

Assessing Seroprevalence of Dengue Fever in US Army Special Operations Forces

LTC Jennifer Caci
USASOC ESO
GMCA 2009



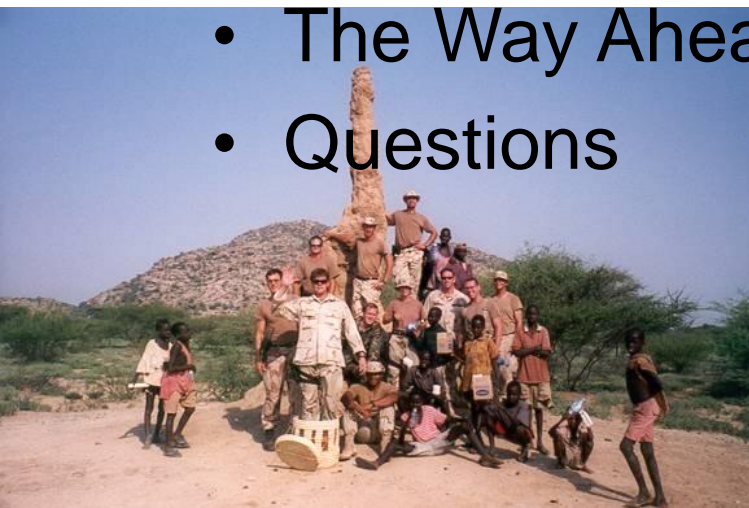
Acknowledgements

- USASOC Surgeon's Office
- LTC Art Lyons, WRAIR
- MAJ Danielle Tack, 98th CA Bn
- Dr. Angie Eick, AFHSC
- LTC Steven Tobler, AFHSC
- MAJ Chris Perdue, AFHSC
- MAJ Cecil Sessions, AFHSC



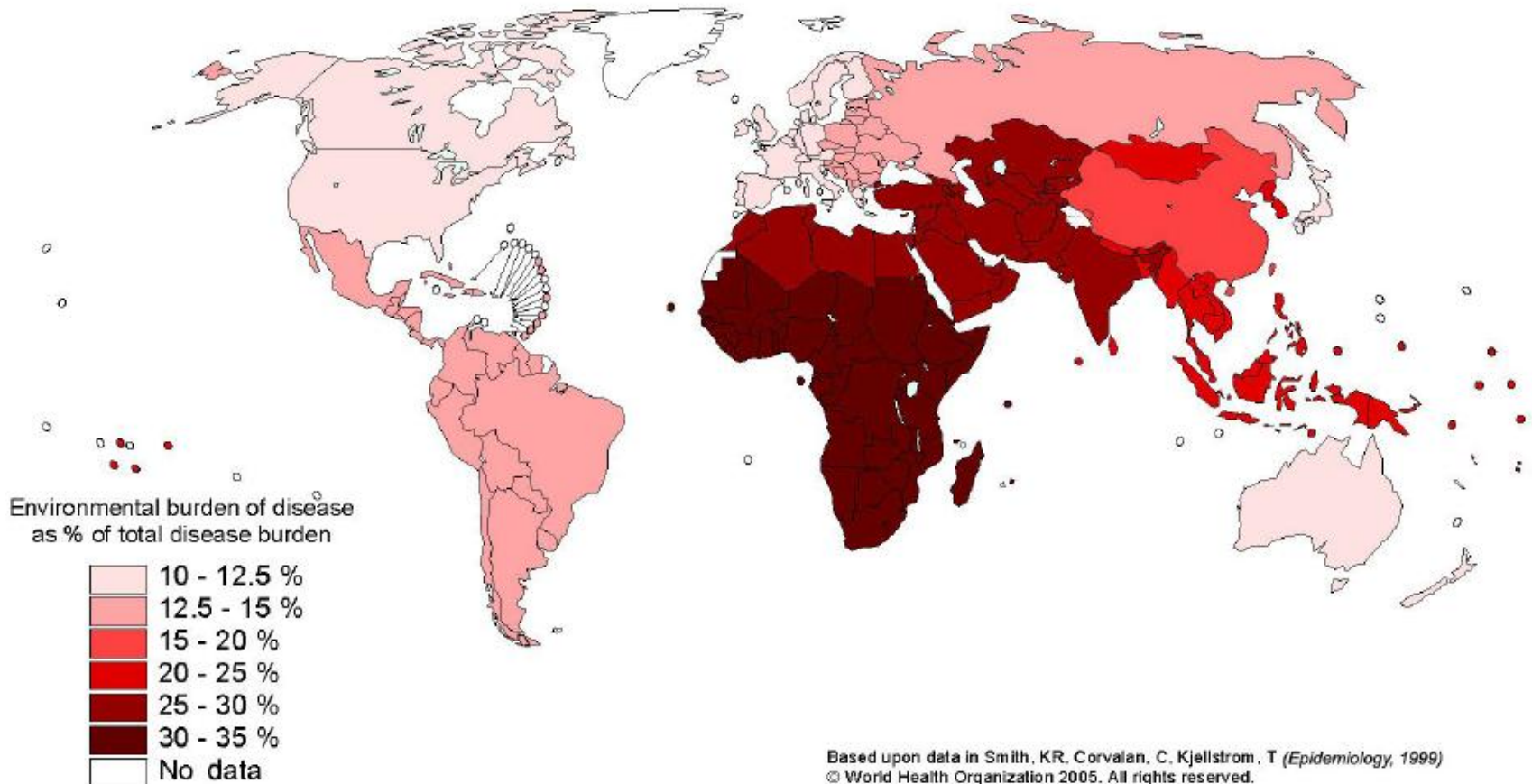
Agenda

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



Setting the Stage

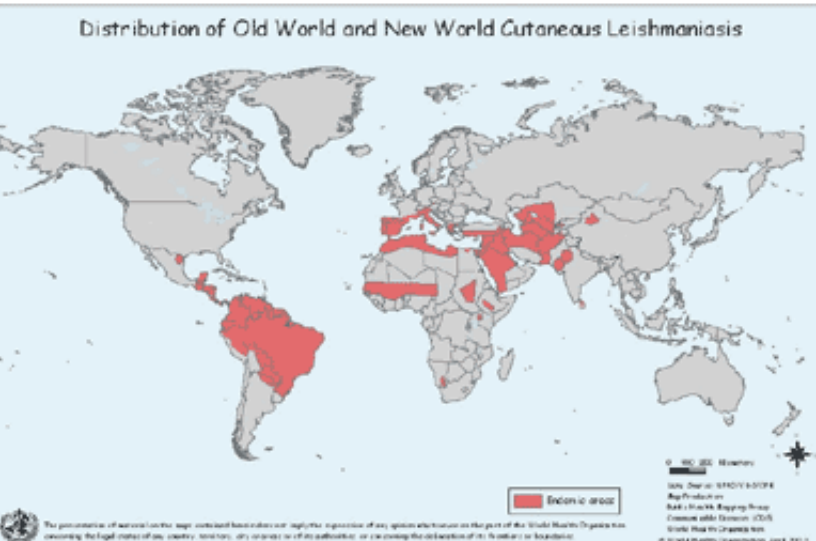
Environmental burden of disease globally



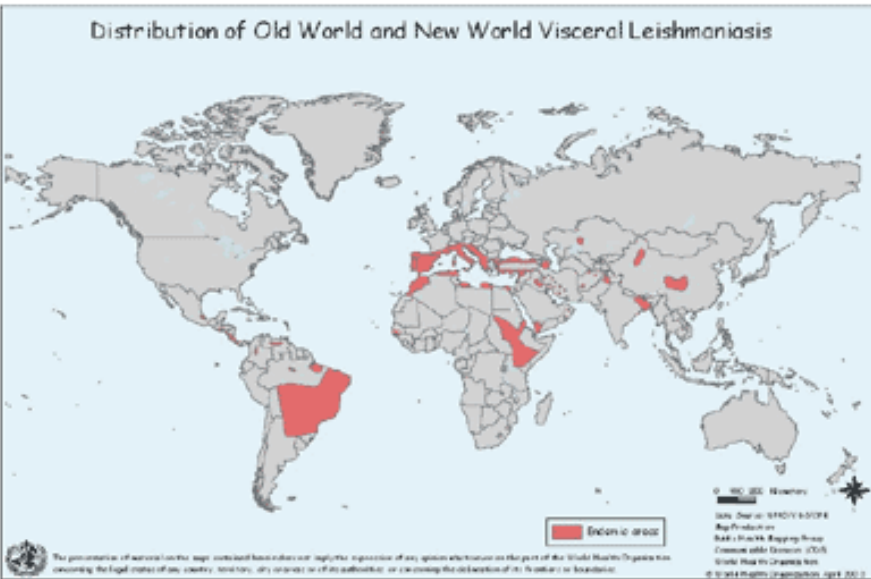


Other Disease Risks

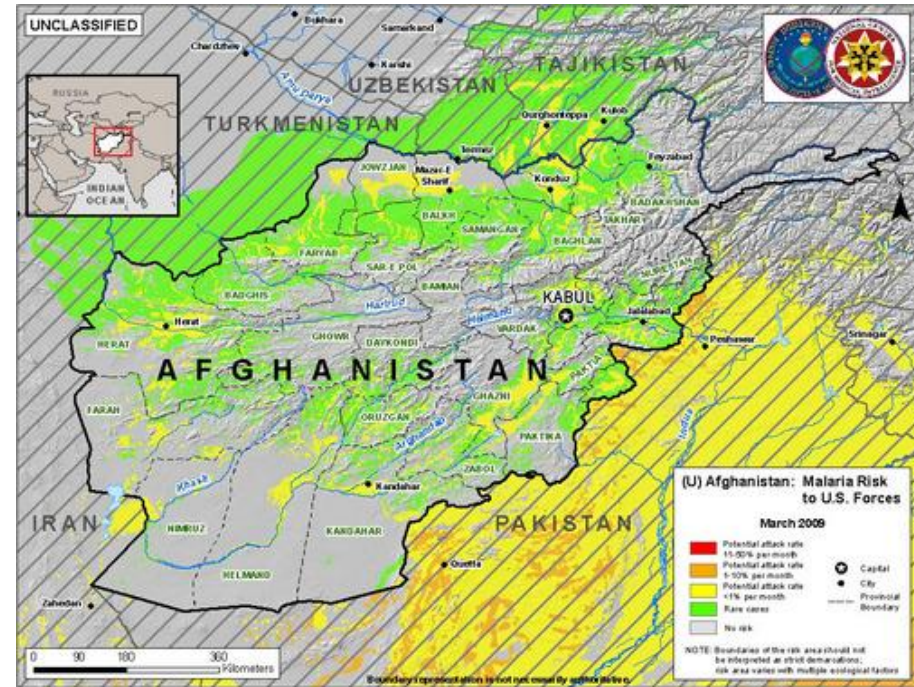
Distribution of Old World and New World Cutaneous Leishmaniasis



Distribution of Old World and New World Visceral Leishmaniasis



Dr. P. Jeseaux, WHO



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

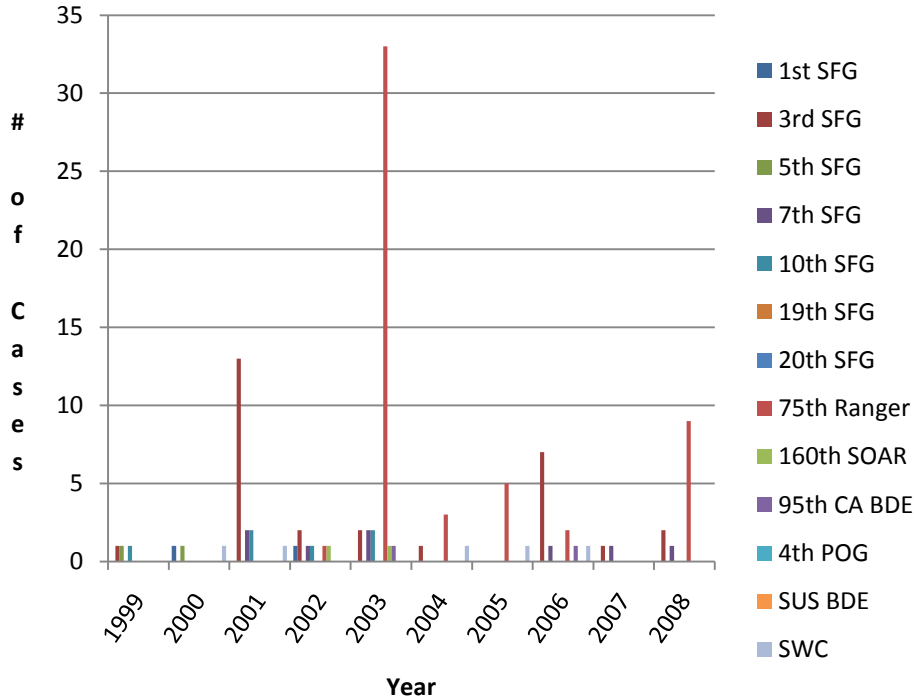
- Increase in *P. falciparum* and mixed infections

Visceral and Cutaneous Leishmaniasis

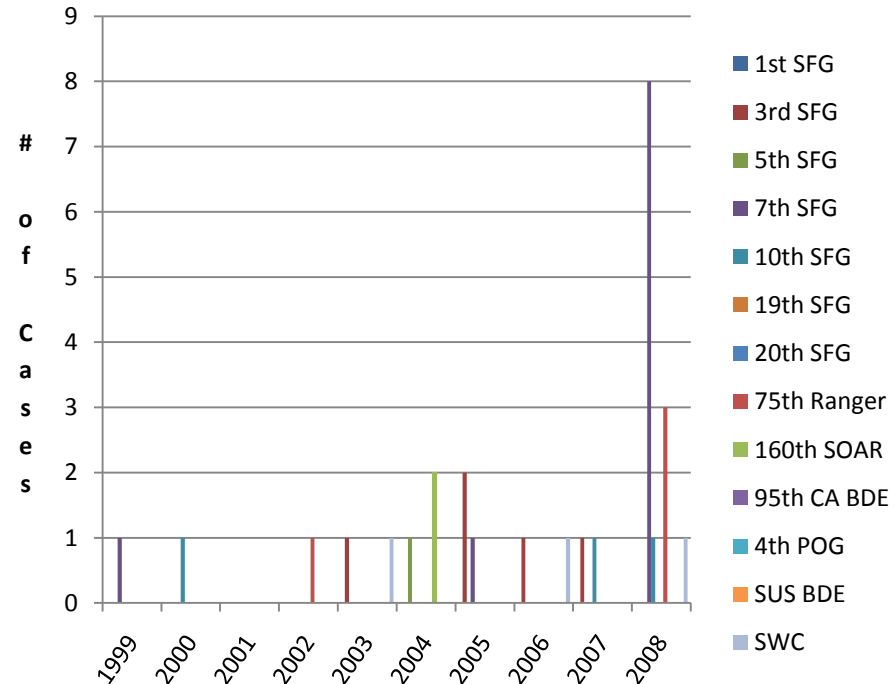


Reported Cases of Prevalent Diseases

Malaria in USASOC 1999-2008



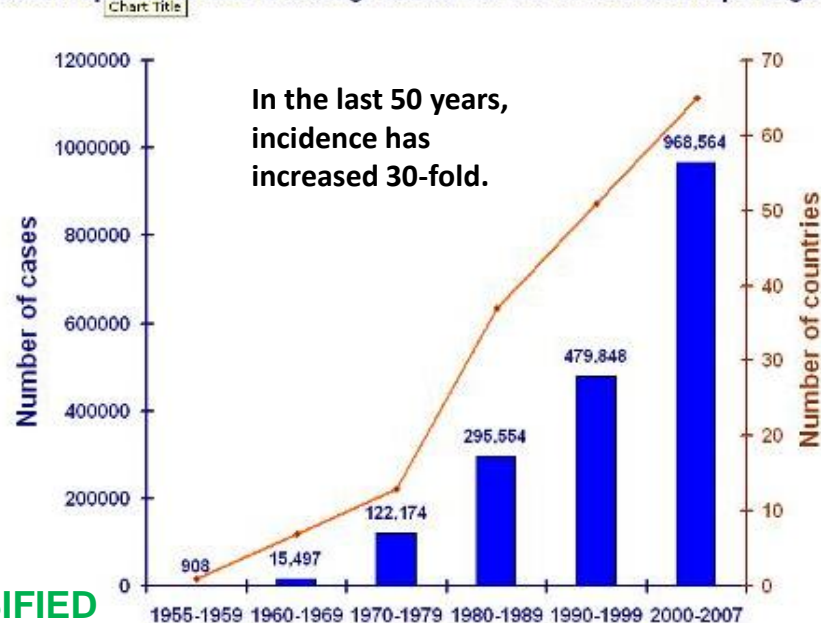
Leishmaniasis in USASOC 1999-2008



Dengue- In General

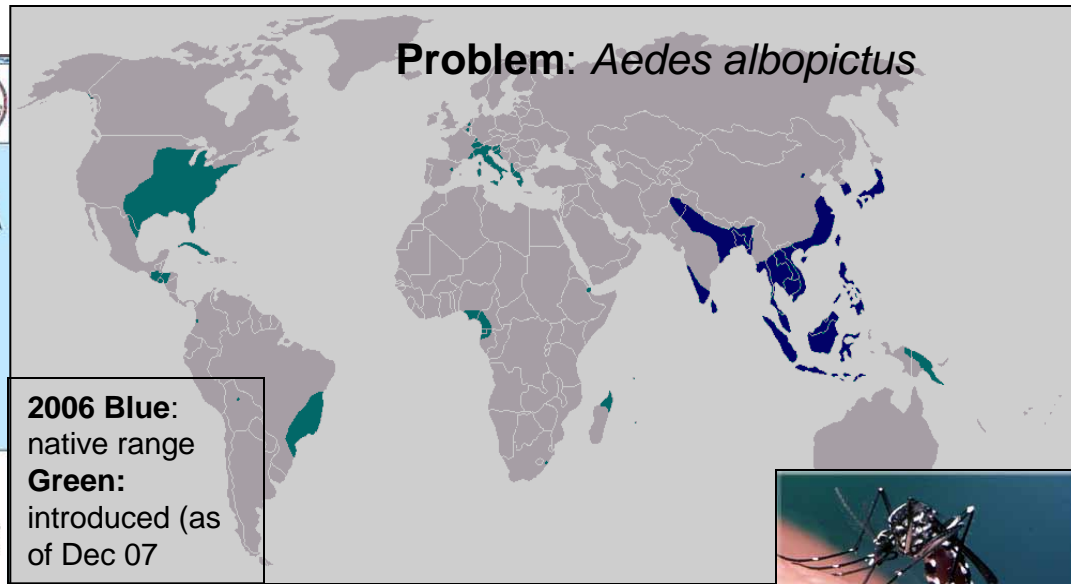
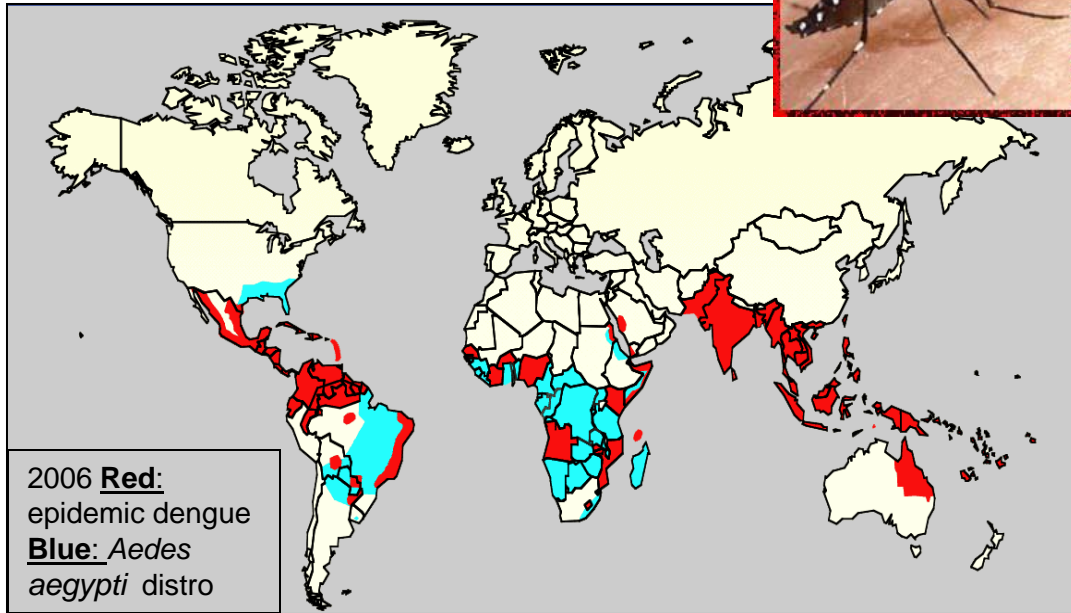
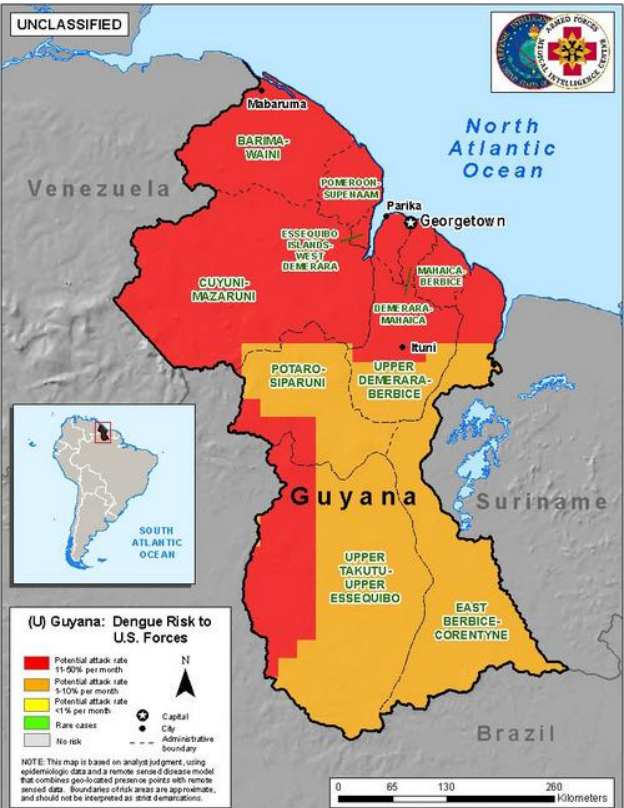
- Ranks as the most important mosquito-borne viral disease in the world; “Break bone fever”
- Range is increasing due to introduced vector (*Ae. albopictus*); number of cases is increasing worldwide
- Infection with serotype 1,3 or 4 followed by infection with serotype 2 within 5 years increases the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

Average annual number of DF/DHF cases reported to WHO & average annual number of countries reporting dengue

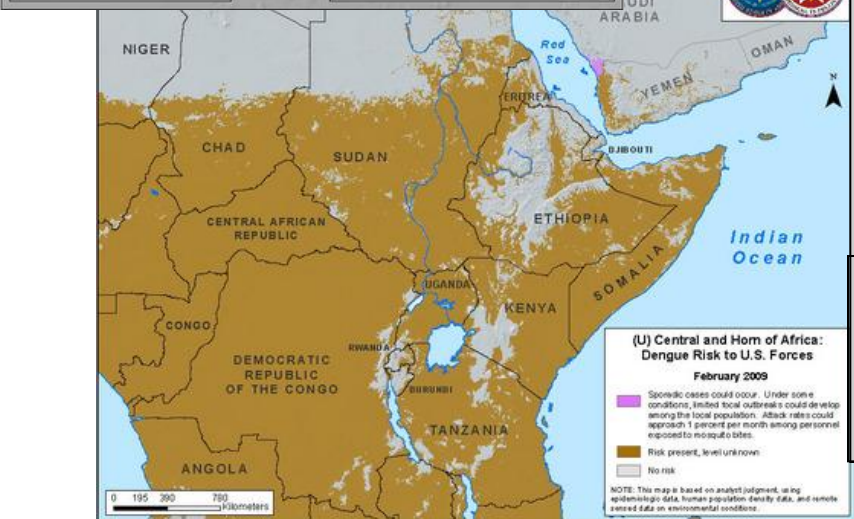


UNCLASSIFIED

USASOC Surgeon's Office

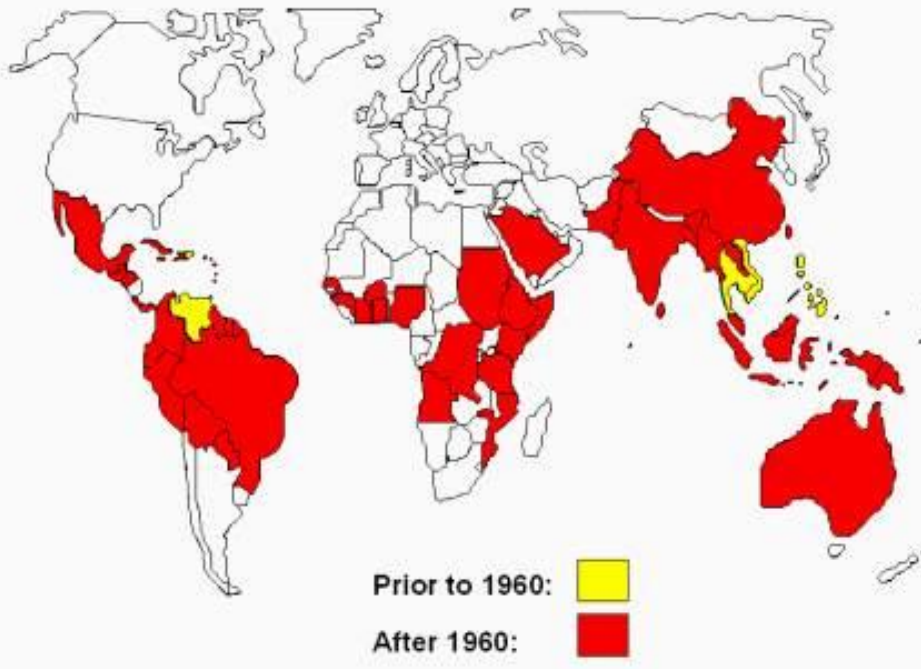


UNCLASSIFIED



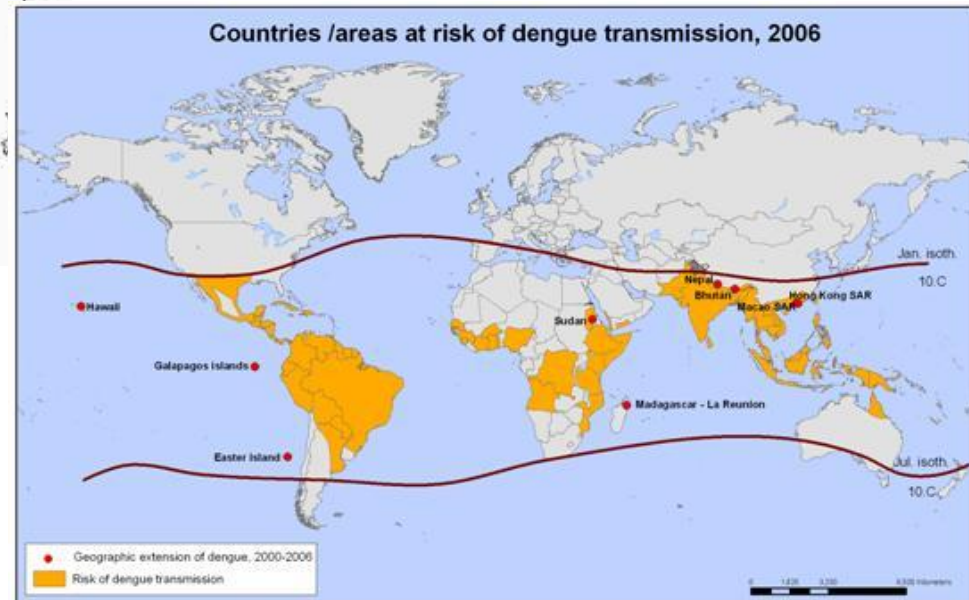
Dengue Hemorrhagic Fever (DHF)

Emergence of DEN/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





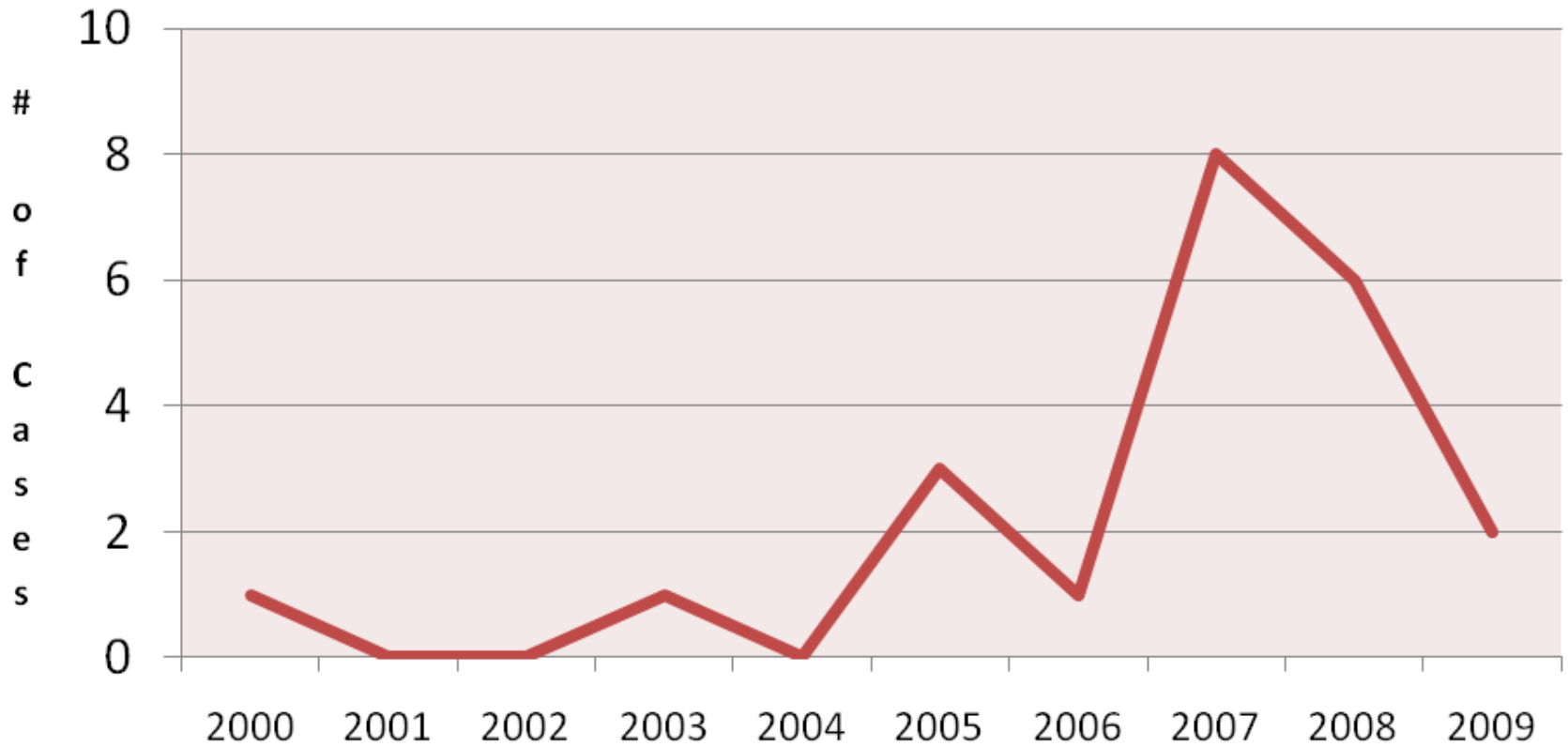
Why Special Operations?

- 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

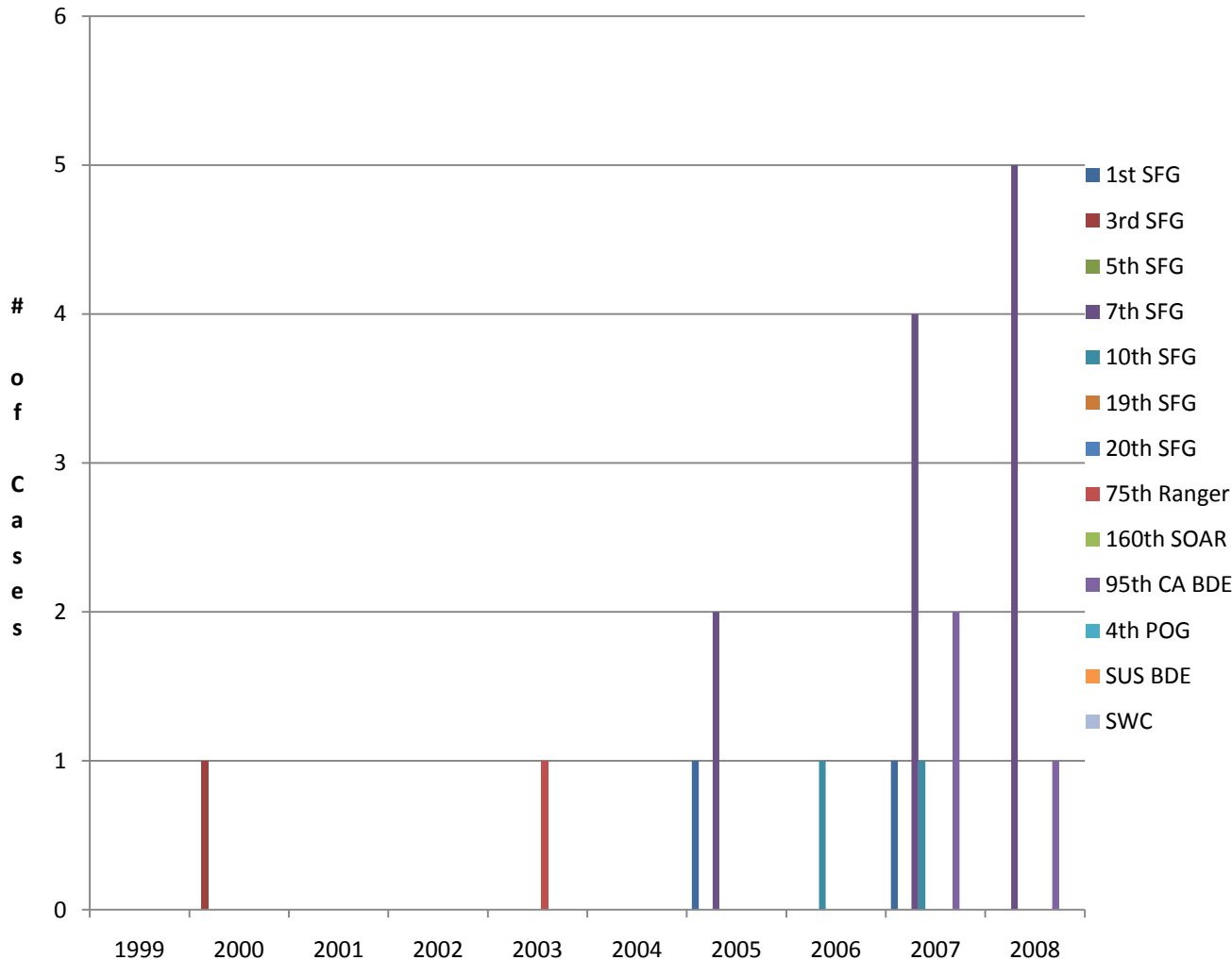
Dengue in USASOC Personnel



2009 data is through Aug 09



Cases by Unit



Reported
Cases of
Dengue

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

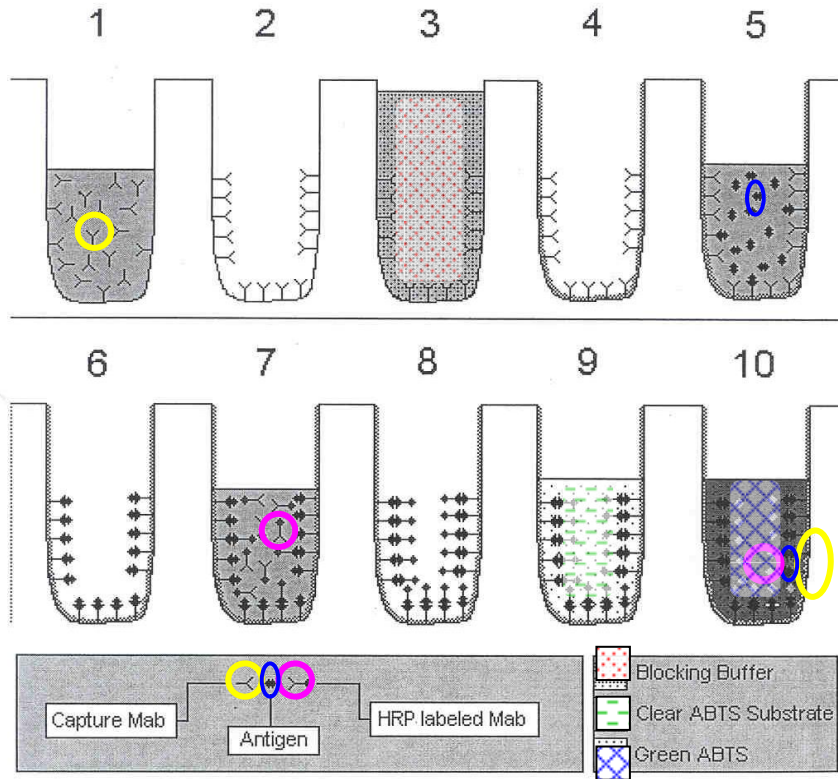
- A collaborative effort between USASOC, WRAIR and AFHSC
- Seroprevalence study of personnel from CA and two SF Groups who have deployed to dengue endemic areas (approximately 1000 samples)
- Samples are from the DoD Serum Repository (DoDSR)
- Lab will look for all 4 serotypes in all samples in the cohort
- 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

This assay is based on the CDC's microneutralization assay for dengue viruses published by Vordam and Beltran in 2002, *Am. J. Trop. Med. Hyg.*, 66, pp. 208-212.

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

REPORTABLE MEDICAL EVENT

PATIENT DATA:

Last Name		First Name	
FMP	Social Security Number	Grade	Date of Birth (DDMMYY)
Base, Camp, Site of Incident (Location)		Gender (Male/Female)	
Country*	APO	Category*	Race:
			White
			Black
			Hispanic
			Asian
			Am Indian
			Other
Unit		UIC	
Unit Location (nearest town)		Duty Phone	

DISEASE DATA: *SEE PAGE 2 FOR CODES

Diagnosis Code*	Diagnosis - Refer to Tri-Service Case Definitions	Onset of Symptoms (DDMMYY)
Confirmed	Method of Confirmation	Admitted
YES	CLINICAL	YES
NO	CULTURE	NO
PENDING	SLIDE	
	BIOPSY	
	SEROLOGY	
	OTHER	

Travel in Previous 3 Years:	Yes	Country #1
	No	Country #2
Malaria Chemoprophylaxis:	Yes	Prophylaxis #1
	No	Prophylaxis #2

HEAT OR COLD INJURIES

Ambient temperature (°F)	WBGT	Previous Heat or Cold Injury	Yes
			No
Wind Speed (MPH)	Body Part or Organ System Affected:	Multi-system involvement:	Yes
			No
Rectal Temperature (°F)		Water Consumption:	
Uniform:			
DCU/Armor/MOPP/Athletic			

REPORTING SOURCE:

Health Care Provider:	Comments/Additional Information:
PM POC:	(See Tri-Service Reportable Events Guidelines)
Phone #:	
Reporting Medical Unit Individual MTF:	
Reported to:	Yes No
Unit Commander	
Higher HQ	
USASOC PM	

USASOC:

Case Entered in JMeW AFIOH Database	Yes	No	Date Transmitted to JMeW
-------------------------------------	-----	----	--------------------------

DISEASE CODES

000 Anthrax	050 Lead Poisoning	090 Syphilis, congenital
002 Arthritis	052 S Legionellosis	095 Syphilis, latent
007 Biological Warfare Agent Exposure	055 C Leishmaniasis, cutaneous	095 Syphilis, late (tertiary)
008 Botulism	055 P Leishmaniasis, mucocutaneous	095 Syphilis, primary/secondary
009 Brucellosis	055 U Leishmaniasis, unspecified	097 S Syphilis, unspecified
009 C2 Campylobacter	056 Leishmaniasis, visceral	097 T Tetanus
009 Carbon Monoxide Poisoning	057 Leprosy	100 S Toxic Shock Syndrome
009 Chemical Agent Exposure	100 Legionellosis	100 Trichinosis
009 C1 Chlamydia	101 Listeria	100 Trypanosomiasis
001 Cholera	058 D1 Lyme disease	011 Tuberculosis, pulmonary
110 Coccioidiomyces	056 Malaria, falciparum	011 Tuberculosis
091 C Cold Injury, Frostbite	056 S Malaria, malariae	002 Typhoid fever
091 C Cold Injury, Hypothermia	056 S Malaria, ovale	002 Typhus fever
091 C Cold Injury, Immersion Type	056 U Malaria, unspecified	099 C Tuberculosis, non-gonococcal
091 P Cold Weather Injury, Unspecified	056 V Malaria, vivax	979 S Vaccine, adverse event
100 S Cryptosporidiosis	058 Malaria	052 S Yersinia, acute duty only
007 S Cytolysis	058 M Meningococcal dis. Meningitis	000 Yellow Fever
001 Dengue fever	058 S Meningococcal dis. Septicemia	
002 Diphtheria	070 Mumps	
002 E coli O157NT	001 Pertussis	
002 E Shigelloidosis	002 Plague	
002 E Meningitis	001 Pneumococcal Pneumonia	
105 Filariasis	002 Rabies	
007 F1 Giardiasis	001 Rabies, human	
009 Gonorrhea	007 Relapsing fever	
009 H1 Haemophilus influenzae, invasive	000 Rheumatic fever, Acute	
009 H2 Haemophilus influenzae	066 S Rocky Mountain Spotted fever	
009 H3 Haemophilus influenzae	000 Rubella	
009 H4 Haemophilus influenzae	000 Salmonellosis	
009 H5 Haemophilus influenzae	100 Schistosomiasis	
070 A Hepatitis A, Acute	006 Shigellosis	
070 B Hepatitis B, Acute	000 Smallpox	
070 S1 Hepatitis C, Acute	000 Streptococci, Grp. A, Invasive	
007 Influenza		

CATEGORY CODES

A11 Army Active Duty	F01 DEP Air Force Active Duty	N01 Navy Active Duty
A21 Army Retired	F02 DEP Air Force Retired	N02 Navy Retired
A61 DEP Army Active Duty	N011 Marine Active Duty	N021 DEP Navy Active Duty
A62 DEP Army Retired	N021 Marine Retired	N022 DEP Navy Retired
F11 Air Force Active Duty	N061 DEP Marine Active Duty	N029 Civilian DEP Civilian
F21 Air Force Retired	N062 DEP Marine Retired	N079 Local National

PRIVACY ACT INFORMATION

Authority: Section 123, Title 10, United States Code (10 USC 123)

Purpose: The purpose of this form is to compile relevant patient information concerning communicable disease and injuries occurring among Department of Defense personnel and family members stationed or operating in Europe.

Responsible: Used to monitor for the emergence of specific communicable disease or outbreaks which pose a public health threat and to prepare data for inclusion in the U.S. Army Medical Surveillance System.

Disclaimer: The requested information is mandatory for compliance with U.S. Non-Nation and Army disease reporting laws and regulations. Failure to provide the requested information will prevent effective public health action and contribute to higher disease and injury rates.

References

- Guzman, M. and G. Kouri. Dengue haemorrhagic fever integral hypothesis: confirming observations, 1987-2007. Trans. of the Royal Soc. of Trop. Med. Hyg. (2008) 102, 522-523.
- Knowlton, K., Solomon, G. and M. Rotkin-Ellman. Mosquito-Borne Dengue Fever Threat Spreading in the Americas. NRDC Issue Paper. July 2009.
- WRAIR 1367 Project 002. USASOC Dengue Seroprevalence Protocol. 10 Sep 09.
- <http://www.promedmail.org/pls/otn/f?p=2400:1000>

An aerial photograph of a rural valley. In the foreground, there are dry, brownish hillsides with sparse vegetation. The middle ground shows a village with several clusters of small, simple buildings, interspersed with fields and some trees. The background features a range of mountains, with the highest peaks covered in snow under a clear blue sky with a few wispy clouds.

Questions?

UNCLASSIFIED