A Virus to Die for: Influenza 2018

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Disclosures

• Related Activities:
  – Member, Technical Advisory Panel on Evaluating the Use of Rapid Influenza Testing in Outpatient Medical Settings, Centers for Disease Control/The Joint Commission
  – Member, Infectious Diseases Society of America (ISDA), Influenza Testing and Antiviral Treatment Guidelines Panel

• Commercial Relationship:
  – Pfizer consultant related to Sickle Cell Disease
What We Will Cover Today:

• Influenza 2018
  – Brief historical and scientific review
  – Discussion of this season’s impact
  – Current testing and treatment recommendations

• Respiratory hygiene in the emergency department (ED)
Zombie Apocalypse!!
Why Discuss Influenza?

• Common disease that causes significant morbidity and mortality
  – Both seasonal and pandemic influenza
  – Preventable with vaccination
  – Potential treatment to decrease severity of disease
Influenza Quiz: Question #1

• Which killed more people, the 1918 “Spanish” Influenza or World War I?
1918 Influenza Pandemic

- World War 1 (The Great War):
  - Killed over 16.5 million individuals
    - 2/3 died in battle, 1/3 from diseases including influenza
    - Of note, approximately 60 million were killed in World War II

*http://wwwnc.cdc.gov/eid/article/12/1/05-0979_article.htm*
Influenza Quiz: Question #2

• Which killed more people, the 1918 “Spanish” Influenza or World War I?

• Approximately what percentage of the world’s population was infected with the Spanish Flu?
1918 Influenza Pandemic

• World War 1 (The Great War):
  – Killed over 16.5 million individuals
    • 2/3 died in battle, 1/3 from diseases including influenza
    • Of note, approximately 60 million were killed in World War II

• 1918 H1N1 Influenza pandemic infected an estimated 500 million globally*
  – Approximately 20% of the world’s population was infected

*http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3167391/
Influenza Quiz: Question #3

• Which killed more people, the 1918 “Spanish” Influenza or World War I?

• Approximately what percentage of the world’s population was infected with the Spanish Flu?

• What percentage of the world died from the Spanish Flu?
1918 Influenza Pandemic

- **World War 1 (The Great War):**
  - Killed over 16.5 million individuals
    - 2/3 died in battle, 1/3 from diseases including influenza
    - Of note, approximately 60 million were killed in World War II

- **1918 H1N1 Influenza pandemic infected an estimated 500 million globally**
  - Approximately 20% of the world’s population was infected

- **Killed an estimated 50 million (maybe as high as 100 million)**
  - 2%-3% of the world’s population died

*http://wwwnc.cdc.gov/eid/article/12/1/05-0979_article.htm*
What is Influenza?
Influenza is...

• A major, acute respiratory illness resulting from infection with an influenza virus

• Highly infectious (depending on strain)
  – Can spread rapidly from person to person
  – Can cause severe illness

• Severity of illnesses also depends on the baseline health of the individual
Influenza Virus

• Orthomyxoviruses
  – RNA virus
    • negative-sense, single-stranded, segmented
  – 6 genera:
    • Influenzavirus A, Influenzavirus B, Influenzavirus C, Isavirus, Thogotovirus, newly discovered 6th genera

• Influenza A- characterized by viral surface proteins
  – hemagglutinin (HA or H)- 16 serotypes
  – neuraminidase (NA or N)- 9 serotypes
Influenza Virus Types

Influenza viruses that infect humans:

- **A viruses** – infect humans, other mammals and birds; causes pandemics

- **B viruses** – infects humans and seals

- **C viruses** – infects humans and pigs

Swine Flu

http://www.cdc.gov/flu/podcasts/images/SwineFlu.jpg
Where Does Influenza A Virus Come From?

Human influenza A viruses start as avian (bird) influenza viruses
How Influenza Spreads

• Spreads easily from person to person through coughing and sneezing

• Transmitted by:
  – Inhaling respiratory aerosols containing virus
  – Touching an infected person or an item contaminated with the virus and then touching your eyes, nose, or mouth
Seasonal Influenza:  
Minor Changes – Antigenic Drift

• Influenza A & B viruses
  – Results in new variants of prevailing strains every year
    • Result in seasonal influenza each winter
  – Some years are worse than others
    • partly related to degree of ‘drift’
  – Primarily Influenza A

• About 3-5 million severe global cases annually
  – Between 290,000 and 650,000 deaths*

Pandemic Influenza: Major Changes – Antigenic Shift

• Major changes occur in the surface antigens of influenza A viruses
  – Caused by mutation or reassortment

• More significant than those associated with antigenic drift

• Lead to the emergence of potentially pandemic strains
  – Creates a virus that is markedly different from recently circulating strains
  – People have no pre-existing immunity
Seasonal vs. Pandemic Influenza

• Pandemic influenza is not just a “bad flu,”
  – It is a wholly new threat to humans
• Compared to seasonal influenzas, pandemic influenzas infect
  – More people
  – Cause more severe illness
  – Cause more deaths
• Seasonal influenza viruses
  – Most often cause severe disease in the very young, the very old, and those with chronic illnesses
• Pandemic influenza strains
  – Can infect and kill young, healthy people
  – In the 1918-19 pandemic, very high mortality rate among people aged 20-40 years
Influenza Pandemics and Threats

<table>
<thead>
<tr>
<th></th>
<th>Years</th>
<th>Case Fatality</th>
<th>Subtype</th>
<th>Pandemic Severity Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918 Influenza (Spanish Flu)</td>
<td>1918-1920</td>
<td>2%</td>
<td>H1N1</td>
<td>5</td>
</tr>
<tr>
<td>Asian Flu</td>
<td>1957-1958</td>
<td>0.13%</td>
<td>H2N2</td>
<td>2</td>
</tr>
<tr>
<td>Hong Kong Flu</td>
<td>1968-1969</td>
<td>&lt;0.1%</td>
<td>H3N2</td>
<td>2</td>
</tr>
<tr>
<td>Russian Flu</td>
<td>1977-1978</td>
<td>N/A</td>
<td>H1N1</td>
<td>N/A</td>
</tr>
<tr>
<td>2009 Flu Pandemic</td>
<td>2009-2010</td>
<td>0.03%</td>
<td>H1N1/09</td>
<td>N/A</td>
</tr>
</tbody>
</table>
## Pandemic Severity Index

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Category 1</th>
<th>Category 2</th>
<th>Category 3</th>
<th>Category 4</th>
<th>Category 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case Fatality Ratio (percentage)</td>
<td>&lt;0.1</td>
<td>0.1 - &lt;0.5</td>
<td>0.5 - &lt;1.0</td>
<td>1.0 - &lt;2.0</td>
<td>≥ 2.0</td>
</tr>
<tr>
<td>Excess Death Rate (per 100,000)</td>
<td>&lt;30</td>
<td>30 - &lt;150</td>
<td>150 - &lt;300</td>
<td>300 - &lt;600</td>
<td>≥ 600</td>
</tr>
<tr>
<td>Illness Rate (percentage of the population)</td>
<td>20 - 40</td>
<td>20 - 40</td>
<td>20 - 40</td>
<td>20 - 40</td>
<td>20 - 40</td>
</tr>
<tr>
<td>Potential Number of Deaths (based on 2006 U.S. population)</td>
<td>&lt;90,000</td>
<td>90,000 - &lt;450,000</td>
<td>450,000 - &lt;900,000</td>
<td>900,000 - &lt;1.8 million</td>
<td>≥ 1.8 million</td>
</tr>
<tr>
<td>20th Century U.S. Experience</td>
<td>Seasonal Influenza (illness rate)</td>
<td>1957, 1968 Pandemic</td>
<td>None</td>
<td>None</td>
<td>1918 Pandemic</td>
</tr>
</tbody>
</table>
Influenza Season: 2018
We Knew It Was Coming:
Current Influenza Activity: Week 8

https://www.cdc.gov/flu/weekly/usmap.htm
What Should You Do During the Influenza Season?
Symptoms of Influenza

Central
- Headache

Systemic
- Fever
  (usually high)

Muscular
- (Extreme) tiredness

Joints
- Aches

Nasopharynx
- Runny or stuffy nose
- Sore throat
- Aches

Respiratory
- Coughing

Gastric
- Vomiting
Influenza Differential Diagnosis

- Acute Respiratory Distress Syndrome
- Adenoviruses
- Arenaviruses
- Cytomegalovirus
- Dengue Fever
- Echoviruses
- Hantavirus Pulmonary Syndrome
- HIV Disease
- Legionnaires Disease
- Parainfluenza Virus

Which ED Patients Should be Tested?

• **Immune-compromised and high-risk patients**
  – Presenting with influenza-like illness, pneumonia, or nonspecific respiratory illness (e.g., cough without fever)

• **Patients with exacerbation of chronic conditions**
  – E.g., asthma, COPD, heart failure

• **Patients with known complications of influenza**
  – E.g., pneumonia
Patients at Higher Risk of Complications

- Children aged <5 years (especially aged <2 years);
- Adults aged ≥65 years;
- Persons with chronic diseases:
  - Pulmonary (including asthma)
  - Cardiovascular (except hypertension alone)
  - Renal
  - Hepatic
  - Hematologic (including sickle cell disease)
  - Metabolic disorders (including diabetes mellitus)
  - Neurologic, neurodevelopment and muscle conditions, such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or prior spinal cord injury
Patients at Higher Risk (cont.)

• Persons with immunosuppression, including that caused by medications or by HIV infection;
• Women who are pregnant or postpartum (within 2 weeks after delivery);
• American Indians/Alaska Natives;
• Persons who are morbidly obese (i.e., BMI ≥40);
and
• Residents of nursing homes and other chronic-care facilities.
Which ED Patients Might be Tested?

• **Consider testing patients, who are not high risk and likely to be discharged**
  – Presenting with influenza-like illness, pneumonia, or nonspecific respiratory illness

• **If the testing will influence**
  – Treatment choice,
  – Further diagnostic testing
  – ED length of stay
What Specimens Should Be Collected?

- Collect **upper respiratory tract specimens** from outpatients for influenza testing as soon after illness onset as possible,
  - Preferably within 4 days of onset
- Nasopharyngeal > Combined nasal and throat swab > Mid-turbinate nasal swab > Throat swab
What Tests Should Be Used?

• Outpatient (ED) setting
  – Rapid molecular assays > Rapid Influenza Diagnostic Tests (RIDTs)

• Hospitalized patients
  – Multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses
<table>
<thead>
<tr>
<th>Influenza Diagnostic Test</th>
<th>Method</th>
<th>Availability</th>
<th>Typical Processing Time</th>
<th>Sensitivity</th>
<th>Distinguishing Subtype Strains of Influenza A</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid influenza diagnostic tests (RIDTs)</td>
<td>Antigen detection</td>
<td>Wide</td>
<td>&lt;30 minutes</td>
<td>10-80%</td>
<td>No</td>
<td>$</td>
</tr>
<tr>
<td>Direct and indirect immunofluorescence assays (DFA and IFA)</td>
<td>Antigen detection</td>
<td>Wide</td>
<td>1-4 h</td>
<td>70-100%</td>
<td>No</td>
<td>$</td>
</tr>
<tr>
<td>Viral cell culture</td>
<td>Virus isolation</td>
<td>Limited</td>
<td>3-10 d</td>
<td>100%</td>
<td>Yes</td>
<td>$$</td>
</tr>
<tr>
<td>Rapid cell culture (shell vials and cell mixtures)</td>
<td>Virus isolation</td>
<td>Limited</td>
<td>1-3 d</td>
<td>100%</td>
<td>Yes</td>
<td>$$</td>
</tr>
<tr>
<td>Nucleic acid amplification tests (including rRT-PCR)</td>
<td>RNA detection</td>
<td>Limited</td>
<td>1-6 h</td>
<td>86-100%</td>
<td>Yes</td>
<td>$$$</td>
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<tr>
<td>Rapid Influenza molecular assays</td>
<td>RNA detection</td>
<td>Wide</td>
<td>&lt;15 minutes</td>
<td>86-100%</td>
<td>No</td>
<td>$$$$</td>
</tr>
</tbody>
</table>

Who Should Be Treated?

- Patients, of any age, with documented or suspected influenza
  - Hospitalized, regardless of illness duration
  - Outpatients with severe or progressive illness, regardless of illness duration
  - Outpatients at high risk of complications from influenza
  - Pregnant women and those within 2 weeks postpartum
Who Might Be Treated?

• Outpatients with illness onset <2 days
• Symptomatic outpatients who have high risk household contacts
  – Especially if household contacts are severely immune-compromised
What Antivirals Should Be Used?

• A single neuraminidase inhibitor
  – E.g.: oral oseltamivir, inhaled zanamivir, or intravenous peramivir
  – Do not use a combination of neuraminidase inhibitors

• Treatment duration for uncomplicated influenza
  – 5 days
Issues with Oseltamivir

• Expensive:
  – $135 average retail price

• Common side effects
  – Nausea/vomiting
  – Diarrhea
  – Headaches
  – Nose bleeds

• Other side effects include:
  – Dizziness, mood changes, sleep problems, seizures, abdominal pain
When Should Co-Infections Be Considered?

- Severely ill patients
  - Respiratory failure, hypotension and fever
- Patients who deteriorate after initial improvement
- Patients who fail to improve after 3-5 days of treatment
Should adjunctive therapy be administered to patients?

• Clinicians **should not** administer
  – Adjuvant corticosteroid therapy
  – Routinely administer immune-modulation using immune globulin preparations
    • E.g. IVIg

• Remember symptomatic treatment
  – Rest, fluids, antipyretics (acetaminophen)
Protecting Yourself and Your Patients from Killer Respiratory Viruses
Disease Containment Measures

- **Isolation**: restriction of movement/separation of *ill* infected persons with a contagious disease

- **Quarantine**: restriction of movement/separation of *well* persons presumed *exposed* to a contagious disease

- **Self-shielding**: self-imposed exclusion from infected persons or those who may be infected

- **Social distancing/cohorting**: reducing interactions between people to reduce the risk of disease transmission

- **Snow days**: days on which offices, schools, transportation systems are closed or cancelled, as if there were a major snowstorm
Containing Pandemic Influenza

• Surveillance and diagnostic services
• Information sharing and dissemination
• Community support
• Hospital and physician capacity
• Supply and delivery of vaccines and drugs

— Note: There are significant concerns lack of surge capacity within the US health system to deal with significant influenza events
Special Report: Tracking the new killer viruses - MERS & H7N9 Bird Flu
Personal Transmission Reduction Methods

• Hand hygiene (cleaning hands with soap and water or an alcohol-based hand rub)

• Respiratory hygiene, e.g., “Cover your cough”

• Cleaning and disinfection of contaminated objects, surfaces

• Physical barriers (e.g., glass or plastic “windows” to protect front desk workers)

• Use of personal protective equipment (PPE) in some settings (e.g., healthcare) such as gowns, gloves, eye, and respiratory protection
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