

Southern Hemisphere Influenza Vaccines and Circulating Strains

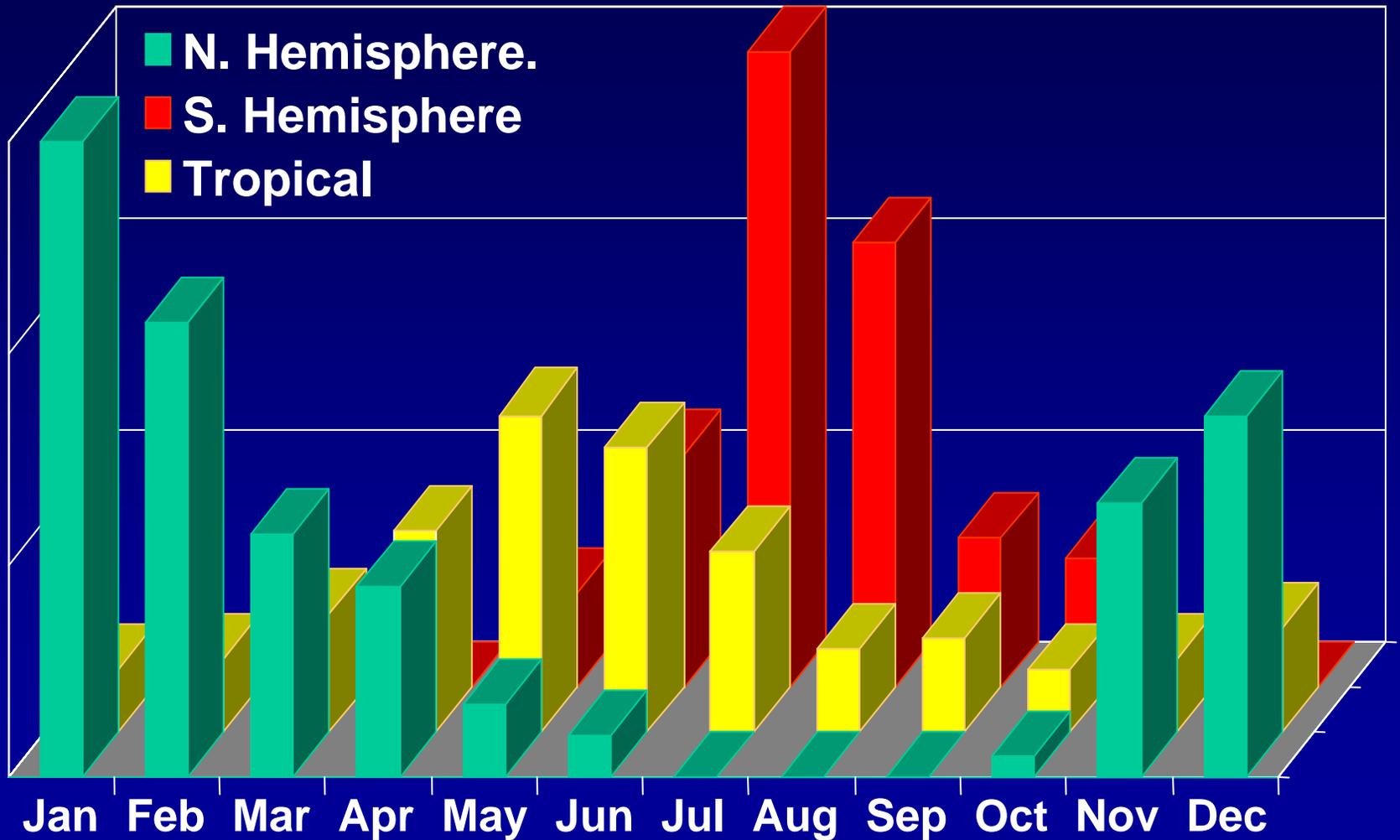
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Questions to be Addressed

- 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?

Seasonal Occurrence of Influenza



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

Methodology

- Looked 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

Vaccine Strain Decisions 1998-2003

	H3N2	H1N1	B
1998-99	A/Sydney/5/97	A/Beijing/262/95	B/Beijing/184/93
1999 - S.H.	A/Sydney/5/97	A/Beijing/262/95	B/Beijing/184/93
1999-2000	A/Sydney/5/97	A/Beijing/262/95	B/Beijing/184/93 B/Shangdong/7/97
2000-S.H.	A/Moscow/10/99	A/NewCal/20/99	B/Beijing/184/93 B/Shangdong/7/97
2000-2001	A/Moscow/10/99	A/NewCal/20/99	B/Beijing/184/93
2001-S.H.	A/Moscow/10/99	A/NewCal/20/99	B/Sichuan/379/99
2001-2002	A/Moscow/10/99	A/NewCal/20/99	B/Sichuan/379/99
2002-S.H.	A/Moscow/10/99	A/NewCal/20/99	B/Sichuan/379/99
2002-2003	A/Moscow/10/99	A/NewCal/20/99	B/HK/330/2001

Vaccine Strain Decisions 2003-Present

	H3N2	H1N1	B
2003-S.H.	A/Moscow/10/99	A/NewCal/20/99	B/HK/330/2001
2003-2004	A/Moscow/10/99	A/NewCal/20/99	B/HK/330/2001
2004-S.H.	A/Fujian/411/2002	A/NewCal/20/99	B/HK/330/2001
2004-2005	A/Fujian/411/2002	A/NewCal/20/99	B/Shanghai/2002
2005-S.H.	A/Wellington/2004	A/NewCal/20/99	B/Shanghai/2002
2005-2006	A/Calif/7/2004	A/NewCal/20/99	B/Shanghai/2002
2006-S.H.	A/Calif/7/2004	A/NewCal/20/99	B/Malaysia/2004
2006-2007	A/Wisc/67/2005	A/NewCal/20/99	B/Shanghai/2002
2007-S.H.	A/Wisc/67/2005	A/NewCal/20/99	B/Shanghai/2002

SH vaccine 2000 and H3N2 Viruses

- SH H3N2 recommended A/Moscow/10/99*
- NH vaccine contained A/Sydney/5/97**

Percent circulating strains April 2000-September 2000 in the Southern hemisphere

A/Sydney-like**	69%
A/Moscow-like*	28%
A/Moscow-low	3%

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%

SH Vaccine 2005 H3N2 Vaccine Virus

- SH recommended A/Wellington/1/2004
- NH vaccine contained A/Fujian/411/2002

Percent of strains circulating February 2005-July 2005-SH (not including South America)

A/California/07/04-like	49%
A/Wellington/1/2004	51%

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

The Special Case of B Viruses-Continued

- Both lineages of B virus continue to circulate globally
- Studies have shown that most adults have been exposed to both viruses
 - Vaccination with either strain generally shows a boost in titer to both virus lineages, albeit lower for the mismatched lineage
 - Vaccination of naïve children show a titer rise against only the vaccine strain

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%	

SH Vaccine 2006- B Vaccine Virus

- SH recommended B/Malaysia/2506/2004* } **B-Victoria**
- NH vaccine contained B/Shanghai/361/2002 } **B-Yam**

Percentage of strains circulating Feb 2006 – August 2006 in the Southern hemisphere

B/Ohio/01/2005-like*	50%	} B-Victoria
B/Ohio/01/2005-like-low	34%	
B/Shanghai/361/2002-like	12.6%	} B-Yamagata
B/Florida/07/2004-low	3.4%	

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
- The most recent vaccine is probably the best vaccine

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