Emerging Infectious Diseases & Ebola

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MEASLES
2015 Measles Cases in the U.S.
January 1 to March 13, 2015

*Provisional data reported to CDC's National Center for Immunization and Respiratory Diseases*
Measles Cases and Outbreaks
January 1 to March 13, 2015*

176 Cases
reported in 17 states and the District of Columbia: Arizona, California, Colorado, Delaware, Georgia, Illinois, Michigan, Minnesota, Nebraska, New Jersey, New York, Nevada, Pennsylvania, South Dakota, Texas, Utah, Washington

4 Outbreaks
representing 90% of reported cases this year
U.S. Measles Cases by Year

* Provisional data reported to CDC’s National Center for Immunization and Respiratory Diseases
Measles

- Initial signs & symptoms
  - High fever,
  - Cough,
  - Runny nose (coryza),
  - Conjunctivitis

- Koplik spots may appear 2-3 days after symptoms begin
Measles

- Rash appears 3-5 days after symptoms begin
  - Initially red macules appear at the hairline and spread downward to the neck, trunk, arms, legs, and feet.
  - The rash may become papular and may coalesce.
- Temperature may increase to > 104°F Fahrenheit.
Measles: Complications

- Complications: more frequent in persons < 5 or > 20
- Common complications:
  - Ear infections: 10%; can lead to hearing loss
  - Diarrhea < 10%
- Severe complications:
  - Pneumonia: 5%; the most common cause of death from measles in young children
  - Encephalitis: 0.1%; can cause convulsions, deafness, mental retardation
  - Death: 0.1%-0.2%
  - Subacute sclerosing panencephalitis (SSPE): 0.004%-0.11%
Measles: Infection Prevention

- Airborne isolation
  - N95 respirators
  - Negative pressure rooms

- If a patient requests an evaluation for fever & rash that could be consistent with measles contact the Iowa Department of Public Health immediately: 1-800-362-2736

- Measles is a public health emergency!
Measles
PERTUSSIS
Reported NNDSS pertussis cases: 1922-2014*

*2014 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Reported pertussis incidence by age group: 1990-2014*

*2014 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System
Clinical Manifestations

- Incubation period 7-10 days (up to 21 days)
- Catarrhal Phase (few days-2 weeks)
  - Rhinorrhea
  - Lacrimation
  - Mild Conjunctivitis
  - Low grade fever
Clinical Manifestations

- Paroxysmal Phase (2-4 weeks)
  - Paroxysmal coughing
  - Inspiratory gasp = whoop
  - Cyanosis
  - Post-tussive vomiting

- Convalescent Phase (weeks-months)
  - Decreasing frequency & intensity of coughing spells
  - 100 day cough
Pertussis: Complications

- Hemorrhagic
  - Epistaxis
  - Subconjunctival hemorrhage
  - Subdural/spinal epidural hematoma

- Pressure effects
  - Hernias
  - Pneumothorax
  - Rectal prolapse
  - Mediastinal/subcutaneous emphysema
Pertussis: Complications

- **Secondary Infections**
  - Otitis media
  - Pneumonia

- **Central Nervous System**
  - Seizures
  - Encephalopathy

- **Other**
  - Lacerated lingual frenulum
  - Nutritional compromise
Treatment

- Needs to be early in the course to be effective
- Antimicrobial agents
  - Erythromycin estolate 500 mg QID x 14 d
  - Azithromycin 500 mg x 1 day; 250 mg x 4 d
  - Clarithromycin 500 mg BID x 7 d
  - TMP-sulfa DS BID x 7 d
  - Ciprofloxacin 250 mg BID x 7-14 d; no published data on efficacy
Pertussis: Infection Prevention

• Droplet precautions:
  – Put the patient in a surgical mask & put the patient in a room immediately
  – Wear a surgical mask when within 3 feet of the patient
  – Add eye protection if doing a cough inducing procedure

• Report confirmed cases of pertussis to the Iowa Department of Public Health within 3 days.
ANTI-VACCINE BODY COUNT

Number of Preventable Illnesses
146623
From June 3, 2007 To February 21, 2015

Number of Preventable Deaths
8973
From June 3, 2007 To February 21, 2015

Number of Autism Diagnoses Scientifically Linked to Vaccinations
0
From June 3, 2007 To February 21, 2015

WELCOME TO THE ANTI-VACCINE BODY COUNT
CHIKUNGUNYA
Chikungunya Virus (CHIKV)

- Family *Togaviridae*; genus *Alphavirus*
- Lipid-enveloped, 11.8 kb positive strand RNA
- Two clades:
  - Semliki Forest clade (CHIKV, O’nyong-nyong, Ross River)
  - Sinbis-equine encephalitis clade (Sinbis, VEE, WEE, EEE)
- Three genotypes: West African, East/Central/South African, & Asian
- Cause either encephalitis or fever/arthritis/rash
- Spread by *Aedes* species mosquito vector
- Reservoir: humans and nonhuman primates
Chikungunya Virus

- 1952-53: Tanzania
- 1958: Bangkok Thailand
- 2005: Comoros Islands (1st time in SW Indian ocean) & subsequently in Mayotte, Mauritius, La Réunion, etc.
- 12/2013: local transmission identified in St. Martin

Subsequently:
- By 7/18/2014, > 440,000 cases occurred in > 20 countries in the Caribbean, Central America, & South America
- Local transmission has been identified in 44 countries or territories in the Americas

- US
  - > 230 imported cases
  - Locally acquired cases in Florida
  - 10/2014: 3 cases identified in Iowa

TE Morrison J Virol 2014;88:11644-11647
LH Chen & ME Wilson 2010;23:438-444
Countries and territories where chikungunya cases have been reported*
(as of March 10, 2015)

*Does not include countries or territories where only imported cases have been documented. This map is updated weekly.
Chikungunya: In the Americas

- Large populations of immunologically naïve individuals.
- Spread of *Aedes* spp. Vector: *Aedes albopictus* in N. & S. America via airplanes & container shipping
- Increasing mobility of persons to & from endemic regions
- CHIKV can be maintained within a human reservoir
Recent Epidemics

- Very large:
  - Kenya: 500,000
  - La Reunion: 265,000/770,000 (34.4%)
  - India: 1,300,000

- Attack rates: 35%-75%

TE Morrison J Virol 2014;88:11644-11647
The Mosquito Vector

- **Aedes aegypti** (yellow fever mosquito) aggressive daytime biter
  - Primary vector of chikungunya virus to humans.
- **Aedes albopictus** (the Asian tiger mosquito)
  - Recent human transmission in Asia, Africa, Europe.
- Other forest-dwelling *Aedes* spp. mosquitoes in Africa

- CHKV introduced into:
  - Comoros & Seychelles by *Ae. aegypti*
  - La Reunion & Mauritius Is. viruses introduced by *Ae. albopictus*
Chikungunya: Transmission

- Person to person via the mosquito vector
- Maternal to child during birth
- During outbreaks in La Reunion & Italy, blood donations were halted & they imported blood products.
Clinical Manifestations

- Incubation period: 3-7 days (range 2-12)
- Asymptomatic infection: 3%-25%
- Symptoms
  - High fever (mean 38.9F; 89%)
  - Symmetrical joint pain, > 1 joint, distal & lower limbs (96%)
  - Myalgia, low back & legs, may have objective changes on biopsy
  - Rash (40%, sometime bullous)
  - Pruritus (50%)
  - Gastrointestinal symptoms (47%)
  - Persistent arthralgia & arthritis (64% at 18 mns)
- Severe disease:
  - Especially newborns & the ≥ 65
  - Occasional rhabdomyolysis with very high CPK
  - Mortality: 1:1000 in La Réunion & India

TE Morrison J Virol 2014;88:11644-11647
LH Chen & ME Wilson 2010;23:438-444
S Ozden et al., Plos One 2007;2:e527
Chronic Joint Involvement

- Risk factors for long-term arthralgia: age > 35 years & arthralgia 4 months after disease onset.
- Patients with long-term arthralgia did not have biological markers typically found in autoimmune or rheumatoid diseases
- High prevalence of mixed cryoglobulinemia: 94%
- Concurrent arthralgias & cryoglobulinemia: > 90%, some persisting for a year.
- The positivity & level of cryoglobulins declined w/ time & as patients recovered; could serve as a prognostic marker

Chikungunya: Unusual Manifestations

- Meningoencephalitis, encephalopathy, encephalitis
- Seizures
- Neuropathy
- Guillain-Barre’
- Optic neuritis, iridocyclitis, episcleritis, retinitis
- Myocarditis, pericarditis
- Heart failure
- Arrhythmias
- Hepatitis, pancreatitis
- Nephritis
- Bullous dermatosis
- DIC
- Fetal death

LH Chen & ME Wilson 2010;23:438-444
Chikungunya: Diagnosis

- Viral culture
- Reverse transcriptase-PCR to detect viral RNA
- Antibody tests: ELISAs, immunofluorescence assays, and plaque reduction neutralization test

LH Chen & ME Wilson 2010;23:438-444
Chikungunya: Treatment & Prevention

● Treatment
  – No specific antiviral therapy
  – Nonsteroidal anti-inflammatory agents
  – Corticosteroids

● Prevention
  – No vaccine
  – Prevention of mosquito bites
  – Eliminating standing water

D Parashar & S Cherian BioMed Research Int 2014; http://dx.doi.org/10.1155/2014/631642
Are you a Mosquito Breeder?

You are if you make needless road ruts where water collects and mosquitoes breed.

You are if you leave holes unfilled.

Fight the peril behind the lines.
DENGUE
Dengue Map

50-100 million cases per year

1022 alerts last 3 mns; blues: absent/unlikely; yellow: unknown; reds: likely/present
Dengue Virus Transmission

- DENV is transmitted between people by the mosquitoes Ae. aegypti & Ae. albopictus:
  - Found throughout the world.
  - Remains infected for life (days - few weeks).
- Mosquitos must feed on a person during the 5- day period of viremia just before symptom onset.
- Virus incubates 8-12 days in the mosquito before it can be transmitted to another person.
Dengue Symptoms by Phase

Symptoms: begin 4 - 7 days after bite & last 3 - 10 days.

Asymptomatic to Symptomatic infection: 2 : 1 to 10 : 1

Symptoms of Dengue fever

- **Febrile phase**: sudden-onset fever
- **Critical phase**: hypotension, pleural effusion, ascites, gastrointestinal bleeding
- **Recovery phase**: altered level of consciousness, seizures, itching, slow heart rate

~48 hrs around defervescence
Assessment of Patients with Dengue: Febrile Phase

- Look for dengue warning signs
- Assess for signs of other infections suggested by the travel history:
  - Eschar in rickettsial infections
  - Prominent arthralgia in chikungunya
  - Koplik spots in measles
- Obtain baseline CBC (early leucopenia or thrombocytopenia support a dx of dengue)
- Liver enzymes may be elevated
- Renal function is usually normal unless the patient has had persistent vomiting or has comorbidities

Fig 1. Spectrum of dengue associated rashes. (a) Macular-papular rash may be seen during the febrile phase; (b) petechial rash may develop during the febrile/critical phase particularly on arms and legs; (c) erythematous rash with ‘islands of white’ can be widespread and develop during the recovery phase.
Dengue: Hemorrhagic Manifestations

CP Simmons, et al. NEJM 2007; 366: 1423-1432
Assessment of Patients with Dengue: Critical Phase

- Assess hemodynamic status: cool clammy peripheries, tachycardia, & pulse pressure narrowing usually precede shock from plasma leakage
- Watch for fluid accumulation: pleural effusions & ascites
- Watch for evidence of mucosal bleeding
- ↑ hematocrit suggests significant plasma leakage
- Coagulopathy: ↑ APTT & ↓ fibrinogen
- LFTs peak during this period
- Renal function usually preserved except in severe shock
- Ultrasound: assess serosal fluid accumulation
- Echocardiography: assess cardiac function

- Continued IV fluids → fluid overload
- Hematologic parameters normalize
- LFTs may lag behind other parameters
- Benign bradyarrhythmias may occur; obtain EKG if the patient has symptoms

WHO Dengue Diagnostic Criteria

Dengue without warning signs:

- Fever & 2 of the following:
  - Nausea, vomiting
  - Rash
  - Aches & pains
  - Leukopenia
  - Positive tourniquet test

http://www.cdc.gov/dengue/clinicalLab/caseDef.html
Dengue Diagnostic Criteria

Dengue with warning signs = dengue plus > 1 of:

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical signs of fluid accumulation
- Mucosal bleeding
- Lethargy or restlessness
- Liver enlarged > 2 cm
- Increased hematocrit concurrent with rapid decrease in platelet count

Dengue Diagnostic Criteria

Severe dengue = dengue plus ≥ 1:

- Severe plasma leakage leading to:
  - Shock
  - Fluid accumulation with respiratory distress

- Severe bleeding

- Severe organ involvement
  - Liver: AST or ALT ≥ 1,000
  - CNS: Impaired consciousness
  - Organ failure: heart & other organs

Severe Disease

- Hemorrhagic fever & shock syndrome: **Increasing**
- Risk factors
  - Age
  - Ethnicity
  - Chronic disease
  - Secondary heterotypic infection
- DENV: 4 serotypes
- Immunity: temporary to all 4, lasting to infecting serotype
- 2 mechanisms of immune evasion induced by DENV complexed with preexisting antibody to a different serotype ➔ higher levels of viremia
## Dengue: Diagnostic Testing

<table>
<thead>
<tr>
<th>Suggestive</th>
<th>Confirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td>One of the following:</td>
<td>One of the following:</td>
</tr>
<tr>
<td>IgM + in one serum sample</td>
<td>PCR +</td>
</tr>
<tr>
<td>IgG + in one serum sample with titer $\geq 1280$</td>
<td>Virus culture +</td>
</tr>
<tr>
<td></td>
<td>IgM seroconversion</td>
</tr>
<tr>
<td></td>
<td>IgG seroconversion or 4-fold increase</td>
</tr>
</tbody>
</table>

Differential Diagnosis

- Depends on the geographical site of the exposure
- **Non-dengue flaviviruses**: Yellow fever, Japanese encephalitis, St Louis encephalitis, Zika, West Nile,
- **Alphaviruses**: Sinbis & Chikungunya
- **Rickettsia**: *Rickettsia prowazeki, R. mooseri, R. conori, R. rickettsi, Orientia tsutsugamushi, Coxiella burnetii*, etc.
- **Hemorrhagic fevers**:  
  - Arenaviridae: Junin, etc.  
  - Filoviridae: Marburg, Ebola  
  - Bunyaviridae: Hantaviruses, Crimean-Congo haemorrhagic fever
- **Other**: Malaria, Leptospirosis, Typhoid, Measles, Enteroviruses, Influenza, & Influenza-like illnesses

Dengue & Chikungunya

- Both transmitted by *Ae. Aegypti* & *Ae. Albopictus*.
- Geographic areas of transmission overlap.
- Have relative short incubation periods → consider diagnosis for febrile travelers whose symptoms begin within 2 weeks of their last exposures.
## Dengue vs. Chikungunya

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dengue</th>
<th>Chikungunya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Rash</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Arthralgia/arthritis</td>
<td>−</td>
<td>+++</td>
</tr>
<tr>
<td>Myalgia</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>++</td>
<td>+/−</td>
</tr>
<tr>
<td>Hypotension</td>
<td>++</td>
<td>+/−</td>
</tr>
<tr>
<td>Bleeding</td>
<td>++</td>
<td>+/−</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>++++</td>
<td>+</td>
</tr>
</tbody>
</table>

COID Dengue Chik Table 2010.

LH Chen & ME Wilson Curr Opin Infect Dis 2010;23:438-444
Dengue Treatment & Prevention

• **Treatment**
  – No specific treatment
  – Treatment is supportive

• **Prevention**
  – No vaccine
  – Prevention of mosquito bites
  – Eliminating standing water
EBOLA
Ebola in West Africa: Timeline

- 12/2013: first cases
- 3/23/14: Guinea Ministry of Health announces hemorrhagic fever outbreak, suspect Ebola
- 3/26/14: Confirmed to be Zaire Ebolavirus
- Subsequent recognition in Liberia and Sierra Leone
- July 27, case reported in Lagos, Nigeria
Cases in the most affected countries

Guinea

Cases: 3,285
Deaths: 2,170

Liberia

Cases: 9,343
Deaths: 4,162

Sierra Leone

Cases: 11,619
Deaths: 3,629
• 116 new confirmed cases vs 132 the previous week.
• **Liberia**: 0 new confirmed cases x 2 weeks, but 1 case reported 3/20/2015.
• **Guinea**: 58 new confirmed cases vs. 51 cases the previous week.
• **Sierra Leone**: new confirmed cases 58
Ebolavirus

- Ebolavirus is a filovirus
- African Bats may be the primary reservoir
- 29 outbreaks from 1976-2013
  - 1-425 people affected
  - 50-100% of patients died
- The primary transmission event from animals to the 1st human case has been difficult to identify.
Ebolavirus

**Good News**
- Not transmissible until symptoms are present
- Average number of people 1 sick person will infect = 2 vs. 18 for measles & 4 for HIV & SARS
- Enveloped virus: easier to kill with disinfectants

**Bad News**
- High mortality rate
- No vaccine
- No approved treatments
Clinical Findings

- Early signs of infection:
  - Non-specific and flu-like
  - Sudden onset of fever, diarrhea, headache, myalgia, arthralgia, vomiting, and abdominal pains
  - Less common: conjunctival injection, sore throat, rashes, bleeding.

- Later:
  - Shock, cerebral edema, coagulation disorders, secondary bacterial infection.
  - Hemorrhagic sx (4 - 5 days after onset): hemorrhagic conjunctivitis, pharyngitis, bleeding gums, oral/lip ulceration, hematemesis, melena, hematuria, epistaxis, and vaginal bleeding

- Terminal:
  - Obtundation, anuria, shock, tachypnea, normo- to hypothermia
Treatment

• Supportive care
  – Fluid and electrolytes
  – Antiemetics

• Ebola-specific therapy
  – Nucleoside Analogs: Brincidofovir
  – Monoclonal antibodies: ZMapp
  – Antibody from persons who have recovered
Ebola: Principles of Care

- Provide care that maximizes the patient’s benefit and minimizes the likelihood of harm to the staff members
- Minimize the number of healthcare workers and the number of invasive procedures and tests
- Do necessary invasive procedures early and preemptively
- Do not move the patient out of the unit for any tests or treatments
### Table: Hospital costs to treat one patient with Ebola

<table>
<thead>
<tr>
<th>Cost component</th>
<th>Cost (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel costs</td>
<td></td>
</tr>
<tr>
<td>Medical doctors</td>
<td>116511.23</td>
</tr>
<tr>
<td>Nursing</td>
<td>141135.12</td>
</tr>
<tr>
<td>Other</td>
<td>46352.54</td>
</tr>
<tr>
<td>Total</td>
<td>303998.89</td>
</tr>
<tr>
<td>Medical treatment costs</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>25248.29</td>
</tr>
<tr>
<td>Other treatment costs</td>
<td>7844.64</td>
</tr>
<tr>
<td>Decontamination</td>
<td>110805.84</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>9410.91</td>
</tr>
<tr>
<td>Clothing/waste</td>
<td>6882.00</td>
</tr>
<tr>
<td>Cardiology/angiology</td>
<td>257.64</td>
</tr>
<tr>
<td>Endoscopy</td>
<td>424.57</td>
</tr>
<tr>
<td>Radiology</td>
<td>2272.98</td>
</tr>
<tr>
<td>Clinical chemistry</td>
<td>50572.84</td>
</tr>
<tr>
<td>Technical support intern/ extern</td>
<td>33218.94</td>
</tr>
<tr>
<td>Infrastructure</td>
<td>97385.07</td>
</tr>
<tr>
<td>Total</td>
<td>344323.73</td>
</tr>
<tr>
<td>Cost of closed ICU and infectious disease beds</td>
<td>395991.68</td>
</tr>
<tr>
<td>Other costs (not classified)</td>
<td>18475.00</td>
</tr>
<tr>
<td><strong>Overall total</strong></td>
<td><strong>1062789.30</strong></td>
</tr>
</tbody>
</table>

ICU-intensive care unit.
Ebolavirus Transmission

- Person-to-person transmission requires close personal contact between an infected person or their body fluids and another person.
- Persons who:
  - Cared for (fed, washed, medicated) or
  - Worked very closely with infected persons
- Nosocomial (hospital) transmission through contact with infected body fluids:
  - Reuse of unsterilized syringes, needles, or other medical equipment contaminated with these fluids
  - Improper use of personal protective equipment (PPE)
- Can be prevented with correct use of PPE
MONROVIA, Liberia — Liberian officials fear Ebola could soon spread through the capital’s largest slum after residents raided a quarantine center for suspected patients and took items including bloody sheets and mattresses.
“West Point is the worst slum in Liberia, which makes it one of the worst slums in Africa, which makes it one of the worst slums in the world.”
Patient Transportation Route

UIHC Special Isolation Unit

Note: If Secondary Inpatient Room is active, doffing zone setup is mirror of Primary Inpatient Room.
SNICU Bay 4 – Special Isolation Unit
Anteroom & Doffing Area
PPE: Inpatient Setting

The “Iowa Hood”
Iowa Waders

![Iowa Waders](image1.png)

![Iowa Waders](image2.png)

![Iowa Waders](image3.png)
Do you notice any similarities?
Take Home Messages

• Think about **measles & pertussis** in patients with febrile exanthems & cough illnesses, respectively!

• Think about **dengue & chikungunya** in febrile travelers whose last exposure to endemic/epidemic areas was < 2 weeks before the onset of symptoms!

• Ensure that your patients are vaccinated against vaccine preventable infections & that they understand the importance of vaccinating children.
Resources

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- Dr. Michael Ohl
- Dr. Kunatum (Jin) Prasidhrathsint
- Dr. Judy Streit

BEWARE
OF UNVACCINATED CHILDREN