Emerging Infectious Diseases and Risk

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LOCKTON
Introduction -- topics

- Brief overview of Viruses
- Emerging viral disease(s)
- Clinical elements of viral infections
- Relationship to costs
Virus: A small infectious particle that replicates only inside the living cells of other organisms (any/all life forms)

Two – three key components

- Genetic material: DNA or RNA
- Protein coat
- Lipid coat or envelope over the protein coat
- Viruses also called ‘virions’
7 genetic types or categories

I: dsDNA viruses
II: ssDNA viruses
III: dsRNA viruses
IV: (+)ssRNA viruses
V: (−)ssRNA viruses
VI: ssRNA-RT viruses
VII: dsDNA-RT viruses
Reservoir – long-term live host of an infectious pathogen.

Hosts either don’t get the disease or carry the pathogen in a subclinical infectious state without symptoms

**Vector** is any agent (person, animal or microorganism) that carries and transmits an infectious **pathogen** into another living organism.
**Vector** is any agent (person, animal or microorganism) that carries and transmits an infectious pathogen into another living organism.
Viral DNA or RNA >>>>>> proteins, more DNA/RNA

Genetic Evolution of H7N9 Virus in China, 2013

The eight genes of the H7N9 virus are closely related to avian influenza viruses found in domestic ducks, wild birds and domestic poultry in Asia. The virus likely emerged from "reassortment," a process in which two or more influenza viruses co-infect a single host and exchange genes. This can result in the creation of a new influenza virus. Experts think multiple reassortment events led to the creation of the H7N9 virus. These events may have occurred in habitats shared by wild and domestic birds and/or live bird/poultry markets, where different species of birds are bought and sold for food. As the above diagram shows, the H7N9 virus likely obtained its HA (hemagglutinin) gene from domestic ducks, its NA (neuraminidase) gene from wild birds, and its six remaining genes from multiple related H9N2 influenza viruses in domestic poultry.

1918: H1N1
1957: H2N2
1959: H7N7
1968: H3N2
1977: H1N1
2003–present: H5N1
2003: H7N7
2003: H9N2
2004: H7N3
1998–1999: H9N2
1997: H5N1
1995: H7N7

Emerging infectious disease

Emerging:  *Newly identified, previously unknown infectious agents that cause public health problems locally or internationally*

Example:  MERS Coronavirus or Middle Eastern Respiratory Syndrome Coronavirus (identified in 2012)
Re-emerging (or resurging) infectious disease

Re-emerging: *Infectious disease known for decades or centuries that now returns in a different form or location.*

Examples: West Nile virus in Western Hemisphere, dengue now in South America and the Caribbean, Monkeypox in the USA

Add to the list: resurgence of measles and other preventable infectious diseases

- **Note:** ‘deliberately emerging’ is bioterrorism, i.e. Anthrax
A Mammalian Example
23 EBOLA OUTBREAKS, 1976-PRESENT

- **1976**: 2nd worst year
  - Sudan, Democratic Republic of Congo
  - 602 cases
  - 431 deaths
  - 71.5% mortality

- **1995**: 5th
  - Democratic Republic of Congo
  - 315 cases
  - 254 deaths
  - 80.6% mortality

- **2000**: 3rd
  - Uganda
  - 425 cases
  - 224 deaths
  - 52.7% mortality

- **2007**: 4th
  - Uganda, Democratic Republic of Congo
  - 413 cases
  - 224 deaths
  - 54.2% mortality

- **2014**: 1st
  - Sierra Leone, Guinea, Liberia, Nigeria
  - 16,899 cases*
  - 5,987 deaths
  - 35.4% mortality

*10,553 lab confirmed cases, Number includes Presumed/Probable Cases
As of November 28, 2014

1976 - Nzara, Sudan
284 cases, 151 deaths

Workers at a cotton factory were infected from an unknown source, possibly roosting bats. The outbreak spread to nearby towns and through a hospital. This was the earliest known outbreak of the Ebola virus, but because of delays in recognizing the outbreak it was not the first international response. Click the map or timeline for other outbreaks.
Drivers of disease emergence vary by region, but common drivers are population growth, land-use change, agricultural intensification and related factors like bushmeat hunting and consumption.

Pool of about 320,000 viruses (lower than many had previously suggested) is the pool from which the next pandemic likely emerges.
Emergence/Re-emergence: Key Factors

SOME POSITIVES:
- Sanitation
  - Urban/sewage
- Improved housing
  - Less crowding
- Hygiene
- Anti-sepsis
- Vaccinations
- Medical care
  - antibiotics

Microbial agent – genetic mutation(s)
Host – nutrition, immunocompromised, aging, chronic dz.
Environment – climate, ecosystems, deforestation
Social/Political – war, civil unrest, lack of political will
Clinical Aspects
Ebola hemorrhagic fever can cause:

**Acute phase:**
- Multiple organ failure
- Severe bleeding
- Jaundice
- Delirium
- Seizures
- Coma
- Shock
- Hair loss

**Sequelae:**
- Sensory changes
- Liver inflammation (hepatitis)
- Weakness
- Fatigue
- Headaches
- Eye inflammation
- Testicular inflammation
- Joint pain, muscle pain
- Skin peeling
- Alopecia - hair loss
Treatment Costs

- Nebraska: $30K/day
- NIH: $50K/day
- Range: $8.5K -- $50K+ per day
- 30+ Nurses for 24 hours ICU coverage
- Several $1 million patients

- PPE costs
- Opportunity costs
- Training costs for 100s or 1,000s of hospital workers to use PPEs
- Building or enhancing clinical facilities for bio-containment
Ebola Specific Therapy

- AVI-7537; Phase II
- CMX-001, brincidofovir
- TKM-Ebola, Phase I
- Zmapp, Phase I
- Perimavir (BCX4430)
- 5+ agents in pre-clinical status or earlier

- 60-80% NHP Survival
- Phase III
- 100% NHP Survival
- 100% NHP Survival
- NHP studies underway

Research/Govt. >>>>>>>>>>>> MED/PHARMA Claims

USA Cost per treatment: HIGH vs LOW?
- pricing model for newer Hepatitis C drugs
Medical Care Costs
- Diagnostic
- Supportive Therapy
  - ICU Plus
  - New Treatments

Continuing Medical Costs
- Related to organ failure
- Joint pain
- Fatigue
- Others
- Combination of Diagnostic and Treatment Costs

Cofactors:
- Age
- Nutritional Status
- Co-morbidities
- Access
- SES
- Others

Generally lead to worsened outcomes but hard to predict.
Medical Care Costs
- Diagnostic
- Supportive Therapy
  - ICU
  - Ventilator status

Continuing Medical Costs
- Related to organ COPD
- Asthma
- Nosocomial infection
- Others
- Combination of FU Diagnostic and Treatment Costs

COFACTORS
- Age
- Nutritional Status
- Co-morbidities
- Access
- SES
- Others

Generally lead to worsened Outcomes but hard to predict.
Medical Care Costs
- Diagnostic
- Supportive Therapy
  - Pain meds OTC
  - Fever control

Continuing Medical Costs
- Joint pain
- Fatigue
- Others
- Combination of Diagnostic and Treatment Costs

Complications: uveitis, retinitis, myocarditis, hepatitis, arthritis, G-B Syn, cranial n. palsy

COFACTORS
- Age
- Nutritional Status
- Co-morbidities
- Access
- SES
- Others

Generally lead to worsened Outcomes but hard to predict.
Chikungunya Virus (formerly Dengue)
CDC Flu models

- FluSurge 2.0: [http://www.cdc.gov/flu/pandemic-resources/tools/flusurge.htm](http://www.cdc.gov/flu/pandemic-resources/tools/flusurge.htm)
  - Models the surge in demand for hospital-based services
  - Part of Pandemic Flu Preparedness Tools
  - Also Excel SS models called
    - Community Flu 2.0 – simulates the spread of influenza through a model community and the impact of potential interventions and some cost calculations
    - FluAid 2.0 – modeling for Pediatric age (<18 years)
    - FluLabSurge 1.0 – models surge in flu related laboratory services
    - FluWorkLoss 1.0 – models flu related work loss
    - Influenza Risk Assessment Tool (IRAT) – assess risk for influenza A
Step 1: Determine population of locale by age groups:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19 yrs</td>
<td>1,350,707</td>
</tr>
<tr>
<td>20-64 yrs</td>
<td>2,106,171</td>
</tr>
<tr>
<td>+ 65 yrs</td>
<td>1,153,154</td>
</tr>
</tbody>
</table>

Step 2: Determine basic hospital resources:

- Total licensed non-ICU beds: 7,300
- Total staffed non-ICU beds: 7,300
- Total licensed ICU beds: 759
- Total Staffed ICU beds: 759
- Total number of ventilators: 691
- % ventilators available: 100%
- Total number of ventilators available: 691

Step 3: Determine duration (6, 8, or 12 weeks) and attack rate (15%, 25% or 35%) of the pandemic:

Duration: 8  
Attack rate: 25%

Step 4: Click to View Results
Pandemic Influenza Impact / Attack Rate: 25%

<table>
<thead>
<tr>
<th>Total Hospital Admissions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Likely Scenario</td>
<td>22,200</td>
</tr>
<tr>
<td>Minimum Scenario</td>
<td>12,605</td>
</tr>
<tr>
<td>Maximum Scenario</td>
<td>29,504</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Deaths</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Likely Scenario</td>
<td>5,378</td>
</tr>
<tr>
<td>Minimum Scenario</td>
<td>4,293</td>
</tr>
<tr>
<td>Maximum Scenario</td>
<td>7,814</td>
</tr>
</tbody>
</table>

Distribution of admissions: By week, 8 week outbreak 25% attack rate

<table>
<thead>
<tr>
<th>Hosp Adm. / Week</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Likely Scenario</td>
<td>1,332</td>
<td>2,220</td>
<td>3,330</td>
<td>4,218</td>
<td>4,218</td>
<td>3,330</td>
<td>2,220</td>
<td>1,332</td>
</tr>
<tr>
<td>Minimum Scenario</td>
<td>756</td>
<td>1,261</td>
<td>1,891</td>
<td>2,395</td>
<td>2,395</td>
<td>1,891</td>
<td>1,261</td>
<td>756</td>
</tr>
<tr>
<td>Maximum Scenario</td>
<td>1,770</td>
<td>2,950</td>
<td>4,426</td>
<td>5,606</td>
<td>5,606</td>
<td>4,426</td>
<td>2,950</td>
<td>1,770</td>
</tr>
</tbody>
</table>
It almost stopped the works in 1918!
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