Global Emerging Infections Surveillance & Response System

The Armed Forces Health Surveillance Center

FISCAL YEAR 2010

"Partnering in the Fight against Emerging Infections"

Overview of AFHSC-GEIS

The Armed Forces Health Surveillance Center (AFHSC) was created to centralize Department of Defense (DoD) domestic and international healthcare surveillance efforts. The organization provides relevant, timely, actionable, and comprehensive health information and supports the military and military-associated populations. The Global Emerging Infections Surveillance and Response System (GEIS) at AFHSC promotes national and international preparedness for emerging infections while maintaining its focus on protecting the health of all DoD health care beneficiaries.

GEIS was established in response to President Clinton's call to address the inadequate protection of US and global public health communities from emerging infectious disease threats. Today, GEIS continues to partner with Continental US (CONUS) and Outside the Continental US (OCONUS) laboratories to provide expertise in infectious disease surveillance. The primary AFHSC-GEIS CONUS research laboratories are: the Walter Reed Army Institute of Research (WRAIR) in Silver Spring, Maryland; the Naval Medical Research Center (NMRC) in Silver Spring, MD; the US Air Force School of Aerospace Medicine (USAFSAM) in San Antonio, Texas; and the Naval Health Research Center (NHRC) in San Diego, California. The five DoD OCONUS research laboratories that serve as primary AFHSC-GEIS partners are: the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, Thailand; the US Army Medical Research Unit – Kenya (USAMRU-K) in Nairobi, Kenya; the US Naval Medical Research Unit No. 2 (NAMRU-2) based in Pearl Harbor, Hawaii; the US Naval Medical Research Unit No. 3 (NAMRU-3) in Cairo, Egypt; and the US Naval Medical Research Unit No. 6 (NAMRU-6) in Lima, Peru. Working in conjunction with their host nations, these partner labs conduct disease surveillance and rapid outbreak response, encourage research and innovation, and build capacity.

The surveillance programs of GEIS focus on five categories of infectious diseases: respiratory infections (RI) with an emphasis on avian and pandemic influenza, gastrointestinal infections (GI), febrile and vector-borne infections (FVBI), antimicrobial resistance (AR), and sexually transmitted infections (STI). In an effort to improve the efficiency and effectiveness of survelliance activities and impose scientific rigor, GEIS initiated steering committees to serve sdvisors in FY10.

Figure 1. AFHSC-GEIS Priority Surveillance Pillars

Another significant undertaking in 2010 was the integration of World Health Organization's (WHO) International Health Regulations (IHR (2005)) core capacities into all surveillance activities. The IHR (2005) mandates that all Member States have the ability to detect, analyze, report, and respond to public health events of international concern (PHEICs). AFHSC-GEIS moves the global public health community closer to achieving IHR (2005) compliance by strengthening surveillance and detection, response and readiness, integration and innovation, and cooperation and capacity building through long-standing relationships between the network partners and their sponsor host countries. In an era of increased globalization where the demarcation between diseases of resource-limited countries and those likely to be encountered by deployed DoD personnel continues to converge, the need for an agile surveillance and response capability becomes more essential. AFHSC-GEIS, with its expansive network of renown international researchers, continues to strive for surveillance products of benefit for force health protection and the global health community.

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Top 10 accomplishments of the AFHSC-GEIS supported network:

- Conducted "Conferencia Regional Andina sobre Enfermedades Infecciosas", a three day conference on emerging infectious diseases (EIDs) with participants and regional health experts from 11 countries in Central and South America (NAMRU-6)

- Developed steering committees for respiratory infection, gastrointestinal infection, malaria and febrile and vector-borne infection programs to improve the efficiency and effectiveness of Department of Defense surveillance activities (AFHSC-GEIS Partner Network)

- Supported pandemic surge response through collection and analysis of over 81,000 samples (approximately 400% increase over the FY08 pre-pandemic period); one specimen (A/Iraq/8529/2009) was selected as a World Health Organization Northern Hemisphere 2010-2011 seasonal vaccine A/H1N1 reference strain (USAFSAM, NHRC, LRMC)

- Published over 1,000 sequences to GenBank, increasing our scientific knowledge of circulating influenza viruses and assisting public health officials with vaccine selection (AFHSC-GEIS Partner Network)

- Established and maintained Influenza-like Illness (ILI) surveillance in 10 South and Central American countries, totaling 52 sites (NAMRU-6, PHCR-South)

- Supported training in surveillance, diagnostic testing and response of influenza, febrile illness, leishmaniasis, and bacterial/enteric disease diagnosis to over 200 medical and laboratory personnel from the South American region (NAMRU-6, PHCR-South)

- Trained 1,049 Royal Thai Army (RTA) staff in support of military unit-based surveillance at five border areas in Thailand as well as 20 civilian and over 70 Cambodian military personnel in basic malaria microscopy and diagnostics (AFRIMS)

Sequence data obtained from GEIS' Influenza Surveillance Program as part of a collaboration between NIH's GenBank and USAFSAM

- Trained five Cambodian National Institute of Public Health/NAMRU-2 technicians and 30 Cambodian nationals in influenza strain sequencing, surveillance and epidemiology; provided bacterial laboratory testing support to six Ministry of Health District/Provincial hospitals (NAMRU-2)

- Provided training in laboratory testing and epidemiology of influenza, malaria, diarrheal disease and other EIDs to 1,614 medical and laboratory personnel from 31 countries in Central Asia, the Middle East, North Africa and sub-Saharan Africa (NAMRU-3, USAMRU-K)

- Supported training of 40 medical and laboratory personnel from four countries in East/Central Africa on basic malaria microscopy, influenza, diagnoses of sexually transmitted infections, enteric infections and other febrile illness; helped establish National Influenza Centers (NICs) in Ghana, Burkina Faso, Togo and Cote d'Ivoire, and supported NICs in Kenya, Tanzania, and Uganda (NAMRU-3, USAMRU-K)

An example of training malaria microscopists in Kenya, using blood film identification examinations

65TH MEDICAL BRIGADE, SEOUL, REPUBLIC OF KOREA: Serves as the strategic link between the Republic of Korea and the CONUS medical base and plans/coordinates US Army medical support at the operational and tactical levels through the early stages of conflict

AUSTRALIAN ARMY MALARIA INSTITUTE, ENOGGERA, AUSTRALIA: An Australian Defense Force organization, providing ADF personnel with the best possible protection against vector borne diseases

ARMED FORCES INSTITUTE OF PATHOLOGY, SILVER SPRING, MARYLAND: Includes research in basic science, environmentalpathology and toxicology, geographic and infectious disease pathology, oncology, and molecular diagnostics; maintains the DoD Medical Mortality Registry

ARMED FORCES RESEARCH INSTITUTE OF MEDICAL SCIENCE (AFRIMS), BANGKOK, THAILAND: Originating as the SEATO Cholera Research Laboratory in Thailand in 1958, AFRIMS has expanded to encompass a range of emerging infectious diseases. As the US Army's largest overseas disease research laboratory, the research institute serves as a collaborating center of the WHO for Diagnostic Reference, Training, and Investigation of Emerging Infectious Diseases. GEIS-funded projects began in the late 1990s and monitors disease trends in Thailand, Myanmar, Laos and Nepal

BROOKE ARMY MEDICAL CENTER (BAMC), SAN ANTONIO, TEXAS: Part of the United States Army Medical Command, serves as a teaching hospital to University of Texas Health Science Center and Uniformed Services University of the Health Sciences (USUHS), and contains the Army Burn Center

GLOBAL VIRAL FORECASTING INITIATIVE (GVFI), SAN FRANCISCO, CALIFORNIA: An independent organization whose team has spent the last 10+ years developing a global system to prevent pandemics

JOHNS HOPKINS UNIVERSITY/APPLIED PHYSICS LAB (JHU/APL), LAUREL, MARYLAND: Solves complex research, engineering, and analytical problems that present critical challenges to the US through utilizing hands-on operational knowledge of the military and security environments

LANDSTUHL REGIONAL MEDICAL CENTER (LRMC), LANDSTUHL, GERMANY: Provides world class comprehensive and compassionate care to our Nation's Warriors, their families, retirees and all other directed beneficiaries in Europe, while maintaining unit and personal readiness

NATIONAL AERONAUTICAL SPACE ADMINISTRATION (NASA), WASHINGTON, DISTRICT OF COLUMBIA: Partners with others to substantially improve science, technology, engineering and mathematics (STEM) education nationwide

NAVY ENVIRONMENTAL PREVENTIVE MEDICINE UNIT 2 (NEPMU-2), NORFOLK, VIRGINIA: Supports the Atlantic Fleet and operational forces with preventive medicine expertise and specialized training, laboratory, and deployment capabilities to increase readiness, promote health, and prevent disease

NAVY ENVIRONMENTAL PREVENTIVE MEDICINE UNIT 5 (NEPMU-5), SAN DIEGO, CALIFORNIA: Maximizes readiness of operational forces and Navy Medical Commands within the Pacific region by providing specialized public health support to train, equip, support, and deploy expert preventive medicine

NAVAL HEALTH RESEARCH CENTER (NHRC), SAN DIEGO, CALIFORNIA: Manages and executes expeditionary operational medical research, development and test and evaluation programs for the Naval Medical Research Center.

NAVY MARINE CORPS PUBLIC HEALTH CENTER (NMCPHC), PORTSMOUTH, VIRGINIA: Serves as the Navy and Marine Corps center for public health services by providing leadership and expertise to ensure mission readiness through disease prevention and health promotion

NAVAL MEDICAL RESEARCH CENTER (NMRC), SILVER SPRING, MARYLAND: Through basic and applied biomedical research, NMRC enhances the health, safety, readiness and performance of Navy and Marine Corps personnel

PACIFIC AIR FORCES (PACAF), HICKAM AIR FORCE BASE, OAHU, HAWAII: PACAF's primary mission is to provide ready air and space power to promote US interests in the Asia-Pacific region during peacetime, through crisis and in war

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES (USUHS), BETHESDA, MARYLAND: Serves the uniformed services and the Nation as an outstanding academic health sciences center and medical school with a worldwide perspective for education, research, service and consultation

UNIVERSITY OF FLORIDA/EMERGING PATHOGENS INSTITUTE, GAINESVILLE, FLORIDA: Created in 2006, the Institute provides a world-class research environment to facilitate interdisciplinary studies of emergence and control of human, animal, and plant pathogens of concern to Florida, the nation, and the world

US ARMY PUBLIC HEALTH COMMAND REGION – EUROPE (PHCR-EUROPE), LANDSTUHL, FEDERAL REPUBLIC OF GERMANY: Supports US European, Africa and Central Commands (EUCOM, AFRICOM and CENTCOM) area of responsibilities (AOR) through military public health programs to sustain force health protection and readiness

US ARMY PUBLIC HEALTH COMMAND REGION – PACIFIC (PHCR-PACIFIC), CAMP ZAMA, JAPAN: Focuses on health promotion and preventive medicine expertise and services for soldiers, family members, and civilians located throughout the Pacific Theater

US ARMY PUBLIC HEALTH COMMAND REGION– SOUTH (PHCR-SOUTH), FORT SAM HOUSTON, TEXAS: Identifies, assesses, and counters environmental, occupational, injury and disease threats through providing health promotion and preventive medicine leadership and services; provides infectious disease surveillance, response, and capacity building support in Central America

US ARMY VETERINARY COMMAND (VETCOM), FORT SAM HOUSTON, TEXAS: Provides military veterinary services in support of United States Army Medical Command (MEDCOM) and Department of Defense (DoD) missions; it is now part of US Army Public Health Command (Provisional)

US NAVAL MEDICAL RESEARCH UNIT NO. 2 (NAMRU-2) PEARL HARBOR, HI: Headquartered in Hawaii, supports American interests in the Pacific Theater and advances US diplomacy in the region by studying infectious diseases of critical public health importance to the United States and other regional partners. With a continued forward presence, the research unit combines virology, microbiology, epidemiology, immunology, parasitology, and entomology into a comprehensive capability to study tropical diseases

US NAVAL MEDICAL RESEARCH UNIT NO. 3 (NAMRU-3), CAIRO, EGYPT: Hosted by the Egyptian government in Cairo, NAMRU-3 has projects in the Africa, East Europe, the Middle East, and Southwest Asia regions and serves as the Eastern Mediterranean Regional World Health Organization (WHO) reference laboratory for influenza and meningitis. NAMRU-3 is the only research institution in North Africa with an Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International accredited animal facility and is one of the only two institutions in Africa with a Biosafety Level-3 (BSL-3) laboratory. In 1999, a partnership was developed with GEIS which led to the recognition of NAMRU-3 as a WHO Collaborating Center for Emerging and Re-emerging Infectious Diseases in 2001

US NAVAL MEDICAL RESEARCH UNIT NO. 6 (NAMRU-6), LIMA, PERU: Established in 1983, NAMRU-6, formerly known as Naval Medical Research Center Detachment-Peru (NMRCD) is hosted by the Peruvian Navy and conducts projects throughout South America and priority regions in Central America. Countries include Argentina, Bolivia, Ecuador, El Salvador, Honduras, Nicaragua, Paraguay, Venezuela, and Colombia. The NAMRU-6 and GEIS partnership began in 1999

US AIR FORCE SCHOOL OF AEROSPACE MEDICINE (USAFSAM), SAN ANTONIO, TEXAS: First-call consultants in Aerospace Medicine, USAFSAM determines solutions to operational needs and prepares new aeromedical experts for future global challenges; began transitioning to its new headquarters at Wright-Patterson Air Force Base, Ohio during FY10

US ARMY MEDICAL RESEARCH INSTITUTE OF INFECTIOUS DISEASE (USAMRIID), FORT DETRICK, MARYLAND: Conducts basic and applied research on biological threats resulting in medical solutions to protect the warfighter

US ARMY MEDICAL RESEARCH UNIT – KENYA (USAMRU-K), NAIROBI, REPUBLIC OF KENYA: Hosted by the Kenya Medical Research Institute (KEMRI), USAMRU-K originated as a temporary site studying trypanosomiasis in 1969. The research unit was permanently established in 1973 and serves as an overseas research activity of the Walter Reed Army Institute of Research (WRAIR). Current activities include malaria, trypanosomiasis, leishmaniasis, entomology, HIV/AIDS and arboviruses, covering Western and sub-Saharan Africa. The mission of USAMRU-K is to develop and test improved means for predicting, detecting, preventing and treating infectious disease threats to military and civilians in East Africa

US NORTHERN COMMAND (USNORTHCOM), COLORADO SPRING, COLORADO: USNORTHCOM conducts homeland defense, civil support and security cooperation to defend and secure the United States and its interests

WALTER REED ARMY INSTITUTE OF RESEARCH (WRAIR), SILVER SPRING, MARYLAND: Conducts biomedical research that is responsive to DOD and US Army requirements and delivers life saving products including knowledge, technology, and medical materiel that sustain the combat effectiveness of the warfighter

WALTER REED ARMY MEDICAL CENTER (WRAMC), WASHINGTON, DISTRICT OF COLUMBIA: Integrates patient care, teaching and research, and provides care to past, present, and future warriors

Capacity Building and Other Efforts

Program Goals

With the aim of providing central coordination of efforts among global network partners, AFHSC-GEIS works to build core public health capacities within partner host countries as defined by the World Health Organization's (WHO) International Health Regulations (IHR (2005)). Core capacities and program functions include, but are not limited to, human resources capacity (training); preparedness activities; early warning, electronic disease surveillance; laboratory infrastructure enhancement and support; assistance with host country outbreak response capabilities; and reporting and notification of outbreak findings. In building and enhancing these core capacities the global network:

Figure 1. NAMRU-3 researchers train many regional organizations on laboratory techniques

- Has a coordinated approach for how network partner efforts fit within the guiding principles of capacity building under the IHR (2005)
- Establishes a mechanism to track, to monitor and to quantify core capacity building efforts for coordination with other US government and international public health entities within partner countries
- Further develops investments in global partners to transition program capabilities and functions toward a sustained, host country-led effort

Achievements

- Trained 39 students from 18 countries toward their Certification in Emerging Infectious Diseases (University of Florida)
- Provided capacity building and technical training support for National Influenza Centers (NICs) in El Salvador, Honduras and Guatemala (PHCR-South)
- Trained over 200 laboratorians and scientists throughout Central and South America on epidemiology, outbreak response and laboratory diagnostic techniques (NAMRU-6)
- Conducted regional conference for over 120 public health leaders from 12 Central and South American countries and multiple international health organizations on public health challenges throughout the Americas (NAMRU-6)
- Conducted 14 training sessions, training 607 individuals from 19 countries in support of US Combatant Command partnerships improving the abilities of local Ministries of Defense and Health to respond to and prevent emerging disease threats (CDHAM)
- Collaborated with WHO's Eastern Mediterranean Regional Office to conduct training on molecular genetics and sequencing for students from the NICs of Egypt, Morocco and Oman, thereby helping these NICs identify new influenza strains and track the emergence of antiviral drugs resistance (NAMRU-3)
- Worked with host country counterparts to establish new NICs in Burkina Faso and Togo and provided continued support to existing NIC in Cote d'Ivoire (NAMRU-3)
- Continued support and enhancement of electronic Unit-Based Surveillance (UBS) project in collaboration with the Royal Thai Army (AFRIMS)
- Partnered and coordinated with Institute Pasteur and host country counterparts to support and enhance the NIC capabilities in the Kingdom of Cambodia (NAMRU-2)
- Initiated the first phase of deployment for open source electronic surveillance and early warning system for resource limited settings (JHU/APL)

Capacity Building and Other Efforts

An Electronic Disease Surveillance Initiative guided by the International Health Regulations (2005)

Emerging and re-emerging diseases are a well-defined threat to global public health. Over the last five years, the World Health Organization (WHO) has identified 1100 disease epidemics worldwide. Recent events, such as the 2009 H1N1 influenza pandemic and the SARS epidemic of 2003, have demonstrated how quickly these newly emerging diseases can spread globally. Furthermore, these events have helped to reshape the most recent version of the International Health Regulations (IHR (2005)), which was adopted by 194 member states in 2007. The IHR (2005) provides Member States with a mechanism and legally-binding framework to help them build public health capacities required to identify, respond and report public health emergencies of international concern (WHO, 2008).

Keeping the threat of emerging infectious diseases in mind, the AFHSC-GEIS program and the Johns Hopkins University Applied Physics Laboratory (JHU/APL) began developing the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE II) in early 2001. Over the past decade, the evolution of the ESSENCE system has aided in the development of a new electronic disease surveillance tools meant for deployment in resource-limited settings around the world. The Suite for Automated Global Electronic bioSurveillance (SAGES) initiative uses innovative ways of capturing clinical and public health data at all government levels to generate information for reliable and timely public health action. SAGES was built to be used as an early warning system by host country sponsors to achieve IHR (2005) compliance for sustainable disease surveillance. The toolkit is broken down into four categories: 1) data acquisition,2) analysis and visualization (available free for download over the internet), 3) communications, and 4) modeling/simulation/evaluation (Figure 2). Data collection is customizable and supports data sources such as text messaging (SMS) and interactive voice response (IVR) allowing for near-real time reporting. The analysis and visualization tools provide public health professionals with the ability to detect and monitor trends of disease or syndromes of interest. The communication tools allow for timely notification of important findings to the appropriate levels of national public health systems. Participating countries will greatly benefit from having a robust, open-source electronic surveillance capability that fulfills six of the eight core public health capacities defined under Annex 1 of the IHR (2005) (WHO, 2008). The SAGES initiative allows countries to enhance their public health systems and meet the July 2012 deadline for IHR compliance.

Figure 2. SAGES, An electronic disease surveillance collaboration between JHU/APL and AFHSC/GEIS initiated in 2010

Future Directions

- Develop and expand relationships with global health partners to work toward further building core public health capacities by the target implementation date of 2012, as outlined by the IHR (2005)
- Develop monitoring and evaluation framework to measure effectiveness and global health impact of program activities throughout the global network

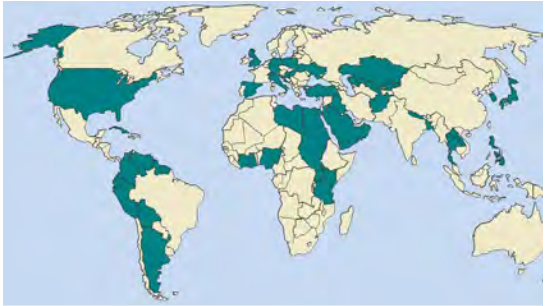
References:

WHO: International Health Regulations (2005). 2nd edition. Geneva, Switzerland: World Health Organization Press 2008.

Respiratory Infections

Program Goals

Successfully develop, implement, support and monitor a respiratory disease surveillance system that contributes to Force Health Protection and global public health through a centrally-coordinated worldwide network of partners. These partners promote, maintain, coordinate, and enhance a responsive and informative surveillance system which provides the Department of Defense (DoD) with critical information regarding the circulating subtypes, epidemiologic patterns, disease severity and burden associated with influenza and other respiratory pathogens:



Respiratory Infections 2010 Surveillance Projects

- Provide timely, accurate and actionable data, for decision makers within the DoD and global public health community
- Augment genetic sequencing capacity at regional labs to enhance timely analysis of circulating influenza viruses and identify samples for further genetic characterization (such as partial or full length genomic characterization for shift/drift or antiviral resistance)
- Strengthen diagnostic laboratory capacities in the DoD and host countries

Achievements

- Established the Respiratory Pathogen Surveillance Steering Committee to improve the efficiency and effectiveness of DoD influenza and other respiratory disease surveillance activities (AFHSC)
- Supported pandemic surge response through collection and analysis of over 81,000 samples (an approximately 400% increase over the FY08 pre-pandemic period); one specimen (A/Iraq/8529/2009) was selected as a World Health Organization Northern Hemisphere 2010-2011 seasonal vaccine A/H1N1 reference strain (USAFSAM, NHRC, LRMC)
- Published over 1,000 sequences to GenBank, increasing our scientific knowledge of circulating viruses and assisting public health officials with vaccine selection (AFHSC-GEIS Partner Network)
- Expanded surveillance capabilities of deployed veterinary personnel to screen for highly pathogenic avian influenza in animals by validating the National Veterinary Service Laboratory avian influenza matrix assay for H5N1 and H7N3 strains, on the Joint Biological Agent Identification and Diagnostic System (FADL)
- Developed new military-to-military (mil-mil) partnerships in Africa, Central America, and Southeast Asia for respiratory disease surveillance (AFRIMS, GVFI, NAMRU-3, USAMRU-K, PHCR-S)
- Established influenza hemagglutinin-inhibition testing capability enabling the feasibility of using convalescent plasma for treatment of severe influenza disease, in peacetime and in wartime (NMRC)
- Conducted influenza surveillance at the human-animal interface in seven countries in Africa, Asia, and Europe to identify transmission risk factors and potential new zoonotic influenza virus strains (AFRIMS, GVFI, NAMRU-2, University of Florida, USAMRU-K)
- Established a bioinformatics coordination group and standalone server enhancing high throughput genomic sequencing analysis and reduced the time between sample processing and result reporting from months to days (WRAIR)
- Identified and reported the emergence of adenovirus serogroup B species (Ad3, Ad7, Ad14, and Ad21) at various US military basic training centers (NHRC)

Respiratory Infections

Figure 1. Tracking the spread of H1N1 pandemic in Northern Europe in November 2010

AFHSC-GEIS Partners Aid in Outbreak Support in the Ukraine for the 2009 A/H1N1 virus through Molecular Sequence Analysis

During the second wave of the H1N1 influenza pandemic in November, reports were received from North Europe of serious respiratory disease resulting in increased hospitalizations and mortality, raising concerns of the potential for an increase in virulence. Responding to these concerns, the Polish Military Institute of Hygiene and Epidemiology (MIHE) provided 58 respiratory specimens to the AFHSC-GEIS influenza sentinel surveillance network for analysis. The specimens, collected by Polish military personnel providing outbreak support in Ukraine, were shipped to Landstuhl Regional Medical Center (LRMC) for identification, and subsequently were sent to the US Air Force School of Aerospace Medicine (USAFSAM) for viral culture and molecular sequencing. The 2009 A/H1N1 virus was identified (by rRT-PCR) in 28 specimens and full-length sequencing of segment seven of influenza A (matrix gene and M2 proton ion channel gene) was performed on six of the specimens. Phylogenetic analysis revealed that all six specimens aligned closely with the current vaccine strain virus, A/California/7/2009, exhibiting an overall nucleotide similarity of 99.2-99.3%. A Blastη analysis of one specimen, A/Ukraine/4898/2009 resulted in a 99.8% match with specimens reported from Scandinavia (Norway) and Eastern Europe (Russia). USAFSAM used nine culture results for sequencing of the full hemagglutinin gene (HA), portions of the neuraminidase gene (encompassing H274); none of the specimens revealed genetic evidence of Oseltamivir resistance. In addition, review of the full-length HA sequences suggested the Ukrainian isolates were 99% similar to 2009 A/H1N1 isolates collected from the US, Asia, Canada, Mexico, and Europe. The AFHSC-GEIS collaboration between USAFSAM, LRMC, and the Polish MIHE highlights military-to-military cooperation during a world-wide pandemic. The findings provided evidence of the molecular changes, or lack thereof, in the HA portion of the 2009 A/H1N1 virus and supported the continued use of Oseltamavir for treatment. In addition, the relative molecular stability of specimens sequenced by USAFSAM, as compared to the vaccine strain, provided confidence that the monovalent vaccine would continue to provide protective immunity during critical periods of the pandemic.

Future Directions

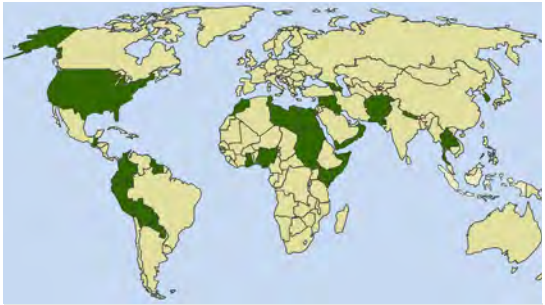
- Expand and incorporate respiratory disease surveillance at the human-animal interface into existing efforts
- Establish standardized (PCR- and/or genetic screening-based), multi-centered, collaborative projects among partners using existing respiratory surveillance systems or samples for discovery of novel EID pathogens or co-infections (e.g. pathogen discovery)
- Examine the effectiveness of non-pharmaceutical interventions (e.g. temperature screening, hand-washing, cohorting, environmental/air controls) in controlling respiratory illness, especially among military recruit populations
- Strengthen existing mil-mil partnerships and incorporate surveillance activities with host country civilian surveillance programs

Febrile and Vector-borne Infections

Program Goals

Aimed at utilizing remote-sensing and ecologic-niche modeling, the Febrile and Vector-borne Infections program integrates pathogen discovery, febrile illness, arthropod-vectors and animal surveillance by:

- Characterizing febrile illness risk and outbreak threats
- Providing actionable information for health care & public health professionals, and DoD decision makers on patient care, case/outbreak mitigation, and outbreak prevention and control
- Promoting measures to lessen the burden of disease of febrile patients and communities



Febrile and Vector-borne Infections 2010 Surveillance Projects

Achievements

- Identified West Nile Virus seropositive samples, from Kabul, Kandahar and Helmond Provinces in Afghanistan, with seroprevalences similar to those documented in Egypt (11% IgG, and 0.7% IgM positive)(NAMRU-3)
- Collaborated with Syrian scientists in diagnosing 31 cases of *Leishmania tropica*. (NAMRU-3)
- Successfully transported, tested, and diagnosed 29 cases of undiagnosed febrile illness in rural Kenya using improved laboratory infrastructure (*P. falciparum*: 27, *P. vivax*: 1, and *Burkholderia meliodosis* (*B. cepacia* complex): 1) (USAMRU-K)
- Confirmed scrub typhus infection in 2.5% of serum samples from febrile patients in Cambodia (NAMRU-2)
- Identified two new Dengue virus type-1 (DENV-1) lineages in Myanmar, one indistinguishable from a 2006 circulating DENV-1 strain in southern China, and the other indistinguishable from a strain circulating in Vietnam (AFRIMS)
- Created an accurate model for predicting Japanese encephalitis (JE) risk (using presence of the vector Culex tritaeniorhynchus and other factors) in Korea, and piloted expansion of the predictive model using JE & other illnesses in Southeast Asia (JE, Chikungunya), South and Central Asia (JE, leishmaniasis), Indonesia (malaria) and Peru (Bartonellosis) (USUHS)
- Forecasted the January-February 2010 Rift Valley Fever outbreaks in South Africa (NASA)
- Developed monthly normalized difference vegetation index (NDVI) and land surface temperature anomaly maps and space-time (Hovmoller) plots for Ukraine/SE Europe, the Middle East, Turkey and Afghanistan as part of the development of a predictive analysis tool for tick-borne diseases (CCHF and rickettsial diseases) in the region (NASA)
- Established VectorMap (www.vectormap.org) which now contains over 13,200 datasets in MosquitoMap (www.mosquitomap.org) from 140 countries; 50,000 datasets from 52 African countries in TickMap (www.tickmap.org); and 3,400 datasets in SandflyMap (www.sandflymap.org) (WRAIR)
- Characterized the prevalence of spotted fever group (30.4%) and typhus group (5.8%) rickettsial infections in undiagnosed febrile illness cases in Kenya (NMRC, USAMRU-K)
- Increased Lassa Diagnostic Laboratory capability in Sierra Leone's Kenema Government Hospital by adding a state-of-the-art satellite system for email communication, and a liquid nitrogen generator for improved sample storage and shipping (USAMRIID)

Febrile and Vector-borne Infections

Understanding the etiology of febrile illnesses in South America

In the forest regions of South America, such as the Amazon and the Chaco, infectious pathogens are among the leading causes of morbidity and mortality among humans. The increasing threat of infection is due to rapid population growth, urbanization, air travel, environmental changes, and the lack of effective intervention strategies. Some of the emerging and re-emerging diseases include cholera, dengue fever, dengue hemorrhagic fever, yellow fever, Venezuelan equine encephalitis, Oropouche fever, Mayaro fever, hantaviral syndromes, epidemic typhus, leptospirosis, leishmaniasis, and falciparum malaria. Except for yellow fever, reliable and universally applicable prevention strategies are lacking.

Figure 1. NAMRU-6 researchers in a BSL-3 field laboratory conducting animal necropsies

To facilitate timely development and implementation of intervention measures that minimize the impact of emerging diseases on human health, investigators at Naval Medical Research Unit No. 6 (NAMRU-6) and collaborating colleagues undertook a proactive strategy. They combined human case and population-based surveillance with arthropod-vector and animal surveillance, to recognize pathogen emergence at its earliest stages. Initial findings included the characterization of viruses in animals (rodents and canines) and arthropod-vectors not yet isolated from human febrile-illness cases at the survey site in Iquitos, Peru. Findings support the belief that there exist a number of infectious diseases that can potentially emerge in South America.

Future Directions

- Continue to conduct human febrile-illness case and population-based surveillance, diagnostic testing support and development, and pathogen discovery
- Support greater understanding of human febrile illness emergence, incidence and prevalence through multi-disciplinary collaborations that elucidate factors that contribute to febrile illness and vector-borne disease risks and human disease outbreak threats

Malaria

Program Goals

Successfully execute a global surveillance system capable of reducing the threat posed by malaria to force health protection and global public health through:

- Coordinated surveillance to characterize the burden, transmission and distribution of malaria drug resistance
- Research, training and capacity building to foster expertise in containing and characterizing malaria threats in Department of Defense (DoD) partner countries
- Monitoring vector populations and their geographical distributions to assess malaria risks and effectiveness of control measures

Malaria 2010 Surveillance Projects

Achievements

- Engaged the Malaria Surveillance Steering Committee to identify and prioritize surveillance needs, formulate surveillance goals, and improve the overall effectiveness of AFHSC malaria surveillance products (AFHSC)
- Geographically expanded surveillance of artemisinin resistant Plasmodium falciparum in Southeast Asia to better characterize the spread, and inform malaria containment efforts executed by World Health Organization (WHO) and local malaria control programs (AFRIMS and NAMRU-2)
- Investigated a cluster of malaria cases among DoD personnel deployed to Liberia in support of Operation Onward Liberty, focusing on malaria drug resistance, personal protective measures, vector efficiency, and environmental factors affecting force health protection (NAMRU-3)
- Examined epidemiological factors and clinical characterization of Plasmodium vivax malaria in Peru, including risk factors for severe disease and investigation of various primaquine treatment regimens for relapse prevention (NAMRU-6)
- Continued characterization of drug sensitivity patterns in Kenya to inform DoD product development and malaria public health officials in Kenya (USAMRU-K)
- Sponsored a symposium of key officials from the Armed Forces, Centers for Disease Control and Prevention (CDC), the Presidential Malaria Initiative (PMI) and other US government organizations to examine and reduce the impact of malaria on US civilians and military forces (AFHSC)
- Conducted a Malaria Microscopy Training Medical Civil Action Program (MEDCAP) as part of Honest Talon 10-01, training 43 Tanzanians and identifying seven trainees as mentors (USAMRU-K)
- Identified two divergent chloroquine resistant “genetic fingerprints” in Oceania, which have implications for potential spread of drug resistant strains from Southeast Asia throughout the western Pacific (Australian Army Malaria Institute)

Malaria

Artemisinin Resistant *Plasmodium falciparum* Malaria: A Threat to Department of Defense (DoD) and Global Populations

Although limited in scope, the recent emergence of artemisinin resistance is relevant for the DoD and the global malaria community. The artemisinin combination therapies (ACT) have been adopted worldwide as the drug of choice for uncomplicated *Plasmodium falciparum* malaria. Furthermore, resistance to the artemisinin class may affect the efficacy of artemether-lumenfantrine, an ACT now licensed in the US. As artemisinin resistance surveillance data become available, they are made accessible to malaria public health authorities to contain and eliminate resistant strains. By incorporating the latest drug resistance data from the global AFHSC-GEIS malaria network, DoD and the larger drug development community may accelerate the advancement of other drug classes for optimal effect.

Figure 1. AFRIMS researcher questions a patient in a high risk area for resistant *P. falciparum*

Figure 2. NAMRU-3 and NEPMU-2 personnel deploy ultraviolet light traps in Liberia to monitor for Anopheles gambiae species mosquitoes

Outbreak Response to Malaria in US Service Members Deployed in Liberia

An outbreak of *P. falciparum* malaria in Liberia, in 2010, resulted in the fatality of a US service member. The Navy Medical Research Unit No. 3 (NAMRU-3), together with colleagues at the Navy Environmental Preventive Medicine Unit 2 (NEPMU-2), US Army Public Health Command Region Europe and US Africa Command, played an important role in investigating the outbreak by conducting an epidemiologic assessment of factors affecting malaria risks of deployed service members. Important findings highlighted the need to improve malaria prevention, vector control measures, and training of healthcare providers. Results of the NAMRU-3 outbreak investigation were presented in the AFHSC sponsored symposium in Washington, DC, entitled "Malaria Surveillance and Epidemiology: Reducing the Impact on US Civilians and Military Forces" and informed AFRICOM malaria practices aimed at reducing the risk of infection during deployment.

Future Directions

- Continue to study artemisinin resistant *P. falciparum*, with an emphasis on in vitro, molecular, clinical and information management approaches to monitor geospatial and temporal spread
- Develop surveillance products and capacities to mitigate the impact of malaria on both global and US DoD populations
- Monitor the evolution and spread of malaria drug resistance to support DoD malaria vaccine, diagnostic, and drug development
- Initiate clinical and laboratory studies to better understand risk factors, pathology and epidemiology of severe *Plasmodium vivax*
- Integrate vector and human surveillance approaches to better aid transmission blocking and containment strategies

Gastrointestinal Infections

Program Goals

Perform surveillance of unique or regional enteric diseases to provide actionable information and threat assessments to Department of Defense (DoD) personnel and related populations by:

- Characterizing enteric pathogens among diverse populations in environments relevant to force health protection (e.g. Norovirus, enterovirus, etc)
- Conducting surveillance to monitor transmission dynamics and to determine the prevalence of enteric pathogens causing acute diarrhea
- Improving laboratory surveillance capabilities during deployment and peri-deployment periods

Gastrointestinal Infections 2010 Surveillance Projects

Achievements

- Established an Enterics Surveillance Steering Committee to assist GEIS in identifying surveillance needs, formulating surveillance goals and improving overall effectiveness of the DoD enteric surveillance (AFHSC)
- Provided enteric infections surveillance support for Cobra Gold exercises (AFRIMS)
- Estimated that the risk of travelers' diarrhea was low for those eating at popular tourist restaurants in Bangkok (AFRIMS)
- Provided laboratory support for cholera outbreaks in collaboration with the Nepalese National Public Health Laboratory (NPHL) and the Walter Reed/AFRIMS Research Unit Nepal (WARUN). In October 2009, WARUN reported 52% of stool samples from a diarrheal outbreak had *Vibrio cholerae*. In April 2010, *V. cholera* was detected in 14 NPHL samples from an outbreak in western Nepal (AFRIMS)
- Assisted in funding two surveillance sites in Kericho, Kenya as part of an enteric infections surveillance field network and proposed vaccine testing sites (USAMRU-K)
- Provided laboratory support to the Cambodian Ministry of Health during a *V. cholera* outbreak and demonstrated resistance to the first-line antibiotic, tetracycline, among most of the isolates; thereby contributing to public health officials' modifications of their guidance (NAMRU-2)
- Shared antibiograms for shigella and other enteric pathogens in collaboration with the Cambodian Ministry of Health and other in-country health partners (NAMRU-2)
- Provided epidemiologic and laboratory support for diarrheal disease and influenza-like illness surveillance for Operation Bright Star, with emphasis on providing real-time data for preventive medicine officers (NAMRU-3)

Gastrointestinal Infections

- Worked with World Health Organization (WHO) to enhance laboratory diagnostics for Iraq, Iran, Sudan, and Yemen by providing Enzyme Immunoassay (EIA) kits for rotavirus detection (NAMRU-3)
- Trained the Cairo University pediatric hospital laboratory staff to diagnose *C. difficile* infections using commercially available antigen and toxin detection Enzyme-linked Immunosorbent Assay (ELISA) Kits (NAMRU-3)

Enhancement of Norovirus Detection Capability at Navy Environmental and Preventive Medicine Units

Acute gastroenteritis is a significant problem among US deployed forces, particularly for the US Navy, as well as, recruit and training populations. The Navy Environmental and Preventive Medicine Unit 2 (NEPMU-2) undertook the task of establishing and building the Navy's diagnostic capabilities for norovirus among shore and ship-based platforms. In FY2010, NEPMU-2 sent a team to the Centers for Disease Control and Prevention (CDC) for norovirus detection training. The training provided guidance in utilizing the CDC protocols for development of the current NEPMU-2 protocol. NEPMU-2 then worked with Navy Environmental and Preventive Medicine Unit 5 (NEPMU-5) to train laboratory personnel on detection methods for norovirus. With the new laboratory competencies, both labs are testing diarrheal cases during routine outbreak investigations. Also, East and West Coast fleets were provided with sample collection kits for sample submission to the appropriate NEPMU for diagnostic support to enhance preparedness for gastrointestinal illness outbreaks.

Figure 1. Ten diarrheal samples received from USS Bonhamme Richard (pictured above) were tested in the 4th quarter of FY2010 and all 10 were found to be Norovirus type 1

Future Directions

- Develop an enteric infections network to integrate the collection of standardized data on pathogens of DoD and host country importance for comparable data across regions
- Emphasize surveillance within military populations in regional exercises and long-term deployment settings
- Develop and field a forward-deployed capability to characterize enteric pathogens circulating in US forces in theater
- Increase projects examining the presence and scope of antibiotic-resistant enteric pathogens

Antimicrobial Resistant Organisms

Program Goals

Enhance and implement antimicrobial resistant organism (ARO) surveillance initiatives among all partners to better understand evolving drug resistance and generate actionable recommendations for treatment of military and host nation populations by:

- Analyzing and archiving antimicrobial resistance patterns of regional pathogens
- Linking collaborative antimicrobial resistance efforts with food safety and security initiatives
- Complying with the GEIS Acinetobacter Strategic Initiative (GASI), National Antimicrobial Resistance Monitoring Network, and Department of Defense (DoD) Clinical Laboratory Improvement Program Standards
- Aligning surveillance outcomes with other DoD efforts such as medical diplomacy, capacity building, and investments in outbreak detection and response

Antimicrobial Resistance 2010 Surveillance Projects

Achievements

- Confirmed the presence of *Plasmodium falciparum* artemisinin resistance in Cambodia, and studied the dose-dependent risk of neutropenia occurring after 7-day courses of artesunate monotherapy in Cambodian patients with acute falciparum malaria (AFRIMS)
- Initiated surveillance methods to track New Delhi Metallo-beta-lactamase (NDM-1) infections using the Antibiotic Resistant Organisms project (NMCPHC)
- Developed information papers on bacteroides, Methicillin-resistant *Staphylococcus aureus* (MRSA)/Methicillin-sensitive *Staphylococcus aureus* (MSSA), and *Clostridium difficile* through a collaboration between the Navy and Marine Corps Public Health Center and Brooke Army Medical Center Infectious Disease Service (NMCPHC, BAMC)
- Piloted Health Level 7 Dashboard for antibiotic resistant infections in preparation for broad scale use by public health professionals (NMCPHC)
- Instituted a surveillance system in intensive care units in Egyptian and Jordanian hospitals to estimate infection rates and antimicrobial resistance patterns associated with medical devices
- Assisted in the identification of *Streptococcus suis* from a specimen referred to Naval Medical Research Unit No. 2 for antimicrobial susceptibility testing, prompting an epidemiological investigation by World Health Organization and Cambodia-Centers for Disease Control and Prevention (NAMRU-2)

Antimicrobial Resistant Organisms

Supporting Global Antimicrobial Resistance Initiatives

Antimicrobial resistance has proven to be one of the growing issues within the fields of medicine and public health. For instance, *Acinetobacter baumanni* has been found to cause serious wound infections, with devastating prosthesis infections and catheter-related sepsis. Some strains of *A. baumannii* are resistant to all known antibiotics, and estimates of death rates from resistant *Acinetobacter* infections range from 30 to 40 percent (Choffnes, 2010). The frequency of multi-drug resistant *Acinetobacter baumannii* infections among US military personnel returning from Iraq and Afghanistan is increasing and becoming more significant. Other infections of military importance are hospital-acquired and community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), which have been associated with increased skin and soft-tissue infections among recruits and soldiers (Choffnes).

Figure 1. IOM Report on the Implication for Global Health and Novel Interventions Strategies Workshop

Knowing the implications of antimicrobial resistance on combat readiness and understanding the need to enhance global surveillance programs that rapidly identify genetic and phenotypic patterns of resistance, AFHSC-GEIS developed several Antimicrobial Surveillance initiatives in 2010. In early April 2010, the Institute of Medicine's (IOM's) Forum on Microbial Threats convened a public workshop in Washington, DC to consider the implications of antimicrobial resistance for global health and strategies to mitigate the impact of antimicrobial resistance and bring together subject-matter experts from various US government organizations and other stakeholders. AFHSC-GEIS contributed support to the workshop and was invited to discuss antimicrobial resistant infections of military importance. Resulting from the two-day event was the 2010 IOM "Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies- Workshop Summary" (Choffnes, 2010).

Future Directions

- Foster military force health protection and medical diplomacy through community-acquired and healthcare-associated infection surveillance activities
- Increase and sustain surveillance capabilities to rapidly identify genotypic and phenotypic patterns of resistance in the ever-changing field of microbiology and antimicrobial resistance
- Create a subject matter expert steering committee to develop strategic goals to better direct, coordinate, and identify surveillance gaps by avoiding redundancies and assuring state-of-the art technologies

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Sexually Transmitted Infections

Program Goals

Enhance ongoing sexually transmitted infections (STI) surveillance efforts and build laboratory capabilities to identify, isolate, and report the impact of STIs on military and host country populations by:

- Evaluating the geographic breadth and burden of *Chlamydia trachomatis* and antimicrobial-resistant *Neisseria gonorrhoeae* among at-risk US military and host country populations
- Providing timely, actionable, and relevant data to guide future treatment policies
- Assessing extent of antimicrobial resistance and epidemiologic factors associated with STIs

Sexually Transmitted Infections 2010 Surveillance Projects

Achievements

- Instituted surveillance at the primary STI referral clinic in Djibouti and enhanced clinic laboratory capabilities to culture *N. gonorrhoeae* and perform antimicrobial susceptibility testing (NAMRU-3)
- Initiated a study among Kenyan commercial sex workers and military personnel at nine sites examining *N. gonorrhoeae* resistance patterns (USAMRU-K)
- Documented lack of appropriate treatment for *N. gonorrhoeae* infection among active duty service members between 2006-2008. Only 30% of single-infection cases and 49% of co-infected cases (*N. gonorrhoeae* plus another STI), received treatment as recommended by the 2006 Centers for Disease Control treatment guidelines (NMCPHC)
- Evaluated US Army medical laboratory STI testing practices and found 74% of Army hospital laboratories used CDC's recommended nucleic acid amplification testing technology for identification of *C. trachomatis* and *N. gonorrhoeae* (AFHSC, USAMEDCOM, USAPHC)

Sexually Transmitted Infections

Chlamydia in the US Army

Detailed trend analyses of nationally reported chlamydia cases across the four military services are limited. To address the information gap, the Defense Medical Surveillance System was queried for chlamydia case reports from non-deployed active duty personnel. Reported trends within the Army were compared to those nationally, and demonstrated that chlamydia incidence rates were considerably higher among soldiers compared to civilians (Figure 1). Incidence rates were roughly 4 times higher among Army women and 2.5 times higher among Army men compared to civilians; these results prompted interest in further examining chlamydia incidence rate data among other military services. The higher rates were possibly attributed to increased screening opportunities available in the Army. Additional studies of chlamydia and STIs in deployed active duty personnel were planned. The poster "*Chlamydia trachomatis* Reported Among US Active Duty Army Members, 2000-2008", based on the chlamydia study described above, was presented in June 2010 at the 12th International Symposium on Human Chlamydia Infections and won an NIH travel award (Jordan, in press).

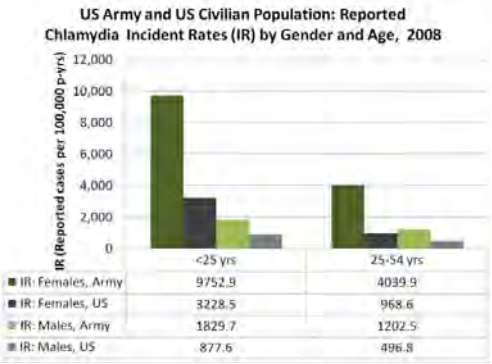

Figure 1. Comparison of Chlamydia incidence rates between US Army and US Civilian populations

Future Directions

- Develop a gonorrhea resistance surveillance network and build laboratory capacity to identify, isolate, and conduct antimicrobial susceptibility testing
- Incorporate the US military into Center for Disease Control and Prevention's (CDC) Gonococcal Isolate Surveillance Project (GISP)
- Assess the impact of chlamydia and other STIs (such as Herpes Simplex virus) among US military personnel and at-risk host country populations

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