INFLUENZA VACCINE PRIMER
LONG-TERM CARE FACILITIES

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OBJECTIVES

▪ Explain how new strains of influenza virus are created so that you understand why we need to continually update the vaccine

▪ Recognize which myth about influenza vaccine your friends use as a reason not to get immunized so that you can discuss it with them

▪ List the range of influenza vaccine effectiveness over the last 10 years and explain how it is determined and what it really means

▪ Describe key differences between the influenza products available this year so that you can use the appropriate product for each patient
I have no financial disclosures related to this presentation

I did get an influenza vaccine this year
Immunized health care personnel

- Reduce transmission of influenza
- Reduce staff illness and absenteeism
- Reduce influenza-related illness and death

www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm
INFLUENZA VIRUS NOMENCLATURE

A / Sydney / 184 / 93 (H3N2)

INFLUENZA-NEW STRAINS ARE CONSTANTLY BEING CREATED
Influenza Strains

- Influenza A H3N2
  - Tends to be more severe
  - Predominant strain in 6/8 years since the 2009-10 pandemic

- Influenza A H1N1
  - Caused the pandemic of 2009-2010 (and 1918!)

- Influenza B-Yamagata lineage

- Influenza B-Victoria lineage

Only one in trivalent vaccine products
INFLUENZA-HOW IT HAPPENS
1918 INFLUENZA PANDEMIC

- H1N1 virus
- Rapid escalation in each community
  - Army camp admissions went from 80/day in early September to 1000/day a few weeks later
- 3 waves of disease over less than 1 year: March 2018, Fall 2018, Spring 2019
- 40-50 million deaths worldwide; 500,000-675,000 deaths in the U.S.
  - 9 million deaths over 4 years in World War I
  - In less than 1 year 1918 influenza killed more people than HIV has in over 20 years
- Unusually high mortality in healthy adults 20-40 years of age
  - Very rapid onset
  - Pulmonary hemorrhage
  - Intense inflammatory response
- Spread facilitated by troop movements

Reid AH, Microbes and Infection 2001;3:81-87; Proceedings HHSA Workshop October 17, 2006
The big pandemic of 1918

U.S. life expectancy 1900-1960

<table>
<thead>
<tr>
<th>Year</th>
<th>Life Expectancy</th>
</tr>
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<tbody>
<tr>
<td>1900</td>
<td>30</td>
</tr>
<tr>
<td>1910</td>
<td>38</td>
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<tr>
<td>1915</td>
<td>38</td>
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<tr>
<td>1920</td>
<td>46</td>
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<td>1925</td>
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<td>1930</td>
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<td>1935</td>
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<td>1945</td>
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<td>1950</td>
<td>70</td>
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<tr>
<td>1955</td>
<td>70</td>
</tr>
<tr>
<td>1960</td>
<td>70</td>
</tr>
</tbody>
</table>
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2017-2018 Season

- A (subtyping not performed)
- A (H1N1)pdm09
- A (H3N2)
- H3N2v
- B (lineage not performed)
- B (Victoria Lineage)
- B (Yamagata Lineage)
INFLUENZA IMPACT-U.S.

- 79,400 deaths in 2017-2018
- 185 pediatric deaths in 2017-2018
  - 80% had not been immunized
  - Many were perfectly healthy
- 959,000 hospitalizations
- 60 million people ill with influenza

https://www.cdc.gov/flu/about/burden/estimates.htm
Are you 65 years of age or older?

Are you under 2 years of age?

Are you pregnant?

Do you have a chronic medical condition like heart, lung (asthma), liver, kidney disease neurologic disease/diabetes/cancer/immune deficiency?

Do you live in a long-term care facility?

Are you and American Indian or Alaskan Native?

Are you extremely obese (BMI > 40)?

Lot’s of people are at risk from influenza!
WHAT YOU HEAR (OR READ) ABOUT INFLUENZA VACCINE

- Influenza vaccine doesn’t work
- Influenza vaccine makes me sick
- I’m healthy/I never get the flu
- I’m allergic to eggs so I can’t get it
- Influenza isn’t that big a deal
2017-2018 INFLUENZA VACCINE EFFECTIVENESS

- Overall = 36%
- Influenza A H3N2 = 25%
- Influenza A H1N1 = 67%
- Influenza B = 42%
## HISTORY OF INFLUENZA VACCINE EFFECTIVENESS

<table>
<thead>
<tr>
<th>Year</th>
<th>Influenza vaccine effectiveness</th>
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<tbody>
<tr>
<td>2004-05</td>
<td>10</td>
</tr>
<tr>
<td>2005-06</td>
<td>21</td>
</tr>
<tr>
<td>2006-07</td>
<td>52</td>
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<td>2007-08</td>
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<td>2008-09</td>
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<td>2009-10</td>
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<td>2010-11</td>
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<td>2011-12</td>
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<td>2013-14</td>
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<td>2014-15</td>
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<tr>
<td>2015-16</td>
<td>48</td>
</tr>
<tr>
<td>2016-17</td>
<td>39</td>
</tr>
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</table>

[https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm](https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm); Downloaded 1/4/2018
INFLUENZA VACCINE EFFECTIVENESS DEPENDS ON:

- How you decide if someone has influenza
- What population you study—most vaccines work less well in the very young and very old
- What you mean by effective:
  - Prevents death
  - Prevents hospitalization
  - Prevents a visit to the doctor or emergency room
  - Prevents any symptoms
WHAT IS EFFECTIVENESS ANYWAY?

The same vaccine could be:

- 100% effective at preventing death
- 80% effective at preventing hospitalization
- 60% effective at preventing a visit to the doctor
- 40% effective at preventing any symptoms
- 20% effective at preventing transmission
IN GENERAL INFLUENZA VACCINE EFFECTIVENESS IS:

- 50-70% for healthy populations
- 20-50% for the elderly (preventing disease)
- 60-80% for the elderly (preventing death)
- 50-70% for newborns if their mother’s get immunized when pregnant
Table 3. Unadjusted and Adjusted Vaccine Effectiveness Estimates for Trivalent Influenza Vaccine Against Influenza Hospitalization

<table>
<thead>
<tr>
<th>Strain</th>
<th>Cases</th>
<th>Controls</th>
<th>Unadjusted</th>
<th>Adjusted</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>No.</td>
<td>VE, % (95% CI)</td>
<td>VE, % (95% CI)</td>
</tr>
<tr>
<td>All strains</td>
<td>320</td>
<td>564</td>
<td>45.0 (25.7–59.3)</td>
<td>58.0&lt;sup&gt;a&lt;/sup&gt; (34.2–73.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>43.3&lt;sup&gt;b&lt;/sup&gt; (22.1–58.9)</td>
<td></td>
</tr>
<tr>
<td>Influenza A</td>
<td>96</td>
<td>191</td>
<td>51.7 (15.1–72.6)</td>
<td>62.6&lt;sup&gt;c&lt;/sup&gt; (2.4–85.7)</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>34</td>
<td>74</td>
<td>88.7 (48.1–97.5)</td>
<td>...</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>43</td>
<td>87</td>
<td>30.3 (–53.7 to 68.4)</td>
<td>276&lt;sup&gt;d&lt;/sup&gt; (–227.3 to 84.0)</td>
</tr>
<tr>
<td>Influenza B</td>
<td>224</td>
<td>373</td>
<td>37.3 (16.0–53.2)</td>
<td>58.3&lt;sup&gt;e&lt;/sup&gt; (29.6–75.3)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>44</td>
<td>78</td>
<td>59.3 (8.6–81.9)</td>
<td>64.4&lt;sup&gt;f&lt;/sup&gt; (–0.7 to 87.4)</td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>135</td>
<td>222</td>
<td>32.4 (–6.2 to 56.9)</td>
<td>54.7&lt;sup&gt;g&lt;/sup&gt; (8.6–77.5)</td>
</tr>
</tbody>
</table>

Vaccine effectiveness against test positive illness=47% this season

Andrew MK et al, J Infect Dis 2017:216:405-14
“INFLUENZA VACCINE GAVE ME THE FLU”

- It’s an inactivated vaccine, so it can’t give you the flu.
- Influenza is a disease with fevers to 102-103 degrees, severe cough, muscle aches that makes most adults sick for 3-4 days.
- Common side effects from influenza vaccine are low-grade temperature, headache, or muscle aches for 1 day.
- People get influenza vaccine during a time of year when other respiratory infections are common.
- In a randomized trial the only difference between people who received influenza vaccine and placebo was a sore arm.

“I’M HEALTHY SO I DON’T NEED A FLU SHOT”
“I NEVER GET THE FLU”

- 80% of 200,000 world wide 2009 pandemic H1N1 deaths were in people younger than 65 years
- 28 pregnant women died in the U.S. in 2009-2010 due to influenza
- Once you’ve actually had influenza you will always get a flu shot
- Most of the deaths during the 1918 pandemic were in healthy people
2018-2019 INFLUENZA VACCINES

• **New** Influenza A (H3N2) strain A/Singapore

• **New** Influenza B Victoria strain B/Colorado

• Same Influenza A (H1N1) strain A/Michigan

• Same Influenza B Yamagata strain B/Phuket

“It’s tough to make predictions, especially about the future.” *Yogi Berra*
WHO Chooses (GuesSes) What to put into each year’s influenza vaccine?

- More than 100 national influenza centers around the world isolate circulating strains of influenza.

- Representative viruses are sent to five WHO Collaborating Centers.

- Twice per year, in September for the Southern hemisphere and February for the Northern hemisphere, the WHO brings together to Collaborating Centers and influenza experts to review the pattern of circulating strains and attempts to predict what will happen over the next 6 months.

- In late February/early March the FDA convenes the Vaccines and Related Biologics Advisory Committee (VRBPAC) who then usually agrees with the WHO and that determines the strains for the fall influenza vaccine in the United States.
Influenza Manufacturing Process
INFLUENZA-WHAT TO EXPECT THIS FALL

▪ ? A mismatch between some circulating strains and the vaccine strains
▪ ? A mild season: 2017-2018 was the biggest season in the U.S. since the pandemic of 2009
▪ ? A late season: 2017-2018 started earlier than usual
▪ ? An H1N1 season: we are due
▪ ? Something unexpected…..
# 2018-2019 INFLUENZA VACCINE PRODUCTS

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Trade Name</th>
<th>How Supplied</th>
<th>Mercury Content (mcg Hg/0.5mL)</th>
<th>Age Range</th>
<th>Vaccine Product Billing Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>GlaxoSmithKline</td>
<td>Fluarix (IIV4)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>6 months &amp; older</td>
<td>90686</td>
</tr>
<tr>
<td>ID Biomedical Corp. of Quebec, a subsidiary of GlaxoSmithKline</td>
<td>FluLaval (IIV4)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>6 months &amp; older</td>
<td>90686</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL (multi-dose vial)</td>
<td>&lt;25</td>
<td>6 months &amp; older</td>
<td>90686</td>
</tr>
<tr>
<td>MedImmune</td>
<td>FluMist (LAIV4)</td>
<td>0.2 mL (single-use nasal spray)</td>
<td>0</td>
<td>2 through 49 years</td>
<td>90672</td>
</tr>
<tr>
<td>Protein Sciences Corporation, a Sanofi company</td>
<td>Flublok (RIV4)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>18 years &amp; older</td>
<td>90682</td>
</tr>
<tr>
<td>Sanofi Pasteur, Inc.</td>
<td>Fluzone (IIV4)</td>
<td>0.25 mL (single-dose syringe)</td>
<td>0</td>
<td>6 through 35 months</td>
<td>90685</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>3 years &amp; older</td>
<td>90686</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL (single-dose vial)</td>
<td>0</td>
<td>3 years &amp; older</td>
<td>90686</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL (multi-dose vial)</td>
<td>25</td>
<td>6 through 35 months</td>
<td>90687</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL (multi-dose vial)</td>
<td>25</td>
<td>3 years &amp; older</td>
<td>90688</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluzone High-Dose (IIV3-HD)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>65 years &amp; older</td>
</tr>
<tr>
<td>Seqirus</td>
<td>Afuria (IIV3)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>5 years &amp; older</td>
<td>90656</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL (multi-dose vial)</td>
<td>24.5</td>
<td>5 years &amp; older</td>
<td>90658</td>
</tr>
<tr>
<td></td>
<td>Afuria (IIV4)</td>
<td>0.5 mL (single-dose vial)</td>
<td>0</td>
<td>5 years &amp; older</td>
<td>90686</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL (multi-dose vial)</td>
<td>24.5</td>
<td>5 years &amp; older</td>
<td>90686</td>
</tr>
<tr>
<td></td>
<td>Fluad (aIIV3)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>65 years &amp; older</td>
<td>90653</td>
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<tr>
<td></td>
<td>Flucelvax (ccIIV4)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>4 years &amp; older</td>
<td>90674</td>
</tr>
</tbody>
</table>
Influenza Vaccines
How Do You Keep Them Straight?

- Is it an injectable vaccine or a nasal vaccine?
- Is it trivalent or quadrivalent?
- Is it made in eggs or in cell culture?
- Is it a special product?
- What are its age restrictions?
- Who makes it/brand name?
- Does it really matter?
IS IT INJECTABLE OR NASAL?

- IIV-injectable influenza vaccine
  - Includes both trivalent (IIV3) and quadrivalent (IIV4) products
  - Includes egg based and cell culture products
  - Includes high dose, adjuvanted, and intradermal products

- LAIV-live attenuated influenza vaccine is back this year as an option
  - Only quadrivalent (LAIV4)
  - Only one manufacturer
WHAT IS A QUADRIVALENT INFLUENZA VACCINE?

➢ Contains 4 strains of influenza

➢ Prior to 2012 influenza vaccines contained 3 strains; 2 influenza A strains (e.g. H1N1, H3N2) and 1 influenza B strain

➢ There are two influenza B lineages (families) circulating; Victoria and Yamagata

➢ When the influenza vaccine “doesn’t work” it is sometimes because the influenza B strain is not matched with the predominant strain in the community

➢ Proportion of B strains causing disease changes every year

➢ About 75% of the vaccine supply this year is quadrivalent
IS IT MADE IN EGGS?

- All are except FluBlok/Protein Sciences Corp and Flucelvax/Novartis
- Flublok is a recombinant vaccine (like Hep B vaccine) and may be referred to as RIV
- Flucelvax is a whole virus vaccine but made in cells and may be referred to as ccIIIV
- These vaccines are ultra-safe for egg-allergic individuals
- This is less important this year given changes in recommendations for egg-allergic patients
▪ Current manufacturing techniques have lowered the amount of ovalbumin contained in influenza vaccines to an amount that doesn’t trigger allergic reactions

▪ Review of published data on 4,172 egg-allergic patients: No cases of anaphylaxis after IIV

▪ Anaphylaxis to influenza vaccine in egg-allergic patients is no more common than anaphylaxis to any other vaccine

▪ Any influenza vaccine product can be given to egg allergic individuals—including those who have had anaphylaxis to egg. You should be just as prepared to treat an anaphylactic reaction to influenza vaccine as you are for any other vaccine

▪ 30 minute waiting period dropped to 15 minutes

ACIP Recommendations. MMWR 2016;65:1-54
IS IT A SPECIAL PRODUCT?

- IIV High dose-Fluzone High Dose/Sanofi (only trivalent)
  - Recommended for those 65 years of age and over
  - More antigen
  - More local side effects
  - Does appear to be slightly more effective based on one recently published study

- Adjuvanted-Fluad (only trivalent)-new this year
  - Licensed for 65 years and above
ADJUVANTED INFLUENZA VACCINE FOR SENIORS

- Fluad-New for the 2016-17 influenza season in the US
- Licensed in 38 countries
- Contains MF-59 (squalene) adjuvant
- Enhances the immune response compared to regular influenza vaccine
- More local side effects (pain, redness at the injection site)
## WHO IS NOT GETTING A FLU VACCINE?

<table>
<thead>
<tr>
<th>Group</th>
<th>2015-2016 Unvaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seniors</td>
<td>37%</td>
</tr>
<tr>
<td>Adults ≥18 years</td>
<td>58%</td>
</tr>
<tr>
<td>Adults, 18-64 years high risk</td>
<td>54%</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>50% overall</td>
</tr>
<tr>
<td></td>
<td>33% if offered</td>
</tr>
<tr>
<td></td>
<td>80% if not offered</td>
</tr>
<tr>
<td>Children</td>
<td>41%</td>
</tr>
</tbody>
</table>

Flu vaccination coverage among health care personnel by November and April, for 2010-11, 2011-12, 2012-13, 2013-14, and 2014-15 flu seasons, and November for 2015-16 flu season, Internet panel survey, United States

www.cdc.gov/flu/weekly
• Protects us from disease
• Decreases the likelihood that we will give influenza to our patients
• Provides a good example for our patients
• Mandatory immunization policies endorsed by AAP and many other professional societies
DON’T FORGET PNEUMOCOCCAL VACCINES

- Many adults of all ages need both pneumococcal polysaccharide (PPSV23/Pneumovax 23) and pneumococcal conjugate (PCV13/Prevnar13) vaccines. Some younger than 65 years just need PPSV23.

- High risk conditions for pneumococcal infections are similar to those for influenza and include: chronic heart/lung disease, diabetes, chronic liver disease or renal failure, asplenia, immunocompromising conditions, CSF leak, cochlear implants, smoking, alcoholism

- For the details go to https://www.cdc.gov/vaccines/vpd/pneumo/hcp/who-when-to-vaccinate.html

- All adults 65 years of age and older need both vaccines

- When giving both the preference is to give PCV13 first followed by PPSV23 8 weeks to 1 year later
THE FUTURE OF INFLUENZA VACCINE

- Continued effort to immunize pregnant women
- Universal vaccine
- Microneedle Patch delivery
- Vaccine for infants less than 6 months of age
- More adjuvanted vaccines
New strains of influenza are continuously being created

Vaccine efficacy is variable and depends on how it is assessed

We are all at risk from influenza

LAIV is an option for influenza vaccination in 2018-2019

We need to immunize ourselves and our staff
QUESTIONS OR COMMENTS