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 rality

- 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 $\leq$ 9 months)

- Infection with **one serotype** **does not protect agains 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**

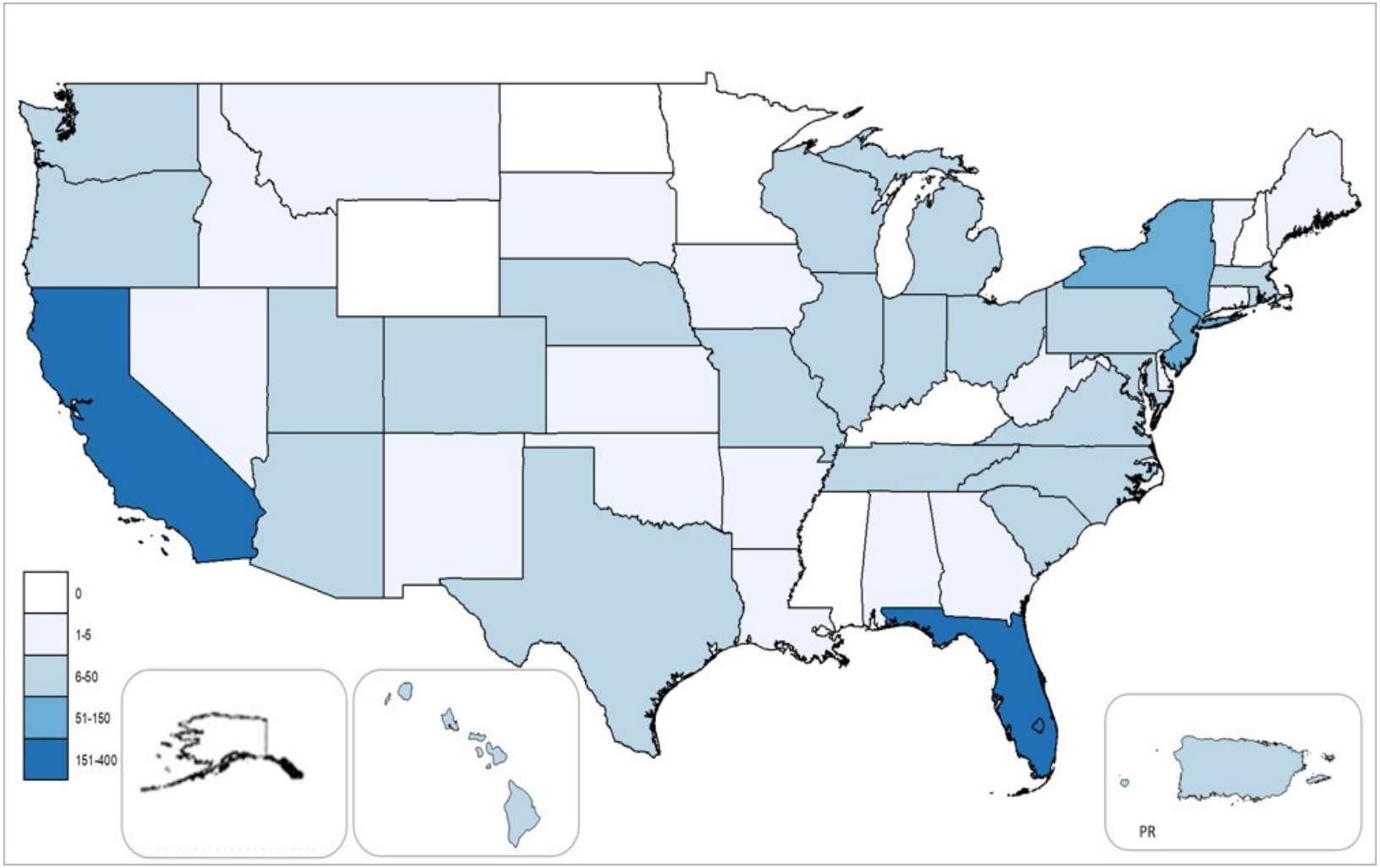
- Vector (*Aedes*) and virus is present throughout **the tropical and subtropical zones**
  - Between
    - 35 degrees North latitude
    - 40 degrees South latitude

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



www.cdc.gov/dengue/statistics

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 occuring

Global Dengue

Before World War II:

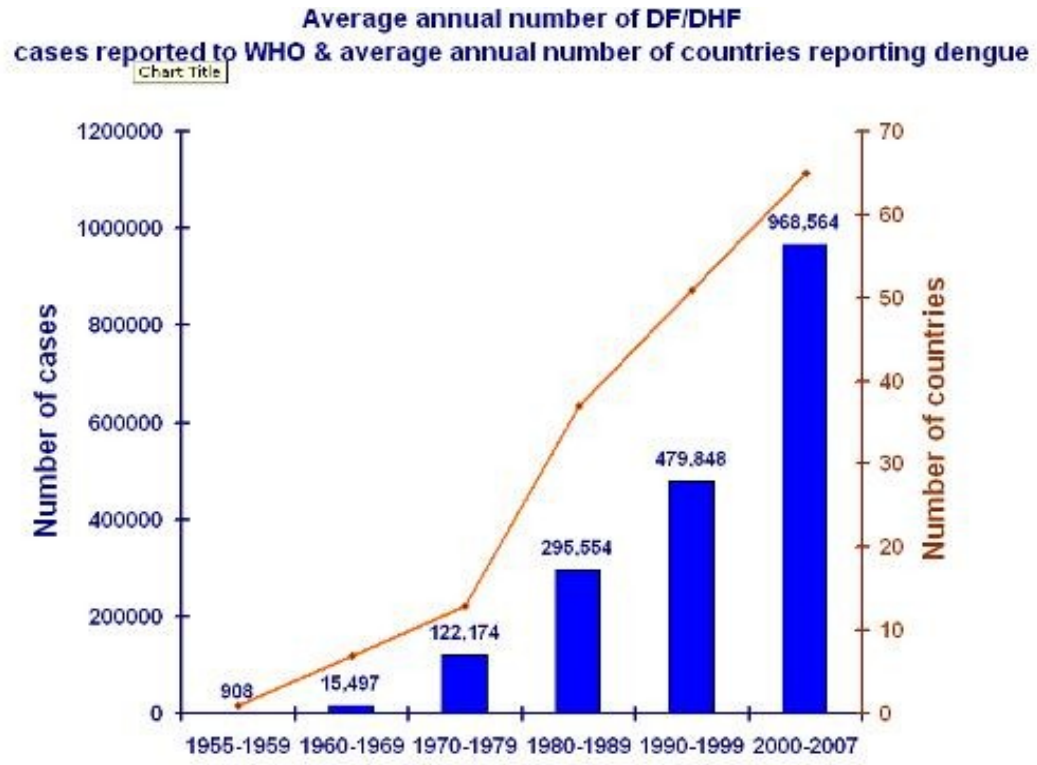
- Sporadic outbreaks were reported
  - throughout the tropics and subtropics

After World War II:

- The start of the 1st pandemi
  - 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 feets (bites) during these hours.

The most risk for DF

- During the **rainy season**

  (when *Aedes* mosquito populations are high)

- However, mosquitoes may feed

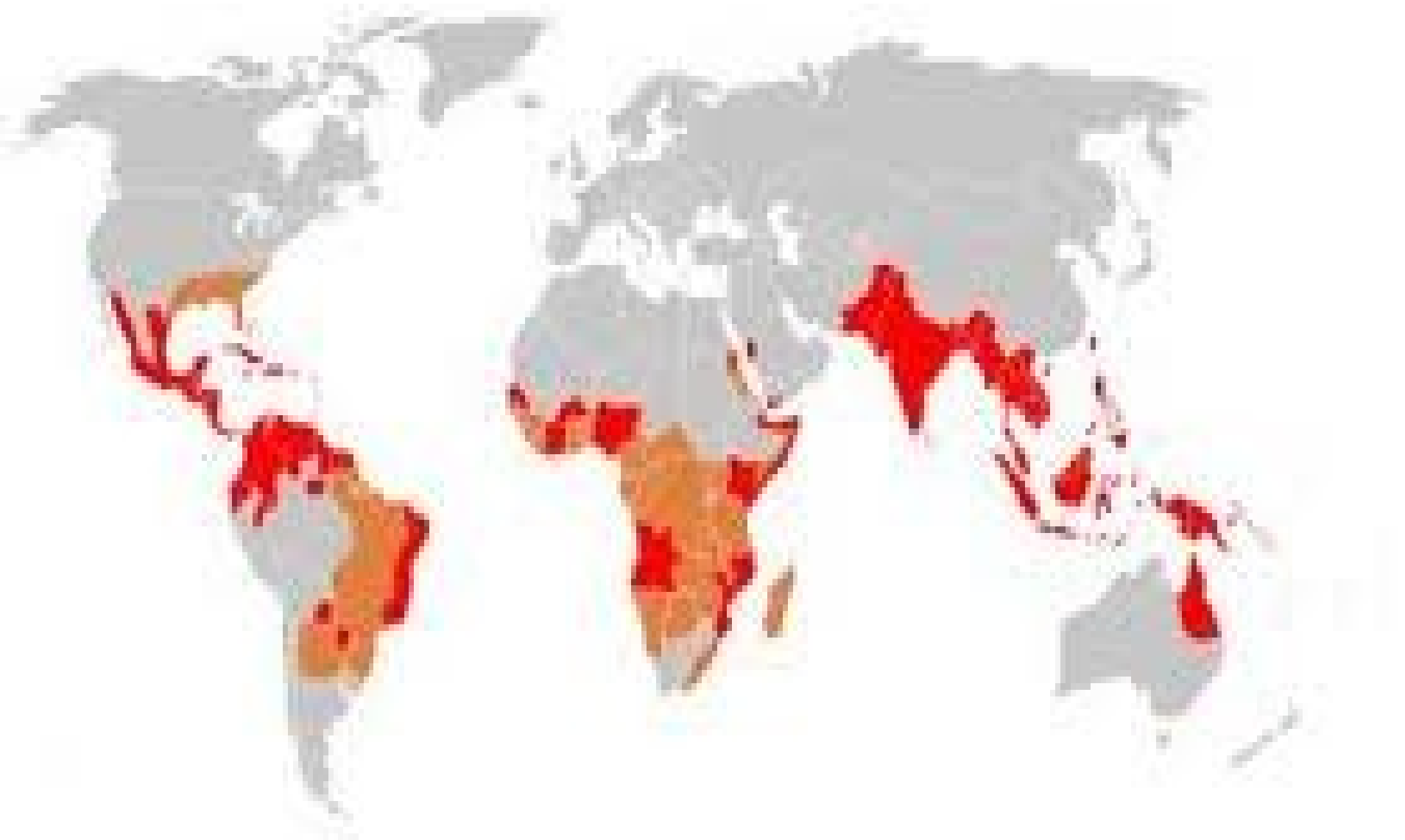
  at any time during the day.
  - **Globally risk**
    - especially for travelers
      - **All year**
      - **All day**

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

Geografic distribution of Dengue



Mosquito *Aedes aegypti* – breeding habitats

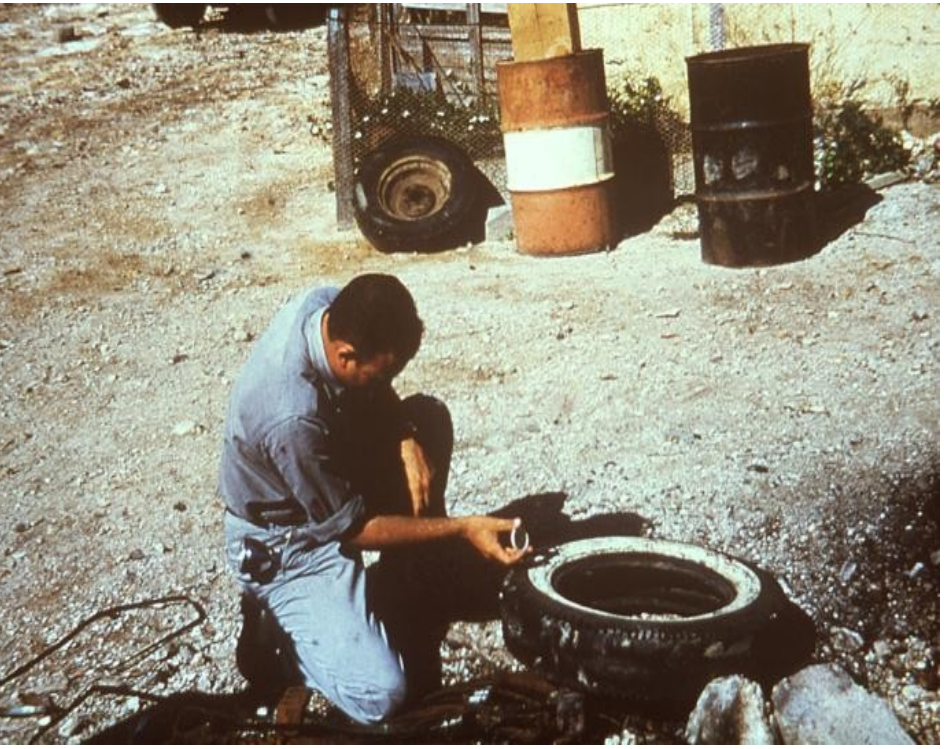
Is adapted to breed **around human dwellings,** where insects oviposit **in uncovered water storage containers** as well as miscellaneous containers **holding water:**

- 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…)

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

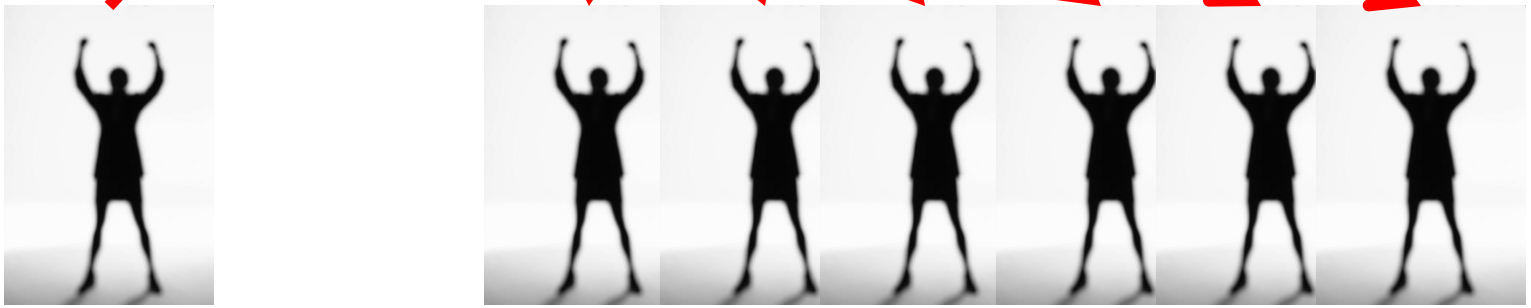
  who have not been previously exposed

  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:

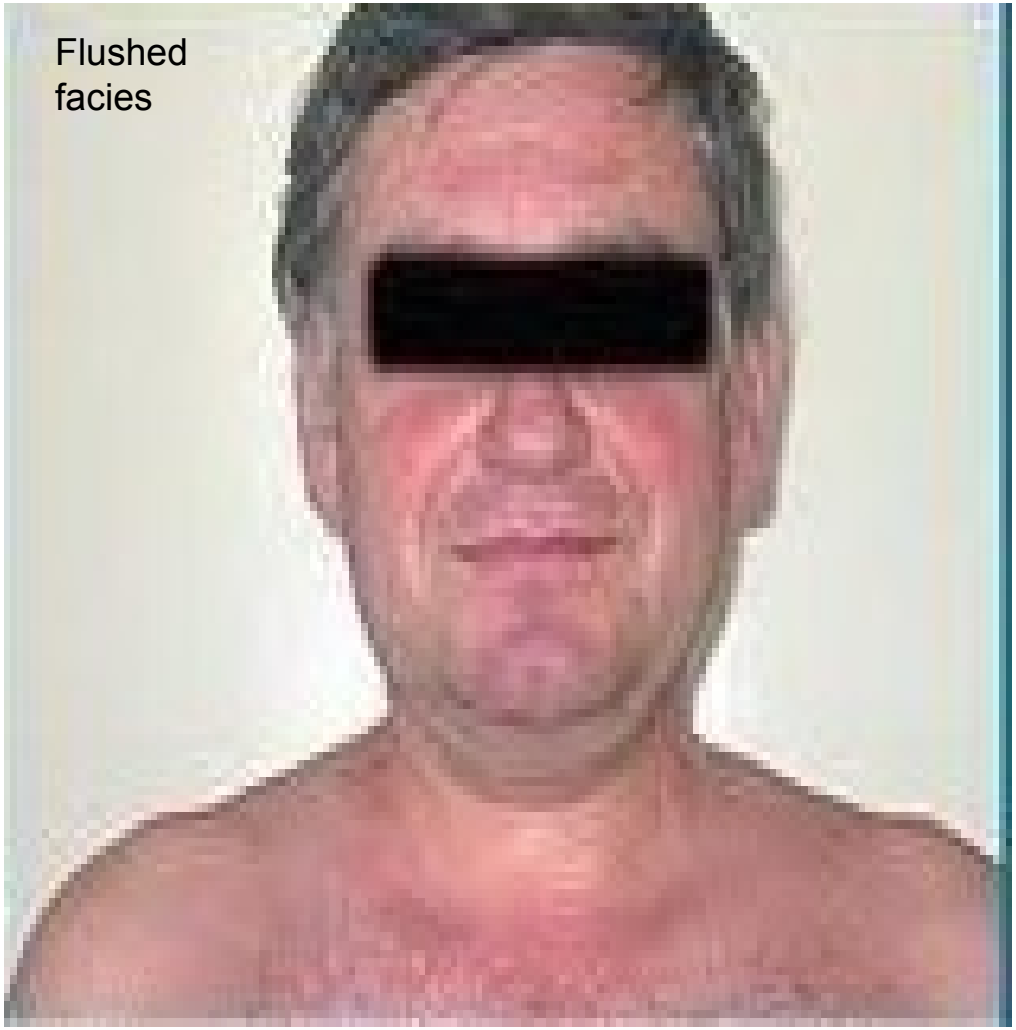
  - Headache, retro-orbital pains
  - Generalized pains in the muscles and bone („breakbone fever“)
  - Lack of appetite, Chills, leucopenia…
- **Fever**
  - Occuring for a period of 5 to 6 days

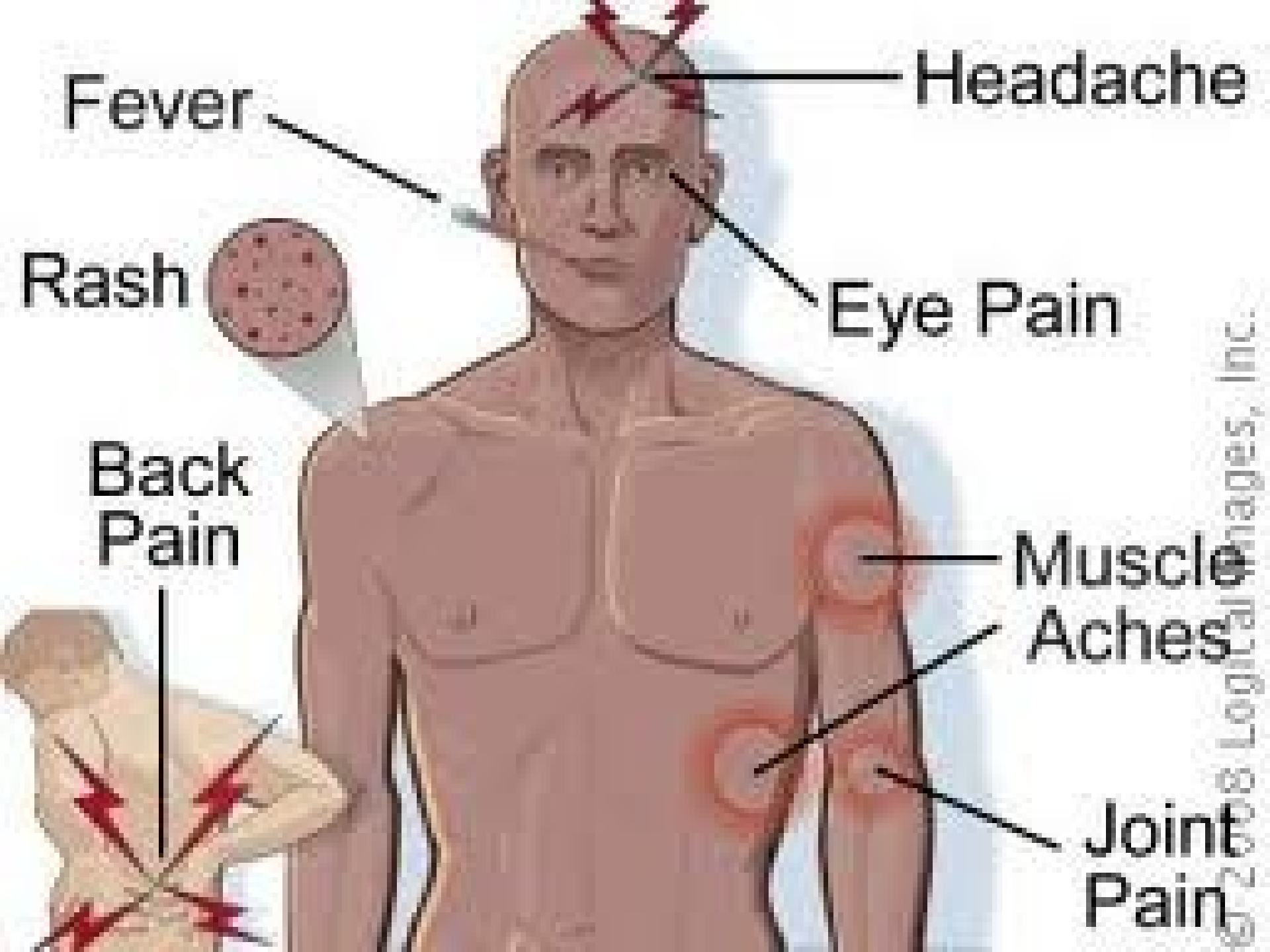
Clinical Manifestations

- **Skin rash**
  - ussually 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)

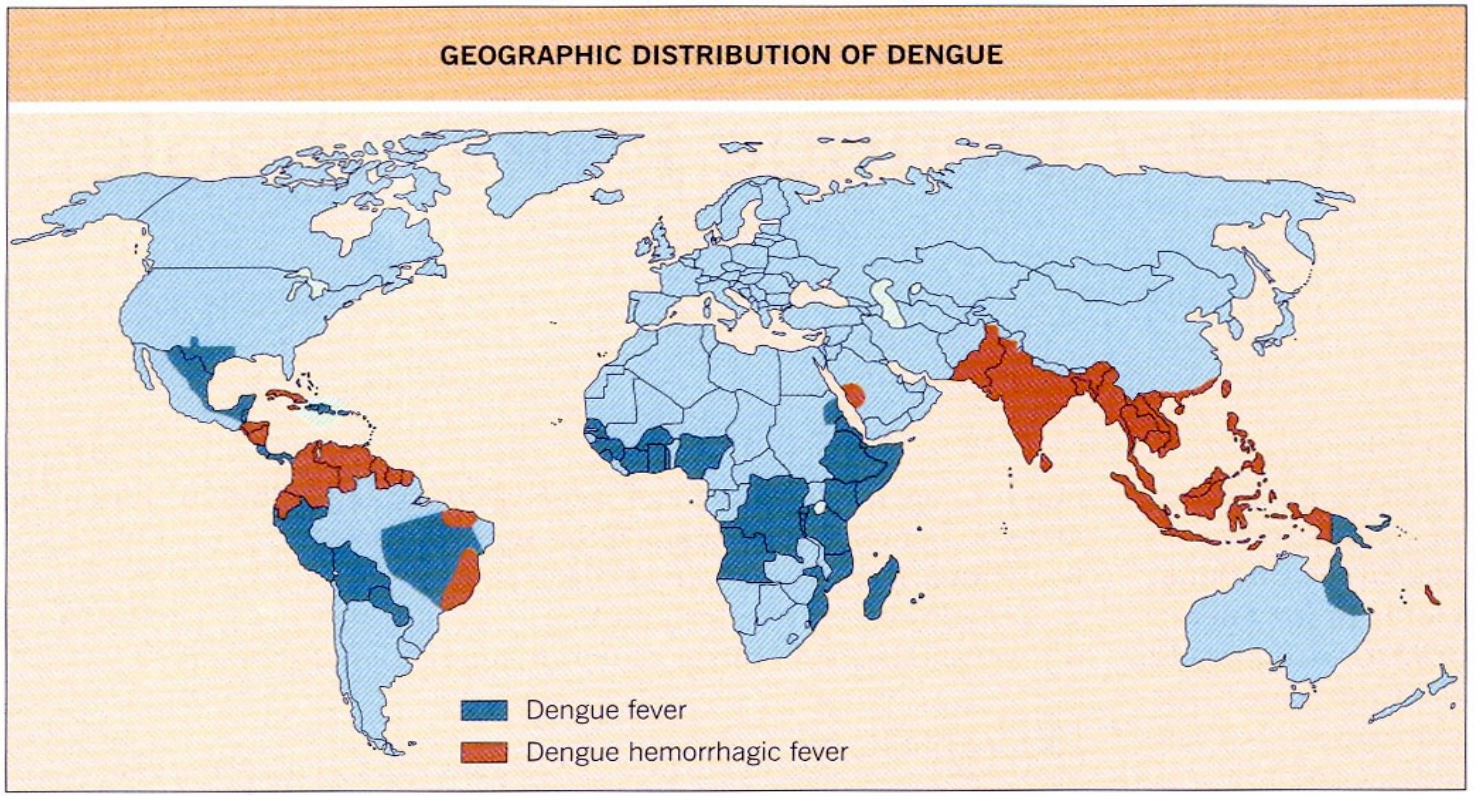
Dengue hemorrhagic fever (DHF)

- 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**

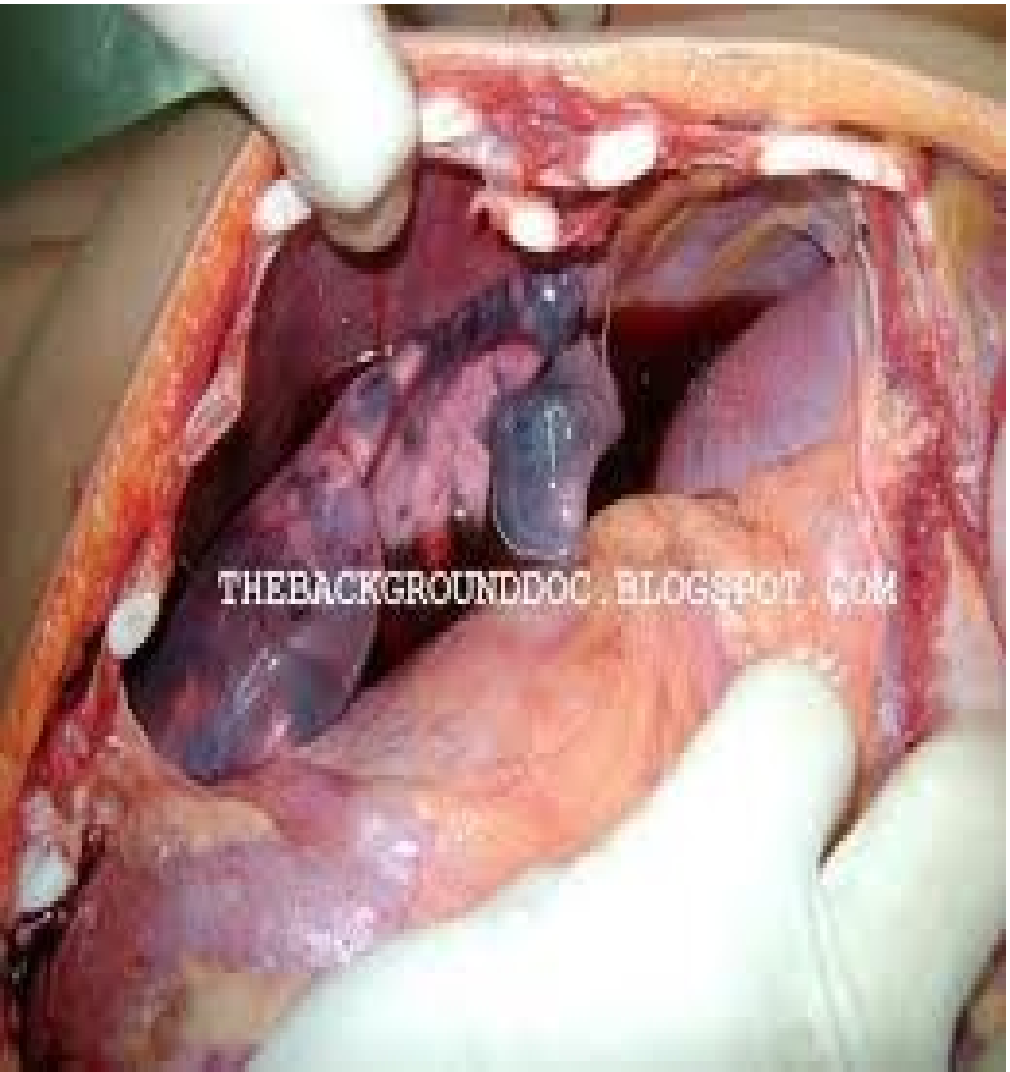
- **Severe cases** are diagnosed based on the following:
  - **High fever** for 2 to 7 days
  - **Hemorrhage**
    - Gastrointestinal bleeding, Ecchymoses, Effusions…
  - **Hepatomegaly**

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 $< 100\,000\ mm^3$
  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**

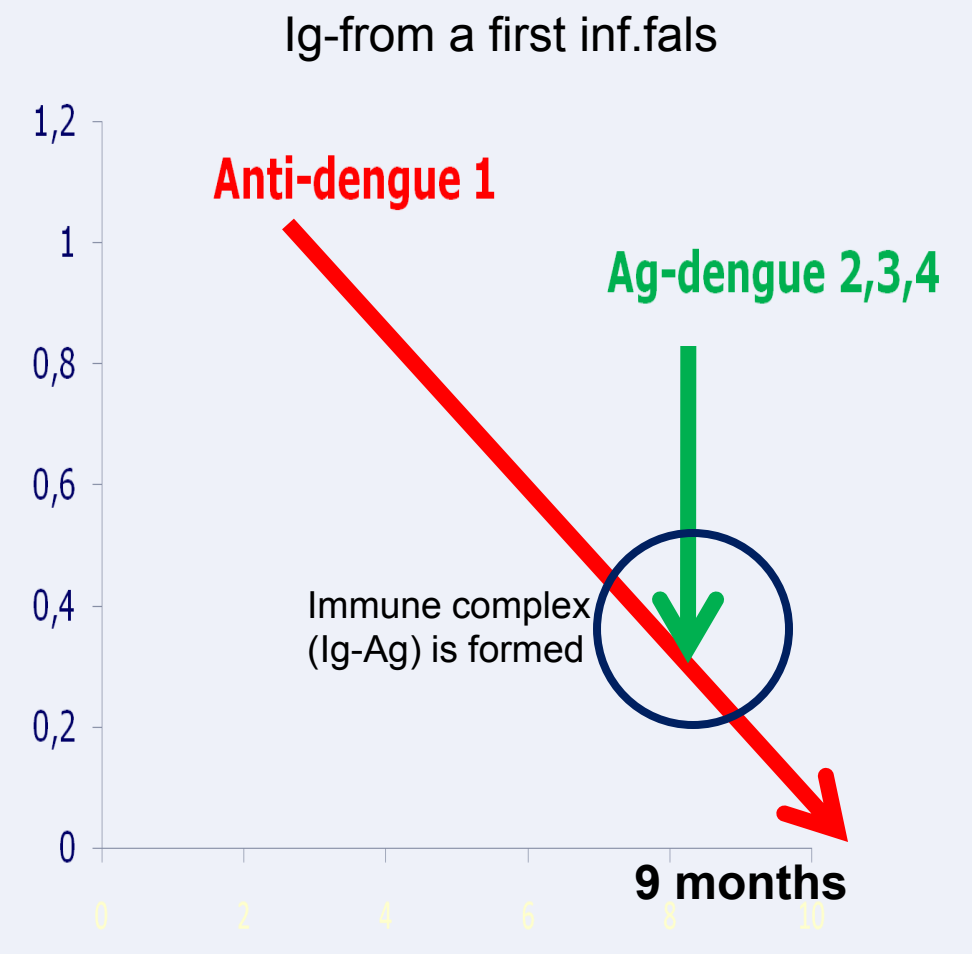
  and has

- **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 ≤ months)
- Infection with **one serotype** **does not protect agains 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 fals

  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…**