Assessing Seroprevalence of Dengue Fever in US Army Special Operations Forces

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USASOC ESO
GMCA 2009
Acknowledgements

- USASOC Surgeon’s Office
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- LTC Steven Tobler, AFHSC
- MAJ Chris Perdue, AFHSC
- MAJ Cecil Sessions, AFHSC
Agenda

• References
• The Dengue Threat
• Dengue Hemorrhagic Fever (DHF)
• Why Special Operations?
• The Study Protocol
• Expected Results
• The Way Ahead
• Questions
Setting the Stage

Environmental burden of disease globally

Environmental burden of disease as % of total disease burden

- 10 - 12.5%
- 12.5 - 15%
- 15 - 20%
- 20 - 25%
- 25 - 30%
- 30 - 35%
- No data

Based upon data in Smith, KR, Corvalan, C, Kjellstrom, T. (Epidemiology, 1999)
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Other Disease Risks

Visceral and Cutaneous Leishmaniasis

Malaria in Afghanistan
(U) 2008: approximately 70,000 cases (28 deaths)
(U) 2007: 433,412 cases (25 deaths)
(U) 2006: 271,881 cases (25 deaths)
(U) 2005: 245,881 cases
(U) 2004: 261,456 cases
(U) 2003: 595,602 cases
(U) 2002: 628,839 cases
(U) 2001: 384,243 cases

- Increase in *P. falciparum* and mixed infections

Dr. P. Jeseaux, WHO
Reported Cases of Prevalent Diseases

Malaria in USASOC 1999-2008

Leishmaniasis in USASOC 1999-2008
Dengue - In General

- Ranks as the most important mosquito-borne viral disease in the world; “Break bone fever”
- Range is increasing due to introduced vector (Ae. albopictus); number of cases is increasing worldwide
- Infection with serotype 1, 3 or 4 followed by infection with serotype 2 within 5 years increases the risk for DHF or highly fatal DSS
- Full recovery can take up to a year
- Currently no FDA approved rapid test
- Currently no vaccine

In the last 50 years, incidence has increased 30-fold.
USASOC Surgeon’s Office

Problem: Aedes albopictus

2006 Blue: native range
Green: introduced (as of Dec 07)

2006 Red: epidemic dengue
Blue: Aedes aegypti distro

UNCLASSIFIED
Dengue Hemorrhagic Fever (DHF)

- Up to 50 million dengue infections occur annually with 500,000 cases of dengue haemorrhagic fever and 22,000 deaths mainly among children.

- Prior to 1970, only 9 countries had experienced cases of dengue hemorrhagic fever (DHF); since then the number has increased more than 4-fold and continues to rise.
Why Special Operations?

- Nearly continuous operations in various dengue endemic areas
- Multiple deployments to dengue endemic areas is not uncommon
- Typically austere living conditions
- Work in small teams so the loss of one person is critical to mission accomplishment
- Hubris sometimes interferes with the application of personal protective measures
Ten Years of Dengue

Dengue in USASOC Personnel

2009 data is through Aug 09
Reported Cases of Dengue

Cases by Unit

- 1st SFG
- 3rd SFG
- 5th SFG
- 7th SFG
- 10th SFG
- 19th SFG
- 20th SFG
- 75th Ranger
- 160th SOAR
- 95th CA BDE
- 4th POG
- SUS BDE
- SWC
Recent Dengue Cases

• Civil Affairs (CA) soldier in Guyana- positive for all four serotypes
• Confirmed in 5 out of 11 soldiers from one SF unit in Suriname and Guyana
• 3 of the 5 were positive for two serotypes and one had some indication of hemorrhagic symptoms
• Cases were not reported so response was slowed
• 2 cases in attached personnel in the Philippines
• CA soldier in Bangladesh
Discussion- Bangladesh Case

• Did not meet criteria for DHF, DSS
• Supportive Care
  – Under observation at Embassy during the day
  – Home at night with RN on call
• Concerns:
  Remain in theater? Redeploy?
Clinical vs. Operational Concerns

- **Redeploy**
  - Potential for clinical deterioration
  - Prolonged limitations
    - Fatigue
    - Muscle/Joint aches
    - Anorexia
    - Depression
  - If second infection with one of other 3 serotypes
    - worsened severity
    - Increased risk DHF, DSS

- **Stay In The Fight**
  - 2 man element
    - 50% strength
  - Difficult to Replace
    - 6 month rotations
    - Large learning curve
  - Evacuation logistics
  - Desires of individual team member
A better knowledge of the prevalence of dengue exposure in our population is needed!
About the Study

• A collaborative effort between USASOC, WRAIR and AFHSC
• Seroprevalence study of personnel from CA and two SF Groups who have deployed to dengue endemic areas (approximately 1000 samples)
• Samples are from the DoD Serum Repository (DoDSR)
• Lab will look for all 4 serotypes in all samples in the cohort
• Results could justify a human use project; exposure data will allow medics and docs to know about higher risk personnel
Protocol

• Samples are labeled with a unique 9 digit number linked to the SSN; links are maintained by a disinterested party; 1000 of the ~1700 available samples are randomly chosen for analysis
• Analysis for the presence of neutralizing antibody against all 4 serotypes, DEN-1-4
• Enzyme linked immunosorbent assay (ELISA) microneutralization test identifies and measures dengue (1-4) from primary and secondary infections
The ELISA Procedure

4G2 monoclonal and an HRP-conjugated anti-mouse antibodies detect and quantify dengue cell based associated viral antigens


A dilution takes place and the dilution tested is either negative or positive for neutralization of the tested virus.
Analysis of Data

• Determine percentage of seronegative and seropositive subjects for each serotype
• Calculate the seroprevalence of antibodies to DEN 1-4
• Stratify results according to age, race, gender and location of deployment
• Test for significance in proportional differences for demographic variables and subsample homogeneity (Fisher’s Exact Tests)
Expected Results

• Seroprevalence of dengue is much higher in our population than currently realized
• If so, a human use protocol will be pursued for follow-up studies to eliminate the need for anonymity
The Way Ahead

• Food for thought:
  – How much dengue are people bringing into the US? Military... travelers... immigration...

• How do we make the results of our study actionable? How can the results help soldiers and commanders?

• Ideally the study results will provide support for faster vaccine development

• Keep pushing the Personal Protective Measures and disease reporting
Disease Prevention

• Vaccines are not available for many high risk diseases
• Personal protective measures must be employed to mitigate disease risk
  – KNOW THE THREAT!
  – Use prophylaxis as directed (i.e. mefloquine, doxy)
  – Sleep under a bed net
  – Use 30% DEET on exposed skin
  – Treat uniforms with permethrin (except NOMEX or FRACUs)
Reporting is Required and Important

- USASOC Reg 525-1 Appendix A Para 9b
- OPREP-3 Reporting Matrix:
  “A medical situation involving marked increase of a disease among personnel or any disease incident of potential significance which may prevent mission accomplishment.”
- Operational impact, combat effectiveness
- Many of these diseases can have long term, unforeseen consequences
- Tracking is necessary in order to evaluate risk and also gather information on resistance
- Reporting emphasizes risk to the command and supports acquisition of needed equipment
# Reportable Medical Events

## Patient Data

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
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<tbody>
<tr>
<td>FMF</td>
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<table>
<thead>
<tr>
<th>Social Security Number</th>
<th>Grade</th>
<th>Date of Birth (DDMMYY)</th>
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<table>
<thead>
<tr>
<th>Base, Camp, Site of Incident (Location)</th>
<th>Gender (Male Female)</th>
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<table>
<thead>
<tr>
<th>Country*</th>
<th>APO</th>
<th>Category*</th>
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<thead>
<tr>
<th>Race:</th>
<th>White</th>
<th>Asian</th>
<th>Black</th>
<th>Am. Indian</th>
<th>Other</th>
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<tr>
<th>Unit Location (nearest town)</th>
<th>Duty Phone</th>
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## Disease Data

**Diagnosis Code**

<table>
<thead>
<tr>
<th>Diagnosis Code</th>
<th>Diagnosis - Refer to Tri-Service Case Definition</th>
<th>Onset of Symptoms (DDMMYY)</th>
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**Confirmed**

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<tr>
<th>Confirmed</th>
<th>Method of Confirmation</th>
<th>Admitted</th>
<th>Date of Admission (DDMMYY)</th>
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<tbody>
<tr>
<td>YES</td>
<td>CLINICAL</td>
<td>YES</td>
<td></td>
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<tr>
<td>NO</td>
<td>BIOLOGY</td>
<td>NO</td>
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**Travel in Previous 3 Years**

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**Malaria Chemoprophylaxis**

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## Heat or Cold Injuries

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<thead>
<tr>
<th>Ambient temperature (°F)</th>
<th>WBGT</th>
<th>Previous Heat or Cold Injury</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Multi-system involvement:</td>
<td></td>
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<td>Water Consumption:</td>
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**Uniform: DCU/Armor/MOPP/Athletic**

## Reporting Source

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<th>Health Care Provider:</th>
<th>Comments: Additional Information: (See Tri-Service Reportable Events Guidelines)</th>
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<th>PM/F:</th>
<th>Phone:</th>
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## USASOC:

**Case Entered in JMS/MIP/APOH Database**: Yes | No

**Date Transmitted to MIPH**:

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<th>Disease Codes</th>
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**Disease Codes**

<table>
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<th>Disease</th>
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**Privacy Act Information**

By entering information concerning reportable diseases and injuries occurring among Department of Defense personnel and family members assigned to or stationed in Europe, the purpose of this form is to comply with federal and military regulations for privacy protection. The information may be used to provide public health assistance and to prevent data from inclusion in the U.S. Army Medical Surveillance System.
References


• WRAIR 1367 Project 002. USASOC Dengue Seroprevalence Protocol. 10 Sep 09.

• http://www.promedmail.org/pls/otn/f?p=2400:1000
Questions?