DENGUE Objectives and handout by jonathan Rakofsky, M.D.

Goals and Objectives
• What is Dengue Fever
• What is the pathophysiology of Dengue Fever
• What is Dengue Hemorrhagic Fever
• What is the treatment for DF and DHF

Dengue Fever (DF): what is it?
• A tropical disease caused by the dengue virus, a flavivirus, that is transmitted by multiple species of mosquitoes, principally the Aedes aegypti.
• Most common arthropod-borne viral illness in humans.
• Characterized by fever, headache, severe muscles and joint pains, with a particular rash that is similar to measles.

Dengue Fever: History
• Earliest known documentation
  Chinese Encyclopedia of symptoms during Chin Dynasty 265-420 AD.
  “The water poison”
• first confirmed report
  1779-1780
  outbreak occurred simultaneously in Asia, North America, and Africa.
• 1789 Benjamin Rush,
  “breakbone fever
  “ki denga pepo”
  “Dengue”

Epidemiology of Dengue Fever: Why should you care?
• 3 billion people
  112 countries
  In the U.S.
  endemic areas.
• According to the CDC:
  2006-2008,
  average of 244 confirmed dengue cases reported in the U.S.
• Dengue cases in returning US travelers have increased steadily during the past 20 years,
• leading cause of acute febrile illness in US travelers returning from the Caribbean, South America, and Asia
• Each year
  an estimated 100 million cases of dengue fever
  500,000 cases of dengue hemorrhagic fever occur worldwide
  22,000 deaths which mainly are children.

Clinical Presentation: Dengue
• History of recent travel to endemic region
• Incubation period 3-14 days (avg 4-7)
• Prodrome
  chills, facial flushing (sensitive and specific indicator)
  • Sudden onset of fever
  • Chills and severe (breakbone) aching of head, back, and extremities
  • Rash- maculopapular or macular
  Face, thorax, flexor surfaces, with islands of skin sparing. Spares palms and soles.
Rash begins on day 3 and persists for 2-3 days
• Other symptoms may include
  Retro-orbital pain
  Nausea and vomiting
  Weakness
  Altered taste sensation
  Sore throat
  Anorexia
  Mild hemorrhagic manifestations
  • Petechiae, bleeding gums, epistaxis, hematuria, menorrhagia
  Lymphadenopathy
  • Fever
  Typically abates with cessation of viremia
  • A second rash may occur within 1-2 days of defervescence, lasting 1-5 days.

Dengue Fever: Physical Exam
• Head
  injected conjunctivae
  facial flushing
  Inflamed pharynx
  Lymphadenopathy
  Nausea and vomiting
• Skin: Characteristic Rash
• Tourniquet Test:
  Inflate BP cuff on upper arm to midway between diastolic and systolic blood pressures for 5 min.
  Positive result if more than 20 petechiae per square inch are observed on the skin in the area that was under pressure.

Dengue: workup/diagnosis
• Laboratory criteria for diagnosis:
  Isolation of the dengue virus from serum, plasma, leukocytes, or autopsy
  Demonstration of a fourfold or greater change in reciprocal immunoglobulin G (IgG) or IgM antibody titers to one or more dengue virus antigens in paired serum samples
  Characteristic findings
  Thrombocytopenia, leukopenia, and mild to moderate elevation of aspartate aminotransferase and alanine aminotransferase.

Dengue Hemorrhagic Fever (DHF): what is it?
• a life-threatening manifestation of DF.
  • characterized by
bleeding, plasma leakage, and thrombocytopenia,
• ultimately transitioning to Dengue Shock Syndrome (DSS).
• less frequently but more dramatic presentation
• Primarily disease of children in Asia, 
equal age distribution in Americas
• Typically begins with initial manifestations of dengue fever, however, the 
fever can reappear (saddleback fever).
• Critical feature: plasma leakage d/t capillary permeability and bleeding d/t 
capillary fragility and thrombocytopenia that develops.
• There are 4 cardinal features defined by the WHO
• 1. Increased vascular permeability 
Hemoconcentration > 20% in hematocrit above baseline value
Pleural effusion
Ascites
• 2. marked thrombocytopenia 
100,000 cells/mm or lower
• 3. fever lasting 2-7 days
• 4. a hemorrhagic tendency
Positive tourniquet test
Spontaneous bleeding

**Dengue Hemorrhagic Fever: immunopathology**
• Most patients have had prior infection with one of the 4 serotypes.
• Antibody dependent Enhancement.
Non-neutralizing antibodies enhance second viral serotype entry into host cell 
(macrophages)
Increase replication in the host cell
A Trojan Horse
• The affected macrophages release vasoactive mediators that increase 
vascular permeability, leading to the vascular leakage, hypovolemia, and 
ultimately the shock.

**Dengue Shock Syndrome**
• DHF progression into circulatory failure
Hypotension
Narrow pulse pressure (<20 mmHg)
Death 8-24 hours after onset of signs of circulatory failure
Most common clinical findings in impending shock:
Hypothermia, abdominal pain, vomiting, restlessness

**Treatment for manifestation of fever**
• Usually self-limited
• Acetaminophen for fever, NSAIDS and Corticosteroids not recommended.
Nsaisds and aspirin to avoid Reye’s syndrome
Oral fluid to avoid dehydration

**Treatment for manifestation of significant bleeding and plasma leakage**
  − Can be severe enough to require blood transfusion
  − H2 receptor antagonist or PPI for GI bleed
- Intravascular volume repletion for plasma leakage to prevent hypovolemic shock
- Corticosteroids showed no benefit vs. placebo

Patient with known or suspected dengue fever:
- Platelet count and hematocrit
  - Measured daily from the third day of illness until 2 days after defervescence
  - Patient with rising hematocrit or dropping platelet
    - Intravascular volume replacement