

DENGUE FEVER

DENGUE HEMORRHAGIC FEVER

DENGUE SHOCK SYNDROME

Infectious Agent of DF

- **Four** immunologically related, single positive-stranded **RNA viruses** known as dengue viruses (four serotypes)
 - DENV – 1
 - DENV – 2
 - DENV – 3
 - DENV – 4
- Of the genus **Flavivirus**, family **Flaviviridae**
- Are responsible for causing DF and DHF

Global Dengue – historical reality

- ▣ The four dengue viruses originated in **monkeys**
- ▣ Independently **jumped to humans from monkeys** in Africa or Southeast Asia
between 100 and 800 years ago

Immunity

- Infection with one DENV produces **immunity** against reinfection with **that one viruses** (short-term ≤ 9 months)
- Infection with **one serotype** **does not protect against the others**, and sequential infections (others serotypes) **put people at great risk for DHF/DSS**

Epidemiology

Transmission occurs from the bite of an infected mosquito



- *Aedes aegypti*
- *Aedes albopictus* (rarely)
- Which are found **throughout the world**
- Insects that transmit disease are **vectors**

- Vector (*Aedes*) and virus is present throughout **the tropical and subtropical zones**
 - Between
 - 35 degrees North latitude
 - 40 degrees South latitude

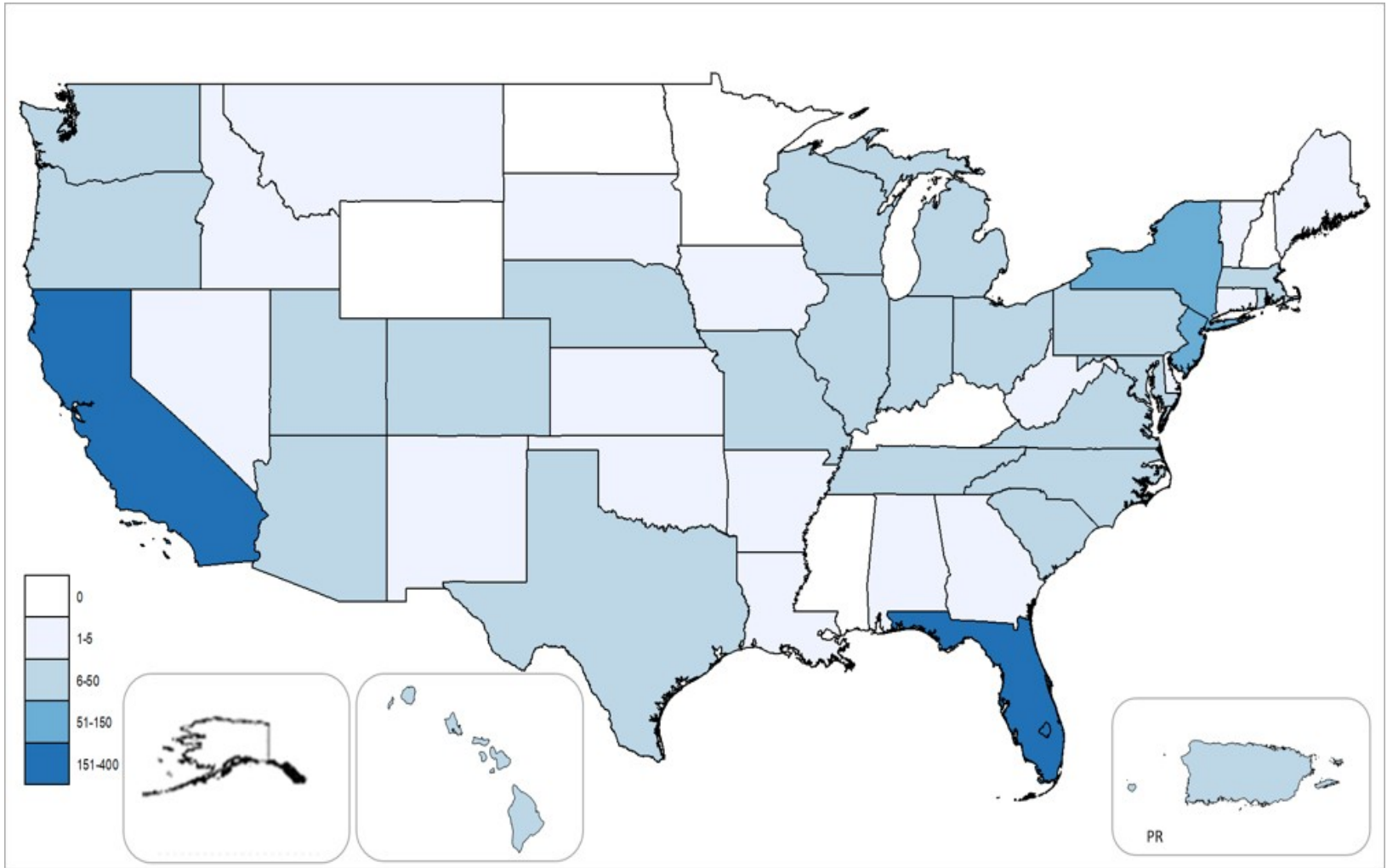
Geografic distribution of Dengue



Epidemiology

- Today about **2,5 billion people**, or about 40% of the world's population, live in areas where **is a risk of dengue** transmission
- Dengue is **endemic in at least 100 countries** in Asia, the Pacific, the Americas, Africa and the Caribbean
- **South-east Asia and Western Pacific** are the most serious affected by DF

Dengue USA 2019



Epidemiology

- The main risk of exposure for the traveler
 - Is in populated **urban and residential areas**
 - Dengue infections are often found in the **urban areas of tropical nations**, including Thailand, Singapore, Taiwan, Indonesia, Philippines, India and Brasil

Epidemiology

- The World Health Organization (WHO) estimates that
 - **50 to 100 million infections occur yearly**
 - Including **500 000 DHF** cases
 - **22 000 deaths**, mostly among children
- Not only is the **number of cases increasing** as the disease **is spreading to new areas**, but explosive outbreaks are occurring

Global Dengue

Before World War II:

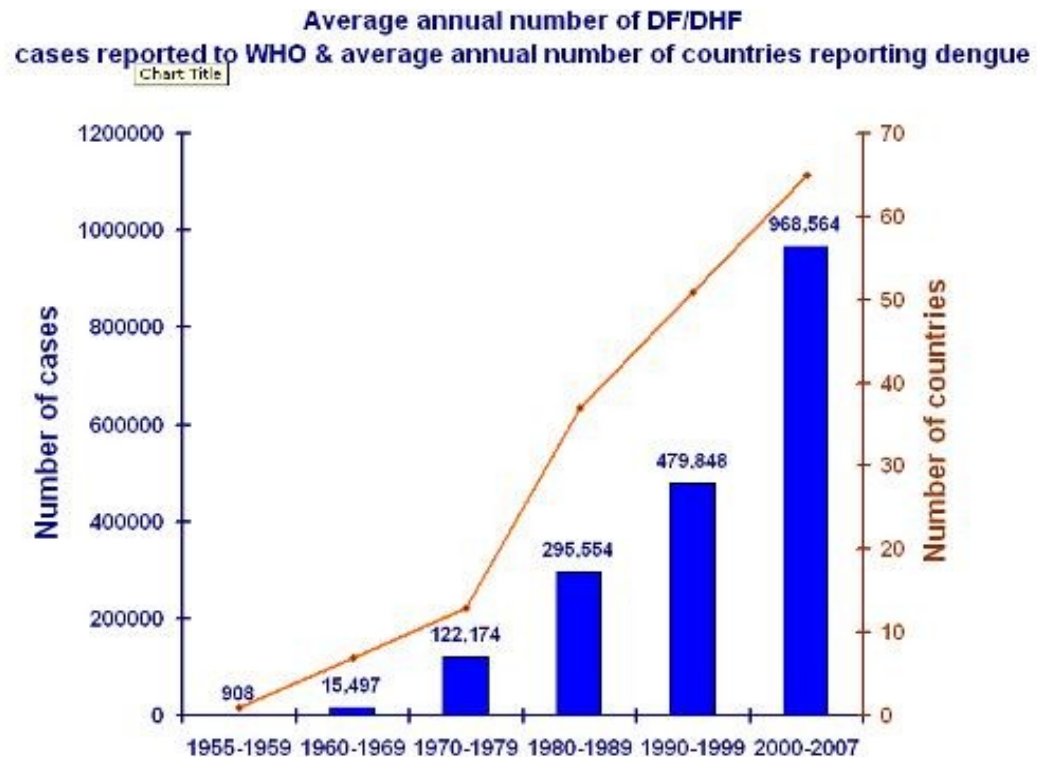
- Sporadic outbreaks were reported throughout the tropics and subtropics

After World War II:

- The start of the 1st pandemic due to transport of *Aedes* around the world in cargo

Past 30 years:

- Next pandemic of DF increased and developed (urbanization, population growth...)



Risk for Dengue

The bite of one infected mosquito can result in infection.

The risk of being bitten is highest during

- **The early morning**
(several hours after daybreak)
- **In the late afternoon**
(several hours before sunset)

Because the female mosquito typically feeds (bites) during these hours.

The most risk for DF

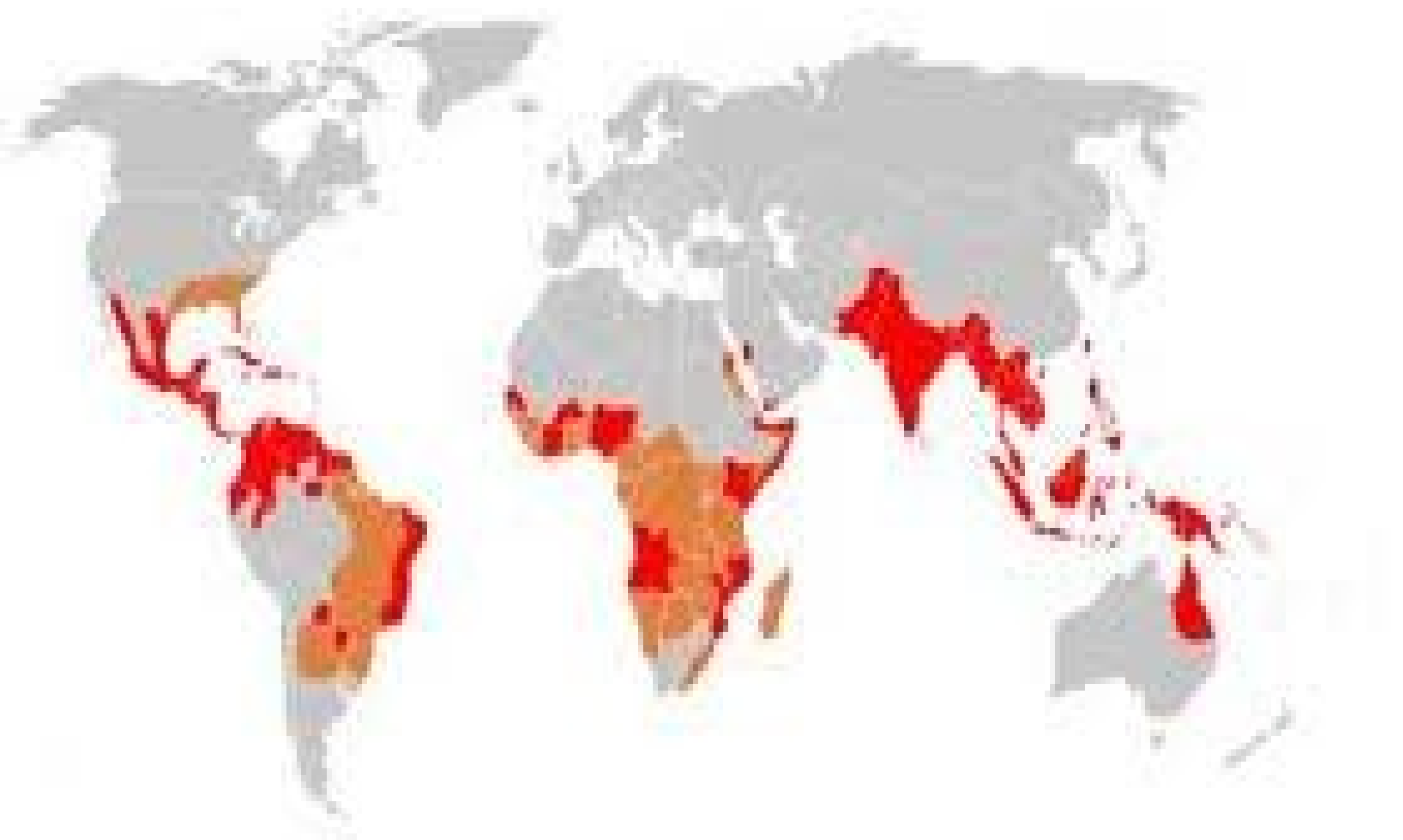
- During the **rainy season**
(when *Aedes* mosquito populations are high)
- However, mosquitoes may feed
at any time during the day.
 - **Globally risk**
 - especially for travelers
 - **All year**
 - **All day**



Dengue

- Is the **second** most common cause of hospitalization among travelers returning from the tropics (malaria is the most common)
- More than **17 000 of travelers** are hospitalised with dengue every year

Geographic distribution of Dengue



Mosquito *Aedes aegypti* – breeding habitats

Is adapted to breed **around human dwellings**, where insects oviposit **in uncovered water storage containers** as well as miscellaneous containers **holding water:**

- The outdoor sculptures
(due to ability to retain water)
- A small outdoor container, **vases**, flower dishes, **cans**
- The interior of a drainage pipe
- Automobile tires
- Standing water containers...

Breeding habitats – stagnant water



The international trade in used tires is responsible for the significant worldwide expansion of dengue fever



Numerous eggs of the DF mosquito vector, *Aedes aegypti*
in any container in or around houses,
which can hold water (jars, tins...)

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Transmission of the Dengue Virus

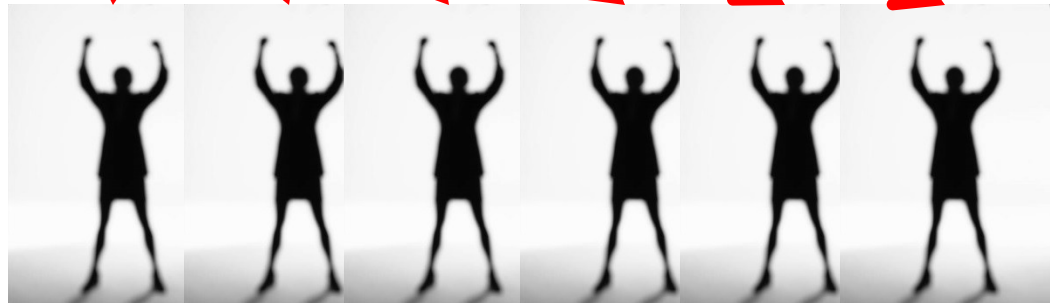
- Mosquitoes first become infected with DENV **by feeding** on the blood of **a dengue-infected person**
- After the virus replicates for 8 – 12 days in the mosquito
 - The mosquito can transmit DENV **to many other people**
- During epidemic of dengue, **infection rates** among those who have not been previously exposed to the virus are often **40% to 50%** of population
- But can reach **80% to 90%**

3. The virus replication for 8-12 days in the mosquito



2. Feeding on the blood by *Aedes*

4. Transmission of DENV to many other people by mosquito



1. Dengue-infected person (viremia)

Mode of transmission

- **In the vast majority of infections**
 - A mosquito bite is responsible
- **In rare cases** dengue can be transmitted
 - Blood transfusion from infected donors
 - In solid organ or bone marrow transplants
 - Needlestick injuries
 - Mucous membrane contact with dengue-infected blood
 - From an infected pregnant mother to her fetus
- Direct **person – to – person** transmission
has not been documented

Incubation

- Usually begin 4 – 7 days after the mosquito bite
- Typically last **3 – 10 days**
- Some people
never have significant symptoms
but can still **infect mosquitoes**
- About **half of people** infected with DENV
who live in areas where the virus is widespread
are asymptomatic

Clinical Manifestations

- Dengue is a febrile illness
due to mosquito-borne viruses

flu – like illness

- The clinical manifestations of symptomatic illness range
from **mild, undifferentiated febrile illness**
to classic DF or DHF.

Clinical Manifestations of DF

- DF is defined clinically by **an acute febrile illness**
with two or more of the following symptoms:
 - Headache, retro-orbital pains
 - Generalized pains in the muscles and bone („breakbone fever“)
 - Lack of appetite, Chills, leucopenia...
- **Fever**
 - Occuring for a period of 5 to 6 days

Clinical Manifestations

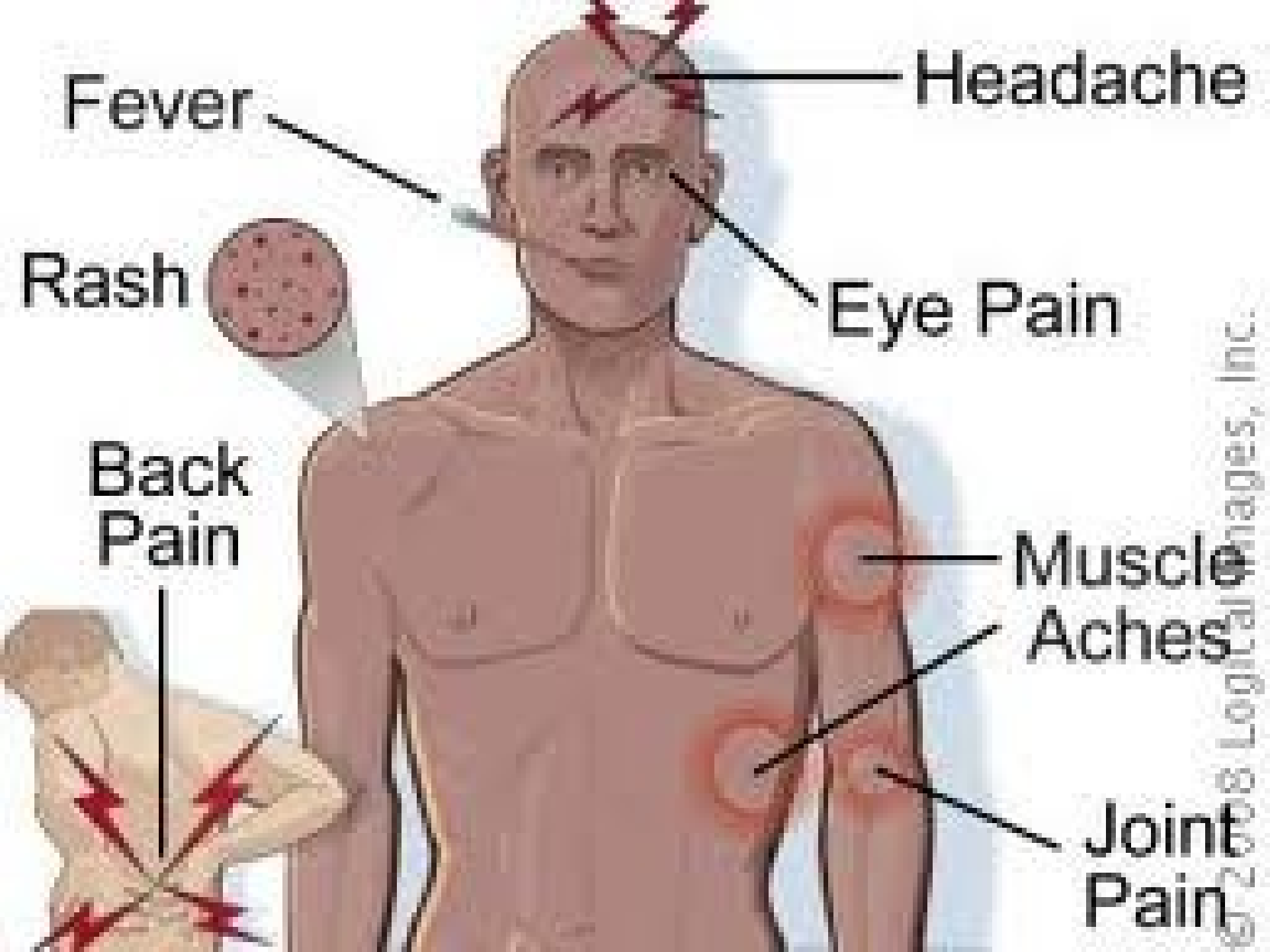
- **Skin rash**
 - usually appears as the fever subsides
 - and last 2 – 4 days
 - may be fleeting and maculopapular, generalized, often confluent
 - seen in about 10% of cases



Clinical Manifestations

- **Other signs and symptoms** include:
 - Flushed facies
(usually during the first 24 – 48 hours)
 - Nausea
 - Vomiting
 - Gastrointestinal disturbances...





Fever

Headache

Rash

Eye Pain

Back Pain

Muscle Aches

Joint Pain

Diagnosis, laboratory

- Mild cases are very hard to diagnose
- Clinical symptoms of DF is very resemble of influenza symptoms - Flu – like illness
- Fever is accompanied by:
 - Leucopenia, relative lymphocytosis
 - Moderate trombocytopenia
 - **AST > ALT** (liver enzyme)
 - Serology (ELISA) for IgG and IgM antibodies
- In case of febrile illness exlude:
 - Malaria, yellow fever, leptospirosis...
 - Chikungunya, rickettsial illness...

Treatment

- There is **no specific treatment for DF**
- **MAINSTAY = Symptomatic and supportive care**
- **HYDRATATION !!!** – essential
 - Is the most important
 - Oral and intravenous replacement of fluid and electrolytes
 - **Sufficient circulating fluid volume** is the central feature of DF care

Prevention (how can we prote

- control of mosquito vector in urban and rural
- mosquito net
- garment cover (for travelers), long-sleeved ga
- repellents and insecticidal sprays



DENGUE

HEMORRHAGIC FEVER

(DHF)

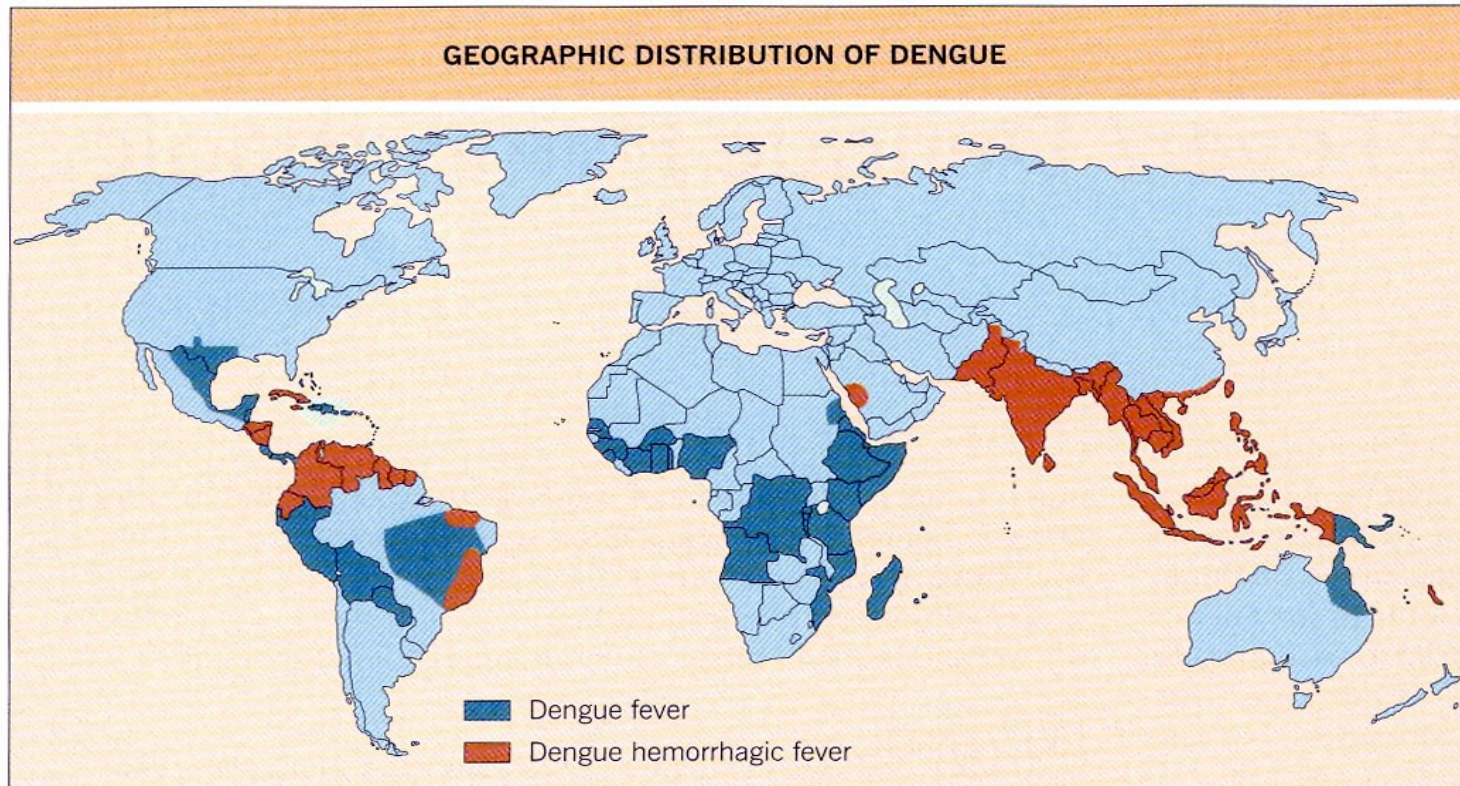
Dengue hemorrhagic fever (DHF)

- A potentially **lethal complication of dengue fever** with hemorrhage and occasional shock
- Was first recognized the 1950s during dengue epidemic in the Philippines and Thailand

- Affects most **Asian countries**
- Has become a leading cause of hospitalization and **death among children** in the region
- Has not been seen in Africa

Dengue hemorrhagic fever (DHF)

- An estimated **500 000** people with DHF require hospitalization each year
- A very large proportion of whom are **children**
- Without proper treatment, **fatality rates** can exceed **20%**
- Adequate **treatment** can reduce death rates to less than **1%**



Clinical Manifestations of DHF

- Approximately **1%** of patients **with DF** develop **DHF** as the fever subsides
- Usually **3 – 7 days** following the onset
- The hallmark of DHF is evidence of **vascular leakage**

- **Severe cases** are diagnosed based on the following:
 - **High fever** for 2 to 7 days
 - **Hemorrhage**
 - Gastrointestinal bleeding, Ecchymoses, Effusions...
 - **Hepatomegaly**

DHF is defined:

- By the presence of all the following symptoms:
 1. **Fever**
 - or recent history of fever lasting 2 – 7 days
 2. **Any hemorrhagic manifestation**
 3. **Trombocytopenia**
 - Platelet count $< 100\ 000\ \text{mm}^3$
 4. Evidence of increase **vascular permeability**
 - Hemoconcentration
 - Pleural or abdominal effusion
 - Hypoalbuminemia, hypoproteinemia

Dengue HF



Dengue HF



Laboratory

- Leucopenia, relative lymphocytosis
- Trombocytopenia
- Anemia
- Elevated hematocrit, hemoconcentration
- Dehydratation
- AST > ALT (liver enzyme)
- Serology (ELISA)
 - for IgG and IgM antibodies (to dengue virus)

Treatment

- There is **no specific treatment for DF/DHF**
- **Symptomatic and supportive care**
- **Aspirin is avoided**
 - (it may exacerbate the bleeding tendency due to the hemorrhagic nature of the severe illness)
- **HYDRATATION !!!** – essential
 - Oral and intravenous replacement of fluid and electrolytes
 - **Circulating fluid volume** is the central feature of DF care

**DENGUE
SHOCK SYNDROME
(DSS)**

Dengue Shock Sy is defined:

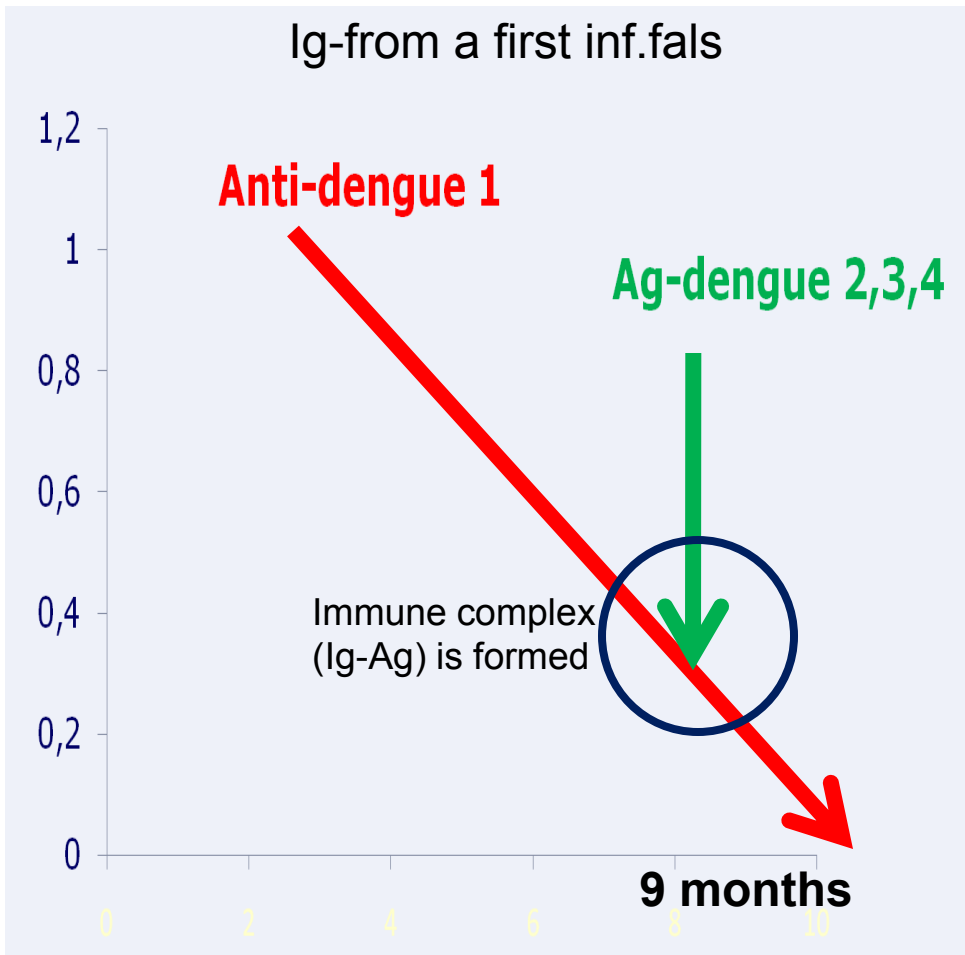
As a syndrom in any case patient
who meets the

- **Criteria for DHF**
and has
- **Hypotension**
- **Narrow puls pressure** (≤ 20 mmHg)
- **Or frank shock**
- **Circulatory failure**
- **Death within 12 to 24 hours**

Patophysiology of DHF/DSS

- Infection with one DENV produces **immunity** against reinfection with **that one viruses** (short-term \leq months)
- Infection with **one serotype** **does not protect** against the others, and sequential infections (others serotypes) **put people at great risk for DHF/DSS**

DHF/DSS



- Is an **immunopathologic syndrome**
- Antibody from a first infection falls and second dengue virus type infection is present
- Even very small numbers of antibody to one serotype of dengue form **immune complex** with other serotype of dengue
- Followed an **acute vascular permeability syndrome**

DHF/DSS

Occurs in:

- Infants infected **for the first time** who have acquired **maternal dengue antibody** in utero
- Children and, less commonly, adults during **a second dengue virus infection**

□ Is more severe in:

- **Whites and Asians** (versus black people)
- **Females** (versus males)
- **Well-nourished children**





Dengue prevention

currently relies
on public health
and community-based
Aedes aegypti
control programs

**to remove and destroy mosquito-breeding
sites**

□ **Thank you for your attention...**