PRIMEVIEW

DENGUE INFECTION

nature REVIEWS DISEASE PRIMERS

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Dengue is a mosquito-borne disease caused by infection with dengue virus (DENV). Clinically, the disease can range from a mild febrile illness (previously called dengue fever) through to dengue with warning signs and severe dengue, which includes what were previously called dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).

EPIDEMIOLOGY

DENVs are transmitted by *Aedes aegypti* mosquitoes and are widespread throughout the tropics. The global expansion of DENVs began with the South-East Asian dengue pandemic in the 1950s and was facilitated by the effects of globalization, such as increased air travel. Over half of the world's population are at risk of DENV infection. Each year, an estimated 360 million DENV infections occur, resulting in 2 million cases of severe disease and 21,000 deaths.

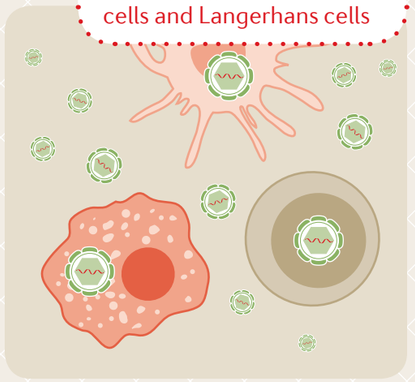
PREVENTION

Prevention focuses on mosquito control using strategies such as larval source reduction, insecticide spraying and community outreach and education. Although some countries, such Singapore and Cuba, achieved temporary dengue control using these approaches, their inconsistent application and the introduction of DENVs from neighbouring countries eventually led to the re-emergence of epidemic DENV transmission.

PATHOPHYSIOLOGY

INFECTION

The bite of an infected mosquito leads to DENV infection of several cell types, including macrophages, dendritic cells and Langerhans cells

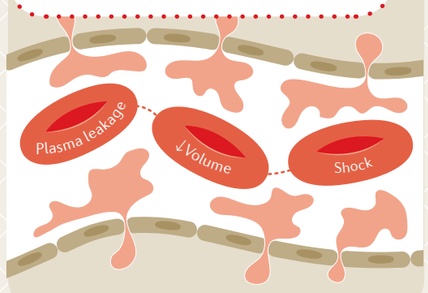


ACUTE PHASE

High viral loads and fever follow 4–7 days later

CRITICAL PHASE

Plasma leakage and abnormal haemostasis underlie DHF and DSS. Although their causes are not well understood, antibody-dependent enhancement and the DENV protein NS1 are probably important contributors.



Second DENV infections are often more severe than the first because non-neutralizing anti-DENV antibodies can enhance infection

CONVALESCENCE

Recovery involves cessation of plasma leakage and reabsorption of lost fluids

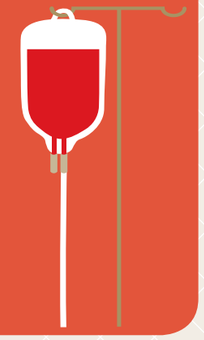
DIAGNOSIS

The 2009 WHO guidelines are used to clinically classify dengue and identify patients at risk of progressing from mild to severe illness. Diagnosis of presumptive dengue with or without warning signs is made if the patient lives in or has recently travelled to a dengue-endemic area and has symptoms such as fever, vomiting or aches and pains. Warning signs of severe disease include abdominal pain, mucosal bleeding and clinical fluid accumulation, whereas hallmarks of severe disease include severe plasma leakage leading to DSS, severe bleeding and severe end-organ involvement.

Confirmation of a dengue diagnosis is made by laboratory testing. This can involve assaying for DENV RNA or the NS1 protein in blood, serum or plasma, as well as for anti-DENV IgM.

MANAGEMENT

As there is no antiviral therapy for dengue, management involves supportive care. The majority of patients with dengue have mild febrile illness and treatment is commonly bed rest, oral fluids and analgesics. Treatment of dengue with warning signs and severe dengue involves the replacement of fluids lost owing to capillary leakage with intravenous fluid therapy. Haemorrhages most commonly occur in the gastrointestinal system, where they can manifest as haematemesis (vomiting of blood) and/or melaena (black, tar-like faeces), and are treated using blood transfusions.



OUTLOOK

To succeed in preventing dengue, mosquito control efforts will need to be sustained in the long term and conducted at the regional level to prevent the spread of DENVs from adjacent endemic areas. This effort will be aided by the development of new control tools, the study of insecticide resistance and improved surveillance. Several dengue vaccines are currently being tested in clinical trials, including recombinant subunit vaccines, an inactivated vaccine and live attenuated vaccines. Recently, a live recombinant tetravalent vaccine received approval from the WHO and is now registered in several countries, providing a promising new pathway towards dengue control.

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