Viruses – Something Old & Something New

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Disclosure

• None
Viruses – Something Old & Something New

Measles

One of the most contagious pathogens – 90% attack rate

Pre vaccine era

90% of Children contracted it before age 15
Over 2 million deaths …. Majority in children < 5 years

Post Vaccine era - 1963; schedule 1st dose 12-15 months

Deaths (2013) – 146,000
Children < 5 years old, 5th leading cause of mortality in children
Majority of measles in US – children less than 12 months
**Viruses – Something Old & Something New**

**Measles**

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
</tr>
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<tbody>
<tr>
<td>2010</td>
<td>63</td>
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<tr>
<td>2011</td>
<td>220</td>
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<tr>
<td>2012</td>
<td>55</td>
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<tr>
<td>2013</td>
<td>187</td>
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<tr>
<td>2014</td>
<td>667 (Ohio)</td>
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<tr>
<td>2015</td>
<td>189 (Disney)</td>
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<tr>
<td>2016</td>
<td>54 (Eloy)</td>
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**Arizona – Eloy**

- Eloy Detention Center: Corrections Corporation of America & ICE
- Inmates - 1500
- Contracted Employees - 1100
- ICE Employees - 100

**Illness**

- May 18 – July 2, 2016
- N = 22, 13 inmates & 9 Employees .... 1 hospitalized
- Initial Cases: 1 inmate & 1 Employee
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Measles

Public Exposure

AK Chin Casino, ARCO, Golden Corral, Apostolic Assembly
Villa Oasis High School, Denny’s, Walmart, Dollar Tree, Circle K
Safeway, Walgreen’s

Factors that Frustrated Public Health Response

Refusal to get vaccinated or provide proof of vaccination – Employees

Factors that Improved Employee Compliance with Vaccination

Wear Mask at work
Stay at home

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Measles

DisneyLand Park - California 2015

N = 125 (110 in California)
39 visited 1 or both Disney Parks
34 household contacts
37 unknown exposure

Vaccination Status

49 Unvaccinated
47 Unknown or Undocumented vaccination status
5 1 dose of vaccine
7 2 doses of vaccine
1 3 doses of vaccine

Reason For Not being Vaccinated

28/37 (67%) 18 children & 10 adults - Personal Belief
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Measles

Transmission

- Respiratory Droplets – 6 feet
- Small Particle Aerosols – Remain in air for 2-4 hours
- Contact with Secretions
- Contact with Contaminated surfaces

Incubation

- Typical – 10 days to fever, 14 days to rash
- Range – 6 to 21 days

Signs & Symptoms

- Fever - Malaise - Anorexia
- Cough - Coryza - Conjunctivitis
- Koplik Spots
- Rash – Face > Trunk > U & L extremities (6-7 days)
- Headache - Abdominal Pain - Vomiting - Diarrhea - Myalgia

Symptoms start to improve 2-3 days after rash began

Fever that persists more than 4 days after rash began….. Complications?
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Measles

Severity of clinical symptoms

Days after infection

Conjunctivitis
Cough
Fever
Koplik’s spots
Rash

A
B
C
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Measles

Transmission – Efficiency

Flight on January 17: Gate X - 4 hour period - All are unvaccinated

- Patient 1 - Rash on Feb 1
- Patient 2 - Rash on Feb 1
- Patient 3 - Rash on Jan 30
- Patient 4 - Rash on Feb 5

Flight on April 17 - Chicago

19 month old with fever & rash ... Waiting for connecting flight at front of gate
Exposed Individual was on incoming flight and passed by child - ?? Vaccination

Identical D8 genotype – Endemic in country of origin of child

mmwr- Dec 19, 2014; 63/1211
mmwr- June 26, 2015; 64/679

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Measles

Vaccination

Children: MMR - 1st dose at 12-15 months, 2nd at 4-6 years

Adults:
- Born Before 1957 - Considered Immune
- Born After 1957 - Suggest 2 doses spaced apart by 28 days

* 1963-1967 - Inactivated vaccine; give these individuals 2 doses

Immunity is 99% after 2 doses and is lifelong
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Measles

Vaccine – Contraindications (Live virus vaccine)

- Pregnant or planning pregnancy in next 28 days
- Anaphylaxis to Eggs – Neomycin – Gelatin
- HIV with CD4 < 200 or 15%
- Solid Organ Transplant
- BMT - Within first 2 years or if with GVHD
- Acute Lymphoblastic Leukemia

Postpone

- Immune globulin therapy: 6 months IM, 8 months IV
- Steroids: Prednisone > 20 mg/day for more than 2 weeks

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Dengue

Most Prevalent Mosquito Borne Viral Illness in the World
390 million infections / 96 million illnesses
Mexico - 78,000 cases
Caribbean - 2 million cases
Brazil - 1.4 million cases
Puerto Rico - 41,000 cases
USA - 341 cases

Arizona - 2014: 93 cases, 2015: 24 cases, 2016 - 14 cases
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Dengue

US Outbreaks … Local Transmission

2005 – Brownsville, TX : N=25

2010 – Key West, FL : N = 28

2013 – Cameron, Hidalgo, Willacy TX : N=58 (26 local)

2015 – Hawaii : N= 261
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Dengue

Arizona Experience – 2014

Outbreak in Sonora Mexico – 6000 cases

AZ – 93 cases, Yuma 70 cases

86% traveled to Mexico in prior 2 weeks
53% hospitalized

Household Cluster investigation

44% Lacked screens on windows & doors
35% left windows open
24 container/100 homes are aedes aegypti mosquitoes

mmwr-may 20, 2016, 60(19) 495-499

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Dengue

Transmission

Bite of Mosquito – Aedes aegypti

Incubation Period

Median: 4-7 days after bite
Range: 3-14 days

Asymptomatic

Less than age 15: 53%
Older than age 15: 14%
Dengue

Signs & Symptoms - Dengue Fever

- Fever (90%) lasts for 2-4 days, 5% biphasic phase of relapse
- Muscle & Joint Pain (80%) "Break bone Fever" (70%)
- Retrorkibital Pain (50%)
- Rash (50%) 2-5 days after fever starts
- Fatigue
- Bleeding
- Conjunctival injection
- Lymphadenopathy
- Hepatomegaly

Ecchymosis of skin, epistaxis, melena, hematochezia

Am J Epid 1995;142: 1204
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Dengue

Signs & Symptoms - Dengue Hemorrhagic Fever: Dengue Shock Syndrome: Severe Dengue

Heralded by abdominal pain, vomiting, restlessness, dyspnea, bleeding that commences with defervescence

A) Vascular Permeability: Pleural effusion - Acute Lung Injury - Ascites - Hemoconcentration
B) Thrombocytopenia - < 100 k
C) Persistent Fever - > 7 days
D) Hemorrhagic Tendency - Tourniquet test or spontaneous bleeding

Laboratory Values

Leucopenia
Thrombocytopenia
Elevated Transaminases - 2 to 5 times normal
Hemoconcentration - Hct > 20% from baseline
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Dengue

Treatment

Tylenol – Avoid NSAIDS and Aspirin
IV fluids
Transfusions as needed

Preventions

Vaccine

Dengavac 
Recombinant live virus vaccine
attenuated yellow fever virus with 4 dengue virus proteins
3 doses at 0,6,12 months
75% effective for severe dengue
Only recommended for countries with > 70% Endemic rate

Mosquito & Stagnant water Precautions

Chikungunya

Origins

July 1952 – Epidemic of Fever with intense arthritis
Near lake Tanganyki in Tanzania
Local Dialect – Kimakonde
Kungunyala – ‘One who slouches’

It spread to Central, Southern and Western Africa – 30 to 50% have Antibodies

In Late 1950-60 small Outbreaks in Southern and South East Asia
Chikungunya

Resurgance

1999 – Democratic Republic of Congo
2004 – Kenya
2005 – Reunion island, Comoros, Madagascar, Seychelles, Maldives
2006 – India, Malaysia
2008 – Thailand
2010 – China
2007 – Sporadic Cases in Europe from Travelers
2013 – Caribbean Islands
2014 – Americas ... Florida with some local transmission
2016 – Nearly 2 million cases in Central and South America

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Chikungunya

Areas infected with A. aegypti
Areas infected with A. albopictus
Areas infected with A. aegypti and A. albopictus
West African enzootic
ECHI enzootic
Asian urban
IOI urban
Chikungunya Incidence 2014 2015 2016

<table>
<thead>
<tr>
<th></th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
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<tbody>
<tr>
<td>USA</td>
<td>2799(12)</td>
<td>885(1)</td>
<td>93</td>
</tr>
<tr>
<td>AZ</td>
<td>19</td>
<td>24</td>
<td>2</td>
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</tbody>
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Chikungunya Reservoir
- Primates
- Rodents
- Birds
- Small mammals
- Humans

Transmission
- Mosquitoes – Aedes aegypti & Aedes albopictus
- Exposure to blood products from infected patients
- Blood transfusion
- Corneal grafts
- Perinatal transmission at delivery
**Chikungunya**

**Incubation Period**
- Median: 2 to 4 days
- Range: 1 to 14 days

**Attack Rate**
- 70-97% of infected people will get illness

**Signs & Symptoms**
- Sudden onset of fever
- Polyarthralgia / arthritis
- Rash - maculopapular or macular, sometimes bullous
- Lymphadenopathy
- Hyperemia of outer ear

- Up to 40°C, lasts 3-5 days
- Symmetric: Hands - wrists - ankles - knees
- 10 or more joints, 2 to 4 days after fever
- 2-4 days after fever, lasts 3-7 days, pruritic
- chondral cartilage
Chikungunya

Complications

- Seen in Age > 65, underlying chronic medical issues
  - ARDS
  - Myocaditis
  - Acute Hepatitis
  - Renal Failure
  - Meningoencephalitis / Flaccid Paralysis / GBS
  - Retinitis / Sensory neural hearing loss

Persistent Symptoms

- From 3 to 18 months out:
  - Poly arthritis - Poly arthralgia
  - Severe Tenosynovitis
  - Raynaud’s Phenomenon
  - Cryoglobulinemia
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Chikungunya

Lab Findings
Leucopenia
Thrombocytopenia
Elevated AST / ALT –
Joint Xray - > 1 year: Erosive changes, articular space narrowing

Diagnosis
First week - RT - PCR in blood
IgM Ab - > 7 days
IgG Ab - > 14 days

Treatment
Supportive with fluids, Tylenol, nsaid

Prevention
Mosquito bite prevention
Stagnant water management
Zika

Yap Island, Micronesia

6 km wide by 15 km long
Northeast of Papua New Guinea
Population 7391

April & May of 2007

Outbreak of illness: fever, macular or popular rash
arthritis or arthralgia and nonpurulent conjunctivitis
3/200 people tested (+) for Dengue IgM

Serum Sample sent to CDC Arbo virus Lab in Fort Collins Colorado
10/71 samples contained Zika virus RNA by RT-PCR

NEJM 2009; 360:2536-43

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The Origins

Entebbe, Uganda
Uganda Virus Research Institute
Field Study of Yellow Fever
Rhesus Monkey’s Placed as Sentinels in nearby forest - Zika Forest

New Virus isolated from monkeys and mosquitoes
Seroprevalence in neighboring province: 6.1%

Zika

The spread

1953 Nigeria First recognized cases

1953 to 2007 13 isolated cases
Seroprevalence - Egypt/India/Thailand/Vietnam/Phillipines/Malaysia

2007 Yap Island - 5000/6700 people

2013 French Polynesia - 32,000 cases

2014 New Caledonia
Cook Island
American Samoa
Samoa
Easter Island
Zika

The Americas

August 2014 Natal Province, Brazil
Illness of fever, maculopapular rash, myalgia, arthritis, conjunctivitis
Dengue tests were negative

March 2015 Bahia Province, Brazil
May 2015 - 7/24 samples had Zika by RT-PCR

How did it get here?
Confederation Cup - June 2013; Tahiti soccer team and fans
Molecular clock - based on mutations in identical strains
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Zika

The spread - Oct 2016

**Americas** - 56 countries, islands and territories
- Brazil - 300,000
- Columbia - 100,000
- Venezuela - 60,000
- Honduras - 30,000
- El Salvador - 11,000
- Mexico - 4000

**United States**
- 3000 cases
- Florida - 708 / 128 local acquisition

**Arizona**
- 36 - All travel related


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Zika

*Something New.....*

Recife, Brazil: Pop 3.7 million
Dr Vanessa & Ana Van der Linder
Neuropediatricians

- Newborns with small heads
- Heads were draped with excess skin
- Limbs were crumbles at odd angles
- Calcifications on cranial xray
- Instead of 1 every 2 months, 12/month

70% of mothers mentioned an itchy rash with fever while pregnant
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Zika

Transmission

Mosquito Born

Africa: Mosquito – Non human primates – Mosquito
Asia: Mosquito – Human – Mosquito

Aedes Aegypti – More tropical & warmer climates, urban

Feeds primarily on humans
Bites Multiple Humans in a single feeding spree
Impercitible Bite
Lives indoors .... Bottle caps – tires – trash
Bites during day light hours: dawn & dusk

Aedes Albopictus – More temperate Climate, suburban, forests

NEJM 2016; 374:16,1552-63

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Aedes Mosquitoes

Key to Aedes

Scutum with lyre-shaped white markings-------------- Aedes aegypti
Scutum with a long median longitudinal white stripe extending from anterior margin to about level of wing root----------- Aedes albopictus
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Zika

Zika Virus RNA in body fluids after onset of symptoms

- **Blood**
  - Serum: 1 week
  - Whole blood: 58 days
  - Pregnancy: 10 weeks

- **Urine**: Up to 91 days

- **Semen**: Up to 188 days; viral load can be 100,000 x higher

- **Saliva**: Up to 91 days

- **Female Genital Secretions**: Up to 11 days

- **Sweat**: Up to 7 days

- **Breast Milk**: ?

UpToDate 10/19/2016
Zika

Transmission

- Bite of an infected Mosquito
- Maternal Fetal Transmission: In utero & perinatal
- Sex: Vaginal, Anal & Oral... Even asymptomatic from endemic area
- Blood Product Transfusion
- Organ transplantation
- Laboratory Exposure
- Breast Feeding??

Zika

Incubation Period

- Mean of 5 days
- Range of 2-14 days
- 80% of individuals do not develop symptoms

NEJM 2016; 374: 1552 - 1563
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Zika

Signs & Symptoms

- Maculopapular Rash (pruritic) - 90%
- Fever (low grade) - 65%
- Arthritis / arthralgia - 65%
- Conjunctivitis (non purulent) - 55%
- Myalgia - 48%
- Headache - 45%
- Retro-Orbital Pain - 39%
- Edema (hands/ankles) - 19%
- Vomiting - 10%

NEJM 2009:360-25536-43
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Zika

Laboratory Findings

- Mild Leucopenia – lymphopenia
- Mild Thrombocytopenia
- Elevation of Transaminases

Diagnosis

- RT - PCR for Zika virus ... 1st Week or < (Low level Viremia)
- IgM Ab -> 1 week - months
  - Cross reacts with dengue, west nile virus,
  - Recent immunization with yellow fever or japanese encephalitis virus vaccine
  - follow up positive results with neutralization antibody via APRT (>10)
- IgG Ab -> 2 weeks – persists for years

Zika

Pregnancy

- Pregnant Women Who Got Rash in previous 5 days
- N=88
- 72 / 88 (82%) zika RT – PCR (+) in blood / urine or both
  - Rash – Conjunctivitis – lymphadenopathy
- Fetal US : 28/42

Abnormalities – 12 /42 (29%) vs 0/16 Controls
- Fetal Death in 2, In utero growth retardation, ventricular calcifications
- abnormal amniotic fluid volume, impaired cerebral or placental blood flow

NEJM 2016 March 4, 2016 / NEJMoa1602412
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Zika

[Images of a child and a medical professional with a child, possibly related to Zika virus case]
Viruses – Something Old & Something New

Zika
Zika

Microcephaly

Occipital to Frontal Circumference - < 3% for Age and Sex

Average Incidence in USA  6/10,000 births (2-12)
French Polynesia … 95/10,000 births

Indicative of problem with Brain Growth

Highest Risk – First Trimester

Ocular abnormalities in 35% of cases with microcephaly

Viruses – Something Old & Something New

Zika

Advise on Plans for Pregnancy

Inside areas of Ongoing Zika Infection

a) Use Barrier Protection for duration of epidemic
b) If pregnant; partner should use barrier protection

Outside of Areas of Zika Infection

a) Men with symptomatic infection should wait 6 months before unprotected sex
b) Women with symptomatic infection should wait 2 months before unprotected sex
c) Asymptomatic men & women with zika exposure should wait 6 months before unprotected sex
Viruses – Something Old & Something New

Zika

Neurologic Complications

- Guillain Barre Syndrome – OR 34 in French Polynesia
- Meningoencephalitis
- Myelitis

Viruses – Something Old & Something New

Zika
**Viruses – Something Old & Something New**

**Zika**

**Treatment**

**Supportive**

- IV fluids
- Tylenol
- Rest
- Avoid aspirin and nsaids

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**Viruses – Something Old & Something New**

**Zika**

**Compare & Contrast**

<table>
<thead>
<tr>
<th></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>
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<tr>
<td>Rash</td>
<td>+++</td>
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