INFLUENZA PREDICTABILITY

W. Paul Glezen, M.D

Baylor College of Medicine
Objectives

- Discuss potential candidate viruses for the 2010-2011 influenza season.
- Review the variability of influenza viruses related to:
  - Virulence
  - Antigenicity
  - Timing of emergence
Continuing Education

Requirements for successful completion:

- Complete registration form
- Sign In
- Attend entire educational activity
- Complete evaluation
Continuing Education Disclosures

❖ Commercial Support
  • This educational activity received no commercial support.

❖ Disclosure of Conflict of Interest
  • The planning committee members have disclosed no conflict of interest.
  • Dr. Glezen is the study chair of the Central Texas Field Trial supported by an investigator-initiated grant funded by MedImmune Vaccines.

❖ Non-Endorsement Statement
  • Accredited status does not imply endorsement by the Department of State Health Services, Continuing Education Services, Texas Medical Association, or American Nurses Credentialing Center of any commercial products displayed in conjunction with an activity.

❖ Off Label Use
  • If applicable, speakers will clearly delineate any off label use of FDA drugs or devices.
Age Specific Rates of Medically Attended Acute Respiratory Illness (MAARI)
Houston, 1981-83
Glezen et al: J Infect Dis 1987; 155:1119-26
Figure 3. Rates of hospitalizations with acute respiratory disease for children less than five years of age and for persons five years and older in Harris County (Houston), Texas, 1981-1983.
- Influenza Herald Wave, 1976
NUMBER OF PATIENTS WITH FEBRILE RESPIRATORY ILLNESSES AND NUMBER POSITIVE FOR INFLUENZA VIRUSES WITH INFLUENZA A/Texas Herald Wave, Houston, 1976-78

Number of Cultures

Week No.: 35 40 45 50 5 10 15 20 25 30 35 40 45 50 5 10 15 20 25

Number Positive

B/Hong Kong

Influenza A/USSR

Influenza A/Texas - A/Victoria

Febrie Respiratory Illness
NUMBER OF PERSONS WITH RESPIRATORY ILLNESSES AND NUMBER WITH INFLUENZA A/USSR AND A/BRAZIL INFECTIONS
HOUSTON, 1977 - 1979

NUMBER POSITIVE

INFLUENZA A/USSR

INFLUENZA A/BRAZIL

NUMBER OF PATIENTS TESTED

WEEK NUMBER:

1977  1978  1979

25  30  35  40  45  50  5  10  15  20  25  30  35  40  45  50  5  10  15  20  25
### Shift in Age Distribution of Persons with Culture-Positive Illness Presenting to Sentinel Clinics during Influenza Epidemics, Houston, 1974-1981

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Early (%)</th>
<th>Peak (%)</th>
<th>Late (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>236(18.4)</td>
<td>489(24.3)</td>
<td>248(24.5)</td>
</tr>
<tr>
<td>5-19</td>
<td>687(53.6)</td>
<td>741(36.8)</td>
<td>356(35.2)</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>359(28.0)</td>
<td>785(39.0)</td>
<td>407(40.3)</td>
</tr>
<tr>
<td>Total</td>
<td>1,282</td>
<td>2,015</td>
<td>1,011</td>
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</table>
Epidemic Period

After School Holiday

Percentage

Years

Epidemic Period

Interrupted by School Holiday

Percentage

Epidemic Period

<5

6-19

>19

Early  Peak  Late

Early  Peak  Late
<table>
<thead>
<tr>
<th>Year</th>
<th>Month Epidemic Started</th>
<th>Virus</th>
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<tbody>
<tr>
<td>2000-2001</td>
<td>November 2000</td>
<td>A (H1N1)</td>
</tr>
<tr>
<td>2001-2002</td>
<td>January 2002</td>
<td>A (H3N2)</td>
</tr>
<tr>
<td>2002-2003</td>
<td>November 2002</td>
<td>B (Victoria Lineage)</td>
</tr>
<tr>
<td>2003-2004</td>
<td>October 2003</td>
<td>A (H3N2)</td>
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</tbody>
</table>
Texas Influenza Activity

School district/campus closures due to flu-like illness

9/29/02 to 4/5/03
Hemagglutinin Subtypes of Influenza A Virus

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Human</th>
<th>Swine</th>
<th>Horse</th>
<th>Bird</th>
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</thead>
<tbody>
<tr>
<td>H1</td>
<td></td>
<td>🐷</td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H2</td>
<td></td>
<td>🐷</td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H3</td>
<td></td>
<td>🐷</td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H4</td>
<td></td>
<td></td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H5</td>
<td></td>
<td></td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H6</td>
<td></td>
<td></td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H7</td>
<td></td>
<td></td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H8</td>
<td></td>
<td></td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H9</td>
<td></td>
<td></td>
<td>🐴</td>
<td>🐦</td>
</tr>
<tr>
<td>H10</td>
<td></td>
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<td>🐦</td>
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<tr>
<td>H11</td>
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<td>🐦</td>
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<td>H12</td>
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<td>🐦</td>
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<td>H13</td>
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<td>🐦</td>
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<td>H14</td>
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<td>🐦</td>
</tr>
<tr>
<td>H15</td>
<td></td>
<td></td>
<td>🐴</td>
<td>🐦</td>
</tr>
</tbody>
</table>
Influenza Virus Nomenclature

**Type of Nucleoprotein**

**Hemagglutinin**

**Neuraminidase**

**A/USSR/90/77 (H1N1)**

- **Virus Type**
- **Geographic Origin**
- **Strain Number**
- **Year of Isolation**
- **Virus Subtype**
FluMist®: Preparation of Vaccine Strains

Reassortants for each of three vaccine strains are derived by coinfection.

Master donor virus

New wild-type strain

Co-infect cells

Six genes from MDV confer attenuation

HA and NA genes from wild-type confer immunity

### Antigenic Variants of Influenza A (H3N2) and Changing Hemagglutinin Amino Acid Positions

<table>
<thead>
<tr>
<th>Year</th>
<th>Variant</th>
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<tbody>
<tr>
<td>1968-72</td>
<td>A/Hong Kong/68</td>
</tr>
<tr>
<td>1972-73</td>
<td>A/England/72</td>
</tr>
<tr>
<td>1974-75</td>
<td>A/Port Chalmers/73</td>
</tr>
<tr>
<td>1974-75</td>
<td>A/Victoria/75</td>
</tr>
<tr>
<td>1977-78</td>
<td>A/Texas/77</td>
</tr>
<tr>
<td>1980-83</td>
<td>A/Bangkok/79</td>
</tr>
<tr>
<td>1984-85</td>
<td>A/Philippines/73</td>
</tr>
<tr>
<td>1985-86</td>
<td>A/Stockholm/85</td>
</tr>
<tr>
<td>1987-88</td>
<td>A/Sichuan/87</td>
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<tr>
<td>1989-90</td>
<td>A/Shanghai/87</td>
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<td>1991-92</td>
<td>A/Beijing/89</td>
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<td>1993-94</td>
<td>A/Beijing/92</td>
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<tr>
<td>1994-95</td>
<td>A/Shangdong/93</td>
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<tr>
<td>1995-96</td>
<td>A/Johannesburg/94</td>
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<tr>
<td>1996-97</td>
<td>A/Wuhan/95</td>
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<td>1997-00</td>
<td>A/Sydney/97</td>
</tr>
<tr>
<td>2001-02</td>
<td>A/Panama/99</td>
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<tr>
<td>2003-04</td>
<td>A/Fujian/02</td>
</tr>
<tr>
<td>2004-05</td>
<td>A/California/04</td>
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<tr>
<td>2005-06</td>
<td>A/Wisconsin/05</td>
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</table>

Position of amino acid differences in pair 4 on the hemagglutinin trimer looking down the three-fold axis. Amino acids 2 and 6 are at the carboxy terminus and cannot be seen in this orientation.

<table>
<thead>
<tr>
<th>Gene segment</th>
<th>Year</th>
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<tbody>
<tr>
<td></td>
<td>1968</td>
</tr>
<tr>
<td>PB1</td>
<td><strong>Avian</strong></td>
</tr>
<tr>
<td>PB2</td>
<td>Human</td>
</tr>
<tr>
<td>PA</td>
<td>Human</td>
</tr>
<tr>
<td>HA</td>
<td><strong>Avian</strong></td>
</tr>
<tr>
<td>NA</td>
<td>Human</td>
</tr>
<tr>
<td>NP</td>
<td>Human</td>
</tr>
<tr>
<td>M</td>
<td>Human</td>
</tr>
<tr>
<td>NS</td>
<td>Human</td>
</tr>
</tbody>
</table>

*1968 and 1957 viruses were reassortants of human and avian strains.
The 1918 virus was an avian strain that mutated to allow human-to-human transmission.
Several viruses have been sequenced

Unusual constellation of genes derived from 2 swine viruses has resulted in a virus capable of human-to-human spread

EURASIAN SWINE VIRUS  X  NORTH AMERICAN SWINE VIRUS (present >10 yrs)

HUMAN H1N1 VIRUS

NA  PB1 (HUMAN)
M  PA, PB2 (AVIAN)

HA, NP, NS (SWINE)
Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, October 1, 2006 – January 23, 2010
Number of Influenza-Associated Pediatric Deaths by Week of Death: 2006-07 season to present

2006-07
Number of Deaths Reported = 78

2007-08
Number of Deaths Reported = 88

2008-09
Number of Deaths Reported = 132

2009-10
Number of Deaths Reported = 248

Legend:
- Yellow: 2009 Influenza A (H1N1) Deaths Reported Current Week
- Purple: 2009 Influenza A (H1N1) Deaths Reported Previous Weeks
- Cyan: Other Influenza Deaths Reported Current Week
- Green: Other Influenza Deaths Reported Previous Weeks
Timeline of Emergence of Influenza Viruses in Humans

- H1: Spanish Influenza (1918)
- H2: Hong Kong Influenza (1997)
- H3: Russian Influenza (1977)
- H5, H9, H7: Avian Influenza
- nH1

Year Timeline:
- 1918
- 1957
- 1968
- 1977
- 1997
- 2004
- 2009

CDC
Annual Impact of Seasonal Influenza in the US: Measuring Disease Burden and Costs

- **Annual Disease Burden** based on 2003 US population
  - 610,660 life-years lost
  - 3.1 million hospitalized days
  - 31.4 million outpatient visits

- **Annual Costs**
  - Direct medical costs: $10.4 billion
  - Direct cost and projected lost earning: $16.3 billion
  - Total economic burden (using projected life values): $87.1 billion

NAM Molinari et al., Vaccine 2007;25:5086 (Immunization Service Division, CDC)
Areas with confirmed human cases of H5N1 avian influenza since 1 January 2010 *

Status as of 06 May 2010
Latest available update

Country, area or territory
Cases: cumulative number
Deaths: cumulative number

Areas with confirmed human cases

* All dates refer to onset of illness

Egypt
Cases: 19
Deaths: 7

Viet Nam
Cases: 7
Deaths: 2

Cambodia
Cases: 1
Deaths: 1

Indonesia
Cases: 3
Deaths: 2

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2010. All rights reserved.

Data Source: WHO
Map Production: Public Health Information and Geographic Information System (GIS)
World Health Organization
PROBABILITY OF INFLUENZA PREVALENCE FOR 2010-2011

1. Influenza A(H1N1) 2009 (Novel or Pandemic H1N1)
2. Influenza A/Perth/2009 (H3N2)
3. Influenza B lineage not in vaccine
4. Influenza A(H1N1) – “seasonal”
5. Influenza B, vaccine lineage
6. Influenza A/avian(H5N1) – mutated to spread readily in humans
CONCLUSIONS

- Virus detection will be the earliest epidemic indicator
- Culture-based surveillance
  - Need viruses for characterization
    - Antigenic
    - Antiviral Sensitivity
- Start early with dedicated clinics (no later than 1 October)
- Maintain high index of suspicion (send suspicious viruses to reference laboratory)