Emerging Infections

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Emerging Infections: Outline

I. Definitions and contributing factors
II. Fungal meningitis
III. Carbapenem-resistant Enterobacteriaceae
IV. Novel coronavirus
V. Influenza

“Emerging Infections”

• New or reemerging disease
• Past 35 years
• Many caused by zoonotic agents
• Seen with increasing frequency
• Contributing or precipitating factors
• Can result from combination of factors

Examples

• Cholera
• Hantavirus, Hantaanvirus
• SARS, coronavirus
• HIV
• Hepatitis C
• Hemolytic Uremic Syndrome
• Novel influenza viruses
• Exserohilum rostratum / fungal meningitis
Factors Contributing to Disease Emergence¹, ²

- **Ecological changes** (economic development, land use; agriculture; dams; deforestation and reforestation)

- **Human demographic factors** (population growth, migration, war and conflict; sexual behavior, IV drug use)

- **International travel and commerce** (movement of goods and people)

¹ Institute of Medicine Report, 1992; ²Stephen Morse, EID Vol. 1, No. 1, Jan-March 1995

Contributing Factors (2)

- **Technology and industry** (mass food production, globalization of food supply, organ transplants)

- **Microbial adaptation**, evolution, e.g., genetic drift and genetic shift in Influenza A, selective (antimicrobial) pressure

- **Breakdown in public health measures** (conflict, bankruptcy, premature program cuts, inadequate sanitation / inadequate sterile environment)

Factors in Combination

- **Egypt**: Schistosomiasis (product of dam and irrigation), followed by hepatitis C outbreak resulting from inadequate mass injectable treatment in 1060s-80s

- **Travel and poverty**, introducing cholera in areas previously free: South America in the 1990s (ballast water of freighters); Haiti in 2010 (South Asian strain, outbreak onset following foreign aid arrival after earthquake)

FUNGAL MENINGITIS

http://www.cdc.gov/hai/outbreaks/meningitis-map.html
Conclusion

- **Largest healthcare-associated infection outbreak in US history**
  - Contaminated Methylprednisolone Acetate (MPA) caused substantial morbidity and mortality
- **Large number of exposed persons required rapid identification and notification**
  - Likely resulted in earlier diagnosis and treatment
  - Likely to have reduced morbidity and mortality

Anne Purfield, Epidemic Intelligence Service Conference, April 22, 2013

Scope of Problem with Compounding Pharmacies

- Compounding pharmacies intended to provide customized medication on small scale
- Production en masse without regulatory oversight for good manufacturing practices might result in compromised quality assurance

Anne Purfield, Epidemic Intelligence Service Conference, April 22, 2013

Epidemic Curve (n=680)

- MPA was distributed from May 21, 2012
- CDC-EOC Activated
- Patient notification
- First case diagnosed

Case-Patient Diagnoses by April 1, 2013 (n=730)

- **584 had a single diagnosis**
  - 308 had parameningeal infection
  - 236 had meningitis
  - 33 had peripheral joint infection
  - 7 had a stroke
- **146 had more than one diagnosis**
  - 144 had parameningeal infection and meningitis
  - 2 had parameningeal infection and peripheral joint infection

Anne Purfield, Epidemic Intelligence Service Conference, April 22, 2013
### Incubation Period*

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Median days</th>
<th>(range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke (n=7)</td>
<td>24</td>
<td>(3 - 157)</td>
</tr>
<tr>
<td>Meningitis (n=231)</td>
<td>36</td>
<td>(0 - 146)</td>
</tr>
<tr>
<td>Parameningeal infection (n=403)</td>
<td>49</td>
<td>(7 - 182)</td>
</tr>
<tr>
<td>Peripheral joint infection (n=34)</td>
<td>62</td>
<td>(22 - 190)</td>
</tr>
</tbody>
</table>

*Defined as the time between the date of the last injection prior to diagnosis to the date of diagnosis

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### Organisms Isolated from Unopened MPA Vials

- **Exserohilum rostratum**
  - Predominant organism from clinical specimens and vials of MPA
- **Other bacteria and fungi**
- **Aspergillus spp. not recovered from vials**

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### CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE)

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### Superbugs You Should Take Seriously

**The Nearly Unstoppable Superbugs**

A particularly virulent type of bacteria called CREs, which include E. coli and Salmonella, is gaining in strength. Can we develop better antibiotics to fight them off?

[Read more](http://www.takepart.com/article/2013/05/10/superbugs-CREs-ecoI-salmonella)
What are CRE?

• Enterobacteriaceae:
  – Family of bacteria normally found in the GI tract
  – E. coli, Klebsiella, etc.
  – Cause infections when they get into the bladder, blood, or other areas where germs don’t belong

• CRE:
  – Enterobacteriaceae that have become resistant to all or almost all antibiotics, including last-resort drugs called carbapenems

Why Should We Care?

• CRE infections are hard to treat, and in some cases, untreatable
• CRE easily spread their antibiotic resistance to other kinds of germs, making those potentially untreatable as well
• New carbapenemases (NDM, VIM) spreading from other countries

KPC in the United States

Unravelling and hard to treat infections from CRE, germs are on the rise among patients in medical facilities. CRE germs have become resistant to all or nearly all the antibiotics we have today. Types of CRE include KPC and NDM. To follow CDC guidelines, we can halt CRE infections before they become widespread in hospitals and other medical facilities and potentially spread to otherwise healthy people outside of medical facilities.
Frequency of CRE Identification among North Carolina Hospitals by Region

<table>
<thead>
<tr>
<th>NCHQ County</th>
<th>Number Facilities Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1-Buncombe</td>
<td>(n=11)</td>
</tr>
<tr>
<td>R2-Guilford</td>
<td>(n=13)</td>
</tr>
<tr>
<td>R3-Wake</td>
<td>(n=7)</td>
</tr>
<tr>
<td>R4-Pitt</td>
<td>(n=12)</td>
</tr>
<tr>
<td>R5-New Hanover</td>
<td>(n=9)</td>
</tr>
<tr>
<td>R6-Mecklenburg</td>
<td>(n=16)</td>
</tr>
<tr>
<td>All Facilities</td>
<td>(n=68)</td>
</tr>
</tbody>
</table>

2012 CDC CRE Toolkit

- Guidance for healthcare facilities
- Guidance for regional prevention

NOVEL CORONAVIRUS (NCoV)

Images: CDC, Google Maps
NCoV: Background

- First identified in patient from Saudi Arabia, September, 2012
- Different from other coronaviruses in humans, including SARS
- Most similar to coronaviruses found in bats
- No specific treatment

NCoV: Current Situation

- 34 cases from Arabian Peninsula (29), UK (3), and France (2)
- Severe acute respiratory illness
- 20 cases (59%) fatal
- “Clear evidence of limited, not sustained, human-to-human transmission”

NCoV: Public Health Actions

- New recommendations for diagnosis and management of patients under investigation—e.g., patients who develop pneumonia within 10 days of travel to the Arabian Peninsula
- New recommendations for infection control during care for confirmed or probable cases
- No travel warnings or restrictions

INFLUENZA

H7N9 virus, WHO Collaborating Centre for Reference and Research on Influenza, National Institute of Infectious Diseases, Japan
Seasonal Flu is a Big Deal

- Affects 5–20% of population each year
  - >200,000 hospitalizations*
  - Average 24,000 deaths (range, 3–49,000)**
- $10 billion direct medical costs,
- $87 billion total economic burden***

*Thompson, JAMA 2004; **MMWR 59(33) 2010; ***Molinari, Vaccine 2007

Pandemic Influenza

Three Conditions:
1. New ("novel") virus; all or most susceptible
2. Transmissible from person to person
3. Wide geographic spread

Infectious Disease Mortality in the US, 1900–1996

Armstrong, et al., JAMA 1999;281:61-66. Adapted from CDC slide set
Impact of Past Influenza Pandemics

<table>
<thead>
<tr>
<th>Pandemic, or Antigenic Shift</th>
<th>Excess Deaths in US</th>
<th>Populations Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918-19 (A/H1N1)</td>
<td>500,000</td>
<td>Persons &lt;65 years</td>
</tr>
<tr>
<td>1957-58 (A/H2N2)</td>
<td>70,000</td>
<td>Infants, elderly</td>
</tr>
<tr>
<td>1968-69 (A/H3N2)</td>
<td>36,000</td>
<td>Infants, elderly</td>
</tr>
<tr>
<td>2009-10 (A/H1N1)</td>
<td>12,500</td>
<td>Persons &lt;65 years</td>
</tr>
</tbody>
</table>

Current Influenza Threats

H5N1
H7N9
H3N2v

H5N1 Avian Influenza

- First human cases identified in 1997
  - Hong Kong
  - 18 cases, 6 deaths
- Reemergence, 2003–present
  - Continued sporadic cases
  - Limited person-to-person spread
  - Progression from Asia to Middle East, North Africa
- WHO update — November, 2011:
  - 15 countries
  - 628 cases
  - 374 deaths (60%)
H3N2 variant (H3N2v)

• “Variant”: Virus that normally infects pigs
• 2010: Swine H3N2 with matrix (M) gene from H1N1 virus first identified in US pigs
• 2011: 12 human cases of H3N2v infection detected in IN, IA, ME, PA, and WV
• 2012: 307 cases in 11 states

H3N2v

• Illness similar to seasonal influenza
• Majority of cases were among children
• Most associated with prolonged exposure to pigs at agricultural fairs

Images: www.cdc.gov/flu

H7N9

• First human infection with avian H7N9 virus detected March, 2013
• 131 cases, 32 deaths (May 8, 2013)
• Most with severe respiratory illness
• Many cases had contact with poultry
• No sustained person-to-person transmission
• (Yet)

H7N9: Public Health Actions

• NC DPH issued memos to all providers with recommendations for detection, testing, and treatment of possible H7N9 cases
• State Lab able to provide testing
• CDC working with pharmaceutical companies on candidate vaccines
• No travel restrictions, special recommendations for US public
Take Home Point

“Public health preparedness is vital for detecting and responding to emerging infections. Despite our prevention efforts, everyday systems malfunction and cause harm, new infections emerge, and unforeseen illnesses arise. Although such events cannot be fully predicted, they should be expected, and effective responses to routine health events strengthen our ability to prevent, detect, and respond to the unusual.”

Bell and Khabbaz, JAMA, Published online January 30, 2013