Dengue

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Dengue Virus

Overview

- Causative agent: Dengue virus (Flavivirus, genus *Flavivirus*; RNA virus)
- Vector: *Aedes aegypti* mosquito (daytime biter)
- Transmission: Human–mosquito–human cycle
- Global impact:
  - ≈ 20 million infections annually worldwide
  - Most common insect-borne viral disease globally
- In the United States:
  - Not endemic
  - 100–200 imported cases/year (mostly from Caribbean & tropical regions)
  - No indigenous transmission reported

🦠 Pathogenesis

Infected mosquito bite → Virus enters bloodstream →
→ Infection of monocytes, macrophages, and endothelial cells → Cytokine release → Increased vascular permeability → Fever, rash, and in severe cases, hemorrhage & shock

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💥 Clinical Forms of Dengue Infection

1. Classic Dengue Fever ("Breakbone Fever")

Onset: Sudden, after incubation of 4–7 days

Symptoms:

- High fever 🌡️
- Malaise and retro-orbital pain 👁️
- Severe myalgia (muscle pain) and arthralgia (joint pain) — feels like bones are breaking ("breakbone")

- Headache 
- Facial flushing
- Maculopapular rash 
- Enlarged lymph nodes (lymphadenopathy)
- Leukopenia (↓ WBC count)

Course:

- Symptoms usually last about a week
- Recovery followed by prolonged weakness (post-viral fatigue)
- Rarely fatal and has few long-term complications

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2. Dengue Hemorrhagic Fever (DHF) / Dengue Shock Syndrome (DSS)

More severe form with ~10% fatality rate ⚠

Initial phase: Same as classic dengue

Progression:

- Hemorrhages in skin and gastrointestinal tract
- Plasma leakage → ↓ blood volume → shock
- Thrombocytopenia, petechiae, and bleeding tendencies
- Commonly seen in southern Asia

Flow of Events:

Classic dengue symptoms → Vascular permeability increases → Plasma leakage → Hypovolemia → Shock → Bleeding (GIT, skin) → Multi-organ involvement (in severe cases)

✿ Comparison Table: Classic vs Hemorrhagic Dengue

Feature	Classic Dengue Fever	Dengue Hemorrhagic Fever / DSS
Fatality	Rarely fatal	Up to 10%

Rash	Common maculopapular	Petechiae, purpura, ecchymoses
WBC Count	Leukopenia	Leukopenia + Thrombocytopenia
Shock	Absent	Present (due to plasma leakage)
Geographic Distribution	Worldwide tropics	Southern Asia predominantly

🧠 Exam Tip

🔷 Remember: Dengue hemorrhagic fever is often due to secondary infection with a different serotype → antibody-dependent enhancement (ADE) leading to more severe immune response.

🧠 Pathogenesis of Dengue Hemorrhagic Fever / Shock Syndrome

⚙️ Key Mechanism: Secondary Infection with a Different Serotype

Dengue virus has 4 serotypes (DEN-1 to DEN-4).

Severe Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS) occurs during a second infection with a different serotype of the virus.

Stepwise Pathogenesis Flowchart

1 First Infection (Primary Dengue):

→ Infection by one serotype (e.g., DEN-1)
→ Body produces antibodies specific to that serotype
→ Patient recovers completely

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2 Second Infection (Different Serotype, e.g., DEN-2):

→ Anamnestic (memory) response occurs
→ Body rapidly produces cross-reacting antibodies against the *first* serotype (heterotypic response)

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3 Two Possible Mechanisms

A. Immune Complex Hypothesis:

→ Virus + Antibody → Immune complex formation →
→ Complement activation →

→ ↑ Vascular permeability + Thrombocytopenia →
→ Hemorrhage & Shock

B. Antibody-Dependent Enhancement (ADE) Hypothesis:

→ Cross-reacting antibodies facilitate virus entry into monocytes/macrophages →

→ Massive cytokine release →
→ ↑ Vascular leakage + Shock →
→ Severe hemorrhagic manifestations

💧 Result:

Both mechanisms lead to plasma leakage, hypotension, shock, and bleeding — hallmark features of DHF/DSS.

🦟 Transmission & Reservoirs

Aspect	Details
Vector	*Aedes aegypti* mosquito (same vector as Yellow Fever)
Reservoir (main)	Humans
Suspected jungle cycle	Monkeys (reservoir) + other *Aedes* species (vectors) in forests
Mode of spread	Mosquito bite → virus transmitted through mosquito saliva during feeding

Flowchart: Transmission Cycle

Infected human → A. aegypti mosquito bites → Virus multiplies in mosquito → Mosquito bites another human → Transmission continues

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Laboratory Diagnosis

Diagnostic Method	Key Points

Virus Isolation	Dengue virus can be isolated in cell culture (confirmatory)
Serology (IgM, IgG ELISA)	Detects IgM antibody or a 4-fold rise in IgG titer between acute & convalescent samples
PCR (Polymerase Chain Reaction)	Detects viral RNA in blood — rapid and sensitive
CBC findings	Leukopenia + Thrombocytopenia common in DHF

🧪 Tip for Exams: PCR and serology (IgM detection or rising IgG titers) are mainstay diagnostic tools.

💊 Treatment & Prevention

❌ Treatment

- No specific antiviral therapy available
- Supportive care only:
  - IV fluids for shock
  - Blood/platelet transfusion if severe thrombocytopenia

- Monitoring for signs of bleeding or hypovolemia

🦟 Prevention & Control

- Vector control is key 🔑
  - Use insecticides to kill mosquitoes
  - Drain stagnant water (eliminate breeding sites)
  - Use mosquito nets, repellents, and full-coverage clothing

💉 Vaccine

- No widely available vaccine in the U.S.
- Dengvaxia (CYD-TDV) — a recombinant live-attenuated vaccine (yellow fever virus genetically engineered to express dengue antigens)
  - Approved in Mexico (2015) and several other countries
  - Not approved in the United States

🧠 Exam Pearl 💡

Severe dengue (hemorrhagic shock) = secondary infection + antibody cross-reaction → complement

activation or ADE → vascular leakage, shock, and hemorrhage