

Introduction and Objectives

Dengue is an enveloped ssRNA virus that is grouped into four serotypes belonging to the genus *Flavivirus*. Dengue infection represents the most destructive arboviral disease for humans. Approximately 50-100 million infections occur each year resulting in about 25,000 deaths. The disease has become more common in high-income countries as a result of vector dissemination and increased travel. Recently, neurological manifestations have been increasingly described. I have defined the following objectives:

- ① Get to know the dengue virus, its replication cycle, transmission and risk factors
- ② Understand the disease, the neurological complications and laboratory diagnosis
- ③ Comprehend the available vaccines and therapeutic approaches
- ④ Show the preventive actions, current situation and epidemiology

Virus entry

DENV replicates within the cells of the immune system (Figure1), particularly macrophages and monocytes

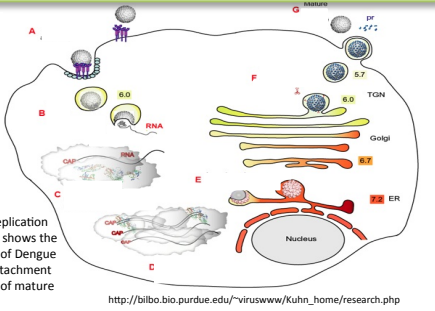


Figure1. DENV replication cycle. This figure shows the replication cycle of Dengue virus from the attachment until the release of mature virus

http://bilbo.bio.purdue.edu/~viruswww/Kuhn_home/research.php

Transmission and Risk factors

Dependent on the vector *Aedes aegypti* and to lesser extent *Ae. albopictus*

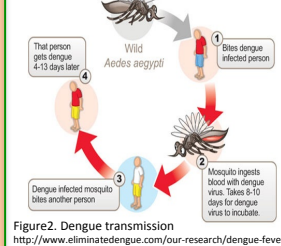


Figure2. Dengue transmission <http://www.eliminatedengue.com/our-research/dengue-fever>

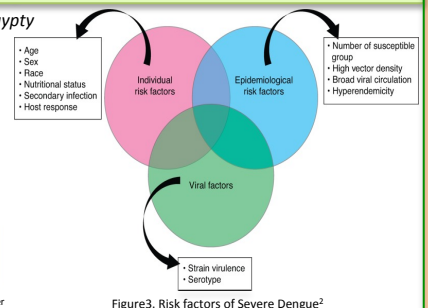


Figure3. Risk factors of Severe Dengue²

Disease

Most DENV infections are asymptomatic



Figure4. The 2009 revised dengue case classification²

Laboratory Diagnosis

- ❖ Often is unavailable at the time of care
- ❖ Isolation of virus from serum or autopsy tissue specimens
- ❖ Identification of specific DENV genome by RT-PCR
- ❖ Limit use in rural areas due to the necessity of biosafety level 3, keeping infectious patient material cold and necessity of qualified personnel
- ❖ Use of several techniques currently available to confirm a case of dengue

Neurological manifestations

Dengue Encephalopathy

- ❖ Hepatic failure, metabolic acidosis, severe hyponatraemia, prolonged shock, disseminated intravascular coagulation, or brain haemorrhage
- ❖ Normal Cerebrospinal fluid (CSF)

Encephalitis

- ❖ Presence of dengue virus RNA, IgM, or NS1 antigen in CSF
- ❖ CSF pleocytosis without other neuroinvasive pathogens

Post-dengue immune-mediated syndromes

- ❖ Acute transverse myelitis, acute disseminated encephalomyelitis, and Guillain-Barré syndrome

Cerebrovascular complications

- ❖ Intracranial haemorrhages during convalescence stage of dengue
- ❖ Can arise without other visible haemorrhagic manifestations

Vaccination

- ❖ No licensed vaccine exists for dengue
- ❖ It should protect against all four serotypes
- ❖ A single dose live attenuated vaccine is expected
- ❖ There are dengue vaccine candidates at different stages of preclinical and clinical development
- ❖ Use of different types of vaccines depends on the purpose of vaccination and target group

Therapeutic approaches

- ❖ Supportive care
- ❖ Monitoring of consciousness
- ❖ Maintenance of airways
- ❖ The design of novel therapeutical approaches is focused on various stages of the viral replication cycle → Targeting mature virus entry into host cells
- ❖ Main concern → not validated for inhibitory effects on all four DENV serotypes

Prevention

- ❖ Educate people in affected areas about basic protection measures
- ❖ Anti-vector control programs:
 - ❖ Rigorous surveillance
 - ❖ Spraying pesticides
 - ❖ Genetically modified mosquitoes
 - ❖ Minimizing potential breeding sites



<http://4.bp.blogspot.com/-aUv8m5D84M/UgmL4013kI/AAAAAAAAABtw/qngd8aMK2M4/s1600/dengue.jpg>

Current situation and epidemiology

- ❖ Dengue affects over a 100 million people annually
- ❖ Dengue is endemic in almost all tropical and subtropical countries
- ❖ The highest incidences are reported in Asia and in Central and South America (Figure5)
- ❖ Global warming is potentially placing a higher proportion of population at risk

Conclusions

- ❖ Transmission of DENVs is dependent on the mosquito *Aedes aegypti* and *Ae. albopictus*
- ❖ Dengue can manifest with a wide range of neurological features
- ❖ The accuracy of diagnosis has to be improved
- ❖ The development of dengue vaccine needs to be the focus of research efforts
- ❖ Stages of viral replication are the focus of new therapeutical approaches
- ❖ Vector control and people education are the two ways to prevent the disease
- ❖ The transmission area of the disease is expanding

References

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2. Hadinegoro, S. R. S. The revised WHO dengue case classification: does the system need to be modified? *Pediatr. Int. Child Health* 32, 33–38 (2012).
3. Bäck, A. T. & Lundkvist, A. Dengue viruses - an overview. *Infect. Ecol. Epidemiol.* 3, 1–21 (2013).
4. WHO. *Dengue: guidelines for diagnosis, treatment, prevention, and control. Spec. Program. Res. Train. Trop. Dis.* (2009). at <http://whqlibdoc.who.int/publications2009/9789241547871_eng.pdf>

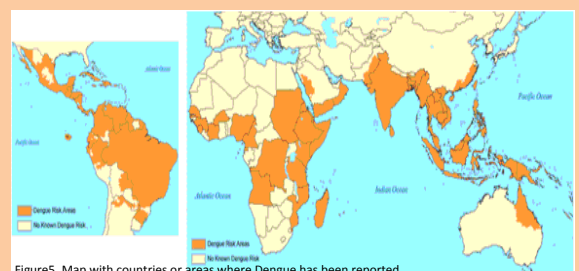


Figure5. Map with countries or areas where Dengue has been reported <http://www.cdc.gov/dengue/epidemiology/>

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