Announcements

- Register for the Epi-Tech Trainings:
  1. Log-on or Request log-on ID/password: https://tiny.army.mil/r/zB8A/CME

- Please enter your name/service and e-mail into the chat box to the left or email the disease epidemiology program at: usarmy.apg.medcom-phc.mbx.disease-epidemiologyprogram13@mail.mil
  - You will receive a confirmation email within the next 48 hours with your attendance record

- Please mute your phones and DO NOT place us on hold. Press *6 to mute/unmute your phone.
Influenza in the DoD

USAF School of Aerospace Medicine / Epidemiology Consult Services
Presented by: DoD Global, Laboratory-based, Influenza Surveillance Program
Lt Col Federinko, MD, MPH, Gregory Wolff, MPH, Jeffrey Thervil, MPH, Amber Brown, MPH
DSN: 798-3196 (Comm: 937 938-3196)
29 September 2015
I. About Influenza
   I. Clinical Information
   II. Subtypes and Strains
   III. Immunity-related Changes: Antigenic Drift/Shift
   IV. 2015-2016 Vaccine
   V. 2014-2015 Influenza Vaccine Facts

II. Influenza Surveillance in Military Populations
   I. Reportable Medical Event Case Definition
   II. Influenza-like Illness (ESSENCE)
   III. Surveillance Activities by Service

III. Contact Information
Clinical Information

• An acute viral disease of the respiratory tract
  – Fever, cough, sore throat, runny nose, headache, fatigue, body aches
• Spread by droplets or touching contaminated surfaces
• Incubation period is 1-4 days (2 days on average)
• Contagious 1 day prior, and up to 5-7 days after symptom onset (longer for children & immunocompromised)
• Severity depends on flu virus, vaccination status, and health status
• Recovery: few days to two weeks (1 week on average)
Subtypes and Strains

- **Influenza A**
  - Evolves rapidly & responsible for most epidemics and pandemics
  - Subtypes:
    - Divided into subtypes based on two surface proteins:
      - Hemagglutinin (HA)
      - Neuraminidase (NA)
    - Combine to create a single subtype (Example: H5N1, H1N1)
    - Are further divided into strains
      - Found in many different animals

- **Influenza B**
  - Gradually changing virus
  - Classified by strains based on their lineage:
    - Examples are Yamagata and Phuket
  - Found primarily in humans
  - May cause epidemics, but not pandemics
Antigenic Drift

• Immunity-related changes to influenza A virus
  – Changes to regions of the HA surface protein can affect human antibody responses to the virus

• Antigenic Drift
  – Small gradual changes that occur over time and create a new strain that may not be recognized by immune system
    • Reason that new influenza vaccine is manufactured and distributed each year
  – USAFSAM conducts molecular sequence analysis on influenza specimens to monitor these changes
Antigenic Shift

- **Antigenic Shift**
  - Abrupt major change that produces a novel (not seen previously in humans) influenza A virus, for example pandemic H1N1
  - Result of direct animal-to-human transmission or mixing of human and animal viral genes within the same individual (reassortment)
  - Most people have little or no protection against the new virus

- **Example: 2009 influenza A(H1N1)pdm**
Vaccine

• Get Vaccinated Early
  – Flu seasons can be unpredictable and begin as early as October
  – Takes about 2 weeks for antibody production after vaccination
  – Influenza vaccine cannot give you influenza
    – The virus injected is inactivated (killed) or is attenuated (weakened)
    – Designed to only cause mild infection at cooler temperatures (not in the lungs)

• This year, DoD ordered over 3.5M doses of trivalent (injection) and quadrivalent (injection & mist) vaccines for service members and beneficiaries
  – Trivalent: A(H3N2), A(H1N1)pdm09, B/Yamagata
  – Quadrivalent: A(H3N2), A(H1N1)pdm09, B/Yamagata, B/Phuket
Annual Influenza Vaccine Manufacturing Timeline for entire US Supply

- **Strain Selection**
  - CDC
  - FDA
  - WHO
  - Surveillance & Reassortants

- **Produce & Standardize Reagents for New Strains**

- **Annual License Approval**

- **Vaccination**

- **Production (at risk)**
  - Produce Working Seed
  - Production

- **Production (may be at risk)**
  - Production

- **Strain Balancing**

- **Formulation**

- **Filling & Packaging**

- **Distribution**

---

**~6 Months to produce ~140 Million doses**
- 2 weeks of production = >10 Million doses

**~4 Months to vaccinate ~140 Million people**
- 2 weeks represents >16 Million vaccinations
In mid to late February 2014, WHO and FDA recommended for the 2014-2015 influenza vaccine (Northern Hemisphere) to include the following components:

- A/California/7/2009 (H1N1)pdm09-like virus
- A/Texas/50/2012 (H3N2)-like virus
- B/Massachusetts/2/2/2012-like virus
- Quadrivalent vaccine also included an additional B virus (B/Brisbane/60/2008-like virus)

Late March 2014: drifted A(H3N2) viruses were detected during routine surveillance testing (4% antigenically distinct from A/Texas)

Jun-Aug 2014: approximately 1/3 of circulating viruses are antigenic drift variants

Sept 2014: nearly 2/3 of circulating viruses are drifted; WHO recommends A/Switzerland/2013-like virus for the southern hemisphere

52% of influenza A(H3N2) viruses collected and analyzed in the U.S. from 1 October – 22 November 2014 were antigenically different from the A(H3N2) vaccine virus.

- Reason for the reduced vaccine effectiveness against A(H3N2) viruses this season.
- Most of the drifted A(H3N2) viruses were A/Switzerland/9715293/2013 viruses, which was the A(H3N2) virus selected for the 2014 Southern Hemisphere influenza vaccine.
Influenza A/H3N2 HA
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)

3C.2A
27%
3C.3
73%

3C.3a

3C.3

2014-2015

2015-2016

Influenza A/H3N2 HA Analysis
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)

3C.2A
27%
3C.3
73%

3C.3a

3C.3

2014-2015

2015-2016

Influenza A/H3N2 HA Analysis
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)

3C.2A
27%
3C.3
73%

3C.3a

3C.3

2014-2015

2015-2016

Influenza A/H3N2 HA Analysis
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)

3C.2A
27%
3C.3
73%

3C.3a

3C.3

2014-2015

2015-2016

Influenza A/H3N2 HA Analysis
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)

3C.2A
27%
3C.3
73%

3C.3a

3C.3

2014-2015

2015-2016

Influenza A/H3N2 HA Analysis
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)

3C.2A
27%
3C.3
73%

3C.3a

3C.3

2014-2015

2015-2016

Influenza A/H3N2 HA Analysis
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)

3C.2A
27%
3C.3
73%

3C.3a

3C.3

2014-2015

2015-2016

Influenza A/H3N2 HA Analysis
Phylogenetic Analysis 2014-2015

N=523
A(H3N2) Vaccine strain: A/Texas/50/2012
Reference Strain
October 2014 4%
November 2014 13%
December 2014 68%
January 2015 15%
ADD GLY Create Glycosylation Motif
LOSS GLY Loss of Glycosylation Motif
F CDC Reference Antigen
e Egg Isolate
LR Low Reactor to: A/Texas/50/2012 (≥8 fold)
Testing for Influenza

• **Rapid Diagnostic Tests**
  – Fast & easy but....
    • High specificity (correctly identifies negatives)
    • Low sensitivity (does not pick up positives very well)
    • Accuracy depends on the prevalence of circulating viruses

• **Confirmatory Tests**
  – Much more sensitive & specific
  – Common
    • RT-PCR detection (24-48 hours)
    • Tissue cell culture (up to 10 days for negative result)
  – Others
    • Immunofluorescent antibody staining (IFA) antigen detection
    • Hemagglutination inhibition (HI) 4-fold rise in antibody titer in paired acute and convalescent sera
    • Immunohistochemical (IHC) staining antigen detection (autopsy)
Influenza Surveillance

• Surveillance in military populations

• Varied approaches
  – Reportable Medical Events (RME)
  – Syndromic
  – Sentinel - AF
  – Shipboard, Recruit, & Population - Navy
  – Population - Army
Influenza and Military Populations

- Even with modern medical advances, influenza and influenza-like illness can cause high morbidity rates, undermining readiness

- Military members and their families:
  - Are stationed where new strains are likely to appear
  - Are highly mobile across the globe and could quickly spread a pandemic strain
  - May live in areas that represent "gaps" in the World Health Organization (WHO)/Centers for Disease Control and Prevention (CDC) influenza surveillance network

- Training environments are well suited for the spread of emerging respiratory pathogens

- Highly immunized military plus electronic vaccination data registry facilitate rapid assessment of vaccine protection against emerging strains
Reportable Medical Events (RMEs)

• “A reportable event may represent an inherent, significant threat to public health and military operation. These events have the potential to affect large numbers of people, to be widely transmitted within a population, to have severe/life threatening clinical manifestations, and to disrupt military training and deployment. Timely accurate reporting of probable, suspected or confirmed cases ensures proper identification, treatment, control, and follow-up of cases

• DRSi
  – Web-based application
  – Identify, collect, document, manage, and track information on RMEs
  – Completeness/timeliness of data is user-driven
## Influenza-associated Hospitalization

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Details</th>
</tr>
</thead>
</table>
| Included population | < 65 years of age  
                      | Any beneficiary type/mandate status                                    |
| Patient status    | Influenza-associated hospitalization                                    |
|                   | Fever ≥ 100.5°F with cough or sore throat in absence of other diagnosis |
| Laboratory        | Positive rapid or confirmatory test                                    |
|                   | < 4 days after hospital admission                                       |

### Case Classification

<table>
<thead>
<tr>
<th>Case Classification</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed</td>
<td>Meet criteria with confirmatory lab test (RT-PCR, culture, IFA, IHC, HI titer)</td>
</tr>
<tr>
<td>Probable</td>
<td>Meet case definition with positive rapid antigen test</td>
</tr>
</tbody>
</table>

### Notes

For all confirmed cases, a nasal wash specimen should be submitted to an appropriate lab for further influenza lab testing (i.e. sequencing)
ILI Syndromic Surveillance

- Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE)
  - Designed by Johns Hopkins University Applied Physics Laboratory and DoD
  - Internet-based syndromic disease surveillance system
  - Used by DoD and some civilian health departments
- Useful for early detection with maximum sensitivity
  - Often at the cost of specificity (false alerts)
ILI Syndromic Surveillance

- **ILI**
  - No influenza specific ICD codes
  - Includes ICD, CPT and Chief Complaint data
- **Influenza Specific**
  - Influenza specific ICD codes only
- For more information on ESSENCE, please refer to https://gumbo2.area52.afnoapps.usaf.mil/epi-consult/training/index.cfm
DoD Global, Lab-based, Influenza Surveillance Program

- **AF Influenza Program “Project Gargle”: 1976-1997**
- **National Science and Technology Council Presidential Decision Directive (NSTC PDD-7)**
  - U.S. not prepared for threat posed by emerging infectious diseases
  - Action taken and AF was assigned lead executive agent for DoD influenza surveillance
- **DoD Global, Lab-based Influenza Surveillance Program : 1998 – present**
  - Sentinel-based, across services
    - Selected according to mission, location, gap in international surveillance
  - Collect 6-10 specimens/week meeting ILI case definition
  - Complete patient information on influenza surveillance questionnaire
  - Submit specimens and questionnaires to the USAFSAM lab
DoD Global, Lab-based, Influenza Surveillance Program

• USAFSAM provides collection kits to sentinel and participating sites

• Nasal wash collection kit
  – Questionnaire
  – Syringe
  – Collection cup
  – VTM vial
  – Biohazard bag
  – Bib
DoD Global, Lab-based, Influenza Surveillance Program

Sentinel Surveillance Sites 2014-2015

CONUS Sites: 55
- Air Force: 33
- Army: 11
- Navy & Marine Corps: 7
- Coast Guard: 6
- JTF CAPMED/DHA: 2

OCONUS Sites: 36
- Air Force: 18
- Army: 9
- Navy & Marine Corps: 7
- Coast Guard: 2
DoD Global, Lab-based, Influenza Surveillance Program

Prevent Influenza Infections
Reduce Morbidity & Mortality
Force Health Protection

Identify current strains & outbreaks
Analyze vaccine effectiveness
Track genetic changes of viruses in circulation (molecular sequence analysis)
Detect and monitor antiviral resistance
Contribute to annual vaccine selection
Monitor severity trends
Surveillance Process and Vaccine Development

- Sentinel Sites
- Participating Non-Sentinel Sites
- National Respiratory & Enteric Virus Surveillance System Labs (U.S.)
- WHO Influenza Labs

USAFSAM DoD Global Lab-Based Sentinel Surveillance

CDC/Viral Surveillance

FDA's VRBPAC* meets to decide strains for annual flu vaccine

*Food and Drug Administration, Vaccines and Related Biological Products Advisory Committee
DoD Global, Lab-based, Influenza Surveillance Program

https://gumbo2.area52.afnoapps.usaf.mil/epi-consult/influenza

- Site-specific surveillance dashboard
  - Submission data
  - POC information
  - Shipping/storage
- Welcome packet
- Weekly reports
- Other sentinel site resources
- Novel virus information
- Historical data
- Program publications

Note: If you would like to receive these reports by email, send a request to the program at: usafsam.phrflu@us.af.mil
Influenza Dashboard

- Online dashboard that displays base-level information
  - Submission data
  - POC information
  - Shipping & storage information

https://gumbo2.area52.afnoapps.usaf.mil/epi-consult/influenza/dashboard/
Navy Influenza Surveillance Activities

• Shipboard and Recruit ILI surveillance
  – Fleet Disease and Injury Surveillance (D&I)
  – Naval Health Research Center (NHRC) FRI program
• Participate in USAFSAM sentinel surveillance program
• NMCPHC Epi Data Center Influenza SITREPs
• NMCPHC Influenza Advisory
  – Guide to tracking pneumonia in ESSENCE
Navy Influenza Surveillance Activities

• Fleet D&I surveillance (formerly known as DNBI)
  – Shift from weekly reporting of xls reports to electronic D&I tracking of AHLTA-T/SAMS encounters
    • Develop D&I report, including Fever and Respiratory categories
  – Units who wish to continue to report via xls spreadsheet - templates and reporting guidance can be found at: website http://www.med.navy.mil/sites/nmcphc/program-and-policy-support/disease-and-injury-reports
Navy Influenza Surveillance Activities

• NHRC FRI program
  – Includes recruit training centers and participating ships
  – Describe circulating respiratory pathogens, including influenza
  – Identify pathogens in support of outbreaks
  – Contributes to FDA’s VRBPAC discussion for development of next year’s influenza vaccine
  – Contact NHRC at nhrc-fri@med.navy.mil for more information and to receive routine reports

• Can describe ILI outbreaks, anticipate duration of illness, describe extent of outbreak, and identify patterns to curtail disease spread
Navy Influenza Surveillance
Activities

- Weekly SITREP including:
  - Vaccination rates
  - Overall flu burden
  - Active Duty/recruit burden
  - Description of hospitalized and outpatient cases and trends
  - Noteworthy information in the open media

- Other reports to track vaccine use and disease burden for BUMED

- For more information and to access the latest SITREP, email:
  usn.hampton-roads.navmcpubhlthcenpors.list.nmcphc-epi@mail.mil
Navy Influenza Surveillance Activities

- NMCPHC Seasonal Influenza Advisory:
  - Navy flu reporting requirements in DRSi
  - Surveillance recommendations for upcoming season
  - Includes guidance on pneumonia surveillance in ESSENCE
  - http://www.med.navy.mil/sites/nmcphc/program-and-policy-support/Pages/Influenza.aspx for more information
Army Influenza Surveillance

- Uses a combination of CHCS Ad Hoc Reporting, DRSi and ESSENCE
- CHCS flat files are sent from each Army lab on a weekly basis to USAPHC containing all positive and negative results of PCRs, cultures and rapid antigen testing
- Army influenza reports can be found at: http://phc.amedd.army.mil/whatsnew/Pages/PublicationDetails.aspx?type=USAPHC%20Influenza%20Surveillance%20Activity
Resources

USAFSAM/PHR Epidemiology Consult Service: Influenza Surveillance
https://gumbo2.area52.afnoapps.usaf.mil/epi-consult/influenza/

Navy and Marine Corps Public Health Center: Influenza homepage
http://www.med.navy.mil/sites/nmcphc/program-and-policy-support/Pages/Influenza.aspx

Army Public Health Center: Influenza Reports
http://phc.amedd.army.mil/whatsnew/Pages/PublicationDetails.aspx?type=APHC%20Influenza%20Surveillance%20Activity

DHA Public Health Division, Immunization Healthcare Branch, Influenza – Seasonal vaccine information:
http://www.vaccines.mil/Influenza_-_Seasonal

FLU.GOV “Know what to do about the flu”
http://www.flu.gov/

CDC Influenza Home Page
http://www.cdc.gov/flu/

WHO Global Influenza Surveillance Network: Manual for the laboratory diagnosis and virological surveillance of influenza
QUESTIONS?
Contact Information

- **Army:** APHC – Disease Epidemiology Program
  Aberdeen Proving Ground – MD
  Comm: (410) 436-7605  DSN: 584-7605
  usarmy.apg.medcom-phc.mbx.disease-epidemiologyprogram13@mail.mil

- **Navy:** Contact your cognizant NEPMU
  NEPMU2: COMM: (757) 950-6600; DSN: (312) 377-6600
  Email: usn.hampton-roads.navhospporsva.list.nepmu2norfolk-threatassess@mail.mil
  NEPMU5: COMM: (619) 556-7070; DSN: (312) 526-7070
  Email: HealthSurveillance@med.navy.mil
  NEPMU6: COMM: (808) 471-0237; DSN: (315) 471-0237
  Email: usn.jbphh.navenpvtmedusixhi.list.nepmu6@mail.mil
  Email: NEPMU7@eu.navy.mil

- **Air Force:** Contact your MAJCOM PH or USAFSAM/PHR
  USAFSAM / PHR / Epidemiology Consult Service
  Wright-Patterson AFB, Ohio
  Comm: (937) 938-3207  DSN: 798-3207
  episervices@us.af.mil