CDC Influenza Epidemiology and Surveillance

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Outline

• Biology of influenza
• Impact of seasonal influenza in U.S. and the world
• U.S. and worldwide influenza surveillance
• Drift of viruses
Influenza background
Influenza Virus

- Eight RNA segments code for 11 proteins
- Virus needs one of each of the 8 gene segments to be viable
- HA (hemagglutinin) and NA (neuraminidase) genes code for surface proteins
- Other genes are responsible mostly for virus structure and replication
Influenza virus transmissibility

- Influenza transmission not fully understood
  - Large droplets: coughing, sneezing
  - Airborne droplet nuclei
  - Direct and indirect fomite contact possible
- Incubation 1 - 4 days
- Infectious from 1 day before to 3-7 days after symptom onset
  - Longer in children and immune compromised
Symptoms of influenza infection

- Acute febrile respiratory infection
  - Abrupt onset fever, chills, muscle aches, headache, fatigue
  - Cough, pharyngitis, rhinitis
- Varies by age
  - GI symptoms (↑ in children)
  - Elderly often without fever
- Sepsis-like syndrome in infants
Complications from influenza

- Primary viral pneumonia
- Secondary bacterial pneumonia
- Bronchitis
- Sinus infections
- Ear infections
- Worsening of underlying illness, e.g., asthma, CHF
- Hospitalization (less frequent)
- Death (less frequent)
Groups at High Risk for Serious Complications

- Persons with chronic conditions
  - Heart or lung disease (asthma); blood or endocrine disorders (diabetes); kidney, liver, and metabolic disorders; neurologic conditions; immunosuppression (HIV/AIDS, cancer); and the morbidly obese
- Children <5 (especially <2 years old)
- Adults ≥65 years of age
- Pregnant women
- American Indian and Alaskan Natives
- Persons <19 receiving long-term aspirin therapy
Types and subtypes of the influenza virus

• Type A
  • Subtypes determined by surface proteins HA (1-18) and NA (1-11)

• Type B
  • Divided into 2 distinct lineages (Victoria and Yamagata)

• Type C
  • Does not typically cause substantial human disease, not routinely tested for
An Ever Changing Virus (1)

- Can change in two different ways
  - Antigenic drift and antigenic shift

- Antigenic drift refers to small changes that happen continually over time (Types A&B)
  - Results in need to get flu vaccine each year to be protected against current influenza viruses
Antigenic shift refers to an abrupt, major change in that results in a new influenza A subtype (e.g. H2N2)

Also occurs when an influenza A subtype from animals emerges that is different from the same subtype in humans

- Results in little population immunity to the new (novel) virus
- Occurred in 2009: H1N1 virus with a new combination of genes (from American pigs, Eurasian pigs, birds, and humans) emerged in people, causing a pandemic

Influenza viruses constantly changing by antigenic drift

Antigenic shift happens only occasionally
Influenza Type A

- Current human subtypes: H1N1 & H3N2
- Infects multiple species besides humans
  - Birds, swine, horses, whales, seals
  - Capacity for ‘species jumping’
- Birds reservoir for new subtypes
  - H1 - H18 (bats: H17,H18)
- Capable of epidemics and pandemics
Influenza A susceptible hosts
### Influenza A HA and NA Subtypes

<table>
<thead>
<tr>
<th>H1</th>
<th>N1</th>
<th>Other animals</th>
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<tbody>
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<td>N2</td>
<td></td>
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<tr>
<td>H3</td>
<td>N3</td>
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<tr>
<td>H4</td>
<td>N4</td>
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<td>H18</td>
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</table>
Generation of new influenza A subtypes

Nonhuman virus

Human virus

Reassortant pandemic strain
Timeline of the emergence of major influenza A subtypes

Human influenzas
- H1
- H2
- H3

Avian influenzas
- H5
- H7
- H9

Variant influenzas
- H1–H3v

Timeline:
- 1918
- 1957
- 1968
- 1977
- 1997
- 1998/9
- 2003
- 2009
- 2015
Impact of Influenza, Seasonality, and Drift
United States
Seasonal Activity in the U.S.

- Occurrence is "predictable"
  - Peak of activity in winter
- Individual seasons unpredictable
  - Onset & peak of activity
  - Pattern and duration of geographic activity
  - Predominant strain(s)
  - Public health impact (attack rate and severe outcomes)
Seasonal Impact in the U.S.: Hospitalization

- Average of 226,054 influenza-associated respiratory and circulatory hospitalizations per year
- Rates highest in children < 5 years and adults ≥ 65 years
- Rates highest in A(H3N2) years

Seasonal Impact in the U.S.: Deaths

- Average of 23,607 influenza-associated respiratory and circulatory hospitalizations per year (range: 3,349–48,614)
- Highest in A(H3N2) years
- Most deaths in adults ≥ 65 years

How are data collected on influenza activity and seasonality in the U.S.?
Five Categories of Influenza Surveillance

- Virologic Surveillance
  - WHO (World Health Organization) and NREVSS (National Respiratory and Enteric Virus Surveillance System) Collaborating Laboratories
  - Novel influenza A virus reporting
- Outpatient Illness Surveillance
- Hospitalization Surveillance
- Mortality Surveillance
- Summary of the Geographic Spread of Influenza
- Summarized weekly in FluView (www.cdc.gov/flu)
Outbreak Investigations

• Done in response to unusual outbreaks of seasonal or novel influenza
• Can either be in the field or coordinated from Atlanta
  • Emergency Operations Center
• Recent Examples
  • H7N9 outbreak in China (2013/14)
  • Seasonal outbreak in Ohio at residential facility for children with severe neurologic/neurodevelopmental conditions (2011)
  • H3N2v outbreak among fairgoers in Ohio (2012) and Pennsylvania (2011)
What about vaccine effectiveness (VE)?
US Flu VE Network: 5 Sites and Principal Investigators

Group Health Cooperative
Lisa Jackson
Mike Jackson

Marshfield Clinic Research Foundation
Ed Belongia

University of Michigan
Arnold Monto
Suzanne Ohmit

Baylor Scott and White Health
Manju Gaglani

University of Pittsburgh
Rick Zimmerman
Patricia Nowalk
CDC-supported seasonal vaccine effectiveness studies, 2005–2013

- Case-control
- Outcomes – Medically attended acute respiratory illness
- PCR-confirmed
- Controls are influenza-negative
- VE estimated using logistic regression

<table>
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<tr>
<th>Year</th>
<th>Site</th>
<th>No.</th>
<th>VE (%)</th>
<th>95% CI</th>
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<td>WI</td>
<td>356</td>
<td>10</td>
<td>-36, 40</td>
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Refs: http://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm
The World
Global Seasonality of Influenza

- Seasonal epidemics in temperate regions
  - Severity varies from year-to-year
  - Most available data from industrialized countries
- Year-round activity in tropical and subtropical climates
  - Equatorial Africa, Southeast Asia
  - Very limited data on disease burden
- Sporadic outbreaks
  - Rural populations
- Travelers
  - Cruise Ships
Seasonal Occurrence of Influenza

Relative Influenza Activity

JAN   FEB    MAR  APR   MAY  JUN   JUL   AUG  SEP  OCT   NOV DEC

N. Hemisphere Temperate
Tropical
S. Hemisphere Temperate

(Reichelderfer PS, et al. Current Topics in Medical Virology, 1988)
Global Burden of Influenza

- Largely unknown
- Data from temperate climates
- One billion cases of influenza
- Estimated 3-5 million severe cases/year
- Estimated 300,000 - 500,000 deaths/year

http://www.who.int/mediacentre/factsheets/fs211/en/
How are data collected on influenza activity and seasonality worldwide?
The WHO Global Influenza Program

• 1947 WHO Global influenza system initiated
  – First WHO Collaborating Center in UK
• Global Influenza Surveillance and Response System (GISRS)
  – Established in 1952 as the Global Influenza Surveillance Network (GISN) comprised of National Influenza Centers (NICs)
  – Changed name to GISRS in 2011
• Excellent example of international collaboration and cooperation
Objectives of GISRS

• Monitor circulating influenza viruses to determine new antigenic variants worldwide to update the vaccine annually
• Serve as the “early warning system” for novel influenza viruses
• Understand the impact of influenza on populations to guide policy and resource decisions
WHO Influenza Network
How does GISRS achieve their objective?

- Monitors emergence and spread of influenza variants
- Records levels of influenza activity by country/region
- Distributes reagents worldwide for identifying influenza viruses
- Disseminates information
- Makes twice yearly recommendations for influenza vaccine composition
- Pandemic planning
WHO GISRS

National Influenza Centers
(~136 Laboratories in 106 Countries)
- Isolate influenza viruses
- Identify viruses and send to International Collaborating Center(s)
- Collect epidemiologic information
- May coordinate in-country networks

World Health Organization
(Geneva)
- Collect information for the Weekly Epidemiological Record (WER) for distribution
- Make annual vaccine recommendations

International Collaborating Centers
(Atlanta, Beijing, London, Melbourne, Tokyo)
- Analyze influenza viruses received
- Provide data for annual vaccine recommendations
- Prepare and distribute candidate vaccine strains

Vaccine Producers
What does this data show us about virus evolution and migration?

H3N2 as an example

Antigenic drift of H3N2, 2002–2007

- Figure shows antigenic distance from A/Sydney/5/1997 plotted against time of isolation
- One unit corresponds to a twofold dilution of antiserum in the HI assay
  - Two units generally be considered enough difference to warrant vaccine update
- Antigenic evolution has been similar on a global scale

Global patterns of drifted H3N2

- New drifted strains of H3N2 appeared in east and Southeast Asia (E-SE Asia) on average 6–9 months before other regions.
- Long delays for drifts to appear in South America.
- No country in E-SE Asia consistently was the source of these viruses.

Black circles indicate the average antigenic distance from the best fit line for all strains isolated in a region, and the thin horizontal black line indicates the standard error of the mean. Colored circles split this overall average by epidemic; circle color indicates time.

H3N2 Drift, summary

- H3N2 virus epidemics worldwide were seeded by viruses originating in E-SE Asia
  - Overlapping epidemics in E-SE Asia create a circulation network within the region
  - E-SE Asian drift viruses first seed epidemics in Oceania, North America, and Europe and later in South America
  - Direction is mostly one way, suggesting that once H3N2 viruses leave E-SE Asia, they no longer contribute to long-term viral evolution

Conclusions

- Influenza viruses constantly changing and emerging
- Influenza burden of disease substantial
- Seasonal and pandemic influenza unpredictable and can vary in origin, duration, and impact
- U.S. and worldwide influenza surveillance systems overlap and work together to provide comprehensive regional, national, and local situational awareness
- Seasonal and novel influenza require constant vigilance and investigation
Thank You!

Questions?

For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov  Web: www.cdc.gov

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