



Dengue

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14 AUG 2012

UNCLASSIFIED



Dengue Lecture Outline

- Dengue Virus
- Dengue Epidemiology
- Military Significance
- Clinical Presentation and Management
- Diagnosis
- Pathophysiology



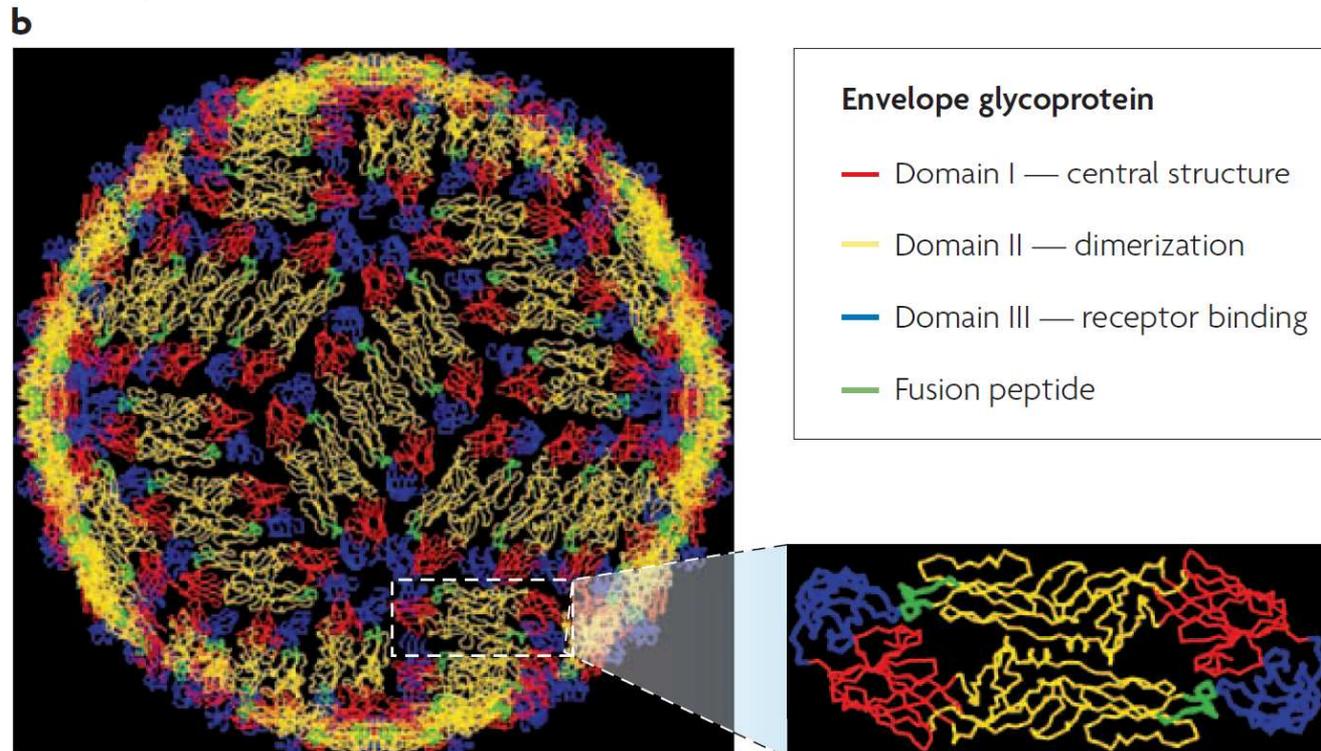
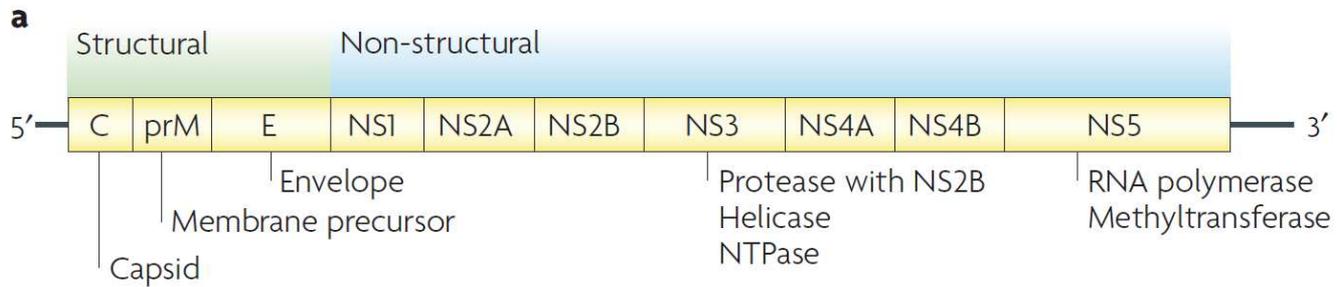
Dengue Virus (DENV)

- Virus
 - Positive-polarity, single-stranded RNA genome
 - Flavivirus (YF, JE, WNV, DENV)
 - 4 serotypes: DENV-1-4
 - Multiple genotypes
- Vector
 - Mosquito (*Aedes aegypti/albopictus*)
- Transmission
 - Feeding mosquito vector
 - Laboratory



Aedes aegypti

Dengue Virus



Dengue Epidemiology



Dengue Ward: QSNICH, Bangkok, Thailand (Photo: Christopher Brown, IHT)



Facts

- Leading arboviral infection of humans
- >120 countries reporting indigenous transmission
- >3.5 billion people living at risk for infection
- >50 million infections annually
- >500,000 severe cases annually
- >30,000 deaths annually
- No licensed vaccine / therapeutic
- Effective vector control very difficult

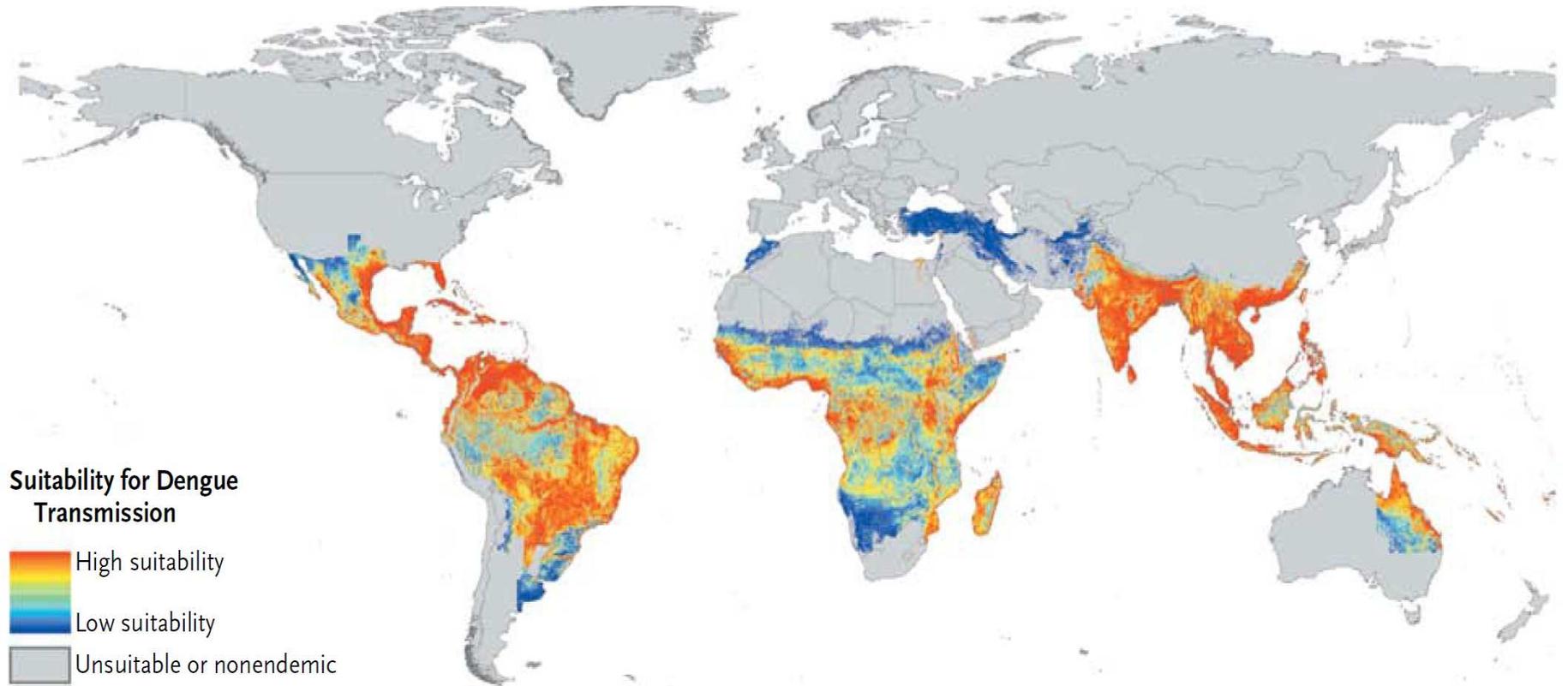


Dengue Ward: QSNICH, Bangkok, Thailand (Photo: Christopher Brown, IHT)



Dengue

Areas supporting dengue virus transmission.



Factors Driving Transmission

- Population increases
 - Migration
 - Urbanization
 - Poverty
 - Vector expansion
 - International travel
-
- Changing global ecology
 - Vector evolution
 - Viral evolution



Dengue ↔ Aedes

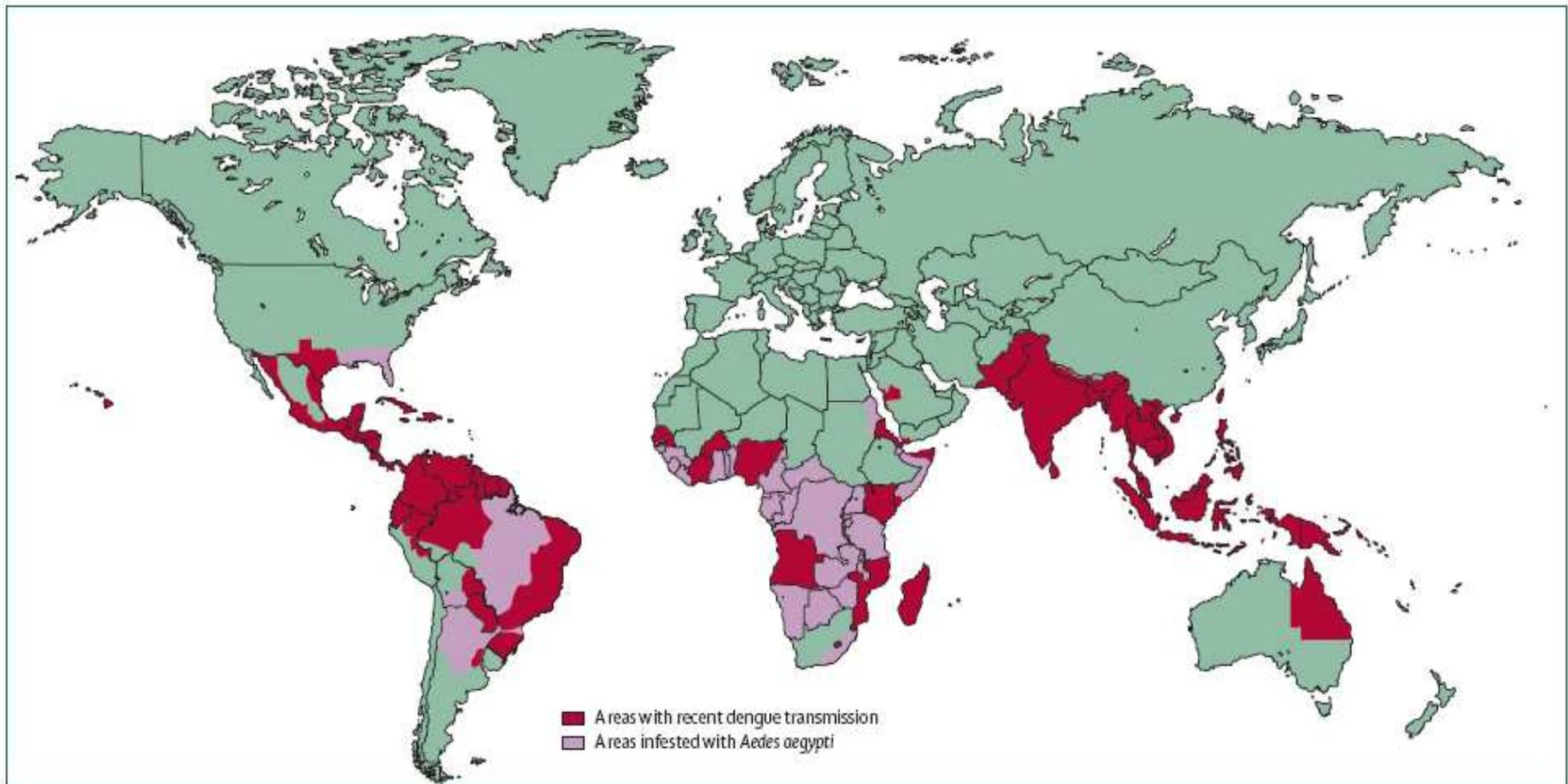
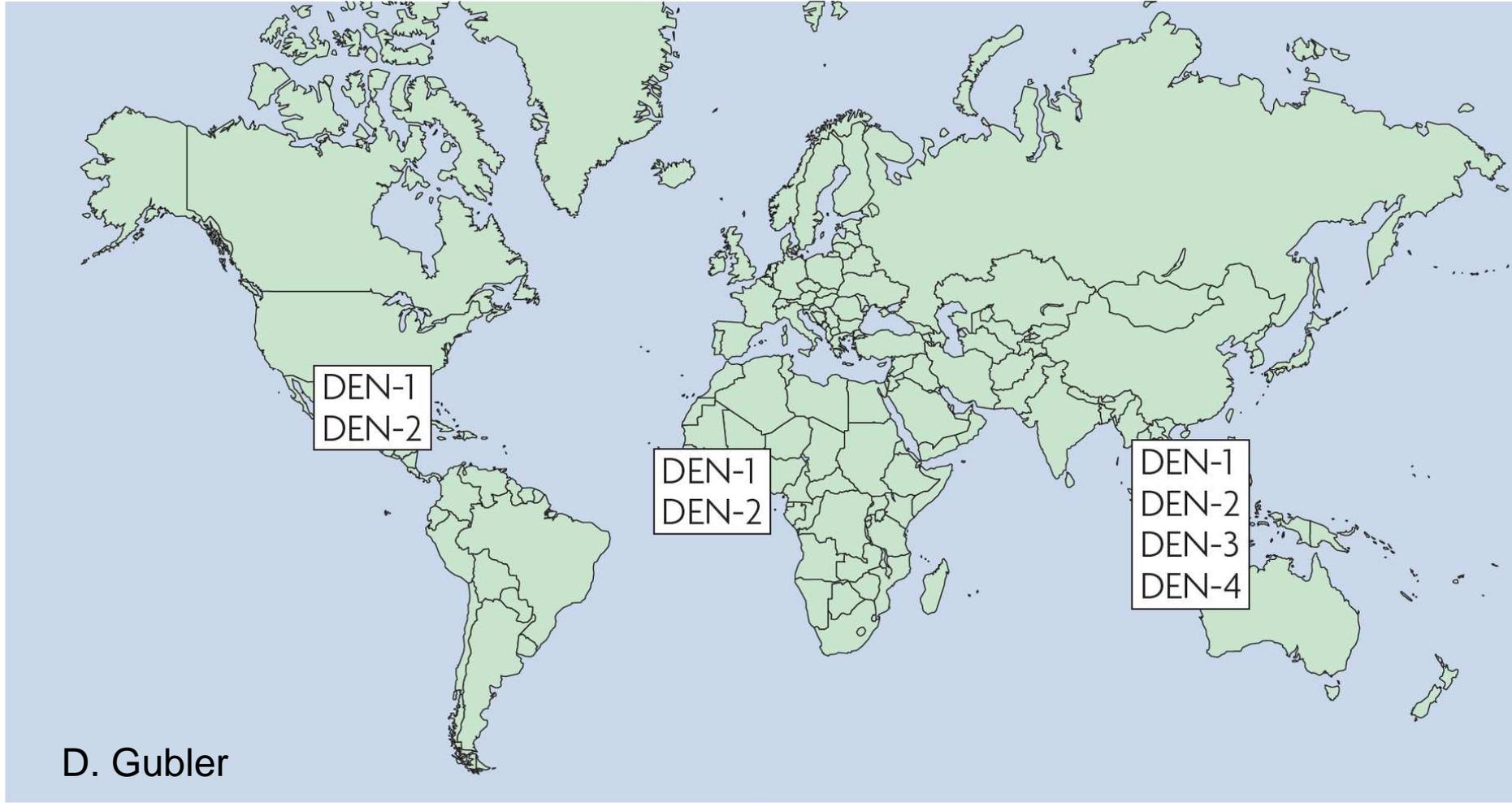


Figure 1: Approximate global distribution of dengue and *Aedes aegypti* in 2005
Reprinted with permission of the US Centers for Disease Control and Prevention.

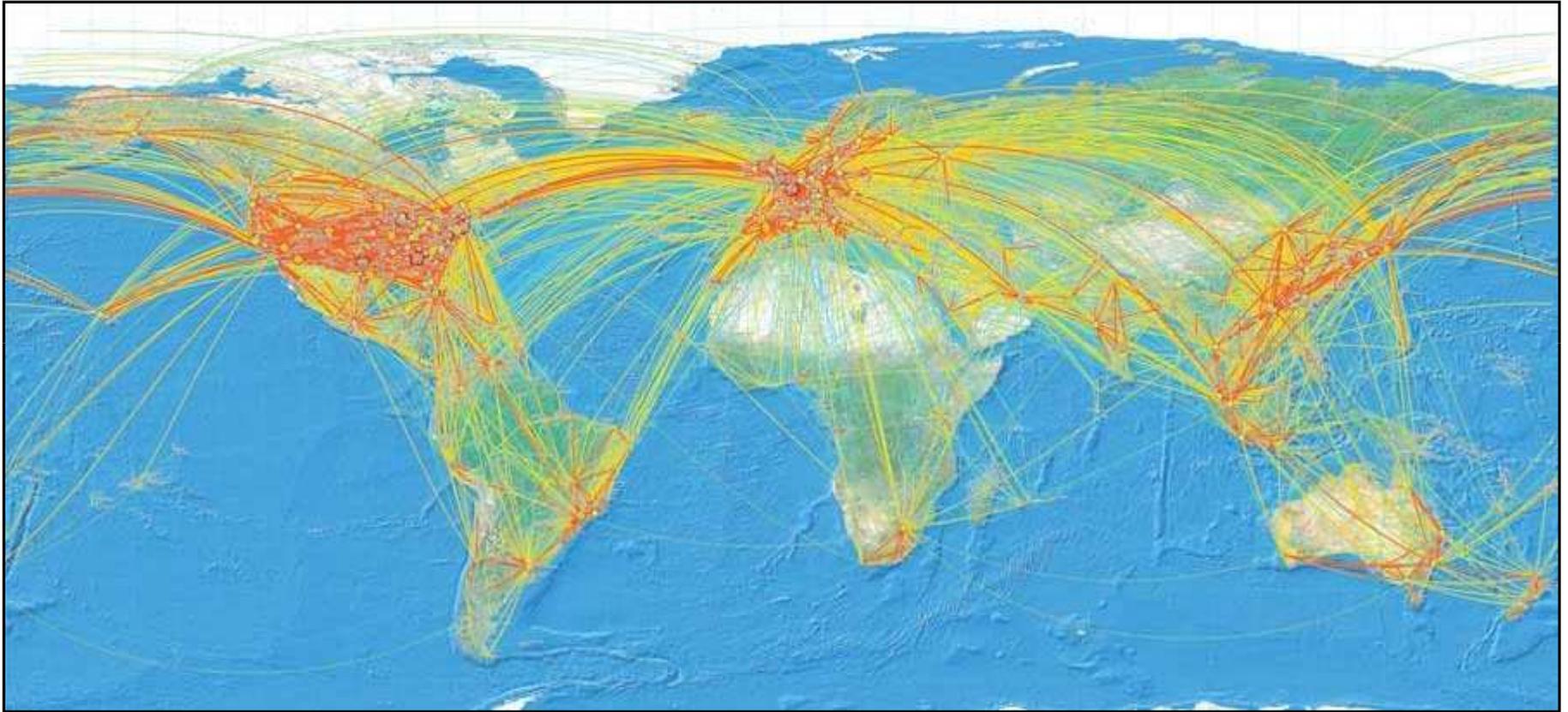
www.thelancet.com Vol 370 November 10, 2007



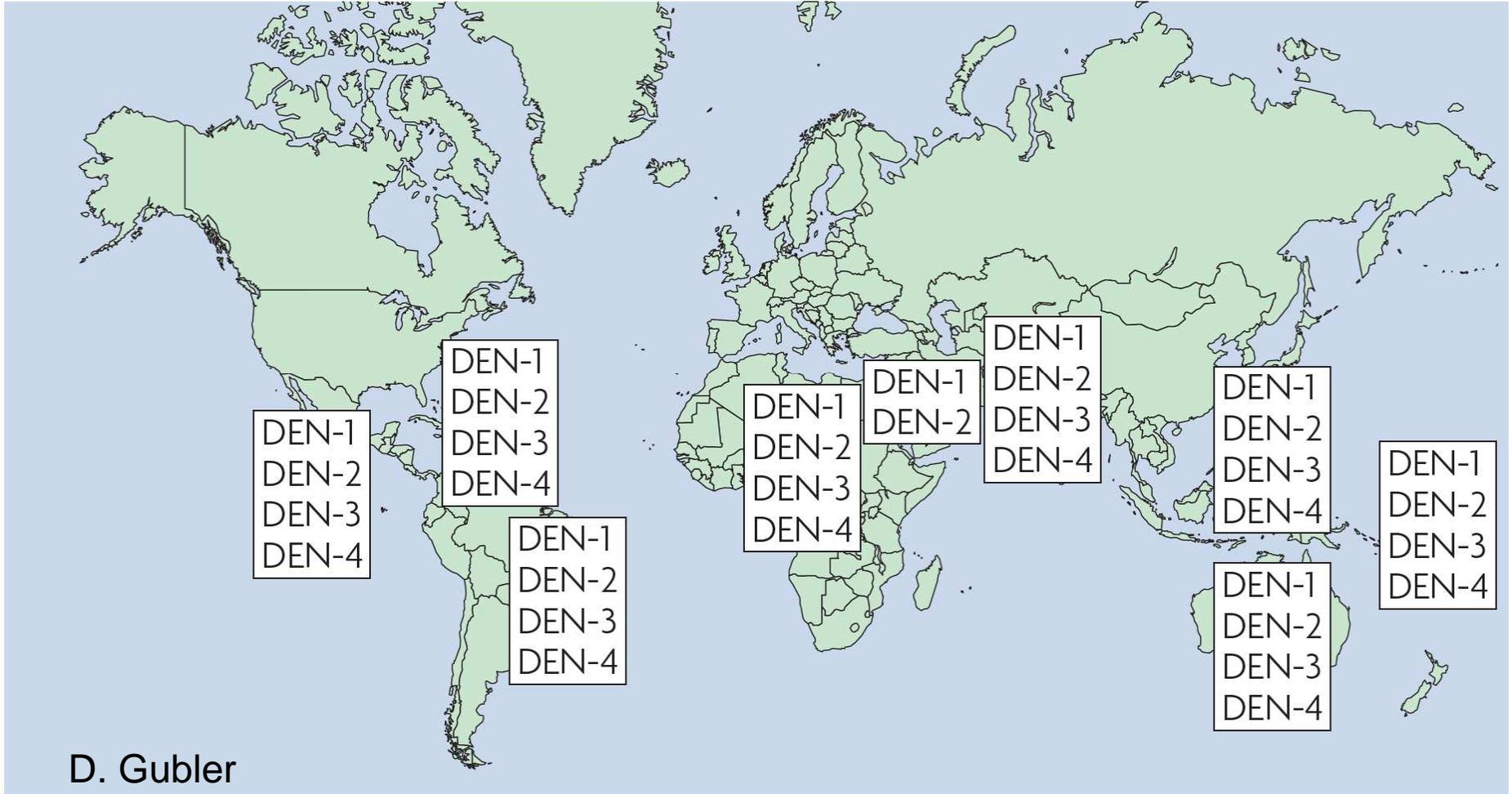
DENV Type Distribution - 1970



Global Air Travel Flight Patterns



DENV Type Distribution - 2004



DENGUE

GUIDELINES FOR DIAGNOSIS, TREATMENT, PREVENTION AND CONTROL



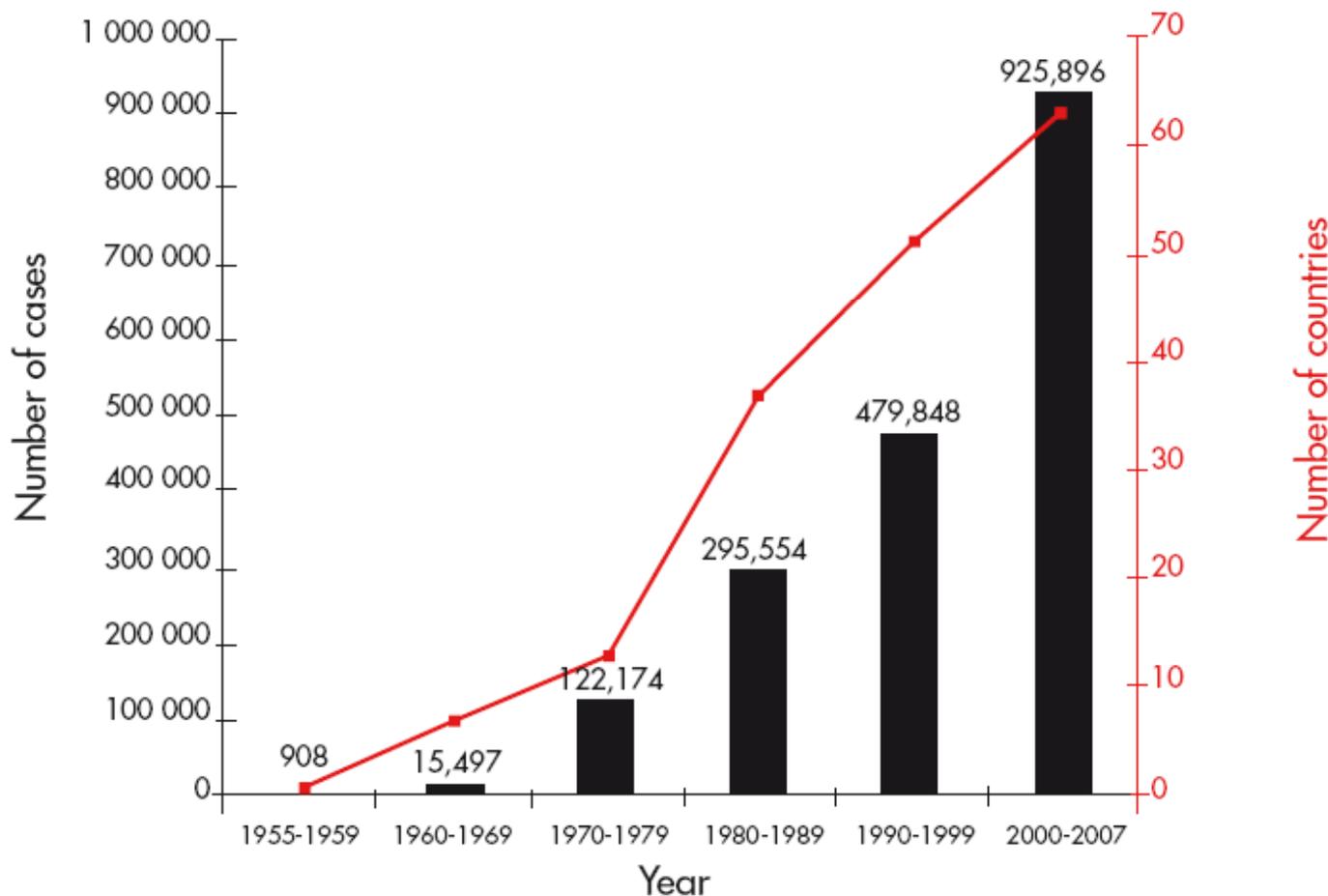
For research on
diseases of poverty
UNICEF · UNDP · World Bank · WHO



World Health
Organization

New edition
2009

Figure 1.2 Average annual number of dengue fever (DF) and dengue haemorrhagic fever (DHF) cases reported to WHO, and of countries reporting dengue, 1955–2007

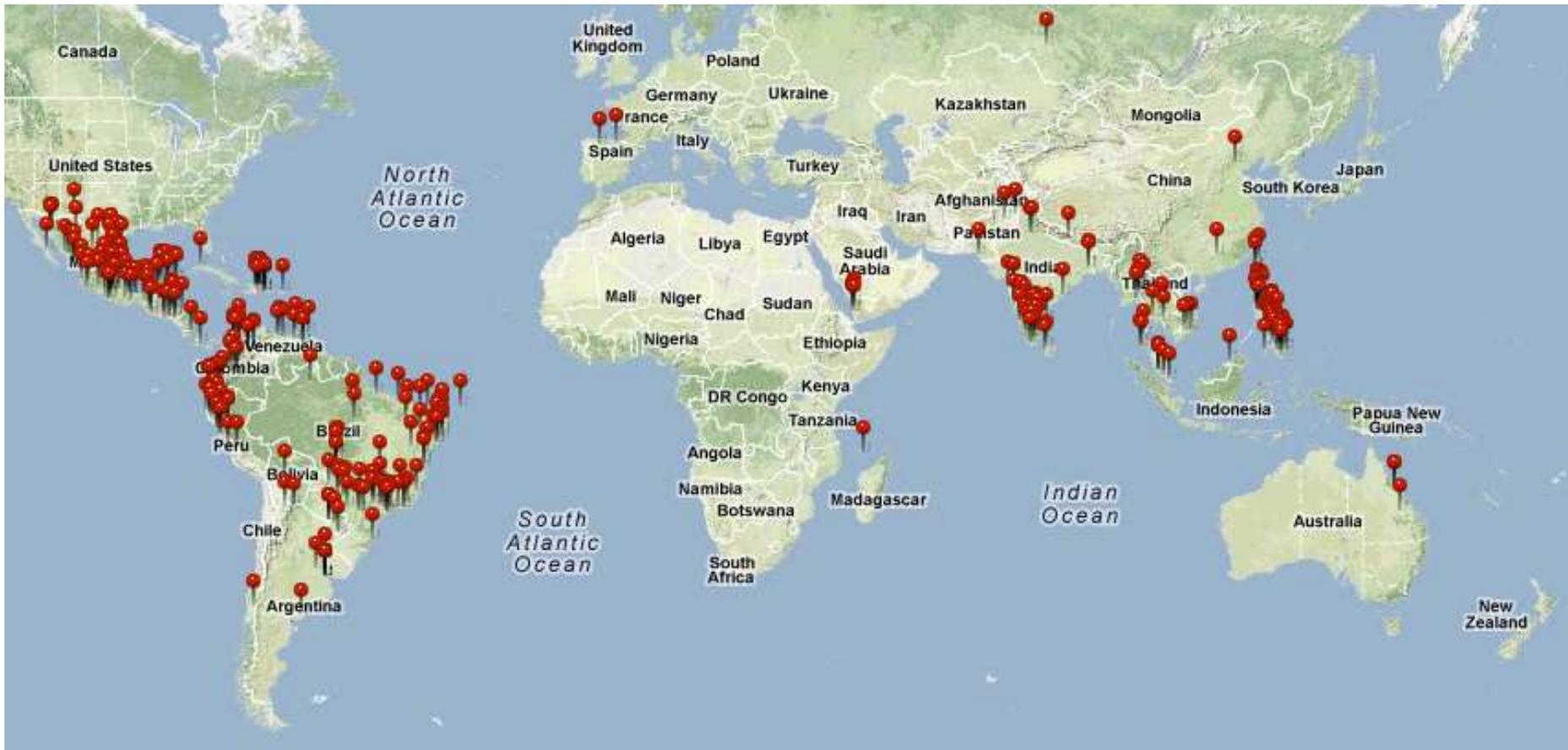




DengueMap

A CDC-HealthMap Collaboration

14 AUG 2012



The Epidemiology of Dengue in the Americas Over the Last Three Decades: A Worrisome Reality

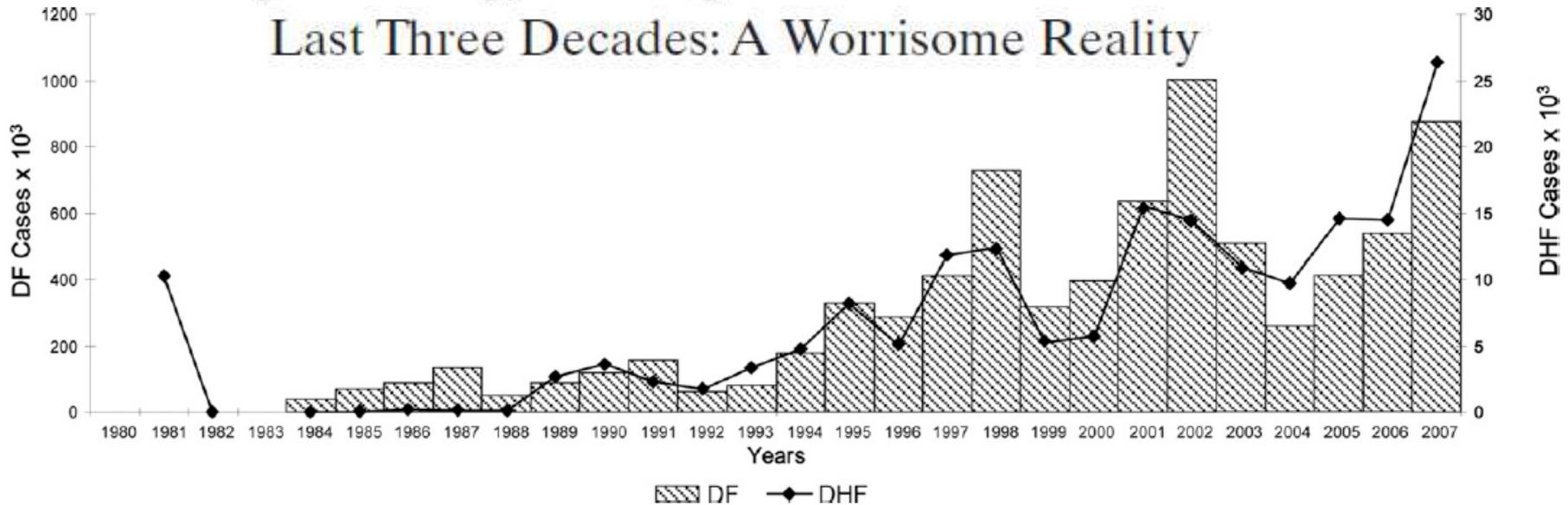


FIGURE 1. Number of dengue fever (DF) and dengue hemorrhagic fever (DHF) cases, Region of the Americas, 1980–2007.

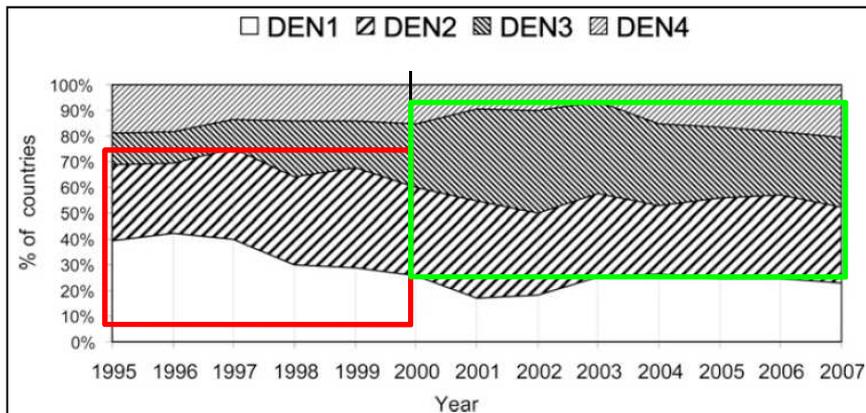


FIGURE 4. Percentage of countries reporting serotypes 1–4 to the Pan American Health Organization by year, Region of the Americas, 1995–2007.

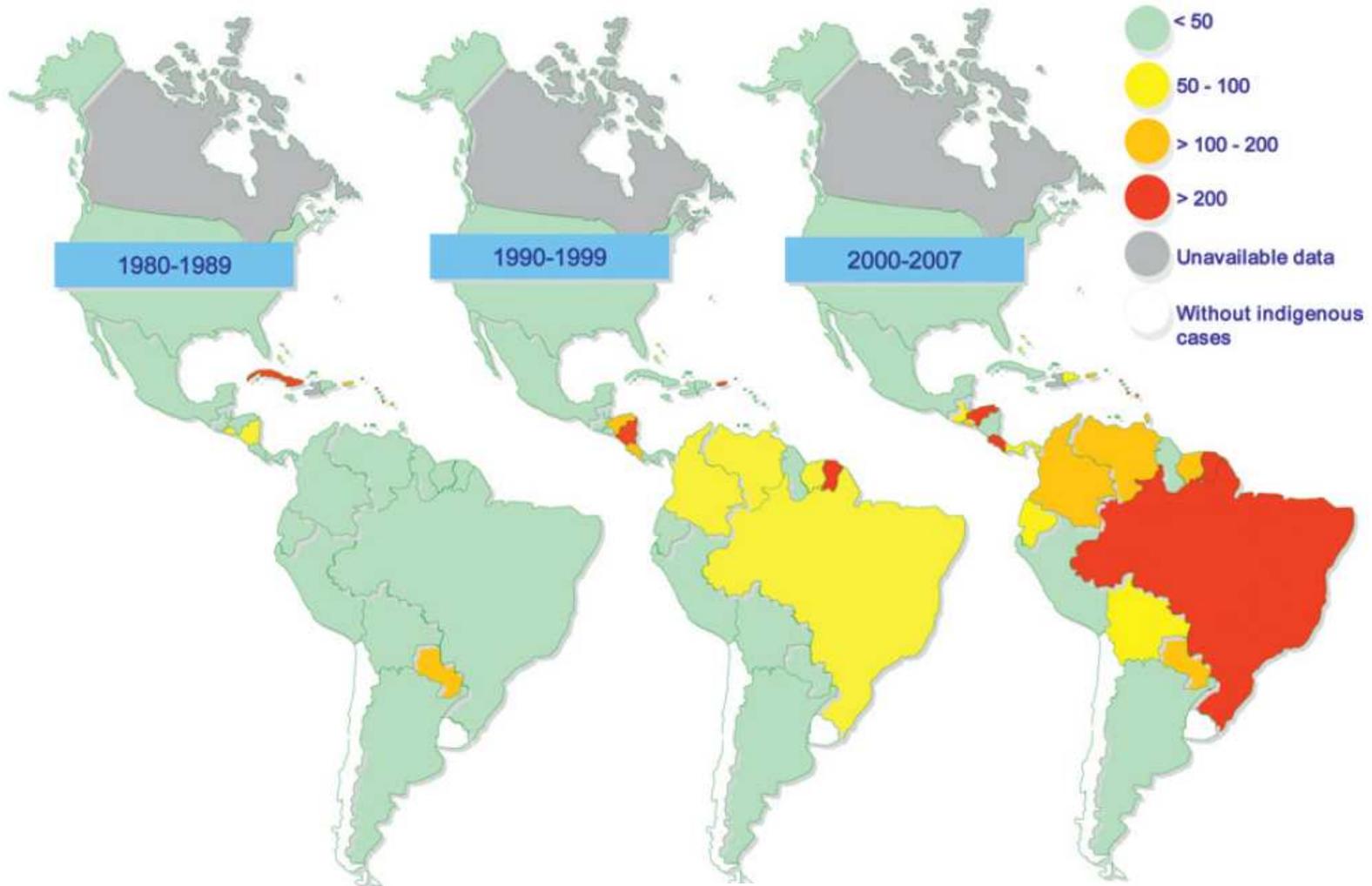
José Luis San Martín,* Olivia Brathwaite, Betzana Zambrano, José Orlando Solórzano, Alain Bouckenooghe, Gustavo H. Dayan, and María G. Guzmán

Dengue Regional Program, Pan American Health Organization (PAHO), Panama, Republic of Panama; Clinical Department, Sanofi Pasteur, Swiftwater, Pennsylvania; General Directorate of Health Surveillance, Secretariat of Health, Tegucigalpa, Honduras; Virology Department, PAHO/World Health Organization Collaborating Center for the Study of Dengue and its Vector, Institute of Tropical Medicine Pedro Kouri, Havana, Cuba

Am. J. Trop. Med. Hyg., 82(1), 2010, pp. 128–135



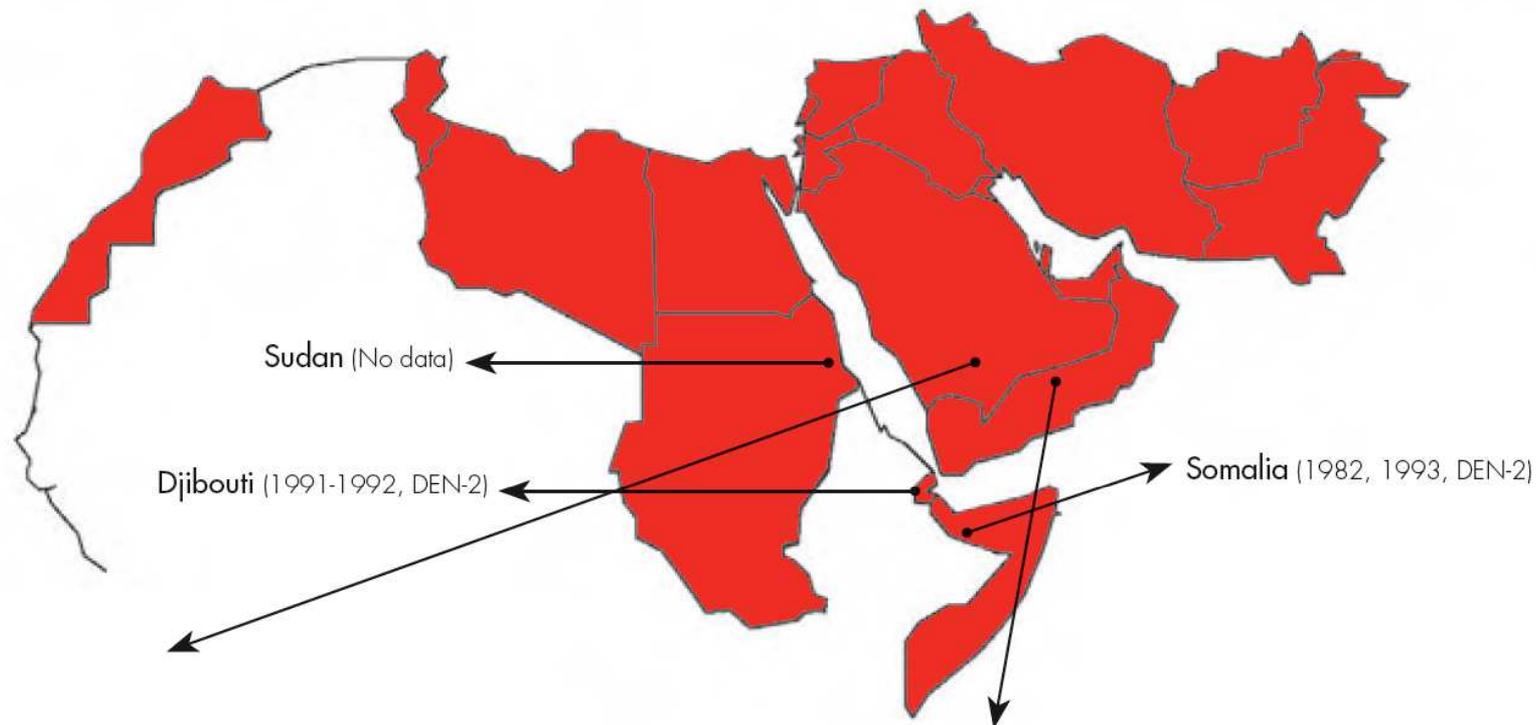
Average dengue incidence per 100,000 by country, Region of the Americas, 1980–2007.



Am. J. Trop. Med. Hyg., 82(1), 2010, pp. 128–135



Figure 1.3 Outbreaks of dengue fever in the WHO Eastern Mediterranean Region, 1994–2005



DEN-2:

1994:	673 suspected cases,	289 confirmed cases
1995:	136 suspected cases,	6 confirmed cases
1996:	57 suspected cases,	2 confirmed cases
1997:	62 suspected cases,	15 confirmed cases
1998:	31 suspected cases,	0 confirmed cases
1999:	26 suspected cases,	3 confirmed cases
2000:	17 suspected cases,	0 confirmed cases
2001:	7 suspected cases,	0 confirmed cases
2005:	32 suspected (confirmed)	

Al-Hudaydah, Makkala, Shaabwa

(1994, DEN-3, no data);

Al-Hudaydah, Yemen

(September 2000, DEN-2, 653 suspected cases, 80 deaths (CFR = 12%));

Al-Hudaydah, Yemen

(March 2004, 45 suspected cases, 2 deaths);

Al-Hudaydah, Makkala

(March 2005, 403 suspected cases, 2 deaths);



Pakistan

NO. OF REPORTED DEATHS

211

DENGUE FEVER

This fever is caused due to the bite of a specific kind of mosquito. What's special about this mosquito is it has white and black stripes on its body, and it bites only in the day time.

Identification of the disease:

The presence of virus of this disease in the body can only be ascertained through blood test in the laboratory.

INDICATIONS:

The specific indications of this disease

include fever with:

- Pain in back, body and joints
- Presence of spots on the body
- Pain in eyeballs
- Shortage of white cells in the blood
- Severe headache, cold and flu
- In case of serious illness, blood may be emitted from different parts of the body like mouth and the nose.

TREATMENT

This disease neither has a specific cure nor a vaccine available. Therefore, as soon as there are any such indications, give the patient as much liquids as possible and contact the nearest health centre.

PRECAUTIONARY MEASURES:

- Keep your homes and offices protected against mosquitoes
- Keep homes and offices airy, bright and safe from moisture.
- Fix nets on doors and windows
- Wear full sleeves clothes
- Use mosquito nets while sleeping
- Don't leave the overhead tanks open
- Don't keep water in containers for more than a week. Instead, empty them every week, let them dry and then fill again
- Don't let the water falling from the overhead tanks to accumulate permanently. Instead dry it.
- Don't let the water accumulate in any case both inside or outside the home.
- Be mindful of your home and mohallah's cleanliness.
- Keep the fence and hedge boundaries duly cut both inside and outside the home, and spray over them with insecticides, particularly in the evening
- Don't let the water stay all the time in the flowers pots, gamias of plants. Instead water them only in the morning every alternate day.

Please Remember!
This is neither hereditary
nor epidemic disease

Health Education Cell, Health Group of Offices



CITY DISTRICT GOVERNMENT KARACHI

CDGKIADVT1247/006 RECONSTRUCTION OF KARACHI – CITY GOVERNMENT'S RESOLVE



Brown – dengue reported

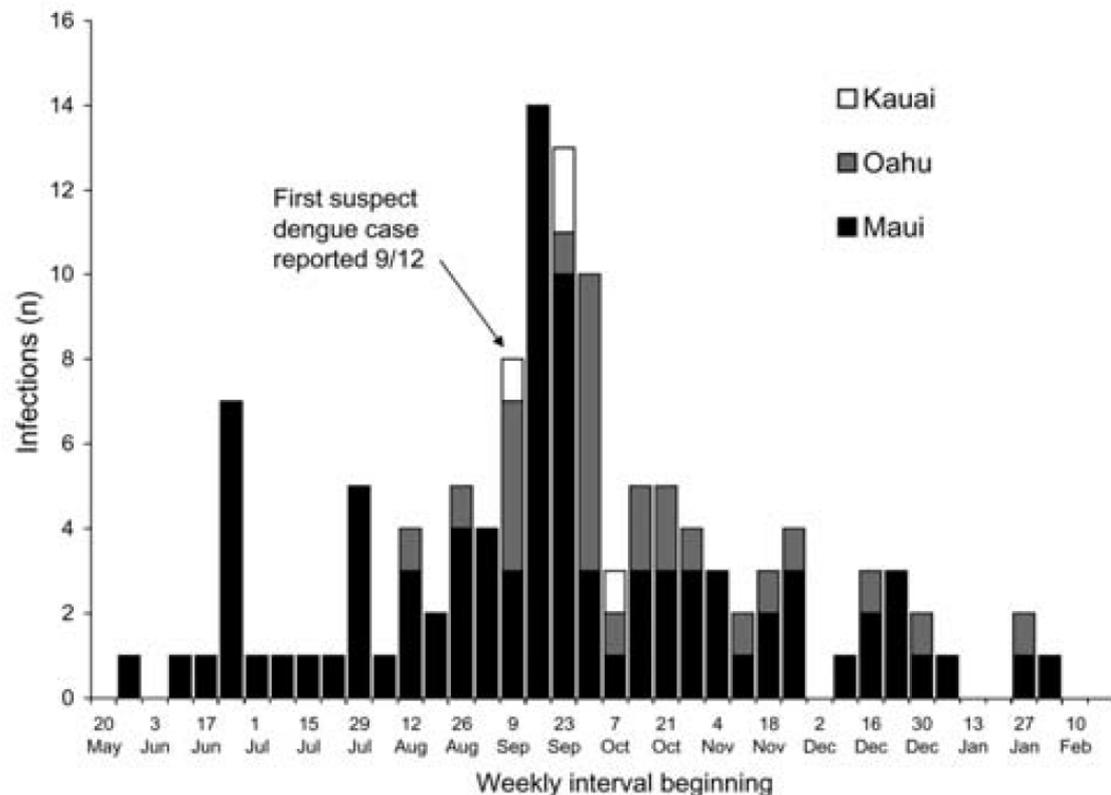
Light Brown – dengue not reported but vector exists

White – data not available



Dengue Fever, Hawaii, 2001–2002

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 11, No. 5, May 2005



Am. J. Trop. Med. Hyg., 59(1), 1998, pp. 95–99

DENGUE SURVEILLANCE IN TEXAS, 1995

JULIE A. RAWLINGS, KATHERINE A. HENDRICKS, CHRISTINE R. BURGESS, RICHARD M. CAMPMAN,
GARY G. CLARK, LAURA J. TABONY, AND MARY ANN PATTERSON

Infectious Disease Epidemiology and Surveillance Division and Bureau of Laboratories, Texas Department of Health, Austin, Texas; Dengue Branch, Centers for Disease Control and Prevention, San Juan, Puerto, Rico

Dengue Hemorrhagic Fever --- U.S.-Mexico Border, 2005

Weekly
August 10, 2007 / 56(31);785-789

Am. J. Trop. Med. Hyg., 78(3), 2008, pp. 364–369





Table 3. Etiologic Diagnoses within Selected Syndrome Groups, According to Travel Region.*

Syndrome and Cause	All Regions	Caribbean	Central America	South America	Sub-Saharan Africa	South Central Asia	Southeast Asia	Other or Multiple Regions†
<i>number of cases per 1000 patients with syndrome</i>								
Systemic febrile illness (n= 3907)								
Specific pathogen or cause reported‡	594	459	527	446	718	522	547	454
Malaria‡	352	65	133	133	622	139	130	234
Dengue‡	104	238	123	138	7	142	315	35
Mononucleosis (due to Epstein–Barr virus or cytomegalovirus)‡	32	70	69	79	10	17	32	63
Rickettsial infection‡	31	0	0	0	56	10	16	24
<i>Salmonella typhi</i> or <i>S. paratyphi</i> infection‡	29	22	25	17	7	141	26	24
No specific cause reported‡	406	541	473	554	282	478	453	546

‡ P<0.01 for the comparison among regions.

*“With respect to specific diagnoses, malaria was one of the three most frequent causes of systemic febrile illness among travelers from every region, **although travelers from every region except sub-Saharan Africa and Central America had confirmed or probable dengue more frequently than malaria.**”*



Seasonality, Annual Trends, and Characteristics of Dengue among Ill Returned Travelers, 1997–2006

Table 1. Dengue and malaria diagnoses as a proportion of all morbidity in ill returned travelers according to region or country of acquisition

Region* or country of exposure	No. ill returned travelers with dengue	No. ill returned travelers with malaria	Total no. ill returned travelers	Dengue proportionate morbidity†	Malaria proportionate morbidity†
Southeast Asia	264	103	3,694	71	28
Thailand	154	9	1,523	101	5
Indonesia	38	53	652	58	81
South Central Asia	90	70	3,303	27	21
India	66	57	2,119	31	27
Caribbean	47	14	1,470	32	9
South America	40	49	2,427	16	20
Brazil	22	12	685	32	18
Central America	37	27	1,867	20	14
Africa	25	1,216	7,231	3	168
Sub-Saharan Africa	23	1,201	6,201	4	194
Oceania	11	91	303	36	300
Other‡ or multiple regions of exposure	7	23	4,443	2	5
Country missing	1	12	182	5	66
Total	522	1,605	24,920	21	64

*Regions defined per (9).

†Proportionate morbidity expressed per 1,000 ill returned travelers seen at GeoSentinel clinics.

‡No cases were acquired in Canada, United States, Western Europe, Japan, or Australia.



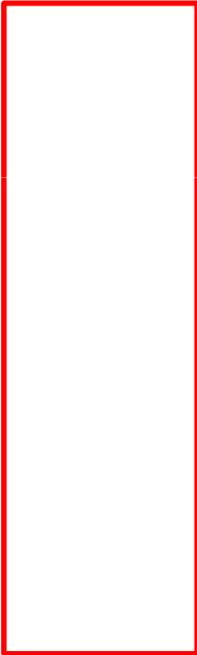
Dengue's Military Significance

- Philippines
- World War II
- Vietnam
- Philippines
- Haiti
- Somalia



Disease	2010 COCOM panel rank	ID-IDEAL Rank
Malaria	1	2
Dengue	2	3
Diarrhea, bacterial	3	1
MDR wound pathogens	4	NA
Leishmaniasis	5	19
Q fever (Coxiella burnetti)	6	26
Norovirus and other viral diarrhea	7	NA
Influenza	8	NA
Leptospirosis	10	7
Diarrhea, protozoal	11	11
TB	12	NA
CCHF	13	10
HIV	14	8
HFRS	15	17
Chikungunya	16	4
Meningococcal meningitis	17	20
Plague	18	27
Rickettsioses	19	18
Viral encephalitides	20	NA





Dengue During Viet Nam War



DENGUE FEVER IN U.S. TROOPS DURING OPERATION RESTORE HOPE, SOMALIA, 1992–1993

TRUEMAN W. SHARP, MARK R. WALLACE, CURTIS G. HAYES, JOSE L.
SANCHEZ, ROBERT F. DEFRAITES, RAY R. ARTHUR, SCOTT A. THORNTON,
ROGER A. BATCHELOR, PATRICK J. ROZMAJZL, R. KEVIN HANSON, SHUENN
JUE WU, CRAIG IRIYE, AND JAMES P. BURANS

Am. J. Trop. Med. Hyg., 53(1), 1995, pp. 89–94

- Hospitalized troops with fever / Unit survey of 494
- 129 / 289 hospitalized w/ fever = no diagnosis
 - 41 / 96 had DENV isolated (39 = DENV-2, 2 = DENV-3)
 - 18 / 37 culture negative had IgM antibodies vs. dengue
- Survey of 494 = 77% prevalence of dengue antibodies



Dengue Fever in US Military Personnel in Haiti JAMA, May 21, 1997—Vol 277, No. 19

Andrew F. Trofa, MD; Robert F. DeFraités, MD; Bonnie L. Smoak, MD; Niranjan Kanesa-thasan, MD; Alan D. King, VMD; Jeanne M. Burrous, MS; Phillip O. MacArthy, PhD; Cindy Rossi, MS; Charles H. Hoke, Jr, MD

- **OBJECTIVE:** Describe outbreak of dengue fever (DF) during Operation Uphold Democracy, Haiti, 1994.
- **PATIENTS:** 101 US military personnel with acute febrile illnesses.
- **RESULTS:** Febrile illnesses accounted for 103 (25%) of the 406 combat support hospital admissions during the first 6 weeks of deployment. A total of 30 patients had DF. Dengue virus serotypes 1, 2, and 4 were isolated from 22 patients, and 8 patients developed IgM antibody to dengue virus. Patients with DF could not be distinguished from other febrile patients on clinical grounds alone.
- **CONCLUSIONS:** **DF accounted for at least 30% of the febrile illnesses among hospitalized US troops.**



59th Annual Meeting ASTMH

- USASOC
- DODSR
- 500 samples
- Dengue ELISA
- **11% seroprevalence**



WRAIR USASOC DODSR Study - 2012

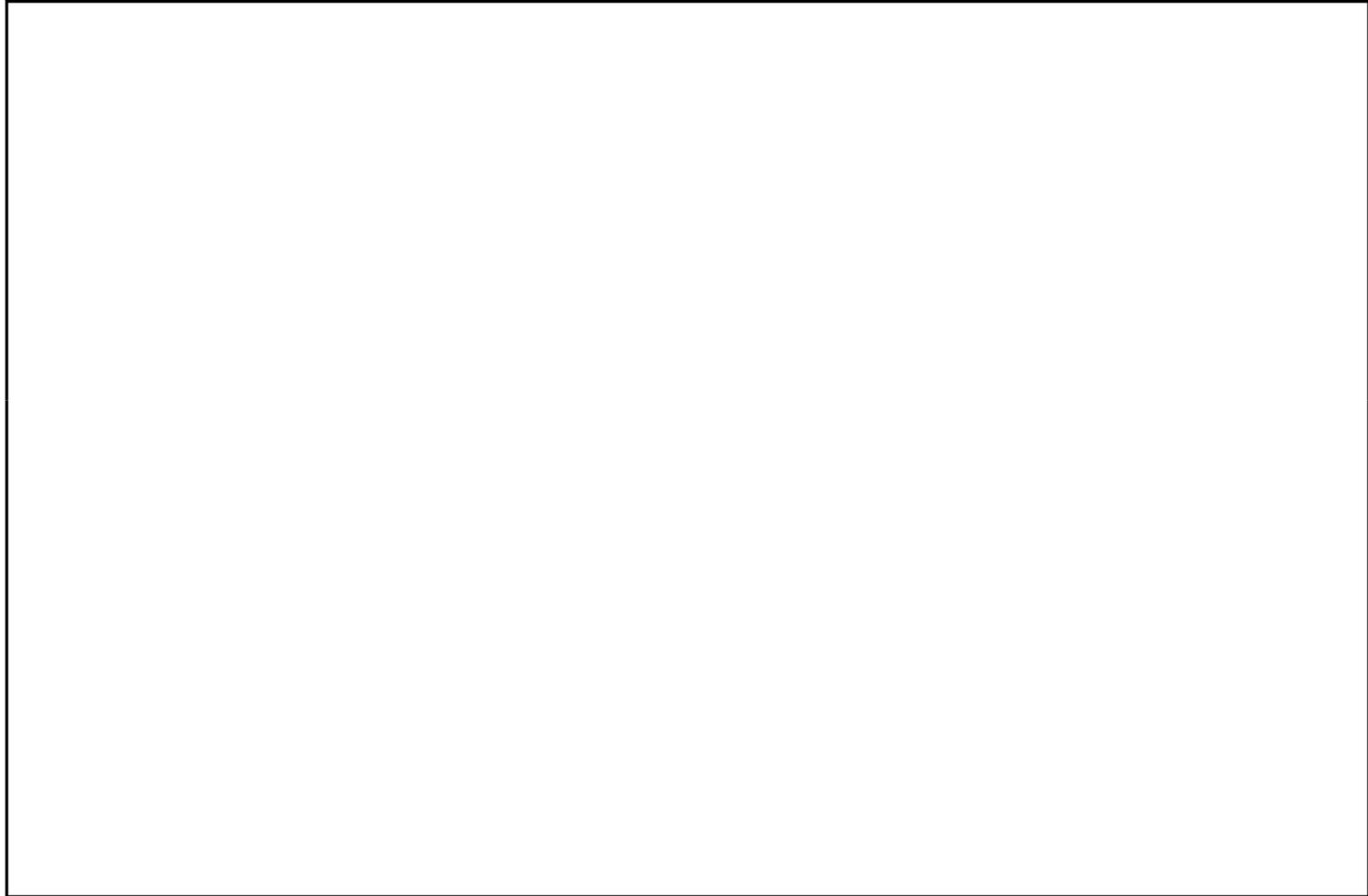
Seroprevalence Based on 1,000 Post-Deployment Samples in First Time Deployers

	Central America*	South America	Asia	Africa*	Total
Percent	4.8	12.4	7.2	6.0	7.6

- **Overall seroprevalence = 7.6%**
- Highest prevalence among those serving in the Army
- Positive association with older age
- No effect of deployment length
- Increased self-report of fever among those w/ antibodies



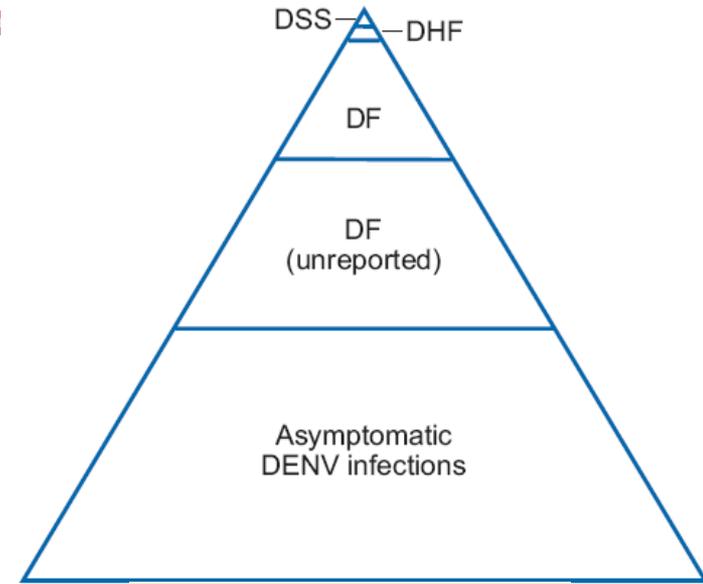
Dengue Clinical Presentation / Management



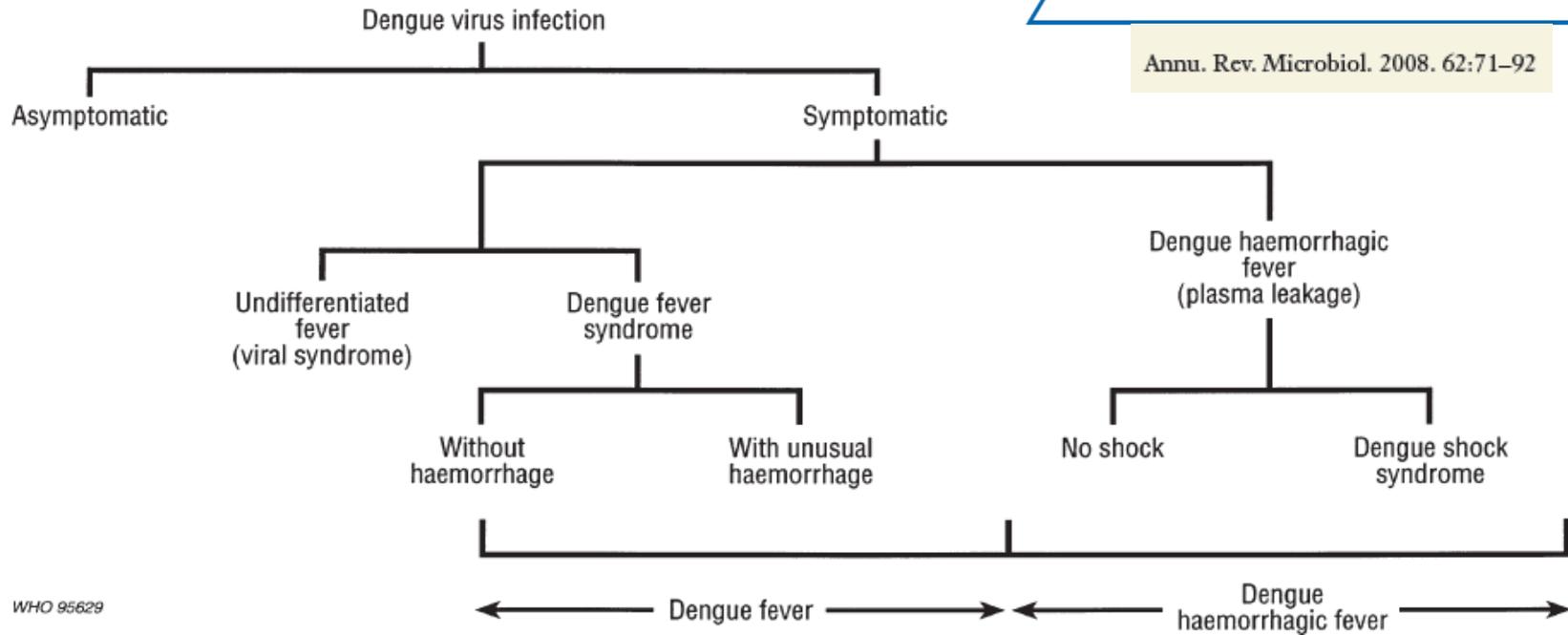
Dengue Ward: QSNICH, Bangkok, Thailand (Photo: Christopher Brown, IHT)



Dengue Infection Clinical Phenotypes

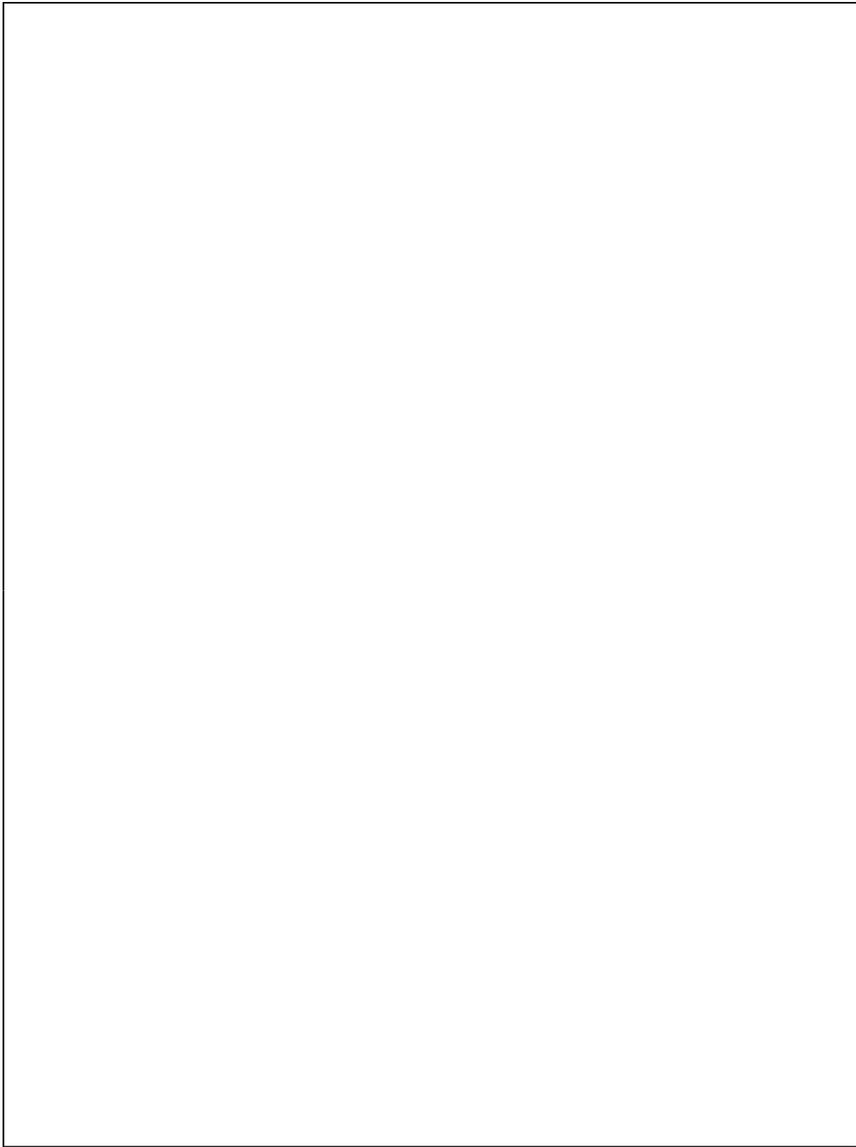


Annu. Rev. Microbiol. 2008. 62:71-92



WHO 95629





Probable dengue

live in /travel to dengue endemic area.

Fever and 2 of the following criteria:

- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leukopenia
- Any warning sign

Laboratory-confirmed dengue

(important when no sign of plasma leakage)

Warning signs*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargement >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

*(requiring strict observation and medical intervention)

Severe plasma leakage

leading to:

- Shock (DSS)
- Fluid accumulation with respiratory distress

Severe bleeding

as evaluated by clinician

Severe organ involvement

- Liver: AST or ALT \geq 1000
- CNS: Impaired consciousness
- Heart and other organs



Dengue Hemorrhagic Fever

Table 1. WHO Classification of DHF

Grades	Increase in Hematocrit*	Hemorrhage†	Shock‡	Profound shock§
1	+	-	-	-
2	+	+	-	-
3	+	±	+	-
4	+	±	+	+

*Hematocrit increased by at least 20%.

†Spontaneous bleeding in skin and/or other sites.

‡Hypotension and/or narrowing of pulse pressure to 20 mmHg or less, with cold clammy skin and restlessness.

§Undetectable blood pressure or pulse.



Dengue Fever in US Military Personnel in Haiti

JAMA 1997;
277:19:1546-1548

Symptoms in Febrile Patients
Admitted to the 28th Combat
Support Hospital, Port-au-
Prince, Haiti, SEP 27, 1994 -
NOV 4, 1994

Symptoms	Dengue Fever, No. of Patients (%) (n=30)	Non-dengue Fever, No. of Patients (%) (n=40)
Malaise	30 (100)	40 (100)
Headache	27 (90)	38 (95)
Chills	26 (87)	34 (85)
Backache	22 (73)	24 (60)
Loss of appetite	21 (70)	30 (75)
Rigors	19 (63)	20 (50)
Arthralgia	18 (60)	21 (53)
Myalgia	18 (60)	27 (68)
Nausea	17 (57)	31 (78)
Neck stiffness	11 (37)	24 (60)
Diarrhea	11 (37)	25 (63)
Conjunctival irritation	10 (33)	21 (30)
Abdominal pain	10 (33)	23 (58)
Coryza	10 (33)	24 (60)
Photophobia	8 (27)	15 (38)
Cough	7 (23)	16 (40)
Sore throat	6 (20)	18 (45)
Altered taste	5 (17)	2 (5)
Vomiting	5 (17)	11 (28)



Physical Findings in Febrile Patients

Finding	Dengue Fever (n=30)	Non-dengue Fever (n=40)
Maximum temperature, mean °C (range)	39.2 (38.4-40.8)	38.9 (38.1-40.7)
Maximum pulse rate, Mean	88	91
Conjunctival injection, No. (%)†	16 (53)	9 (23)
Pharyngeal erythema, No. (%)	5 (17)	5 (13)
Neck stiffness, No. (%)	2 (7)	3 (8)
Abdominal tenderness	6 (20)	17 (43)
Lymphadenopathy, No. (%)	10 (30)	9 (23)
Rash, No. (%)‡	16 (53)	1 (3)

**P* values indicate probabilities associated with χ^2 of difference in proportions between the 2 groups.

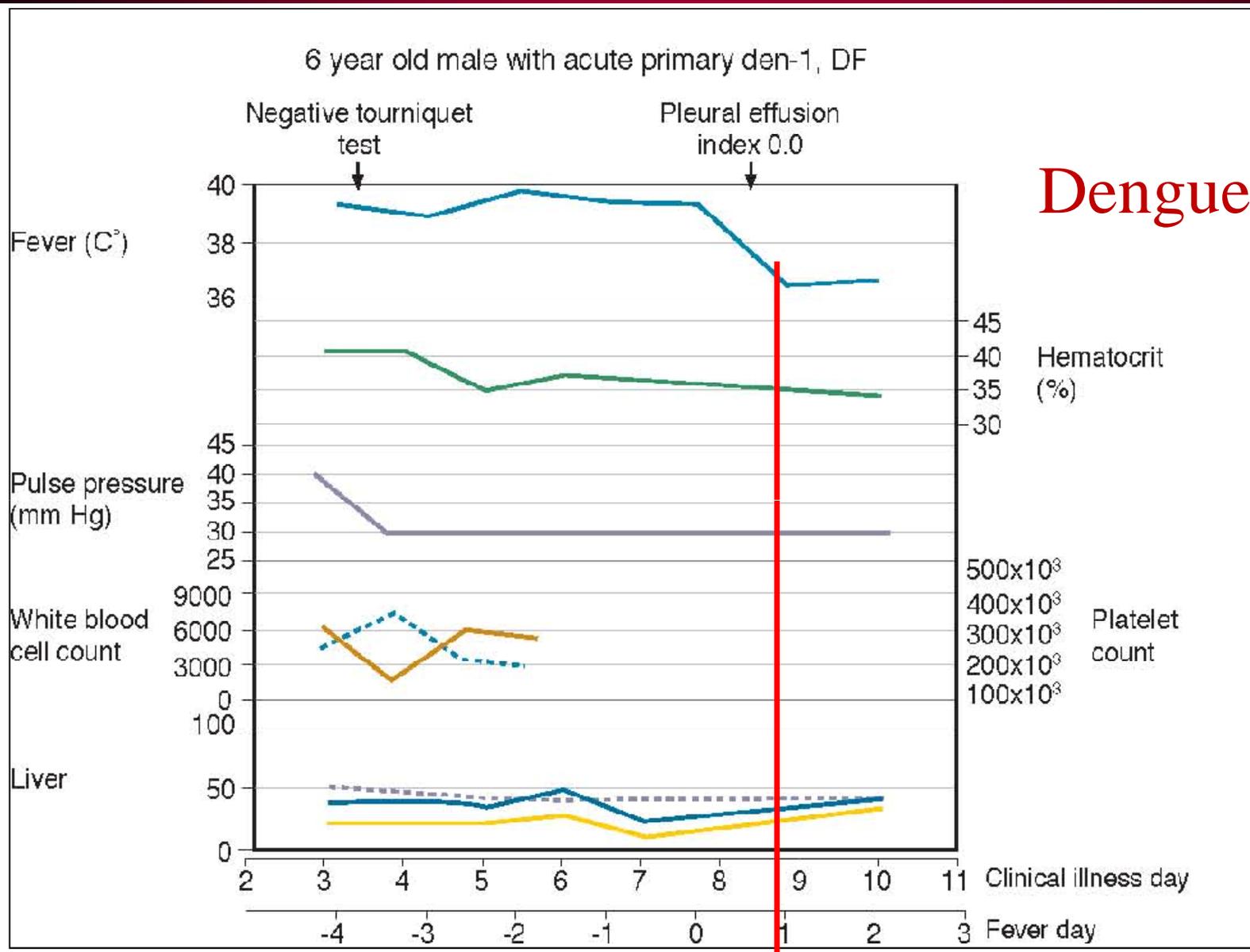
†*P*=.02.

‡*P*<.001.

**Febrile Patients Admitted to the 28th Combat Support Hospital,
Port-au-Prince, Haiti, September 27, 1994 to November 4, 1994***



Dengue Fever



WHO Treatment Guidelines DF/DHF (1999)

Dengue Fever

Febrile phase	Manifestation	Management
Duration 2-7 days	<ul style="list-style-type: none">– Temp 39-40°C– Headache– Retro-orbital pain– Muscle pain– Joint/bone pain– Flushed face– Rash– Skin haemorrhage, bleeding from nose, gums– Positive tourniquet test– Liver often enlarged– Leucopenia– Platelet/haematocrit normal	<ul style="list-style-type: none">– At home*– Bed rest– Keep the body temperature below 39^o– Paracetamol-Yes**– Aspirin-No– Brufen-No– Oral fluids and electrolyte therapy– Follow-up for any change in platelet/haematocrit

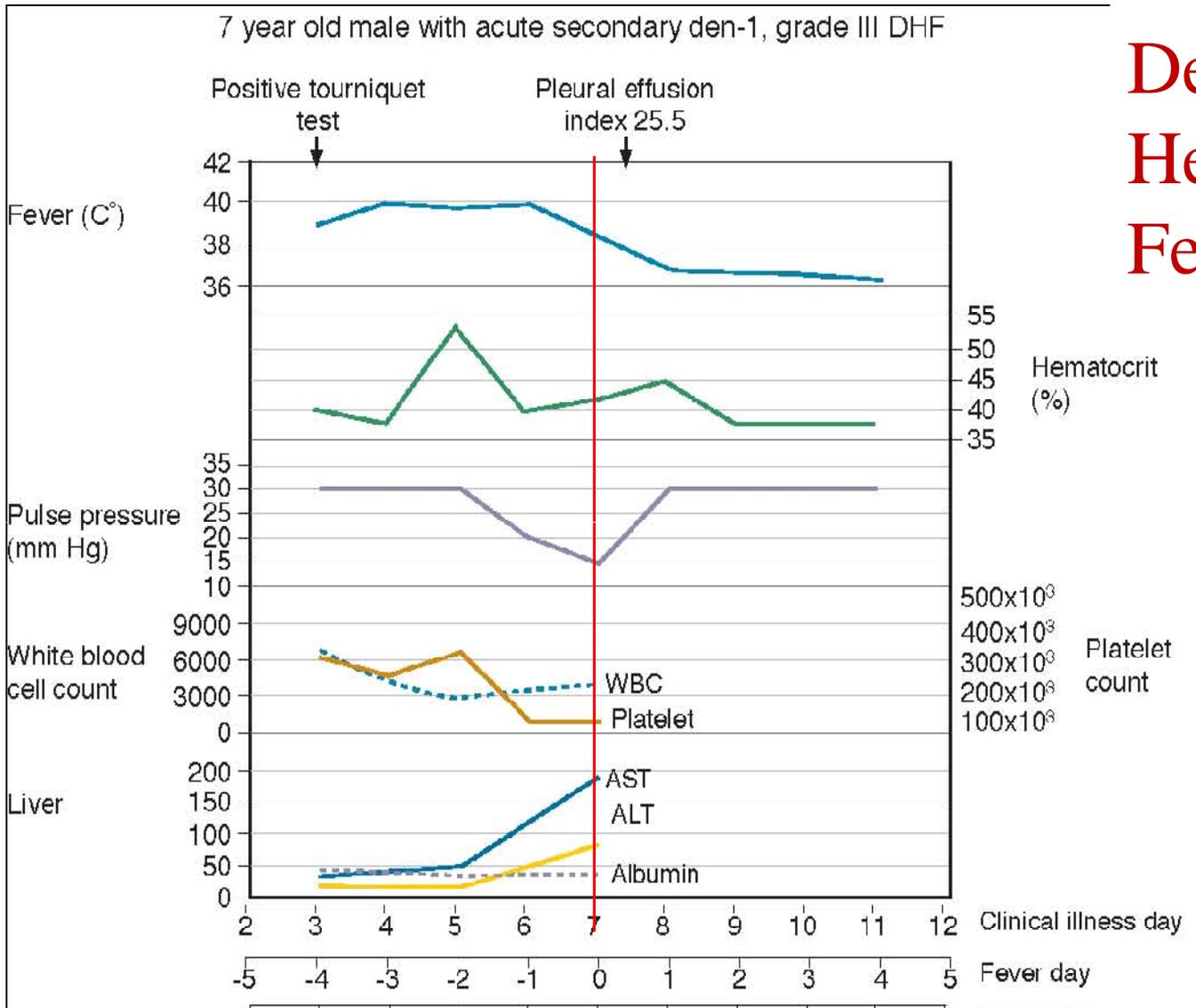


WHO Treatment Guidelines DF/DHF (1999)

<p>Afebrile phase (critical stage)</p> <p>Duration –2-3 days after febrile stage</p>	<p>Manifestation</p> <ul style="list-style-type: none"> – Same as during febrile phase – Improvement in general condition – Platelet/haematocrit normal – Appetite rapidly regained 	<p>Management</p> <ul style="list-style-type: none"> – Bed rest – Check platelets/haematocrit – Oral fluids and electrolyte therapy
<p>Convalescence Phase</p> <p>Duration –7-10 days after critical stage</p>	<p>Manifestation</p> <ul style="list-style-type: none"> – Further improvement in general condition and return of appetite – Bradycardia – Confluent petechial rash with white centre/ itching – Weakness for 1 or 2 weeks 	<p>Management</p> <ul style="list-style-type: none"> – No special advice. – No restrictions. – Normal diet



Dengue Hemorrhagic Fever

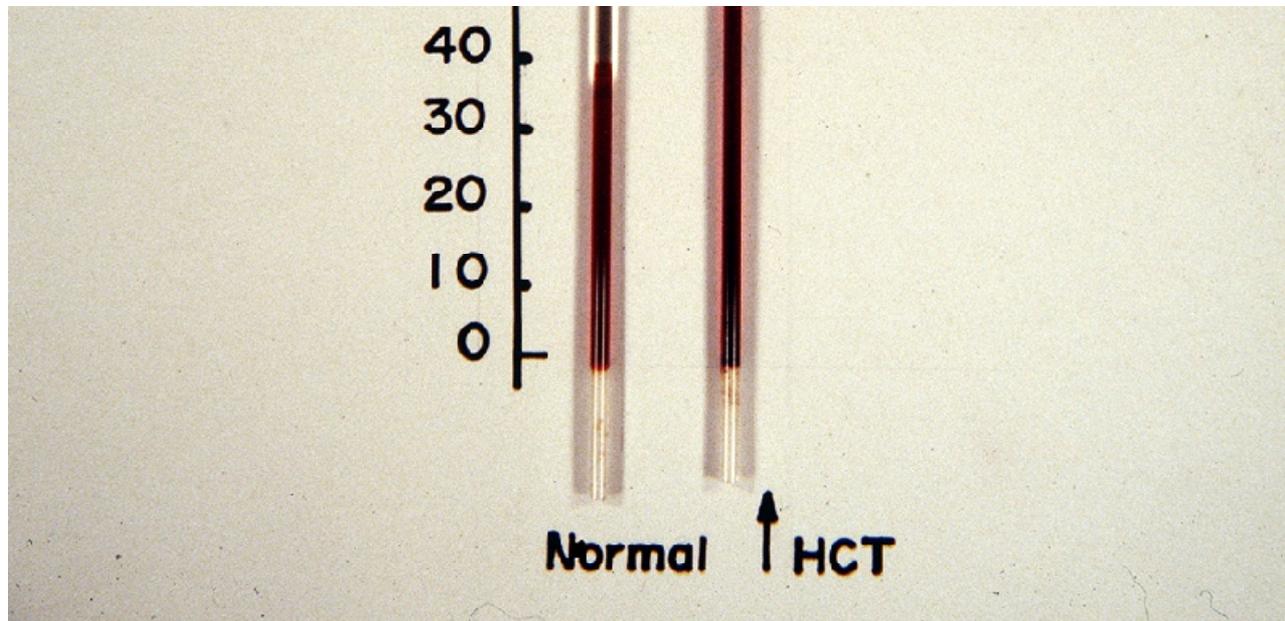


Pleural Effusion Index

R LAT decubitus X-ray showing a large pleural effusion, DHF the day after defervescence. Degree of plasma leakage may be quantified by means of the pleural effusion index. The pleural effusion index is calculated as 100 times the maximum width of the R pleural effusion, divided by the maximal width of the R hemithorax.



Hemoconcentration



DHF: I / II

Afebrile Phase (critical stage)	Manifestation	Management
Duration 2-3 days	<ul style="list-style-type: none"> – Same as during febrile phase. – Thrombocytopenia and rise in haematocrit level (more than 20%) 	<ul style="list-style-type: none"> – OPD or hospital – ORS – Check platelets/haematocrit. If haematocrit is more than 20%: – Initiate IV therapy (5% D/NSS) 6 ml/kg/hr (for 3 hours) – Check haematocrit/vital signs/urine output after 3 hours, and in case of improvement⁴ – Reduce IV therapy to 3ml/kg/hr (for 3 hours) – In case of further improvement, continue IV therapy at 3ml/kg/hr (6-12 hours) and then discontinue IV therapy – In case of no improvement⁵ increase IV therapy to 10 ml/kg/hr (for 1 hr). In case of improvement now, reduce the volume of IV from 10ml/kg/hr to 6ml/kg/hr and further to 3ml/kg/hr accordingly. – Generally, DHF Grades I and II do not give complications
Convalescence Phase	Manifestation	Management
Duration 2-3 days after critical stage	<ul style="list-style-type: none"> – Further improvement in general condition and return of appetite – Bradycardia – Confluent petechial rash with white centre/ itching – Asthenia and depression (sometimes for a few weeks, common in adults) 	<ul style="list-style-type: none"> – Normal diet – No need for any medication

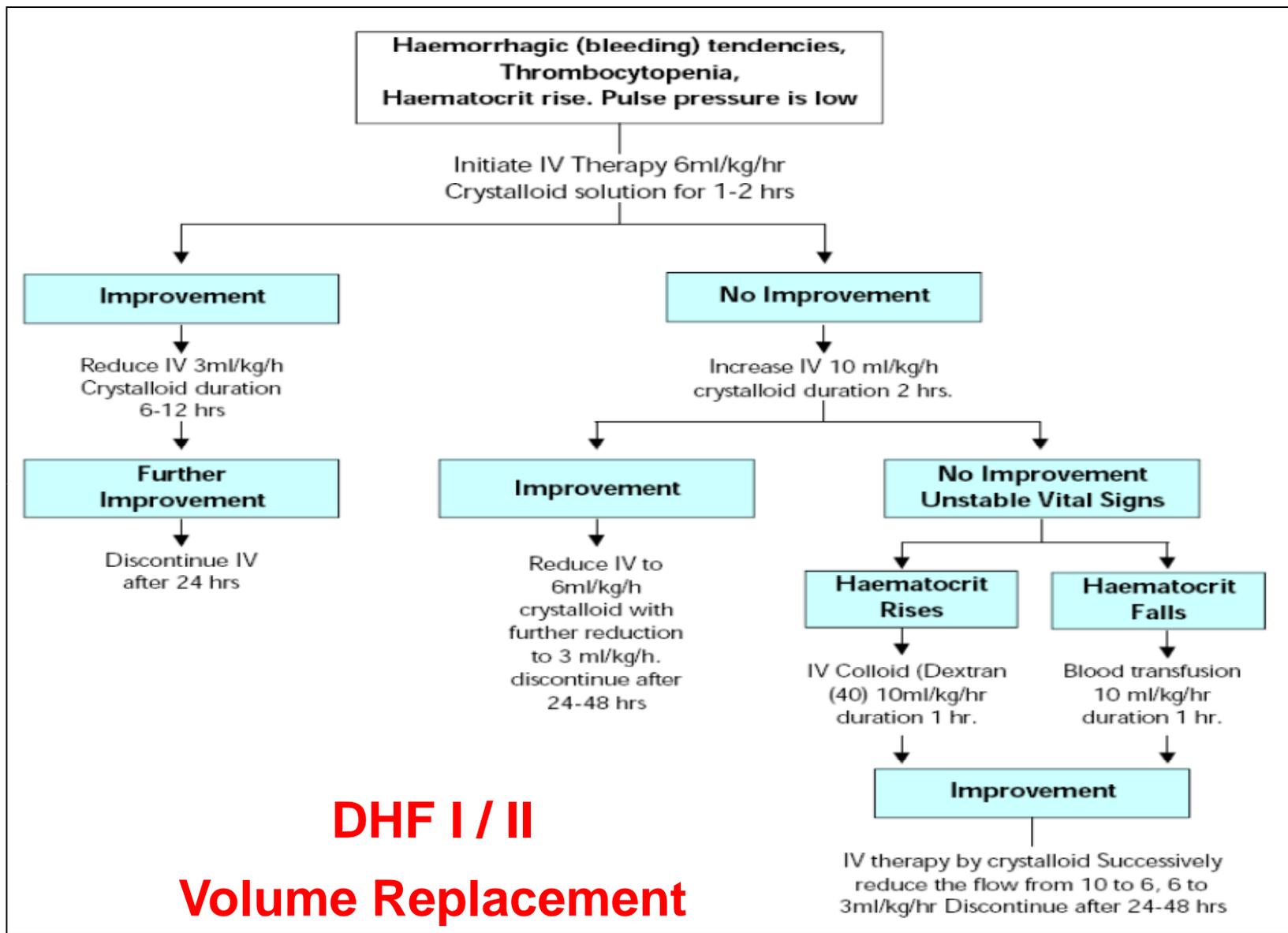




Petechiae on chest wall in child
with DHF.

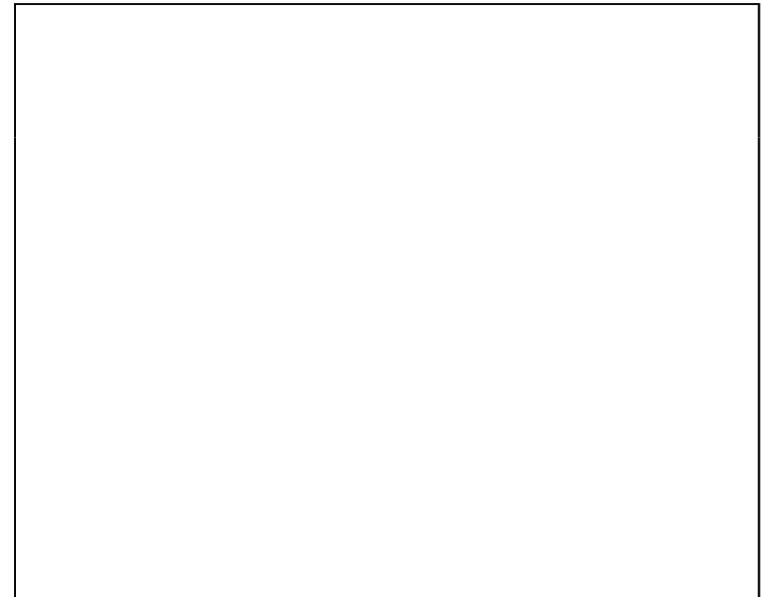
Subcutaneous hemorrhage in
child with DHF.





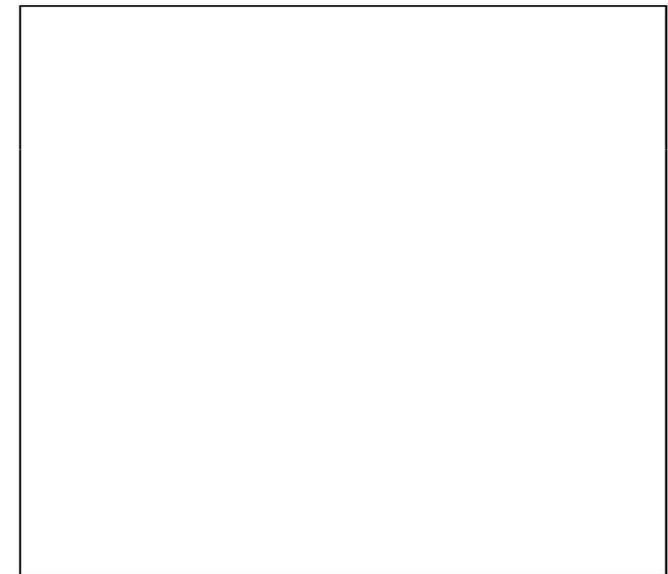
Afebrile phase	Manifestation	Management
<p>Duration two days after febrile stage</p>	<p>In addition to the manifestations of DHF Grade II:</p> <ul style="list-style-type: none"> - Circulatory failure manifested by rapid and weak pulse, narrowing of pulse pressure (20 mmHg or less) or hypotension with the presence of cold clammy skin and restlessness - Capillary relief time more than two seconds <p>Profound shock with undetectable pulse and blood pressure</p>	<ul style="list-style-type: none"> - Check haematocrits/platelet - Initiate IV therapy (5% D/NSS) 10 ml/kg/h - Check haematocrit, vital signs, urine output every hour - If patient improves, IV fluids should be reduced every hour from 10 to 6, and from 6 to 3 ml/kg/h which can be maintained up to 24 to 48 hours - If patient has already received one hour treatment of 20 ml/kg/hr of IV fluids and vital signs are not stable, check haematocrit again and - If haematocrit is increasing, change IV fluid to colloidal solution preferably Dextran or Plasma at 10 ml/kg/h every hr. - If haematocrit is decreasing from initial value, give fresh whole blood transfusion, 10 ml/kg/h and continue fluid therapy at 10 ml/kg/h and reducing it stepwise bring down the volume to 3 ml/kg/h and maintain it up to 24-48 hours - Initiate IV therapy (5% D/NSS) 20 ml/kg as a bolus one or two times - Oxygen therapy should be given to all patients⁶ - In case of continued shock, colloidal fluids (Dextran or Plasma) should be given at 10-20 ml/kg/hr.

DHF: III / IV



Afebrile phase	Manifestation	Management
	<p>Profound shock with undetectable pulse and blood pressure</p>	<ul style="list-style-type: none"> – If shock still persists and the haematocrit level continues declining, give fresh whole blood 10 ml/kg as a bolus – Vital signs should be monitored every 30-60 minutes – In case of severe bleeding, give fresh whole blood 20 ml/kg as a bolus – Give platelet rich plasma transfusion exceptionally when platelet counts are below 5,000–10,000/ mm³. – After blood transfusion, continue fluid therapy at 10 ml/kg/h and reduce it stepwise to bring it down to 3 ml/kg/h and maintain it for 24-48 hrs
Con. Phase	Manifestation	Management
<p>Duration 2-3 days after recovery from critical/shock stage</p>	<ul style="list-style-type: none"> – 6-12 hours after critical/shock stage, some symptoms of respiratory distress (pleural effusion or ascites) – 2-3 days after critical stage, strong pulse, normal blood pressure – Improved general condition/return of appetite – Good urine output – Stable haematocrit – Platelet count > 50,000 per mm³ – Patient could be discharged from hospital 2-3 days after critical stage – Bradycardia/arrhythmia – Asthenia and depression (few weeks) in adults 	<ul style="list-style-type: none"> – Rest for 1-2 days – Normal diet – No need for medication

DHF: III / IV



Petechiae



Gastric Bleeding

Melena



**UNSTABLE VITAL SIGNS
Urine Output Falls
Signs Of Shock**

Immediate, rapid volume replacement*: Initiate IV therapy
10-20ml/kg/h Crystalloid solution for 1 hr

Improvement

IV Therapy by crystalloid
successively reducing from 20
to 10, 10 to 6, and 6 to 3ml/kg/hr

**Further
Improvement**

Discontinue intravenous
therapy after 24-48 hrs

No Improvement

Oxygen

**Haematocrit
Rises**

IV Colloid (Dextran 40)
or plasma 10ml/kg/hr as
intravenous bolus
(repeat if necessary)

**Haematocrit
Falls**

Blood transfusion
(10 ml/kg/hr) if
haematocrit is
still >35%

Improvement

IV therapy by crystalloid,
successively reducing the flow
from 10 to 6, 6 to 3ml/kg/hr
Discontinue after 24-48 hrs

**DHF III / IV
Volume Replacement**



Diagnosing Dengue

Infant w/ dengue: Thai – Cambodia border

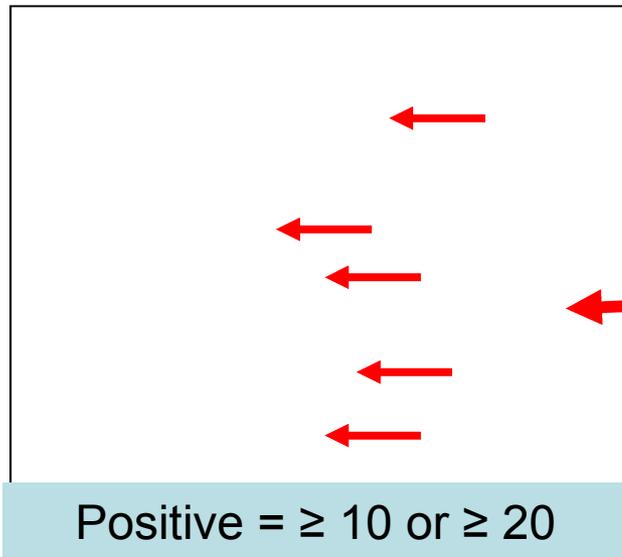
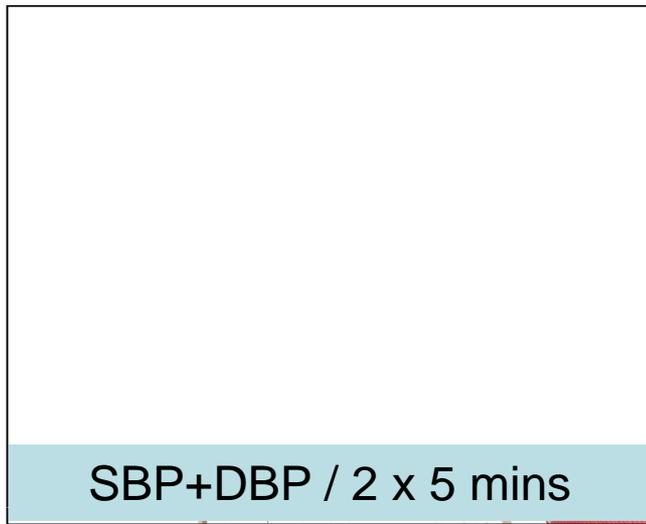


Diagnosing Dengue - Basics

- Maintain high degree of suspicion
 - Geographic location
 - Clustering of cases
- History and physical
 - Clinical presentation consistent with dengue
 - Vital signs (T, BP, pulse pressure, HR)
 - Dengue tourniquet test
- Clinical lab assessment
 - CBC (WBC, HCT, PLT), AST/ALT, Bilirubin
- Endemic area, +Clinical, +Tourniquet test, $WBC < 5k$ = High PPV



Dengue Tourniquet Test





Disease Course – Windows of Diagnostic Opportunity







Dengue Pathophysiology

AN
ACCOUNT
OF THE
Bilious Remitting Fever,
AS IT APPEARED IN PHILADELPHIA, IN THE SUMMER
AND AUTUMN OF THE YEAR 1780.

The pains which accompanied this fever were exquisitely severe in the head, back, and limbs. The pains in the head were sometimes in the back parts of it, and at other times they occupied only the eyeballs. In some people, the pains were so acute in their backs and hips, that they could not lie in bed. In others, the pains affected the neck and arms, so as to produce in one instance a difficulty of moving the fingers of the right hand. They all complained more or less of a soreness in the seats of these pains, particularly when they occupied the head and eyeballs. A few complained of their flesh being sore to the touch, in every part of the body. From these circumstances, the disease was sometimes believed to be a rheumatism. But its more general name among all classes of people was, the *Break-bone fever*.

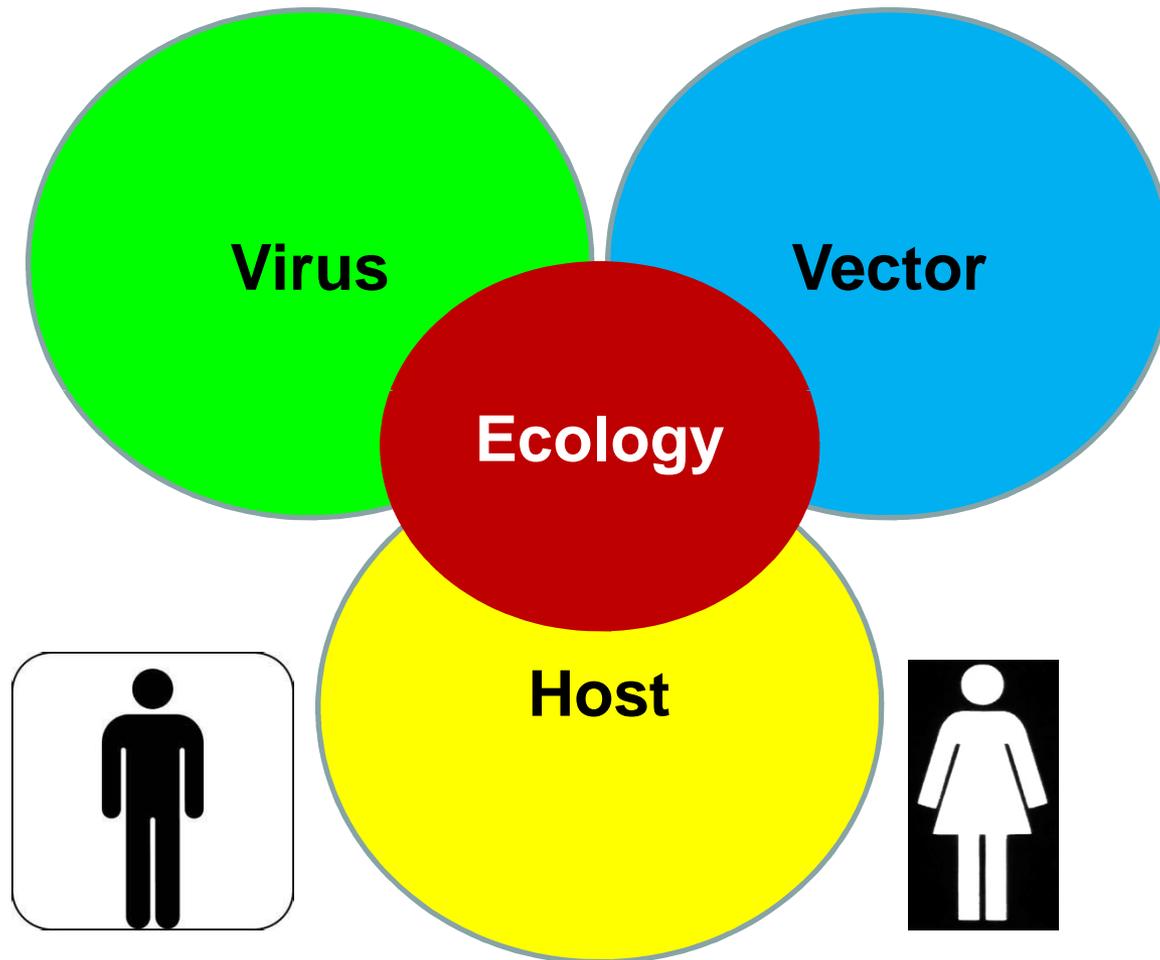


Infection / Disease Determinant Questions

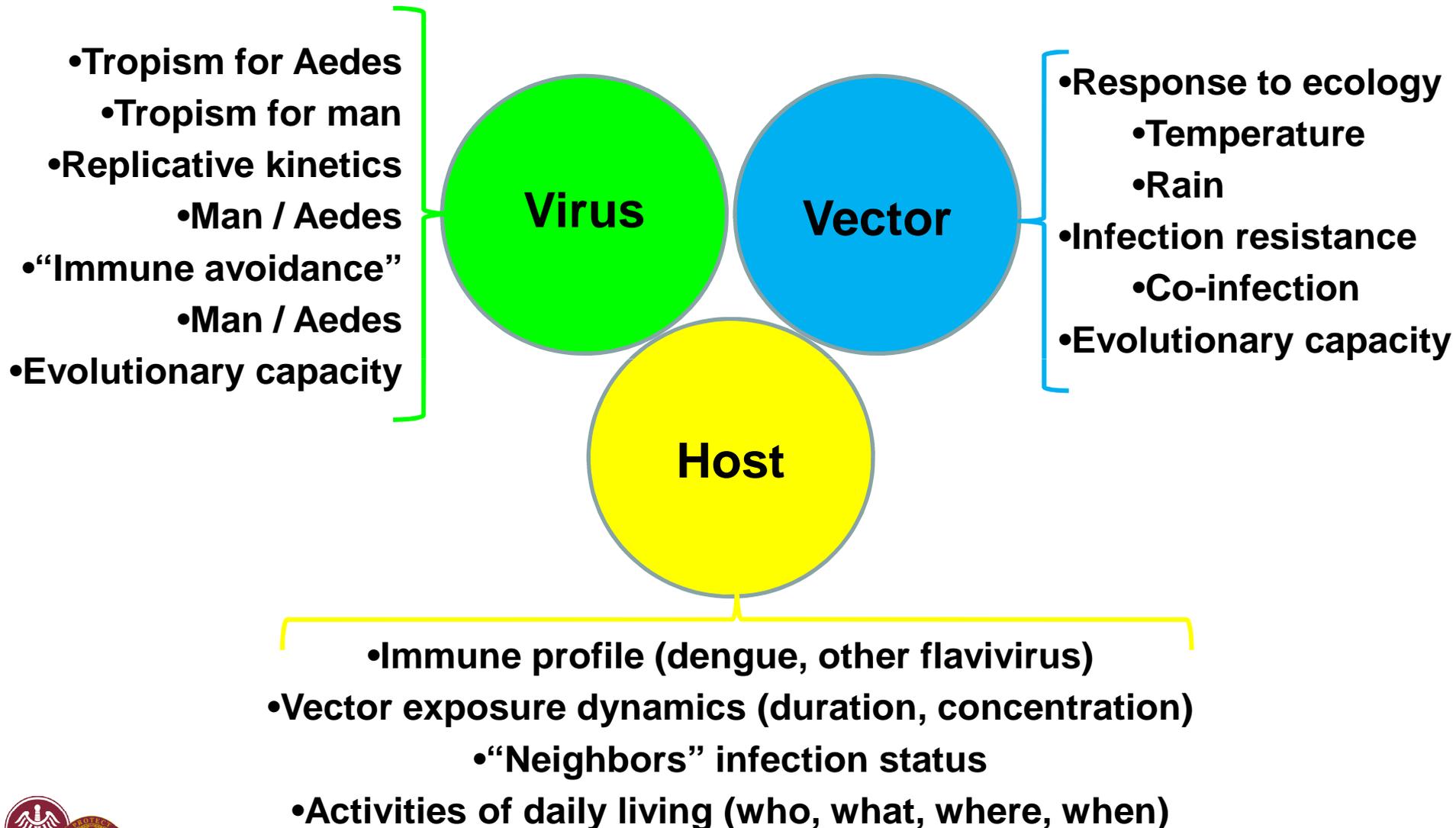
- What places a person at risk for acquiring a dengue virus infection?
- Why do some Aedes feeding episodes result in infection and others do not?
- Why do some people experience disease following infection and others do not?
- Why is the dengue clinical phenotype spectrum so broad?



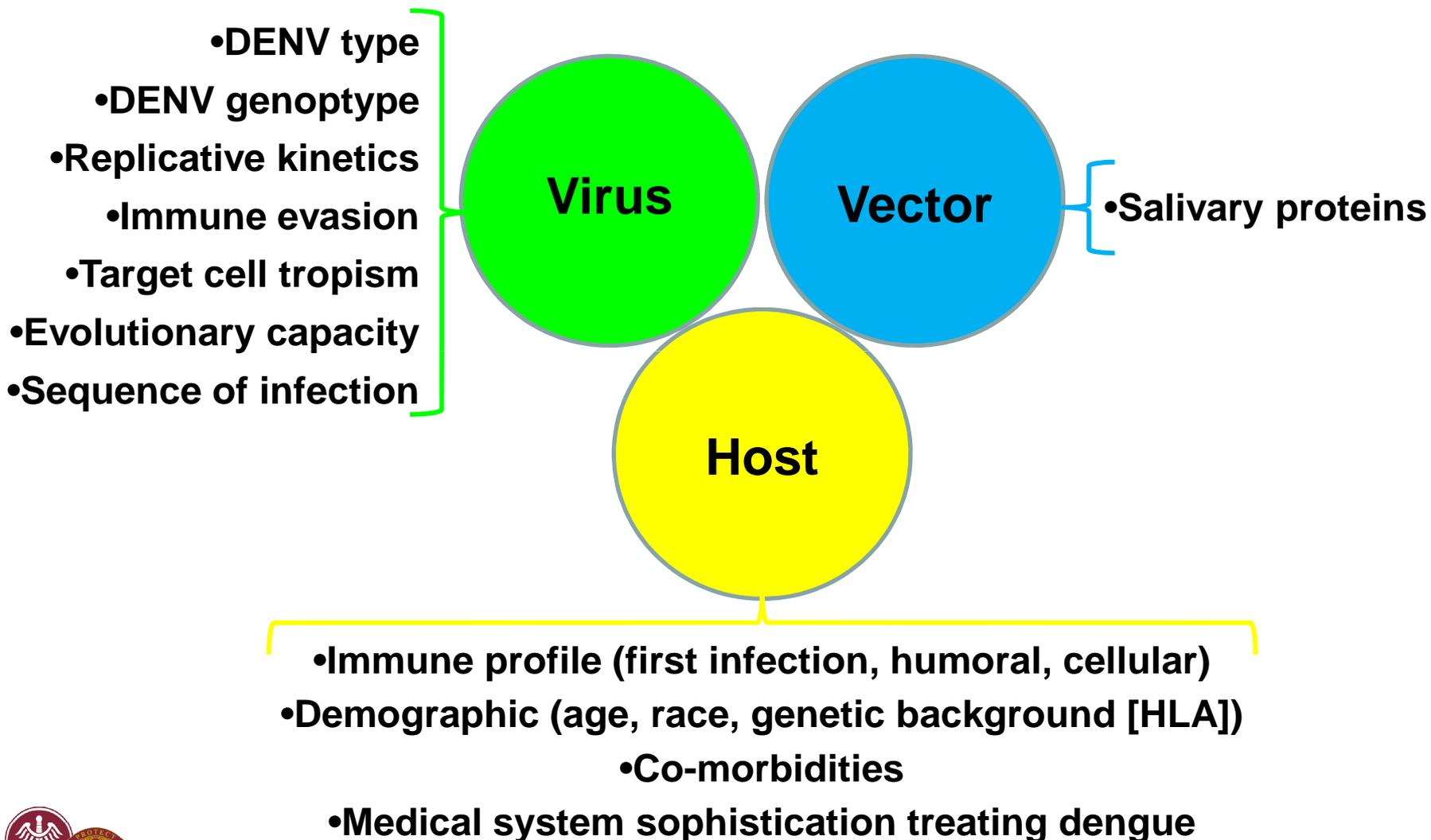
Exposure and Infection Outcome Determinants



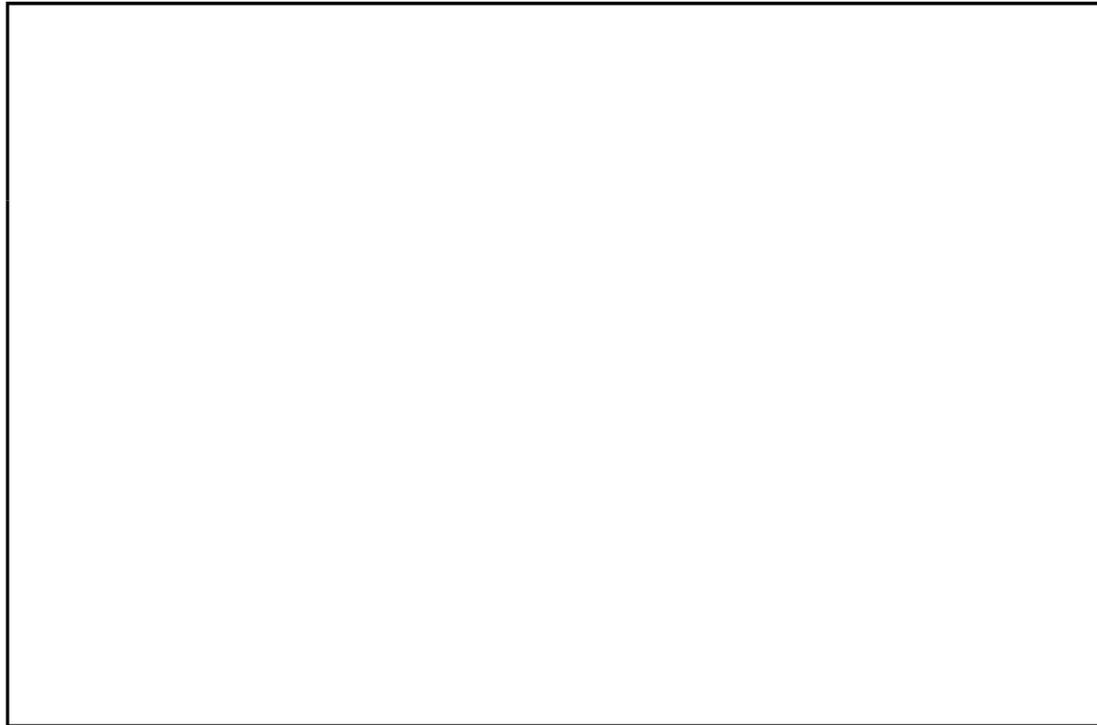
Exposure Determinants – Risk of Infection



Infection Outcome Determinants – Risk of Disease

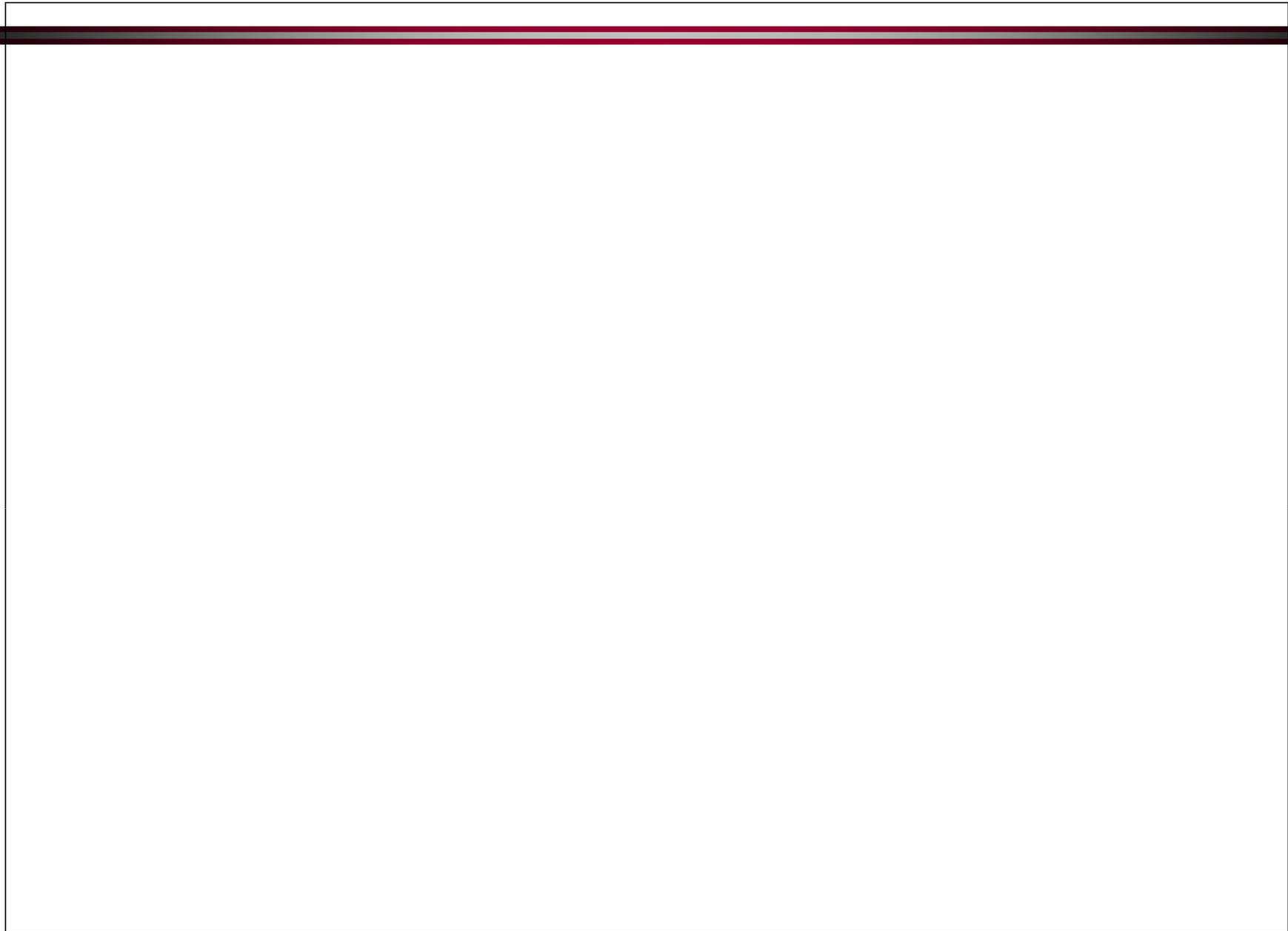


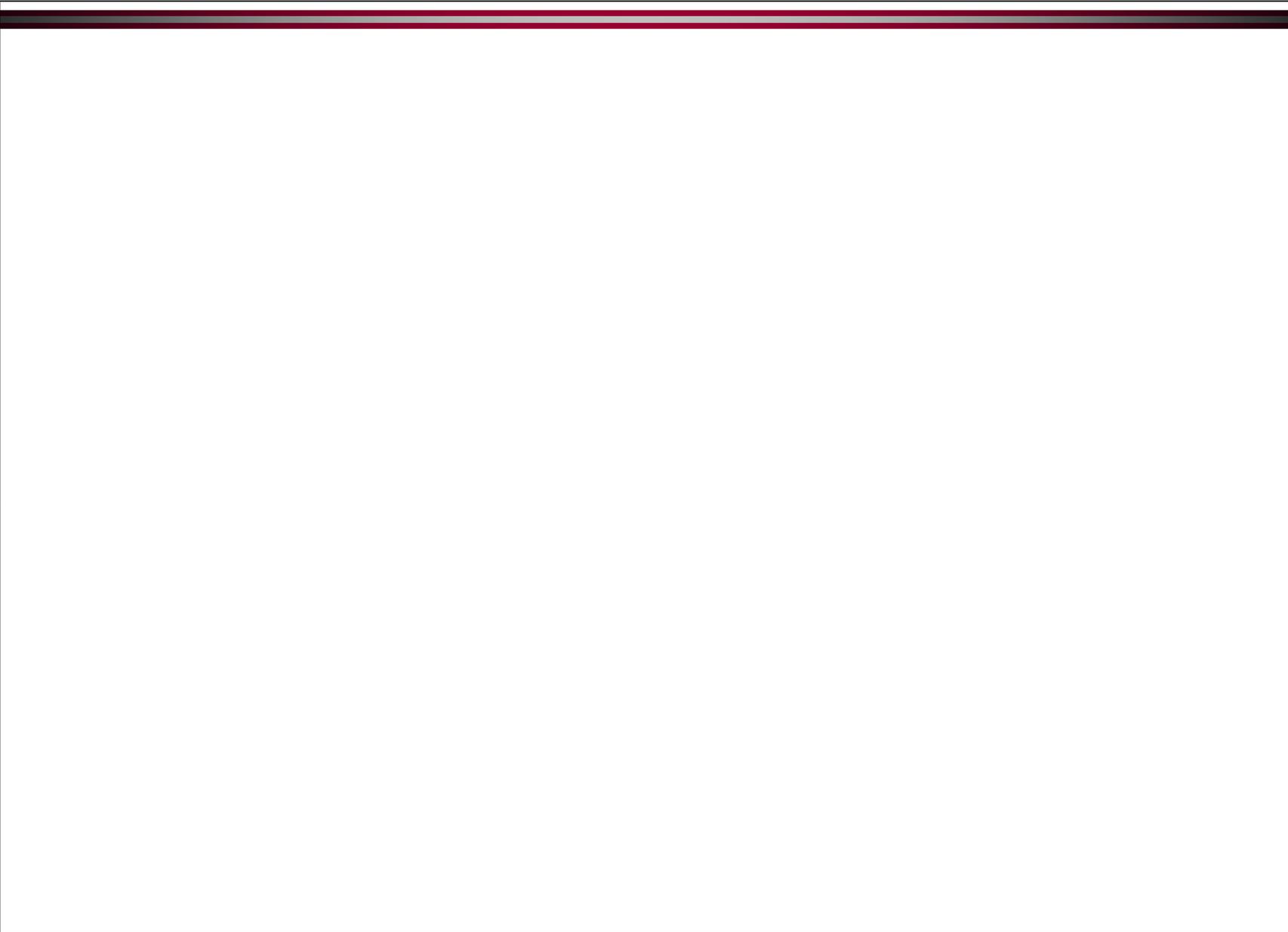
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Dengue Ward: QSNICH, Bangkok, Thailand (Photo: Christopher Brown, IHT)







Immunologic Response – Clinical Phenotype (Rothman)



Questions?

