MHRP EXCHANGE

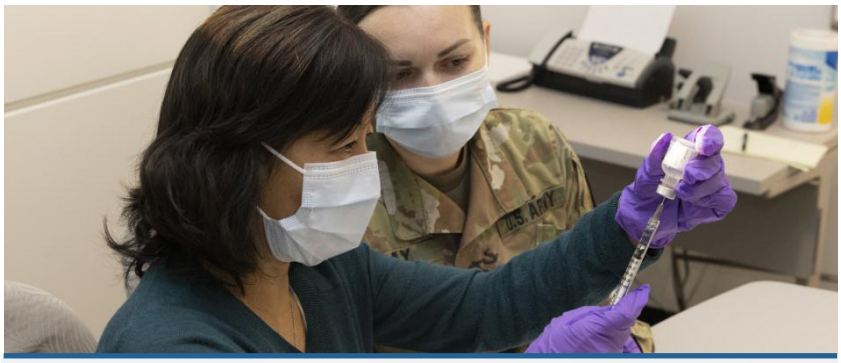
FALL 2022

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

MHRP Launches New HIV Vaccine Trial to Optimize ALFQ Adjuvant Dosage

In October of this year, MHRP launched a Phase 1 trial that evaluates the safety, tolerability and immunogenicity of varying doses of the Army's novel ALFQ adjuvant in a candidate HIV vaccine to optimize adjuvant dosage.

The new trial, RV575, is a randomized double-blind study that is enrolling a total of 60 healthy adult participants at the Walter Reed Army Institute of Research (WRAIR) Clinical Trials Center in Silver Spring, Maryland. Three arms of 20 participants will receive identical doses of the candidate vaccine antigen formulated with a different dose of ALFQ adjuvant, either 50, 100 or 200 micrograms.



Lei Zhu and Maj. Kelly Ray, WRAIR Clinical Trials Center research coordinators, prepare vaccine prior to the RV575 research study. (Mike Walters/WRAIR)

The trial tests the hypothesis that the 50-microgram dose of ALFQ will be equally immunogenic as the previously tested 100 and 200 microgram doses with a similar safety profile. ALFQ adjuvant dose optimization has the potential to improve efficiency and cost effectiveness of vaccine administration.

Adjuvants are vaccine components that help activate the immune system and improve immune responses. Preclinical and clinical studies have shown the WRAIR-developed Army Liposome Formulation (ALF) family of adjuvants to be safe and effective. The ALFQ formulation is the most potent in the family, and it is being studied in combination with several vaccines, including COVID-19, Campylobacter and malaria candidates.

The candidate vaccine antigen in RV575 combines two investigational protein products provided by Duke University: A244 and B.63521. A244 is a protein vaccine similar to the subtype E component of the AIDSVAX®B/E vaccine that was safely administered to more than 8,000 participants in MHRP's RV144 Thai trial, the only human vaccine trial to demonstrate modest efficacy in preventing HIV-1 infection. B.63521 is a subtype B recombinant protein vaccine developed by the Duke Human Vaccine Institute with the support of the National Institute of Allergy and Infectious Diseases, one of the National Institutes of Health.

ALFQ Adjuvant Tested in Vaccines Against Multiple Infectious Diseases

"ALFQ displays promising immune-enhancing effects and is also being tested with vaccines against a number of infectious diseases," said Dr. Gary Matyas, Chief of MHRP's Adjuvants and Formulation Section. ALFQ is currently being evaluated in multiple Phase 1 clinical trials as part of candidate vaccines against several pathogens:

COVID-19: ALFQ is being tested as part of WRAIR's Spike Ferritin Nanoparticle (SpFN) vaccine against COVID-19. SpFN entered Phase 1 human trials in April 2021, and early analyses showed it induces highly potent and broadly-neutralizing antibody responses against major SARS-CoV-2 variants of concern as well as the SARS-CoV-1 virus that emerged in 2001.

Malaria: WRAIR conducted a first-in-human evaluation of a novel malaria vaccine candidate containing the WRAIR-developed FMP013 antigen and the ALFQ adjuvant. Results, published in the journal *Vaccine*, showed the vaccine was safe and well tolerated by adults. ALFQ is also currently being tested as part of a malaria candidate vaccine with the FMP014 antigen.

HIV: In addition to RV575, earlier this year MHRP launched RV546, a Phase 1 trial in Thailand to evaluate two HIV vaccine candidates with and without the ALFQ adjuvant to gain insight into late boosting strategies and the effects of fractional dosing.

Campylobacter: The National Risk Management Center and NIAID launched a Phase 1 clinical trial at the Cincinnati Children's Hospital Medical Center to evaluate a *Campylobacter jejuni* conjugate vaccine with ALFQ as an adjuvant.

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WRAIR
Walter Reed Army Institute of Research

MHRP to Explore Monkeypox Risk Among Cohort Participants

MHRP has received funding from the Defense Health Agency to characterize monkeypox disease burden and associated predictors among MHRP's international cohort studies of HIV and other sexually transmitted infections (STIs).

This observational study will describe monkeypox disease epidemiology, transmission and clinical presentation by leveraging existing and prospective cohort data and specimens from MHRP studies in Africa (Nigeria, Uganda, Kenya, Tanzania) and Asia (Thailand). Researchers will analyze study samples to describe the recent burden of unrecognized monkeypox in international populations and prospectively characterize monkeypox disease presentation and epidemiologic risk factors.

Monkeypox virus is endemic in Central and West Africa, but since May 2022 more than 75,000 people from at least 100 nonendemic countries without traditional risk factors have been diagnosed with monkeypox infection. In July the World Health Organization declared the outbreak a Public Health Emergency of International Concern.

MHRP's cohort research helps identify and characterize populations that are at risk for HIV and other STIs to inform the development of prevention and treatment tools. Developing relationships with key populations through observational research facilitates engagement of these population for future studies of product safety and efficacy. This foundational work will also inform eventual deployment of safe and efficacious products to the populations that need them most. This research supports Force Health Protection and Readiness by describing an infectious disease threat in regions where Joint Forces operate and informing effective prevention and mitigation strategies.

The Uganda MOCHI cohort study team meets for protocol training. The study launched in-country in October.

MOCHI Cohort Study Launches in Uganda

MHRP and the Makerere University Walter Reed Project (MUWRP) began enrolling participants in Uganda for the Multinational Observational Cohort of HIV and Other Infections (MOCHI) study, an observational study of HIV and other sexually transmitted infections (STIs).

The MOCHI study has already enrolled over 230 participants at risk for HIV and other STIs at clinics in Homa Bay and Kericho, Kenya. An additional 500 participants will be enrolled in Kampala, Uganda.

"In order to develop safe and efficacious interventions to prevent HIV and other STIs, it is critical to understand, engage, and actively involve the populations that may someday benefit from these interventions," explained Dr. Trevor Crowell, the Protocol Chair for MOCHI. "The launch of MOCHI in Uganda allows MHRP to continue a robust collaboration with local researchers and community members to better understand the evolving epidemiology of HIV and other STIs."

MOCHI will estimate HIV and STI incidence and track the evolution of participants' sexual behaviors, risk mitigation such as use of condoms and pre-exposure prophylaxis (PrEP), and healthcare engagement. The study also facilitates sites' preparedness for future HIV and STI prevention studies by building capacity, evaluating site recruitment and retention, and maintaining relationships with affected communities.

MOCHI engages community members who may participate in future studies, including those designed to test HIV prevention tools as well as interventions to achieve HIV remission. Every 12 weeks, participants respond to behavioral questionnaires and receive clinic-based HIV and STI testing. They are also linked to PrEP and provided HIV home testing kits for use between scheduled visits. Participants diagnosed with HIV will be connected to antiretroviral therapy and continue with follow-up visits to monitor early events in HIV pathogenesis and response to antiretroviral therapy. The study is employing a novel biometric technique, iris scanning, for participant identification.

MOCHI is designed to provide one unified protocol and set of data collection instruments for deployment across multiple sites in diverse regions of world. Homa Bay and Kericho, Kenya, are located in a part of Western Kenya with exceptionally high HIV prevalence. MOCHI is the first MHRP study at the Homa Bay site, which serves a fishing community on the shore of Lake Victoria as well as female sex workers and other key populations who congregate at nearby bars in tourist areas. The MUWRP team in Kampala, Uganda, has a long history of engaging key populations at risk for HIV and other STIs, including in prior MHRP studies such as the RV217 Early Capture Cohort Study. Now that the MOCHI study model has been established, MHRP can leverage the platform in additional countries in the coming years, with a target of enrolling 500 participants in each country where the study is opened.

MHRP PEPFAR Programs Provide Preventive HIV and COVID Services in Tanzania and Nigeria

Since 2005, MHRP has implemented the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), delivering HIV prevention, care and treatment services across four countries in Africa. Though COVID presented new challenges for those populations, longstanding efforts and infrastructure ensured a resilient, capable response as staff worked to provide COVID vaccinations alongside a full slate of HIV programs.

In Tanzania, MHRP's PEPFAR staff had an exhibition booth at the agricultural trade fair celebrating the Nane Nane public holiday. The exhibition highlighted HIV program interventions, the DREAMS initiative for adolescent girls and young women, and offered COVID vaccinations on site through close collaboration with Tanzania Regional Governments. In just six days, a total of 1,717 adults were vaccinated during the exhibition. The Johnson & Johnson COVID vaccinations were funded from the American Rescue Plan Act through PEPFAR.

Apart from showcasing the impact and milestones of the HIV services, staff also provided Voluntary Medical Male Circumcision (VMMC) at the fair using a mobile clinic van. A total of 175 people accessed the VMMC services on-site.

MHRP PEPFAR services in Nigeria support the Centre for Population Health Initiatives (CPHI), a drop-in community health center that offers a wide range of specialized, free health services to key populations. This One-Stop Shop is a community-led resource where vulnerable populations and people living with HIV can access HIV screening, testing and treatment, TB screening and treatment, cervical cancer screening, prevention of mother-to-child transition, partner counseling and more in one safe, convenient location. In addition to HIV prevention and treatment services, this One-Stop Shop is a hub for trusted information and access to COVID vaccines.

"Clients have trust because they see the same people and faces," said Dooshima Uganden, Prevention Program Manager for HJFMRI and the Walter Reed Program-Nigeria, which supports CPHI. "Staff spend time explaining what the vaccine does, how it works, what the benefits are – and clients are free to ask questions and know if there are issues they can come back."

Convenience is at the heart of the One-Stop Shop model. Clients who drop in for HIV counseling or preventive services, or just to spend time in the CPHI center, may use the opportunity to discuss or receive the COVID vaccination. And, like all CPHI One-Stop Shop services, the COVID vaccines are free.

Dr. Hamada Shaban (pictured) was recognized as a Hero of the Fight Against COVID-19 by the U.S. Embassy in Tanzania. Honorees were rendered as comic book-style superheroes for artwork displayed at the Heroes Night event. Photo courtesy of U.S. Embassy in Tanzania

Dr. Hamada Shaban Recognized for COVID-19 Vaccination Efforts in Tanzania

The U.S. Embassy in Tanzania has recognized Dr. Hamada Shaban as a "Hero of the Fight Against COVID-19" for his contributions to the success of MHRP's PEPFAR-funded vaccination campaign in the Southern Highlands region. The embassy celebrated Dr. Shaban and other honorees at a November 10 celebration in Dar es Salaam.

MHRP's COVID-19 response activities were implemented in the Mbeya, Songwe, Katavi and Rukwa regions of Tanzania, where vaccination rates lagged behind targets. In collaboration with a regional council health management team including representatives from the Ministry of Health and Presidents Office Regional Administration and Local Government, MHRP initiated a baseline assessment to identify the gaps and areas for improvement in vaccination efforts.

"The baseline helped us to task each region and council to come up the work plan and areas where they needed support," said Dr. Shaban. "A majority had logistical challenges distributing COVID-19 vaccine from national, regional, and district centers to local facilities."

Raising community awareness of coronavirus prevention and control measures was another main priority. The team engaged healthcare providers to work with local leaders to improve vaccination uptake through door-to-door visits, presence at community events and social functions, and outreach at churches, markets and other high-traffic locations.

Targets were set to vaccinate 75% of the adult population in the four Southern Highland regions. By the end of October, vaccination rates exceeded targets in three regions, with a total of more than 2.9 million clients receiving their COVID vaccination across all four regions.

MHRP at MHSRS

In September, MHRP participated in the Military Health System Research Symposium (MHSRS) in Kissimmee, Florida. The session entitled "Mitigating Bloodborne Infection Risk in Large Scale Combat Operations" was planned by MHRP Director COL Julie Ake and co-chaired by Baishali Kanjilal and Dr. Nelson Michael, Director of WRAIR's Center for Infectious Diseases Research. The session featured various oral and poster presentations from Army, Air Force, Uniformed Services University and industry researchers, including epidemiology and countermeasure development progress for HIV, syphilis and malaria. MHRP scientists presented vaccine and monoclonal antibody research in that session and contributed to other MHSRS sessions with abstracts describing prevention of sexually transmitted infections (STIs) and also PEPFAR-based implementation science.

CAPT Joseph Sean Cavanaugh, MHRP's chief of international HIV prevention and treatment, presented findings from MHRP's African Cohort Study survey of infection prevention and control practices at HIV care and treatment facilities supported by MHRP in four African countries.

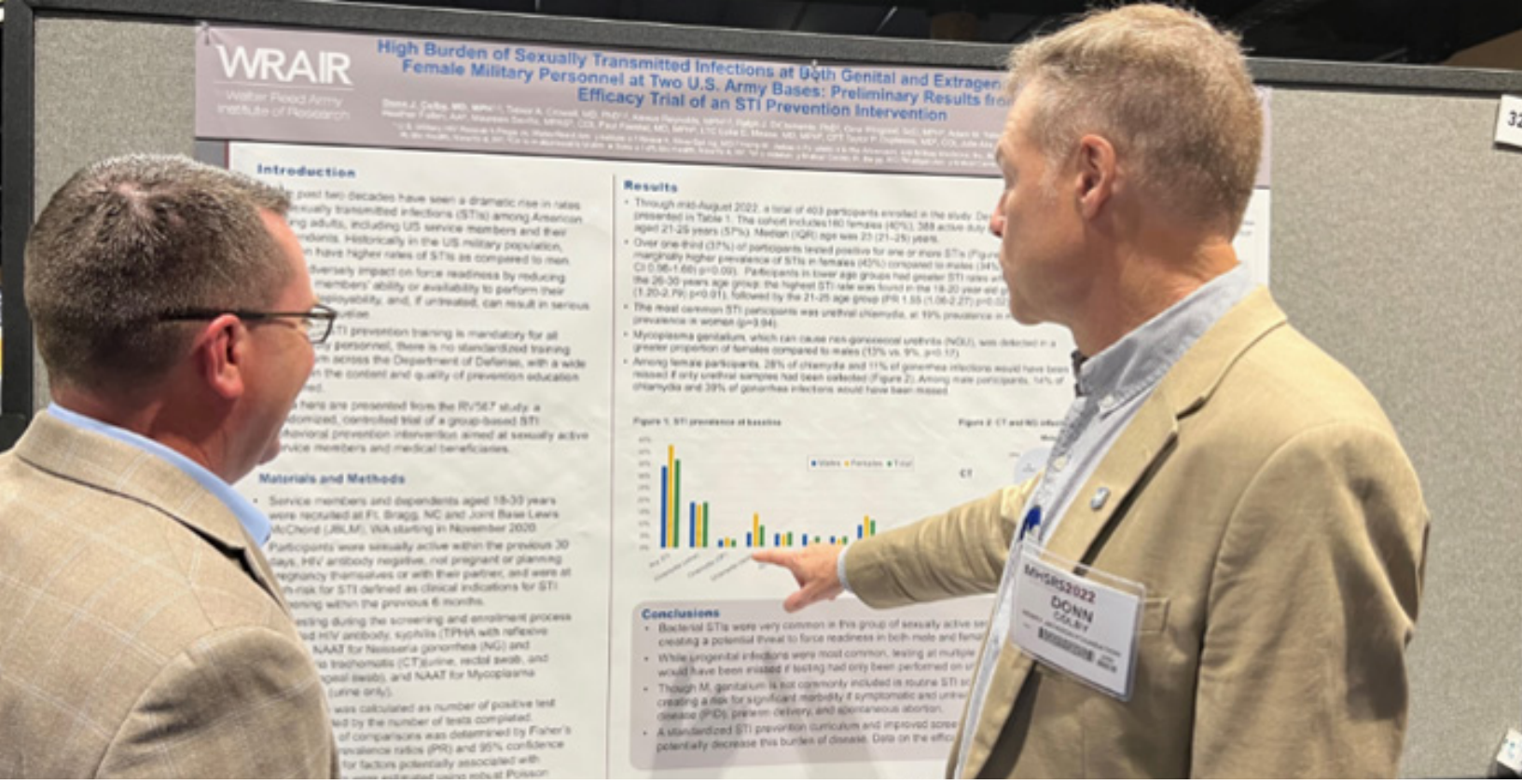
Other MHSRS presentations:

1. Denise Hsu - HIV Immunoprophylaxis with Bispecific Antibodies
2. Hannah King - Anti-SIV Monoclonal Antibodies in Macaques Are a Robust Model for HIV Monoclonal Antibody Countermeasures in Humans
3. Samantha Townsley - Modulations to HIV-1 Specific B Cells Expressing Activation Markers Associate with Antibody Responses within the First 2 Weeks of Infection
4. Paul Adjei - Depression in People Living with Human Immunodeficiency Virus During the SARS-CoV-2 Pan-demic in the Military HIV Research Program-President's Emergency Plan for AIDS Relief Pro-gram Sites in 4 African Countries
5. Shelly Krebs - Low-dose in vivo protection and neutralization across SARS-CoV-2 variants by monoclonal antibody combinations

Dr. Shelly Krebs, Chief of the B Cell Biology Core, presented her team's research on broadly neutralizing monoclonal antibody combinations against HIV.

MAJ Baishali Kanjilal co-chaired a session on mitigating bloodborne infection risk.

Dr. Sandhya Vasan, Director of the HJF component of MHRP, presented on monoclonal antibodies with multiple targets to prevent bloodborne HIV transmission in combat settings.



STI Behavioral Intervention Study Wins First Place MHSRS Poster Award

MHRP researcher Dr. Donn Colby and the RV567 study team won first place in the third poster session at the 2022 Military Health System Research Symposium (MHSRS). The poster highlighted findings from MHRP's sexually transmitted infection (STI) behavioral intervention study conducted at Ft. Bragg, North Carolina, and Joint Base Lewis-McChord, Washington.

Over the past two decades, STIs have significantly increased in American young adults, including U.S. service members and their dependents. In the U.S. military population, women have higher rates of STIs compared to men. STI prevention training is mandatory for all active-duty personnel, but there is no standardized training curriculum across the Department of Defense.

Study RV567 is a randomized, controlled trial of a group-based STI behavioral prevention intervention aimed at sexually active service members and medical beneficiaries. To date, the study has recruited a total of 403 participants aged 18-30, with 97% of participants on active duty.

Over one-third (37%) of participants tested positive for one or more STIs. Though not commonly included in routine STI screening, *M. genitalium* bacterial infection was diagnosed in more than 1 in 10 females, creating a risk for significant morbidity if symptomatic and untreated.

Bacterial STIs create a potential threat to Force Readiness in both male and female soldiers by reducing service members' ability or availability to perform their duties, or to be deployed. If untreated, bacterial STIs can result in medical complications including chronic pain and infertility.

The researchers conclude that standardized prevention curriculum and improved screening practices in the military health system could potentially decrease the burden of STIs.

The study is currently enrolling, and data on the efficacy of the RV567 intervention are expected in fiscal year 2024.

The 44th World Congress of the International Committee of Military Medicine

MHRP researchers travelled to Brussels, Belgium, in September to present at the 44th World Congress of the International Committee of Military Medicine (ICMM).

The main objective of the ICMM is to ensure that medical services personnel have the means to work together, using similar practices, in operations involving international cooperation. The 44th World Congress was chaired by Dr. David Smith, Acting Principal Deputy Assistant Secretary of Defense for Health Affairs, and head of the U.S. delegation to the ICMM.

MHRP's various presentations at the meeting highlighted recent HIV, Ebola and SARS-CoV-2 research, includes findings from MHRP's implementation of U.S. President's Emergency Plan for AIDS Relief (PEPFAR) initiatives:

Shared Lessons: COVID-19 and HIV Vaccine Development

MHRP Director COL Julie Ake gave an oral presentation at a session on pandemics and vaccines discussing the interaction of COVID-19 and HIV vaccine efforts. She described HIV as a global destabilizing force, impacting partner militaries and challenging public health in strategic geographies, necessitating the longstanding Army mission to develop a globally effective HIV vaccine. The presentation showed how lessons learned from earlier HIV prevention efficacy trials as well as the COVID-19 vaccine development experience can be leveraged to achieve the ultimate public health tool of an effective HIV vaccine.

Infection Prevention and Control

CAPT Joseph Sean Cavanaugh, MHRP Chief of International HIV Prevention and Treatment, presented findings from a recent survey of infection prevention and control (IPC) practices at MHRP PEPFAR-supported HIV treatment facilities, particularly pertaining to airborne pathogens. The presentation reviewed basic tenets of IPC and the various aspects that were assessed in the survey. Results highlighted IPC gaps and risks for amplification of respiratory pathogens in healthcare facilities. These results are being used by MHRP partners to identify and prioritize facilities for outreach and remediation.

Preclnical and Clinical Vaccine Trials

MAJ Kathryn McGuckin Wuertz presented preclinical findings showing the U.S. Army-developed Spike Ferritin Nanoparticle (SpFN) COVID-19 vaccine protects against challenge with alpha and beta virus variants in Syrian golden hamsters. MAJ Gina Griffith gave an oral presentation on research showing shortened regimens of the Janssen MVA-BN-Filo and Ad26. ZEBOV Ebola vaccines are safe and immunogenic in people living with and without HIV, and may be of benefit to deploying military personnel and first responders.

From left to right: MHRP Director COL Julie Ake; Armed Forces of the Philippines Surgeon General COL Fatima Claire Navarro; MHRP Chief of International HIV Prevention and Treatment CAPT Sean Cavanaugh (USPHS), Deputy Director of the Infectious Disease Department at the Naval Medical Research Center Navy Cmdr. Andrew Letizia; and Air Force COL (Dr.) Jessica Cowden, chief medical officer of the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense and the Infectious Disease Programs at the Defense Institute for Medical Operations at Lackland Air Force Base.

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