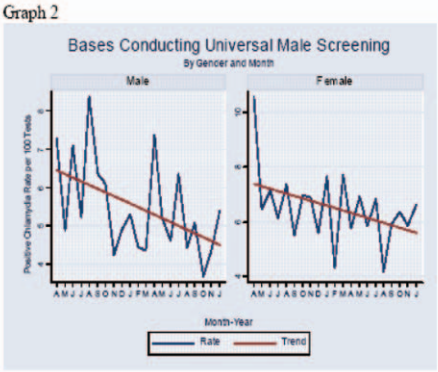
Mosquito surveillance has been conducted at many U.S. Air Force installations in the continental United States, using a variety of traps. During 2004, AFRIOH/RSRH identified a total of over 46,200 mosquitoes from 43 installations, almost all within the known range of WNV in North America, indicating that potential vectors of WNV were present at almost every installation. A total of 3,371 female mosquitoes in 181 pools were screened for WNV and SLE. Emphasis was given to potential vectors collected on 18 installations in the western United States where WNV had only recently appeared. WNV was detected and confirmed in two *Culex tarsalis* pools from Minot AFB, ND. A *Culex quinquefasciatus* pool at Goodfellow AFB, TX, negative by VecTest™ was determined to be positive by RT-PCR. SLE was not detected in any of the pools, and there were no false positives.

During fiscal year 2004, AFIOH began a surveillance project for *Chlamydia trachomatis*. *Chlamydia trachomatis* infections are highly prevalent, often latent, and can produce serious sequelae and a health-care burden. There is general agreement in recommending annual *Chlamydia* screening for sexually active young women, but the evidence for universal screening of men is less clear. The presence of an AFIOH database of *Chlamydia* and gonococcal results allows DoD to investigate this question. Eight of 17 participating bases performed routine *Chlamydia* screening for both sexes. The rest screened young women and only tested young men when clinically indicated. Specimens were tested at a central laboratory for *C. trachomatis* using a commercially available test kit. Analysis on 27,000 urine samples submitted from young men between April 2002 and January 2004 compared bases conducting universal screening with bases conducting focused male screening. Both types of screening showed a substantial decline in positive *Chlamydia* tests for both men and women. Overall rates in women between the two were similar, suggesting that universally screening young men made no difference in *Chlamydia* positive test rates among young women.

Graph 1



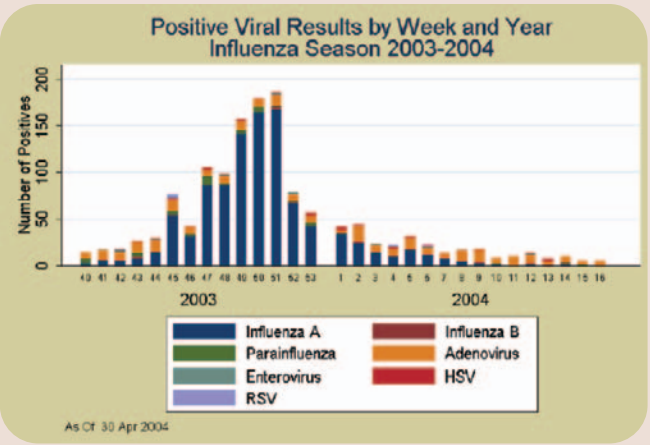
Graph 2



Influenza Outbreak Surge Response

The daily workflow of any clinical program can be stressed during an outbreak. The AFIOH virology laboratory faced this situation in December 2003 when there was an unusually early influenza peak. In that month 1,567 respiratory samples were received, and 40% of those were positive for influenza. The respiratory program has dealt with surges in demand for laboratory testing, but the previous peak was 929 samples received in February 2003.

The December surge served as an example of what would be needed to handle future outbreaks or even a pandemic. A Flu Surge plan was developed by identifying tasks that could be accomplished by lab techs not trained in viral isolation procedures. Individuals from other parts of AFIOH were identified and scheduled to spend a rotation in the virology laboratory to become familiar with those tasks. Competency checklists and safety briefings were updated and documented. Should there be a need, these individuals can be scheduled to work with the virology staff to facilitate timely processing and reporting of specimens. Cooperative arrangements with NHRC were strengthened in case lab capacity is exceeded.



Naval Medical Research Center Detachment: Lima, Peru

The only US Department of Defense overseas medical research unit in the Western Hemisphere, Naval Medical Research Center Detachment (NMRCD) supports the GEIS mission in South and Central America through surveillance of malaria, diarrhea, respiratory infections, and other febrile diseases; development of outbreak early warning systems; outbreak response; and epidemiologic training.

Over the past decade, malaria emerged as a major public health threat in the Amazon Region. Collaborative studies done by the Peruvian Ministry of Health and NMRCD since 1998 demonstrated that *P. falciparum* was no longer sensitive to chloroquine (CQ) and sulfadoxine-pyrimethamine (SP) in parts of the Peruvian Amazon. These studies contributed to Peru becoming the first country in the Americas to adopt combination treatment with artesunate (AS) for uncomplicated *P. falciparum malaria*. NMRCD extended malaria resistance mapping in FY04. An in vivo efficacy trial identified areas in the northwest Peruvian Amazon where *P. falciparum* continues to be sensitive to SP, refining previous resistance maps. NMRCD has leveraged this and other *in vivo* studies to validate molecular predictors of drug resistance. This on-going project, which will expand beyond the Peruvian Amazon, could ultimately contribute to an inexpensive and rapid method of predicting resistance profiles. NMRCD also initiated in FY04 the first assessment of Peru's implementation of combination treatment for uncomplicated *P. facliparum*, providing a critical link between surveillance and public health action. To assess adherence to and acceptability of mefloquine (MQ)-AS and SP-AS combination therapy, NMRCD staff performed 334 observations of health worker-patient interactions, 334 independent patient interviews, and 174 interviews with health workers. The high cost of combination therapies and limited availability of AS were the primary impediments to combination treatment.

Diarrhea surveillance activities in FY04 included a prospective study of acute diarrheal disease (ADD) among 560 Peruvian military recruits at the

Vargas-Guerra (VGE) army base in Iquitos, Peru. Baseline and acute stool samples were evaluated for pathogenic parasites microscopically and by enzyme-linked immunosorbent assay, and for bacterial pathogens by culture, serum agglutination, and polymerase chain reaction. Over 4 weeks of follow-up, 19% of recruits experienced ADD. *Shigella spp*. was the most common identified bacterial pathogen, suggesting opportunities for future *Shigella*-related research in this population. In another study, NMRCD staff conducted active surveillance for ADD in Cuzco, Peru among tourists, whose enteropathogen profile may be similar to what deployed U.S. troops would experience. Of 53 patients with ADD, enterotoxigenic *E. coli* (ETEC), enteroaggregative *E. coli* (EAEC), and *Cryptosporidium* were the most common identified pathogens (27%, 21%, and 12%, respectively, of 33 patients with at least one identified pathogen). Of concern, 3 of 5 *Campylobacter jejuni* isolates were resistant to ciprofloxacin.

NMRCD participates in the U.S. Department of Defense Influenza and Respiratory Virus Surveillance Program (coordinated by AFIOH as described above), and in FY04 identified 778 cases of acute respiratory disease (ARD) at 10 sentinel sites in Peru, Nicaragua, and Ecuador. Analysis at AFIOH identified influenza A as the most frequent etiology (10%). Comparison of current and previous data from specimens obtained by NMRCD with data from Northern Hemisphere specimens showed moderate seasonal correlation of isolate type distribution. This suggests that influenza activity in South America may help predict activity during the following influenza season in North America.

ARD surveillance is partially integrated into a febrile illness surveillance network of 8 sites in Peru, 6 in Bolivia and 3 in Ecuador. FY04 accomplishments include the isolation and description of the American genotype of dengue-2 virus, for which cross-protection from other genotypes of dengue-2 virus is incomplete; isolation of a new sabia-like Arenavirus from a patient with hemorrhagic fever from Bolivia; identification of dengue-3 as the agent responsible for the epidemic of dengue fever and dengue hemorrhagic fever in Tumbes; laboratory confirmation of murine typhus in Tumbes; identification of a new spotted fever group rickettsia in Northern Peru; serological confirmation of spotted fever group rickettsial infections in Yurimaguas and La Merced; confirmation of illness caused by rocio, St. Louis encephalitis, murutucu and caraparu viruses in Iquitos; and isolation of cardiovirus from humans for the first time in Cusco and Iquitos. Expanding beyond sentinel surveillance, NMRCD initiated active, community-based surveillance for dengue in Iquitos as part of a joint project with the NMRCD Entomology Department to evaluate insecticide control of *Aedes aegypti* and dengue.

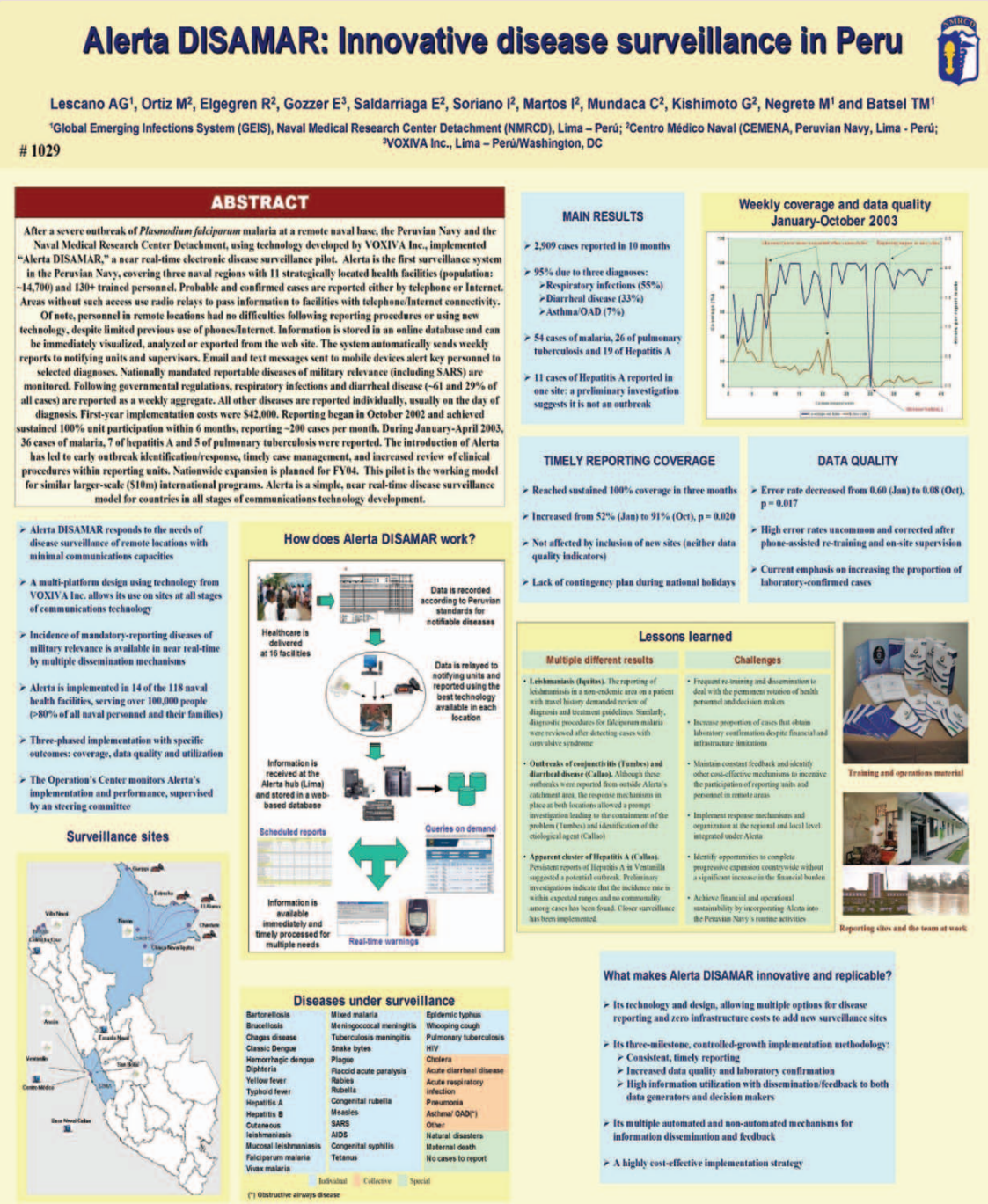
NMRCD continues to develop and operate early warning surveillance systems based on cost-effective strategies affordable in resource-constrained countries. In FY04, efforts focused on timely outbreak detection using Alerta DISAMAR and EWORS. Alerta connects remote Peruvian Naval clinic locations across Peru to a central coordination and analysis hub in Lima using internet, telephone, or radio. It expanded to 8 additional facilities in FY04, covering 80% of Peruvian military personnel, and reported >200 disease events including outbreaks of dengue, malaria, and diarrhea. EWORS is being developed in collaboration with GEIS partners at NAMRU-2 (Jakarta, Indonesia), where it was first implemented. This syndromic surveillance system will provide highly sensitive, real-time detection capacities in minimally-implemented facilities. Two pilot sites are planned for early 2005. The Peruvian Ministry of Health continues to use PHLIS, a laboratory information-based surveillance network developed in collaboration with NMRCD and with SOUTHCOM support which ended in FY03. PHLIS currently covers 70% of Peru's health regions and supports country-level weekly reports, documenting the emergence of Dengue 1 in at Peru's northern border in FY04.

GEIS supported responses to outbreaks of diarrhea, dengue, yellow fever, and leptospirosis during FY04. The leptospirosis outbreak in a village near Iquitos, Peru manifested as a surge in cases of undifferentiated febrile illness at a regional hospital. Using a combination of classical epidemiologic investigation methods and molecular diagnostic techniques, NMRCD staff identified a stream running through the village, where children bathed, as the likely source. Contamination likely had occurred at a pig farm upstream from the village. Following the investigation, NMRCD and regional Ministry of Health officials communicated their findings and recommendation to avoid the stream to community leaders.

NMRCD significantly expanded its outbreak response training program in FY04 to enhance regional

outbreak response capacity with courses for Ministry of Health staff in Peru, Argentina, Chile, and Ecuador. Over 300 participants were trained. The course adapts a CDC model to a developing country setting, where personnel may not have received as much training previously and laboratory capacity often is limited. Host countries have demonstrated support for the course by sharing approximately 60% of the cost.

Alerta DISAMAR poster presented at ASTMH in December 2003



Alerta DISAMAR: Innovative disease surveillance in Peru

Lescano AG[1], Ortiz M[2], Elgegren R[2], Gozzer E[3], Saldarriaga E[2], Soriano I[2], Martos I[2], Mundaca C[2], Kishimoto G[2], Negrete M[1] and Batsel TM[1]

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ABSTRACT

After a severe outbreak of *Plasmodium falciparum* malaria at a remote naval base, the Peruvian Navy and the Naval Medical Research Center Detachment, using technology developed by VOXIVA Inc., implemented "Alerta DISAMAR," a near real-time electronic disease surveillance pilot. Alerta is the first surveillance system in the Peruvian Navy, covering three naval regions with 11 strategically located health facilities (population: ~14,700) and 130+ trained personnel. Probable and confirmed cases are reported either by telephone or Internet. Areas without such access use radio relays to pass information to facilities with telephone/Internet connectivity.

Of note, personnel in remote locations had no difficulties following reporting procedures or using new technology, despite limited previous use of phones/Internet. Information is stored in an online database and can be immediately visualized, analyzed or exported from the web site. The system automatically sends weekly reports to notifying units and supervisors. Email and text messages sent to mobile devices alert key personnel to selected diagnoses. Nationally mandated reportable diseases of military relevance (including SARS) are monitored. Following governmental regulations, respiratory infections and diarrheal disease (~61 and 29% of all cases) are reported as a weekly aggregate. All other diseases are reported individually, usually on the day of diagnosis. First-year implementation costs were $42,000. Reporting began in October 2002 and achieved sustained 100% unit participation within 6 months, reporting ~200 cases per month. During January-April 2003, 36 cases of malaria, 7 of hepatitis A and 5 of pulmonary tuberculosis were reported. The introduction of Alerta has led to early outbreak identification/response, timely case management, and increased review of clinical procedures within reporting units. Nationwide expansion is planned for FY04. This pilot is the working model for similar larger-scale ($10m) international programs. Alerta is a simple, near real-time disease surveillance model for countries in all stages of communications technology development.

- Alerta DISAMAR responds to the needs of disease surveillance of remote locations with minimal communications capacities
- A multi-platform design using technology from VOXIVA Inc. allows its use on sites at all stages of communications technology
- Incidence of mandatory-reporting diseases of military relevance is available in near real-time by multiple dissemination mechanisms
- Alerta is implemented in 14 of the 118 naval health facilities, serving over 100,000 people (>80% of all naval personnel and their families)
- Three-phased implementation with specific outcomes: coverage, data quality and utilization
- The Operation's Center monitors Alerta's implementation and performance, supervised by an steering committee

Surveillance sites

How does Alerta DISAMAR work?

Healthcare is delivered at 16 facilities

Data is recorded according to Peruvian standards for notifiable diseases

Data is relayed to notifying units and reported using the best technology available in each location

Information is received at the Alerta hub (Lima) and stored in a web-based database

Scheduled reports

Queries on demand

Information is available immediately and timely processed for multiple needs

Real-time warnings

Diseases under surveillance

Bartonellosis	Mixed malaria	Epidemic typhus
Brucellosis	Meningococcal meningitis	Whooping cough
Chagas disease	Tuberculosis meningitis	Pulmonary tuberculosis
Classic Dengue	Snake bytes	HIV
Hemorrhagic dengue	Plague	Cholera
Diphteria	Flaccid acute paralysis	Acute diarrheal disease
Yellow fever	Rabies	Acute respiratory infection
Typhoid fever	Rubella	Pneumonia
Hepatitis A	Congenital rubella	Asthma/ OAD(*)
Hepatitis B	Measles	Other
Cutaneous leishmaniasis	SARS	Natural disasters
Mucosal leishmaniasis	AIDS	Maternal death
Falciparum malaria	Congenital syphilis	No cases to report
Vivax malaria	Tetanus	

Individual Collective Special

(*) Obstructive airways disease

MAIN RESULTS

- 2,909 cases reported in 10 months
- 95% due to three diagnoses:
  - Respiratory infections (55%)
  - Diarrheal disease (33%)
  - Asthma/OAD (7%)
- 54 cases of malaria, 26 of pulmonary tuberculosis and 19 of Hepatitis A
- 11 cases of Hepatitis A reported in one site: a preliminary investigation suggests it is not an outbreak

Weekly coverage and data quality January-October 2003

TIMELY REPORTING COVERAGE

- Reached sustained 100% coverage in three months
- Increased from 52% (Jan) to 91% (Oct), p = 0.020
- Not affected by inclusion of new sites (neither data quality indicators)
- Lack of contingency plan during national holidays

DATA QUALITY

- Error rate decreased from 0.60 (Jan) to 0.08 (Oct), p = 0.017
- High error rates uncommon and corrected after phone-assisted re-training and on-site supervision
- Current emphasis on increasing the proportion of laboratory-confirmed cases

Lessons learned

Multiple different results

- **Leishmaniasis (Iquitos).** The reporting of leishmaniasis in a non-endemic area on a patient with travel history demanded review of diagnosis and treatment guidelines. Similarly, diagnostic procedures for falciparum malaria were reviewed after detecting cases with convulsive syndrome
- **Outbreaks of conjunctivitis (Tumbes) and diarrheal disease (Callao).** Although these outbreaks were reported from outside Alerta's catchment area, the response mechanisms in place at both locations allowed a prompt investigation leading to the containment of the problem (Tumbes) and identification of the etiological agent (Callao)
- **Apparent cluster of Hepatitis A (Callao).** Persistent reports of Hepatitis A in Ventanilla suggested a potential outbreak. Preliminary investigations indicate that the incidence rate is within expected ranges and no commonality among cases has been found. Closer surveillance has been implemented.

Challenges

- Frequent re-training and dissemination to deal with the permanent rotation of health personnel and decision makers
- Increase proportion of cases that obtain laboratory confirmation despite financial and infrastructure limitations
- Maintain constant feedback and identify other cost-effective mechanisms to incentive the participation of reporting units and personnel in remote areas
- Implement response mechanisms and organization at the regional and local level integrated under Alerta
- Identify opportunities to complete progressive expansion countrywide without a significant increase in the financial burden
- Achieve financial and operational sustainability by incorporating Alerta into the Peruvian Navy's routine activities

Training and operations material

Reporting sites and the team at work

What makes Alerta DISAMAR innovative and replicable?

- Its technology and design, allowing multiple options for disease reporting and zero infrastructure costs to add new surveillance sites
- Its three-milestone, controlled-growth implementation methodology:
  - Consistent, timely reporting
  - Increased data quality and laboratory confirmation
  - High information utilization with dissemination/feedback to both data generators and decision makers
- Its multiple automated and non-automated mechanisms for information dissemination and feedback
- A highly cost-effective implementation strategy

Naval Medical Research Unit—2: Jakarta, Indonesia

Naval Medical Research Unit –2 (NAMRU-2) is an overseas research laboratory in Jakarta, Indonesia with projects in Southeast Asia and the Pacific Islands. The lab is recognized as a World Health Organization Collaborating Center for Emerging and Re-emerging Diseases.

In addition to its BSL2+ laboratory, insectory, and animal facility in Jakarta, NAMRU-2 also supports a satellite laboratory in Phnom Penh, Cambodia in collaboration with the Cambodian National Institute of Public Health. NAMRU-2 supports the GEIS mission through four programs: Emerging Diseases, Enteric Diseases, Parasitic Diseases, and Virology.

Timely and reliable surveillance data and investigative capabilities are the cornerstones of an effective public health outbreak response system. GEIS-funded projects at NAMRU-2 have been on the forefront in characterizing and mitigating regional infectious disease threats and assisting developing countries to build effective outbreak surveillance, investigative, and diagnostic infrastructures. NAMRU-2 has fostered an extensive network of collaborative relationships throughout the region.

FY 2004 was marked by significant regional public health challenges. Dengue fever killed at least 600 people in Indonesia in just a few months. Avian influenza swept across Southeast Asia just one year after the SARS epidemic, demonstrating to the inadequacy of many countries public health policies and outbreak response infrastructures. While malaria rates in Indonesia have fallen in some areas, epidemic transmission in other areas has continued to challenge containment efforts.

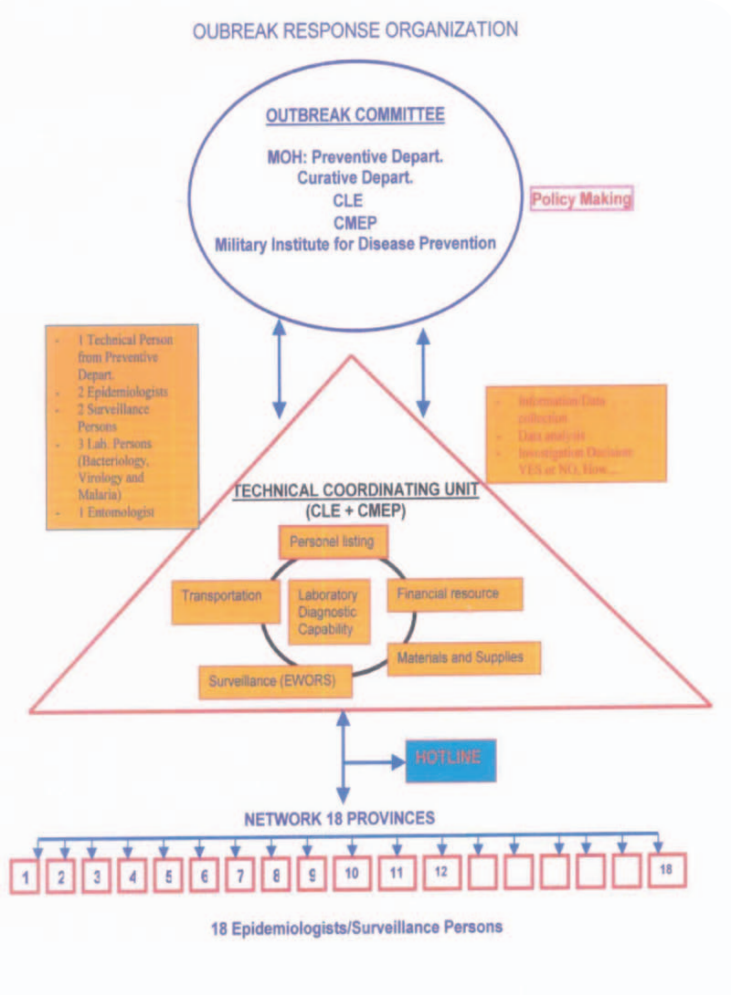
Media attention has highlighted the problem of epidemic disease spread; in response NAMRU-2 was able to bolster diagnostic and epidemiological capabilities at local, national and regional levels. NAMRU-2 also helped develop new surveillance strategies, such as the novel syndromic surveillance initiative Early Warning Outbreak Recognition System (EWORS). Other NAMRU-2 projects in FY04 included: 1) *Plasmodium vivax* antimalarial resistance rapid screening initiative; 2) surveillance studies to characterize the epidemiology, including molecular and resistance patterns, of infectious disease threats and their vectors; and 3) capacity building measures that include guidance and training to develop effective outbreak response infrastructures, outbreak response training workshops, and disease-specific laboratory diagnostic courses accompanied by technology transfer.

The innovative syndromic surveillance system, EWORS (version 3.5) began its first year integrated into newly organized central government outbreak investigation committees in Cambodia, Laos and Vietnam and was effective in triggering timely, targeted, and effective outbreak responses. EWORS has been successfully accepted as a local regional initiative. This plays to the strengths of NAMRU-2's strategic positioning in Jakarta, with collaborative host-country satellite surveillance platforms throughout Southeast Asia.

NAMRU-2 continued its comprehensive influenza surveillance project in Indonesia, providing useful prevalence data and temporal, genotype data of circulating strains. Indeed, the success of this initiative has prompted formal funded collaborations between the CDC and NAMRU-2 in FY05 and FY06 that effectively increased DoD-GEIS capacity support of NAMRU-2 by 37%. This new relationship with CDC is tangible evidence of the value CDC places on DoD-GEIS supported capacities at NAMRU-2.

Malariometric surveys, antimalarial surveillance, and vector surveillance in Indonesia provided the Ministry of Health with valuable data to evaluate existing antimalarial treatment strategies and vector control strategies in endemic areas, and provided researchers with a new understanding of how antimalarial resistance occurs and spreads in *P. vivax*. Investigations into molecular markers of antimalarial resistance in *Plasmodium vivax* to define location-specific chloroquine (CQ)-resistance patterns provided insights that may be used to identify molecular epidemiological tools for rapidly defining location-specific resistance patterns.

In FY04, NAMRU-2 provided investigative support and intervention guidance in the many instances of outbreak crisis that have plagued the region. NAMRU-2 mobilized epidemiologic and diagnostic resources to assist host-national surveillance, investigative, and intervention efforts, including those recognized as contributing to the successful containment of the SARS epidemic by Vietnamese officials. NAMRU-2 is currently engaged collaboratively in preparing the region through training, equipping, and monitoring, to survive an anticipated avian influenza epidemic. NAMRU-2 provides direct epidemiological and diagnostic support in assisting the Indonesian Ministry of Health to devise effective vector control programs and public education campaigns. NAMRU-2 has contributed to national efforts in providing clinical, epidemiological, entomological and diagnostic assistance for malaria outbreaks like that which occurred in Sukabumi, West Java (Indonesia), along with follow-up surveillance to assess control efforts.



This example from Laos, details the organization created to facilitate efficient outbreak investigations and interventions

Even as the WHO makes pessimistic predictions of a new influenza pandemic, NAMRU-2 supported the development of outbreak and diagnostic infrastructure in countries with inadequate healthcare and monitoring systems to support outbreak surveillance and response. NAMRU-2 has played a critical regional role in capacity building programs that have trained over 400 participants from six nations in outbreak response, microscopy, and laboratory training for influenza (e.g., H5N1), dengue, Chikungunya virus, malaria, and filariasis. NAMRU-2 also provided training in specific and advanced technologies, including PCR. NAMRU-2 designed and developed new standardized malaria diagnostic sets for the education and training of diagnosticians to improve the sensitivity of blood smears worldwide.

NAMRU-2 also provided advice to host country governmental agencies. In Indochina NAMRU-2 facilitated the reorganization of predominantly decentralized outbreak response structures towards more effective, multidisciplinary, centrally directed ones. NAMRU-2 provided advice to local and host country government agencies on devising new anti-malarial treatment and malaria control strategies.

NAMRU-2 continues to provide direct support for military operations. In response to a suspicious cluster of pneumonia cases at USNH Yokosuka, Japan, including one fatality, NAMRU-2 provided diagnostic support, and helped to rule out H5N1 and SARS as diagnostic etiology in partnership with NHRC and AFIP. In partnership with NAMRU-3, NAMRU-2 contributed to Iraq operations in assessing the impact of diarrheal disease occurrence. This study resulted in changes to treatment recommendations that would reduce morbidity and maximize troop readiness.

Naval Medical Research Unit—3: Cairo, Egypt

The five elements of the GEIS program at U.S. Naval Medical Research—3 (NAMRU-3) are: 1) Enhanced surveillance for priority infectious diseases in Egypt, 2) Regional syndrome-based surveillance for selected diseases, including influenza, in the Middle Eastern, African, Eastern European, and Western Asian regions, 3) Surveillance for emerging infectious diseases in military populations, 4) Strengthening surveillance and response to regional disease outbreaks, and 5) Archiving of selected specimens and their associated laboratory and epidemiologic data.

The NAMRU-3 influenza surveillance program provides the only source of information on circulating strains of virus in 6 nations (Kazakhstan, Ukraine, Syria, Egypt, Saudi Arabia, and Oman) in a region of >500 million people and intense U.S. military involvement. In recognition of the sustained excellence of this program, in FY04 NAMRU-3 was designated as the WHO influenza reference laboratory for the Eastern Mediterranean Regional Office (EMRO). Over 4,730 samples were collected from patients with acute febrile respiratory illness during FY04, thus far yielding 348 influenza isolates and 449 other viral isolates which are pending full identification. During FY04, effort was made to expand influenza surveillance regionally by initiating new partnerships in Kenya (USAMRU-K, CDC, and Kenya Medical Research Institute [KEMRI]), Kyrgyzstan, Pakistan, and Ghana (Noguchi Institute). NAMRU-3's partnership with Saudi Arabia was of single importance in sampling international Hajj pilgrims during April, 2004, netting >400 samples from 26 different nationalities and yielding 58 viral isolates. GEIS supported surveillance of birds as carriers of potentially dangerous strains of influenza in Egypt's Nile Valle, a concentrating point for migratory birds. In this first year of study, 1,020 migratory birds were sampled, representing 21 bird species. More than 11% of the birds, mainly ducks, were influenza A positive by PCR, and 10 different subtypes have been identified, indicating broad host and geographic sources. The Kenya influenza surveillance initiative will sample from both migratory waterfowl and commercial poultry in collaboration with the Kenya National Museum and the International Livestock Research Institute. The NAMRU-3 influenza surveillance program provides isolates and data to CDC and WHO for annual upgrade and modification of each year's influenza vaccines.

FY04 saw the strongest ever GEIS-funded direct operational support by NAMRU-3 to deployed U.S. military forces in the Middle East. The Military Surveillance Network, initiated during 2004, was designed to support field commands in addressing the threat of enteric disease among the >140,000 US troops deployed to Afghanistan, Iraq, and support locations in the CENTCOM and EUCOM regions. These studies have taken the form of 1) Mid- and post-deployment questionnaire-based surveys (Incirlik, Turkey; Rhein-Main, Germany; As Sayliyah, Qatar), 2) Case-control studies (Camp As Sayliyah, Qatar), 3) Cross-sectional surveys (Al Asad Air Base, Anbar Province, Iraq), 4) Military provider knowledge, attitude, and practice surveys (As Sayliyah, Qatar, 5) Cohort studies (Multinational Forces and Observers [MFO] peacekeeping force, Sinai, Egypt; and Incirlik Air Base, Turkey), and 6) Randomized, double-blinded treatment trial (azithromycin vs. levofloxacin; Incirlik Air Base, Turkey).

Mid- and post-deployment survey of >3000 troops revealed that diarrhea occurred during Afghanistan or Iraq deployment in 76% of respondents. More than one half reported multiple episodes, 62% sought medical care, and 45% reported job/duty impairment. Estimated clinic burden due to diarrhea was 13 clinic visits/100 person-months and manpower loss per month was estimated to be almost 4 duty-days per 100 person-months. In a large post-deployment health survey of American troops, NAMRU-3 employed a novel design and analysis to survey >15,000 Operation Iraqi Freedom (OIF) personnel to identify seasonal disease trends. Among the 10% reporting utilization of health care resources for any reason during deployment, >25% received IV hydration. Diarrhea was the most commonly reported illness (75%), prompting clinic

visits in 48% of cases, while respiratory illness, although the second most common health complaint (69%), prompted health care visits in only 17%.

Although diarrhea was acknowledged by medical providers to be the most common ailment in theater requiring medical care, only 14% knew that enteric bacteria were usually responsible and fewer than half reported using combination quinolone + loperamide treatment for diarrhea. NAMRU-3 equipped and staffed fully functional microbiology laboratories complete with real-time PCR pathogen detection at military air bases in Iraq (Al Asad) in collaboration with NAMRU-2, and Incirlik (Turkey), and established enrollment and collection facilities at US military facilities in Qatar and Sinai. In both peacekeeping (Sinai [MFO]) and battleground (Iraq) deployments in the CENTCOM region, pathogenic *E. coli* (enterotoxigenic [ETEC] and enteroaggregative [EAEC], primarily) was identified as the primary cause of diarrhea and was associated with an average 4.6 days of illness and duty downtime. Against a theater-wide medical policy of withholding diarrhea treatment for at least 3 days, NAMRU-3 advised CENTCOM medical authorities to treat early with single dose quinolone + loperamide on the basis of previously demonstrated effectiveness for ETEC. Within 30 days of conclusion of the study, this advisement was adopted by the Force Surgeon as standard treatment policy for the entire theater. Enrollment in NAMRU-3's azithromycin vs. levofloxacin treatment trial has ended (n=220), and data is being analyzed. Antimicrobial sensitivity testing of ETEC at Incirlik, Turkey, suggests that long-term exposure or accumulative flouroquinolone usage in such a closed population may increase resistance to these medications.

Enteric studies in civilian populations in FY04 included surveillance of severe diarrhea among young children living in urban slum and rural village in Egypt. In both populations, ETEC, rotavirus, and Campylobacter comprised the majority of etiologies with the majority of cases occurring under the age of 12 months. High levels of flouroquinolone resistance to *Campylobacter* were seen in both urban and rural sites.

To enhance surveillance for priority infections in Egypt, NAMRU-3 developed a surveillance network of infectious disease hospitals in 1998 in partnership with the Egyptian Ministry of Health. The network currently includes 7 hospitals and focuses on acute febrile illness, meningitis, diarrhea, and hepatitis. In FY04, antibiotic susceptibility testing yielded clinically relevant information on resistance patterns. For example, blood culture of *Staphylococcus aureus* from acute febrile illness patients demonstrated methicillin resistance in >11%, and forty-six percent of *Streptococcus pneumoniae* isolates from meningitis patients demonstrated poor susceptibility to penicillin, tetracycline, and trimethoprim-sulfamethoxazole.

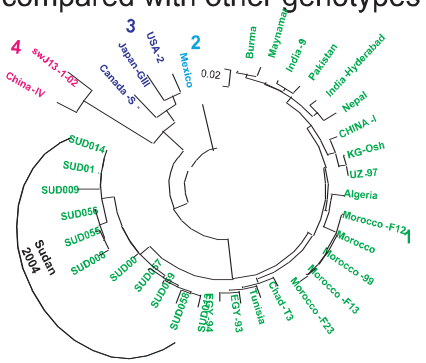
For over 45 years, NAMRU-3 has enjoyed a strong medical research partnership with the Sudanese Ministry of Health despite strained international relations with the current Sudanese Government. WHO called upon NAMRU-3 in September 2004 to assist in diagnosis of severe illness occurring among Darfur refugees. NAMRU-3 identified Hepatitis E Virus (HEV) as the dominant pathogen in Darfur refugees with acute febrile illness, and also identified two cases of Congo Crimean Hemorrhagic Fever. Soon thereafter, NAMRU-3 mobilized personnel, equipment, and supplies to establish serological capability in Sudan, and is currently working to bring appropriate epidemiological expertise onto the scene. Also in Sudan, a new hospital laboratory-based study was begun of meningitis etiology and antimicrobial resistance profiles. Over time, it is hoped that this project will evolve into a surveillance network for epidemic-prone diseases following the same plan as implemented and maintained in Egypt. Thus far, 5 hospitals in the Khartoum and Om Durman regions have received training in surveillance methods, clinical microbiology, and good laboratory practices, and quality control.

As a WHO collaborating center, NAMRU-3 will support training and development of laboratory-based surveillance throughout the EMRO region. In FY04, laboratory-based disease surveillance was introduced into Yemen and Pakistan, and plans were developed for expansion to Morocco, Jordan, Lebanon, and Iran.

Isolation of Hepatitis E Virus (HEV) from cases of Acute Jaundice Syndrome from Refugee Camps in Darfur, Sudan – Darwish M, Earhart KC

Background: HEV is an unclassified non-enveloped single stranded RNA virus that was first identified in 1980. It causes epidemic and sporadic acute viral hepatitis in many developing countries worldwide and has been identified globally. It is usually transmitted through faecally contaminated water, with humans as the natural host, however zoonotic spread is also suspected. It is a disease of young adults, self-limited with low mortality however can result in fulminant hepatitis and characteristically affects pregnant women with a mortality of 20% or more during the third trimester of pregnancy. Frequent reports on Epidemic and Sporadic hepatitis outbreaks in Sudan date back to the 1920s. The CDC reported a large outbreak of what was presumed to be hepatitis E in refugee camps in Eastern Sudan in 1985. Hepatitis E was subsequently documented in Sudan in 1987 and was responsible for an outbreak of hepatitis in August 1988 associated with severe flooding. In late May 2004 an outbreak of acute jaundice syndrome was noted in displaced persons in the Darfur region. In late June, similar reports were made from the camps in neighboring Chad. Onset coincided with onset of the rainy season. Of interest, there was also a report in June 2004 of hepatitis E in the neighboring Central African Republic as well. From 22 May - 17 Sep 2004, a total of 6861 cases and 87 deaths of suspected hepatitis E were reported from Greater Darfur region, Sudan through the early warning alert and response system (EWARN). The greatest number of cases was apparently from West Darfur.

NJ Tree for Sudan strains compared with other genotypes



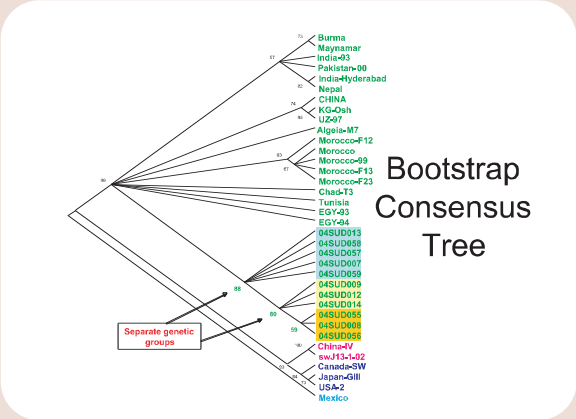
Methods: Samples were collected by WHO staff from patients identified with acute jaundice syndrome in three camps located in El Geneina and Habilla regions, which are located here in West Darfur. Serum was obtained from a total of 53 individuals, placed into a liquid nitrogen dry shipper supplied by NAMRU-3, and made available for testing. Basic clinical and demographic information was only available on 48 patients. Laboratory testing was conducted using serologic and molecular techniques at NAMRU-3. First, testing focused on ruling out yellow fever through a flavivirus screen and ruling in hepatitis E, which was suspected, through IgG assay.

Results: The age of patients ranged between 3 and 70 years old, with a mean and median of 25 years. Samples were obtained from 38 women and 10 men. 11 of the 38 women were pregnant. Samples were obtained during case finding and selected at the discretion of local WHO staff. One death occurred in a woman in her third trimester of pregnancy who had PCR confirmed HEV. All samples screened negative for flavivirus. IgG for HEV was detected in over 40% of the samples, and confirmed for HEV using a nested PCR. Ninety percent of PCR positive samples had a high EIA index above 5.7. Subsequent testing for Hepatitis A virus, which can occur concomitantly with HEV, revealed two additional cases IgM positive for Hepatitis A. Leptospirosis is highly endemic in Sudan, however no samples tested positive for leptospirosis. Sampling was likely of differing quality, as all samples with detectable virus by PCR originated from one camp in Geneina. We subsequently received another set of samples that were collected in September and early October 2004. An additional 134 samples were collected and tested. Of these, almost 70% tested positive by IgG for HEV, and again, many confirmed by PCR. None have been sequenced yet. Once again, testing for Hepatitis A IgM showed no serologic evidence of acute Hepatitis A infection among the patients with acute jaundice syndrome.

HEV genome: The PCR product which was used for sequencing and phylogenetic analysis was a 310 base pair section that covers the junction of the 3 open reading frames. Phylogenetic analysis, as shown in the neighbor joining tree, demonstrated that all of

the Sudan isolates clustered with the endemic countries as genotype 1. It also shows that they cluster together as a unique group, separate from other known isolates. The boot strap consensus tree suggests that not only are the Sudan isolates a unique cluster with a bootstrap support value greater than 85%, but among the Sudan isolates there are two distinct subgroups within this cluster.

Conclusions: The epidemiological and clinical picture suggested HEV as an etiology of the acute hepatitis outbreak in 2004 occurring in Darfur. Laboratory diagnosis confirmed that HEV is at least in part responsible for the hepatitis outbreak. Poor hygienic and sanitary conditions including contaminated water sources are believed to be responsible for the outbreak. Strains of HEV recovered from within one geographic location within a country generally are genetically similar and characteristic of that area and differ from strains indigenous to other locations and countries. NAMRU-3 derived sequence data indicates that HEV strains from this outbreak are distinct from viruses characterized during other outbreaks and from other geographic



regions. The viruses identified thus far in Western Sudan suggest that they are indigenous to Sudan, and that this outbreak did not originate elsewhere. In addition the data suggests that there are a variety of indigenous strains within Sudan, and that this outbreak is likely complex. The outbreak response by NAMRU-3 participating as WHO collaborating center helped to inform DoD medical leadership about important regional medical events and contribute in an important way to global health.

Armed Forces Research Institute of Medical Sciences: Bangkok, Thailand

The GEIS program at The Armed Forces Research Institute of Medical Sciences (AFRIMS) monitors and prevents infectious disease emergence in Southeast Asia, a region of critical importance to global health. In FY04, AFRIMS conducted important surveillance of malaria prevalence and drug resistance in Cambodia, where malaria is a leading health problem with an estimated annual incidence of 1026/100,000 and a population mortality rate of 3.7/100,000. AFRIMS is partnering with the Cambodian National Malaria Center and NGOs on a five year effort to reduce malaria morbidity involving prevalence, risk factor, and health care infrastructure assessment. Investigators, research technologists, and expert microscopists have developed a comprehensive training plan to introduce novices to the fundamentals of malaria blood film reading. An AFRIMS expert developed reference slide sets to train and test Cambodian microscopists.

The application of remote-sensing based geographic information systems to predict malaria transmission risks in North-Western Thailand has been explored. Malaria transmission is associated with location since it is typically related to specific mosquito breeding sites. There is clustering of people with malaria infections at particular locations. Information on the distribution of malaria can permit controls to be targeted towards the foci of transmission. The mapping of locations using GIS should improve control measures though more accurate targeting.

AFRIMS is also involved in an emerging disease surveillance system along the Thai borders. The potential for outbreaks is higher at the borders; therefore, collecting information on the syndrome of illness in those regions could signal early signs of an outbreak. GEIS sought to leverage the existing health-care resources along the Burmese, and Cambodian

borders and create a communications network to relay the syndrome information to AFRIMS for analysis. This network of communication has proven effective and an outbreak response team has been created. The surveillance has clearly identified clusters of febrile illness as the most common syndrome and malaria the most common diagnosis for febrile diseases.

Febrile illness surveillance has been conducted at AFRIMS-Kwai River Christian Hospital (KRCH) Clinical Center on the Thai-Myanmar border since 1999. The objectives have been to provide a greater knowledge of the causes of febrile illness; in particular, what zoonotic and vector-borne emerging infectious diseases might be prevalent at this sentinel site, and to evaluate prototype test kits for diagnosis of arthropod-borne and zoonotic diseases. Adults presenting with fever are enrolled and blood samples are obtained at baseline and after three weeks. Diagnosis is made through a combination of culture, serologic, and molecular laboratory techniques, as well as clinical data. Rapid diagnostics tests are then evaluated through comparison with reference laboratory results. To date, a total of 1,113 cases have been enrolled. Major findings include a high incidence of leptospirosis, identification of a broad spectrum of febrile illness, and identification of a high frequency of co-infection, particularly of malaria and leptospirosis.

In a joint effort with the Ministries of Public Health and Livestock Development a zoonotic illness surveillance system is being developed in Thailand. Current case-reporting and sharing of information requires a paper-based system, using either fax machines or the postal system. The recent outbreak of avian influenza in the region highlights the need for rapid, secure information sharing capabilities both within and between involved ministries. AFRIMS-GEIS has funded the development and piloting of a secure internet-based system for case reporting of zoonotic illnesses in Thailand. Illnesses reported through this system by both medical doctors and veterinarians are anthrax, rabies, and leptospirosis. This system has been deployed to two provinces.

Antimicrobial resistance among enteric pathogens in developing countries is of critical public health concern. Much of the emerging antibiotic resistance observed today, such as fluoroquinolone-resistant *Campylobacter*, is thought to originate in Southeast Asia. The region's extraordinary population density, proximity to domestic animals by much of the population, and marginal infrastructure provides ample opportunities for genetic information transfer between microorganisms. The long term goal of AFRIMS and GEIS is to determine regional diarrhea etiology (pathogens and risk factors) and drug resistance patterns. This data will be crucial to guiding antimicrobial use for treatment and prevention of disease. To date, 725 cases and 444 controls have been tested. *Campylobacter spp*. and *Salmonella spp*. are the principle pathogens from Bangkok, while these plus *Aeromonas* spp. comprise the majority of isolates from other regions.

To further expand enteric disease surveillance throughout Southeast Asia, site visits, collaborator coordination visits, staff training, and infrastructure development projects were undertaken in Thailand, Cambodia, Maldives, and Nepal in FY04. These projects form the cornerstone of the Department of Enterics projects to provide timely and accurate surveillance and antimicrobial resistance data for the SE Asian region. As a result of substantial new laboratory infrastructure and training in Cambodia and Maldives, the National Pediatric Hospital in Phnom Penh, Cambodia and the regional hospital in Male, Maldives are now prepared to begin patient enrollments into enteric surveillance and antimicrobial resistance studies during FY 2005-06.

An epidemic of highly pathogenic avian influenza is spreading through domestic poultry and other birds in Asia. Human cases with a high fatality rate have been reported in Vietnam and Thailand. AFRIMS has established sentinel sites for surveillance of influenza in Nepal and Thailand in areas not otherwise covered by the WHO Global Influenza Surveillance Network. Samples are collected from patients with suspected influenza and shipped to AFIOH for isolation, typing and subtyping. Selected isolates are forwarded to CDC for further characterization and vaccine component determinations.

In July 2004, AFRIMS responded to an outbreak of febrile respiratory illness among refugees in Nepal. Testing by AFIOH confirmed influenza A/H3N2 in 42/62 samples. Molecular sequencing revealed that these were closely related to the Wellington strain, which had also caused outbreaks in Europe earlier in 2004. These findings influenced the WHO's recommendation that the 2005 Southern Hemisphere vaccine include a Wellington-like strain.

Early Season Influenza A H3N2 Outbreak in Southeast Nepal

In July 2004, the Walter Reed-AFRIMS Research Unit Nepal detected an outbreak of influenza A (H3N2) at three Bhutanese refugee camps located in southeastern Nepal. Sixty-four patients were evaluated by the team of investigators and throat swabs were obtained. Basic case histories were taken with symptoms and presence or absence of fever at the time of specimen collection. Specimens were both tested by rapid flu test kit (OIA Flu Rapid Diagnostic®, Thermo-Electron) and submitted to the Air Force Institute for Operational Health (AFIOH) for definitive culture and PCR analysis. Sixty-one (61) of the persons involved in the outbreak were refugees from Bhutan, but the patients also included 1 foreign aid worker from Japan, and 2 Nepalese nationals. The majority of patients were under the age of 10 (38, 59%), and about equal genders (F: 28, 44%; M: 36, 56%). None of the patients had been vaccinated against influenza. Of the 64 specimens collected, 42 (65%) tested positive for influenza A by culture. Clinical criteria of fever plus either cough or sore throat were relatively sensitive for influenza (83%), but not specific (13%). Rapid influenza testing on location during the outbreak showed relatively low sensitivity (36%) but good specificity (95%). Combining clinical criteria with rapid influenza testing improves the sensitivity to 40%, with no change in specificity (95%). Molecular subtyping using RT-PCR revealed all 42 specimens were H3N2 subtype, but showed some changes in several regions that were different from most of the specimens collected by the WHO in the 2003-2004 seasons. This outbreak shows the value of continued influenza surveillance even during the off-peak influenza season.

Figure 1

Figure 1. Unrooted phylogenetic analysis of HA1 hemagglutinin proteins from 25 Nepal isolates and H3 vaccine strains. The Nepal isolates have drifted from the 2004/05 A/Fujian/411/03 vaccine strain (and A/Wyoming/03/03 vaccine seed strain) and are more genetically related to A/Wellington/1/04, the new 2004/05 southern hemisphere H3 vaccine strain. A K145N substitution (branch point indicated) was observed in 25/27 Nepal isolates and represents a genetic marker for a growing lineage of H3N2 viruses since the 2003/04

U.S. Army Medical Research Unit–Kenya: Nairobi, Kenya

GEIS activities at the US Army Medical Research Unit-Kenya (USAMRU-K) are centered on a developing infectious disease surveillance network. Hospitals are selected in each province of Kenya to serve as infectious disease surveillance sites. Additionally, a site is operated in southern Uganda. Each site is then provided with the infrastructure and personnel support required to perform case identification, sample collection, sample processing, and secure record maintenance. The staffs at these sites are trained in outbreak identification and control techniques and in infection control measures.

Using the established 6-site infectious disease surveillance network in Kenya, all patients with suspected hemorrhagic fever and ten patients per site per week with fevers of unknown etiology have serum tested for viral hemorrhagic fevers, other arborviruses including dengue, rickettsia, hepatitis, malaria, and leptospirosis. A total of 255 samples have been processed. Six acute cases of West Nile Virus illness were detected. Exposure history to dengue was found in 11% of those tested from Alupe and 38% from Malindi. USAMRU-K cooperatively responded to outbreaks of febrile illnesses due to leptospirosis at a boarding school, as well as malaria and o'nyong-nyong virus, assisting the Kenyan Ministry of Health.

The Department of Enterics maintains the capability to do both standard microbiologic determination of bacterial pathogens and antimicrobial sensitivity. This capability is enhanced by the ability to do molecular characterization of numerous pathogens and parasitologic diagnosis through collaborative arrangements. Integration with other projects in USAMRU-K's surveillance network will facilitate collection of stool samples on up to 200 subjects per year from each of five surveillance sites across Kenya. These samples will be tested for susceptibility against commonly used antimicrobials and will be molecularly characterized for a variety of pathogenic characteristics.

The increased population mobility arising from the migration from rural to urban centers has not only contributed to the development of slum areas but also the introduction of malaria into new areas. Two clinical studies conducted in Nairobi suggests that previously unrecorded malaria transmission could be

occurring in Kibera, a sprawling slum estate in Nairobi. Between 2001 and 2003, intensive mosquito surveillance was conducted in Kibera.

Day resting indoor collections were made daily in 120 randomly selected and GPS mapped houses using mouth aspirators. CS ELISA and PCR techniques were used to test *P. falciparum* infection. Concurrently, mosquito larvae were collected from polluted water along the only stream passing through the study area. Eight-four An. *Gambiae s.l.* mosquitoes were identified by PCR as *An. Arabiensis* (98%), and as *An. Gambiae s.s.* (2%) Human Blood Index was 0.97. *Plasmodium falciparum* infection rate was 2.5%.

Active surveillance was performed for epidemiology and drug sensitivity of malaria in Kenya using five of the surveillance sites in the surveillance network. Each site provides up to five samples per day. Results are reported to the National Malaria Control Program. This is the only national in vitro antimalarial surveillance activity in Kenya, and had significant impact on the Ministry of Health's decision to change recommended treatment of malaria in Kenya from sulfadoxine-pyrimethamine (SP) to the artemisinin derivative combination CoArtem. Demonstration of significant mefloquine resistance could impact prophylaxis recommendations, particularly for deployed forces. Geographical expansion and *in vivo* antimalarial testing is planned for the near future.

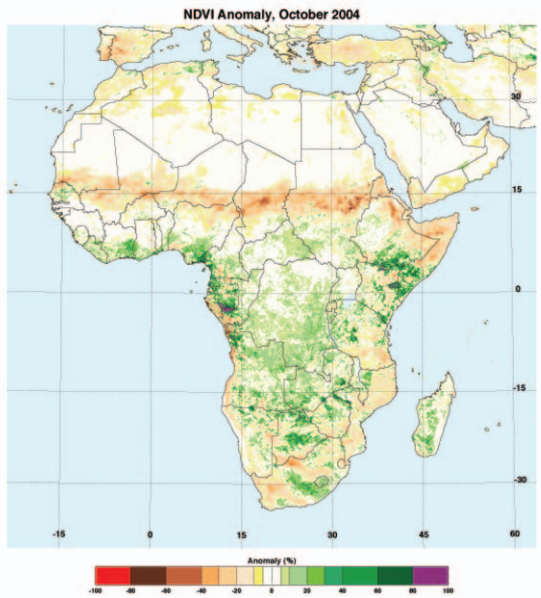
USAMRU-K also embarked on a survey of arboviral illnesses and surrogate markers for exposure in East Africa. This survey examined the socioeconomic factors as determinants of exposure to infectious diseases, particularly arboviral illnesses. The goal is to develop a model for estimating disease risks in the absence of specific health data from a region. Upon completion this project will provide the Ministry of Health with much more complete health-risk information. It will also be available to medical planners in the U.S. military for threat assessment.

In an ongoing collaborative study with the Rakai Project and the Henry M. Jackson Foundation, febrile illness surveillance was conducted in Uganda using the established surveillance network site in the Rakai District. Laboratory support for this activity includes *in vitro* antimalarial susceptibility testing on samples with malaria parasitemia and analysis for other pathogens including arboviruses in collaboration with the WHO Regional Arbovirus Reference Laboratory.

National Aeronautical Space Administration

In collaboration with the National Aeronautical Space Administration (NASA) at the Goddard Space Flight Center (GSFC), DoD-GEIS continues utilization of remotely sensed satellite data to monitor and forecast Rift Valley fever and other vector-borne disease outbreaks.

The purpose of this project is to provide detailed analyses of satellite vegetation data for Africa and related satellite derived global climate data sets (including sea surface temperatures and outgoing long wave radiation and rainfall (where available)) to support DoD-GEIS monitoring of the ecological dynamics and climate anomalies associated with Rift Valley fever outbreaks in Africa and the Saudi Arabian Peninsula. In addition, the analyses of global climate data will support other DoD-GEIS vector-borne disease monitoring activities elsewhere.



Normalized Difference Vegetation Index (NDVI) anomaly for Africa, showing above normal vegetation conditions in parts of East Africa in October 2004 where RVF epidemics occurred during October 1997 – April 1998.

The GSFC produces monthly vegetation anomalies for Africa and the Saudi Arabian Peninsula and global Sea Surface Temperature (SST) and Outgoing Long wave Radiation (anomalies) to assist in identifying regions of anomalous climatic conditions that may lead to an increase in RVF outbreak risk. Identification and mapping of risk areas involves tracking and computation of a persistence index of above normal vegetation conditions, associated with above normal rainfall, in RVF endemic regions.

Time series satellite data was provided for six surveillance sites maintained by USAMRU-K for characterization of eco-climatic dynamics. Monthly electronic reports on RVF monitoring are also provided to WHO in support of continental efforts to monitor and suppress RVF activity.

Collaborators used the satellite information products in surveillance of RVF activity and to emphasize mosquito control measures where needed. Project staff has on various occasions during FY04 been invited to provide expert support to other programs and institutions interested in the use of remote sensed data in vector-borne disease surveillance.

Acronyms

ADD	Acute Diarrheal Disease
AFEB	Armed Forces Epidemiological Board
AFI	Acute Febrile Illness
AFIOH	Air Force Institute for Operational Health
AFIP	Armed Forces Institute of Pathology
AFRIMS	Armed Forces Research Institute for Medical Science
AMSA	Army Medical Surveillance Activity
APEC	Asia Pacific Economic Cooperation
AR	Antibiotic Resistance
AS	Sodium Artesunate
ASTMH	American Society of Tropical Medicine & Hygiene
BDU	Battle Dress Uniform
BSL	Bio Safety Level
CCHF	Crimean-Congo Hemorrhagic Fever
CDC	Centers for Disease Control and Prevention
CENTCOM	Central Command
CHCS	Composite Health Care System
CHPPM	Center for Health Promotion and Preventive Medicine
CHPPM-W	Center for Health Promotion and Preventive Medicine – West
CoCOM	Combatant Commanders
CoV	Coronavirus
CQ	Chloroquine

DHFR	Dihydopteroate Reductase
DHPS	Dihydopteroate Synthage
DMZ	Demilitarized Zone
DNBI	Disease and Non-Battle Injury
DoD	Department of Defense
DoE	Department of Energy
EAEC	Enteroaggregative *E. coli*
ECL	Electro-Chemoluminescence
ELR	Electronic Laboratory Reporting
EMRO	Eastern Mediterranean Regional Office
EPICOM	Epidemiological Consultation
EPI-X	Epidemic Information Exchange
ESSENCE	Electronic Surveillance System for the Early Notification of Community-Based Epidemics
ET	Experimental Therapeutics
ETEC	enterotoxigenic *Escherichia coli*
EUCOM	European Command
EWORS	Early Warning Outbreak Recognition System
FDPMU-E	Forward Deployed Preventive Medicine Unit
FRI	Febrile Respiratory Illness
FY	Fiscal year
GAS	Group A Strep
GEIS	Global Emerging Infections System
GIS	Geographic Information System
GLP	Good Laboratory Practices

GOARN	Global Outbreak Alert and Response Network
GPS	Global Positioning System
GSFC	Goddard Space Flight Center
HA	Health Affairs
HEV	Hepatitis E Virus
HHS	Health and Human Services
HMPV	Human Metapneumovirus
ICU	Intensive Care Unit
IEIP	International Emerging Infections Program
IFA	Immunofluorence
ILI	Influenza-Like-Illness
In CONUS	Inside Continental United States
INS	Instituto Nactionale de Salude
JE	Japanese Encephalitis
KEMRI	Kenya Medical Research Institute
KRCH	Kwai River Christian Hospital
MCRD	Marine Corps Recruit Depot
MFO	Multinational Forces and Observers
MHS	Military Health System
MMWR	Mortality and Morbidity Weekly Report
MQ	Mefloquine
MSD	Mortality Surveillance Division
MTF	Military Treatment Facility
NAMRU-2	Naval Medical Research Unit - 2

NAMRU-3	Naval Medical Research Unit - 3
NASA	National Aeronautical Space Administration
NDVI	Normalized Difference Vegetation Index
NEHC	Navy Environmental Health Center
NEPMU	Navy Environmental Preventive Medicine Unit
NGO	Non Government Organization
NHRC	Naval Health Research Center
NMRC	Naval Medical Research Center
NMRCD	Naval Medical Research Center Detachment
NORTHCOM	Northern Command
NREVSS	National Respiratory & Enteric Virus Surveillance System
NV	Norovirus
OCONUS	Outside Continental United States
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OSD	Office of the Secretary of Defense
OTSG	Office of the Surgeon General
PCR	Polymerase Chain Reaction
PHLIS	Public Health Laboratory Information System
PMOH	Peruvian Ministry of Health
PPM	Personal Protective Measures
QC	Quality Control
QC	Quinidine Gluconate
RDD	Rickettsial Disease Department

RME	Reportable Medical Event
ROK	Republic of Korea
RVF	Rift Valley Fever
SADR	Standard Ambulatory Data Record
SARS	Severe Acute Respiratory Syndrome
SLE	St. Louis Encephalitis
SP	Sulfadoxine-Pyrimethamine
SST	Sea Surface Temperature
STI	Sexually Transmitted Illness
TRANSCOM	Transportation Command
TSN®	The Surveillance Network®
TYCOMS	Type Commander
USAMRIID	U.S. Army Medical Research Institute for Infectious Disease
USAMRU-K	U.S. Army Medical Research Unit - Kenya
USDA	U.S. Department of Agriculture
USFK	U.S. Forces Korea
USNH	U.S. Naval Hospital
USUHS	Uniformed Services University of the Health Sciences
VGE	Viral Gastroenteritis
VGE(Peru)	Vargas-Guerra
WHO	World Health Organization
WNV	West Nile Virus
WPRO	Western Pacific Regional Office
WRAIR	Walter Reed Army Institute of Research

Appendix A: Strategic Plan

GEIS Strategic Plan of 1998 (Excerpt): Addressing Emerging Infectious Disease Threats: A Strategic Plan for the Department of Defense

The Vision of DoD-GEIS, 1998: To Enhance Force Protection and Preventive Defense

Goal I: Surveillance
Detect and monitor emerging pathogens, the diseases they cause, and the factors influencing their emergence to protect military readiness, the health of DoD beneficiary populations, and other national interests. Surveillance priorities included : 1) influenza; 2) drug resistant malaria; 3) antibiotic resistant diarrhea; 4) febrile illnesses including viral hemorrhagic fevers and dengue.

Goal II: Systems Research, Development, and Integration
Integrate public health practices and improve capabilities in clinical medicine, military medicine, laboratory science, epidemiology, public health, and military medical research to facilitate rapid identification and response to emerging infections.

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

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

Appendix B: DoD–GEIS Overseas Laboratory Partners

United States	Kazakhstan	Jamaica	Myanmar
United Kingdom	Panama	Kenya	Suriname
S. Korea	Syria	Haiti	Laos
Belize	Antigua	Uganda	Ecuador
Czech Republic	Egypt	St. Kitts	Vietnam
Japan	Bahamas	Ghana	Peru
Costa Rica	Jordan	St. Lucia	Cambodia
Hungary	Barbados	Pakistan	Brazil
El Salvador	Qatar	St. Vincent	Philippines
Ukraine	Dominica	Nepal	Argentina
Guatemala	Yemen	Trinidad	Singapore
Uzbekistan	Dominican Republic	Bangladesh	Bolivia
Honduras	Sudan	Tobago	Indonesia
Tajikistan	Grenada	Thailand	
Nicaragua	Djibouti	Guyana	

Influenza Isolates:

http://www.cdc.gov/flu/weekly/weeklyarchives2003-2004/03-04summary.htm
http://www.geis.fhp.osd.mil/GEIS/SurveillanceActivities/Influenza/Reports/influenza_2004-06-00.pdf

influenza isolates: Peru, Thailand, Nepal, Germany, Korea, Japan, Turkey, Kyrgyzstan, USA, Italy, Qatar, Egypt, Saudi Arabia, Oman, Kazakhstan, Ukraine, Syria, Indonesia

Appendix C: Selected Activities in Support of Our Partners

Military Infectious Disease Research Program
- Norovirus Conference: September 2003
- Military Infectious Disease Program Review: 3 presentations
- Leishmaniasis Emergency Funding

United States Army
- U.S. Center for Health Promotion & Preventive Medicine, Force Health Protection Conference: 20 poster/presentations

United States Navy
- Navy Occupational Health and Preventive Medicine Workshop: 11 poster/presentations
- Global Influenza Surveillance Working Group Annual Meeting

Office of the Assistant Secretary of Defense (Health Affairs)
- XXXV International Congress on Military Preventive Medicine: 11 poster/presentations

U.S. Regional Commands
- PACOM: Asia Pacific Military Medicine Conference: 8 poster/presentations
- SOUTHCOM: Pan American Conference on Military Medicine
- CoCOM Surgeons Conference
- J4 Staff Brief
- Acinetobacter baumanii Meeting

U.S. Centers for Disease Control & Prevention
- International Conference on Emerging Infectious Diseases: 29 poster/presentations
- EIS Annual Conference
- Antimicrobial Resistance Grant Symposium
- Epi-X Workshop
- NCID Global Health Meeting

United States Department of State
- Indo/US Symposium
- International Health Office Meeting on Zoonoses and Inter Federal Agency Information Sharing & Networking
- Biological Weapons Convention Meeting of Experts: 3 presentations

Pan American Health Organization
Meeting Regional Surveillance Networks Emerging & Reemerging Infectious Diseases

World Health Organization
Eastern Mediterranean Regional Office Annual Meeting: 6 poster/presentations
Global Consultation on Strengthening National Capacities for Surveillance, Response and Control of Communicable Diseases
Global Outbreak Alert and Response Network Meeting

Professional Societies
American Society of Microbiology Annual Meeting: 10 poster/presentations
Infectious Disease Society of America Annual Meeting: 4 poster/presentations
American Society of Tropical Medicine & Hygiene Annual Meeting: 47 poster/presentations
Institute of Medicine Forum on Microbial Threats
Institute of Medicine Annual Meeting – SARS Lessons Learned
Institute of Medicine Vaccine Meeting
Board on Global Health – Pandemic Influenza Meeting
Meeting of the European Society for Chlamydia Research

Appendix D: Publications/Presentations By Category

Respiratory Diseases:

Manuscripts

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Poster/Presentations

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