Introduction and Objectives

Dengue is an enveloped sRNA 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 (Figure 1), particularly macrophages and monocytes.

Disease

Most DENV infections are asymptomatic.

Transmission and Risk factors

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

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

Cerebrovascular complications

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

Neurological manifestations

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

Post-dengue immune-mediated syndromes

- Supportive care
- Monitoring of consciousness
- Maintenance of airways
- The design of novel therapeutic 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

Therapeutic approaches

- Supportive care
- Monitoring of consciousness
- Maintenance of airways
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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

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 (Figure 5)
- 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 therapeutic approaches
- Vector control and people education are the two ways to prevent the disease
- The transmission area of the disease is expanding

References