Infectious Diseases
2017

Michael F. Parry, M.D., FACP, FIDSA, FSHEA
Professor of Clinical Medicine, Columbia University
Thomas J. Bradsell Chair of Infectious Diseases
The Stamford Hospital
October 2017
Disclosure

Research support from

• Cidara Pharmaceuticals
• Glaxo/Smith-Kline
<table>
<thead>
<tr>
<th>Year</th>
<th>Disease/Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>Candida auris</td>
</tr>
<tr>
<td>2016</td>
<td>Colistin resistance (mcr-1 gene)</td>
</tr>
<tr>
<td>2015</td>
<td>Zika virus</td>
</tr>
<tr>
<td>2014</td>
<td>Powassan, Heartland, Bourbon virus, etc</td>
</tr>
<tr>
<td>2014</td>
<td>Enterovirus D68</td>
</tr>
<tr>
<td>2013</td>
<td>Chikungunya</td>
</tr>
<tr>
<td>2012</td>
<td>MERS</td>
</tr>
<tr>
<td>2009</td>
<td>H1N1pdm influenza</td>
</tr>
<tr>
<td>2008</td>
<td>CRE (KPC, NDM-1, etc) infections</td>
</tr>
<tr>
<td>2007</td>
<td>Parechovirus</td>
</tr>
<tr>
<td>2005</td>
<td>H7N9 and H9N2 influenza</td>
</tr>
<tr>
<td>2004</td>
<td>ESBL infections</td>
</tr>
<tr>
<td>2003</td>
<td>SARS</td>
</tr>
<tr>
<td>2002</td>
<td>VRSA</td>
</tr>
<tr>
<td>1999</td>
<td>Nipah virus</td>
</tr>
<tr>
<td>1999</td>
<td>West Nile Virus (new world)</td>
</tr>
<tr>
<td>1997</td>
<td>H5N1 influenza</td>
</tr>
<tr>
<td>1996</td>
<td>nCJD (mad cow disease)</td>
</tr>
<tr>
<td>1995</td>
<td>HHV-8 (Kaposi sarcoma virus)</td>
</tr>
<tr>
<td>1994</td>
<td>Hantavirus</td>
</tr>
<tr>
<td>1992</td>
<td>MDR-Tuberculosis</td>
</tr>
<tr>
<td>1989</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>1988</td>
<td>Hepatitis E, HHV-6</td>
</tr>
<tr>
<td>1983</td>
<td>HIV/AIDS, Helicobacter</td>
</tr>
<tr>
<td>1983</td>
<td>E. coli O157:H7, Lyme disease</td>
</tr>
<tr>
<td>1980</td>
<td>HTLV I, II</td>
</tr>
<tr>
<td>1978</td>
<td>Clostridium difficile colitis</td>
</tr>
<tr>
<td>1976</td>
<td>Ebola, Legionnaires disease</td>
</tr>
</tbody>
</table>
Outline

• Antibiotic resistance
• Zika
• Candida auris
• Influenza
Dramatic decline in infectious disease mortality preceded the antibiotic era

FIGURE 1. Crude death rate* for infectious diseases — United States, 1900–1996†

*Per 100,000 population per year.
The crisis in antibiotic resistance 1992

The synthesis of large numbers of antibiotics over the past three decades has caused complacency about the threat of bacterial resistance. Bacteria have become resistant to antimicrobial agents as a result of chromosomal changes or the exchange of genetic material via plasmids and transposons.

*Streptococcus pneumoniae*, *Staphylococcus aureus*, organisms that cause respiratory and cutaneous infections; and members of the *Enterobacteriaceae* and *Pseudomonas* families, organisms that cause diarrhea, urinary infection, and sepsis, are now resistant to virtually all of the older antibiotics.

The extensive use of antibiotics in the community and hospitals has fueled this crisis. Mechanisms such as antibiotic control programs....and better hygiene....need to be adopted in order to limit bacterial resistance.

BAD BUGS, NO DRUGS

As Antibiotic Discovery Stagnates ...
A Public Health Crisis Brews

ID Physicians Warn of Brewing “Superbug” Crisis

Infectious Diseases Society of America Proposes Federal Measures to Spur Antibiotic Development

http://www.idsociety.org
A 'slow catastrophe' unfolds as the golden age of antibiotics comes to an end

Research scientist Rosslyn Mayback was part of the team that identified a strain of E. coli bacteria with a gene that could spread antibiotic resistance. (Walter Reed Army Institute of Research)

By Melissa Healy

JULY 11, 2016, 10:05 AM | REPORTING FROM BETHESDA, MD.

In early April, experts at a military lab outside Washington intensified their search for evidence that a dangerous new biological threat had penetrated the nation’s borders.
Proposed CMS rule on infection control and inappropriate antibiotic use

Today, the Centers for Medicare and Medicaid Services (CMS) proposed new standards to advance healthcare quality and equity in our nation’s hospitals. In a proposed rule open for public comment, CMS recommends strengthening Conditions of Participation (CoPs) related to infection prevention and antibiotic prescribing in U.S. hospitals and critical-access hospitals (CAHs).

The rule includes provisions for preventing healthcare-associated infections, stopping spread of antibiotic-resistant germs and reducing inappropriate antibiotic prescribing. Hospitals and CAHs would be required to have and demonstrate adherence to facility-wide infection prevention and control programs, as well as antibiotic stewardship programs.

The proposed rule builds on the Department of Health and Human Services (HHS) quality initiatives, including the National Quality Strategy, the Centers for Disease Control’s Antibiotic Resistance Solutions Initiative and the Partnership for Patients.
Trends in Antimicrobial Resistance 2017:  
**ESCAPE pathogens**

- *Enterococcus* (VRE)
- *Staphylococcus aureus* (MRSA and VISA)
- *Carbapenem resistant Enterobacteriaceae (CRE)*  
  *E. coli, Klebsiella, Enterobacter* (and others: NDM-1, etc)
- *Acinetobacter* (multi-drug resistant)
- *Pseudomonas* (FQ resistant)
- *Extended spectrum beta-lactamase producing GNR* (ESBL positive  
  *E. coli, Klebsiella, Enterobacter*)
  plus
- *Clostridium difficile* (NAP-1 strains, and others)
Multi-drug resistant organisms
MDRO Infections
Fluoroquinolone resistance Stamford

Pseudomonas -- Percent resistant to Cipro
Are our work-horse agents in the hospital eroding in value due to emerging resistance?
Growing Resistance in *Enterobacteriaceae*

**Extended Spectrum Beta-lactamases (ESBL)**

- Enzymes confer resistance to cephalosporins and penicillins, including third generations
  - Gram negative bacilli (E coli, Klebsiella, etc)
  - Varying phenotypes
  - 700 different profiles
- Prevalence of ESBLs is unappreciated
  - Laboratories fail to detect ESBL in 25% of instances depending on the type of enzyme present (Tenover, CDC, 2009)
- Chronic intestinal carriage for months / years
- High rate of treatment failure
- Inpatient and community prevalence
  - 80% outpatient
  - 80% UTIs
ESBL-positive isolates at Stamford
ESBL Treatment Options

- **Oral**
  - Nitrofurantoin
  - Fosfomycin
- **Parenteral**
  - Carbapenems
    - Ertapenem, imipenem, meropenem, doripenem
  - Tigecycline
  - Avycaz and Zerbaxa (new ceph+BLI)
  - Gentamicin (some)
  - Ciprofloxacin (some)
  - Cefamycins: cefoxitin and cefotetan (some)
Carbapenem Orders / ESBL isolates

Carbapenem orders
Carbapenem Susceptibility

Imipenem Susceptibility Stamford

- B. fragilis
- E. coli
- Klebsiella
- Enterobacter cloacae
- Enterobacter aerogenes
- Morganella
- Pseudomonas

percent susceptible
Emergence of Carbapenem-resistant Enterobacteriaceae (CRE)

• Carbapenems have remained effective against most of the Enterobacteriaceae, including ESBL producing strains.
  – imipenem, meropenem, ertapenem

• CRE (KPC most common)
  – Appeared 1996; 2690 cases in NYS, 50% hospital acquired in 2014
  – Klebsiella, E. coli, Enterobacter and others
  – Confer resistance to all β-lactams including extended-spectrum cephalosporins and carbapenems
  – Usually co-resistant to multiple other agents
  – Multiple enzyme profiles (KPC, NDM, VIM, OXA, others)
  – High mortality due to co-morbidities and lack of effective treatment
  – **Plasmid mediated**
PCR technology will allow rapid patient screening for CRE enzymes in the laboratory

**THE NEED**
- Carbapenem resistance results in increased mortality in hospitalized patients and is associated with higher total hospital costs.1

**THE SOLUTION**
- Xpert® Carba-R can detect and differentiate the most prevalent carbapenemase gene families in just 48 minutes.
Evolution of CRE in the United States

KPC-producing CRE

NDM-producing CRE

This map was last updated on February 2015

This map was last updated on January 2015
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Result</th>
<th>Verified</th>
<th>Ent.</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLUID CULTURE</td>
<td>Preliminary (continued)</td>
<td>08/04/16-1220</td>
<td>08/04-1220 GOCAMPO</td>
<td>PERITONEAL FLUID</td>
</tr>
<tr>
<td>Method: AEX</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perf Site: TSH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source: PERITONEAL FLUID</td>
<td>BAP</td>
<td>GHR #2^</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNM</td>
<td>#3^ #4^ #5^</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Which of the following agents is an appropriate choice for systemic infection due to CRE-producing *E. coli*?

- Amikacin
- Levofloxacin
- Colistin
- Fosfomycin
- Zosyn
- Minocycline
- Avycaz / Vabomere
Action Plan for CRE Control

• Active surveillance
• HCW education
• Laboratory enhanced detection
  – lab education
• Strict isolation / contact tracing / screening
• Antibiotic stewardship
• Mandatory Reporting to DOH
• Preserve the limited antibiotic options for treatment
A Nasty Bug Breaks Out

Dog-resistant staph bacteria now spread even students

By: Luisa Lyon

The bacteria started to spread in February when a student brought the bacteria to school. The bacteria quickly spread throughout the school and has caused a number of illnesses. The school has been closed for two weeks and is currently being disinfected. The bacteria is resistant to most antibiotics and is a serious threat to student health.

Dead Student Had Infection, Officials Say

New York City health officials said yesterday that a Brooklyn middle school student who died on Oct. 14 had become infected with a dangerous strain of bacteria that has become increasingly common in schools.

The bacteria, which can cause serious skin infections and bloodstream infections, is resistant to many antibiotics and can be difficult to treat. Health officials said the student, who attended a middle school in the borough of Brooklyn, became infected with the bacteria and later died.

The bacteria, known as Staphylococcus aureus, has become a major concern in schools in recent years as the number of cases has increased. The bacteria can spread quickly through schools and is difficult to control.

The school district has been working closely with health officials to prevent the spread of the bacteria. They have implemented extra cleaning measures and are providing extra hand sanitizer to students and staff.

The bacteria is spread through contact with contaminated objects or by direct contact with an infected person. The bacteria can live on surfaces for long periods of time, so it is important to clean surfaces frequently to prevent the spread of the bacteria.

Health officials are advising schools to follow proper cleaning procedures and to keep students who are sick away from school. They are also advising schools to monitor their students for any signs of illness.

The bacteria is especially dangerous for people who have weak immune systems, such as children and elderly people.

The school district is working with health officials to ensure that students and staff are safe and healthy.

The New York Times
Emergence of MRSA over 45 years in Fairfield County
(Stamford Hospital Microbiology Lab data)
(community and hospital strains)
National Trends in MRSA

*American Society for Microbiology annual meeting 6/4/17*
Impact of an “MRSA Bundle” on MRSA rates:
Veterans Affairs (VA) Intensive Care Units.

Hand hygiene, Active Surveillance testing, Contact Precautions

Stamford – Hospital-acquired MRSA cases

Hospital-acquired MRSA cases per 1000 patient days


0.36 0.29 0.24 0.20 0.14 0.25 0.27 0.24 0.29 0.13 0.13 0.12 0.07 0.16 0.03 0.07

rate per 1000 pt-days
Hospital-acquired infection = Medical Mistake
MRSA Treatment Options

• Oral
  – Bactrim, Doxy/Minocycline, Linezolid >90%
  – Clindamycin 60%

• Parenteral
  – Vancomycin
  – Bactrim, Doxy/Mino, Linezolid
  – Daptomycin
  – Ceftaroline
  – Telavancin / Dalbavancin / Oritavancin

• Decolonization
  – CHG bathing or cloth wipes
  – nasal / wound rx (mupirocin / povidone iodine / alcohol)
  – oral agent
Rising Incidence of Hospital-acquired *Clostridium difficile* Infection.

Difficulties in controlling the spread of *C. difficile*

- High community prevalence
- Prolonged fecal and skin carriage
- Frequent recurrence
- Persistence of spores in the environment
- “Incident density” pressure – carriers + symptomatic
- Antibiotic use and overuse
Risk of C. difficile with Perioperative Antibiotic Prophylaxis

Carignan, Sherbrooke Hospital, Quebec. SHEA, 2007

• 7256 class 1 and 2 surgeries

• CDAD rate 9.2/1000 cases
  – 5.1 / 1000 cases after only prophylactic antibiotics
  – 21.8 / 1000 cases after treatment

• Risk related to number of antibiotic doses received

<table>
<thead>
<tr>
<th>0 doses</th>
<th>0 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 dose</td>
<td>1.6 / 1000</td>
</tr>
<tr>
<td>2 to &lt;48hrs</td>
<td>3.4 / 1000</td>
</tr>
<tr>
<td>≥48 hrs</td>
<td>13 / 1000</td>
</tr>
</tbody>
</table>
Persistence of *C. difficile* During and After Treatment

Sethi, Al-Nassir, Donskey, et al  ICHE 2010; 31:22
PCR Detection of **Asymptomatic** *C. difficile* Colonization and Rising *C. diff* Rates

Only 35% of cases were genetically related to at least one previous case (i.e., ≤2 SNVs). These data show that in the majority of cases, *C. difficile* infection is not transmitted from another symptomatic patient. We observed diverse subtypes in patients with *C. difficile* infection, each representing a separate transmission event from a reservoir or asymptomatic carrier.
<table>
<thead>
<tr>
<th>Core element</th>
<th>NHSN Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Leadership Commitment</td>
<td>23 Written Antibiotic Stewardship support?</td>
<td>Yes to both</td>
</tr>
<tr>
<td></td>
<td>26 Salary for Antibiotic Stewardship Activities?</td>
<td></td>
</tr>
<tr>
<td>2 Accountability: Leader</td>
<td>24 Physician Steward?</td>
<td>Yes</td>
</tr>
<tr>
<td>3 Drug Expertise: Pharmacist</td>
<td>25 Pharmacist Responsible for Improving Antibiotic Use?</td>
<td>Yes</td>
</tr>
<tr>
<td>4 Action: at least one</td>
<td>29 Procedure for Antibiotic Treatment Review?</td>
<td>Yes to either</td>
</tr>
<tr>
<td></td>
<td>30 Antibiotic Approval?</td>
<td></td>
</tr>
<tr>
<td>5 Tracking: prescribing, resistance</td>
<td>27, 27.1 Policy to Require Prescribers to Document Antibiotic Use in Medical Record?</td>
<td>Yes to one</td>
</tr>
<tr>
<td></td>
<td>28, 28.1 Document indications for antibiotic order?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31* Antibiotic Audit with Feedback?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32** Monitor Antibiotic Use?</td>
<td></td>
</tr>
<tr>
<td>6 Reporting: antibiotic use,</td>
<td>31* Antibiotic Audit with Feedback?</td>
<td>Yes to one</td>
</tr>
<tr>
<td>resistance: doctors, nurses, staff</td>
<td>32, ** Monitor Antibiotic Use? -&gt; Antibiotic Use Shared with Prescribers?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32.1 Monitor Antibiotic Use? -&gt; Antibiotic Use Shared with Prescribers?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33 Stewardship Program Feedback?</td>
<td></td>
</tr>
<tr>
<td>7 Education: to clinicians on</td>
<td>34 Stewardship Program Education?</td>
<td>Yes</td>
</tr>
<tr>
<td>resistance, prescribing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* NHSN survey question 31 applies to two Core Elements (5, 6); ** 32 to Core Element 5 and 32.1 to Core Element 6
Aedes species transmit:

- Dengue
- Yellow fever
- West Nile
- Eastern Equine Encephalitis
- Zika virus
- Chikungunya
Zika virus

- Single stranded RNA virus
- Genus *Flavivirus*, family *Flaviviridae*
- Closely related to Dengue, Yellow Fever, Japanese encephalitis, and West Nile viruses
- Primarily transmitted through the bite of an infected *Aedes* species mosquito (*Ae. aegypti* >> *Ae. albopictus*).
- Aggressive biter, indoors and outdoors, rural and urban, day-time > night-time
Aedes Distribution in United States

*Aedes aegypti* and *Aedes albopictus* Mosquitoes: Geographic Distribution in the United States

*Aedes aegypti*

*Aedes albopictus*
Where has Zika virus been found?

- Before 2015, Zika outbreaks occurred in Africa, Southeast Asia, and the Pacific Islands.
- Outbreaks are occurring in over 50 countries past 2 years
- Recent focus in South America, Central America and the Caribbean
- Mainland US cases are most related to travel (over 5000 cases)
- Local cases in Florida
  - Other gulf coast states to follow
Declining Trends in Reported Zika Cases in the Americas

Confirmed and suspected Zika virus in the Americas, 2015–2017 (as of May 25, 2017)

PAHO Regional Zika Epidemiological Update (May 25, 2017):
Figure 2. Number of potential Zika-related infections by month (n=179)-Connecticut, February 1, 2016-June 30, 2017
Modes of transmission

- Bite from an infected mosquito
- Sexual transmission
  - Primarily from infected male partners
  - Mainly from symptomatic partners
- Maternal-fetal-Intrauterine or perinatal
- Laboratory exposure
- Likely (with screening recommendations)
  - blood transfusion, organ and tissue transplant
  - fertility treatment
  - breast feeding
  - other blood and body fluid exposure
Incubation and viremia

- Incubation period for Zika virus disease is 3–14 days.
- Zika viremia ranges from a few days to 1 week.
- Virus remains in urine longer than in blood – up to 3 weeks.
- Virus remains in semen even longer – infectious virus up 3-6 months by PCR.
- Duration of virus in vaginal secretions, saliva also prolonged
- Virus may be secreted by infected newborns for several weeks
Zika virus clinical disease course and outcomes

- Clinical illness is usually mild.
- Symptoms last several days to a week.
- Severe disease requiring hospitalization is uncommon.
- Fatalities are rare.
- Guillain-Barré syndrome (GBS) reported in patients following suspected Zika virus infection.
- Intrauterine infections problematic
Symptoms

- Many infections asymptomatic
  - 80%
- Most common symptoms
  - Fever
  - Maculopapular rash
  - Joint pain
  - Conjunctivitis
- Other symptoms include muscle pain and headache.
Clinical features: Zika virus compared to dengue and chikungunya

<table>
<thead>
<tr>
<th>Features</th>
<th>Zika</th>
<th>Dengue</th>
<th>Chikungunya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Rash</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Myalgia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Shock</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Rabe, Ingrid MBChB, MMed
“Zika Virus- What Clinicians Need to Know?”
(presentation, Clinician Outreach and Communication Activity (COCA) Call, Atlanta, GA, January 26 2016)
Skin rashes seen in Zika infections

Cruz, O.: www.thelancet.com/infection Vol 16 July 2016
Skin rashes seen in Zika infections

Cruz, O:. www.thelancet.com/infection Vol 16 July 2016
Table. Descriptive epidemiology among persons testing positive for Zika and unidentified Flavivirus infections—Connecticut, February 15, 2016-June 30, 2017

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total infections (n=179)</th>
<th>Zika positive (n=118)</th>
<th>Unidentified Flavivirus positive (n=61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>134 (75%)</td>
<td>78 (66%)</td>
<td>56 (92%)</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>32 yrs. (3-88)</td>
<td>34.5 yrs. (3-88)</td>
<td>30 yrs. (10-56)</td>
</tr>
<tr>
<td>≥1 primary symptom</td>
<td>127 (71%)</td>
<td>114 (97%)</td>
<td>13 (21%)</td>
</tr>
<tr>
<td>Rash</td>
<td>114 (90%)</td>
<td>103 (90%)</td>
<td>11 (85%)</td>
</tr>
<tr>
<td>Fever</td>
<td>71 (56%)</td>
<td>65 (57%)</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>82 (65%)</td>
<td>76 (67%)</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>47 (37%)</td>
<td>45 (39%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>Pregnant Females</td>
<td>55 (31%)</td>
<td>8 (7%)</td>
<td>47 (77%)</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; trimester</td>
<td>14 (25%)</td>
<td>4 (50%)</td>
<td>10 (21%)</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; trimester</td>
<td>12 (22%)</td>
<td>1 (13%)</td>
<td>11 (23%)</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; trimester</td>
<td>29 (53%)</td>
<td>3 (38%)</td>
<td>26 (55%)</td>
</tr>
<tr>
<td>Travel to affected area outside CT</td>
<td>179 (100%)</td>
<td>118 (100%)</td>
<td>61 (100%)</td>
</tr>
</tbody>
</table>
Diagnostic testing for Zika virus

- **PCR** for viral RNA in clinical specimens collected ≤ 7 days (serum) or ≤ 21 days (urine) after illness onset.
- **Serology** for IgM and neutralizing antibodies in serum collected 1 to 12 weeks after illness onset.
- Zika virus serology (IgM) can be positive due to antibodies against related flaviviruses (e.g., dengue and yellow fever viruses)
- **Plaque reduction neutralization test (PRNT)** for presence of flavivirus-specific neutralizing antibodies in paired serum samples.
Zika and pregnancy outcomes

- Zika virus can be transmitted from a pregnant woman to her fetus during pregnancy or around the time of birth.
- Greatest risk is in first trimester
- “Congenital Zika Syndrome” -- fetal brain atrophy – interference with neuronal migration during embryogenesis
  - Microcephaly and cerebral calcifications
  - Poorly developed brain structures
  - Defects of the eye
  - Hearing deficits
  - Impaired intrauterine growth
  - Neurodevelopmental delay
  - Cognitive impairment
## Results from Zika Pregnancy and Infant Registries

<table>
<thead>
<tr>
<th>Findings</th>
<th>US States and DC USZPR(^1) % (95% CI)</th>
<th>US Territories USZPR/ZAPPS(^2) % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic vs. Asymptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Symptomatic with birth defects</td>
<td>8 (4-13)</td>
<td>5 (4-6)</td>
</tr>
<tr>
<td>% Asymptomatic with birth defects</td>
<td>12 (7-19)</td>
<td>7 (4-11)</td>
</tr>
<tr>
<td>Birth Defects by Trimester of Infection at DX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First trimester</td>
<td>15 (8-26)</td>
<td>8 (5-12)</td>
</tr>
<tr>
<td>Second trimester</td>
<td>--</td>
<td>5 (4-7)</td>
</tr>
<tr>
<td>Third trimester</td>
<td>--</td>
<td>4 (3-6)</td>
</tr>
</tbody>
</table>


---

Zika Update: Findings from the U.S. Zika Pregnancy Registry and Updated Clinical Guidance

CDC May 4, 2017
Congenital Defects US data

Box. Birth Defects Potentially Related to Zika Virus Infection During Pregnancy and Monitored by the US Zika Pregnancy Registry for Enhanced Surveillance

**Brain Abnormalities With and Without Microcephaly**
- Confirmed or possible congenital microcephaly
- Intracranial calcifications
- Cerebral atrophy
- Abnormal cortical formation (eg, polymicrogyria, lissencephaly, pachygryria, schizencephaly, gray matter heterotopia)
- Corpus callosum abnormalities
- Cerebellar abnormalities
- Porencephaly
- Hydranencephaly
- Ventriculomegaly/hydrocephaly (excluding "mild" ventriculomegaly without other brain abnormalities)
- Fetal brain disruption sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)
- Other major brain abnormalities including intraventricular hemorrhage in utero (excluding postnatal intraventricular hemorrhage)

**Neural Tube Defects and Other Early Brain Malformations**
- Neural tube defects including anencephaly, crania, encephalocele, spina bifida
- Holoprosencephaly (arhinencephaly)

**Eye Abnormalities**
- Micophthalmia/anophthalmia
- Coloboma
- Cataract
- Intracocular calcifications
- Chorioretinal anomalies involving the macula (eg, chorioretinal atrophy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage; excluding retinopathy of prematurity)
- Optic nerve atrophy, pallor, and other optic nerve abnormalities

**Consequences of Central Nervous System Dysfunction**
- Congenital contractures (eg, arthrogryposis, clubfoot, congenital hip dysplasia) with associated brain abnormalities
- Congenital deafness documented by postnatal audiological testing

*Live births: measured head circumference (adjusted for gestational age and sex) less than the third percentile at birth or, if not measured at birth, within first 2 weeks of life. Pregnancy loss: prenatal head circumference more than 3 SDs below the mean based on ultrasound or postnatal head circumference less than the third percentile. Birth measurements are evaluated using the Intergrowth-21st standards [http://intergrowth-21st.org] based on measurements within 24 hours of birth.*

Zika Update: Findings from the U.S. Zika Pregnancy Registry and Updated Clinical Guidance
CDC May 4, 2017
## Eye Findings in Congenital Infections

<table>
<thead>
<tr>
<th></th>
<th>Zika</th>
<th>Toxoplasmosis</th>
<th>Rubella</th>
<th>CMV</th>
<th>Herpes Simplex</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjunctivitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Keratitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Macular Mottling</td>
<td>+ focal pigmentary clumping</td>
<td>+ granular (Salt-and-pepper retinopathy)</td>
<td></td>
<td></td>
<td></td>
<td>+ granular (Salt-and-pepper retinopathy)</td>
</tr>
<tr>
<td>Chorioretinal Atrophy</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Optic Nerve abnormalities</td>
<td>Hypoplasia, cupping, pallor</td>
<td></td>
<td>paller</td>
<td>paller</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Cataract</td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Microphthalmia</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Iris Coloboma</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Active inflammation:</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Zika Update: Findings from the U.S. Zika Pregnancy Registry and Updated Clinical Guidance
CDC May 4, 2017
Symptomatic Pregnant Women with Possible Zika virus Exposure

**UPDATED INTERIM PREGNANCY GUIDANCE:**
**SYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE**

**Testing Recommendations and Interpretation of Results for Healthcare Providers**

**ASK PREGNANT WOMEN ABOUT**
- Travel to or residence in any areas with risk for Zika virus transmission during and prior to pregnancy
- Possible sexual exposure before or during current pregnancy
- A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy
- Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia)
- If no symptoms reported, refer to asymptomatic guidance

Before testing, discuss testing limitations and potential risks for misinterpretations of test results.

**WHOM to test?**
- Pregnant women reporting possible exposure during current pregnancy and symptoms of Zika virus disease

**WHEN to test?**
- Test as soon as possible, through 12 weeks after symptom onset

**WHICH tests?**
- Zika virus NAT on serum and urine AND Zika virus IgM serology on serum

**RESULTS and ADDITIONAL tests**
- **Positive Zika virus NAT (if Zika IgM negative, see footnote 4)**
  - Zika virus PRINT ≥10 AND dengue virus PRINT <10
  - Acute Zika virus infection

- **Negative Zika virus NAT AND non-negative Zika virus IgM**
  - Zika virus PRINT ≥10 AND dengue virus PRINT ≤10
  - **Zika virus infection, timing of infection cannot be determined**
  - For pregnant women without Zika virus exposure before the current pregnancy, a positive IgM result represents recent Zika virus infection.

- **Negative Zika virus NAT AND negative Zika virus IgM**
  - Zika virus PRINT <10
  - **No evidence of Zika virus infection**
  - For pregnant women without Zika virus exposure before the current pregnancy, a positive IgM result represents recent unspecified flavivirus infection.
Long term follow up for infants with positive or inconclusive Zika virus test results

- Auditory and ophthalmological screen at 6 months intervals
- Continued evaluation of developmental characteristics and milestones, as well as head circumference, through 1st year of life
- Consultation with appropriate medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy) if any abnormalities are noted and as concerns arise
Prevention: couples who are pregnant

- Do not travel to Zika area
- If patient must travel to Zika area, use mosquito bite protection and take steps to prevent sexual transmission during and after travel.
- Not having sex can eliminate the risk of getting Zika from sex.
- Condoms can reduce the chance of getting Zika from sex.
- Male partner who has traveled should use a condom correctly from start to finish every time they have vaginal, anal, or oral sex throughout the pregnancy.
Prevention: Non-pregnant couples with female partner who traveled

• Discuss signs and symptoms and potential adverse outcomes associated with Zika
• CDC says wait at least 8 weeks after symptom onset or last date of exposure to have sex and attempt conception (CDC).
• WHO applies the 6 month wait recommendation to both men and women returning from Zika transmission area.
CDC’s Response to Zika

PREGNANT? READ THIS BEFORE YOU TRAVEL

What we know about Zika

- Zika can be passed from a pregnant woman to her fetus.
- Zika infection during pregnancy can cause certain birth defects.
- Zika is spread mostly by the bite of an infected Aedes species mosquito. These mosquitoes are aggressive daytime biters. They can also bite at night.
- There is no vaccine to prevent or medicine to treat Zika.
- Zika can be passed through sex from a person who has Zika to his or her sex partners.

What we don’t know about Zika

- If there’s a safe time during your pregnancy to travel to an area with Zika.
- If you do travel and are infected, how likely it is that the virus will infect your fetus and if your baby will have birth defects from the infection.

Travel Notice

CDC has issued a travel notice (Level 2-Practice Enhanced Precautions) for people traveling to areas where Zika virus is spreading.

- For a current list of places with Zika outbreaks, see CDC’s Travel Health Notices: http://wwwnc.cdc.gov/travel/page/zika-travel-information
- This notice follows reports in Brazil of microcephaly in babies of mothers who were infected with Zika virus while pregnant.

Symptoms of Zika

Most people with Zika won’t even know they have it. The illness is usually mild with symptoms lasting for several days to a week.

The most common symptoms of Zika are:
- Fever
- Rash
- Joint pain
- Red eyes

Bed Net

- If your room is not well screened and air conditioned, use a bed net when sleeping or resting.
- Mosquitoes can live indoors and will bite at any time, day or night.

Insect Repellent

- Use EPA-registered insect repellent containing DEET, picaridin, OLE, PMD, or IR3535.
- Always use as directed.
- Do not apply repellent under clothing.
- If you are also using sunscreen, apply sunscreen first and insect repellent second.
- When used as directed, these insect repellents are proven safe and effective even for pregnant and breastfeeding women.
- Most repellents, including DEET, can be used on kids older than 2 months. Mosquito netting can be used to cover babies <2 months old in carriers, strollers, or cribs to protect them from mosquito bites.

Condoms

- Zika can be passed through sex. Bring male or female condoms with you when traveling. Use condoms during and after travel to protect yourself and your partner.
- If you are pregnant, use condoms for the rest of your pregnancy.
- Not having sex eliminates the risk of getting Zika through sex.

Permethrin Spray

- Spray your clothing and gear with permethrin to help protect you from mosquito bites or bring pre-treated items.
- Always follow the directions on the bottle. Reapply as directed.
- Do not spray permethrin on your skin.
- Long sleeves and long pants help protect against Zika.
Tackling an Invasive, Emerging, Multi-drug Resistant Yeast: *Candida auris*—What Healthcare Providers Need to Know
What the public thinks

What the healthcare professionals think

Why Do We Care About an Obscure Candida Species called C. auris?
Candida auris Rapid Emergence since 2009

But This Really Got Our Attention...

- C. auris outbreak in a UK hospital
- 9 C. auris bloodstream infections
- >40 people colonized
- Clear patient-to-patient transmission

Hard to Control

- Contact precautions
- Screening for colonization
- Chlorhexidine bathing
- Cleaning room with bleach 3X/day
- Terminal cleaning with higher concentration bleach
- Eventually closed unit

C. auris cultured from many hospital surfaces
Candida auris in the US

Clinical C. auris cases by date
May 2013–April 2017
(current case count through July 2017=99)

Tackling an Invasive, Emerging, Multidrug Resistant Yeast: Candida auris—CDC August 15, 2017
C. *auris* clinical case features

**Epidemiologic Characteristics of US Cases**

- 75% of isolates from blood
- Median age: 70; one case in a neonate
- Multiple underlying medical conditions and indwelling devices
  - Tracheostomy tube, central venous catheter, gastrostomy tube
- Extensive healthcare exposure (acute care hospitals, LTACHs, vSNFs)
- Resistant: 80% to Fluconazole, 40% to Ampho B, ~3% to Echinocandins
- ~30% 30-day mortality

Tackling an Invasive, Emerging, Multidrug Resistant Yeast: Candida auris—CDC August 15, 2017
Global *C. auris* Situation

- Now common in some international hospitals
  - Up to 40% of *Candidas* in 1 Indian and 1 Kenyan hospital
  - 10% of *Candidas* in private South African hospitals
  - Probably well-established in Venezuela (limited dx capacity)
  - Cases now in Colombia and Panama
- UK continues to have introductions; seem to have controlled initial spread
- No further isolates in Japan; relatively few in South Korea
- Major unknowns in most of Africa and parts of Latin America
Influenza in Fairfield County 2016-7

Influenza Testing Stamford 2016-2017

Number of tests performed

- Positive Tests
- Negative Tests

STAMFORD HOSPITAL
Annual Variation in Flu Seasons

Laboratory-Confirmed Influenza-Associated Hospitalizations, 2016–2017* and Selected Previous Seasons

*As of February 10, 2017
Not all “ILI” is Influenza

Biofire Results  December 2016 - May 2017

35% positive

number of isolates

Chlamydia  mycoplasma  rhino/enterovirus  influenza  para influenza  adeno virus  coronavirus  RSV  metapneumovirus
Testing for Influenza

The overall pooled specificity was high for all influenza testing modalities (at least 98.3%). Sensitivity, however, varied.

<table>
<thead>
<tr>
<th></th>
<th>NAAT</th>
<th>DIA</th>
<th>RIDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza A</td>
<td>91.6%</td>
<td>80.0%</td>
<td>54.4%</td>
</tr>
<tr>
<td>Influenza B</td>
<td>95.4%</td>
<td>76.8%</td>
<td>53.2%</td>
</tr>
</tbody>
</table>
Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2017–18 Influenza Season
2017–18 U.S. influenza vaccines will contain:

- A/Michigan/45/2015 (H1N1)pdm09–like virus
- A/Hong Kong/4801/2014 (H3N2)–like virus
- B/Brisbane/60/2008–like virus (Victoria lineage)
- B/Phuket/3073/2013–like virus (Yamagata lineage)*
Guidance for Use in Specific Populations and Situations
Populations at Higher Risk for Medical Complications
Attributable to Severe Influenza

- All persons aged ≥6 months without contraindications should be vaccinated annually. However, vaccination to prevent influenza is particularly important for persons who are at increased risk for severe complications
  - all children aged 6 through 59 months;
  - all persons aged ≥50 years;
  - adults and children who have chronic pulmonary (including asthma) or cardiovascular (except isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus);
  - persons who are immunocompromised due to any cause (including immunosuppression caused by medications or by HIV infection);
  - women who are or will be pregnant during the influenza season;
  - children and adolescents (aged 6 months through 18 years) who are receiving aspirin- or salicylate-containing medications
  - residents of nursing homes and other long-term care facilities;
  - American Indians/Alaska Natives; and
  - persons who are extremely obese (BMI ≥40).
- ACIP recommends that LAIV4 not be used during the 2017–18 season
<table>
<thead>
<tr>
<th>Trade name</th>
<th>Manufacturer</th>
<th>Presentation</th>
<th>Age indication</th>
<th>Mercury (from thimerosal, μg/0.5 mL)</th>
<th>Latex</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated influenza vaccines, quadrivalent (IIV4s), standard-dose†</td>
<td>Seqirus</td>
<td>0.5 mL prefilled syringe</td>
<td>≥18 years</td>
<td>24.5</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥18 years</td>
<td>24.5</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL prefilled syringe</td>
<td>≥3 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL single-dose vial</td>
<td>≥3 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥6 months</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>GlaxoSmithKline</td>
<td>0.5 mL prefilled syringe</td>
<td>≥3 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>ID Biomedical Corp. of Quebec (distributed by GlaxoSmithKline)</td>
<td>0.5 mL prefilled syringe</td>
<td>≥3 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>Sanofi Pasteur</td>
<td>0.25 mL prefilled syringe</td>
<td>6 through 35 months</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL prefilled syringe</td>
<td>≥3 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL single-dose vial</td>
<td>≥3 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥6 months</td>
<td>25</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td>Inactivated influenza vaccine, quadrivalent (cclIV4), standard-dose,† cell culture-based</td>
<td>Seqirus</td>
<td>0.5 mL prefilled syringe</td>
<td>≥4 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥4 years</td>
<td>25</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td>Inactivated influenza vaccine, quadrivalent (IIV4), standard-dose, intradermal§</td>
<td>Sanofi Pasteur</td>
<td>0.1 mL single-dose prefilled microinjection system</td>
<td>18 through 64 years</td>
<td>NR</td>
<td>No</td>
<td>ID**</td>
</tr>
<tr>
<td>Inactivated Influenza Vaccines, trivalent (IIV3s), standard-dose†</td>
<td>Seqirus</td>
<td>0.5 mL prefilled syringe</td>
<td>≥5 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥5 years</td>
<td>24.5</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL prefilled syringe</td>
<td>≥4 years</td>
<td>≤1</td>
<td>Yes††</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥4 years</td>
<td>25</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td>Adjuvanted inactivated influenza vaccine, trivalent (allV3),† standard-dose</td>
<td>Seqirus</td>
<td>0.5 mL prefilled syringe</td>
<td>≥65 years</td>
<td>NR</td>
<td>Yes††</td>
<td>IM</td>
</tr>
<tr>
<td>Inactivated Influenza Vaccine, trivalent (IIV3), high-dose$§§</td>
<td>Sanofi Pasteur</td>
<td>0.5 mL prefilled syringe</td>
<td>≥65 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td>Recombinant Influenza Vaccine, quadrivalent (RIV4)$¶¶</td>
<td>Protein Sciences</td>
<td>0.5 mL prefilled syringe</td>
<td>≥18 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td>Recombinant Influenza Vaccine, trivalent (RIV3)$¶¶</td>
<td>Protein Sciences</td>
<td>0.5 mL single-dose vial</td>
<td>≥18 years</td>
<td>NR</td>
<td>No</td>
<td>IM</td>
</tr>
<tr>
<td>Live Attenuated Influenza Vaccine, quadrivalent (LAIV4)$*** (not recommended for use during the 2017–18 season)</td>
<td>MedImmune</td>
<td>0.2 mL single-dose prefilled intranasal sprayer</td>
<td>2 through 49 years</td>
<td>NR</td>
<td>No</td>
<td>NAS</td>
</tr>
</tbody>
</table>
2016-2017 Vaccine Match

Antigenic Characterization of U.S. Viruses Collected October 1, 2016 to present

- Antigenically Similar to 2016-17 Vaccine
- Antigenically Low to 2016-17 Vaccine

<table>
<thead>
<tr>
<th>Antigenic Group</th>
<th>Characterized</th>
<th>Antigenic Similarity</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1pdm09</td>
<td>74 (100%)</td>
<td></td>
</tr>
<tr>
<td>H3N2</td>
<td>258 (96.6%)</td>
<td></td>
</tr>
<tr>
<td>B Yamagata</td>
<td>66 (100%)</td>
<td></td>
</tr>
<tr>
<td>B Victoria</td>
<td>70 (90.9%)</td>
<td></td>
</tr>
</tbody>
</table>

*Against reference viruses representing NH 2016-2017 vaccine component
A(H1N1)pdm09 - A/California/07/2009
A(H3N2) - A/Hong Kong/4801/2014
B/Vic - B/Brisbane/60/2008
B/Yam - B/Phuket/3073/2013 (quadrivalent vaccine only)
Data collected [CDC] through the U.S. Influenza Vaccine Effectiveness Network during 11/28/16–4/14/17 indicate that influenza vaccination reduced the overall risk for influenza-associated medical visits by 42%  

- Vaccine effectiveness against the predominant influenza A(H3N2) viruses was 34% (95% CI=24%–42%)  
- Vaccine effectiveness against influenza B viruses was 56% (95% CI=47%–64%).
HCW Flu Vaccination
Hospital Compare Data for 2015-2016 season

Healthcare workers given influenza vaccination

Why is this important?

Hide Graph

For this measure, the rate for the top 10% of hospitals was Not Available.
Neuraminidase Treatment of Influenza

- FDA approved for patients with proven or highly suspect influenza infection within 48 hours of onset of symptoms
- Observational studies of hospitalized patients suggest that treatment might still be beneficial when initiated 4 or 5 days after symptom onset
- Observational data in pregnant women has shown antiviral treatment to provide benefit when started 3-4 days after onset
- A randomized placebo controlled study suggested clinical benefit when oseltamivir was initiated 72 hours after illness onset among febrile children with uncomplicated influenza

Thank You!

Questions?