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DENGUE FEVER: A REVIEW OF EPIDEMIOLOGY, CLINICAL FEATURES, AND PREVENTION

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ABSTRACT

Dengue fever is an acute, mosquito-borne viral disease of major global health importance, transmitted primarily by Aedes aegypti and Aedes albopictus mosquitoes. The infection is caused by any of the four antigenically distinct dengue virus serotypes (DENV-1 to DENV-4), resulting in a clinical spectrum ranging from mild febrile illness to severe manifestations such as dengue hemorrhagic fever and dengue shock syndrome. This review article compiles key findings from peer-reviewed studies and international guidelines to summarize the virology, transmission cycle, pathophysiology, clinical features, diagnostic approaches, management strategies, and preventive measures for dengue. Globally, an estimated 390 million infections occur annually, with a rising trend attributed to rapid urbanization, climate change, and inadequate vector control. Current management remains supportive, focusing on timely recognition of warning signs, careful fluid resuscitation, and prevention of complications. Prevention relies on integrated vector control, community education, and selective vaccination. This review highlights the urgent need for strengthened surveillance, sustainable mosquito control, and continued research into antivirals and vaccines to mitigate dengue's growing burden.

INTRODUCTION:

Dengue is an acute, mosquito-borne viral infection caused by dengue viruses (DENV) that produces a wide clinical spectrum from asymptomatic infection and a self-limited febrile illness to life-threatening disease characterized by plasma leakage, major bleeding, shock and organ use impairment; it is an increasingly common cause of serious illness in tropical and subtropical regions worldwide. [1][2]

The World Health Organization's (2009) case classification groups symptomatic dengue into:

1) Dengue without warning signs
2) Dengue with warning signs (eg, abdominal Kpain/tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, liver enlargement, rising hematocrit with falling platelets)
3) Severe dengue (severe plasma leakage leading to shock or fluid overload, severe bleeding, or severe organ involvement). [3]

Major complications to watch for are hypovolemic (dengue) shock from plasma leakage, profound thrombocytopenia with hemorrhage (dengue hemorrhagic manifestations), severe hepatic injury, severe central-nervous-system or cardiac involvement, and maternal fetal complications in pregnancy; mortality is preventable with timely recognition and supportive care. [4] [5]

➢ STRUCTURE OF DENGUE VIRUS:

The dengue virus is a roughly spherical, enveloped virion about 50 nm in diameter, featuring an icosahedral nucleocapsid containing its positive-sense single-stranded RNA genome and a capsid (C) protein. This core is surrounded by a host-derived lipid envelope embedded with 180 copies of the E (envelope) and M (membrane) proteins, which form the virus's protective outer layer and are crucial for cell attachment, entry, and replication.

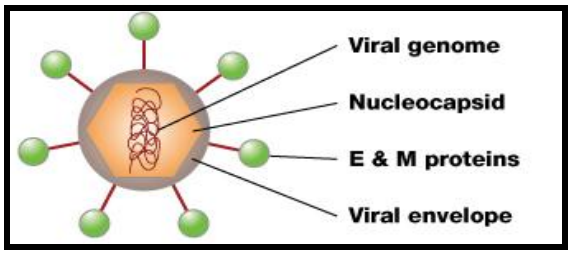

Fig 1. Structure of dengue virus

➢ ETIOLOGY:

Dengue is caused by four antigenically related but distinct serotypes (DENV-1, 2, 3, 4) of an enveloped single-stranded positive-sense RNA virus in the genus Flavivirus. Human infection is transmitted primarily by Aedes aegypti and secondarily by Aedes albopictus mosquitoes; these vectors bite during daytime and breed in small collections of water near human habitation. [4][6]

Severe disease is strongly linked to host immune responses: secondary infection with a heterologous serotype can produce subneutralizing antibodies that enhance viral entry and replication (antibody-dependent enhancement, ADE), and immune-mediated mechanisms contribute to plasma leakage and coagulopathy. [6]

➢ EPIDEMIOLOGY:

Dengue is endemic in >100 countries; global estimates vary by method, but widely cited analyses estimate hundreds of millions of infections per year (Bhatt et al. Estimated ~390 million infections annually, many asymptomatic) and WHO reporting documents very large recent waves, for example 2023–2024 saw historic increases with millions of reported cases and thousands of severe cases/deaths in the Americas and elsewhere. Transmission is highest in tropical/subtropical urban and peri-urban settings where Aedes mosquitoes thrive. [4][5]

Key drivers of the recent expansion are urbanization with high human population density, increased international travel, inadequate vector control, and climatic and environmental changes that expand mosquito habitat and seasonality. Surveillance systems

under-report true incidence (many infections are asymptomatic or mild), so local burden can be substantially higher than reported case counts. [7]

- **TRANSMISSION OF DENGUE VIRUS:**

Dengue virus transmission occurs primarily through the bite of infected Aedes mosquitoes, specifically Aedes aegypti and Aedes albopictus. Aedes aegypti is the primary mosquito vector responsible for dengue transmission, thriving in densely populated urban environments. The transmission cycle involves the virus being transmitted between humans and mosquitoes, with the mosquito remaining infected for its entire lifespan. The extrinsic incubation period in mosquitoes is 8-12 days, while the intrinsic incubation period in humans is 3-14 days, with an average of 4-7 days.[8]

The viral load present in the host at the time of feeding influences the mosquito's ability to become infected. Genetic differences among mosquito populations can affect their susceptibility to dengue virus infection and transmission, and studies have shown variations in vector competence among Aedes aegypti populations from different regions. All four serotypes (DENV-1 to DENV-4) can be transmitted by Aedes aegypti, with varying levels of susceptibility and dissemination efficiency.[8,9]

- **LIFE CYCLE OF DENGUE VIRUS:**

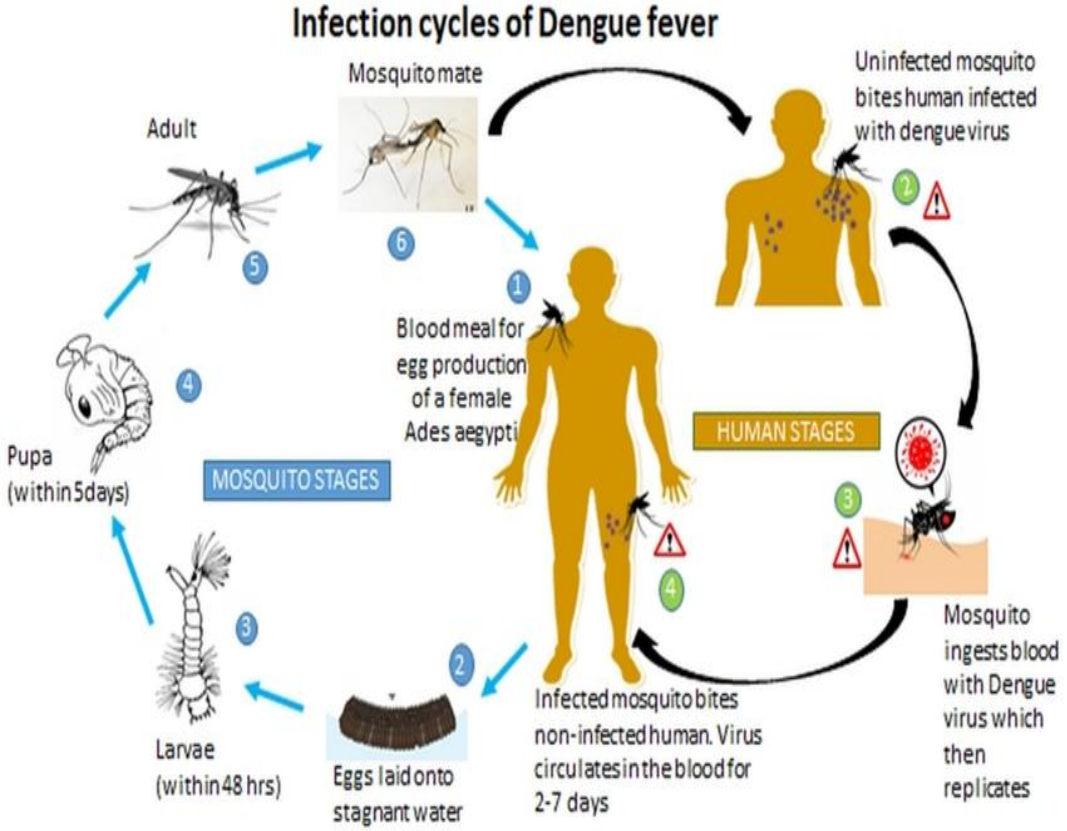

Fig .2 : Life Cycle of Dengue Virus in human body

Fig 2 illustrates the life cycle of the Aedes mosquito, which is the primary vector for transmitting dengue fever, and the process of virus infection. The mosquito life cycle includes stages from egg to adult, with female mosquitoes requiring a blood meal for egg production. The eggs are laid onto standing water surfaces, and larvae hatch from these eggs in water, progressing through four stages before becoming pupae and eventually adult mosquitoes.

In terms of virus infection, uninfected Aedes aegypti and Aedes albopictus mosquitoes can bite a human infected with the dengue virus. After ingesting blood with the dengue virus, the virus takes 10-12 days to incubate in the mosquito. Once the mosquito is infected, it can bite another human and transmit the virus. After 4-13 days, the human becomes virus infectious. The image highlights the role of wild mosquitoes in bringing people into contact with the virus and spreading it.

- **PATHOPHYSIOLOGY OF DENGUE VIRUS:**

Dengue virus infection triggers a complex interplay of immunological mechanisms that contribute to its pathophysiology. The immune response plays a crucial role in responding to secondary dengue virus infections, with CD4+ and CD8+ T cells targeting viral antigens and inducing cytokine production. However, this response can also lead to a cytokine storm, characterized by the production of cytokines like TNF-α, IL-6, and CXCL10, which contribute to vascular leakage and disease severity. Additionally, pre-existing antibodies can enhance dengue virus infection in cells expressing Fcγ receptors, leading to increased viral replication and severity through a phenomenon known as antibody-dependent enhancement (ADE).[10]

Vascular leakage and endothelial dysfunction are also key features of dengue pathogenesis. Dengue virus infection induces endothelial activation, leading to increased vascular permeability and leakage. Mast cells contribute to vascular leakage through the release of mediators that disrupt endothelial function. Furthermore, the interaction between dengue virus and CLEC5A/TLR2 receptors on immune cells exacerbates vascular leakage and disease severity.[10][11]

Other key factors that influence dengue pathogenesis include viral load and serotype, with higher plasma viremia associated with adverse outcomes and different serotypes contributing to varying levels of disease severity. Host genetic factors, such as genetic variations in immune response genes, can also influence disease susceptibility and severity. Finally, dengue virus employs various strategies to evade the host immune response, including suppression of type I interferon signaling.[11]

- **SIGNS AND SYMPTOMS:**

Mild symptoms of dengue can be confused with other illnesses that Cause fever, aches and pains, or a rash. .[12]

The most common symptom of dengue Is fever (40°C/104°F) with any 2 of the Following:

Nausea, vomiting

Rash

Aches and pains (eye pain, typically

Behind the eyes, muscle, joint, or Bone pain)

Swollen glands

Severe dengue (Dengue Hemorrhagic Fever DHF OR Dengue Shock Syndrome DSS) occurs less frequently than dengue fever but has a more dramatic clinical presentation. .[12]

Severe dengue is defined by one or more of the following:

Plasma leakage that may lead to shock (dengue shock) and/or fluid accumulation,

With or without respiratory distress

Severe bleeding, and/or severe organ impairment.

Patients with severe dengue shows:

Biphasic fever

- Thrombocytopenia
- Increasing hematocrit
- Low albumin
- Hemorrhagic manifestations
- Progressive effusions
- Lymphocytosis

➢ **DIAGNOSIS:**

Dengue should be suspected in a febrile patient who has lived in or traveled to an endemic area and who has two or more of: nausea/vomiting, rash, myalgia/arthralgia, leukopenia, or WHO warning signs.[13][14]
Laboratory confirmation is best achieved by RT-PCR or NS1 antigen testing during the first 5 days of illness, while IgM and IgG serology become useful afterwards.[13][15]
Additional monitoring with complete blood count, hematocrit, liver enzymes, coagulation profile, and renal function is essential to assess severity and guide fluid management.[13][14]

➢ **COMPLICATIONS:**

1. Plasma leakage and hypovolaemic shock (dengue shock syndrome): This is the principal life-threatening complication.
2. Severe bleeding: Can range from mild mucosal bleeding to severe gastrointestinal or intracranial hemorrhage.
3. Severe organ involvement: May include hepatitis, acute kidney injury, myocarditis, pancreatic or pulmonary disease.[15]
4. Neurological complications: Encephalopathy, encephalitis, Guillain-Barré–like syndromes, seizures.
5. Secondary infections and prolonged recovery Patients risk secondary bacterial infections and prolonged fatigue.[15]
6. Coagulopathy and multiorgan failure: Combination of thrombocytopenia, coagulopathy, and shock can be fatal.[13][14]

➢ **WARNING SIGNS:**

At defervescence, urgent escalation is warranted if any of the following appear: abdominal pain, persistent vomiting, clinically detectable fluid accumulation, mucosal bleeding, lethargy/restlessness, or a rapid drop in platelet count with rising haematocrit.[14]

Fig 3 . Warning signs of Dengue Fever

TREATMENT OR MANAGEMENT OF DENGUE:

There is no specific antiviral therapy for dengue; care is purely supportive. WHO recommends managing symptoms, hydration, and close monitoring. The treatment approach for dengue fever varies depending on the patient's illness phase. Patients without warning signs can typically be treated as outpatients with acetaminophen and sufficient oral fluids. In addition, educating patients about the warning signs and advising them to seek immediate medical attention if any of these signs occur is important (15). Following are the management of dengue:

Fluid Management:

IV crystalloids: first-line therapy for patients with warning signs or shock. Adjust infusion rate according to:
Vital signs (pulse pressure >20 mmHg).
Urine output (>0.5 mL/kg/hr).
Hematocrit dynamics.

Colloids: reserved for patients with persistent shock despite crystalloids.

Avoid fluid overload → risk of ARDS and abdominal compartment syndrome.

Transition to oral rehydration after 24–48 hours once stable. .[15] [16]

Hematocrit and Fluid Response:

- Rising hematocrit despite fluids → persistent capillary leak syndrome (CLS) → repeat fluid bolus.
- Falling/normal hematocrit with no improvement → suspect bleeding → transfuse blood. [16]

Blood and Platelet Transfusion:

- Blood transfusion: for severe/suspected bleeding with instability despite fluids or hematocrit <45% in adults with hemorrhage.
- Platelet transfusion: if <20,000/μL with high bleeding risk.
- Routine prophylactic platelet transfusion in thrombocytopenia without bleeding is not beneficial.

Complications and Their Management:

- Bleeding: GI or vaginal hemorrhage requires prompt transfusion. Mucosal bleeding (oral/nasal) → monitor only.
- Fluid overload: oxygen support; consider furosemide (0.5 mg/kg) if indicated.
- Neurological complications (~5%): usually self-limiting (paresthesias). Severe cases like Guillain-Barré syndrome require specific therapy. [17]

Experimental/Investigational Therapies

- Corticosteroids, immunoglobulins, and chloroquine showed no benefit in trials.
- JNJ-A07, targeting viral NS proteins, is under clinical evaluation. [17] [18]

➢ PREVENTION OF DENGUE:

Personal Protection

- Avoid mosquito bites by using EPA-registered repellents (DEET, IR3535, icaridin).
- Wear loose-fitting, long-sleeved clothing and pants.
- Sleep under bed nets, especially if screened rooms or AC are not available.

Use mosquito coils or insecticide-treated materials (curtains, nets). [18]

Environmental Control

Eliminate mosquito breeding sites: cover water containers, dispose of stagnant water, clean rooftops and sunshades.

Maintain proper household sanitation and drainage. [18]

Biological Control

Introduce larvivorous fish (e.g., guppy *Poecilia reticulata*) in tanks and wells.

Use predatory copepods in water containers.

Employ Wolbachia-infected mosquitoes, which are less susceptible to dengue virus. (20)(21) [20] [21]

Chemical Control

Apply larvicides in large breeding containers.

Use space sprays (thermal fogs or aerosols) and insecticides (e.g., malathion, pyrethroids).

Oil-based formulations to reduce evaporation and prevent breeding. [22]

Travel-Related Precautions

Before travel: review health advisories, visit a travel clinic, pack repellents and paracetamol.

During travel: stay in screened or air-conditioned rooms, prevent mosquito bites, seek care if fever develops.

After travel: prevent mosquito bites for 3 weeks to avoid spreading dengue.

Health Education

Raise awareness through mass campaigns and community education about dengue prevention and early medical consultation. [23]

Dengue Vaccine

Dengvaxia® (CYD-TDV, authorized as Dengvaxia) approved for children 9–16 years with laboratory-confirmed prior infection in endemic regions (e.g., U.S. territories).

Not approved for travelers from non-endemic areas. [23]

➢ METHODOLOGY:

This review is structured as an evidence-based review drawing exclusively from high-quality published literature. Articles were retrieved from databases such as PubMed, Google Scholar, and official health agency portals using search terms including “dengue virus,” “pathophysiology,” “clinical management,” and “prevention.” Preference was given to authoritative sources: World Health Organization (WHO) guidelines (2009 and updates), Centers for Disease Control and Prevention (CDC) reports, and key peer-reviewed studies in journals such as Nature, The New England Journal of Medicine, Lancet, and Frontiers in Cellular and Infection Microbiology. Only articles with clear methodologies and relevant clinical or epidemiological data were included. Information was critically appraised for accuracy, relevance, and recency, ensuring that data reflect current global trends, including the surge of cases reported in 2023–2024. References were compiled in Vancouver style as per academic requirements. No human or animal subjects were directly involved in this assignment, and all data are secondary, drawn from the cited literature.

➢ DISCUSSION:

The collected literature underscores dengue as a rapidly expanding public health challenge. Epidemiological evidence indicates that the virus has spread to more than 100 countries, with the highest transmission in tropical and subtropical urban areas. The convergence of climate variability, urban crowding, and insufficient vector control has intensified the incidence of large outbreaks. Pathophysiological insights reveal that severe dengue is primarily immune mediated; antibody-dependent enhancement (ADE) during secondary infections increases viral replication and triggers cytokine storms, resulting in plasma leakage and coagulopathy. Clinically, early recognition of warning signs, abdominal pain, persistent vomiting, rapid hematocrit rise is critical to prevent shock and fatal complications. Diagnostic advances such as NS1 antigen detection and RT-PCR allow timely confirmation in the acute phase, while serology assists in later stages. Management remains supportive, emphasizing careful fluid therapy and close monitoring of hematocrit and platelet counts to prevent both shock and fluid overload. Despite ongoing research into antivirals like JNJ-A07 and novel vaccine strategies, Dengvaxia® remains the only licensed vaccine and is limited to individuals with prior dengue infection in endemic regions. Effective control therefore hinges on integrated vector management, community education, and innovative biological controls such as Wolbachia-infected mosquitoes.

➢ CONCLUSION:

Dengue continues to pose a formidable challenge to global health systems, with incidence and geographic spread escalating each year. Evidence from recent outbreaks highlights the interplay of environmental, social, and immunological factors driving disease severity and spread. While mortality can be minimized through timely diagnosis and meticulous supportive care, the absence of widely available antivirals and universally safe vaccines underscores the importance of prevention. Sustainable mosquito-control programs, public awareness, and surveillance remain the backbone of effective dengue control. Future priorities should include investment in next-generation vaccines, targeted antivirals, and strengthened public health infrastructure to mitigate climate-driven increases in vector populations. A coordinated, evidence-based approach,spanning research, community engagement, and policy, is essential to reduce

the global burden of dengue and prevent future large-scale outbreaks.

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