Public Health:
What Clinicians Need to Know

Mary-Margaret A. Fill, MD
PHM 2017 | July 22, 2017

Disclosures

• None
Objectives

1. Understand reportable versus notifiable conditions
2. Explain the role of healthcare providers in the public health system
3. Discuss the public health approach to outbreak investigations, including the role of the laboratory and environmental health
4. Describe clinical features and understand when to suspect measles infection
5. Implement appropriate actions upon identifying a suspect measles case
6. Understand how to use public health as a resource in uncertain diagnoses
Public Health Disease Surveillance: Data for Action

Healthcare Providers
Hospitals
Laboratories
Local & State Public Health
Centers for Disease Control
Key Terms

Reportable Diseases

Notifiable Diseases
Reportable vs. Notifiable

State Reportable Conditions
Set by state department of health
Updated annually

Nationally Notifiable Conditions
Set by CDC and CSTE
Updated when needed

Information Feedback

Healthcare Providers
Hospitals
Laboratories
Local & State Public Health
Centers for Disease Control
Notifiable Diseases: Information Feedback

Notifiable Diseases and Mortality Tables

<table>
<thead>
<tr>
<th>Disease</th>
<th>Current week</th>
<th>Cases 2017</th>
<th>5-year weekly average</th>
<th>2016</th>
<th>2015</th>
<th>2014</th>
<th>2013</th>
<th>2012</th>
<th>States reporting cases during current week (%)</th>
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Reportable Diseases: Information Feedback

Communicable and Environmental Diseases and Emergency Preparedness

2016-2017 Annual Report
Reportable vs. Notifiable

State Reportable Conditions
Set by state department of health
Updated annually

Nationally Notifiable Conditions
Set by CDC and CSTE
Updated when needed

State Statute (TN)

COMMUNICABLE AND ENVIRONMENTAL DISEASES
CHAPTER 1200-14-01


1200-14-01-02 REPORTABLE DISEASES.

(1) All healthcare providers and other persons knowing of or suspecting a case, culture, or specimen of a reportable disease or event shall report that occurrence to the Department of Health in the time and manner set forth by the Commissioner in the List.

(2) The Commissioner shall re-evaluate, update, and post the List at least annually and from time to time as appropriate. The Commissioner shall post the annual update on or before November 15th of each year and this new List shall become effective starting January 1st of the following year. If the Commissioner posts an updated List more frequently than on an annual basis, then the updated List will become effective on the date stated in the List. The List shall be available online at the Department of Health’s web page and in print.
Case #1: Ty

CC: diarrhea

HPI: Previously healthy 8 year old male presents to the ED with 4-5 days of watery diarrhea. No blood in stool. No vomiting or fever. Complains of crampy abdominal pain, nausea, and anorexia.

PMH/PSH: None. Immunizations up to date. Last WCC < 6 months ago. Medications: None | Allergies: None

Vital Signs →
T: 37.2°C  HR: 122 bpm  BP: 105/65 mmHg  RR: 16bpm  O₂: 99%

Physical Exam →
GEN: Awake, alert, conversant, but ill-appearing.
CV: Tachycardic. No murmur. Pulses 2+ UE/LE.
ABD: Mildly distended. Generalized tenderness w/o rebound or guarding.
EXT: Warm and well-perfused.
Case #1: Ty

CC: diarrhea

HPI: Previously healthy 8 year old male presents to the ED with 4-5 days of watery diarrhea. No blood in stool. No vomiting or fever. Complains of crampy abdominal pain, nausea, and anorexia.

PMH/PSH: None. Immunizations up to date. Last WCC < 6 months ago. Medications: None. Allergies: None.

Vital Signs: T: 37.2°C HR: 122 bpm BP: 105/65 mmHg RR: 16 bpm O2: 99%


One more thing .... As you’re leaving the room, the parents mention that another member of Ty’s baseball team is sick with similar symptoms. They recently traveled to an out-of-state tournament and wonder if they have been exposed to something there ...

Possible Diagnosis?

1. Shiga-toxin producing E. coli
2. Salmonella sp.
3. Cryptosporidium
4. Norovirus
5. Lactose intolerance
“The Call”

7/30
Local HD alerted to
GI illness among
Hotel A guests

July–August 2015
Investigation Timeline

- **July 30**: Local HD alerted to GI illness among Hotel A guests
- **July 22**: Baseball tournament begins
- **August 3**: TDH joins investigation

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 21</td>
<td>7/30 Local HD alerted to GI illness among Hotel A guests</td>
</tr>
<tr>
<td>July 24</td>
<td>7/22 Baseball tournament begins</td>
</tr>
<tr>
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<tr>
<td>July 30</td>
<td>7/30 Local HD alerted to GI illness among Hotel A guests</td>
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<tr>
<td>Aug 2</td>
<td>7/30 Local HD alerted to GI illness among Hotel A guests</td>
</tr>
<tr>
<td>Aug 5</td>
<td>7/30 Local HD alerted to GI illness among Hotel A guests</td>
</tr>
<tr>
<td>Aug 8</td>
<td>7/30 Local HD alerted to GI illness among Hotel A guests</td>
</tr>
<tr>
<td>Aug 11</td>
<td>7/30 Local HD alerted to GI illness among Hotel A guests</td>
</tr>
</tbody>
</table>

July–August 2015
Investigation Timeline

- **7/22**: Baseball tournament begins
- **7/30**: Local HD alerted to GI illness among Hotel A guests
- **8/3**: TDH joins investigation
- **8/4**: Stool samples positive for Cryptosporidium

July–August 2015

Cryptosporidium

- Protozoan parasite that can cause GI illness in humans & animals
  - Acute, watery diarrhea
  - Symptoms can last up to 4 weeks

- Transmitted by the fecal-oral route
  - Highly infective oocysts

- Average incubation period 7 days
  - Range 4-28 days

- In immunocompromised persons, can cause chronic disease and life-threatening malabsorption

Heymann, 2008; Chappell et al., 2006; Davies & Chalmers, 2009; Heymann, 2008; Hunter et al., 2004; Goodgame, Genta, White & Chappell, 1993; Olhuysen, Chappell, Crabb, Sterling, & DuPont, 1999; http://www.cdc.gov/parasites/crypto/
National Incidence: Age Breakdown

The Problem with Pools ... 

- *Cryptosporidium* is the leading cause of all waterborne outbreaks in the United States during 2001–2010
- *Cryptosporidium* is extremely chlorine-tolerant
  - Can survive > 10 days in CDC recommended chlorine levels
- Single diarrheal contamination incident can introduce $10^7$–$10^8$ *Cryptosporidium* oocysts
- ≤ 10 oocysts can cause infection
Our Investigation ... 

• Interviews with managers of baseball tournament attendees

<table>
<thead>
<tr>
<th>Exposure (Hotel A)</th>
<th>Disease (+)</th>
<th>Disease (-)</th>
<th>Totals</th>
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<tr>
<td>(+)</td>
<td>9</td>
<td>0</td>
<td>9</td>
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<tr>
<td>(-)</td>
<td>0</td>
<td>10</td>
<td>10</td>
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<tr>
<td>Totals</td>
<td>9</td>
<td>10</td>
<td>19</td>
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</table>

\( p < 0.01 \)

\( \chi^2 \) test used
**Investigation**

1. Case-control study

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**Data Collection**

- Questionnaire administered online via REDCap®
  - Demographics, illness, exposures

   ![Diagram]
   
   - 326 survey invitations
   - 156 survey responses
   - 250 individuals
   - 48% response rate
**Epidemic Curve July 18 – August 8, 2015 (n=60)**

![Epidemic Curve](image)

**Case Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Primary (n=55)</th>
<th>Secondary (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (median, range)</td>
<td>11 (3–65)</td>
<td>30 (12–41)</td>
</tr>
<tr>
<td>Sex</td>
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<td></td>
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<tr>
<td>Male</td>
<td>42 (76%)</td>
<td>1 (20%)</td>
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<tr>
<td>Female</td>
<td>13 (23%)</td>
<td>4 (80%)</td>
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</table>
Severity of Illness

Duration of Illness (days)

Mean: 6.3
Median: 5.0
Range: 2 – 21

Sought Medical Care: n (%)

21 (35)

Hospitalized: n (%)

1 (3%)

Selected Exposures

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cases (n=55) No. (%)</th>
<th>Controls (n=190) No. (%)</th>
<th>Odds Ratio</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>Hotel Breakfast (all days)</td>
<td>45 (85)</td>
<td>138 (73)</td>
<td>2.0</td>
<td>0.9–4.8</td>
</tr>
<tr>
<td>Hotel Dinner (all days)</td>
<td>17 (32)</td>
<td>45 (24)</td>
<td>1.5</td>
<td>0.7–3.4</td>
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<tr>
<td>Hotel Refrigerator</td>
<td>48 (89)</td>
<td>161 (86)</td>
<td>1.3</td>
<td>0.5–3.5</td>
</tr>
<tr>
<td>Hotel Ice Machine</td>
<td>36 (65)</td>
<td>97 (52)</td>
<td>1.8</td>
<td>0.9–3.5</td>
</tr>
<tr>
<td>Any Restaurant</td>
<td>50 (94)</td>
<td>165 (89)</td>
<td>2.0</td>
<td>0.4–10.0</td>
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<tr>
<td>Outside Food</td>
<td>23 (45)</td>
<td>59 (33)</td>
<td>1.7</td>
<td>0.8–3.4</td>
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<tr>
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<td>11 (22)</td>
<td>37 (20)</td>
<td>1.1</td>
<td>0.4–2.8</td>
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<tr>
<td>Swimming (all days)</td>
<td>44 (80)</td>
<td>67 (36)</td>
<td>7.3</td>
<td>3.2–17.0</td>
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### Contamination Event

- 5 (10%) case-patients who swam reported swimming for multiple days while ill with diarrhea
  - 3 during or just before time period with highest odds of infection

* Photographs used with permission
Anecdotes

“All our kids got sick except mine who went in the pool for 1 minute and couldn’t stand the foggy water, so he got out! He said he ‘couldn’t even see underwater with his goggles on!’”

* Photographs used with permission

Investigation

1. Case-control study
2. Laboratory testing
**Laboratory Testing**

- Samples from 9 patients analyzed at private and state labs
- Multiple techniques
  - Direct microscopy
  - Antigen detection

- CryptoNet
  - CDC molecular-based surveillance program
  - *Cryptosporidium hominis* subtype IfA12G1

**Investigation**

1. Case-control study
2. Laboratory testing
3. Environmental investigation
Investigation Timeline

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
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<tbody>
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<td>8/3 TDH joins investigation</td>
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<td>8/4 Stool samples positive for Cryptosporidium</td>
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<tr>
<td>Aug 2</td>
<td>8/5 Environmental assessment performed</td>
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<tr>
<td>Aug 5</td>
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<tr>
<td>Aug 8</td>
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<tr>
<td>Aug 11</td>
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July–August 2015

Environmental Investigation

- Standard testing with a water chemistry monitor
- Samples for culture
- Inspection at hotel, interviews with staff
Pool Background and Maintenance

- Sand filtration system
- Disinfection with chlorine
  - Stabilized with cyanuric acid
- Routine maintenance
  - Third party monitoring

Environmental Testing

<table>
<thead>
<tr>
<th>Environmental Test</th>
<th>Hotel A Pool Result</th>
<th>Recommended Level</th>
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</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.2</td>
<td>7.2–7.8</td>
</tr>
<tr>
<td>Free available chlorine</td>
<td>0.5 ppm</td>
<td>2–3 ppm*</td>
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<tr>
<td>Oxidation reduction potential</td>
<td>528 mV</td>
<td>600–900 mV</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>* Escherichia coli</td>
<td>20 MPN/100mL</td>
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<tr>
<td>Total Coliforms</td>
<td>365 MPN/100mL</td>
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</table>

* Recommended range 1-3 ppm without cyanuric acid; 2-3 ppm with cyanuric acid
## Environmental Testing

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**Cryptosporidium**
- Negative

**Escherichia coli**
- 20 MPN/100mL

**Total Coliforms**
- 365 MPN/100mL

*Recommended range 1-3 ppm without cyanuric acid; 2-3 ppm with cyanuric acid

## Investigation Timeline

- **7/22**: Baseball tournament begins
- **7/30**: Local HD alerted to GI illness among Hotel A guests
- **8/3**: Stool samples positive for Cryptosporidium
- **8/4**: TDH joins investigation
- **8/5**: Environmental assessment performed
- **8/11**: Pool closed

July–August 2015
Public Health Recommendations

• Recommendations and remediation procedures
  – Pool closed from August 11th to September 5th

• Individuals and businesses must be vigilant with routine maintenance of pool facilities


Take Home Points

• Cryptosporidium can cause clinically significant disease in immunocompetent persons
  – Consider diagnosis with history of recreational water exposure, or animal exposure.

• Practice caution around recreational water sources and engage in healthy swimming practices!!
Case #2: Minnie

CC: fever

HPI: Previously healthy 16 year old female presents to the ED with complaints of fever and nasal congestion. She has been feeling poorly for about 3-4 days. This morning she also noticed a splotchy rash on her face and neck.

Vital Signs →
T: 40.5°C  HR: 107 bpm  BP: 112/75 mmHg  RR: 12bpm  O₂: 98%

Physical Exam →
GEN: Awake and alert. Somewhat ill-appearing.
CV: Mildly tachycardic. No murmur.
PULM: Clear breath sounds bilaterally. No crackles, rales or wheezes.

Skin Exam

![Skin Exam Image]
Additional history?

1. Travel history
2. Immunization history
3. Medications
4. Past medical history
5. Additional history of present illness
Additional PE Findings

Measles: Background

- Paramyxovirus family
- Humans are the only natural host
- Only 1 serotype
  - > 20 genotypes identified since 1990

https://www.tau.ac.il/lmsc/departments/biotech/members/rosenthal/figs.html
Clinical Presentation

- Acute viral respiratory illness
  - Malaise, anorexia
  - Fever (as high as 104°F)
  - 3 C’s: cough, coryza (runny nose), conjunctivitis
  - Koplik spots
  - Maculopapular rash

Rash

- Maculopapular, blanching rash starts 3-7d after prodrome begins
  - Rash appears ~ 14d after exposure
- Spreads head → trunk → extremities
- Immunocompromised patients may not have rash
Complications

• Common (30%):
  – Diarrhea (8%), otitis media (5-10%), pneumonia (6%)

• Less Common:
  – Subacute Sclerosing Panencephalitis (SSPE)
  – Fatal neurodegenerative disease
  – Occurs 7-10 years post-infection
  – Pre-vaccine era: SSPE rate 1/100,000

Subacute Sclerosing Panencephalitis (SSPE)

• Fatal neurodegenerative disease
• Occurs 7-10 years post-infection
• Pre-vaccine era: SSPE rate 1/100,000

California DOH reviewed all cases during 1998–2016
  – Rate among children < 5 yo: 1/1,367
  – Rate among children < 12 mo: 1/609
Treatment

- No specific antiviral therapy
- Supportive care to relieve symptoms and treat complications

- Severe measles in children (requiring hospitalization) should be treated with vitamin A (2 doses)
  - 50,000 IU for infants < 6 months
  - 100,000 IU for infants 6-11 months
  - 200,000 IU for children > 12 months

Transmissibility

- 9/10 (90%) of exposed, susceptible people will become ill after close contact

HOW CONTAGIOUS IS MEASLES?

$R_0 =$ average number of people who will catch the disease from 1 infected person

<table>
<thead>
<tr>
<th>Disease</th>
<th>(2-3)</th>
<th>(4-7)</th>
<th>(5-7)</th>
<th>(12-18)</th>
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<tr>
<td>EBOLA</td>
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<tr>
<td>FLU</td>
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<tr>
<td>SARS</td>
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<tr>
<td>MUMPS</td>
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<tr>
<td>POLIO</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>MEASLES</td>
<td></td>
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</tr>
</tbody>
</table>
Method of Spread

• Transmitted by direct contact with infectious droplets
• Or, by airborne spread when an infected person breathes, coughs, or sneezes
• Can remain infectious on surfaces and in the air for up to 2 hours after an infected person leaves an area.

Important Time Frames

• **Infectious Period**
  – 4 days before and 4 days after the onset of rash

  ![Rash Timeline]

<table>
<thead>
<tr>
<th>Day</th>
<th>Day</th>
<th>Day</th>
<th>Day</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>-4</td>
<td>-3</td>
<td>-2</td>
<td>-1</td>
<td>0</td>
</tr>
</tbody>
</table>

• **Incubation Period**
  – 7-21 days from exposure to onset of fever
  – Rash usually occurs ~14 days after exposure
Global Epidemiology

- Annually:
  - 20 million cases
  - 146,000 deaths
- A leading cause of death among children: 400 deaths per day (16/hour)

Measles Vaccine

- Introduced in 1963
- Live-virus vaccine
  - 1-dose: 93% effective
  - 2-doses: 97% effective
- Contraindications:
  - Anaphylaxis after previous dose or to a vaccine component
  - Known severe immunodeficiency (malignancy, chemotherapy, congenital immunodeficiency, long-term immunosuppression, HIV)
  - Pregnancy
Measles Incidence — United States, 2001–2017

![Bar graph showing the number of reported cases of measles in the United States from 2001 to 2017.]

Recent Notable Outbreaks

- **2014–2015**: Large, multi-state outbreak linked to Disneyland. No definitive source identified, but thought to have started with a traveler infected overseas.
- **2014**: Large outbreak of 383 cases. Occurred among unvaccinated Amish communities in Ohio.
Measles in Memphis (2016)


4/15: PH alerted to Pt A:
18 moM measles IgM+

4/18: PCR specimen collected on Pt A

4/5: Onset of fever in Pt A
4/9: Onset of rash in Pt A
4/15: PH alerted to Pt A:
18 moM measles IgM+

Measles in Memphis
Measles in Memphis

4/15: PH alerted to Pt A:
18 moM measles IgM+


4/5: Onset of fever in Pt A

4/9: Onset of rash in Pt A

4/18: PH alerted to Pt B:
50 yoM measles IgM+

4/18: PCR specimen collected on Pt A

4/18: PCR specimen collected on Pt B

4/19: PH alerted to Pt A:
18 moM measles IgM+

Measles in Memphis


4/5: Onset of fever in Pt A

4/9: Onset of rash in Pt A

4/15: PH alerted to Pt A:
18 moM measles IgM+

4/18: PCR specimen collected on Pt A

4/18: PCR specimen collected on Pt B

4/19: PH alerted to Pt A:
18 moM measles IgM+
Measles in Memphis

4/5:
Onset of fever in Pt B

4/9:
Onset of rash in Pt B

4/18: PH alerted to Pt B: 50 yoM measles IgM+

4/18: PCR specimen collected on Pt A

4/19: PCR specimen collected on Pt B

4/15: PH alerted to Pt A: 18 moM measles IgM+

4/5: Onset of fever in Pt A

4/9: Onset of rash in Pt A

4/18: PCR specimen collected on Pt A

4/19: PCR specimen collected on Pt B

4/18:
PCR specimen collected on Pt A

4/19:
PCR specimen collected on Pt B

Measles in Memphis

4/5: Onset of fever in Pt B
4/5: Onset of fever in Pt A
4/9: Onset of rash in Pt B
4/9: Onset of rash in Pt A
4/15: PH alerted to Pt A: 18 moM measles IgM+
4/18: PCR specimen collected on Pt A
4/18: PH alerted to Pt B: 50 yoM measles IgM+
4/18: PCR specimen collected on Pt B

4/18: PCR specimen collected on Pt A
4/19: PCR specimen collected on Pt B
4/21: Pt A: PCR +
4/21: PH alerted to Pt C: 7 moF measles IgM+

Immediate Public Health Response

HDOC Activated
Incident Command System
Initiated

Immediate Public Health Response

HDOC Activated (4/22)
Incident Command System
Initiated

Intensive case
investigations

Comprehensive
contact tracing
Immediate Public Health Response

- HDOC Activated (4/22)
- Incident Command System Initiated
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- HDOC Activated (4/22)
- Incident Command System Initiated
- Intensive case investigations
- Comprehensive contact tracing
- Testing symptomatic contacts
- Healthcare infection control
- Communication

Public Health Action
Case Locations

Case Vaccination Status

7 Laboratory-Confirmed Cases

- 6 (86%) Unvaccinated
- 1 (14%) Received 1 Dose MMR

3 (50%) Vaccine Eligible
3 (50%) Vaccine Ineligible

1 (33%) Not ID’d as unvaccinated
1 (33%) Vaccine delayed for illness
1 (33%) Fear of autism from MMR
Exposures: Public Locations

- 25 Locations
  - Hospitals: 6 (24%)
  - Outpatient Clinics: 12 (48%)
  - Non-Medical Public Settings: 7 (28%)

Individual Exposures

- 985 potentially exposed persons
  - 92 (9%): Close contacts of case-patients
  - 893 (91%): Exposed in healthcare settings
    - 235 (26%): Healthcare workers
    - 658 (74%): Non-healthcare workers
Public Health Action

- **385** doses of MMR vaccine administered at public health vaccination clinics and community-located events
- **41** quarantine orders, with subsequent daily active monitoring by public health, issued to close contacts of patients
- **18** doses of post-exposure intramuscular immune globulin (IGIM) administered to 18 infants aged < 12 months within 6d of exposure
- **235** immunization statuses of potentially exposed healthcare workers confirmed
- **9** press releases, press conferences and media updates to keep the public up to date on the outbreak and current guidance

Measles Priorities

1. Identify
2. Isolate
3. Inform
4. Intervene
   - Investigate
   - Immune globulin
   - Immunize
1. Identify

• Prodrome
• Features of rash
  – Direction of spread (cephalocaudal)
  – Maculopapular
  – Lasts at least 3-4 days
• Fever
• Unique features (Koplik spots)
• Risk factors
  – Immunization status (patient, household members, close contacts)
  – International travel
1. Identify

- Registration and triage staff
- Posters for providers and patients

**ALERT: Measles is very contagious and is spreading in our community.**

Tell staff and get a mask if you have:
- a fever
- a rash
- red, watery eyes
- a cough and a runny nose

Protect yourself and others now!
Ask your doctor if you and your family need measles vaccinations.

1. Identify

**Measles Serology (IgM)**
- In susceptible individuals, IgM testing early may be negative
- Test/retest at least 72h after rash onset
- Serologic results can be difficult to interpret in individuals with past immunization

**Measles RNA (RT-PCR)**
- Lower false positive rate early in course of illness
- OP or NP swab, and urine sample
- Dacron swab / viral transport media
- Testing performed at CDC
2. Isolate

- **IMMEDIATELY**
- Surgical mask on patient
  - Decreases risk, but still an exposure
- AIIR
  - Path to AIIR should minimize exposures
  - Confirm negative pressure
  - Private room, door closed
- Airborne precautions (N95) for ALL staff
- Immune staff only

3. Inform

- **As soon** as a case of measles is **suspected**, notify:
  - Hospital Infection Prevention / Infection Control
  - Public Health
    - 24/7, 365
    - Local or regional health department
    - Category 1A reportable disease in TN

  **Do NOT wait for test results!!**
4. Intervene (Immune globulin & Immunize)

- **Immune globulin**
  - Within 6d of exposure for high risk groups
    - **Infants** (< 12 mo) = give IGIM (0.5 mL/kg)
    - **Pregnant** (protected if ≥1 dose of MMR) or severely immunocompromised = give IGIV (400 mg/kg)

- **MMR**
  - If given within 72 hours of exposure for standard risk groups can provide some protective immunity or modify the clinical course of disease
  - MMR is first line (over IG) for infants 6–12 months of age if identified within 72 hours of exposure (as to not delay routine MMR & varicella immunization)

---

**Case #3: Rocky**

**CC:** weakness, falls, fever

**HPI:** Previously healthy 5 year old male presents to the ED with progressive weakness, recurrent falls and unsteady gait over the last ~7-10 days. Subjective fever at home. Intermittent confusion noted by family.

**Vital Signs**
- T: 38.2°C  HR: 110 bpm  BP: 100/70 mmHg  RR: 20 bpm  O₂: 99%

**Physical Exam**
- **GEN:** In no acute distress.
- **CV:** NRRR. No murmur, rub or gallop.
- **PULM:** Clear breath sounds bilaterally, normal work of breathing.
- **GI:** Mildly distended and mildly tender to palpation in all 4 quadrants.
- **NEURO:** Awake and alert. No deficits in CN II-XII. Strength 5/5 UE & LE. Patellar reflexes 2+ bilaterally.
- **SKIN:** Area of erythema (2x2 cm) with central necrosis on left calf.
**Differential Diagnosis?**

1. Viral meningitis or encephalitis
2. Intoxication (alcohol, medication or heavy metal)
3. Tickborne disease
4. Closed head injury / non-accidental trauma
5. Post-infectious (acute cerebellitis, ADEM)
6. Neurodegenerative disorder
Case #3: Rocky

CC: weakness, falls, fever

HPI: Previously healthy 5 year old male presents today with progressive weakness, recurrent falls, and unsteady gait over the last 7-10 days. Subjective fever at home.

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- T: 38.2°C
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- SKIN: Area of erythema (2x2 cm) with central necrosis on left calf.

Clinical Course: Hospital A (HD #1)

- Labs:
  - ALT: 73
  - AST: 99
  - Alk Phos: 235
  - T Bili: 3.1
  - Creatine Kinase: 552

- CT head, MRI brain, CXR, CT A/P all negative for acute processes except for mildly prominent left inguinal LN
- Transitioned to IV doxycycline
- Transferred to Hospital B for LP

One more thing ....

As you’re leaving the room, the parents mention that Rocky was seen at Urgent Care ~ 5 days ago for a rash on his leg. He had been playing outside about a week prior and they noticed a tick on his leg in that area. He was prescribed doxycycline and discharged home. He’s still taking the doxycycline.
Clinical Course: Hospital B (HD #3)

- Labs:
  - ALT: 352
  - AST: 996
  - ALk Phos: 245
  - T Bili: 7.9
  - D Bili: 7.0
  - Lactic Acid: 12.6
  - CSF WBC: 1
  - CSF RBC: 0
  - CSF Glucose: 36
  - CSF Protein: 50

- IgM and IgG for Lyme, Ehrlichia and Rickettsia all returned negative from Hospital A
- Ultimately transferred to Hospital C via LifeFlight

Clinical Course: Hospital C (HD #4-7)

- Labs:
  - ALT: 214
  - AST: 432
  - ALk Phos: 242
  - T Bili: 10.3
  - Lactic Acid: 6.6 – 13.0
  - PT: 20.6 / INR: 1.8
  - PTT: 71.9
  - LDH: 5,093
  - Creatine Kinase: 7,361
  - Ferritin: 46,789

- All bacterial blood, CSF, urine cultures negative
  - Multiple hospitals, sites, dates
- Continue on mechanical ventilation, 3 vasopressors and broad spectrum antibiotics.
- Family ultimately transitioned him to comfort care on HD #7
Gross Autopsy Findings

- **External:**
  - LLE erythema with 2cm area of central necrosis on lateral calf
  - Gangrenous changes of fingers, toes, ears, nose and genitalia

- **Internal:**
  - Geographic necrosis of the liver
  - Splenic infarction
  - Lymphocytic myocarditis
  - Relatively few manifestations of chronic disease
    - Remote infarct in right thalamus (1.2 cm)
    - Renal arterio- and arteriolar nephrosclerosis
    - Left ventricular hypertrophy
    - Mild atherosclerotic heart disease

Dr. Margaret Compton, VUMC Pathology

Unexplained Death Evaluation

- **Centers for Disease Control and Prevention Infectious Disease Pathology Branch (IDPB)**
  - Help identify previously unrecognized or new infectious agents

- **Diagnostic assays for > 150 etiologic agents**
  - Immunohistochemistry
  - Ultrastructural study
  - Molecular evaluation and electron microscopy
  - Microbiological methods
### IDPB Report

**Results:**

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver, gallbladder</td>
<td>Spotted fever group <em>Rickettsia</em> (0070)</td>
<td>Negative</td>
</tr>
<tr>
<td>Liver, gallbladder</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>Pancreas, spleen</td>
<td>Spotted fever group <em>Rickettsia</em> (0070)</td>
<td>Negative</td>
</tr>
<tr>
<td>Pancreas, spleen</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>Lt ventricle heart &amp; LAD</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>LLI lung</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>Lg &amp; xu bowel</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>Rt kidney, adrenal</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>Bladder, prostate</td>
<td>Heartland virus (1447)</td>
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<td>Rt &amp; Lt testis</td>
<td>Heartland virus (1447)</td>
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<tr>
<td>Bone marrow vertebral body</td>
<td>Heartland virus (1447)</td>
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<tr>
<td>Thyroid &amp; hilar lymph nodes</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
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<td>Lower extremity skin lesion</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>Bone marrow rib squeeze</td>
<td>Heartland virus (1447)</td>
<td>Positive</td>
</tr>
<tr>
<td>Pons</td>
<td>Heartland virus (1447)</td>
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<tr>
<td>Rt thalamic lesion</td>
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<tr>
<td>Rt hippocampus</td>
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<table>
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<tr>
<td>Liver, gallbladder</td>
<td>Heartland virus RT-PCR</td>
<td>Positive for Heartland virus</td>
</tr>
<tr>
<td>Pancreas, spleen</td>
<td>Heartland virus RT-PCR</td>
<td>Positive for Heartland virus</td>
</tr>
</tbody>
</table>

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**IDPB Report**

**HRTV IHC Positive**

- Liver, gallbladder (+ PCR)
- Pancreas, spleen (+ PCR)
- Left ventricle
- Lung
- Large and small bowel
- Kidney, Adrenal gland
- Testes
- Bone marrow (x2)
- Thyroid & hilar lymph nodes
- Lower extremity skin lesion
- Rt thalamic infarct

<table>
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<th>Result</th>
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</tr>
</tbody>
</table>
Brain IHC

Myocarditis

Photo Credit: Dr. Wun-Ju Shieh, CDC IDPB
Cardiac IHC

Renal Damage
Renal IHC

Bone Marrow IHC
Heartland Virus (HRTV) Background

• Novel Phlebovirus
  – Single-stranded RNA viruses in Bunyaviridae family
• First identified in two patients in Missouri in 2009
  – Heartland Regional Medical Center

Tick Dragging
Yield

Results To Date

- Collected ~ 4000 ticks → 237 testing pools

<table>
<thead>
<tr>
<th></th>
<th>A. americanum (Lone Star)</th>
<th>D. variabilis (Dog Tick)</th>
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<tbody>
<tr>
<td>Adult</td>
<td>356</td>
<td>48</td>
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<tr>
<td>Nymph</td>
<td>1308</td>
<td>0</td>
</tr>
<tr>
<td>Larvae</td>
<td>2352</td>
<td>0</td>
</tr>
</tbody>
</table>

- 1 positive pool (2015) for HRTV

Data Credit: Stephanie Poindexter and Dr. Abelardo Moncayo, TDH
Conclusions

- Physicians and other healthcare providers are an integral part of the public health system in the United States.

- Public health investigations often include epidemiologic, laboratory and environmental components to understand the full picture.
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- Public health can assist in the identification of novel or emerging pathogens, and can often facilitate testing through state public health laboratories or CDC.
Conclusions

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- Public health investigations often include epidemiologic, laboratory and environmental components to understand the full picture.
- Some diseases and conditions are of extreme public health importance and require immediate reporting.
- Public health can assist in the identification of novel or emerging pathogens, and can often facilitate testing through state public health laboratories or CDC.
- **Learn more about public health in your city, county and/or state!**

Powerful Example

**The Index Case for the Fungal Meningitis Outbreak in the United States**

April C. Pettit, M.D., M.P.H., Jonathan A. Kropski, M.D., Jessica L. Cassillio, M.D., M.P.H., Jonathan E. Schmitz, M.D., Ph.D., Carol A. Krauch, M.D., Ph.D., Bret C. McAlpine, M.D., Xuan J. Wang, M.D., Steven S. Spines, M.D., and Meredith E. Pugh, M.D., M.S.C.J.

**SUMMARY**

Persistent neutrophilic meningitis presents a diagnostic challenge because the differential diagnosis is broad and includes atypical infectious causes. We describe a case of persistent neutrophilic meningitis due to *Acremonium fumigatum* in an immunocompetent man who had no evidence of sinopulmonary or cutaneous disease. An epidural glaecoocostoid injection was identified as a potential route of entry for this organism into the central nervous system, and the case was reported to the state health department.
Impact of Quick Response

Estimated Deaths and Illnesses Averted During Fungal Meningitis Outbreak Associated with Contaminated Steroid Injections, United States, 2012–2013

Rachel M. Smith, Gordana Dorado, Matthew Wise, Julia R. Harris, Thomas Chiller, Martin J. Mehler, Benjamin J. Park

Without prompt recall, rapid public health actions, and early diagnosis and interventions by clinicians, there could have been an additional:

→ 3,150 contaminated injections
→ 153 cases of meningitis
→ 124 deaths
Thank You - Questions?

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Cell: (678) 520-2181