Potential Collaborations: Exploring Strain Circulation, Match and Hemispheres

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Overview

- Armed Forces Epidemiology Board Meeting – September 2006
  - Southern Hemisphere Influenza Vaccines and Circulating Strains
- Seasonality and vaccine timing
- Examples and other considerations
History

• Vaccine strain selection takes place in February for the Northern hemisphere
  – Vaccine is produced for October vaccination
• Since 1999 a second formal vaccine strain selection has taken place in September for the Southern hemisphere
  – Vaccine is produced for March/April vaccination of the following year
• At least twice prior to formalization of this process, the SH vax was updated informally to address newly circulating predominant strains
Questions to be Addressed
(Armed Forces Epidemiology Board Talk)

• Are common circulating influenza viruses different enough to warrant separate Northern and Southern hemispheric vaccines?
• Is there insufficient cross-reactivity between the two vaccines to actually warrant DoD procurement of the two separate hemispheric vaccines?
Methodology

• Look at all Southern hemisphere vaccine recommendations
• Identify when the Southern hemisphere strains were updated prior to the Northern hemisphere vaccine
• For each instance, revisited all surveillance/isolate data to see which strains actually circulated both globally and in the SH between the SH vaccination period and the upcoming NH new vaccine
Frequency Tables

- Look at all circulating viruses by date of collection
- Characterized in HI tests using ferret anti-sera raised against vaccine strains and other common circulating strains
- If a virus is “like” it is antigenically similar to a vaccine strain
- If a virus is “low” it shows a four-fold or greater reduction in titer against ferret anti-sera raised against the vax strain
- Shows the percentages of circulating strains submitted to CDC (or other WHOCC)
<table>
<thead>
<tr>
<th>Year</th>
<th>H3N2</th>
<th>H1N1</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998-99</td>
<td>A/Sydney/5/97</td>
<td>A/Beijing/262/95</td>
<td>B/Beijing/184/93</td>
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<tr>
<td>2000-S.H.</td>
<td>A/Moscow/10/99</td>
<td>A/NewCal/20/99</td>
<td>B/Beijing/184/93 &lt;br&gt; B/Shangdung/7/97</td>
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<tr>
<td>Year-Season</td>
<td>H3N2</td>
<td>H1N1</td>
<td>B</td>
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</tbody>
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SH vaccine 2000 and H1N1 Viruses

- SH recommended New/Caledonia/20/99*
- NH vaccine contained A/Beijing/262/95

Percent circulating strains April 2000-September 2000 in Southern hemisphere

- A/New Caled-like* 85%
- A/New Caled-low 1%
- A/Johannes-like 14%
SH Vaccine 2004 H3N2 Vaccine Virus

- SH recommended A/Fujian/411/2002*
- NH vaccine contained A/Moscow/10/99

Percentage of strains circulating April 2004-September 2004 in the SH

- A/Fujian/411/2002-like* 87%
- A/Fujian/411/2002-low 5%
- A/California/07/04-like 7%
- A/Wellington-like 1%
The Special Case of B Viruses

• Two lineages of B viruses have been circulating since mid-1980’s
• B-Yamagata-circulated globally
• For approximately 10 years B-Victoria’s circulated mainly in China, but has spread globally since 2001
• In two years, 1999 and 2000 local authorities were instructed to choose the strain most relevant to the country
• Both lineages continue to circulate today which poses challenges for vaccine strain selection
• Studies have shown that most adults have been exposed to both viruses
SH Vaccine 2001 - B Vaccine Virus

- SH recommended B/Sichuan/379/99  \( \{ \) B-Yamagata \( \}
- NH vaccine contained B/Beijing/184/93  \( \{ \) B-Yamagata \( \}

Percent strains circulating April 2001 – September 2001 in the Southern hemisphere

B/Sichuan/379/99-like  \( \) 69%  \( \{ \) B-Yamagata \( \}
B/Sichuan/379/99-low  \( \) 31%
Well Matched Circulating Viruses
Summary

H3N2
• 2000  69% match to NH
• 2004  87% match to SH vaccine
• 2005  ~51% matched the SH vaccine

H1N1
• 2000  85% match to SH vaccine

B
• 2001  69% match to SH/100% to lineage of SH
• 2006  50% match to SH/84% to lineage of SH
Questions Revisited

• Are common circulating influenza viruses different enough to warrant separate Northern and Southern hemispheric vaccines?
  – YES, sometimes, and if so WHO recommends a change

• Is there insufficient cross-reactivity between the two vaccines to actually warrant DoD procurement of the two separate hemispheric vaccines?
  – We have looked at differences based on antigenic characterization which does not correlate perfectly with human antibody response. Some degree of cross-reactivity is likely present and varies from strain to strain.
Considerations, Caveats, Conclusions

- Some viruses are more cross-reactive than others ....such as A/Sydney and A/Moscow so some protection could be afforded by a mismatched vaccine
  - Correlation between ferret antibodies and human antibodies is not perfect
- It is possible for some viruses to circulate for short times and in limited areas –like A/Wellington which was almost exclusively Oceania/Aus/NZ
- There could be sampling bias as WHOCCs request new and unusual strains in addition to representative isolates
- Just because a strain is changed doesn’t mean that it will circulate predominantly
- The most recent vaccine is probably the best vaccine
Influenza Seasonality and Vaccine Recommendations

• Influenza vaccine selection based on latest circulating isolates globally (thanks to all the NICs for their contributions!!)

• Influenza vaccination recommended in Oct-Dec for NH and Feb-March for SH

• Most tropics have year round circulation to some level with either peak in rainy season or bimodal peaks in rainy and winter season
Seasonal Occurrence of Influenza

- N. Hemisphere
- S. Hemisphere
- Tropical
Discrete seasonality just 500km Apart:
Srinagar coincides with winter: Case for NH vaccine
Delhi with monsoon: case for SH vaccine

Tale of Two Cities in India
Influenza Peak Coincides with Rainfall:
Advocacy for SH vaccine in April-May in Delhi region
Dynamic pattern …PlosOne, 7:e29129, 2012
Brazil: The Dilemma of Influenza Vaccine Recommendations.....
Mello Wad et al, 2009, PloSOne 4(4)

• Looks at alternate vaccine delivery scenarios
  – SH vaccine, SH schedule (April)**
  – NH vaccine, SH schedule (April)
  – SH vaccine, delivered in January (not feasible)
  – NH vaccine, NH schedule (October)

• Considers “effectiveness” proportion of matches between vaccine strains and those circulating after vaccination

• Assumed cross-protection between same lineage Bs and aggregated them
Brazil Continued

• Used statistics and aggregated isolates from 1991 to 2007 to determine seasonal patterns
  – Compared by looking at P and I deaths ‘65-’05
• Looked at isolates from 2 cities from 1999-2007
• Estimated the proportion of seasons with correct match to that available in vaccine
• Looks at vaccine induced protection of 9 months and overlap with matching strains
• Bottomline-Using NH vaccine and NH timing would have greatest impact in preventing illness
When does Equator not Define Hemispheres?
Influenza Seasonality in Tropics – How to consider timing and which vaccine to use?
Considerations

• When seasonality is year round without a marked peak or with multiple peaks
  – How to account for percent of disease prevented per month?
  – How to deal with the issue of waning immunity?
• Should we consider cross-protective immunity?
• Should we aggregate data from countries?
  – Which to include? Which to exclude?
  – Should each country have their own analyses?
• What data are available to use and how detailed should we be?
Seasonality and better timing
Looking at new policy?

- Some countries may have been using the wrong hemisphere vaccine at wrong time
- Create a comprehensive summary of seasonality from the region (SE Asia to start)
- Should NH be at latitude of 30 degrees or other factors?
- For individuals….the most recent vaccine is the probably best---Department of defense….can drive policies by individuals
- For countries policy needs to be driven by how to protect the most people