DoD Global, Laboratory-Based Influenza Surveillance Program

Vaccines and Related Biological Products Advisory Committee Meeting

February 18, 2009

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Outline

• Introduction & history
• Overview of sentinel & population-based surveillance
• Description & highlights: epidemiology, laboratory, vaccination, molecular analysis
• Discussion
Origin of the program

• 1976 US Air Force begins influenza surveillance

Aims:
– Isolate and identify circulating influenza virus
– Detect emerging variants
– Evaluate effectiveness of vaccine
DoD laboratory-based influenza surveillance program

- Sentinel (etiology) based surveillance
  - USAF School of Aerospace Medicine (USAFSAM)*
    Brooks City-Base, Texas

- Population based surveillance**
  - Naval Health Research Center (NHRC)
    San Diego, California

*Formerly the program was located in the Air Force Institute for Operational Health (AFIOH)

**Recruits, Shipboard and Border Populations
Specimen collection

Collection methods (USAFSAM)
- Patient criteria: fever $\geq 100.5^\circ$F and cough or sore throat (< 72 hr duration)
  - Case definition for Influenza-like Illness -> USAFSAM & sentinel sites

- Collection kits are provided to sentinel sites
  - Instructed to collect 6-10 specimens / week
  - Preferred specimen is nasal wash
- Surveillance questionnaire (e.g. vaccine, symptom and travel history)
DoD Global Influenza Surveillance

..................IN ACTION
DoD Global Influenza Surveillance

.................................IN ACTION

DoD-GEIS

Funding & Guidance

Laboratory

Epi Services
**DoD Global Influenza Surveillance**

**.........IN ACTION**

- **DoD-GEIS**
- **Funding & Guidance**
- **Laboratory**
  - Supplies FedEx, etc, Support
  - Participating Sites
    - Collect & ship Samples
- **Epi Services**
  - Program guidance, routine reports and notifications
DoD Global Influenza Surveillance

...............IN ACTION

DoD-GEIS

Funding & Guidance

Laboratory

Epi Services

Supplies
FedEx, etc,
Support

Conventional/
Molecular
Laboratory
Methods

Participating
Sites

Collect & ship
Samples

Flu Isolated

Program guidance,
routine reports and
notifications
DoD Global Influenza Surveillance

DoD-GEIS

Funding & Guidance

Laboratory

Supplies FedEx, etc, Support

Participating Sites

Collect & ship Samples

Flu Isolated

CDC

Vaccine Decisions

Epi Services

Program guidance, routine reports and notifications

Conventional/ Molecular Laboratory Methods

Selected Samples

All Molecular Sequences
Results by Week Collected

2007-2008
6,751 Specimens
Influenza 30.9%
   Flu A 72.7%
   H1 40%
   H3 60%
   Flu B 27.3%

2008-2009
2,155 Specimens (12 FEB)
Influenza 26.6%
   Flu A 90%
   H1 56.3%
   H3 43.7%
   Flu B 10%

Summary of Processed Specimens
All Sites by Week
Influenza Seasonal Years 2007-08 & 2008-09

As Of 12 Feb 2009
## Comparison of seasons

### 2007-2008 Season

- **Specimens processed:** 6,751
- **Countries:** 20
  - For example:
    - Antarctica
    - Embassy sites in Asia (US Staff)
    - Nepal
  - Ft. Gordon Cluster, Dec 2007 A/H1
  - Ellsworth AFB, vaccine strain contribution July 2007 A/H1

### 2008-2009 Season

- **Specimens processed:** 2,155
- **Countries:** 13
  - For example:
    - Saipan
    - **Deployed sites:** Kyrgyzstan, Kuwait, Iraq, Afghanistan
    - Guam early season
      - B Yamagata
    - S. Korea Dec 2008
      - A/H3 from Osan AB, then A/H1 from Army hospital in Seoul
A Subtype & B Lineage Results by Week Collected (USAFSAM) CURRENT SEASON – ALL SITES

2,155 Specimens (10 FEB)

Influenza 551
Flu A 488
H1 278
H3 210
Flu B 57

Influenza Subtype Results by Week and Year
Influenza Seasonal Year 2008-2009

As Of 10 Feb 2009
Influenza Subtype Results for Season 2008-2009 Across DoD Commands
Pacific Sites

South Korea

2008-2009

307 Specimens

Influenza 144

Flu A 134

H1 119

H3 24

Flu B 0
Vaccination Rates

- AF AD 95.8% ANG 92.0% AFR 84.0%
- All recruits are vaccinated – all services

AD = Active Duty  ANG = Air National Guard  AFR = Air Force Reserve
NHRC conducts population-based surveillance for febrile respiratory illness (FRI) at 8 US military basic training centers

- FRI rates tabulated weekly
- Specimens and clinical data are collected systematically from consenting trainees
- PCR and viral culture testing for influenza A/B, adenovirus, etc.
- Clinical data include vaccination status, type of vaccine, and vaccination date
NHRC Influenza Surveillance, 2008-09

- 70 lab-confirmed influenza A cases Oct 08 – Jan 09
  - 67 (96%) A/H1
  - HA sequencing of A/H1 isolates from recruits shows they are similar to an A/H1 strain circulating in the U.S. that has 5 amino acid mutations from the current A/H1 vaccine strain
  - 3 (4%) A/H3

Vaccination Status of Confirmed Influenza Cases Among Military Basic Trainees, 2008-09

![Graph showing vaccination status and percent flu positive for flu A and flu B cases among military basic trainees from 2008 to 2009.](image)
• Vaccine effectiveness calculation
  – Only considered periods when all trainees on base were vaccinated
    • Majority of recruit vaccination Oct-Jan was LAIV, > 90%
  – Trainees assumed “covered by vaccination” 14 days after arrival/receiving the vaccine
  – Proportion “unvaccinated” at each site estimated as those within their first 14 days of arrival
    • e.g., in 8-week training programs, 2/8 (25%) of the population was assumed to be “unvaccinated” at any given time
  – Previous estimates of 81-94% VE against lab-confirmed influenza using this method during past 5 seasons

• 2008-09 Results
  – 62 lab-confirmed cases (all A/H1) in this analysis
    • 26 cases among vaccinated, rate = 1.0/10,000 person-weeks
    • 36 cases among unvaccinated, rate = 5.1/10,000 person-weeks
  – VE (A/H1) = 79% (95% CI, 66-87%)
    • Other assumptions (7 days for coverage; 10% less vaccination) resulted in VE estimates of 83% and 66%, respectively
  – Vaccine appeared to be effective against A/H1 among U.S. military recruits
Preliminary Vaccine Data USAFSAM

- 2,155 specimens; 551 (25.6%) influenza isolates
  - 37.6% (207 of 551) identified vaccination status (quest avail)
  - 62.3% (129 of 207) characterized as vaccinated
  - 77.5% (n=100) LAIV; 22.5% (n=29) Injection

% Distribution of Influenza Subtypes/Lineage by Vaccination Status (as of 07 Feb 2009)

<table>
<thead>
<tr>
<th></th>
<th>Vaccinated (N=129)</th>
<th>Un-Vaccinated (N=78)</th>
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<tbody>
<tr>
<td><strong>Influenza A</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A sub pending</td>
<td>0.8% (1)</td>
<td>1.3% (1)</td>
</tr>
<tr>
<td>A/H1</td>
<td>81.4% (105)</td>
<td>53.8% (42)</td>
</tr>
<tr>
<td>A/H3</td>
<td>15.5% (20)</td>
<td>23.0% (18)</td>
</tr>
<tr>
<td><strong>Influenza B</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B lineage pending</td>
<td>2.3% (3)</td>
<td>3.8% (3)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>0</td>
<td>17.9% (14)</td>
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Laboratory method

- **Molecular analysis**
  - Nucleic acid extraction
  - PCR analysis – A/H1, A/H3 and B
  - Sequencing of HA1 region for positive flu’s
  - Sequence analysis performed - data to CDC

- **Tissue culture analysis**
  - Influenza A, B, PIV 1,2,3, RSV, Adeno
  - All positive tissue culture archived for additional testing

- **Archiving**
  - Repeat or additional testing as requested by provider
  - CDC request for egg culture production and possible use as vaccine seed virus
Influenza A/H1 HA (HA1) Phylogenetic Analysis

- Overall amino acid sequence identity for the 184 specimens sequenced 98.1 – 100%
- 3 at 98.1%
- 88 at 99.1% or more
- 93 greater than 98.1% but less than 99.1%
- Parallel amino acid changes at 141 and 185

All annotated aa changes are comparisons of submitted specimens to A/Brisbane/59/2007 and do not relate to previous vaccine strains

2008 – 09 Vaccine strain
Previous Vaccine strains

January 09 (collection date)

"_" Parallel Mutation Site
Influenza A/H3 HA (HA1) Phylogenetic Analysis

• Overall amino acid sequence identity for the 118 specimens sequenced 97.9 – 99.4%
  • 15 at 97.9%
  • 73 at 99.1% or more
  • 30 greater than 97.9% but less than 99.1%
• Parallel amino acid changes at 173

2008 – 09 Vaccine strain
Previous Vaccine strains
January 09 (collection date)
December 08 (collection date)
^ Create glycosylation motif
& Loss of glycosylation motif
“_” Parallel Mutation Site

All annotated aa changes are comparisons of submitted specimens to A/Brisbane/10/2007 and do not relate to previous vaccine strains
Influenza B HA (HA1) Phylogenetic Analysis

- Overall amino acid sequence identity for the 35 B Yamagata lineage specimens sequenced to date
  98.2 – 99.7%*
- Overall amino acid sequence identity for the 11 B Victoria lineage specimens sequenced to date
  97.3 – 97.9%**

2008 – 09 Vaccine strain
Previous Vaccine strains
January
A Ten Seasonal Year Review

*1998-1999 through 2008-2009*

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<tr>
<td>Negative</td>
<td>73%</td>
<td>59%</td>
<td>66%</td>
<td>61%</td>
<td>58%</td>
<td>58%</td>
<td>63%</td>
<td>59%</td>
<td>42%</td>
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<tr>
<td>Adenovirus</td>
<td>3%</td>
<td>33%</td>
<td>16%</td>
<td>18%</td>
<td>20%</td>
<td>11%</td>
<td>5%</td>
<td>3%</td>
<td>22%</td>
<td>12%</td>
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<td>1%</td>
<td>1%</td>
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<td>2%</td>
<td>1%</td>
<td>0%</td>
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<tr>
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<td>1%</td>
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<td>1%</td>
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<tr>
<td>Influenza A</td>
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<td>6%</td>
<td>6%</td>
<td>14%</td>
<td>8%</td>
<td>25%</td>
<td>26%</td>
<td>16%</td>
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<tr>
<td>Influenza B</td>
<td>5%</td>
<td>1%</td>
<td>7%</td>
<td>3%</td>
<td>8%</td>
<td>2%</td>
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<td>Parainfluenza</td>
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<td>1%</td>
<td>1%</td>
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<tr>
<td>Respiratory Syncytial Virus</td>
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<td>1%</td>
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<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0.4%</td>
<td>1%</td>
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<tr>
<td>Metapneumovirus</td>
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<td>0.2%</td>
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<tr>
<td><strong>TOTAL</strong></td>
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<td>6933</td>
<td>4561</td>
<td>4094</td>
<td>4357</td>
<td>4311</td>
<td>2610</td>
<td>4485</td>
<td>6751</td>
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</tbody>
</table>

*2008-2009 data includes specimens collected from 28 Sept 2008 through 7 Feb 2009.*
Acknowledgements

• Armed Forces Health Surveillance Center
• DoD-Global Emerging Infections Surveillance and Response System (GEIS)
• NHRC, USAFSAM
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• Military Health System
  – Landstuhl Regional Medical Center
  – Tripler Army Medical Center
• Medical & public health staff
• USACHPPM-S, USACHPPM-EUR

Contact Us!

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