MHRP EXCHANGE

MHRP
U.S. MILITARY HIV RESEARCH PROGRAM

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

MHRP Collaborators Workshop Unites Researchers Around Acute HIV infection

This January, MHRP brought together leading HIV researchers who are collaborating or consulting in the analysis of MHRP's two unique acute HIV infection cohorts, RV254 and RV217.

The meeting included more than 100 researchers from the NIH and academic institutions including Duke, Yale, and UCSF to present data and discuss progress and plans for key research that these cohorts can help answer.

Much of the literature on acute infections is derived from smaller acute infection cohorts that were characterized further out from infection.

"In our cohorts we have samples from volunteers within days of infection," said Merlin Robb, MD, MHRP's Deputy Director of Clinical Research and protocol chair of the one of the studies being conducted in Thailand and Africa. "Data from our cohorts will help explore the very earliest stages of infection which are critical for long term prognosis in the absence of treatment."

Read more about these two acute infection studies on page 4.

MHRP's Dr. Jintanat Ananworanich leads a discussion about data from the acute HIV infections cohorts.

MHRP Researchers Find Viral Burden to be Primary Predictor of HIV Disease Progression

Study suggests predictors of HIV disease progression may be subtype specific

New findings published in the Journal of Infectious Diseases found HIV-1 viral load and subtype to be the primary predictors of disease progression in rural Uganda.

The findings from the collaborative study, lead by researchers at the U.S. Military HIV Research Program (MHRP), is contrary to current understanding that T-cell activation predicts disease progression independently of viral load. Although T-cell immune activation is strongly associated with disease progression in HIV subtype B infections, this study suggests that viral replication is the primary driver of HIV disease in Uganda where subtype A, B, and D containing recombinants circulate.

Michael Eller, Ph. D., lead researcher in the study, said the results reiterate that HIV pathogenesis may be different in the African context.

"There are numerous factors that differ between the African and US or European settings, such as environmental factors, other infections, nutrition, host immunogenetics, HIV viral subtype, predominant mode of transmission, as well as access to treatment," Eller said

"These results are important because more than two-thirds of global infections occur in Africa. We need more studies that characterize what untreated disease looks like in an African setting."

IN THIS ISSUE

MHRP and Ebola Vaccine Development

For more than a century, the US military medical community has solved many significant international health problems, particularly in the area of tropical infectious diseases. This research expertise, along with a robust international clinical trials infrastructure, is being leveraged to help in the US Government's response to the recent Ebola outbreak in West Africa.

Results Published on First Ebola Vaccine Study in Africa

In 2009-10, MHRP's site in Uganda, the Makerere University Walter Reed Project (MUWRP) led the first Ebola vaccine clinical trial in Africa. They tested an early-generation DNA vaccine developed by NIAID's Vaccine Research Center. The study found both the Ebola and Marburg DNA vaccines to be safe and immunogenic in an African setting. The results were published online in the Dec. 2014 edition of The Lancet and helped lead to a clinical evaluation of a more potent ChAd3 vaccine, co-developed by NIAID and GlaxoSmithKline.

Scan the QR code to read MHRP's Ebola article in Lancet

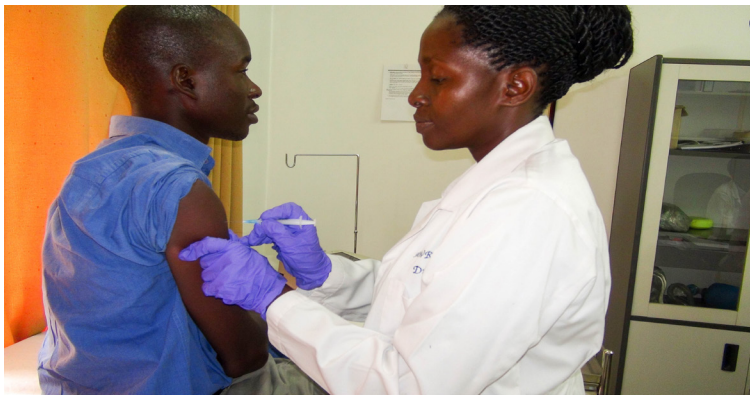
Diagnostic Expertise Provides Crucial Support

The HIV diagnostic research lab within MHRP is providing crucial laboratory support for another novel Ebola vaccine being tested at WRAIR, the VSV-EBOV candidate developed by NewLink Genetics and Merck Vaccines USA in collaboration with the Public Health Agency of Canada.

The team at WRAIR took assays developed at USAMRIID and validated them for wider use within a span of weeks. These lab tests are being used in the clinical studies, and may be used as reference assays in support future trials of this vaccine candidate.

New Ebola Vaccine Trials in Africa

A new Phase Ib clinical trial of two experimental Ebola vaccines began this February in Kampala, Uganda. One vaccine encodes for the Ebola Zaire strain glycoprotein (ChAd3-EBOZ) while the second vaccine encodes for Zaire and Sudan strain Ebola glycoproteins (ChAd3-EBO). As part of this study, some Ugandan volunteers from the 2009 DNA study will receive a boost, or additional injection, with the new vaccine candidate to explore a more long lasting effect of vaccination. Walter Reed Program Nigeria, another MHRP site, will begin testing the Zaire strain Ebola vaccine in a larger Phase II study that will take place at 10 sites in four West Africa countries.



Expertise on the Global Stage: MHRP and the WHO

In addition to the vaccine studies, several MHRP scientists— including Director COL Nelson Michael and LTC Julie Ake — have been consulted by the World Health Organization (WHO) to assist with the planning of upcoming Ebola vaccine studies in West Africa.

World Health Organization

They assisted work with local ethical and regulatory authorities as they strived to expedite these research trials in response to the 2014 Ebola outbreak.

At the Frontlines of an Epidemic: Combating Ebola in Liberia

Last fall, CDR Jennifer Malia, DrPH, MHRP's Assistant Chief of the Department of Laboratory Diagnostics and Monitoring, jumped at the opportunity to deploy to Liberia and treat Ebola patients. Malia spent more than a month in Monrovia, setting up a dedicated Ebola Treatment Center for health care workers and running a laboratory.

CDR Jennifer Malia,DrPH at her station in the Ebola Treatment Unit (ETU) in Monrovia, Liberia.

When the Public Health Service's Chief Medical Officer approached Jennifer Malia about the chance to join the military's team of first responders to treat Ebola in Liberia, Malia didn't hesitate to give her answer.

"I said, 'yes,' right away," she says. "It was scary, but it was an opportunity to be on the ground and making an impact."

After nearly a decade of experience with MHRP setting up and managing HIV laboratories in Africa, Malia said she felt confident in her ability to get the facility off the ground. But she had some difficulty assuring her family of her safety.

"I told my kids, 'This Ebola outbreak – getting it under control and helping people survive – depends on the labs," she said. "I told them, 'Mommy can do this.'"

After a week of safety training at the CDC headquarters in Atlanta, Malia was deployed to Liberia as a part of the first wave of US troops sent to carry out President Obama's directive to set up clinics to combat the virus.

At the time of her deployment, Liberia was climbing toward the peak of its Ebola outbreak. According to the WHO, more than 200 cases were reported each week with transmission spreading rapidly in the country's dense capital of Monrovia.

As a member of the Public Heath Services' "Team One," Malia and her colleagues set up Monrovia's first Ebola treatment unit (ETU) in less than 10 days and immediately began admitting and treating patients.

"We were the first people on the ground and our mission was to see and treat Ebola health care workers," Malia said.

"We were the only team with that directive and part of the President's plan was to assure health care workers that if, God forbid, you had an Ebola exposure risk, there would be a facility that had the capability to run tests, medevac you, if necessary, and provide you with the best level of care possible."

Although Malia didn't treat patients, she spent most of her time in "the hotzone," collecting and testing samples and transporting blood draws to the local USAMRID lab to run Ebola PCR.

Throughout her deployment, Malia said the clinic lost two patients and discharged four. Through it all, she was moved by the sense of community that held Monrovians together, despite a disease that made it impossible to have physical contact.

Members of Team One, the military's first responders to the Ebola outbreak in Monrovia, Liberia.

"The patients we saw were health care workers first. As they got better, they would take care of the sicker patients on the ward with them and they all planned to go back to work at other ETUs after they recovered," she said.

"People lived and they left, and they went back to work. It was truly a unique and emotional experience."

Jennifer Malia is MHRP's Assistant Chief of the Department of Laboratory Diagnostics and Monitoring based at the Walter Reed Army Institute of Research in Maryland.

Cohorts Provide Insight into Crucial Stages of Early HIV Infection

One of the biggest hurdles facing HIV researchers is pinpointing a timeline of viral integration into the host genome. In order to better understand how the immune system responds during the critical moments of acute infection, MHRP hosted a workshop this winter to discuss findings from its two innovative cohort studies in Thailand and East Africa. Learn more about our novel acute cohorts below.

RV254/Search10

In Thailand, MHRP researchers collaborate with the Thai Red Cross AIDS Research Center to identify acutely infected individuals and place them onto ART immediately. Researchers have found that this very early initiation of ART results in immune restoration and a very small or undetectable reservoir of HIV DNA, very similar characteristics to "elite" HIV controllers.

Samples from more than 130,000 individuals have been collected from voluntary testing and counseling clinics in Bangkok. Samples found to be negative with routine testing then underwent a Nucleic Acid Test (NAT). More than 230 people found to be acutely infected were then enrolled in this cohort, and nearly all of them opted to start ART within days of discovering their status.

Early Capture HIV Cohort Study (ECHO) - RV217

Since 2009, MHRP has led an ambitious multi-site study in East Africa and Thailand that follows a group of high-risk volunteers, tracking their HIV status and characterizing their progression through the acute stages of HIV infection. This prospective study has captured samples from some of the earliest stages of HIV infection – in some cases within days – along with blood samples before infection.

To date, more than 2,000 volunteers have been enrolled in the study and 108 incident cases have been observed. Volunteers are enrolled before they begin to show detectable HIV antibodies and if they are subsequently found to be HIV-positive, they are closely monitored for markers of disease progression.

International Consortium Probes HIV-related Neurocognitive Disorders

MHRP is a founding member of the International Neurological HIV Cure Consortium (INHCC), an international alliance dedicated to studying HIV's impact on the central nervous system in the hopes of leveraging those findings to discover a cure for HIV. Using MHRP's novel acute cohorts, INHCC has launched a number of studies aimed at determining the immediate and long-term cognitive and behavioral impacts of acute HIV infection.

The INHCC is lead by Dr. Victor Valcour, of UCSF, Dr. Serena Spudich of Yale University, and MHRP's Dr. Jintanat Ananworanich.

Members of the INCC chat during a meeting focused on neuro-HIV at the Acute Infections Workshop.

New Study to Help Identify Infectious Diseases in Deployed Troops

MHRP is collaborating with Spot On Sciences on a new study for detecting infectious pathogens such as HIV, hepatitis B and hepatitis C and mosquito-borne infections such as dengue, West Nile and chikungunya virus in deployed troops. MHRP seeks to evaluate methods for efficient collection, preservation and transportation of high quality biospecimens, such as blood, from remote locations with limited resources.

"We seek to improve current sampling methods. Specifically, to better preserve specimen integrity, provide ease of transport, maintain rigorous tracking and chain of custody, and permit an accurate result by highly sensitive tests," said Sheila Peel, PhD., Chief, Department of Laboratory Diagnostics and Monitoring at MHRP.

MHRP will investigate whether HemaSpot, facilitates improved specimen integrity for infectious pathogen screening due to its potential ease of use and stability during transportation. HemaSpot is based on dried blood spot (DBS) sampling, a proven technology that has been around for 50 years. The patent-pending device allows blood sample collection to be performed in remote settings, improves sample quality, simplifies collection, and allows for stable sample storage for years at room temperature, all characteristics which facilitate acquisition of blood samples in the field.

The Walter Reed Army Institute for Research (WRAIR) conducts research to diagnose, prevent, and treat infectious diseases, which often pose a unique threat to troops deployed to disease-endemic areas of the world. Screening of soldiers for infectious pathogens requires venipuncture, a process that is not practical in resource-scarce environments. Once whole blood is collected, the next significant challenge is sample transportation under appropriate conditions.

"The US military deploys troops throughout the world for peacekeeping and military missions, exposing soldiers to innumerable infectious diseases. The proposed study will address whether HemaSpot allows efficient collection, preservation and transportation of sufficiently high quality biospecimens for surveillance, epidemiology, and/or diagnostic testing of remote or vulnerable populations," said CPT Brook Postek, the principal investigator of the study at WRAIR.

Spot of Science is supporting this work, with additional funding from the Defense Health Program.

Credit: ARMY

World AIDS Day Round Up

Nigeria:

The Walter Reed Program-Nigeria marked World AIDS Day with a series of coordinated activities alongside the US Embassy in Abuja. WRP-N also hosted several town hall discussions aimed at engaging young adults in taking a greater ownership of their sexual and reproductive health

Thailand:

This World AIDS Day, the ECHO Center collaborated with the city of Pattaya and local government officials 222 to host a World AIDS Day parade and education initiative.

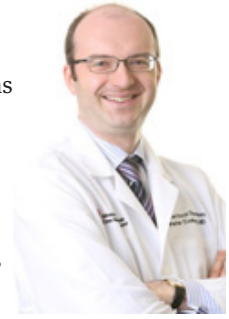
Tanzania:

In Tanzania, The Walter-Reed Program (WRP-T) hosted debates, HIV prevention seminars, and gender-based violence community engagement sessions aimed at opening communication around HIV, sexuality, and prevention.

Welcome Dr. Peter Coakley

MHRP Global Health Program's Associate Director for Medical Affairs

MHRP would like to welcome Dr. Peter Coakley, MD to our Global Health Programs team. Dr. Coakley joins MHRP as the new Associate Director for Medical Affairs. An infectious disease clinician, Dr. Coakley has a passion for improving HIV clinical services through education, mentoring, and the execution of operational research, impact evaluations and clinical studies.



See MHRP and RV144 Collaborators at CROI 2015 in Seattle, Washington

Date	Title	Presenter	Time
Tuesday, 24-February	HIV Burden and Biomarker Associations with Colonic HIV RNA during Acute HIV Infection	Trevor Crowell (MHRP)	Oral presentation 10:15 am
	HIV-1 Infections with Multiple Founders Are Associated with Higher Viral Loads	Morgane Rolland (MHRP)	Oral Presentation 11:00 am
	Efficacy of HIV-1 monoclonal antibody immunotherapy in acute SHIV-infected macaquess	Diane Bolton (MHRP)	Oral Presentation 10:45 am
	HVTN505 Breakthrough Sequences Showed HIV Vaccine-Associated Differences in Env-gp120	Morgane Rolland (MHRP)	Poster Presentation 10 am - 12:15 pm
	Infectious and noninfectious multimorbidity among HIV clinic clients in the African Cohort Study	LT COL Julie Ake (MHRP)	Poster Presentation 2:30 - 4:00 pm
	Acute HIV CSF/Plasma RNA Rations Are Variable and Greater than in Chronic HIV	Joanna Hellmuth (Collab)	Poster Presnetation 2:30 - 4:00 pm
	High Incidence of Syphilis among Thai MSM who Started ART Therapy during Acute HIV Infection	Donn Colby	Poster Presentation 2:30 - 4:00 pm
	Altered Properties of Mucosal NK Cell Subsets during Acute HIV-1 Infection	Aleandra Schuetz (AFRIMS)	Poster Presentation 2:30 - 4:00 pm
	Therapeutic Drug Monitoring of Lopinavir in HIV-infected Children on Second-line ART	Linda Aurpibul (HIV-NAT)	Poster Presentation 2:30 - 4:00 pm
	Correlates of CNS viral transit in acute HIV infection	Joanna Hellmuth (SEARCH)	Poster Presentation 2:30 - 4:00 pm
Wednesday, 25-February	Predictors of Cognitive Performance among HIV-infected Patients in East Africa	Victor Valcour (SEARCH)	Poster Presentation 2:30 - 4:00 pm
Thursday, 26-February	Peripheral T Follicular Helper Cells with Universal Helper Activity in HIV Infection	Hendrick Streeck (MHRP)	Oral presentation 11:00 am
	Inflammation persists despite early initiation of ART in acute HIV infection	Netanya Utay	Oral presentation 10:00 am
	Neutralizing Antibodies Differ Between HIV-1 Infected RV144 Vaccines and Placebos	Shelly Krebs (MHRP)	Oral presentation 12:00 pm
	Higher rate of Hepatitis B antigen and antiHBV antibody seroconversion among HIV/chronic hepatitis B co-infection initiating HBV active HAART from Thailand	Anchalee Avihingsanon (HIV-NAT)	Poster Presentation 2:30-4:00 pm
	Human Papillomavirus and Cervical Cytology in Perinatally Infected Asian Adolescents	Annette Sohn (HIV-NAT)	Poster Presentation 2:30-4:00 pm
	CD14+ PBMC Secrete Cytokines Linked to HIV-Associated Neurocognitive Disorders	Melissa Agsalda-Garcia (SEARCH)	Poster Presentation 2:30 pm - 4 pm
	Astrocyte and microglial activation in acute and chronic HIV pre and post cART.	Michael Psluso (SEARCH)	Poster Presentation 2:30 - 4:00 pm

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

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