WRAIR'S INVESTIGATOR'S DISPATCH

VECTOR-BORNE DISEASE COUNTERMEASURES

WRAIR

WRAIR PROTECTS YOUR SIX

Protecting your brain - the most important six inches on the battlefield

CENTER FOR MILITARY PSYCHIATRY AND NEUROSCIENCE

- Blast Induced Neurotrauma and Neuroprotection
- Sleep & Resilience
- Team Performance and Mental Fitness
- Military Psychiatry

Protecting the most important six microns between you and the threat of disease

CENTER FOR INFECTIOUS DISEASE RESEARCH

- Vaccines & Entomology
- Viral & Bacterial Diseases
- Military HIV Research Program
- Experimental Therapeutics & Emerging Infectious Diseases

WHETHER YOU'RE AT HOME STATION OR SIX THOUSAND MILES AWAY

WALTER REED ARMY INSTITUTE OF RESEARCH'S MISSION

Discover, design, and develop solutions for military relevant infectious disease and brain health threats through innovative research protecting and optimizing Warfighter lethality.

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PROMOTED HASHTAGS

#WRAIR #WRAIRProtectsYourSix
#WRAIREnto #WorldHealth
#VectorThreat #SoldierHealth
#ForgeTheFuture

WALTER REED ARMY INSTITUTE OF RESEARCH IS A SUBORDINATE COMMAND OF MRDC

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Vector-Borne Disease Countermeasures

- Vector-borne disease (VBD) threats exist in 100% of places we send our Warfighters
- Mosquito-, tick- and sand fly-borne diseases, including malaria, leishmaniasis, Lyme disease, dengue, and Zika virus, are significant threats to force readiness
- When deployed to a highly malaria endemic region within AFRICOM without effective countermeasures, a brigade could experience a 35.5% reduction in combat effectiveness in less than two weeks
- 22 out of the top 38 endemic disease threats impacting deployed U.S. troop operations are vector-borne
- Up to one million dollars can be spent evacuating, treating, and redeploying each Warfighter infected with a vector-borne disease
- The optimal method to prevent vector-borne disease remains avoidance of arthropod bites
- To combat vector-borne diseases, WRAIR has established insectaries and vector surveillance sites in important geopolitical areas of interest
- WRAIR, in partnership with other DoD partners, has developed several countermeasures such as: vector control repellents, rapid diagnostic and identification kits, and surveillance knowledge products to protect the Warfighter
- WRAIR's insectary enterprise rears over 3.1 million mosquitoes, 700K sand flies, and 15K scrub typhus mites every year for countermeasure research
- WRAIR's insectary enterprise is a force health multiplier with sought after subject matter experts to combat vector-borne disease research

VECTORS AND DISEASES

Mosquito
- *Aedes*: Dengue, Zika, yellow fever, chikungunya
- *Culex*: Lymphatic filariasis, West Nile, various encephalitis viruses
- *Anopheles*: Malaria, lymphatic filariasis

Ticks
- Tick-borne encephalitis
- Crimean-Congo haemorrhagic fever
- Typhus
- Lyme disease

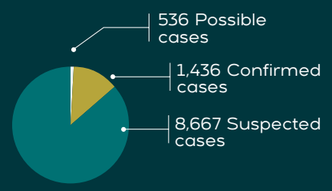
Sand Flies
- Leishmaniasis

Fleas
- Plague
- Murine typhus

Biting Flies
- Human African trypanosomiasis
- Onchocerciasis

Triatomine Bugs
- Chagas disease

IMPACT OF VECTOR-BORNE DISEASES ON FORCE READINESS 2010-2016

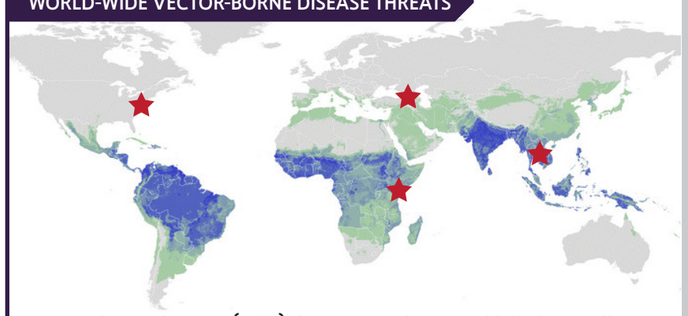


- Suspected: either a non-confirmed reportable medical event or an outpatient medical encounter with a diagnosis of vector-borne disease
- Confirmed: confirmed reportable medical event
- Possible: hospitalization with a diagnosis for vector-borne disease

Lyme disease and malaria were the most commonly diagnosed

February 2018 MSMR vol. 25 no. 2

WORLD-WIDE VECTOR-BORNE DISEASE THREATS



Vector-borne diseases (VBD) threaten readiness and lethality in all 140 countries we send our Warfighters.

Colors indicate the number of vector-borne diseases that pose a risk - darker color = greater disease threat

0 1 2 3 4 5 6

Combined global distribution of seven major vector-borne diseases for which integration of vector control program may be beneficial: malaria, leishmaniasis, dengue, Japanese encephalitis, lymphatic filariasis, yellow fever, and Chagas disease.

★ WRAIR insectaries and vector surveillance sites

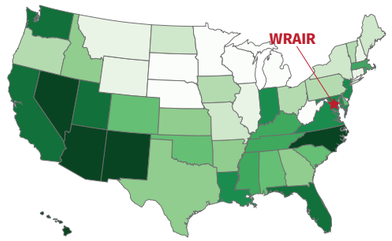
https://www.researchgate.net/figure/Combined-global-distribution-of-seven-major-vector-borne-diseases-for-which-integration_fig2_282334337

VECTOR-BORNE DISEASE THREAT STATESIDE

% of Land Area Contained in Military Installations, 2013

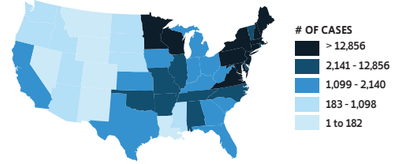
0.005 - 0.04
0.04 - 0.06
0.06 - 0.12
0.12 - 0.21
0.21 - 0.29
0.29 - 0.43
0.43 - 0.66
0.66 - 1.76
1.75 - 3.99
3.99 - 5.6

MOST MILITARY-HEAVY STATES IN THE U.S.

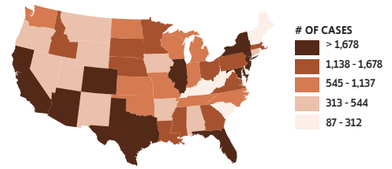


WRAIR leverages its insectary and the Walter Reed Biosystematics Unit to fight the threat stateside.

TICK-BORNE DISEASE CASES IN US STATES: 2004 - 2016



MOSQUITO-BORNE DISEASE CASES IN STATES: 2004 - 2016



https://www.businessinsider.com/how-much-land-military-bases-take-up-in-each-state-2014-11
https://www.cdc.gov/vitalsigns/vector-borne/index.html
https://www.cdc.gov/vitalsigns/vector-borne/index.html

PARTNERSHIPS

These efforts have been supported in part by GEIS, MIDRP and other DoD and non-DoD partners.

LAYERED DEFENSE AGAINST VECTOR-BORNE DISEASES

VECTOR/PATHOGEN SURVEILLANCE
Scientists use environmental traps to detect and understand the vector threat of a region

PREVENTIVE TREATMENT
Preventative measures include medications and vaccines

PERSONAL PROTECTIVE MEASURES
Skin protection and permethrin treated uniforms and bed nets

SPATIAL REPELLENT DEPLOYMENT
Spatial repellents and insecticide applications kill vectors; the DOD is working to develop this capability

LABORATORY & DIAGNOSTICS
Confirms vectors and pathogens, analyzes for pesticide resistance and drug counter resistance, and identifies emerging new VBD threats

THE WALTER REED BIOSYSTEMATICS UNIT (WRBU)

The Walter Reed Biosystematics Unit (WRBU) is a world-renowned center of taxonomic excellence, undertaking cutting-edge research to provide actionable entomological intelligence tools and products that best assess global vector-borne disease risk. In partnership with the Smithsonian Institution, WRBU has grown the U.S. National Mosquito Collection from 200,000 specimens in 1961, into the world's most taxonomically and geographically comprehensive collection of over 1.7 million specimens today. WRBU also manages eight other insect families including sand flies, horse flies, black flies, biting midges, and four other families of non-biting insects.

WRBU CORE COMPETENCIES

- Diagnose and describe species, and develop identification tools
- Map and model vector spatio-temporal distributions
- Utilize cutting-edge genetic and genomic approaches
- Identify, track, and report changing global vector hazards
- Undertake real-time biosurveillance and vector incrimination
- Sustain and develop partnerships with academia, military, and industry

2019 ACCOMPLISHMENTS

Published Findings Show that Malaria Mosquitoes can Migrate Long Distances on High Level Wind Currents

A global team including scientists from the National Institutes of Health and the WRBU used balloons to capture insects up to 290 meters in the air in the Sahel of Mali. Publishing these findings in *Nature*, it was demonstrated that previously blood-fed malaria vectors frequently migrate over hundreds of kilometers, almost certainly spreading malaria over such distances. This study has significant implications for malaria prevention and elimination, indicating that military entomologists can no longer focus solely on endemic mosquitoes and disease threats.

Sequenced the Genomes of Three Novel Mosquitoes

Members of the WRBU worked with WRAIR viral diseases researchers to achieve whole genome assemblies for three New World *Anopheles* mosquito species. To date, WRBU has sequenced 160 whole genomes (including 110 new species). These data allow for forward-facing solutions, identifying specific areas of interest for future vector countermeasure development.

Publishing the First Global Mosquito Atlas in 35 Years

Three authors who either have been or are currently civilian heads of the WRBU published a 1,200 page, two-volume book, "Mosquitoes of the World." The book, placed into production by Johns Hopkins Press, covers mosquito biology, systematics and includes a revised taxonomic catalog of mosquitoes including updated current distribution, key works and taxonomic histories for all 3,527 known taxa. The book will be available for purchase June 2020 and will be the only resource of its kind developed within the last 35 years. This resource cements WRBU as an internationally renowned resource for mosquito identification, supporting novel entomological countermeasures to protect the Warfighter.

WRAIR'S WORLD-CLASS INSECTARY

SILVER SPRING, MD

Sand Flies

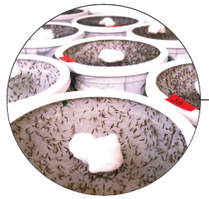
Mosquitoes

- Rears over 20,000 mosquitoes a week that are capable of transmitting malaria in support of new drug countermeasure research
- Maintains the largest and most diverse set of colonies of sand flies in the world

EXPLOITING THE THREAT TOWARDS A SOLUTION

WRAIR's CHMI model has infected >2,200 volunteers across 76 challenges since the 1990s, both in the WRAIR Insectary (47) and at a variety of domestic and overseas locations (29).

CONTROLLED HUMAN MALARIA INFECTION CHALLENGE



REAR MOSQUITOES

Mass rearing of uninfected mosquitoes

INFECTIOUS FEEDS

Mosquitoes are infected with malaria by artificial feed

CHALLENGE

Humans are infected with malaria through infectious mosquito bites

MOSQUITO DISSECTION

Mosquitoes are validated for malaria infection through dissection

★ WORLD'S LARGEST CHMI TRIAL WAS COMPLETED AT WRAIR IN 2018.

COMBATING VECTOR-BORNE DISEASE THREATS

VECTOR CONTROL

- DEET, picaridin, and IR3535 are proven, effective repellents
- Permethrin-treated bed nets
- Permethrin-treated uniform

DIAGNOSTICS & DETECTION

- Rapid vector detection tools
- Rapid pathogen detection kits

KNOWLEDGE PRODUCTS

- Insectary operations training
- Parasite culture
- VectorMap
- World-wide mosquito ID keys
- Online tutorials for mosquito and sand fly identification

USAMRD-AFRICA'S WORLD-CLASS INSECTARY

KISUMU, KENYA


Sand Flies

Mosquitoes

USAMRD-Africa is the only DOD entomology research department in Africa. USAMRD-Africa rears mosquitoes and sand flies to develop novel pest management strategies.

USAMRD-AFRICA ENTOMOLOGY CAPABILITIES & PRODUCTS

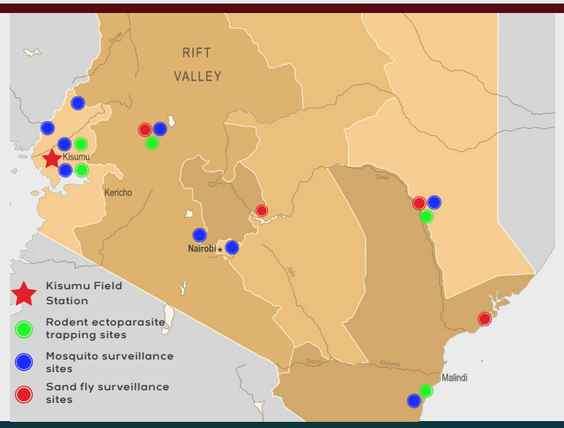
- Robust insectary operations that support membrane and direct feeding research and test for several vector borne pathogens.
- Two semi-field enclosures supporting novel pesticide repellent and resistance studies.
- Researching tomorrow's solutions for mitigating vector-borne diseases through transmission blocking, molecular pesticide knockdown resistance, microbiota effects on resistance, risk hazard communication, community outreach, and integrated pest management control strategies.
- Enhanced partnership with Kenya Defence Forces to increase surveillance locations in areas where Military personnel are supporting contingency or humanitarian efforts.


Mosquito Traps Help Track VBD Threats


Sand Fly Membrane Feeding

TRACKING AND MITIGATING VECTOR-BORNE DISEASE THREATS IN KENYA

- Conducts vector surveillance throughout Kenya resulting in vector hazard maps, and baseline for pesticide resistance for improved targeted control.
- Utilizing ectoparasites from rodents and bats to track associated disease throughout the region.



THE WORLD-CLASS AFRIMS INSECTARY

BANGKOK, THAILAND


Chiggers


Sand Flies


Mosquitoes

Armed Forces Research Institute of Medical Sciences (AFRIMS) rears sand flies, all major Southeast Asian malaria vectors, and has the only scrub typhus-infected chigger colony in the world.

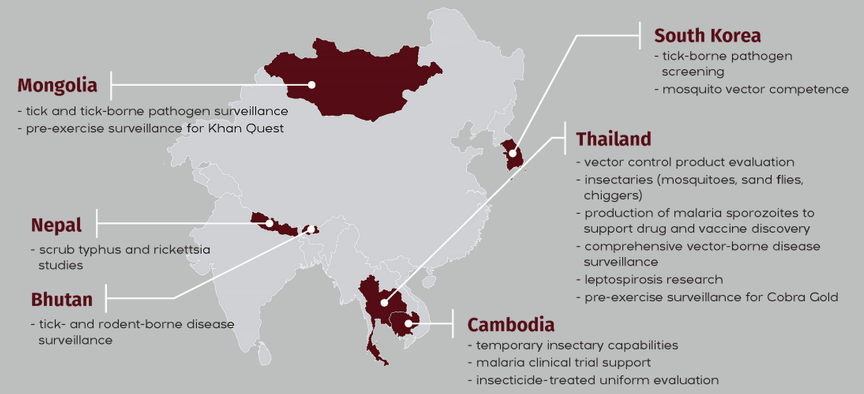
AFRIMS ENTOMOLOGY CAPABILITIES & PRODUCTS

Repellents, uniforms, attractants, and traps to protect from insect vectors of disease at home and abroad are tested year-round against abundant native mosquitoes, sand flies, ticks, and chiggers using facilities such as wind tunnels and large mosquito enclosures.

- One of two DOD labs capable of producing relapsing malaria (*P. vivax*) infected mosquitoes.
- AFRIMS's scrub typhus chigger colonies allow unique studies on pathogen transmission and development of challenge models for vaccines.
- Conducts pre-exercise surveillance at Cobra Gold training sites in Thailand and provides findings to medical planners to enhance force health protection.
- Transport *Anopheles dirus* mosquitoes to Cambodia in support of anti-malarial drug testing.

INSECTARIES AND TEST SITES

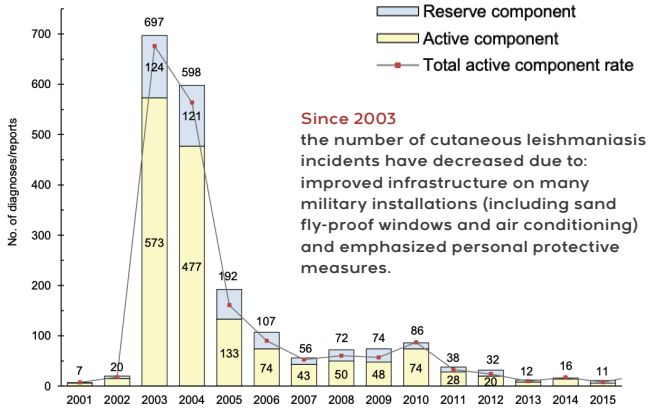
The tropical climate at the six AFRIMS research locations enables testing of vector control products, vector surveillance, and arthropod rearing.



LEISHMANIASIS

TOPLINE MESSAGES

- WRAIR has the most robust pre-clinical cutaneous leishmaniasis (CL) drug and sand fly-vector research program in the world.
- Over 1 billion people at risk worldwide for cutaneous and visceral leishmaniasis, with approximately 90K cases and 30K deaths annually.
- Leishmaniasis continues to be of military medical surveillance interest because of deployments to endemic areas of the Middle East (Iraq, Afghanistan, and Kuwait), North Africa, and Central and South America.
- More U.S. Service Members were potentially exposed to leishmaniasis during their service in OEF and OIF than at any other time since World War II.



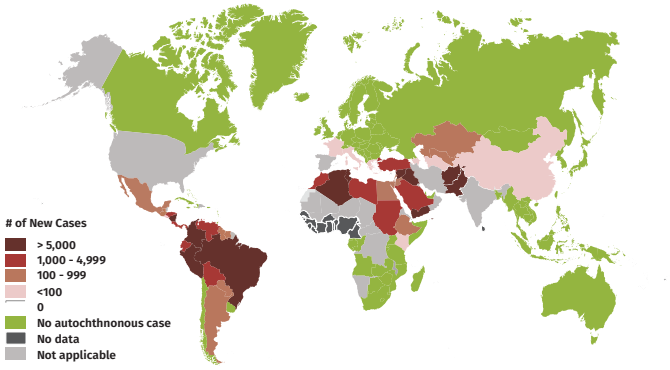
Since 2003
the number of cutaneous leishmaniasis incidents have decreased due to: improved infrastructure on many military installations (including sand fly-proof windows and air conditioning) and emphasized personal protective measures.

Relevance to the Warfighter

- Immature theatres have the highest risk for vector-borne disease
- Sand flies that are competent vectors of leishmaniasis are prevalent in areas where U.S. forces operate.
- No vaccines or preventive treatments for CL exist that can be self-administered by deployed personnel.

COUNTERMEASURES DEVELOPED WITHIN THE USAMRDC

- Leishmania Rapid Diagnostic Device (CLDetectTM, Inbios International), FDA approved.
- Topical paromomycin treatment for CL is in the early phases of transitioning to a commercial partner.
- New strategic surveillance and collection knowledge products.



CASE STUDY: OPERATION ENDURING FREEDOM & OPERATION IRAQI FREEDOM

>2,800
incidents of cutaneous leishmaniasis, a potentially disfiguring parasitic skin disease were reported among U.S. Service Members deployed to OIF/OEF.

100%
of confirmed cutaneous leishmaniasis cases at Walter Reed Army Medical Center received up to 28 days intravenous treatment with Pentostam (an investigational new drug).

WRAIR's Rapid Diagnostic Tool Saves Lives

During OIF/OEF, Soldiers could not donate blood if they served in Saudi Arabia, Kuwait, Iraq, Bahrain, Qatar, the United Arab Emirates, Oman and Yemen at any time since 1990. At the time, blood donations were not being tested for parasites. Without sufficient blood testing during the war, blood could not be accepted, and this constrained the blood supplies. WRAIR's Rapid Diagnostic Tool enabled doctors to test if the pathogen was in the blood and this allowed Service Members to donate blood during OIF and OEF.