Dengue Update

**Epidemiology:** ([www.cdc.gov/dengue/index.html](http://www.cdc.gov/dengue/index.html))
- 4 viruses (DENV-1, DENV-2, DENV-3, DENV-4)
  - Positive sense, single stranded RNA Flavivirus
- 1/3 of the world’s population is at risk
- ~400 million people infected annually
- 75% of infections are asymptomatic
- Endemic in the tropics (Caribbean, Latin America, Southern Asia, Africa, Pacific Islands)
- Rarely in US, but sporadic outbreaks in Florida, Hawaii (2001), and Texas-Mexico Border (2005)
  - Most cases are imported (tourist/traveler)

**Vector/Transmission:**
- *Aedes aegypti & Aedes albopictus* (Same as Zika)
- Distribution in Southern United States, especially Southeastern, ranging up to Ohio
- Vertical transmission at time of delivery, no congenital transmission, but can be transmitted thru breastmilk, no sexual transmission

**Clinical Presentation:**
- Bite (4-7 days) → High Fever (2-7days) → Headache → Retro-orbital pain → myalgias/arthralgias → flushing of face, anorexia, abdominal pain, rash (3-4 days after fever… trunk, medial aspect of arms/thighs, plantar and palmar surfaces) → hemorrhagic (nose bleeds, bleeding gums, internal bleeding)
- Rash does not itch
- Rash can be petechial or macular/papular/maculopapular or purpura
- WHO Classification
  - Dengue: febrile with travel/living in area of risk AND
    - ≥2: Nausea, vomiting, rash, aches/pains, + tourniquet test, leukopenia
    - Warning signs that this is going to progress to Severe Dengue: abd pain/tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, restlessness, hepatomegaly
  - Severe Dengue: Dengue + Severe plasma leakage leading to shock or fluid overaccumulation with respiratory distress, severe bleeding or organ impairment
    - Ex. Transaminases ≥ 1000, impaired consciousness or heart impairment

**Labs:**
- CBC → leukopenia, thrombocytopenia
- CMP → elevated AST, ALT, hyponatremia
- Sed rate usually normal
- RT-PCR: ≤ 5days from onset of symptoms
• NS1 (Nonstructural Protein 1 antigen immunoassay): ≤ 5 days from onset of fever (however, can be positive up to 9 days)
• IgM ELISA ≥ 4 days after fever onset and can test up to 90 days post symptom onset
  o High cross reactivity with other Flaviviruses (Yellow Fever, West Nile, Japanese Encephalitis, St. Louis Encephalitis virus)

Treatment:
• Early recognition and prompt supportive care can lower rates of medical complications and death
• Supportive Care!!!
• No antiviral
• Avoid ASA and NSAIDs
• Do not transfuse platelets, shown to do more harm than good
• No corticosteroids, no benefit shown, possible harm. Unless Immune Thrombocytopenic purpura (ITP)

Vaccine:
• Dengvaxia by Sanofi Pasteur (France)
  o Live attenuated, recombinant, tetravalent
  o 3 dose (0, 6, 12 months)
  o Registered for use in endemic areas
  o Globally 65% effective, but 81.9% effective on seropositive and 52.5% effective in seronegative at baseline
  o Current use in Mexico, Brazil, Thailand, Phillipines
  o www.who.int/immunization/research/development/dengue_vaccines/en/
• Phase III trials
  o Butantan-DV (Brazil)
    ▪ Tetravalent, live attenuated
    ▪ Ongoing Trial (Brazil)
  o Takeda’s-TDV (Japan)
    ▪ Tetravalent, live attenuated
    ▪ TIDES trial (Latin America & Asia)
• Dengue Vaccine Initiative (www.denguevaccine.org)
• GDAC- Global Dengue & Aedes-transmitted Diseases Consortium (www.preventdengue.org)
• Major roadblock... who gets severe dengue? Not well understood, but thought to be immune modulated.
  o Possible Antibody-dependant enhancement
  o Possible Cytokine storm
  o Possible cross reactive T-cells
• Why is the dengue vaccine not available in the US?
  o Because there is a higher incidence of severe dengue in seronegatives that get the vaccine (most of the US population). You can test IgG antibodies (ELISA), but this gets expensive.