

*Military Infectious Diseases
Research Program*

Director
COL Julia Lynch, MD
August 2011

Defense Health Board Brief

**U.S. Army Medical Research and Materiel
Command**

MISSION

Mission and Vision

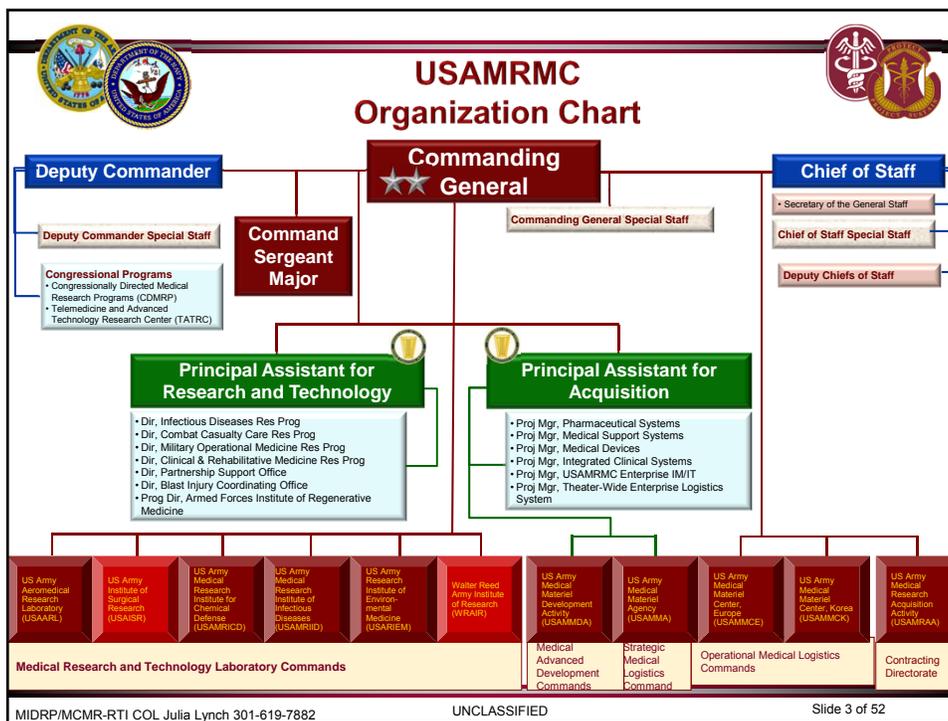
VISION

Responsively and responsibly create and deliver medical information and products for the warfighting family.

ARMY MEDICINE
CARING BEYOND THE CALL OF DUTY

A trusted partner for leading biomedical research and materiel innovation for global health.

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USAMRMC S&T Management–RADs

PA(R&T) Ft. Detrick, MD
Principal Assistant for Research & Technology

- Research Area Directorates (RADs) – Functions**
 - Manage programs; do not execute programs (do not perform research and technology)
 - Fund intramural and extramural research and technology
 - Responsible for both the problem set and the solution set
 - Devise a research strategy (program) and fund research and technology that fit the program
 - Widely networked / many meetings
- Military Infectious Diseases Research Program (MIDRP)**
COL Julia Lynch
 - Medical Readiness
 - Vaccines
 - Biotechnology
 - Prophylaxis/treatment drugs
 - Diagnostics/prognostics
 - Vector control
 - Medical C4ISR
 - HIV countermeasures (congressional mandate)
- Combat Casualty Care Research Program (CCCRP)**
COL Dallas Hack
 - Trauma care and resuscitation
 - Traumatic brain injury care
 - Blood replacement on the battlefield
 - Technology to support combat medic
 - Acute pain management
 - Burn and acute wound management
 - Combat dentistry research
- Military Operational Medicine Research Program (MOMRP)**
COL Carl Castro
 - Injury prevention and reduction
 - Psychological health and resilience
 - Physiological health
 - Environmental health and protection
- Clinical & Rehabilitative Medicine Research Program (CRM RP)**
COL Jan Harris
 - Rehabilitation and prosthetics
 - Regenerative medicine and transplants
 - Restore vision
 - Pain management

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Military Infectious Diseases MISSION



To conduct for the Department of Defense, a **focused and responsive** world class infectious diseases research and development program leading to **fielding of effective, improved means of protection and treatment** to **maintain maximal global operational capability** with minimal morbidity and mortality

- Force Health Protection
 - Naturally occurring threats
- Requirements driven
- Army Lead Agent



WRAIR/NMRC





Naturally Occurring Infectious Diseases Impact U.S. Military Operations



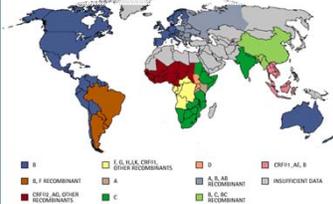
Infectious Diseases...

- Can cause more casualties than enemy fire
- Are present wherever the military is deployed
- Require new tools to combat emerging diseases and evolving drug resistance

Risk Areas for Travelers' Diarrhea



Global Distribution of HIV-1 Strains



Military Cost...

- Lost duty time
- Decreased combat effectiveness
- Morbidity due to drug-related side effects
- Medical logistical burden



Historical Impact of Infectious Diseases on US Military Effectiveness



- Civil War
 - mortality 2/3 disease vs 1/3 combat related trauma
- World War I
 - mortality 1/2 disease vs 1/2 combat related trauma
- World War II
 - 95% battlefield admissions
- Vietnam
 - 69% battlefield admissions
- Gulf War
 - 71% battlefield admissions
- Somalia
 - >95% battlefield admissions

“Montgomery says that the English Army won, however Rommel claimed victory for Dysentery”

-Sir Sheldon Dudley, battle of El Alamein



Military Infectious Diseases

ID Threats to the US Military Prioritization Expert Panel - April 2010

- **Objective:** To identify and operationally prioritize the infectious disease threats to US Forces which will assist in the determination of capability requirements.
- **References:**
 - Initial Capabilities Document (ICD) for Infectious Disease Countermeasures (IDCM), 2006, and "Infectious Diseases Investment Decision Evaluation Algorithm: A Quantitative Algorithm for Prioritization of Naturally Occurring Infectious Disease Threats to the U.S. Military," *Military Medicine* 2008;173:174-181
- **Panel Composition:**
 - The panel was comprised of the following stakeholders and SMEs:
 - ID Consultants to the Army, Navy, and Air Force Surgeon Generals
 - Chief, ID Services at WRAMC; MRMC Liaison to Assistant Secretary for the Army for Acquisition, Logistics, and Technology (ASAALT)
 - Medical Research Consultant to the Army Surgeon General
 - Director, of the Military Infectious Diseases Research Program (MIDRP)
 - Office of the J4; Office of the Assistant Secretary of Defense Health Affairs
 - Directorate of Combat Doctrine Development (DCDD), AMEDD Center and School
 - Combatant and other major Command representatives:
 - (PACOM, Socom, TRANSCOM, NORTHCOM, AFRICOM Surgeon's Offices)

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Military Infectious Diseases

ID Threats to the US Military Prioritization Expert Panel - April 2010

Decision-making Strategy:

- The National Center for Medical Intelligence (NCMI) data using the Global Risk Severity Index (GRSI) were considered
 - GRSI Values (Median Incidence rate X Severity Weight X 1000) calculated for each disease in each country

		AFRICOM	CENTCOM	EUCOM	PACOM	SOUTHCOM
Disease	Global Risk Severity Index (GRSI)	GRSI for 50 countries	GRSI for 20 countries	GRSI for 27 countries	GRSI for 24 countries	GRSI for 27 countries
Pathogen A	5759.98	2735.85	682.50	531.38	868.08	942.18
Pathogen B	4081.59	3166.29	53.77	0.62	515.17	345.73
Pathogen C	1055.86	330.58	16.83	0	500.88	207.57
Pathogen D	400.40	281.06	15.05	18.28	44.90	41.11
Pathogen E	314.70	158.47	38.41	9.88	53.06	54.90

- **Assumptions:**
 - Select agents were included if they were also considered a force health protection risk in their naturally occurring state
 - Existence of a countermeasure for a specific pathogen (i.e., vaccine, prophylactic therapeutic, diagnostic tool), impacted the ranked prioritization
- Consensus pathogen ranking was determined through:
 - Iterative discussion and anonymous voting by participants using a decision support software

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Military Infectious Diseases

ID Threats to the US Military Prioritization Expert Panel - April 2010

Consensus Top 20 Ranked Infectious Disease FHP Pathogens

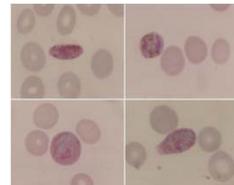
<ol style="list-style-type: none"> 1. Malaria 2. Dengue 3. Diarrhea, bacterial 4. Multidrug-resistant (MDR) wound pathogens 5. Leishmaniasis 6. <i>Q fever (Coxiella burnetti)</i> 7. <i>Norovirus and other viral diarrhea</i> 8. <i>Influenza</i> 9. Adenovirus 10. <i>Leptospirosis</i> 	<ol style="list-style-type: none"> 11. <i>Diarrhea, protozoal</i> 12. <i>Tuberculosis (TB)</i> 13. <i>Crimean-Congo hemorrhagic fever (CCHF)</i> 14. <i>Human immunodeficiency virus (HIV/AIDS)</i> 15. <i>Hemorrhagic fever with renal syndrome (HFRS)</i> 16. <i>Chikungunya</i> 17. <i>Meningococcal meningitis</i> 18. <i>Plague</i> 19. <i>Rickettsioses</i> 20. <i>Viral encephalitides</i>
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- Neither RAD1 nor DHPe funds efforts in these functional areas
- Current efforts on these pathogens fall under Diagnostic Systems Only



Burden of Malaria for Endemic Countries

- | **243 million cases***
 - | 85% Africa
 - | 10% SE Asia
- | **863,000 deaths***
 - | 89% Africa
 - | 6% E. Mediterranean
 - | 5% SE Asia
- | **Risk groups**
 - | **Infants & young children**
 - | **Pregnant women**
 - | **Travelers**



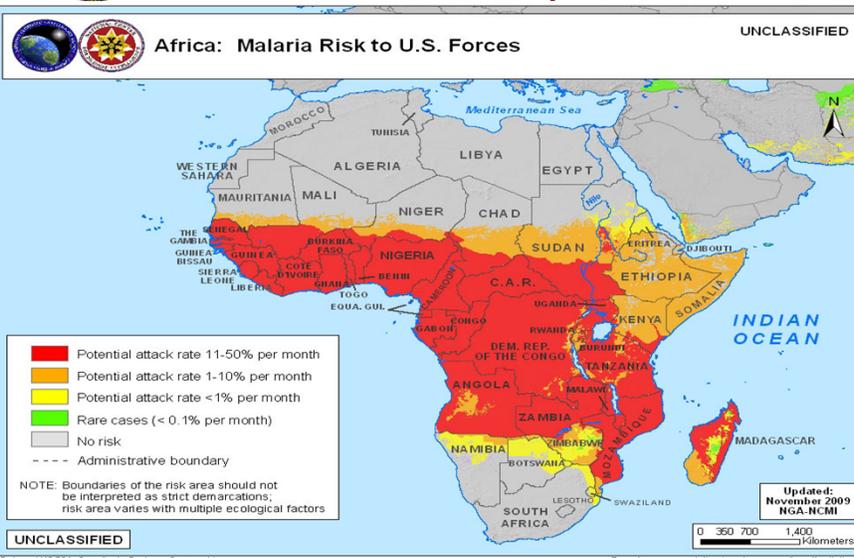


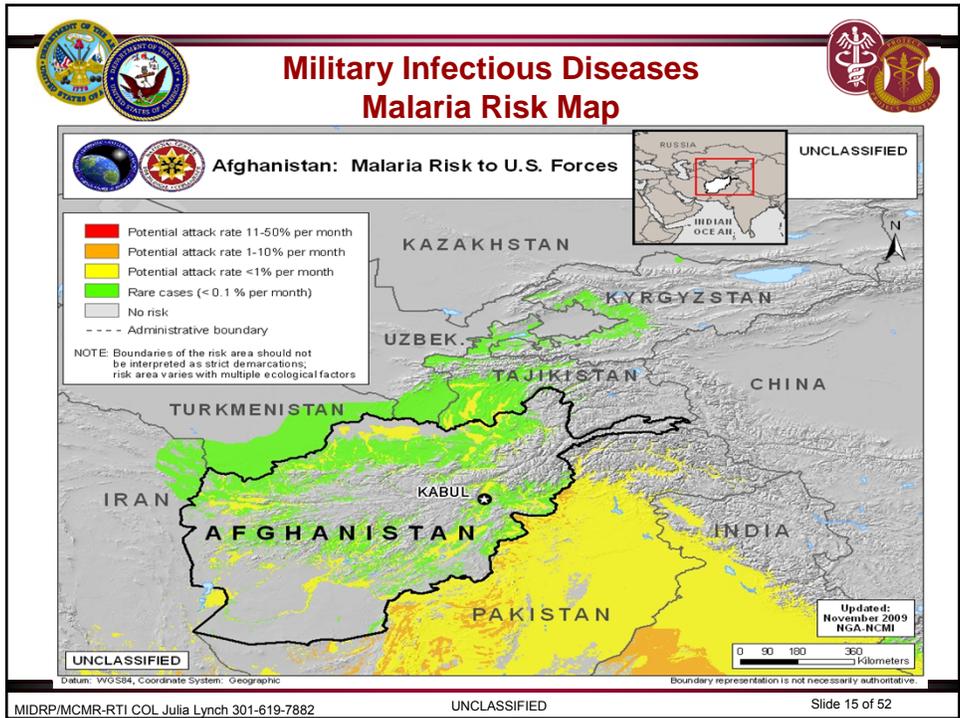
Malaria Risk Assessment

- **Historically the most feared and disabling infectious disease for deployed forces.**
 - 80-100% attack rates experienced by US forces in WWII in Guadalcanal and New Guinea.
 - attack rates are 11-50% /mo in Sub-Saharan Africa and 0.1-1% /mo in Afghanistan for deployed forces.
- **10-14 LDD/malarial episode**
- **~ 100 reported cases and one fatality/year for DoD**
- **Cost of \$31,498/person for evacuation and treatment of a case of malaria in a deployed US Service Member**
- **PPM are effective: chemoprophylaxis is >95% effective when properly used- compliance and tolerance (typically<50%) limits effectiveness.**
 - Standard prophylactic drugs include Doxycycline (gastrointestinal discomfort and photosensitivity); Mefloquine (neurotoxicity); Malarone (cost \$7-\$10/day).



Military Infectious Diseases Malaria Risk Map





Malaria and Recent Military Deployments

Country	Forces	Outcomes
Haiti-2010	US Army/Navy	13 Cases (85% of cases reported non-compliance) 5 Evacuations
Liberia 2009	US Navy	7 Cases 1 Death
Liberia-2003	US Marines ~225 for 2 Weeks	80 Cases 44 evacuation 4 Severe & Complicated
Afghanistan-2002	US Army Rangers 725 man force 4 months	38 cases (>50% of all rangers reported non-compliance)
Nigeria-2001	US Special Forces 300 for Short Term Deployment	7 Cases 2 Severe and Complicated 1 Death

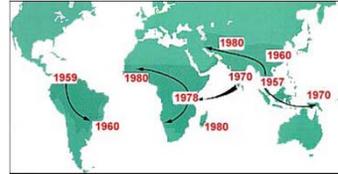
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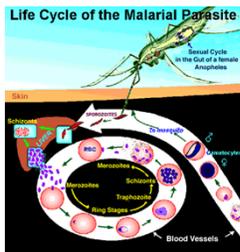
Antimalarial Drug Discovery

Threat:

- Historically caused more casualties than enemy fire; high risk of death
- 80 cases in 225 Marines deployed in Liberia; Approx. 100 confirmed cases/yr
- Parasites developing resistance to current drugs



Spread of Drug Resistance



Program Goals:

- To develop new drugs suitable as prophylaxis (long-term use).
- To develop drugs for radical cure for relapsing malaria

Current Candidates:

- Alternate regimens for Atovaquone/proguanil (Malarone)
- New formulations of doxycycline to improve tolerance
- Tafenoquine under evaluation for radical cure and weekly prophylaxis indication with GSK
- New candidates under pre clinical evaluation.

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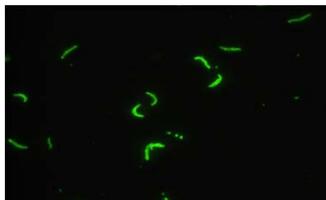
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Malaria Vaccines

Threat:

- Symptoms: Intermittent fever, chills, sweats, may progress to renal & liver failure, pulmonary and cerebral edema, coma, death
- Distributed throughout the tropics, and prevalent in 109 countries



Program Goal: To develop vaccine to protect against *P. falciparum* and *P. vivax* malaria

Current Candidates:

- Protein-Based vaccines
- DNA, viral vector-based vaccines
- Attenuated sporozoite vaccines
- Combination products

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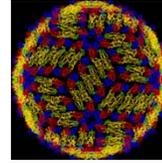
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Military Infectious Disease Dengue Risk Assessment



- **Dengue viruses**
 - Single-stranded RNA viruses
 - 4 antigenically distinct serotypes
 - (DENV-1, -2, -3 and -4)
- **Transmission primarily by peridomestic mosquito species *Aedes aegypti***
 - Daytime feeding
 - Domestic/Peridomestic habits
 - Breeds in freshwater containers
 - Thrives in urban environment



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Dengue Risk Assessment



- **Leading vector-borne viral disease globally**
 - Transmission in ~120 countries
 - Tropics and sub-tropics
 - 50 to 100 million infections annually (25,000 Deaths)
 - Undifferentiated Fever
 - Dengue Fever
 - Dengue Hemorrhagic Fever (DHF)/ Dengue Shock Syndrome (DSS)
secondary infections
- **Currently no U.S. FDA approved vaccine or drug**
 - Supportive care
 - (10-14 LDD per episode)
 - Prevention
 - Personal Protective Measures (PPM) (repellents, bed nets, treated uniforms) difficult to sustain

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Global distribution of dengue virus serotypes, 1970



22 October 2007

FOUO

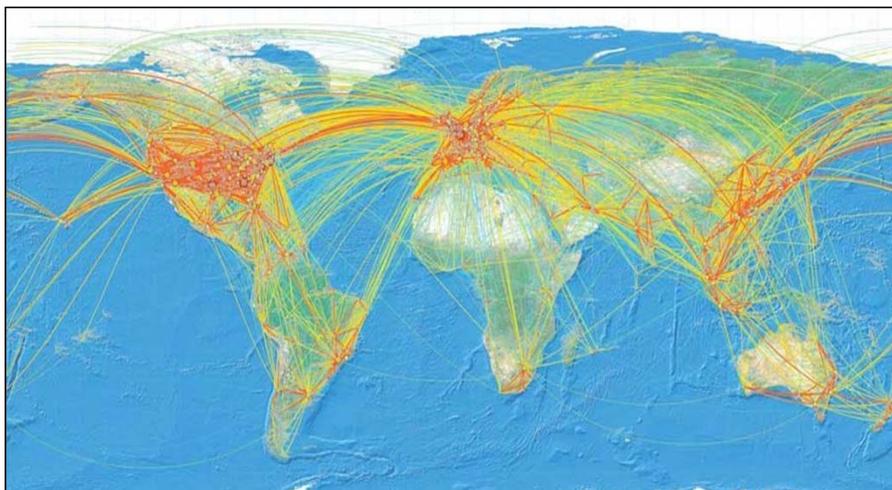
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Air Traffic Global Flight Patterns

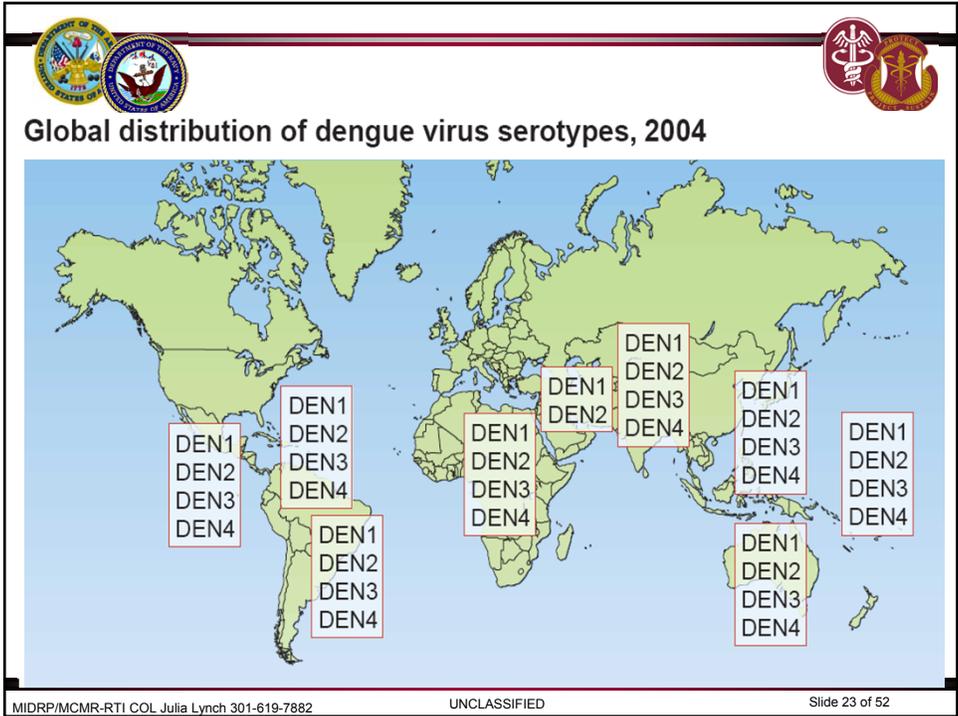


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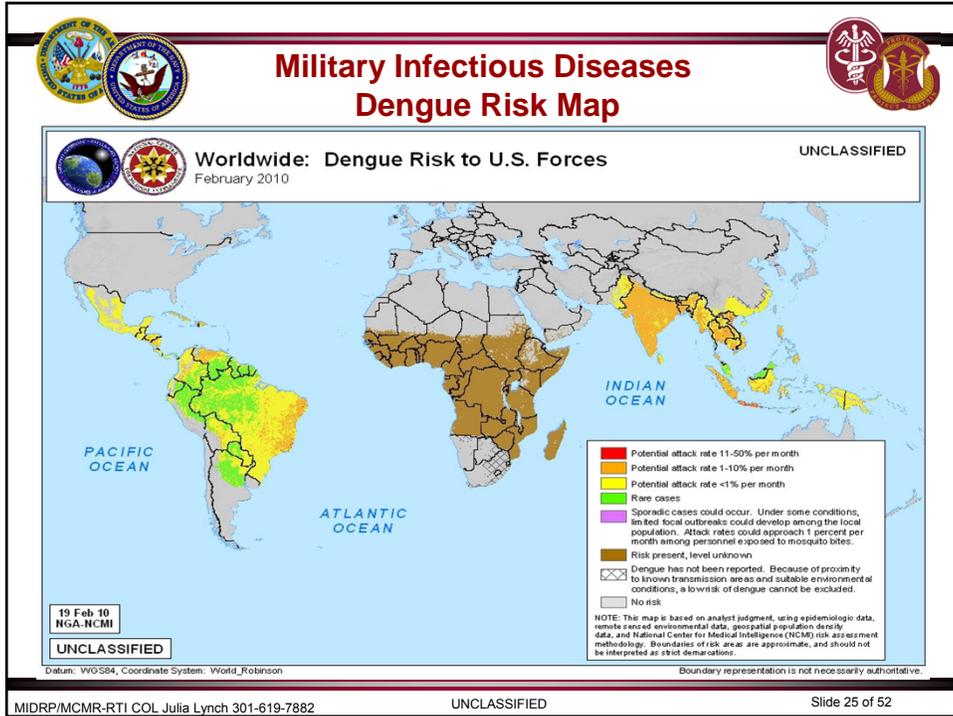
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**Military Infectious Diseases
Dengue and Military Deployments**

Country	Forces	Outcomes
Key West, FI -2010 (~5% Key West residents (~1,000 people) exposed in 2009)	Active duty and veterans	6 Cases (LDD= 84 days)
2000-2009	Defense Medical Surveillance System (DMSS)	46 hospitalized cases (LDD=644) 279 ambulatory (LDD=3906 days)
Haiti - 1997	Active duty	103 hospitalized cases with fever of unknown origin (FUO) in first 6 months (LDD=420 days) ; 29% determined to be dengue by viral isolation or serology
Somalia – 1992/1993	Operation Restore Hope	129 hospitalized cases with FUO (LDD=1078 days) ; 60% determined to be dengue by viral isolation or serology

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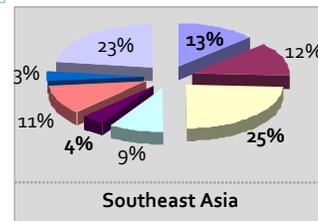
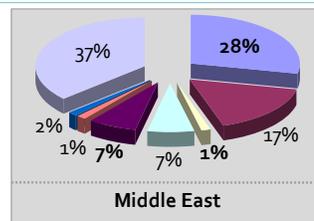
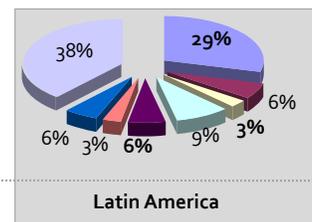
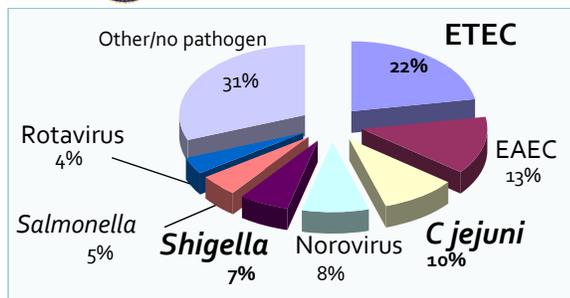


Military Infectious Diseases Enteric Bacterial Pathogens Risk Assessment

- **Monthly attack rate of 29% for Traveler's diarrhea among deployed personnel**
 - Within 3 months, ~ 90% of deployed soldiers will have had diarrhea resulting in substantial duty days lost
 - **Enterotoxigenic *Escherichia coli* (ETEC)** most common cause of traveler's diarrhea worldwide
 - ***Shigella***-induced diarrhea/dysentery more prevalent in the Middle East
 - ***Campylobacter***-induced diarrhea /dysentery more prevalent in Southeast Asia



Bacterial Diarrhea - Prevalence



MS Riddle et al. *Am. J. Trop. Med. Hyg.*, 74(5), 2006



Military Infectious Diseases Bacterial Diarrhea and Dysentery - Burden

- **Cumulative deployments and diarrhea/dysentery burden OEF/OIF '01-'07**

– # of deployments (mean 183 d)	2,134,578
– Cases of diarrhea	3,857,002
– Diarrhea days	11,478,270
– Visits to medical	850,444
– Hospitalizations	17,356
– Duty days lost	1,114,208

- Data provided by AFHSC; Riddle et al Vaccine, 2008



Military Infectious Diseases Countermeasures

Vaccines



Infectious diseases adversely impact military operations. Vaccines are often the most durable and cost-effective solution.

Drugs



New drugs for treatment or prophylaxis are continually required to overcome evolving drug resistance.

Diagnostics



Early diagnosis facilitates prompt, appropriate treatment and aids commanders in the field.

Insect Vector Control



Many militarily relevant infectious diseases are transmitted by biting insects and other arthropods.



Military Infectious Disease RDT&E Programs

<p>Army, RDT&E (RAD-1)</p> <ul style="list-style-type: none"> - Task Areas- management by Lab based Steering Committee <ul style="list-style-type: none"> - Malaria vaccine - Anti-Parasitic Drugs - Flaviviruses (Dengue vaccine) - Bacterial Diarrheal pathogens (ETEC, Shigella, Campy vaccine) - Clinical Diagnostics - Identification and control of vectors - Wound Infections (MDRO) - Lethal Viruses (HFRS vaccine) - HIV vaccine - Rickettsia (tech watch) - Portfolio management by MRM/C/Lab based IIPT - Intramural (WRAIR, NMRC and OCONUS) 	<p>DHPe, RDT&E</p> <ul style="list-style-type: none"> - Task Areas- management by Joint Program Committee (JPC) <ul style="list-style-type: none"> - Rapid Screening of Whole Blood - Antimicrobial Countermeasures - Wound Infection Prevention and Management - Clinical Diagnostics - Acute Respiratory Disease - Innovative-Immunochemoprophylaxis - Portfolio management by JPC - Intra and Extramural Solicitations - NEW IN FY10 <ul style="list-style-type: none"> - POM funding begins in FY12
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Countermeasure Development Strategy

	 <p>Prevention</p>	 <p>Field Interventions</p>	 <p>Long Term Treatment/Management</p>
Points of Use	<ul style="list-style-type: none"> • Pre Exposure • Pre Deployment 	<ul style="list-style-type: none"> • Deployed in the Field 	<ul style="list-style-type: none"> • MTF Definitive Care
Capability Need	<p>Provide Immunity Before Exposure</p>	<ul style="list-style-type: none"> • Reduce Risk of Exposure to Pathogens • Reduce Risk of Illness (LDD) • Identify Agents 	<ul style="list-style-type: none"> • Reduce Exposure to Nosocomial Pathogens • Identify Agents of Wound Infections • Optimize Wound Infection Management
Research Solutions	<ul style="list-style-type: none"> • Understand Epidemiology, Pathophysiology, and Immunity • Develop and Test Candidate Products 	<ul style="list-style-type: none"> • New Drugs • Vector Control Products • Blood Screening Tools • Diagnostics 	<ul style="list-style-type: none"> • New Drugs and Biologics • Diagnostics • Environmental Decon Products • Bio-Marker Assays
Products	<ul style="list-style-type: none"> • Malaria Vaccine • Dengue Vaccine • ETEC Vaccine • HIV vaccine 	<ul style="list-style-type: none"> • Bed Nets • Dengue Rapid Diagnostic • Tafenoquine • Artesunate • Dengue JBAIDS • Repellants • Topical Paromomycin 	<ul style="list-style-type: none"> • Maggot Therapy • Phage Therapy • Arbekacin • MDRO Micro Arrays

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Military Infectious Diseases ASAALT (6.1-6.3) Funding

Program Area	FY11 Science Totals (\$M)	FY12 Science Totals (\$M)	FY13 Science Totals (\$M)
Antiparasitic Drug Research	11.5	9.0	9.4
Malaria Vaccine Research	7.9	8.9	10.0
Flavivirus Vaccine Research	5.8	5.2	5.0
Diarrheal Diseases	7.6	7.7	7.7
Insect Vector Products	3.0	2.8	3.0
Diagnostics	1.4	2.0	2.1
Rickettsial Diseases	1.3	1.0	1.2
Meningococcal Research	1.2	0.7	0
Wound Infection	0.4	0.5	0.8
Hemorrhagic Fever and Renal Syndrome Vaccine	1.6	2.0	2.4
HIV Research	14.2	13.9	14.1
Total	55.9	53.7	55.7



Military Infectious Diseases DHPe Funding (6.1-6.4) FY11-13

Tasks	FY11 (\$M)	FY12 (\$M)	FY13 (\$M)
Rapid Screening of Fresh Whole Blood	5.1	4.5	3.3
Antimicrobial Countermeasures and Wound Infection Prevention and Management	32.4	4.6	8.5
Diagnostic Systems for Infectious Diseases	0.7	0	2.0
Acute Respiratory Diseases	0.5	0	0.6
TOTAL	38.7	9.1	14.4



Military Infectious Diseases Program Process



- **Organized around Task/Program Areas**
 - Task Area Management (Steering Committee vs JPC)
 - Laboratory scientists, stakeholders, external reps
 - Develop near, mid-range and long term goals and objectives
 - Program area goals/objectives reviewed and approved by Senior Leaders (MRMC, OSD-HA)
- **Funding through Peer Reviewed Process**
 - PI centered proposals written annually against published objectives or Program Announcements
 - Externally peer reviewed (Science >programmatic)
 - Internally peer reviewed (Programmatic=Science)
- **Strategic Program Reviews every 3 years**
 - External Panels
 - International senior scientists, industry experts, academia, stakeholders

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Military Infectious Disease Research Program



	Research Effort	Advanced Development	Fielded Products
Antiparasitic Drugs	Malaria (CDD)	Intravenous Artesunate (CPD) Tafenoquine	Atovaquone/Proguanil (Malarone, 2000) Doxycycline (Vibramycin®, 1992) Halofantrine (Halfan®, 1992) Mefloquine (Lariam®, 1989) Sulfadoxine-Pyrimethamine (1983) Chloroquine-Primaquine Tablets (1969) Primaquine (1952) Chloroquine (1949)
	Leishmaniasis	Topical Paromomycin drug (CPD)	
Vaccines	Malaria (CDD) Diarrhea (CDD) Dengue Hemorrhagic fevers Scrub Typhus HIV Global	Dengue Tetravalent (CDD) HIV Regional (CDD)	Japanese Encephalitis - cell based (2009) Hepatitis A (1995) Japanese Encephalitis (1992) Oral Live Typhoid Ty21A (1988) Hepatitis B (1981) Meningococcus (A, C, Y, W-135) (1981) Adenovirus 4 & 7 (1980) - (2011)
	Laboratory-based assays Point-of-need devices (CDD)	Leishmania Rapid Diagnostic Device Leishmania Skin Test Dengue Rapid Diagnostic Device	Scrub Typhus Diagnostic Kit (1998) Scrub Typhus JBAIDS (2010) Malaria Rapid Diagnostic Test (2007) SMART Leish PCR Diagnostic Test (2011)
Vector Control Products	Repellents/Insect control Insect identification Vector Diagnostics (CDD)	Combined Camouflage Face Paint Badnet Alternate Repellent System	DEET-based Insect Repellent (1946) Rift Valley Fever virus Vector Detection Assay (2011) West Nile Virus Diagnostic Kit (2001)

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Military Infectious Diseases What Makes the MIDRP Unique?

- Focused on FDA/EPA approved products for the warfighter (adult indication)- Force Health Protection
 - Enhance global operational capability
 - Enhance Stability operations
- MRMC organized like a pharmaceutical company
 - Product development oriented organizational structure and processes
 - Decision Gate System integrates best industry business practices
 - Historical success of vaccines/therapeutics
- Core research program embedded in Military labs with uniformed researchers
 - Discipline and mission focus
 - Global research platform – Host nation partners
 - Unique OCONUS clinical trial sites



"Because, if we fail to protect them, who will protect us?"
CAPT Meg Ryan



Military Infectious Diseases Critical Resource in Global Research



USAMRIID, Fort Detrick



WRAIR/NMRC, Silver Spring



NMRC-D, Lima



USAMRU-K, Nairobi



NAMRU-3, Cairo



AFRIMS, Bangkok



NAMRU-2, Cambodia/Hawaii





Military Infectious Diseases AFRIMS



● AFRIMS, Bangkok ● Field & Study Sites

Armed Forces Research Institute of the Medical Sciences (USAMC-AFRIMS) Bangkok, Thailand

- Conducted bench science, surveillance, and testing of infectious disease medical countermeasures and diagnostics
- 50-year partnership with the Royal Thai Army conducting infectious disease research
- 28 Active Duty U.S. Army personnel
- 350+ local employees
- Malaria, dengue, scrub typhus, HIV, diarrheal diseases, vector control, disease surveillance (GEIS)
- AAALAC-accredited animal facility with 600 nonhuman primates
- BSL-3 laboratory, CAP certified

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Military Infectious Diseases



Virology Field Site Kamphaeng Phet Province



Pivotal Trials Conducted by MRMC/Thai MoPH

Japanese encephalitis
Virus (JE-VAX®) 1980's
-Biken

Hepatitis A Vaccine
(Havrix) 1990's
-GSK

Dengue vaccine
(Chimerivax) (2011)
-Sanofi Pasteur

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Military Infectious Diseases Phase 3 Prime-Boost HIV Vaccine Trial in Thailand

- Sponsor: US Army Surgeon General
- Trial size: 16,396 vaccinated
- Duration of trial: 6 Years
- Cost: \$105M
- Six partnering organizations
 - MRMCC, NIH, Thai MoPH, Thai Army, Sanofi Pasteur, GSID



The Top 10 Everything of 2009

TIME charts the highs and lows of the past year in 20 wide-ranging lists

Search a Section: [Home](#) [All Best and Worst Lists](#)

The Top 10 Everything of 2009 Top 10 Medical Breakthroughs

2. AIDS Vaccine

In 2009

In a field that has seen more failures than success, experts received the news of an effective new AIDS vaccine with a fair share of skepticism. In September, a \$495 million trial of a novel combination of two older vaccines was the first to show protection against HIV infection. The results of the trial, which involved more than 30,000 volunteers, suggested that the vaccine was 31% effective at preventing infection among those who were inoculated. It was a modest outcome, given that behavior-based prevention



Results announced Sep 2009

- 31.2 % effective
- Safe vaccine regimen
- A major step forward for HIV vaccines
- Provides the first evidence that development of a safe and effective HIV vaccine is possible



Military Infectious Diseases OCONUS LABS

Robust international research infrastructure
and clinical trial capabilities





Military Infectious Diseases Byproducts of Mission



- **Global Public Health Benefits directly related to products developed**

Pathogens of Global Importance are important pathogens for a Global Force

- JE vaccine
- Hep A vaccine
- Malaria drugs

- **Capacity Building**

- Employment, education, training
- Community , academia, government

- **Medical Diplomacy**

- Mil to mil
- Mil to Civ



Military Infectious Diseases Issues/Barriers



The most significant problems confronting the S&T and/or Advanced Development program:

1. Changes in External Partner dynamics make it increasingly difficult to field Force Health Protection products
2. Inadequate funding
 - Leveraging Partners
 - Narrow pipeline
 - Loss of responsiveness to new threats
3. Endangerment of the Force Health Protection mission due to parallel and/or uncoordinated investments in CBD initiative in Emerging Infectious Disease and Threat Reduction



Military Infectious Diseases Issues/Challenges



Changes in External Partner dynamics make it increasingly difficult to field Force Health Protection products

- DoD requires partnerships to successfully develop and sustain products
 - Historically partnerships with industry have led to US FDA products for pathogens with limited US market
 - Industry now has little interest in many FHP relevant diseases (little-to-no profit-margins after development)
 - Increasing costs in product development (science, manufacturing, regulatory...)
 - Helsinki Declaration-hindrance for Industry to conduct clinical trials in disease endemic areas
- Not-for-profit organizations (Gates Foundation, Wellcome Trust, GAVI...) providing resources to make development, fielding and market sustainment of low profit-margin products feasible for industry

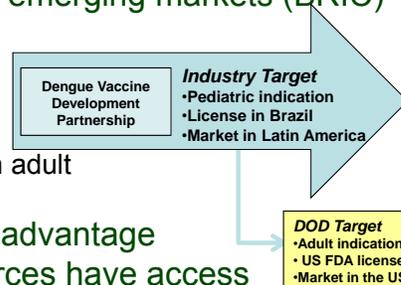


Military Infectious Diseases Issues/Challenges



Changes in External Partner dynamics make it increasingly difficult to field Force Health Protection products

- Industry and Non-profit partners seek pediatric products intended for resource poor and emerging markets (BRIC)
 - If primary commercial market is foreign, trend is to seek approval from other licensing authorities (e.g. China, India, Brazil)
 - DoD requires FDA approval and an adult indication
- DoD at risk of being at FHP disadvantage in future battlefield as other Forces have access to countermeasure not available to US Forces



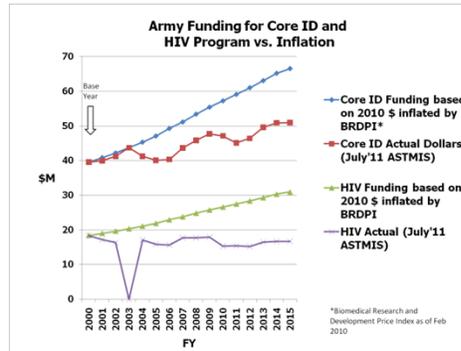


Military Infectious Diseases Issues/Challenges



Impact of Inadequate Funding- Leveraging Partners

- DoD's greatest leveraging power when partnering with industry is derived from intellectual property rights based on early phase research discoveries.
 - Requires sustained and robust 6.1-6.3 investment
- Co-funding product development with substantial Army dollars maintains this leverage throughout the development
 - Reliance on partner funding shifts decision authority
 - delays achieving our target
 - » Ad vector/DNA prime boost
 - inability to assure pursuit of FDA approval
 - » ChimeriVax
- Partners need to see DoD as a strong and viable partner
 - Reduced funding erodes leverage in current partnerships and reduces interest in future engagements



MIDRP/MCMR-RTI COL Julia Lynch 301-619-7882

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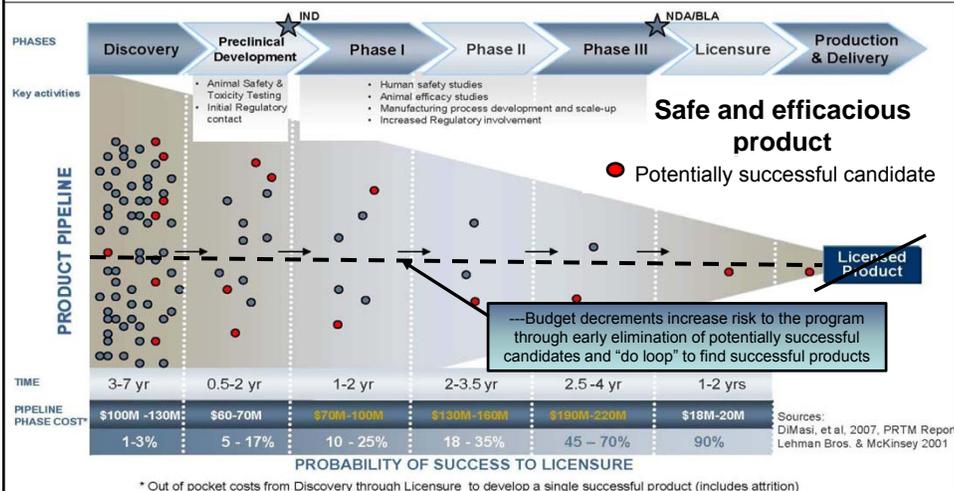
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Military Infectious Diseases Issues/Challenges



Impact of Inadequate Funding- Forces the product pipeline to narrow to too few candidates too early in development impede effective/efficient development of FHP products



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Military Infectious Diseases Issues/Challenges



Impact of Inadequate Funding- *Loss of responsiveness to new (or returning threats)*

- Inadequate funding can result in loss of technology base
 - Leishmaniasis
 - Discontinued in 2001, restarted in 2004
 - Adenovirus
 - No tech base exists to support re-engineering if Ad4/7 vaccine fails due to emergent serotypes
- Increased funding in response to new threats is inefficient—ramp-up time is significant obstacle
- Ability to be agile and adapt to new threats depends on maintenance of a broad technology base



Issues/Challenges



- **Endangerment of the Force Health Protection mission due to parallel investments in Chemical Biological Warfare Defense Program**
 - ASAALT Lead Agent for programming Naturally Occurring ID RDT&E
 - Public Law 50 USC 1522 establishes Chemical and Biological Warfare Defense (CBD) program and requires all CBD funds be budgeted in a defense wide account with oversight provided by ATSD(NCB).
 - WMD Threat Reduction and Countermeasures
 - Prohibits Services from requesting funding for agents in the program
 - Change in scope of the CBD program to include Emerging Infectious Disease (EID)
 - On October 26, 2009, ATSD(NCB) signed a Memorandum for the Secretaries of the Military Departments including EID into the Biodefense Mission Set
 - H5N1, H1N1 first efforts attempted to be funded using CBD dollars (diagnostics)
 - FY11, FY12 congressional appropriations for CBD include "EID"



Issues/Challenges

- **Endangerment of the Force Health Protection mission due to parallel investments in CBD**
 - EID poorly defined and inconsistently used (SARS, H5N1, H1N1, Chik, dengue, manmade/bioengineered...)
 - If EID is in the “program” what is now excluded from Service Programming?
 - CBD focus >> Biowarfare Countermeasures >> EID Countermeasures (for the Homeland)
 - EID-Influenza Therapeutic Acquisition Program underway (~\$200M)
 - CBD focus >> Biowarfare Threat Reduction >> EID Threat Reduction (for the Homeland)
 - Potential impacts on OCONUS labs
 - Blurring of programmatic lines, insufficient coordination between DoD infectious diseases programs
 - Potential duplication of efforts
 - Loss of focus (loss of funding?) on FHP needs in favor of civilian/public health potential threats



Backup