Influenza Vaccination in Older Adults

Stefan Gravenstein, MD, MPH, AGSF
Professor of Medicine, Brown University
Clinical Director, Quality Partners of Rhode Island
Conflict of Interest Disclosure

• I serve as consultant or speaker for:
  – GalxoSmithKline
  – Juvaris
  – Novavax
  – SanofiAventis

• I have grant support from
  – Medicare (Patient Safety)
  – AHRQ (RO1)
  – Novavax (influenza vaccine study)
Objectives

• Understand the importance of routine universal influenza vaccination, especially for older adults and health care workers

• Learn how to increase immunization rates
  – Understand that there is much to do

• Know about new vaccines on the horizon
Influenza: The Impact

- Elderly account for the majority of influenza hospitalizations (1989-2001)\(^1\)

Influenza VE for Reducing Pneumonia Hospitalization in the Elderly

Influenza Mortality and Hospitalization Rates by Age Group

- One Influenza death for every 8 hospitalizations\(^1\)
- M&M increases dramatically after age 50

Influenza: Why the Impact

• Host factors
  – Age
  – Underlying disease
    • Lungs, vascular, immune system, obesity, pregnancy
  – Exposure

• Environmental factors: exposure

• Viral factors
  – Drift-minor antigenic variation
  – Shift-major antigenic variation (>25%)
Age

• Declining immunity (more later)
  – Altered presentation of disease (later diagnosis)
• Difficulty in clearing virus
  – Mucociliary escalator less efficient
  – Cough less forceful
  – Less fever, less impairment of viral replication
• Increase in underlying inflammatory markers
  – Increasingly in a “pro-thrombotic state”
• Change in the way we complain, accept illness
• Physiologic reserve
Underlying disease

• Pulmonary disease
  – Affects viral clearance, pulmonary reserve, inflammatory state

• Endocrine disease
  – Affects immune defense mechanisms, physiologic reserve, inflammatory state

• Obesity
  – Affects pulmonary function

• Pregnancy
  – Affects pulmonary function, immune function
Fomites size, deposition, spread

- **Upper respiratory tract**
- **Lower respiratory tract**
- **Sewage and water sources**

**Direct**
Expelled from infectious host by violent expiration (cough, sneeze) or simply exhalation

**Indirect**
Aerosolization of infectious agent from environmentally contaminated sources (fomites, sewage)

- **Dynamic particle size**
- **Density (settling velocity)**
- **Particle composition**
- **Temperature and relative humidity**
- **Virus particle’s genetic vulnerability**
- **Ultraviolet radiation**

**Physical Decay**

**Biologic Decay**

Chotani, GIDSAS-JHU, 2006
Environmental
(i.e., reasons for Universal Vaccination)

• Children as vectors
  – Viral load
  – Lack of immunity (opportunity to get infected)
  – Aerosilization
  – Hygiene

• Adults as vectors
  – Propelling virus (vigor of cough, sneeze: aerosol)
  – As caregivers

• Herd immunity: 80% of herd immune?
Airborne Influenza Distribution

• Airborne particles collected in urgent care clinic (stationary & personal aerosol samplers),
  – employee and patient testing
  – 11 days, 4-5 h/d

• Influenza A or B +
  – 18% stationary, 19% of personal samplers
  – Correlated with the location of patients with influenza (r=.77)
  – 42% < 4.1 µm diameter

Figure 1. Number of patients with clinically confirmed influenza and percentage of aerosol samplers positive for influenza A or B, by sampling day.
Figure 3. Airborne concentration of influenza A RNA in influenza A–positive clinic locations, by day of sampling. For instances in which >1 examination room or procedure room was positive for influenza A on a particular day, the geometric mean concentration is shown.
1° Approach to Influenza Prevention: Vaccinate!

• Preventing disease spread: herd immunity
  — Universal vaccination
    • Children
    • Healthcare workers

• Preventing primary disease
  — Children
  — Adults

• Preventing secondary complications
  — Children, older adults, people with underlying disease
Healthy People 2010: Goals and Progress for Influenza Vaccination

<table>
<thead>
<tr>
<th>Population</th>
<th>1998 Baseline* (%)</th>
<th>2008-09 † (%)</th>
<th>2009-10 (Feb) Seasonal/H1N1† (%)</th>
<th>2010 Goal (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults aged ≥65 years</td>
<td>64</td>
<td>67</td>
<td>66/14</td>
<td>90</td>
</tr>
<tr>
<td>High-risk adults 18-64 years old</td>
<td>26</td>
<td>36 (32-42)</td>
<td>35/33.2</td>
<td>60</td>
</tr>
<tr>
<td>HCW: ALL</td>
<td>37</td>
<td>49 estimated</td>
<td>62/37</td>
<td>60</td>
</tr>
<tr>
<td>LTC</td>
<td></td>
<td></td>
<td>54/20</td>
<td></td>
</tr>
<tr>
<td>Office</td>
<td></td>
<td></td>
<td>64/39</td>
<td></td>
</tr>
</tbody>
</table>

Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep.* 2009; 58(39);1091-1095 and 2, 2010; 59(12);357-368

*Source = National Health Interview Survey (NHIS), CDC.
Increasing Vaccine Uptake

• Greater vaccine uptake for patients in general, and reduced disparity in vaccine uptake when:
  – there are standing orders for vaccination
  – verbal consent for vaccine is allowed
  – seasonal vaccination campaigns are included
  – Uptake among the health care staff is high (>40%)

• This holds true for long-term care facilities and office practices

Bardenheier B, et al. Academy Health June 2010
Health Care Workers Don’t Know

• They can unwittingly transmit flu to patients and families; 10-50% get it/you, but 50% never know it
• Office exposure to flu during flu season is likely
• Vaccination reduces sick time and protects them from getting flu from children
  – Vaccinated workers 70% less likely to get flu
• Vaccine reduces the likelihood of hospitalization for a vascular event (MI or CVA) or pneumonia, each by about 30%

Common HCW Myths

• If you vaccinate the patients, you do not need to vaccinate staff
  – NO—you need two shields to prevent the flu
• Vaccine contains unsafe preservative
  – NO—the preservatives are safe, and single dose (pre-filled syringes) are preservative-free
• I get flu from the shot
  – NO, NO, NO!
• You can’t trust public programs
  – It’s not just a public program: every major body (CDC and all major medical trade associations) recommends this
  – 15% are afraid of needles
• I can wait until flu is here to get my shot
Influenza Vaccine Reduces Pneumonia, Cardiac, and Cerebrovascular Disease in Older Patients

Policies to Increase Uptake

• Employers that require influenza vaccine to be taken as a condition of employment
• Recommend getting the vaccine
• Free, readily available/frequently offered, vaccine for employees
• Develop strategy to ID those who remain unvaccinated
• Have employers view vaccine administration a measure of patient and workplace safety and quality assurance
• Active declination
• Education program for staff, especially addressing myths

Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep* 2010; 59(12);357-368
## Presentation of Clinical Influenza Differs by Age Group

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>Children</th>
<th>Adults</th>
<th>Elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough (nonproductive)</td>
<td>++</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Fever</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Myalgia</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Malaise</td>
<td>+</td>
<td>+</td>
<td>++++</td>
</tr>
<tr>
<td>Sore throat</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Rhinitis/nasal congestion</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Abdominal pain/diarrhea</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>++</td>
<td>–</td>
<td>+</td>
</tr>
</tbody>
</table>

++++ Most frequent sign/symptom  
+ Least frequent  
– Not found

Caveats

• Influenza only likely when influenza is circulating in the state, and more likely if known to be circulating in the community
• Most individuals do not present with classic symptoms, even if the disease turns out to be lethal
• Fewer than half will ever know if they had the flu most than
When there is a Vaccine shortage

• Follow CDC and state priority guidelines
• Is priority goal to vaccinate vectors or patients
• Consider how to recruit the high priority first without producing a panic in the process.
  – Manage message
  – Anticipate push-back if serial vaccines are to be given
• Recruit help to equitably get vaccine distributed
Immune Responses to TIVs Tend to Be Lower in the Older Adult

Serum hemagglutination-inhibition antibody responses to inactivated influenza virus vaccines by age of vaccinees

<table>
<thead>
<tr>
<th>Vaccine virus</th>
<th>Age Gp (N)</th>
<th>Rise (%)</th>
<th>GMTb</th>
<th>≥40c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PreVac</td>
<td>PostVac</td>
<td>PreVac</td>
</tr>
<tr>
<td>A/Soloman Islands/03/06 (H1N1)</td>
<td>Adults (24)</td>
<td>52</td>
<td>92</td>
<td>1248</td>
</tr>
<tr>
<td></td>
<td>Elderly (24)</td>
<td>92</td>
<td>14</td>
<td>279</td>
</tr>
<tr>
<td></td>
<td>Children (29)</td>
<td>96</td>
<td>6</td>
<td>129</td>
</tr>
<tr>
<td>A/Wisconsin/67/05 (H3N2)</td>
<td>Adults</td>
<td>50</td>
<td>95</td>
<td>457</td>
</tr>
<tr>
<td></td>
<td>Elderly</td>
<td>54</td>
<td>66</td>
<td>267</td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>86</td>
<td>8</td>
<td>48</td>
</tr>
<tr>
<td>B/Malaysia/2506/04</td>
<td>Adults</td>
<td>54</td>
<td>27</td>
<td>220</td>
</tr>
<tr>
<td></td>
<td>Elderly</td>
<td>42</td>
<td>30</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>72</td>
<td>8</td>
<td>65</td>
</tr>
</tbody>
</table>

aData from Vaccine Responses, Zhiping Ye, M.D., Ph.D., FDA, [http://www.fda.gov/ohrms/dockets/ac/08/slides/2008-4348S1and2-00-index.html](http://www.fda.gov/ohrms/dockets/ac/08/slides/2008-4348S1and2-00-index.html).

Standard Dose Influenza Vaccine: GMT, Younger vs Older

Sanofi Pasteur annual release study GRC41
Vaccination, even poor match, reduces fever

New Vaccines

- Increased Antigen and/or adjuvant addition
- Antigen only

Immune response

Time
New Vaccines

• The newest licensed vaccine is a high dose influenza vaccine
  – It contains four times (60 vs 15 µg/strain) the antigen of the regular seasonal vaccine for adults
  – Phase III RCT N=3876, randomized 2:1 to HD
    • Blood collected baseline and day 28 for primary endpoint of immunogenicity
    • Secondary endpoint of safety

## HD Vaccine: Safety (injection site)

<table>
<thead>
<tr>
<th></th>
<th>High-Dose (N = 2573)</th>
<th></th>
<th>Standard-dose (N = 1260)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensity</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>35.6</td>
<td>(33.7; 37.5)</td>
<td>24.3</td>
</tr>
<tr>
<td>Grade III</td>
<td>0.3</td>
<td>(0.2; 0.7)</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Erythema</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>14.9</td>
<td>(13.6; 16.4)</td>
<td>10.8</td>
</tr>
<tr>
<td>Grade III</td>
<td>1.8</td>
<td>(1.3; 2.4)</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Swelling</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>8.9</td>
<td>(7.9; 10.1)</td>
<td>5.8</td>
</tr>
<tr>
<td>Grade III</td>
<td>1.5</td>
<td>(1.1; 2.1)</td>
<td>0.6</td>
</tr>
</tbody>
</table>

HD Vaccine: Safety (systemic)

<table>
<thead>
<tr>
<th>Reaction</th>
<th>High-Dose (N=2573)</th>
<th>Standard-dose (N=1260)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>Any Myalgia</td>
<td>21.4</td>
<td>(19.8; 23.0)</td>
</tr>
<tr>
<td>Grade III</td>
<td>1.6</td>
<td>(1.2; 2.2)</td>
</tr>
<tr>
<td>Any Malaise</td>
<td>18.0</td>
<td>(16.5; 19.5)</td>
</tr>
<tr>
<td>Grade III</td>
<td>1.6</td>
<td>(1.1; 2.2)</td>
</tr>
<tr>
<td>Any Headache</td>
<td>16.8</td>
<td>(15.3; 18.3)</td>
</tr>
<tr>
<td>Grade III</td>
<td>1.1</td>
<td>(0.7; 1.6)</td>
</tr>
<tr>
<td>Any Fever</td>
<td>3.6</td>
<td>(2.9; 4.4)</td>
</tr>
<tr>
<td>Grade III</td>
<td>0.0</td>
<td>(0.0; 0.2)</td>
</tr>
</tbody>
</table>

Immediate and Unsolicited AEs, SAEs

• Similar event rates
  – AEs within 30 minutes post-vaccination: 0.3%
  – Unsolicited AEs within 28 d post-vaccination: 22%
  – SAE event rate: 6.1% HD, 7.4% standard dose
  – No deaths day 0-28; 0.6% after day 28 - “unrelated”

• Only 2 SAEs reported by investigators as vaccine related:
  – Exacerbation of Crohn's disease 2 days post-HD vaccination
  – New diagnosis myasthenia gravis 1 mont post-standard dose vaccination

Phase III study of HD vaccine

Superiority for H1N1 and H3N2; non-inferiority for B; all HD vs SD comparisons, $P<0.0001$

HD response by age

Summary HD Vaccine

• Met FDA superiority requirements for immunogenicity based on seroprotection rates (70-80% higher with influenza A strains; 30% higher –noninferior-- against influenza B) independent of age, health

• Appears similarly safe to standard dose vaccine

• Licensed December 23, 2009, available 2010 season; post-licensure efficacy study underway

• No data yet on clinical superiority
Summary

• Influenza remains the most common cause of infectious death for the elderly for many reasons
• Vaccines not as great for elderly, but still provide important, cost-effective approach to influenza prevention
• Vaccinate all age groups, patients
• Circulating virus change each year (drift and shift)—so need annual vaccination
• Need HCW, office and facility P&P to increase vaccine uptake
• New HD vaccine more immunogenic, may be better for older patients
Resources

- http://www.cdc.gov/mmwr
- http://www.flu.gov