Dengue Virus: A Diagnostic Testing Update

Presenter:
Elitza S. Theel, Ph.D., D(ABMM)
Director, Infectious Diseases Serology Laboratory
Co-Director, Vector-Borne Diseases Service Line

Department of Laboratory Medicine and Pathology
at Mayo Clinic, Rochester, Minnesota
Disclosures

• None

Presentation Outline

• Overview of dengue virus
• Clinical Presentation
• Diagnosis
  • Nucleic Acid Amplification Tests (NAATs)
  • Dengue Virus NS1 Antigen
  • IgM and IgG Antibodies to Dengue Virus
• Treatment and Prevention
Dengue Virus – An Overview

• Member of the Flaviviridae family
  • Enveloped, +ssRNA viruses
• Four dengue virus serotypes (I-IV)
• Mosquito-borne Transmission:
  • Aedes spp
    • A aegypti and A albopictus
• Reservoir: Humans
• Transmission cycle:
  • Mosquito-human-mosquito

Dengue Virus: Epidemiology

Dengue Virus – Clinical Presentation

- Dengue Virus Infection
  - Asymptomatic (~50%)
  - Symptomatic
    - Undifferentiated Fever
    - Dengue Fever
      - Older children or adults
        - High fever, retro-orbital pain, myalgia, arthralgia, rash
    - Dengue Hemorrhagic Fever
      - Three Phases:
        - Febrile
        - Critical
        - Convalescent

Dengue Virus – Diagnostic Approaches

- Diagnosis is based on exposure history, clinical presentation and laboratory findings
- Available laboratory methodologies:
  - Culture (CDC only)
  - NAATs
  - Serology
    - Antigen
    - Antibody

- Graph showing:
  - Viremia
  - NS1 Ag
  - IgM
  - IgG
  - Days 0 to 50
  - Acute Disease
NAATs for Dengue Virus Detection

- Two PCR Assays:
  - Dengue Virus, Molecular Detection, PCR, Serum (Mayo Test ID: DENGs)
  - Dengue Virus, Molecular Detection, PCR, Spinal Fluid (Mayo Test ID: DENGc)

- Useful for acute disease (≤5 days of symptoms)

- No FDA-cleared assays

- Performance characteristics vary
  - Sensitivity: 80%-90%
  - Specificity: >95%

- Negative results do not rule out infection
  - Follow-up with serology

Dengue Virus NS1 Antigen Detection

- NS1 Antigen (Mayo Test ID: DNSAG)
  - Conserved glycoprotein secreted from infected cells
  - **Acute Infection Marker!**
    - Detectable during viremic period
    - Detectable prior to development of IgM
    - Detectable for 1-9 days following symptom onset
  - Alternative to NAATs for detection of acute disease

- Performance characteristics:
  - Sensitivity: 96%
  - Specificity: 86%

- Also detectable following re-infection
**Antibody Detection to Dengue Virus**

- Dengue Virus Antibody, IgG and IgM, Serum (Mayo Test ID: DENGGM)
- Dengue Virus Antibody/Antigen Panel, Serum (Mayo Test ID: DENVPM)

**IgM Antibodies**
- 3-5 days post illness onset
- Persist for 30-90 days
- FDA-cleared assay available
- Sensitivity: 60%-99%
- Specificity: 80%-98%
- Flavivirus cross-reactivity

**IgG Antibodies**
- >10 days post illness onset
- Persist for years/decades
- Flavivirus cross-reactivity

![Graph showing antibody detection](image)

**Treatment & Prevention of Dengue Virus**

- No targeted antiviral agents
- Supportive care only
  - Proper fluid management associated with decrease in disease mortality
  - Pain/fever management
- Avoid mosquito exposure while viremic
- Personal protective measures are recommended
- Dengvaxia vaccine
  - For people ages 9 through 16
  - Prior laboratory confirmed dengue infection
  - Live in an endemic area
References


3. www.cdc.gov

4. www.who.org