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TITLE: Military-Relevant Infectious Diseases Endemic to Kenya: Epidemiology, Immunology, Pathophysiology, Treatment and Prevention

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### Title and Subtitle

Military-Relevant Infectious Diseases Endemic to Kenya: Epidemiology, Immunology, Pathophysiology, Treatment and Prevention

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### Abstract (Maximum 200 Words)

Growth in operations continued particularly in the field sites in Nyanza and the Rift Valley Provinces during the second year of the Cooperative Agreement. State-of-the-art clinical research facilities were opened in Kombewa (November 2003) and Kericho (March 2004) for malaria and HIV/AIDS intervention studies, respectively. Kericho now has a new maternal and child health clinic and construction is underway to extend the Kombewa facility. A pediatric wing and modern research laboratory buildings will be ready for occupancy during the final year of the agreement. A 135 children dose and age stratified Phase I clinical trial for MSP-1 and an epidemiological study involving 276 children is in progress at the Kombewa field site. Both studies are in their follow-up phase. In Kericho, a retrospective economic impact study was completed and published results demonstrate a significant decrease in earnings of both the infected worker and the employer. A prospective comparison of EIA and Western blot testing (reference) with four rapid tests in 486 subjects enrolled in an HIV-1 sero-incidence study was undertaken in Kericho. The sensitivity of all four rapid tests was 100% and specificity ranged from 99.1% to 100% with high positive and negative predictive values. Recruitment into the cohort development protocol in preparation for future HIV/AIDS vaccine intervention studies also commenced this year. Over 2600 subjects have been enrolled with some groups already into their first six month follow-up visit. Work in leishmaniasis was initiated with the arrival of Ellison Fellows to the unit under a special new NRC program. A pathway for prostaglandin synthesis in the parasite has been described and published. A potential role for this novel pathway in the life cycle or pathogenesis of the parasite is under investigation. Laboratory studies on severe anemia in complicated malaria continues with an emphasis on complement regulatory proteins. Recent immuno-fluorescent studies have shown colocalization of parasite antigens and RBC molecules on the surface of uninfected RBC implicating a bystander mechanism in the pathogenesis of malarial anemia. Entomological and GIS capabilities have been extended from Nairobi to support field sites executing clinical studies.
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Military-relevant Infectious Diseases Endemic to Kenya: Epidemiology, Immunology, Pathophysiology, Treatment and Prevention

US ARMY MEDICAL RESEARCH UNIT - KENYA

The mission of USAMRU-K is to develop and test improved means for predicting, detecting, preventing and treating infectious disease threats to US military personnel deployed worldwide and to undertake global surveillance, training, research, and response to emerging infectious disease threats.

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SUMMARY

Growth in operations continued particularly in the field sites in Nyanza and the Rift Valley Provinces during the second year of the Cooperative Agreement. State-of-the-art clinical research facilities were opened in Kombewa (November 2003) and Kericho (March 2004) for malaria and HIV/AIDS intervention studies, respectively. Kericho now has a new maternal and child health clinic and construction is underway to extend the Kombewa clinical research facility. A pediatric wing and modern research laboratory buildings will be ready for occupancy during the final year of the agreement. A 135 children dose and age stratified Phase 1 clinical trial for MSP-1 and an epidemiological study involving 276 children is in progress at the Kombewa field site. Both studies are in their follow-up phase. In Kericho, a retrospective economic impact study was completed and published results demonstrate a significant decrease in earnings of both the infected worker and the employer. A prospective comparison of EIA and Western blot testing with four rapid tests in 486 subjects enrolled in an HIV-1 sero-incidence study was undertaken in Kericho. The sensitivity of all four rapid tests was 100% and specificity ranged from 99.1% to 100% with high positive and negative predictive values. Recruitment into the cohort development protocol in preparation for future HIV/AIDS vaccine intervention studies also commenced this year. Over 2600 subjects have been enrolled with some groups already into their first six month follow-up visit. Work in leishmaniasis was initiated with the arrival of Ellison Fellows to the unit under a special new NRC program. A pathway for prostaglandin synthesis in the parasite has been described and published. A potential role for this novel pathway in the life cycle or pathogenesis of the parasite is under investigation. Laboratory studies on severe anemia in complicated malaria continue with an emphasis on complement regulatory proteins. Recent immuno-fluorescent studies have shown co-localization of parasite antigens and RBC molecules on the surface of uninfected RBC implicating a bystander mechanism in the pathogenesis of malarial anemia. Entomological and GIS capabilities have been extended from Nairobi to support field sites executing clinical studies.
PROGRAMS:

Department of Malaria Immunology
Malaria Clinical Trials
LTC (P) Mark Withers
Background

*Plasmodium falciparum* malaria causes more than 1 million deaths per year. In lowland holoendemic areas of sub-Saharan Africa, such as in western Kenya, it is the children who bear the brunt of the morbidity and mortality due to malaria. Malaria in western Kenya is holoendemic. Malaria transmission occurs all year but at a very high level during the two rainy seasons. Several malaria chemotherapy and epidemiology studies have been done on the adult population for decades. These studies typically demonstrate about 90% prevalence of parasitemia over 12 weeks during a high malaria transmission period.

The Walter Reed Project (WRP) and the Kenya Medical Research Institute (KEMRI) have been involved in malaria research in western Kenya for many years. These studies cover nearly every aspect of the disease - epidemiology, entomology, immunology, hospital-based treatment trials, and community-based studies of antimalarials. The WRP/KEMRI laboratories near Kisumu have served as the base for both phase I and II trials of candidate malaria vaccines and antimalarial drugs over the past decade. In spite of these research efforts, malaria infections in this area continue unabated and improved control strategies are needed.

Worldwide, the populations at risk for malaria include not only the infants, children and adults in malaria-endemic regions, but also non-immune travelers to malarious areas. This includes vacationers and deploying military personnel. A safe and effective vaccine that prevented infection, or even merely checked the clinical symptoms, of *P. falciparum* malaria would be a milestone public health achievement and would bolster efforts to control this most insidious infectious disease around the world. The increasing prevalence of drug resistance in various malaria strains makes the development of an effective vaccine an international priority in the struggle for control of this devastating disease.

The target population for this particular vaccine is children at risk for clinical disease (including severe disease) due to infection with *P. falciparum*. The Walter Reed Army Institute of Research in collaboration with the Malaria Vaccine Initiative and GlaxoSmithKline are undertaking multi-year clinical studies to test the safety and efficacy of MSP-1 at USAMRU-K. MSP-1 can only be tested for proof of concept in populations with high malaria transmission rates, as there is no predictive animal model and no reliable challenge system to detect efficacy against clinical malaria. This vaccine construct has been tested in malaria naïve adults (US) to establish safety, reactogenicity and to identify a dose for further evaluation. It was subsequently evaluated in semi-immune Kenyan adults and has been found to be safe, well tolerated & immunogenic in this population. An epidemiological study and a dose escalating and age stratified Phase 1 clinical trial are in progress to provide safety and baseline data in children in anticipation of Phase 2b efficacy trial in FY05.
Accomplishments:

1. Completed product administration phase of a age-stratified dose escalating Phase 1 clinical trial of MSP-1 adjuvanted with GlaxoSmithKline AS02A (FMP-1) in 135 Kenyan children. Study is now in the active follow-up phase.
2. Completed the dosing phase of a 270 children epidemiological study. Subjects received treatment dose of antimalarial drug (Coartem) or placebo and will be followed parasitologically for one year
3. Commenced construction of a sq ft annex to the clinical research facility in Kombewa. When completed the annex will house offices, conference rooms, IT, data and supplies storage space reserving the existing building for patient and clinical activities.

Malaria Pathogenesis - 1
COL Jose Stoute
Background:

*Plasmodium falciparum* malaria causes more than 1 million deaths per year. Most of these deaths occur as the result of complications such as severe malarial anemia and cerebral malaria. In lowland holoendemic areas of sub-Saharan Africa, such as in western Kenya, it is the children who bear the brunt of the morbidity and mortality due to malaria. Here, the most common complication is severe malarial anemia that occurs from a few months after birth, when transplacental immunity begins to wane, up to 24 months of age. Cerebral malaria is relatively rare in holoendemic areas and, when it occurs, it is usually seen in 2 to 5-year-olds. Adults are not as susceptible as children due to the acquisition of immunity after prolonged exposure. By contrast, in areas of the world with low transmission severe malarial anemia is still confined to young children but cerebral malaria makes up a larger proportion of the cases of severe malaria and is more common in older children and adults. Our research program aims to increase our understanding of the pathogenesis and the pathophysiology underlying the contrasting epidemiology of the severe disease.

To understand the pathogenesis of severe malarial anemia, we have examined the role of RBC complement regulatory proteins in malaria. Complement receptor 1 (CR1, CD35), decay accelerating factor (DAF, CD55), and membrane inhibitor of reactive lysis (MIRL, CD59) are RBC surface proteins that promote the inactivation and binding of C3b in immune complexes (ICs) to (CR1), promote inactivation of C3b convertases (CD55), and interfere with the assembly of the membrane attack complex C5b-9 (CD59). Consequently, complement regulatory proteins may play an important role in protecting RBCs from complement activation and IC formation that occurs during malaria infection. In support of this hypothesis, work from our laboratory has shown that RBCs of children with severe malarial anemia are deficient in the complement regulatory proteins CR1 and CD55.
In addition to its potential role in the development of severe malarial anemia, CR1 has been implicated in the pathogenesis of cerebral malaria. RBCs infected with mature malaria parasites (trophozoites and schizonts) form rosettes by binding to CR1 present on the surface of uninfected RBCs. As the number of CR1 molecules on RBCs increases, so does their propensity to form rosettes. Rosette formation has been linked to the development of cerebral malaria, as it is more common in parasite cultures from patients with cerebral malaria than in cultures from patients with uncomplicated malaria. Rosettes are thought to play a role in the pathogenesis of cerebral malaria by plugging cerebral capillaries thereby interfering with cerebral blood flow.

Accomplishments:

1. Demonstrated differences in level of expression of CR1 and CD55 in children with severe malarial anemia and controls, and children with cerebral malaria and controls (Error! Reference source not found., Error! Reference source not found.).
2. Showed that RBC complement regulatory proteins have an age-dependent pattern of expression increasing from childhood to adulthood (Manuscript in preparation).
3. Showed that children with severe malaria have increased levels of immune complexes (Manuscript in preparation).
4. Showed that monocytes from children with cerebral malaria have high level of expression of the complement receptor 3 (Manuscript in preparation).
5. The study of the pathogenesis of severe malarial anemia is underway supported by a 4-year NIH grant.
6. The training of 3 Kenyan Ph.D. candidates is in progress supported by a grant from the Fogarty International Center.

Publications:


Malaria Pathogenesis -2
Dr. John Waitumbi

Background:
Non-immune patients infected with *P. falciparum* develop varying levels of disease severity. In the individuals who develop severe malaria, one of the most obvious parameter that is associated with severity is the level of parasite density. In the absence of specific anti-parasite immune responses in non-immune individuals, it is reasonable to assume that certain strains of *P. falciparum* cause severe disease because they have an imbalance between cell proliferation and cell loss. This assumption is strengthened by observation: 1) chemoprophylaxis that solely limits parasitemia reduces morbidity and mortality and 2) the in vitro growth rate of parasites differ intrinsically between strains. Thus, understanding the basic mechanisms that underlie cell death may point to potentially new targets for therapeutic interventions to slow cell proliferation. One of the physiological mechanisms of reducing cell numbers is by apoptosis. Apoptosis is an active biochemical process that involves changes on three essential cellular components, namely, DNA, protein and lipid and once initiated irreversibly commit cells to death.

The molecular mechanisms involved in apoptosis are complex but they eventually involve DNA fragmentation, activation of caspaces and externalization of phosphatidylserine (PS). DNA double strand cleavage in apoptotic cells occurs at the linker regions between nucleosomes to produce fragments that are multiples of approximately 185 bp. These fragments can easily be demonstrated by agarose gel electrophoresis as characteristic ladders. *De novo* protein synthesis and/or the modification of existing proteins (such as caspaces) is another important attribute of apoptosis. Finally, lipids are also involved and several apoptotic pathways use signal-transduction pathways based on membrane receptors and membrane-derived phospholipid precursors as second messengers.

This study proposes to determine whether there are fundamental differences in the apoptotic processes between strains of *P. falciparum* that maintain low parasite densities and those that maintain high parasite densities as measured by cell cycle distribution of DNA, DNA fragmentation and externalization of PS.

Accomplishments:

1. Established two *P. falciparum* cell lines with differential growth doubling time: These PF strains will be used to study whether apoptosis is involved in growth rate regulation.

Trainees:
PhD candidate thesis - The role of apoptosis in regulating *P. falciparum* cell numbers in non-immune individuals.

**Department of Anti-malarial Drug Discovery**
MAJ Shon Remich

**Background:**
Our scientific research is conducted in two separate laboratories with distinct but complimentary efforts. The Malaria Drug Screening Laboratory conducts research aimed at malaria drug discovery and drug resistance. Malaria drug discovery efforts currently test natural products, both as plant extracts and purified compounds, for their ability to kill the malaria parasite in culture. These efforts are aimed at identifying a naturally produced compound that can be transitioned into advanced development as a new anti-malarial drug. Drug resistance research is in support of the USAMRU-K GEIS program which has identified several geographically distinct areas of Kenya and Uganda where malaria parasites are collected, transported to the laboratory, and tested against a panel of 15 known anti-malarial drugs for their drug susceptibility profiles. This laboratory also will support malaria drug clinical trials with the culturing and testing of field isolates of malaria. The Molecular Malaria Laboratory conducts scientific research aimed at understanding the molecular mechanisms of drug resistance. Several genes are well characterized as obtaining mutations that confer resistance to several currently prescribed anti-malarial drugs. Identification of these mutations allows our laboratory to assess the severity of drug resistant malaria and provide indications as to the effectiveness of current and future anti-malarial therapies. This laboratory also conducts basic science projects aimed at identifying Plasmodial enzyme pathways that can be targeted for drug discovery.

**Department of Entomology. (STEP I. U):**
LTC Van Sherwood

**Background:**
In FY03, the Entomology program at USAMRU-Kenya supported three primary research programs in Kenya. These programs covered malaria research in western Kenya and the city of Nairobi and arbovirus vector research along the coast of Kenya. Approximately 40 casual (full-time) employees were hired to assist in these programs and two vehicles were dedicated for support of the entomology project in western Kenya. An entomology laboratory was established at headquarters in Nairobi that supports specimen identification, storage (-70°C freezers), and PCR requirements.

The project in western Kenya was designed to study the ecology of malaria vectors with the use of remote sensing and GIS to develop a new dry season malaria vector control strategy. The combined vector, environmental, and map database were used to address questions about malaria transmission focality. Maps of the site were constructed using the differential global positioning system (GPS). The maps include permanent water sources and areas to find malaria vector eggs during the dry season. On-site mosquito collections provided data for Entomological Inoculation Rates (EIRs) which indicated
that the highest monthly EIR was 0.14, or an infective bite every three days in May. It was also determined that An. funestus tend to seek blood meals earlier than infective An. gambiae. This finding will have significant impact on transmission, and on assessment of disease risk since early biting infective vectors are more likely to find unprotected hosts.

In Nairobi, a malaria vector surveillance program established in the Kibera shantytown, a district of the city with >700,000 inhabitants was continued. Urban malaria is having an increasing impact in sub-Saharan Africa and in Nairobi the ecology is further confounded by the fact that the city is at an altitude of approximately 1 mile. Two of the most important vectors, An. gambiae and An. arabiensis, were found throughout the year in Kibera although at extremely low population densities. It appears that during the drier seasons these vectors are breeding in polluted streams that border the edge of the shantytown. No infected vectors were collected; however, our collections were not conducted specifically in areas of suspected local transmission based on travel histories of infected individuals.

Recent data from the Coast Province indicated ongoing dengue transmission. An arbovirus surveillance program was established that initially focused on vector surveillance in the localities of the identified infections. Household vector surveillance was conducted throughout the year and collected eggs from ovicups to determine the presence/absence of the vector in the area. Aedes aegypti is the primary dengue vector but other potential vector species are present. Ae. aegypti is not usually found indoors although larvae are quite abundant especially during the rainy seasons. Temperature and humidity data for the study area was collected. A human use protocol for a dengue serosurveillance study was submitted through KEMRI. Potential study sites were identified in Mombasa and Malindi. In addition to these studies, entomology provided support for CONUS based programs to include phase one of the Dengue Vector Control System device testing. This 15 week test program was designed to evaluate the effectiveness of traps for collecting dengue vectors. Support was also provided for several leishmaniasis programs/protocols.

Accomplishments:
1. Mapped distribution and vector species abundance in Kamonye and Kombewa in support of ongoing malaria drug and vaccine studies.
2. Determined malaria vector species abundance and distribution by ELISA
3. Determined subspecies variance of Anopheles gambiae complex
4. Monitored Entomological Inoculation Rates (EIR) in villages participating in intervention studies. Analyses have been expanded to include PCR analysis of the sporozoites from Plasmodium-positive mosquitoes to determine resistant genotypes in the vector population for comparison with the prevalence in the serological samples from vaccine and drug trial participants.
Department of HIV/AIDS (STEP H.)
MAJ(P) Gimamarie Foglia

Background:
The United States Military HIV Program is a joint collaboration between the Walter Reed Army Institute of Research and The Henry M. Jackson Foundation in Washington, D.C., U.S.A. The United States Army Medical Research Unit – Kenya (USAMRU-K) HIV/AIDS activities is located at the tea growing highlands in Kericho, Rift Valley Province. USAMRU-K provides regional coordination between our programs in Uganda, Tanzania, and Cameroon. The primary mission of the Project is to develop and test strategies to prevent HIV infection globally to include a safe and effective vaccine for HIV. The current rationale is to develop vaccines based on the genetics and subtypes or clades of the viruses prevalent in different regions of the world. The program is already advancing a second-generation, clade E vaccine strategy to efficacy testing in Thailand, where clade E is most prevalent. A similar strategy will be employed in East Africa where clades A, C, and D are contributing in varying proportions to the HIV epidemic in the region.

A key element in developing a vaccine is to appropriately identify cohorts in which to conduct vaccine trials. Cohort development work has already commenced with about 3000 subjects enrolled for follow-up at six monthly intervals. Analysis of the data from the cohort study will inform about: (1) the incidence and prevalence of HIV, (2) characterize the risk factors associated with HIV infection, (3) determine the viral clade and recombinations of HIV-1 in the population, (4) characterize the kinetics of HIV-specific immune responses, CD4 counts and viral loads in early HIV infection and in the face of malaria co-infection, and (5) characterize the drug resistance patterns of Plasmodium species.

In addition to conducting research, the Program also undertakes HIV prevention and treatment programs. Currently, we are actively educating the local communities about HIV through “barazas” where our staff performs drama relating to HIV risk behaviors and illness in Kiswahili and English. Our Program conducts workshops to update the local medical community and facilitates the development of other prevention programs such as mother-to-child transmission and HIV in the workplace. The care and prevention component of the program will be subsumed under the Presidential Emergency Program for Aids Relief (PEPFAR). USAMRU-K is equally engaged with other USG agencies in the planning and execution of this new Presidential Initiative. The Boston University School of Public Health in collaboration with USAMRU-K successfully completed a retrospective study to estimate the impact of HIV-morbidity on labor productivity in the Kenya Highland tea estates. The results of this recently published study will underpin additionally funding from the NIH to undertake prospective studies in the near future. The clinical Research Building and Maternal and Child Health Clinic at the Kericho District Hospital premises was completed and dedicated in March 2004. It is now serving the needs of the program, the hospital and the community.
III. ACCOMPLISHMENTS:
1. Completed HIV Productivity Study in collaboration with Boston University School of Public Health
2. Continued the administration of Nevirapine and free Determine HIV Rapid tests, to HIV-infected mothers and their babies to prevent vertical transmission of HIV (PMTCT) at Kericho hospitals. This work was expanded to over 15 PMTCT sites and over 7,000 pregnant women were counseled and tested. This work was done in collaboration with the Elizabeth Glaser Pediatric AIDS Foundation and Abbott Laboratories.
3. Commenced “HIV and Malaria Cohort Study Among Plantation Workers and Adult Dependents in Kericho, Kenya” in June 2003. Work under this protocol will determine the incidence of HIV-1 in workers and adult dependants on the tea plantation and characterize the risk factors associated with HIV-1 infection.
4. Continued community programs for voluntary counseling and testing which was initiated in 2000.
5. Developed HIV-1 Postexposure Programs (PEP) for Kericho Hospitals and sponsored training of their Medical Officers supervising PEP in September 2002. PEP program has been successfully transferred to other laboratories in Kenya, Uganda and Tanzania.
6. Obtained funding from the AIDS Vaccine Advocacy Coalition (AVAC) to purchase essential medical equipment for the Kericho District Hospital Maternity and Delivery Wards in January 2003. Purchased items will help to prevent the transmission of HIV-1 from mother to child.
7. Commenced Proficiency Testing of all ELISA/Western Blot and rapid HIV tests to maintain quality assurance and control at all laboratory sites involved in the WRP HIV Vaccine Cohort Development and Elizabeth Glaser Pediatric AIDS Fund for Prevention of Mother to Child HIV Transmission.
8. Trained three WRP Staff Medical Officers on the administration and monitoring of HIV–infected patients in a 1 month clinical didactic course at Makerere University in Uganda. These clinicians are now training other WRP staff on HIV care and treatment.
10. Obtained free Donation of Diflucan from Pfizer in December 2003 to treat HIV-infected patients with cryptococcal meningitis and esophageal candidiasis.
11. Developed President’s Emergency Plan for AIDS Relief (PEPFAR) plan for USAMRU-K in conjunction with the U.S. Military HIV Program, in Dec 2003. This program will be implemented in the Kericho, Kenya region in 2004.
12. Commenced antiretroviral pilot program to include building infrastructure and training staff for dispensing antiretroviral therapies and monitoring patients.
GRANTS, CONTRACTS, CRDAs

Cooperative Agreement, Award No: DAMD17-02-2-0022. Military-Relevant Infectious Diseases Endemic to Kenya: Epidemiology, Immunology, Pathophysiology, Treatment and Prevention (a P6 contract awarded by USAMRAA, Fort Detrick, MD; Award amount $4,914,896.00). PI: Dr. Davy K. Koech (Performance period 1 March 2002 to 28 February 2005).

CRADA, Award No: CRADA DAMA-17-02-0148. Research and Development on the Clinical Development of a Malaria Vaccine Made with FMP-1. (a P6 contract awarded by PATH to WRAIR). USAMRU-K component of CRADA administered within the Cooperative Agreement.

National Institutes if Health Grant #1 ROI HL71502-01 to Henry M. Jackson FDN for the Advancement of Military Medicine sub-awardee KEMRI for $327,476.52 – Role of Immune Complex in Severe Malarial Anemia. PI: Dr. Jose Stoute; Project period 15 AUG 2003 to 30 JUN 2004.
PLANS AND STRATEGIES FOR THE FUTURE

USAMRU-K has continued with its rapid expansion in the second year of the Cooperative Agreement. The new clinical Research Facility in Kombewa has successfully completed a Phase 1 FMP-1 vaccine trial in a semi-immune adult population and two additional studies are in progress. A Phase 2b malaria vaccine efficacy trial in children is planned for the first quarter of its last year. An annex building is under construction in Kombewa that upon completion will permit vaccine and drug development studies to be conducted simultaneously at the clinical facility. Thirty kilometers away in Kisumu, a 64 bed pediatric wing and a research laboratory are under construction. The basic malaria immunology and drug studies conducted in the new facilities in Kisumu will complement the resources in Kombewa to transform USAMRU-K into a premier site for clinical, research, and training in parasitic diseases in Africa. This work will be supported by a NIH grant and a Fogarty International Center grant that will both extend into the end of this CA. The challenge of the future is to find major long term funding to keep these invaluable resources solvent after the PATH CRADA, NIH and FIC grants expire in the subsequent CA.

Likewise, Kericho is undergoing a major transformation. A modern clinical research facility and a maternal and child health clinic were dedicated in March 2004 and are now operational. IT assets are also being put in place to support future trials of HIV vaccine candidates. Infrastructural upgrading and institutional strengthening will continue into the final year of the Agreement. Efforts to expand our drug development program are underway and the annex in Kombewa is being constructed to absorb this growth. Future projects will expand our activities to include the Maseno University and KEMRI, Alupe campuses. A seven site surveillance network is now in place under our GEIS program and there are plans to extend it into other countries in sub-Saharan Africa. The unit saw nine of its ten TDA positions occupied by US active duty officers or GS-civilian working as PIs on its programs. Efforts continue at the State Department level to expand the allowable positions from ten to eleven. However, there is a limit to the number of active duty and civilian US personnel that can be deployed into the country to run an ever expanding research and operational mission. Therefore, in the final year of the CA, emphasis would continue to focus on recruitment, training, and the establishment of retention programs for Kenyans at the highest levels of the organization. We look forward to a future where collaboration between the unit and local institutions will increase and integration will be achieved at all levels of our operations.