Influenza and Influenza Vaccine

Epidemiology and Prevention of Vaccine-Preventable Diseases

National Immunization Program
Centers for Disease Control and Prevention
Revised January 2006

Note to presenters:
Images of vaccine-preventable diseases are available from the Immunization Action Coalition website at http://www.vaccineinformation.org/photos/index.asp

Influenza

• Highly infectious viral illness
• First pandemic in 1580
• At least 4 pandemics in 19th century
• Estimated 21 million deaths worldwide in pandemic of 1918-1919
• Virus first isolated in 1933

Influenza Virus

• Single-stranded RNA virus
• Orthomyxoviridae family
• 3 types: A, B, C
• Subtypes of type A determined by hemagglutinin and neuraminidase

Influenza Virus Strains

• Type A - moderate to severe illness
  - all age groups
  - humans and other animals
• Type B - milder disease
  - primarily affects children
  - humans only
• Type C - rarely reported in humans
  - no epidemics

Influenza Virus

- A/Fujian/411/2002 (H3N2)

- Neuraminidase
- Hemagglutinin
- Type of nuclear material
Influenza Antigenic Changes

• Hemagglutinin and neuraminidase antigens change with time
• Changes occur as a result of point mutations in the virus gene, or due to exchange of a gene segment with another subtype of influenza virus
• Impact of antigenic changes depend on extent of change (more change usually means larger impact)

Antigenic Shift

• Major change, new subtype
• Caused by exchange of gene segments
• May result in pandemic
• Example of antigenic shift
  – H2N2 virus circulated in 1957-1967
  – H3N2 virus appeared in 1968 and completely replaced H2N2 virus

Antigenic Drift

• Minor change, same subtype
• Caused by point mutations in gene
• May result in epidemic
• Example of antigenic drift
  – In 2002-2003, A/Panama/2007/99 (H3N2) virus was dominant
  – A/Fujian/411/2002 (H3N2) appeared in late 2003 and caused widespread illness in 2003-2004

Impact of Pandemic Influenza

• 200 million people could be affected
• Up to 40 million require outpatient visits
• Up to 700,000 hospitalized
• 89,000 - 200,000 deaths
Influenza Clinical Features

- Incubation period 2 days (range 1-4 days)
- Severity of illness depends on prior experience with related variants
- Abrupt onset of fever, myalgia, sore throat, nonproductive cough, headache

Influenza Complications

- Pneumonia
  - secondary bacterial
  - primary influenza viral
- Reye syndrome
- Myocarditis
- Death 0.5-1 per 1,000 cases

Impact of Influenza

- ~36,000 excess deaths per year
- >90% of deaths among persons >65 years of age
- Higher mortality during seasons when influenza type A (H3N2) viruses predominate

Impact of Influenza

- Highest rates of complications and hospitalization among young children and persons >65 years
- Average of >200,000 influenza-related excess hospitalizations
- 57% of hospitalizations among persons <65 years of age
- Greater number of hospitalizations during type A (H3N2) epidemics

Hospitalization Rates for Influenza By Age and Risk Group*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Rate** (high-risk)</th>
<th>Rate** (not high-risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-11 mos</td>
<td>1900</td>
<td>496-1038</td>
</tr>
<tr>
<td>1-2 yrs</td>
<td>800</td>
<td>186</td>
</tr>
<tr>
<td>3-4 yrs</td>
<td>320</td>
<td>86</td>
</tr>
<tr>
<td>5-14 yrs</td>
<td>92</td>
<td>41</td>
</tr>
<tr>
<td>15-44 yrs</td>
<td>56-110</td>
<td>23-25</td>
</tr>
<tr>
<td>45-64 yrs</td>
<td>392-635</td>
<td>13-23</td>
</tr>
<tr>
<td>&gt;65 yrs</td>
<td>399-518</td>
<td>125-228</td>
</tr>
</tbody>
</table>

* Data from several studies 1972 - 1995
** Hospitalizations per 100,000 population

Influenza Diagnosis

- Clinical and epidemiological characteristics
- Isolation of influenza virus from clinical specimen (e.g., nasopharynx, throat, sputum)
- Significant rise in influenza IgG by serologic assay
- Direct antigen testing for type A virus
**Influenza Epidemiology**

- **Reservoir**: Human, animals (type A only)
- **Transmission**: Respiratory, Probably airborne
- **Temporal pattern**: Peak December – March in temperate climate. May occur earlier or later.
- **Communicability**: 1 day before to 5 days after onset (adults)

**Month of Peak Influenza Activity United States, 1976-2005**

<table>
<thead>
<tr>
<th>Month</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dec</td>
<td>14%</td>
</tr>
<tr>
<td>Jan</td>
<td>21%</td>
</tr>
<tr>
<td>Feb</td>
<td>45%</td>
</tr>
<tr>
<td>Mar</td>
<td>10%</td>
</tr>
<tr>
<td>Apr</td>
<td>3%</td>
</tr>
<tr>
<td>May</td>
<td>3%</td>
</tr>
</tbody>
</table>

**Influenza Vaccines**

- **Inactivated subunit (TIV)**
  - intramuscular
  - trivalent
- **Live attenuated vaccine (LAIV)**
  - intranasal
  - trivalent

**Composition of the 2005-2006 Influenza Vaccine**

- A/California/7/2004 (H3N2)
  - A/New York/55/2004
- A/New Caledonia/20/99 (H1N1)
- B/Shanghai/361/2002
  - B/Jilin/20/2003 or B/Jiangsu/10/2003

*strains in (parenthesis) are antigenically identical to the selected strains and may be used in the vaccines

**Transmission of LAIV Virus**

- LAIV replicates in the nasopharyngeal mucosa
- Mean shedding of virus 7.6 days – longer in children
- One instance of transmission of vaccine virus documented in a child care setting
- Transmitted virus retained attenuated, cold-adapted, temperature-sensitive characteristics
- No transmission of LAIV reported in the U.S.

**Inactivated Influenza Vaccine Efficacy**

- 70%-90% effective among healthy persons <65 years of age
- 30%-40% effective among frail elderly persons
- 50%-60% effective in preventing hospitalization
- 80% effective in preventing death
Influenza and Complications Among Nursing Home Residents

LAIV Efficacy in Healthy Children
- 87% effective against culture-confirmed influenza in children 5-7 years old
- 27% reduction in febrile otitis media (OM)
- 28% reduction in OM with accompanying antibiotic use
- Decreased fever and OM in vaccine recipients who developed influenza

LAIV Efficacy in Healthy Adults
- 20% fewer severe febrile illness episodes
- 24% fewer febrile upper respiratory illness episodes
- 27% fewer lost work days due to febrile upper respiratory illness
- 18%-37% fewer days of healthcare provider visits due to febrile illness
- 41%-45% fewer days of antibiotic use

Timing of Inactivated Influenza Vaccine Programs
- Actively target vaccine available in September and October to persons at increased risk of influenza complications, children <9 years, and healthcare workers
- Vaccination of all other groups should begin in November
- Continue vaccinating through December and later, as long as vaccine is available

Inactivated Influenza Vaccine Schedule

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dose</th>
<th>No. Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-35 mos</td>
<td>0.25 mL</td>
<td>1* or 2</td>
</tr>
<tr>
<td>3-8 yrs</td>
<td>0.50 mL</td>
<td>1* or 2</td>
</tr>
<tr>
<td>≥9 yrs</td>
<td>0.50 mL</td>
<td>1</td>
</tr>
</tbody>
</table>

*Only one dose is needed if the child received influenza vaccine during a previous influenza season

Inactivated Influenza Vaccine Recommendations
- All persons 50 years of age or older
- Children 6-23 months of age
- Residents of long-term care facilities
- Pregnant women
- Persons 6 months to 18 years receiving chronic aspirin therapy
- Persons ≥6 months of age with chronic illness
### Inactivated Influenza Vaccine Recommendations
- Persons with the following chronic illnesses should be considered for inactivated influenza vaccine:
  - pulmonary (e.g., asthma, COPD)
  - cardiovascular (e.g., CHF)
  - metabolic (e.g., diabetes)
  - renal dysfunction
  - hemoglobinopathy
  - immunosuppression, including HIV infection
  - any condition that can compromise respiratory function or the handling of respiratory secretions

### Pregnancy and Inactivated Influenza Vaccine
- Risk of hospitalization 4 times higher than nonpregnant women
- Risk of complications comparable to nonpregnant women with high-risk medical conditions
- Vaccination (with TIV) recommended if pregnant during influenza season
- Vaccination can occur during any trimester

### HIV Infection and Inactivated Influenza Vaccine
- Persons with HIV at increased risk of complications of influenza
- TIV induces protective antibody titers in many HIV infected persons
- Transient increase in HIV replication reported
- TIV will benefit many HIV-infected persons

### Influenza Vaccine Recommendations
- Healthcare providers, including home care*
- Employees of long-term care facilities
- Household contacts of high-risk persons

*LAIV should not be administered to healthcare workers who have contact with severely immunosuppressed persons who require hospitalization and care in a protective environment

### Influenza Vaccine Recommendations*
- Providers of essential community services
- Students
- Persons traveling outside the U.S.
- Anyone who wishes to reduce the likelihood of becoming ill from influenza

*these groups may receive TIV, and some may be eligible for LAIV

### Influenza Vaccination of Children
- Children <24 months at increased risk of hospitalization
- Inactivated influenza vaccination of healthy children 6-23 months is recommended
- Vaccination of household contacts and other caregivers of children <24 months of age is encouraged
In the 2003 National Health Interview Survey, only 40% of healthcare workers reported receiving influenza vaccine in the previous 12 months.

**Influenza Vaccination of HCWs**
- Educate HCWs about the benefits of vaccination for themselves, their families, and their patients
- Educate staff about vaccine adverse reactions
- Provide free vaccine at the work site to all employees, including night and weekend staff

**Live Attenuated Influenza Indications**
- Healthy* persons 5-49 years of age
  - close contacts of persons at high risk for complications of influenza (except immunosuppressed)
  - persons who wish to reduce their own risk of influenza

*Persons who do not have medical conditions that increase their risk for complications of influenza

**Simultaneous Administration of LAIV and Other Vaccines**
- Inactivated vaccines can be administered either simultaneously or at any time before or after LAIV
- Other live vaccines can be administered on the same day as LAIV
- Live vaccines not administered on the same day should be administered >4 weeks apart

**Inactivated Influenza Vaccine Adverse Reactions**
- Local reactions: 15%-20%
- Fever, malaise: not common
- Allergic reactions: rare
- Neurological reactions: very rare

**Live Attenuated Influenza Vaccine Adverse Reactions**
- Children
  - no significant increase in URI symptoms, fever, or other systemic symptoms
  - significantly increased risk of asthma or reactive airways disease in children 12-59 months of age
- Adults
  - significantly increased rate of cough, runny nose, nasal congestion, sore throat, and chills reported among vaccine recipients
  - no increase in the occurrence of fever
- No serious adverse reactions identified
Inactivated Influenza Vaccine
Contraindications and Precautions

• Severe allergic reaction to a vaccine component (e.g., egg) or following a prior dose of vaccine
• Moderate or severe acute illness

Live Attenuated Influenza Vaccine
Contraindications and Precautions

• Children <5 years of age*
• Persons >50 years of age*
• Persons with chronic medical conditions*
• Children and adolescents receiving long-term aspirin therapy*

*These persons should receive inactivated influenza vaccine

Live Attenuated Influenza Vaccine
Contraindications and Precautions

• Immunosuppression from any cause
• Pregnant women*
• Severe (anaphylactic) allergy to egg or other vaccine components
• History of Guillain-Barré syndrome
• Moderate or severe acute illness

*These persons should receive inactivated influenza vaccine

LAIV Storage and Handling

• Must be stored at < 5°F (-15°C)
• May be stored in a frost-free freezer with a separate door
• May be thawed in a refrigerator and stored at 35°-46°F (2°-8°C) for up to 60 hours before use
• Should not be refrozen after thawing

Influenza Vaccine Strategies to Improve Coverage

• Ensure systematic and automatic offering of TIV to high-risk groups
• Educate healthcare providers and patients
• Address concerns about adverse events
• Emphasize physician recommendation

Influenza Antiviral Agents*

• Amantadine and rimantadine
  —effective against influenza A only
  —approved for prophylaxis and treatment
• Zanamivir and oseltamivir
  —neuraminidase inhibitors
  —effective against influenza A and B
  —oseltamivir approved for prophylaxis

*see influenza ACIP statement or CDC influenza website for details
Influenza Surveillance
• Monitor prevalence of circulating strains and detect new strains
• Estimate influenza-related morbidity, mortality and economic loss
• Rapidly detect outbreaks
• Assist disease control through rapid preventive action

National Immunization Program
Contact Information
• Telephone 800.CDC.INFO
• Email nipinfo@cdc.gov
• Website www.cdc.gov/nip