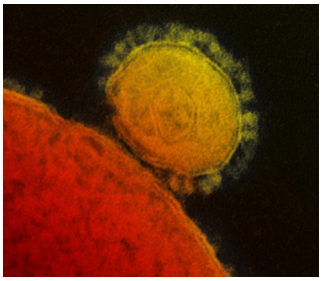
EIDB UPDATES

WRAIR | EIDB EMERGING INFECTIOUS DISEASES BRANCH

Summer 2019

NEWS FROM EMERGING INFECTIOUS DISEASES BRANCH AT THE WALTER REED ARMY INSTITUTE OF RESEARCH

MERS-CoV Vaccine is Safe, Induces Strong Immunity in First-in-human Trial



A Middle East respiratory syndrome coronavirus (MERS CoV) vaccine candidate was shown to be safe, well-tolerated, and induced a robust immune response in a Phase 1 first-in-human clinical trial. Initial findings from the trial were published in The Lancet Infectious Diseases.

MERS is a severe respiratory disease first identified in Saudi Arabia in 2012. MERS CoV has infected more than 2,200 people and killed nearly 40% of those infected. There are currently no licensed vaccines or specific treatments for MERS.

The new study, conducted at WRAIR's Clinical Trials Center, evaluated a candidate DNA vaccine (GLS-5300) co-developed by GeneOne Life Science Inc. and Inovio Pharmaceuticals. Though other vaccine candidates have previously been tested for use in camels, which are the suspected source of the virus that causes MERS, this is the first vaccine candidate to be tested in humans.

More than 85 percent of volunteers exhibited a detectable immune response to MERS CoV after just two vaccinations. The immune response persisted throughout the study and was similar in magnitude to the response seen in survivors of natural MERS CoV infection. The promising results from this study prompted advancement to a second Phase 1/2a trial in South Korea and a Phase 2 study in the Middle East.

"Military personnel are at particular risk for MERS, given the deployments to the Middle East and South Korea where the largest MERS outbreaks have occurred," said Dr. Kayvon Modjarrad, director of WRAIR's EIDB, the principal investigator of the study and first author on the publication. "This study is, therefore, an important advancement for the U.S. Army, the military community as a whole and global stakeholders."

Coalition Warfare Program Awards $1 Million for Severe Acute Respiratory Infection Research

EIDB has won a $1 million award from the Office of the Undersecretary of Defense for Acquisition, Technology and Logistics Coalition Warfare Program (CWP). The funds will support severe acute respiratory infection (SARI) threat characterization in military treatment facilities across the Kingdom of Jordan.

Among all awards, the proposal from EIDB is the only medical- or public health-related project ever selected. The CWP support will be matched by funds from the DoD Global Emerging Infectious Surveillance and Response System and in-kind services by the office of the Director General of the Jordanian Armed Forces Royal Medical Services (RMS).

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This is the inaugural edition of EIDB Updates, a newsletter sharing highlights from the Emerging Infectious Diseases Branch (EIDB) of the Walter Reed Army Institute of Research (WRAIR).

WRAIR announced the creation of its EIDB in August 2018, with the explicit mission to survey, anticipate and counter the mounting threat of emerging infectious diseases of key importance to U.S. forces in the homeland and abroad.

Building on decades of prescient investments into broad capabilities and a product-oriented research infrastructure, the U.S. Army and WRAIR have been able to consistently maintain a posture of readiness and response to the most pressing pathogens that threaten U.S. and allied forces.

This newsletter will serve as a platform to disseminate developments stemming from EIDB efforts in infectious disease surveillance, biopreparedness, research and countermeasure product innovation.

In this issue:

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Meet the Emerging Infectious Diseases Branch Leadership

Dr. Kayvon Modjarrad, Director

Dr. Modjarrad has been working in the field of global health and infectious disease research since 2002 and vaccinology and emerging pathogens research since 2011. Dr. Modjarrad completed his Internship and Residency in Internal Medicine and Fellowship in Infectious Diseases at Yale, Vanderbilt and the NIH.

In 2015, Dr. Modjarrad was seconded to the World Health Organization where he advised on vaccine research and development for Ebola and other EIDs. Prior to this assignment, he served as the Head of the Viral Pathogenesis Translational Science Core at the National Institutes of Health Vaccine Research Center. In this position he led efforts to develop, test and advance vaccine candidates against multiple pathogens of global importance, including HIV, RSV, Ebola, MERS-CoV and Zika.

Dr. Paul Scott, Deputy Director

Prior to joining WRAIR's EIDB, Dr. Scott led the Military HIV Research Program's HIV Epidemiology and Threat Assessment Task Area, characterizing HIV among military personnel, assessing risk associated with the emergency battlefield blood supply and studying HIV in countries where US troops are deployed.

Dr. Scott joined the Army in 1991 and served as a Major in the United States Army Medical Corps, where he was a preventive medicine and family medicine physician.

Ms. Mihret Amare, Associate Director of Programs and Operations

Ms. Amare oversees the implementation of EIDB objectives by managing the administrative, programmatic, financial and operational components for HJF. Ms. Amare has more than 12 years of experience managing scientific projects. Prior to joining EIDB, Ms. Amare worked with the U.S. Military HIV Research Program since 2015 as a Senior Program Manager, most recently overseeing the inception and launch of the Army's Joint West Africa Group (JWARG), which now falls under EIDB's mission.

Ms. Amare has previously worked at the Navy Medical Research Center (NMRC), where her contributions led to multiple peer-reviewed manuscripts and a book chapter. Ms. Amare earned her MBA from George Washington University.

Suzanne Mate, PhD, NISP Project Director and Project Principal Investigator

CPT (P) Mate is a Commissioned Officer in the U.S. Army Medical Service Corps. During her service, CPT (P) Mate responded to the 2013-2015 West African Ebola Outbreak and applied an integrated molecular epidemiologic strategy to reveal sexual transmission of Ebola virus. Within EIDB, she continues her efforts to fill gaps in disease surveillance and response strategies by integrating field researchers with public health and information scientists.

CPT (P) Mate received her Ph.D. in Biochemistry and Molecular Genetics from George Washington University, and reentered into the Armed Services as a Direct Commission, Biochemist, in 2014.

Severe Acute Respiratory Infection Research

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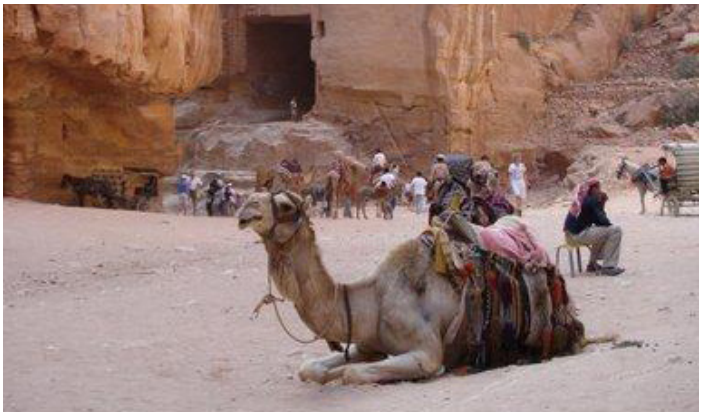
The CWP provides funding on a competitive basis to DoD organizations to conduct cooperative research and development, test and evaluation projects with foreign partners. Among the goals of the program are to collaboratively address strategic technology gaps for current and future missions and strengthen current defense partnerships and developing new relationships.

The World Health Organization defines SARI as an acute respiratory infection with fever, cough, recent onset and hospitalization. Identification and characterization of cases through the CWP-funded research will eventually lead to the advanced development and testing of a vaccine in Jordan against Middle East respiratory syndrome coronavirus, a persistent threat in the Central Command region.

The SARI project, slated to begin in late 2019, will fall under EIDB's Partnership for Research in the Middle East (PRIME) initiative. PRIME was founded on a military-to-military partnership between WRAIR and the Jordanian RMS, with preliminary program activities focused on training, improving biopreparedness and upgrading local laboratories and equipment.



Phase 1 Trial of Ebola Sudan Vaccine Begins in Uganda

EIDB and Makerere University-Walter Reed Project (MUWRP) launched a Phase 1 clinical trial in July to evaluate the safety and immunogenicity of an Ebola vaccine candidate against the Sudan species of the virus in healthy adult volunteers in Uganda.

This study will evaluate two doses of an Ebola Sudan chimpanzee adenovirus vector vaccine, (cAd3-EBO S), developed by the National Institutes of Health Vaccine Research Center. Forty healthy adult volunteers will be enrolled, with 20 in each of the two dosage groups and followed for 48 weeks to evaluate the candidate vaccine's safety and volunteers' immune response to vaccination.

The cAd3-EBO S candidate has not previously been evaluated as a stand-alone vaccine to confirm its safety and immunogenicity. The dose escalation design of the study is intended to provide more data on the extent of cAd3-EBO S' ability to provoke rapid immunity with a single injection. A vaccination strategy to achieve immediate protective immunity against Ebola would be desirable in an outbreak setting, where response workers would need to be deployed rapidly.

Various species of Ebola virus, including Zaire and Sudan, have been associated with large outbreaks of Ebola virus disease (EVD) in Africa and reported case fatality rates of up to 90%. While prior outbreaks of EVD have been localized to regions of Africa, there is a potential threat of spread given the frequency of international travel. This vaccine trial is really unrelated to the ongoing Zaire Ebola outbreak in the Democratic Republic of the Congo, and the vaccine antigen would not protect against Ebola Zaire.

MUWRP, headquartered in Kampala, Uganda, has previously participated in four Ebola vaccine studies, including the first Ebola vaccine trial conducted in Africa in 2009. WRAIR has been involved with more than a half dozen Ebola vaccine studies.

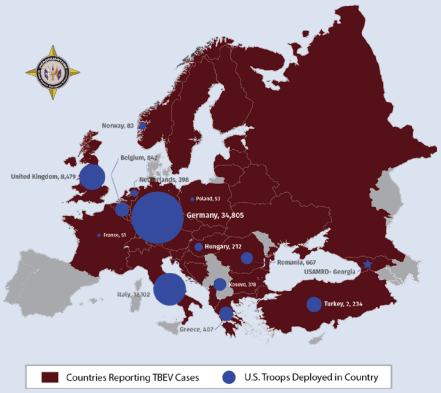
Lassa Epidemiology Study Planned for Nigeria

EIDB is planning a study to determine the prevalence of Lassa fever virus in Nigeria and identify related risk factors. The study, to be conducted in Abuja and Lagos, is expected to start next year.

Lassa fever is a viral haemorrhagic fever endemic in several West African countries including Guinea, Liberia, Nigeria and Sierra Leone. Lassa virus infection causes symptomatic disease in about 20% of cases and approximately 15-20% of hospitalized patients die from the illness.

Evidence of expanding epidemiology of Lassa fever, changing dynamics of disease transmission and case fatality and incidents of imported cases in Europe and North America highlight some critical vulnerabilities of concern to the Department of Defense military medical enterprise. The EIDB in collaboration with other DoD partners and regional and international academic collaborators will implement this community-based survey to promote Global Health Security Agenda aims as well as interests of U.S. Africa Command.

EIDB Works Toward Licensing Tick-Borne Encephalitis Vaccine for U.S. Use



WRAIR's EIDB is planning three studies to speed U.S. Food and Drug Administration (FDA) licensure of an existing tick-borne encephalitis (TBE) vaccine for pre-deployment use in U.S. service member populations.

Two TBE vaccines are available to Europeans but are not approved by the FDA, though service members deployed to Europe may receive the vaccine on a case-by-case basis. The new studies aim to characterize the experience of military personnel who received the non-FDA TBE vaccine in Europe and assess risk for incident TBEV infection among U.S. personnel serving in the European Command region.

TBE is a severe central nervous system disease that can cause long-term complications and death. The virus is prevalent in Central and Eastern Europe, where cases have surged in the last three decades, and U.S. military personnel deployed to the European Command region are at an increased risk of exposure.

Zika Vaccine, Persistence Research Advances

WRAIR's EIDB has been granted a funding award from the Congressionally Directed Medical Research Program to advance a Zika vaccine developed at WRAIR, called a Zika purified inactivated virus (ZPIV) vaccine.

The research is a collaboration with several research institutes totaling $2.6 million, with Trudeau Institute as the primary awardee. Each team will contribute key technology and expertise in this examination of methods to block the impact of Zika virus infection during pregnancy.

WRAIR scientists and collaborators moved rapidly to develop and test the ZPIV vaccine candidate as part of the U.S. Department of Defense response to the 2015 outbreak of Zika virus in the Americas. Though worldwide Zika incidence is down, it's still an issue in regions of South America and Asia. Due to global deployments, Zika is still considered a threat to service members and their families.

Persistence publication

EIDB is also collaborating on an observational prospective cohort study designed to evaluate the persistence of Zika virus in bodily fluids of volunteers diagnosed with the filovirus and relate persistence to a variety of host and environmental factors. The project is a collaboration between the Brazilian Ministry of Health, the World Health Organization, the Wellcome Trust and EIDB.

This study aims to increase understanding of how long virus may be shed via bodily fluids, informing best measures to prevent the transmission of the virus. Results published in the journal *Emerging Infectious Diseases* were the first to show the presence of Zika virus in rectal swabs, a finding that could bring to light a possible route of transmission and aid in diagnosis of Zika virus infection.

JWARG Wins GHERI Award to Further Infectious Disease Surveillance in Ghana

Made possible by the Global Health Engagement Research Initiative at the Center for Global Health Engagement, Uniformed Services University, the Joint West Africa Research Group (JWARG) study of severe infectious disease will soon expand into Navrongo, Ghana, in early 2020.

JWARG is a joint initiative implemented by EIDB that leverages existing research platforms and partnerships in West Africa to improve biopreparedness in the region. The severe infectious disease protocol, RV466, is designed to identify and characterize cases of suspected febrile illness.

The new project is called the Navrongo Integrated Surveillance Project (NISP), because it combines RV466 with community investigations (entomologic surveillance, xenosurveillance , STEM engagements and ethnographic surveys). With rigorous and standardized metadata collection connecting human febrile illness with community biogeography, NISP aims to improve modeling of health risks.

"NISP is a unique project because it's not just detecting pathogens in clinical samples; it's integrating community engagement to understand behaviors and ecology that expose groups to illnesses," said Cpt. Suzanne Mate of the Medical Service Corps and EIDB. "Once we are better able to define and measure the conditions and circumstances for infectious diseases in a community, we can improve risk models that take into account those factors."

Kingdom of Jordan HIV Study Opens

In May the Walter Reed Army Institute of Research opened a protocol that will be the first observational HIV study conducted in the Kingdom of Jordan and the first molecular epidemiologic study of HIV in the Middle East and North Africa (MENA) region.

The study, RV505, seeks to understand the evolving HIV epidemic in Jordan; gathering information on HIV risk factors, outcomes, genotypes and drug resistance profiles. While new HIV cases are declining in most parts of the world, they are rising in the MENA region.

This is the first study to come out of the Partnership for Research in the Middle East (PRIME), a WRAIR collaborative initiative led by EIDB in collaboration with the Jordanian Royal Medical Services and the Jordan Ministry of Health.

PRIME, headed by Dr. Kayvon Modjarrad, launched in 2017 with initiatives focused on training, improving biopreparedness and upgrading laboratories and equipment. Future research activities will focus on emerging infectious diseases including studies on Severe Acute Respiratory Infections, survivors of locally reportable diseases and acute febrile illness.

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