Emerging Infectious Diseases

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Global Warming

Morens and Fauci: Dengue and hemorrhagic fever: a potential threat to public health in the United States
JAMA 299: 214-216; 2008
White Nose Syndrome

- Geomyces destructans
- Millions of bats have died in the northeast USA since 2006
- Bats are the largest consumers of mosquitoes
Emerging Arboviruses in the Western Hemisphere

- West Nile virus: September 27, 1999 (Queens, NY)
- Chikungunya: December 17, 2013 (Saint Martin)
- “Ebola: September 28, 2014 (Dallas, Texas)” (filovirus)
- Zika: May 15, 2015 (Bahia, Brazil)/July 26, 2016 (Miami, FL)/November 29, 2016 (Texas)
- Dengue: expanding range
Ebola Hemorrhagic Fever

- Following incubation period of 2 to 21 days, onset is sudden, marked by high fever, headache, erythematous macules, and myalgia.
- Abdominal pain, arthralgia, and pharyngeal and conjunctival erythema may follow these symptoms.
- Patients may develop a non pruritic, macules and papules, which desquamates by day 5 of the illness.

CDC/Atlanta
Ebola Hemorrhagic Fever

- Bleeding into the gastrointestinal tract is the most prominent, besides petechiae and hemorrhages from puncture wounds and mucous membranes.

- Most of the patients develop severe hemorrhagic symptoms in the next few days, with bleeding from multiple sites such as lungs and gastrointestinal tract.

- The skin and mucous membranes are also affected with echymoses, disseminated nonpalpable petechiae and massive gingival bleeding that usually herald a fatal outcome.

CDC/Atlanta
Filoviruses – Diagnosis and Therapy

- The most commonly used assays to detect antibodies to filoviruses are the ELISA, indirect immunofluorescence assay (IFA), and immunoblot.

- Direct detection of viral particles, viral antigen and genomic RNA can be achieved by electron microscopy, reverse PCR, antigen detection ELISA, immunohistochemistry.

- Treatment: None – only supportive care; Filoviruses are resistant to the antiviral effects of interferon and
Ebola Virus Transmission and Reservoir

- Person-to-person by direct contact with blood, secretions, organs or semen. Virus found in the skin and sweat glands of infected bodies.
- Possible animal reservoirs looked for, e.g. monkeys, bats and blood sucking insects. No evidence.
- However, on the basis of available evidence the reservoir must be zoonotic and normally maintained in an animal host that is native to Africa. The infected monkeys...
Ebola management: 2016

Public health measures:
• Avoid contact with body fluids, e.g. Hazmat suits
• Screening travelers
• Isolating patients
• Dealing with traditional “healers”
• Dealing with traditional burial practices
Ebola Management

- No approved antiviral drugs; supportive care is “standard”, but
- IgG from Ebola survivors appears to help;
- Experimental therapies: brincidofovir; ZMapp (monoclonal antibodies)
- Ebola vaccines are under investigation
About 2.5 billion people, or 40% of the world’s population, live in areas where there is a risk of dengue transmission. Dengue is endemic in at least 100 countries in Asia, the Pacific, the Americas, Africa, and the Caribbean. The World Health Organization (WHO) estimates that 50 to 100 million infections occur yearly, including 500,000 DHF cases and 22,000 deaths, mostly among children.
Dengue: 2016
Dengue

- Four virus types (DENV 1, DENV 2, DENV 3, DENV 4)
- Infection with one serotype does not protect against the others, and sequential infections put people at greater risk for dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).
- Two mosquito vectors: Aedes aegypti and Aedes albopictus
- Incubation Period: 4-7 days
Dengue fever (Flavivirus): "white islands in sea of red" and conjunctival hemorrhages
Dengue: symptoms

- fever
- headache
- pain behind the eyes
- joint and muscle pain
- nausea/vomiting
- mild bleeding, such as nose or gum bleeding or easy bruising
Dengue hemorrhagic fever (DHF): tourniquet test
DHF: Signs and Symptoms

- Severe abdominal pain or persistent vomiting
- Petechiae and ecchymoses
- Bleeding from nose or gums
- Vomiting blood
- Black, tarry stools
- Drowsiness or irritability
- Pale, cold, or clammy skin
- Difficulty breathing
- No antivirals available: treat symptomatically
Dengue Prevention

- Mosquito control
- Quadrivalent vaccine (Sanofi Pasteur): 56% reduction in dengue; approved in Philippines, Mexico and Brazil
Chikungunya

- *Togaviridae*
- *Aedes* Mosquito borne illness.
- Transmission similar to dengue fever.
- Makonde for “that which bends up.”
- Discovered in Africa in 1952 with several outbreaks in Africa, South Asia, and Southeast Asia.
- Emerged in the Caribbean in 2013.
Chikungunya

- Since 2006, over 200 cases have been reported in the United States, but only in people who had traveled to other countries.
- On July 17\textsuperscript{th}, 2014 the first chikungunya case acquired in the United States was reported in Florida by the CDC. A subsequent case in Florida was reported on July 29\textsuperscript{th}, 2014.
- Now: 100,000s of cases
Countries and territories where chikungunya cases have been reported.
Clinical Manifestations

- Fever and malaise
  - Up to 104 F
- Polyarthralgia
  - Usually symmetrical
  - Commonly involves multiple joints
    - Hands, wrists, ankles.
- Skin Manifestations (40 to 75% of patients)
Morbilliform Rash
Morbilliform Rash
Nasal Hyperpigmentation
3) Scrotal erythema with aphthous-like ulcers
Purpuric Macules
Zika Virus

- Single stranded RNA Virus
- Genus *Flavivirus*, Family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
Transmission

- Bite of an infected *Aedes aegyptus* (or *A. albopictus*) mosquito
  - Also spreads dengue, chikungunya and yellow fever viruses

- Rarely, maternal-fetal transmission
  - Intrauterine transmission (congenital infection)
  - Intrapartum transmission

- Through infected blood or sexual contact
  - Only arbovirus documented to be sexually-transmitted
Geographic Distribution

- **1947**: First isolated from a rhesus monkey in Zika forest, Uganda.
Geographic Distribution

- **1951-1981**: Sporadic human infections were found in Africa and Asia.
Geographic Distribution

- **2007**: The first major recognized outbreak occurred in the Yap Island, affecting >70% of the population (5005 cases).
Geographic Distribution

- **2013 to 2014:** Another larger outbreak occurred in French Polynesia, affecting about 28,000 people.
Current Outbreak in the Americas

- **May 2015**: the first locally-acquired cases in the Americas were reported in Brazil

- **Currently**: outbreaks are occurring in many countries in the Americas
Zika in the U.S. (as of November 30, 2016)

**Continental U.S.**
- Travel-associated cases reported: 4310 (1114 pregnant)
- 28 microcephaly & other birth defects/5 neonatal deaths
- Locally acquired through sexual transmission: 36
- Locally acquired vector-borne cases reported: 185 (184 in FL)
- 1 laboratory acquired
- Guillain-Barre syndrome: 13

**U.S. Territories (Caribbean Sea)**
- Travel-associated cases reported: 125
- Locally acquired cases reported: 33,133
- Pregnant: 2561
- Guillain-Barre syndrome: 48
Clinical Manifestations

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>N (n=31)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macular or papular rash</td>
<td>28</td>
<td>90%</td>
</tr>
<tr>
<td>Mild fever</td>
<td>20</td>
<td>65%</td>
</tr>
<tr>
<td>Arthralgia (small joints)</td>
<td>20</td>
<td>65%</td>
</tr>
<tr>
<td>Conjunctivitis (nonpurulent)</td>
<td>17</td>
<td>55%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15</td>
<td>48%</td>
</tr>
<tr>
<td>Headache</td>
<td>14</td>
<td>45%</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>12</td>
<td>39%</td>
</tr>
<tr>
<td>Edema</td>
<td>6</td>
<td>19%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3</td>
<td>10%</td>
</tr>
</tbody>
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Zika Rash

- Blanchable macules and papules
- Start on the face or trunk, 3-5 days after the febrile phase, and become more diffuse
Zika Course and Outcomes

- Symptoms develop in 20% of infected individuals
- Occur 2-12 days after the mosquito bite
- Usually mild
  - Severe disease requiring hospitalization is uncommon
  - Case-fatality rates are low
- Symptoms resolve within 2-7 days
- Guillain-Barré syndrome reported following Zika virus infection
  - Relationship to Zika virus infection is not known
  - Colombia has reported 3 deaths due to GB in Zika patients
## Zika vs Dengue & Chikungunya

- **Diseases have similar clinical features**

<table>
<thead>
<tr>
<th>Features</th>
<th>Zika</th>
<th>Dengue</th>
<th>Chikungunya</th>
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<tbody>
<tr>
<td>Fever</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Myalgia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Pruritus</td>
<td>+++</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>
Diagnosis

- **Clinically**
  - Recent travel history to active transmission area
  - Unprotected sexual contact with a person with recent travel
    - Presence 2 of the 4 major symptoms
      - Rash, fever, arthralgia, conjunctivitis

- **Lab**
  - Viral RNA RT-PCR (≤7 days after illness onset)
  - Antibody testing (≥4 days after illness onset)
    - IgM ELISA
    - Plaque reduction neutralization test (PRNT)
Management

- No specific antiviral therapy

- Treatment is supportive (i.e., rest, fluids, analgesics, antipyretics)

- Suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya

- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage
Zika Virus and Microcephaly

- Reports of a substantial increase in number of babies born with microcephaly in 2015 in Brazil (20-fold increase compared to 2014)
  - Zika virus identified in several infants with microcephaly and in early fetal losses
  - Some infants with microcephaly* have tested negative for Zika virus
  - In February 2016, the WHO declared a “Public Health Emergency of International Concern”

- Studies are underway to characterize the relationship between Zika and congenital microcephaly

- Retrospective investigation in French Polynesia outbreak in 2013-2014

*head circumference <2 SD below mean
Beyond Microcephaly

Other zika-related abnormalities (even with normal head circumference) include:

- Craniofacial disproportion
- Spasticity
- Seizures
- Vision problems including blindness
- Irritability
- Brainstem dysfunction
- Cardiac and GI dysfunction
- Risk greatest if infection during 1st trimester
Reporting Zika Disease Cases

- Zika virus disease is now a nationally notifiable disease
  - Healthcare providers encouraged to report suspected cases to their state health department

- State health departments are requested to report laboratory-confirmed cases to CDC
Prevention

- No vaccine or medication available

- Primary prevention measure is to reduce mosquito exposure

- Pregnant women should consider postponing travel to areas with ongoing Zika virus outbreaks

- Protect infected people from mosquito exposure during first week of illness to prevent further transmission

- Pregnant women should abstain from sex (or use condoms) with male partners who traveled to areas with active Zika transmission (8 weeks if male is asymptomatic/laboratory negative, 6 months after symptoms/laboratory positive)
Prevention: Insect Repellents

- DEET is the topical insect repellent with the best documented effectiveness against mosquitoes; it also repels ticks, chiggers, fleas, gnats and some flies.
- Higher concentrations of DEET provide longer protection, but concentrations >50% have not been shown to improve efficacy.
- Concentrations of DEET from 10% to 30% considered safe in children >2 months old.
- DEET considered safe in pregnancy
- Adverse events: uncommon; severe AEs: rare
Other Insect Repellents

- Picaridin and IR3535: similar efficacy to DEET
- Oil of lemon eucalyptus, citronella and essential oils: less effective than DEET
- Permethrin: used on clothing, mosquito nets, tents, and sleeping bags to repel and kill mosquitoes & ticks
- The repellent should be applied after sunscreen. Applying DEET after sunscreen reduces the SPF of the sunscreen, but applying sunscreen second may increase absorption of DEET.

JAMA 316: 766-767; August 16, 2016
What Comes After Zika?

- Nipah (Malaysia)
- MERS (middle east)
- Hendra (Australia)
- Enteroviruses: e.g. EV71 (southeast Asia)
- Influenza: new human, swine and avian strains
- Hantaviruses: new strains
References

Thank you
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Any questions?