

MHRP EXCHANGE



Volume 2, Issue 1
Winter 2014

NEWS FROM THE U.S. MILITARY HIV RESEARCH PROGRAM AT THE WALTER REED ARMY INSTITUTE OF RESEARCH

MHRP to Join the HVTN and ACTG Networks as an NIH-funded Clinical Trials Unit

The U.S. Military HIV Research Program has been selected as a Clinical Trials Unit (CTU) with four clinical research sites that will receive funding from the National Institute of Allergy and Infectious Diseases (NIAID) to continue HIV vaccine and therapeutics research.

MHRP will conduct research as part of the HIV Vaccine Trials Network (HVTN) and AIDS Clinical Trials Group (ACTG), which it has already been a part of since 2008. The HVTN and ACTG are two of five Clinical Trials Networks directed and funded by NIAID that work together to address NIAID's HIV/AIDS scientific priorities.

"The designation of MHRP as a CTU by NIAID will allow us to extend and expand our current research, leveraging the robust international clinical trial infrastructure we already have in place and working collaboratively with the broader Networks to achieve the shared vision of an AIDS-free generation," said MHRP's Director, Col. Nelson Michael.

Col. Michael will serve as the MHRP CTU's Principal Investigator and will oversee the following clinical research sites:

This award will allow MHRP to expand its HIV research and leverage its robust clinical trial infrastructure in Africa.

- Kenya Medical Research Institute/Walter Reed Project Clinical Research Center, Kericho, Kenya (ACTG)
- Moi University Clinical Research Center, Eldoret Kenya (ACTG)
- National Institute for Medical Research – Mbeya Medical Research Center, Mbeya, Tanzania (HVTN)
- Polana Çanico Health Research and Training Center, National Institute of Health, Maputo, Mozambique (HVTN)

Since becoming a CTU for the ACTG network in Kenya, MHRP has participated in many high-priority therapeutics studies including OCTANE (Prevention of Mother-to-Child Transmission) and STRIDE (TB), both of which were published in the *New England Journal of Medicine*.

Continued on page 6

HIV Incidence Study Begins in Mozambique



CISPOC and MHRP staff convened in Maputo to prepare for the start of RV363.

In December 2013, MHRP began the RV363 study to assess the incidence of HIV and the willingness of adults to participate in future HIV vaccine trials in Mozambique. The study will determine incidence in men and women aged 18–35 in both Maputo and Beira.

The retention rate of the enrolled cohort will be assessed over a 2-year follow-up period with a quarterly follow-up visit. RV363 also will serve as a mechanism to further augment the clinical, laboratory, data management, quality assurance and community engagement capacity at these sites for upcoming HIV vaccine trials.

MHRP is conducting research in collaboration with the National Institute of Health, Polana Çanico Health Research and Training Center (CISPOC) in Maputo and the Catholic University of Mozambique, Research Center for Infectious Diseases (CIDI) in Beira.

IN THIS ISSUE

- 2 MHRP Diagnostics: Unique Capabilities Within DoD
- 3 MHRP's World Aids Day Activities
- 5 Focus on Acute Infection Studies
- 6 NIAID Director Anthony Fauci, M.D. Visits AFRIMS

MHRP Diagnostics: Unique Capabilities Within DoD



MHRP's Department of Laboratory Diagnostics and Monitoring (DLDM) conducts state-of-the-art HIV and HIV-related infections diagnostics and cutting-edge diagnostic research. The diagnostics program boasts unique capabilities that aren't replicated within the Department of Defense (DoD). The following is a Q&A with MHRP Diagnostics Chief, Sheila Peel, MSPH, Ph.D.

What is DLDM's diagnostics mission?

The first mission focus of MHRP was the development, optimization, and deployment of HIV diagnostic, clinical and therapeutic monitoring technologies for soldiers. It was one of two original departments—Retrovirology Diagnostics and Retrovirology Research—authorized by Congress in 1986. Today, MHRP remains a DoD leader in the development of infectious diseases diagnostic countermeasures and militarily-relevant research. Our diagnostics program is intensely focused on solving problems for the warfighter and DoD beneficiary.

What are MHRP's clinical diagnostic capabilities?

DLDM's HIV Diagnostics and Reference Laboratory (HDRL) provides direct HIV testing support to the U.S. Military European and Central Commands and by request to 51 medical treatment facilities. We conduct all U.S. Army HIV confirmatory testing; thus, determine the HIV infection status classification for all Army personnel. To do this, we developed the most advanced HIV diagnostic algorithm in the U.S., setting the standard for HIV diagnostics. Additionally, we provide HIV clinical monitoring (viral load) services for all Army and Navy HIV-infected personnel and HIV resistance genotyping for all HIV-infected DoD service members. Finally, we are the Tri-Service HIV Reference laboratory and provide diagnostic consultative services and resolution of HIV and related disease infection status.

How does Diagnostics play a role in protecting soldiers?

The ability to quickly detect and sequence sexual and/or transfusion-transmitted infections—not just HIV, but others such as hepatitis C

and HTLV—ensures a safe battlefield blood supply, informs clinical decision making and countermeasure development.

Emergency blood transfusion with non-FDA compliant blood products voluntarily donated by service members is a life-saving procedure used on today's battlefields; HIV infection screening of all service members before they deploy and the use of highly sensitive and specific point-of-care (POC) tests for infection detection prior to fresh whole blood transfusion is critical for the well-being of our injured troops. We have been engaged in evaluating and selecting POC products not only for the battlefield, but areas of operation where troops do not have ready access to care.

Are you involved in HIV/AIDS threat assessment for the military?

We work closely with MHRP epidemiologists to monitor HIV infections among soldiers. Our laboratory data assists public health investigations in determining time, location and mode of acquisition for all deployment-related infections as well as identifying potential HIV transmission networks. Data we generate facilitates identification of targets for preventive interventions and informs policy development within the DoD.

What is your role in product development?

DLDM's HDRL and Technology Assessment Laboratory evaluate and deploy new serological and molecular-based tests for HIV and related diseases. We work with many industry partners to develop, license, and acquire new assays, or "products," to guarantee DoD is using the best products available to support the warfighter.

DLDM participates in two to five premarket application FDA clinical trials for new U.S. product approvals per year; 50% of currently used FDA-licensed HIV screening and monitoring assays were evaluated in our laboratories.

How does Diagnostics support MHRP's clinical research and global health programs?

We develop and deploy diagnostic approaches to advance MHRP's HIV cohort, vaccine, and therapeutic clinical trials. For example, we developed a novel way to screen for HIV in RV217, the acute HIV infection study. We are currently developing a diagnostic

Continued on page 6

Dr. Jintanat Ananworanich Joins MHRP



MHRP welcomes Dr. Jintanat Ananworanich as the Associate Director for Therapeutics Research. In this new role, Dr. Ananworanich will oversee adult HIV therapeutic trials as part of the newly funded MHRP Clinical Trials Unit under the ACTG. She comes to MHRP from the Thai Red Cross in Bangkok where she served as the Director of SEARCH and Deputy Director of Scientific Affairs at the HIV Netherlands Australia Thailand

Research Collaboration (HIV-NAT) at the Thai Red Cross. Dr. Ananworanich has collaborated with MHRP since 2005 as part of

the joint HIV research effort between MHRP, the Thai Red Cross AIDS Research Center and the University of Hawaii; she will continue to maintain a strong working relationship between the U.S. and Thailand.

Dr. Ananworanich brings a wealth of expertise in developing protocols and managing adult and pediatric HIV clinical trials. Over the past decade she has led more than 60 studies including the Staccato treatment interruption study that led to a seminal paper in the *Lancet* and the NIAID-funded study, PREDICT, on when to start antiretroviral therapy in children. She has more than 170 publications and is currently the principal investigator on the MHRP/NIAID-funded acute HIV infection study, RV254.

World AIDS Day Activities Around the Globe

Around the world millions of people turned out for activities on December 1 to mark World AIDS Day. See how MHRP’s international sites commemorated the day.

Thailand

Staff from the ECHO Clinic represented the AFRIMS Division of Retrovirology in Pattaya, Thailand’s annual World AIDS Day parade—an event organized by the Pattaya city council. Pattaya, a Thai vacation destination with a large population of MSM and transgender women and an ongoing high rate of HIV, is also home to the ECHO Clinic where MHRP’s acute HIV infection study (known as ECHO or RV217) is taking place in Thailand.



AFRIMS staff took part in Pattaya’s annual World AIDS Day parade, which ended at a local school where city officials publicly thanked those individuals who are working to prevent and treat HIV.

Kenya

At an event in Nairobi, the Kenya Defence Forces (KDF) Vice Chief of Defence Forces Lt. Gen. Samson Mwathethe led soldiers in marking World AIDS Day. Following a speech that touched on stigma, voluntary medical male circumcision and HIV prevention, Lt. Gen. Mwathethe, as well as Chief of Medical Brig. Gen. Christopher Arrum, tested for HIV at the event.

Uganda

To commemorate World AIDS Day, Ugandan and American Embassy staff volunteered at six sites supported by the American people through the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR). The sites included the Mukono District Youth Center that was opened by MHRP’s Makerere University Walter Reed Project in 2012, as well as the Mildmay Uganda, L Giussani Secondary School, Hospice Africa Uganda, Makerere University Hospital and the Kiswa Health Center IV.

Tanzania

The Walter Reed Program (WRP-T) outreach team reached thousands of people with HIV prevention messages and HIV testing in the days leading up to World AIDS Day. Local activities included:

- A series of five debates involving nearly 200 community members. Participants engaged in in-depth discussions on issues such as the driving factors for new HIV infections, stigma and AIDS-related deaths.
- Nineteen peer educators reached more than 2,100 people with HIV and AIDS education and prevention messages. Educators traveled to multiple areas with a mobile cinema van and road show truck to deliver the messages.
- A football and netball tournament that reached large crowds of fans. Additionally, a booth was set up to conduct HIV testing onsite.
- From November 28 through December 1, WRP-T staff conducted mobile voluntary testing and counseling. More than 2,200 individuals were tested for HIV during this time period.



Through the use of mobile testing clinics, over four days WRP-T staff tested more than 2,200 people in five wards of the Sumbawanga Urban District in the Rukwa region of Tanzania.



Nearly 200 people turned out for debates held in five wards of the Sumbawanga Urban District where community representatives discussed issues that precipitate or are fueling the high prevalence of HIV in the Rukwa region of Tanzania.

Care and Treatment Clinics in Tanzania Receive New Laboratory Equipment with the Help of the Walter Reed Program-Tanzania



On December 1, Tanzanian Vice President Dr. Mohamed Gharib Bilal handed over a CD4 machine to the Mbeya region. The machine was the first of 37 to be distributed in the Southern Highlands region of Tanzania where MHRP works and is known locally as the Walter Reed Program (WRP-T). The machines will be used in 21 care and treatment clinics around the Southern Highlands. Support for the machines came from PEPFAR through WRP-T.

In his speech, the Vice President thanked the American people and specifically called out the Walter Reed Army Institute of Research for the support. Additionally, he introduced a new “Zonal Strategy” to respond to HIV/AIDS in Tanzania. The strategy will be carried out in eight zones around the country, the first of which will be the Southern Highlands.

Maryland, U.S.A.

On December 2, the Walter Reed Army Institute of Research (WRAIR) community gathered to mark World AIDS Day. Speakers included Dr. Edmond Tramont of NIAID who was the first leader of MHRP at WRAIR; Dr. Mary Marovich of the NIAID Division of AIDS; MHRP collaborator, Dr. Jintanat Ananworanich (by video) and Col. Shon Remich, WRAIR and who previously led the DoD PEPFAR program in Kenya.



Pictured left to right: Dr. Mary Marovich, Col. Steven Braverman, Dr. Ed Tramont, Col. Shon Remich and Col. Jerome Kim.

Nigeria

Walter Reed Program-Nigeria (WRP-N) World AIDS Day activities took place at two sites: the 45 Nigerian Air Force Hospital, Makurdi and the 2 Division Hospital, Ibadan.

In Makurdi, WRP-N, in collaboration with the Centre for Infectious Diseases Control (CIDC), 45 Nigerian Air Force, Health Initiatives for Health and Safety in Africa (HIFASS) and Benue Breweries Limited, organised a 7-day program that included medical outreach, HIV counseling and testing and a health bazaar. Between November 25 and December 4, 2,803 people attended the various World AIDS Day activities and received information about HIV and other STIs. More than 1,000 people were also tested for HIV.

In Ibadan, celebrations began with a 10-vehicle motorcade, or rally, that traveled through multiple areas while team members distributed HIV information. After the rally participants could take part in health talks, condom use demonstrations and a play, as well as free medical check-ups and HIV testing and counseling.



A 10-vehicle motorcade help spread HIV awareness in Ibadan Nigeria on World AIDS Day.



At the 45 Nigerian Air Force Hospital in Makurdi, Acting Officer in Command receives an HIV test.

Focus on Acute Infection Studies

The study of acute HIV infection is critical to the design and development of HIV vaccines and strategies to achieve an undetectable level of virus without antiretrovirals, or a functional cure. By diagnosing HIV within weeks or even days of infection, scientists are afforded the opportunity to study the early events following infection. This provides the opportunity to look at what the virus and the cells are doing at various places in the body and identify ways to intervene.

MHRP is conducting two unique studies that are enrolling patients within weeks of HIV infection: RV217, the Early Capture HIV Cohort (ECHO) study and RV254/SEARCH 010. Both studies are enrolling in Thailand and RV217 is also underway at multiple sites in east Africa.

Patients who start ART during acute HIV infection have, at one year, levels of virus similar to that of elite controllers

RV217/ECHO

An observational study taking place at multiple sites, RV217 is designed to characterize recruitment, retention, HIV prevalence, HIV incidence and biological characteristics of acute HIV infection in high-risk volunteers such as sex workers and MSM. The study also seeks to provide a unique set of biological specimens including blood and mucosa. In this unprecedented study, researchers collect very small blood samples twice weekly via finger stick collections. These “small blood volume” visits allow clinicians the opportunity to diagnose HIV infection prior to the advent of detectable antibody by the most sensitive nucleic acid detection techniques available. RV217 has screened more than 3,600 individuals and identified 95 acute HIV infections.

RV254/SEARCH 010

RV254—a collaboration between MHRP and the South East Asia Research Collaboration with Hawaii (SEARCH)—is a similar cohort to RV217, but is also comparing early initiation of HAART to megaHAART. Although no difference in outcome has been seen



A volunteer for the RV217 study in Kenya checks in using her thumbprint.

between the different therapies, researchers have noted that patients who start ART during acute HIV infection have, at one year, levels of virus similar to that of elite controllers, or the small percentage of people who can naturally control the HIV virus. Furthermore, the earlier patients start treatment the less integrated HIV DNA they have in their central memory CD4+ T cells, which historically has been a major barrier to curing HIV.

To date, RV254 has screened nearly 88,000 people and identified 158 acute HIV infections. Confirmation of acute infection to enrollment into the study occurs within three days and treatment is initiated within two days following enrollment. The majority of RV254 participants were enrolled within 2-3 weeks of infection.

While researchers believe that early diagnosis and immediate treatment are the stepping stones to a functional cure, more research is needed to better understand the adaptive, innate and host responses that alter viral load set-point and consequently prognosis and infectiousness.

Watch a video about RV254:



Dr. Jintanat Ananworanich, along with colleagues from AFRIMS, describes the RV254 study in greater detail and discusses what makes this research so unique. Watch the video at <http://ow.ly/soAgh> or scan the code with your smartphone.

Moving RV217 Forward: Collaborators Meet in D.C.



MHRP hosted the “laboratory analysis RV217 working group meeting” on January 8 at its headquarters. The meeting included collaborators from AFRIMS, VRC, DAIDS, MHRP, Ragon, Duke, UPenn, VGTI, and UNC. RV217 has many unique elements including the acquisition of samples prior to HIV infection, the potential to acquire samples during the eclipse phase of infection prior to detectable HIV nucleic acid but after actual infection has occurred, and the collection of samples prior to peak viremia and the advent of antibody responses.

The success of the study in collecting these unique samples has attracted world renowned scientists to work as collaborators on the analysis of samples. The meeting, with more than 20 short scientific presentations, provided an update on ongoing laboratory analyses and upcoming research that has been approved by the RV217 Scientific Steering Committee with emphasis on promoting coordination and synergy among the RV217 collaborators.

NIAID Director Tours HIV Laboratories at AFRIMS



NIAID Director Dr. Anthony Fauci was recently in Thailand to receive the Prince Mahidol Award for his contribution to AIDS prevention and control. While there, he paid a visit to the Division of Retrovirology at the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, which played a critical role in executing the RV₁₄₄ HIV vaccine trial. He also visited the Thai Red Cross, where MHRP and collaborators are conducting the acute infection study, RV₂₅₄. AFRIMS staff also escorted Dr. Fauci on a visit to Pattaya, located 60 miles southeast of Bangkok, where MHRP is currently conducting its acute HIV infection study, RV₂₁₇/ECHO.

Diagnostics

Continued from page 2

tool to distinguish a vaccine-induced test result, or Vaccine-induced Seropositivity (VISR), from that of a true HIV infection-induced positive test. We manage MHRP's 2.7 million sample biorepository; receiving and reposing ~60,000 samples per annum and redistributing to our collaborators ~8,000 samples per year. We support our colleagues in global health through diagnostic consultations, laboratory audits, and human and infrastructure capacity building.

MHRP Diagnostics by the Numbers:

119,002 - Average reportable HIV test results generated between 2010 and 2013

85,000 - Approximate number of HIV screening tests conducted per year in support of EUCCOM and CENTCOM

1.2 Million - Yearly number of HIV tests the laboratory provides technical oversight authority (all Army and Military Entrance Processing Stations)

2,722,032 - Samples managed in the Specimen Processing Laboratory (current total)

Exchange is published by the Communications Department of the U.S. Military HIV Research Program through a cooperative agreement with the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. Contents of this publication are not necessarily the official views of, or endorsed by, the U.S. Government or the Department of Defense. Depiction of individuals in photographs does not indicate HIV status.

Please submit your questions and comments via email to communications@hivresearch.org. Editors: Lisa Reilly, Stephanie Stevens

For more information visit: www.hivresearch.org. Connect with us on Facebook and Twitter!



MHRP Selected as CTU

Continued from page 1

MHRP's newest research sites are in Mozambique, where clade C is the predominant HIV subtype. MHRP will participate in planned HVTN-led studies in the region that will test a vaccine regimen similar to the one used in RV₁₄₄ but targeted for subtype C. This research is part of the Pox-Protein Public-Private Partnership (P5).

See MHRP at CROI

MHRP and collaborators will give the following presentations at the annual Conference on Retroviruses and Opportunistic Infections (CROI) taking place March 3–6 in Boston:

Loss of HIV Serological Markers Following Early Treatment of Acute HIV Infection –Mark Manak

Etravirine/Rilpivirine-Specific Mutations Selected by EFV and NVP in Kenyan Patients Failing ART –Keith Crawford

Evaluation of the Hologic Aptima HIV-1 Quant Dx Assay with HIV-1 Subtypes –Mark Manak

CTX Prophylaxis Discontinuation Among ART-treated Adults: a Randomized Non-Inferiority Trial –Christina Polyak

Divergent HIV-specific CD4 T Cell Response Profiles in HIV Vaccine Trials –Franco Pissani

Evaluation of the Proposed US CDC Algorithm for Detection of Acute HIV Infection in Serial Samples –Leigh Anne Eller

Antibody Responses in Anogenital Secretions of RV₃₀₅, a Late Boost Vaccination of RV₁₄₄ Volunteers –Siriwat Akapirat (AFRIMS/MHRP)

Early ART Initiation Prevents Disruption of the Mucosal Barrier and subsequent T Cell Activation –Alexandra Schuetz (AFRIMS/MHRP)

Inflammation in Acute HIV Infection Correlates with Blood and Gut CD4 T-Cell Loss and Viral Burden –Netanya Sandler (MHRP Collaborator)

CNS Outcomes of cART vs. cART plus Maraviroc and Raltegravir Intensification During Acute HIV –Victor Valcour (MHRP Collaborator)

Early Monocyte Inflammation among Treatment-Naïve Acute HIV-infected Thai Subjects –Lishomwa Ndhlovu (MHRP Collaborator)

Immediate Antiretroviral Therapy Mitigates the Development of Neuronal Injury in Acute HIV –Michael Peluso (MHRP Collaborator)

Concentrations of Nevirapine or Efavirenz on and off Anti-Tuberculosis Therapy –Nilesh Bhatt (MHRP Collaborator)