What's the Big Deal about Influenza?

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Learning Objectives

- The participant will be able to discuss and describe:
  - Basic of Viral Structure and Function
  - Epidemiology and Clinical Presentations of Influenza
  - Elements of Influenza Prevention, Control and Intervention
  - Influenza Surveillance Activities
  - Basics of Pandemic Influenza

Really Short Answer

- Kills +/- 36,000 annually across age groups
- May lead to significant health complications
- Increases hospitalizations
- Expensive:
  - fiscally
  - socially
- Viral mutations can result in pandemics

‘Flu Facts

• What is Influenza?

Influenza aka "the flu" is a contagious respiratory illness caused by the influenza virus. Infection with influenza viruses causes illness ranging from mild to severe and life-threatening.

An Ancient Foe;
Origin of the name Influenza 15th century Italy
Epidemics attributed to "influence of the stars"

Cross Species Infectivity

YOU SHOULDN'T HEAR ABOUT THE FLU OR THE FLU.

YOU ARE A PAGAN!
Influenza Virus Types
- 3 types of influenza: A, B, C
- Influenza A and B viruses responsible for annual epidemics
- Influenza C produces mild disease and has not been associated with widespread outbreaks

Influenza Virus Types
- Characterized by ability to change continually and occasionally drastically
- Antigenic drift
  - Influenza A and B viruses
- Antigenic shift
  - Influenza A viruses only

Influenza Type C viruses
- Type C Influenza Viruses
  - Rarely reported as a cause of human illness
  - Most cases probably subclinical
  - Not associated with epidemic disease

Influenza Type A
- Type A influenza viruses:
  - Characterized by moderate to severe illness
  - Affect all age groups
  - Widely distributed in nature
  - Infect a wide variety of animal species (humans, pigs, birds, seals, whales)
  - Undergo antigenic shift and drift
    - Main cause of death among the high risk during epidemics

Structure of the Influenza A Virus
- 2 types of Spikes
  - #1 contains the enzyme hemagglutinin (H)
  - #2 contains the enzyme neuraminidase (N)
  - Both enzymes are antigens*

Role of the Spikes
- *antigen = chemical substance that stimulates a response by the immune system
**Influenza Antigens**

- **Hemagglutinin (H) spike**
  - Essential for viral attachment to the host cell membrane
  - 3 types with established lineage in humans:
    - H1
    - H2
    - H3

- **Neuraminidase (N) spike**
  - Essential for virus penetration into cells
  - Two types with established lineage in humans:
    - N1
    - N2

**Antigenic Drift**

- Gradual, continual process
- Result of an accumulation of point mutations in the HA and NA genes during viral replication
- Allows for repeated infections over a lifetime and recurrent epidemics
- Vaccine updated twice yearly

**Antigenic Shift**

- Replacement of HA or HA + NA (i.e. new subtype)
- Reassortment
- Adaptation of virus from non-human host
- Sporadic event
- Can result in pandemic

**Influenza Type B Viruses**

- Generally causes milder disease than type A
- No subtypes
- Primarily affects children; infects humans almost exclusively
- More stable than A with less antigenic drift with consequent immunologic stability

**Influenza: Nomenclature**

- **Virus Type**
  - Influenza A: HA and NA surface antigens type also contribute to the classification of the strain.

- **Geographic origin**
  - A/Sydney/5/1963 = influenza A strain + Sydney virus subtype + strain number 5/1963 (year) + hemagglutinin type + neuraminidase type + surface antigens:

- **Strain number**

- **Year of isolation**

- **Virus Subtype**
  - In animal viruses, the original host is also included in the classification A/Chicken/Swine/1976 (H3N8).

**Definitions**

- **Seasonal flu** is a contagious respiratory illness caused by influenza viruses
- **Pandemic flu** is flu that causes a global outbreak, or pandemic, of serious illness that spreads easily from person to person. Currently there is no pandemic flu.
- **Avian flu** is caused by avian influenza viruses, which occur naturally among birds.
Seasonal Influenza

- Acute, febrile respiratory illness affecting nose, throat, bronchial tubes and lungs; symptoms appear rapidly.
- Epidemics caused by influenza viruses A and B. (Type C uncommon in people; no epidemics)
- Occurs worldwide, causing considerable morbidity and mortality each year.
- Systemic Symptoms:
  - Last 2-3 rarely > 5 days
  - Recovery usually rapid; some experience lingering depression and asthenia for several weeks
  - Palliative treatment includes aspirin* or acetaminophen
  * Aspirin should NEVER be used for infants, children or teens. Reye Syndrome Concerns
- Occurrence: worldwide.
- Communicability (Infectious Period):
  - Adults can shed virus 1 day before to 5 days after onset
  - Children can shed > 10 days
- Chronic Carrier state: NO
- Temporal Pattern: year round in tropical areas. Peaks from December-March in temperate climates
- Incubation: 1-4 days; average of 2 days

Influenza: A Viral Pirate

- The virus particle lands on the cell surface
- Genetic information + cell nucleus
- viral genome + new viral components + new virus particles
- Budding + infect other cells

“Droplet” Transmission

- Flu virus is present:
  - In large droplets expelled when you cough or sneeze, which fall quickly to the ground or onto surfaces.
  - On the hand of ill people.
- Transmission occurs:
  - Usually from direct hand-to-hand or hand-to-surface contact.
  - Flu virus on the hands is easily transferred to the eyes, nose and mouth where flu virus can enter the body and cause infection
  - Less frequently by direct inhalation of flu virus in the air.
- Implication: hand washing is as important as respiratory precautions.

What is “Droplet Transmission”?

- Droplets from a cough or sneeze of an infected person are propelled (generally up to 3 feet) through the air. Droplet Precautions include:
  - Placing masks in a private room or cohort, when non-patient contact is necessary in patient care
  - Wearing a mask when working within 3 feet of patient
  - Limiting patient transport and visits to a minimum if patient is symptomatic.

Influenza: A Viral Pirate

- Classic Influenza:
  - abrupt onset of fever, sore throat, myalgia and non-productive cough
  - Fever usually 101-102°F, often with prostration
  - Myalgia usually affect back muscles
  - Patients can often recall exact hour of onset; may say “feels like a truck hit me”
**Influenza Love Poem**

I shall seek you and find you...
I shall take you to bed and control you...
I will make you ache, shake and sweat until you groan...
I will make you beg for mercy...
I will exhaust you to the point that you will be relieved when I leave you...
and you will be weak for days.
All my love,
The flu.

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**Influenza: Treatment, Prevention and Control**

- Antiviral Therapy
- Vaccination
- Infection Control
- Diagnostic Testing
- Surveillance

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**Answer Summary**

Check Out "Epidemiology and Prevention of Vaccine-Preventable Disease" ed. "The Pink Book" pub. April 2013

- Influenza causes +/- 36,000 excess deaths per year
- >95% of deaths in people >65 years of age
- Highest rate of complications in senior and young children age 0-4 years
- Average of >200,000 influenza-related hospitalizations annually; 57% among people < age 65
- Nursing home attack rates may = 60% with facility rates as high as 30%
- H3N2 years see even higher rates of hospitalizations
- Estimated cost of a severe epidemic = $12 billion
- Antiviral therapy can
- 
- Antiviral therapy should be initiated within 48 hours of symptom onset
- Antivirals (prophylaxis) to prevent illness in:
  - Persons at high-risk for complications
  - To control outbreaks in nursing homes and other institutions

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**Antivirals**

- Drug resistant viruses can
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- Drug resistant viruses can emerge
- Some strains of flu no longer respond to the most common antiviral drugs
- "Resistant generation" of antivirals (oseltamivir, zanamivir) remains in limited supply
- Not a substitute for vaccination

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**Vaccination**

- In young adults, routine 70-90% effectiveness against clonally and immunocompromised, common circulating strains
- Vaccination is not very effective in reducing illness severity, complications (70%) and deaths (50%)
- Antigens vary:
  - Antigens vary:
    - Antigenic drift:
      - Antigenic drift:
        - Antigenic drift:
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**World Health Organization Meeting**

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This is why major epidemics of influenza recur regularly and why new vaccines have to be developed and produced every year to be effective.
Flu Vaccine is Effective

- Actual efficacy depends on degree of similarity between viruses in vaccine and viruses in circulation currently.
- Vaccine strains chosen 9-10 months prior to influenza season, based on WHO lab data.
- Vaccine efficacy may be reduced because of changes in circulating strains.

- Individuals ≥65 years of age who received influenza vaccine have reduced risk of hospitalization for:
  - Heart disease (reduction of 19%)
  - Stroke (reduction of 16%-23%)
  - Pneumonia (reduction of 25% to 32%)
  - Risk of death from all causes (reduction of 48%-50%)

Influenza Vaccines

- Most efficient method to control influenza
- Must be administered annually
- 2 vaccines available
  - Trivalent inactivated vaccine
  - Live attenuated vaccine

When to Get Vaccinated

- October and November are best times.
- As flu has historically peaked between late December-early March, vaccination efforts should continue through December and beyond.
- It takes about 2 weeks to become immune post vaccination.
- Unsure about getting vaccinated this year??

Infection Control Measures

- respiratory hygiene/cough etiquette
- hand hygiene
- environmental cleaning
- social distancing

What is Respiratory Hygiene/Cough Etiquette?

- Cover mouth/nose when sneezing or coughing
  - If no tissue, use elbow instead of hands
- Use tissues and dispose of appropriately
- Perform hand hygiene after contact with respiratory secretions
- Distance yourself from others (more than 3 feet)

H3N2 virus has been most common in past few decades
- (Letters "H" and "N" refer to molecules on the surface of the virus)
- H3 years tend to be more severe and Southern Hemisphere is reporting H3 this season!
Influenza: Prevention

Cover your nose and mouth
- Cover your mouth and nose with a tissue when coughing or sneezing

Individual Infection Control Strategies

- Respiratory hygiene/cough etiquette and hand hygiene are effective strategies to stop the spread of germs.
- We should make good hygiene a habit now.

What is Hand Hygiene?

- Traditional hand washing
  - Soap and warm water
  - Minimum of 20 seconds (the time it takes to sing "Happy Birthday" twice)
- Alcohol based hand rubs
  - Acceptable means to disinfect/sanitize EXCEPT when hands are visibly soiled

Policy and Personal Decision

Avoid close contact
- Avoid close contact with people who are sick
- When you are sick, keep your distance from others to protect them from catching your illness
- If possible, stay home from work, school, and outside when you are sick. You can help prevent others from catching your illness.

Influenza: Prevention and Control in Healthcare Facilities

- DROPLET CONTACT PRECAUTIONS
  - USE OF GLOVES, GOWNS, MASKS
  - INFECTIOUS WITHIN 3 FEET OF PATIENT
  - CONTAMINATED SURFACES
- DROPLET HYGIENE ETIQUETTE
  - INCORPORATE INTO INFECTION CONTROL PRACTICES
  - DISCOURAGE VISITORS WITH RESPIRATORY SYMPTOMS
- RESTRICT ILL HEALTHCARE WORKERS
- VACCINATION OF RESIDENTS AND HEALTHCARE WORKERS
- IDENTIFY OUTBREAKS
- REPORT TO REGIONAL EPIDEMIOLOGIST
- REPORT TO YOUR LOCAL DEPARTMENT OF HEALTH
Institutional Outbreak Control

Prior planning key to minimizing impact
- Ensure vaccine and antiviral stock
- Educate staff, visitors, patients, families
- Isolate suspected cases and contacts
- Increase room air ventilation
- Prompt diagnosis and institution of control measures

Control Measures
- Early detection and control
- Prevent introduction
- Limit spread within facilities
- Notify and isolate staff and visitors
- Provide宣传教育 for patients and visitors
- Isolate to borders for non-severe and severe

Environmental Disinfection

- Disinfectants that are currently in use should be sufficient to kill the flu virus
- Influenza viruses typically live on inanimate objects for several hours
- Increased environmental cleaning during any cold/flu season should be a part of an infection control program

Influenza: Diagnosis

- Viral culture*
  - only culture isolates can provide specific information regarding circulating influenza subtypes and strains

- Rapid antigen testing*
  - 30 minutes
  - Differentiate between A & B
  - Back-up negatives with culture??

Influenza Surveillance Objectives

Determine:
- which viruses are circulating, where and when they are circulating
- intensity and impact of influenza activity strains and detect new strains
- recent unusual events
- Infection by unusual viruses
- Unusual syndromes caused by influenza viruses
- Unusually large/severe outbreaks of influenza

- Rapid outbreak detection
- Assist disease control through rapid preventive action
- Estimate influenza-related morbidity, mortality and economic loss

Global Surveillance

- World Health Organization Initiative
- Emerging Infections
- Enhanced Communications

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Influenza: Surveillance Systems

- Sentinel Family Physician Network
- Nosocomial Reporting
- Local Health Departments
- Pneumonia and Influenza Mortality Process
- Laboratory Surveillance
  - WHO/INREV virology labs
  - 13 in NYS participate
- HERDS
- Pediatric Death Reporting

Internet sites for influenza surveillance

- NYSDOH:
  www.health.state.ny.us/nysdoh/flu/index.htm
- CDC:
  www.cdc.gov/flu/weekly/fluactivity.htm

Internet sites for avian influenza surveillance

- CDC:
  http://www.cdc.gov/flu/avian/
- WHO:
  http://www.who.int/csr/disease/avian_influenza/en/
- NYSDOH:
  - HAN Advisory dated February 17, 2004:
    "Respiratory Illness Surveillance for Influenza (H5N1) and SARS"
    https://www.health.state.ny.us/topics/infectiousdisease/avianflu/advisory211.pdf

Seasonal vs. Pandemic Flu

A pandemic is a world-wide epidemic.
Pandemics result from the emergence of a new virus to which the overall population has no immunity.

Unlike seasonal flu, which typically affects the elderly, frail, sick and young, pandemic flu could present as much risk to the young and healthy.

Could begin at any time of year.
Asia is the source of many outbreaks
- ex: current Avian Influenza Outbreak

"The pandemic clock is ticking, we just don't know what time it is"

E. Marcuse
What is an influenza pandemic?
- Worldwide outbreak of a novel influenza virus
- Occur infrequently and at irregular intervals
- Potential for substantial impact
  - Morbidity and mortality: 18-42 million outpatient care, 314,000-734,000 hospitalization, 89,100-207,000 deaths
  - Social disruption
  - Economic costs

How does this happen?
- 4 key factors must be present
  - Novel virus
  - Reassortment of animal and human viruses
  - Direct transmission of animal virus to humans
  - Adaptation of non-human virus in intermediate host prior to transmission to humans
  - Susceptible population
  - Virus capable of causing disease in humans
  - Virus that is transmissible from person-to-person

The Great Influenza Pandemic 1918-1919
"For a period of approximately eighteen months influenza ravaged the world, claiming three times the number of lives lost in World War One. It was the worst plague in recorded history, killing more people in a shorter time than even the Black Death of the fourteenth century."

References: Brumley, W. Influenza: The Last Great Plague (1977); Oxford, Alison, Epidemics and Peace, 1918 (1973)

Bird Flu—What's the Big Deal?
- Avian strains can infect humans
- Re-assortment of avian and human strains to create novel strain (antigenic shift)
- Efficient person-to-person transmission
- Little/low immunity/protection to new virus
- Probable higher morbidity/mortality
- Pandemic influenza

Pandemic Strain Emergence: Reassortment of Influenza A Viruses
- Direct Avian - Human Infection
- New reassorted virus
- Other mammal

Pandemic Strain Emergence: Direct Infection
**H5N1 Transmission to Humans**

People who have gotten sick from bird flu had close contact with sick birds and touched them with their bare hands.

Infected birds shed virus in their saliva, nasal secretions, and feces.

Food - oral transmission

Virus from bird droppings can remain in the environment for several weeks.

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**If a Pandemic happens, what to expect...**

- At the peak of a moderately severe pandemic influenza outbreak (i.e. 35% attack rate, 6-week duration), New York State (excluding New York City) can expect:
  - 14,916 influenza-related hospital admissions per week
  - 3,728 influenza-related deaths per week
  - 2,609 deaths in the hospital

- Influenza patients will most likely utilize:
  - 65% of hospital bed capacity
  - 125% of intensive care capacity
  - 65% of hospital ventilator capacity
  - Resource allocation ethical issues

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**General Pandemic Planning Concepts**

- Goals
  - Limit total burden of disease (morbidity & mortality)
  - Decrease social disruption
  - Decrease economic loss
  - Engage all levels of health care system, public health, and emergency response
  - Include public and private sectors
  - Key similarities & differences between pandemic response & other health emergencies
  - Planning, resources, & implementation

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**Will Avian Flu Cause the Next Pandemic?**

- No one knows!

- The H5N1 virus could change to spread more easily among humans—but it might not.

- It could "swap genes" with another animal virus, or with a human flu virus.

- Earth's may vary or may not be lower than with current human H5N1 cases

- Evidence to date finds very few "sub-clinical" cases

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**Influenza Resources**

- [www.cdc.gov](http://www.cdc.gov)
  - U.S. public health guidelines

- [www.pandemicflu.gov](http://www.pandemicflu.gov)
  - U.S. pandemic plan

- [www.who.int](http://www.who.int)
  - Global updates and official case reports

- [www.nyhealth.gov](http://www.nyhealth.gov)
  - New York State surveillance summaries
One day on the road in the English countryside, a clergyman happened to meet the plague.

"Where are you bound?" asked the clergyman. "To London," responded Plague. "To kill a thousand!" They shared a few moments longer, then parted.

Some months later they chanced to meet again, and the clergyman inquired, "As I recall, you were going to kill a thousand. How is it that two thousand died?" "Ah, yes," replied Plague. "I killed but a thousand. Fear killed the rest."

The End and a bit of History

1918 Influenza Fluctuations
Precautions:
- Wearing caputum balls or public balls
- Confining bedpan or penning while
- Blocking with a sheet by the bed
- Public Health:
- Postponed events and social walks
- Periods of daily hours
- Prohibited public and open streets
- Law enforcement:
- Arrested people for not wearing masks and spitting in the streets
- Schools Closed
- Homework placed on paper
- Students wrote in assignments