

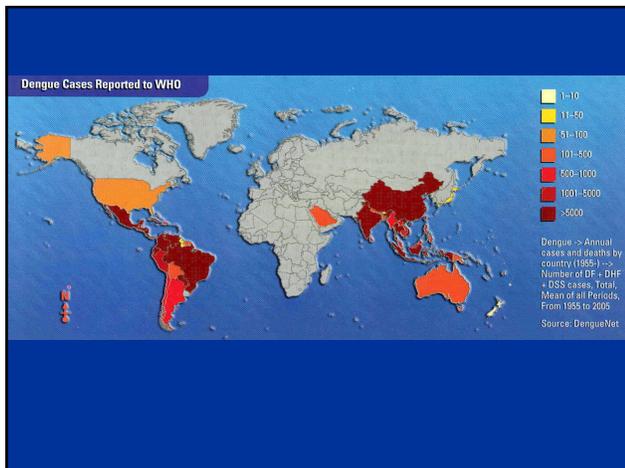
Dengue in the New Millenium

Usa Thisyakorn, M.D.

Professor of Pediatrics
Faculty of Medicine
Chulalongkorn University
Bangkok, Thailand

Factors to global resurgence of dengue

- ▼ Population growth
- ▼ Urbanization
- ▼ Mosquito control
- ▼ Travel
- ▼ Public health infrastructure



NATURAL HISTORY OF DENGUE INFECTION

Spectrum of dengue infection

- ▼ Asymptomatic
- ▼ Undifferentiated fever
- ▼ Dengue fever
- ▼ Dengue hemorrhagic fever

Dengue fever

- ▼ Fever
- ▼ Muscle and bone pain
- ▼ Maculopapular rash

WHO classification of dengue infection

Severity	Platelet	Plasma leakage
DF	variable	absent
DHF grade I	<100,000	present
grade II	<100,000	present
DSS grade III	<100,000	present
grade IV	<100,000	present

Thaithumyanon P, Thisyakorn U, Deerojanawong J, Innis BL

Dengue infection during parturition complicated in severe hemorrhage and vertical transmission.

Clin Infect Dis 1994; 18: 248-9

Major pathophysiologic changes in DHF

- ▼ Leakage of plasma
- ▼ Abnormal hemostasis

Pathogenesis

- ▼ Immune: ADE
- ▼ Viral: loads, strains, virulence
- ▼ Host: genetic factors



**Prommalikit O, et al
AOJPCH 2004; 3: 26-9.**

**Pathogenesis of DSS:
Immune Enhancement or
Viral Virulence**

Prommalikit O, et al .

Presented at the 25th ICP
Aug 25-30, 2007, Athens, Greece

Association between MBL
gene polymorphisms and
susceptibility to dengue.

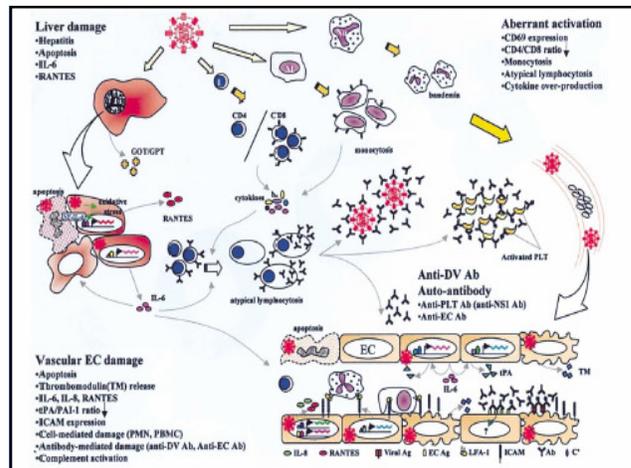
Srettakraikul K, et al. Seroepidemiology
of dengue virus infection in HIV-infected
children in comparison to healthy children.
Presented at the annual meeting of Pediatric
Infectious Diseases Society of Thailand,
4-5 March, 2006.

HIV-infected children and healthy children
had no different seroepidemiology of
dengue virus infection.

Thisyakorn U, et al. Nutritional status of children with DHF

The study confirmed the
observation generally made
that most patients with DHF
are not undernourished.

Clin Infect Dis 1993; 16: 295-7.



DENGUE PATIENTS IN DIFFERENT AGE GROUP

Clinical manifestations and severity of dengue infection varied with age.

Setrkraising K, et al. Asian Biomedicine 2007; 1: 53-7.

The d-dimer, a specific marker for cross-linked fibrin, is often used as a marker for DIC significantly correlated with disease severity.

Sosothikul D, et al. Thromb Haemost 2007; 97: 627-34.

The extent of endothelial cells, coagulation and fibrinolysis activation in children with dengue infection seems to be correlated to disease severity.

Waidab W, et al. Presented at the 25th ICP, Aug 25-30, 2007, Athens, Greece

Association of cytokine-related gene expression levels with dengue disease severity was demonstrated.

BLEEDING PRECAUTIONS

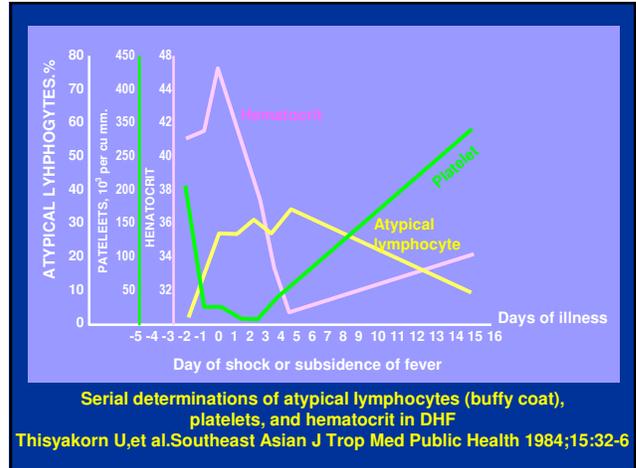
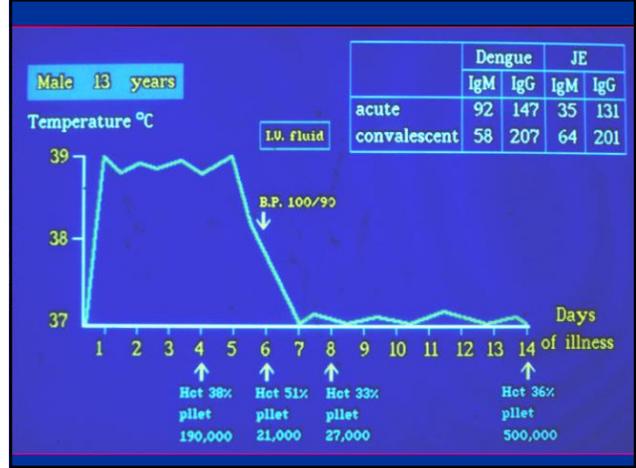


Mitrakul C, Thisyakorn U. Hemostatic studies in DHF

- ▼ Vasculopathy
- ▼ Coagulopathy
- ▼ Platelet abnormalities

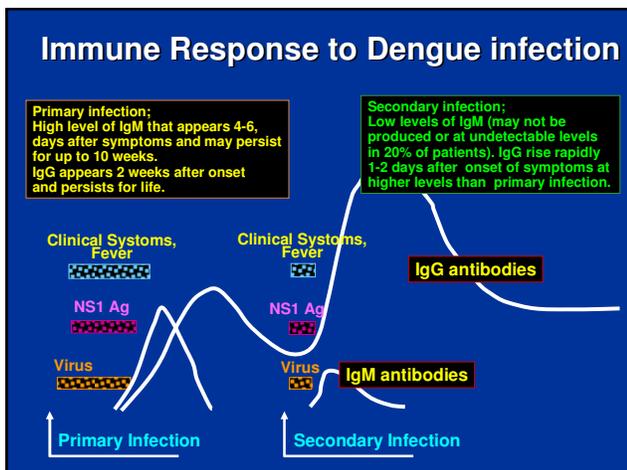
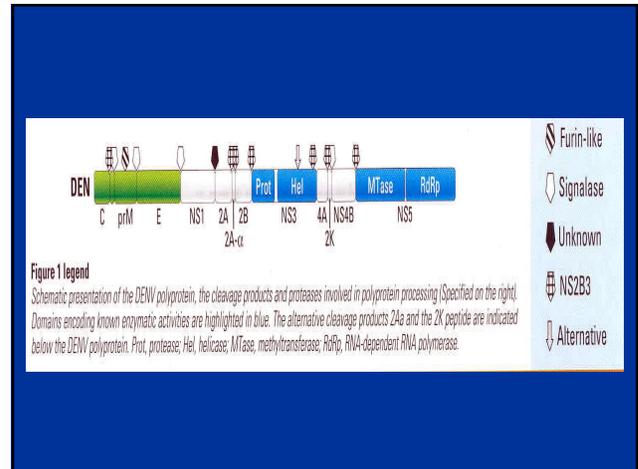
Proceedings of 1st International Congress of Tropical Pediatrics.
Nov 8-12, 1989, Bangkok, Thailand: 215-7.





LABORATORY DIAGNOSIS OF DENGUE INFECTION

- ▼ Serology
- ▼ Virus isolation
- ▼ Molecular technique



Interpretation Guide

Disease Status	Fever	PCR	NS1 Ag	IgM	IgG
No Infection	NA	-	-	-	-
Very Early					
Acute Primary	+	+	+	-	-
Early	+	+	+	-/+	-
Acute Primary					
Late Acute	-	+/-	+/-	+	-/+
Primary					
Convalescent	-	-	-	-	+
Very Early					
Acute	+	+	+	-/+	+
Secondary					
Early Acute	+	+	+	-/+	+
Secondary					
Late Acute	-	+/-	+/-	+/-	+
Secondary					
Convalescent	-	-	-	-	+

DENGUE ENCEPHALITIS

A true entity?

**Thisyakorn U, Thisyakorn C.
Dengue infection with
unusual manifestations**

**Patients tended to be in
the younger age group and
had higher mortality.**

J Med Assoc Thai 1994; 77: 410-3.

**Thisyakorn U, Thisyakorn C.
DHF: Unusual manifestations
and problem in management**

**The unusual manifestations
include encephalopathy,
encephalitis and fulminant
hepatitis**

JAMA.SEA 1994; 10: 102-3.

**Thisyakorn U, Thisyakorn C,
Limpitikul W, Nisalak A.
Dengue infection with CNS manifestations**

**Neurological manifestations of dengue
including alteration of consciousness,
seizures, pyramidal tract signs, meningeal
signs and headache. CSF showed
lymphocytic pleocytosis in 1/5 while
presence of IgM in few patients.**

Southeast Asian J Trop Med Pub Hlth 1999; 30: 504-9

Solomon T, et al. Neurological manifestations of dengue infection.

In dengue endemic areas patients with encephalitis and encephalopathy should be investigated for this infection, whether or not they have other features of the disease.

Lancet 2000; 355: 1053-9.

Innis BL, et al. Acute liver failure is one important cause of fatal dengue infection.

Liver injury is either a direct effect of virus replication in the liver or a consequence of host responses to infection.

Southeast Asian J Trop Med Pub Hlth 1990; 21: 695-6.

Pancharoen C, Rungsarannont A, Thisyakorn U. Hepatic functions in dengue patients.

Hepatocellular injury manifested by hepatomegaly, elevation of ALT And coagulopathy are common in DHF and even in DF, though hepatomegaly is absent.

J Med Assoc Thai 2002; 85: S298-301.

Pancharoen C, Thisyakorn U. Co-infection in dengue patients.

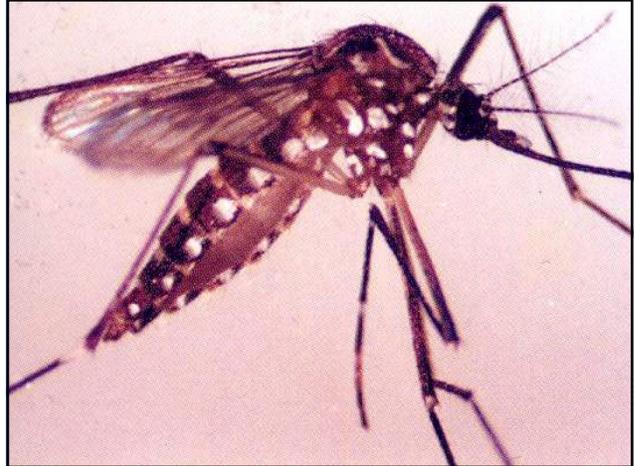
Co - infection can modify clinical presentations of dengue disease and result in missed or delayed diagnosis and treatment and possible misinterpretation as unusual manifestations.

Pediatr Infect Dis J 1998; 17: 81-2.

**Thisyakorn U, Thisyakorn C.
Diseases caused by arboviruses**

Successful treatment of DHF depends on early recognition and careful monitoring of the development of shock.

Med J Aust 1994; 160: 22-6.



Prevention

- ▼ Control of mosquito
- ▼ Vaccine



Vaccines

- ▼ Two live-attenuated
 - ▼ Mahidol-Aventis Pasteur
 - ▼ Walter Reed
- ▼ Four chimeras

Lancet 2002;360:1243-5



Conclusion

The geographical expansion of DHF presents the need for well-documented clinical, epidemiological and virological description of the syndrome.

Both biological and social researches are essential to develop effective mosquito control, medications to reduce capillary leakage and a safe vaccine.

