Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

<table>
<thead>
<tr>
<th>Site</th>
<th>Current Week*</th>
<th>Since Oct. 1, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A/Untyp.</td>
<td>A/H3</td>
</tr>
<tr>
<td>Ft. Benning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ft. Jackson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ft. Leonard Wood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRTC Great Lakes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lackland AFB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCRD Parris Island</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCRD San Diego</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGTC Cape May</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- NHRC also conducts shipboard FRI surveillance that includes large-deck ships of the US Fleet Forces (Atlantic), 3rd (Pacific), and 7th (Far East) Fleets.
- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries in Illinois and San Diego (details on page 7).
- NHRC-CDC-BIDS collaborative border FRI/SARI surveillance program is ongoing at 7 US-Mexico border sites in San Diego (2) and Imperial (5) counties in California. Details on page 8.
- For more information about NHRC FRI surveillance programs, please contact NHRC.

Vaccination Status of Confirmed Influenza Cases Among US Military Basic Trainees, 2014-16

- NHRC is conducting laboratory-based surveillance for meningococcal disease. The program’s purpose is to track and characterize meningococcal cases among DoD medical beneficiaries. For more information and the most recent data, click here.
Adenovirus

- Vaccination against types 4 and 7 adenovirus was instituted at all basic training centers by mid-November 2011.
- FRI rates and the proportion of FRI cases positive for adenovirus have decreased markedly since vaccine was reintroduced.
- Sporadic adenovirus cases at basic training centers 2012-16. FRI rates remain low in general.

FRI Rates

- FRI surveillance is ongoing at 8 U.S. military basic training centers, representing all service branches. As each week’s FRI count is reported, FRI Rate Status is classified into one of 3 categories:
  - At or below expected value (expected value shown as dashed line)
  - Moderately elevated
  - Substantially elevated

Week ending 24 December 2016:
- At or below expected value:
  Fort Benning (trainees on holiday leave, returning the first week in Jan.)
  Fort Jackson (trainees on holiday leave, returning the first week in Jan.)
  Fort Leonard Wood (trainees on holiday leave, returning the first week in Jan.)
  Naval Recruit Training Command, Great Lakes
  Marine Corps Recruit Depot, San Diego
  Lackland Air Force Base (data through 29 Oct.)
  Coast Guard Training Center, Cape May (data through 17 Dec.)

- Moderately elevated:
  None

- Substantially elevated:
  Marine Corps Recruit Depot, Parris Island
Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)
NHRC Respiratory Illness Update
Week Ending: 24 December 2016

MCRD SD FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

MCRD PI FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Back to FRI Report

Observed FRI rate (expected rate = dashed line)  
Moderately elevated  
Substantially elevated  
Pneumonia rate (incl. afebrile)
Lackland AFB FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Cape May FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Back to FRI Report
**DoD Beneficiary Surveillance**

- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries at Lovell FHCC (Great Lakes, IL) and in 4 NMC San Diego facilities: the Emergency Department, Pediatric Department, Naval Branch Health Clinic Kearny Mesa, and NH Camp Pendleton.

- For questions regarding surveillance in this population, please contact the principal investigators at NHRC-FRI_Ben@med.navy.mil.
**US-Mexico Border Surveillance**

- In collaboration with the CDC Border Infectious Disease Surveillance program and San Diego/Imperial Counties, NHRC performs laboratory testing for FRI cases among civilians near the US-Mexico border. Both outpatient (FRI) and inpatient (Severe Acute Respiratory Illness; SARI) cases are included in the program. Current sites are located in San Diego (2) and Imperial (5) counties in California.
Phylogenetic Comparison of Influenza A-pandemic 2009 H1N1 (pH1N1) HA and NA Protein Sequences

- 47 analyzed Influenza A pH1N1 HA sequences were derived from MDCK isolates and 4 belonged to clade 6B while 43 belonged to the subclade 6B.1, defined by mutations S84N, S162T (ADD GLY) and I216T.
- 46 analyzed Influenza A pH1N1 NA sequences were derived from MDCK isolates.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown (both HA and NA sequences) are with respect to A/California/07/2009-like virus.

Summary of Influenza A (pH1N1) Protein Homology When Compared to 2015-2016 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. Isolates</th>
<th>2015-2016 Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/pH1N1 HA</td>
<td>47</td>
<td>A/California/07/2009</td>
<td>97.0-98.0%</td>
</tr>
<tr>
<td>A/pH1N1 NA</td>
<td>46</td>
<td>A/California/07/2009</td>
<td>96.1-97.3%</td>
</tr>
</tbody>
</table>

Summary of Influenza A (pH1N1) N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity.\(^2\) Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server

http://www.cbs.dtu.dk/services/NetNGlyc/

<table>
<thead>
<tr>
<th>A/pH1N1 Segment</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>ADD GLY</td>
</tr>
<tr>
<td>NA</td>
<td>S162N</td>
</tr>
<tr>
<td></td>
<td>N44S, S70N</td>
</tr>
<tr>
<td></td>
<td>N386K</td>
</tr>
</tbody>
</table>

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Phylogenetic Comparison of Influenza A (H3N2) HA and NA Protein Sequences

- 33 analyzed H3N2 HA sequences were derived from MDCK isolates and 17 were derived from clinical specimen.
- 28 analyzed H3N2 NA sequences were derived from MDCK isolates and 9 were derived from clinical specimen.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown are with respect to 2010 vaccine strain A/Perth/16/2009-like virus for HA sequences and A/Norway/1186/2011 for NA sequences.

Summary of Influenza A (H3N2) Protein Homology When Compared to 2015-2016 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No.</th>
<th>2015-2016 Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3N2 HA</td>
<td>50</td>
<td>A/Switzerland/9715293/2013</td>
<td>96.8-99.6%</td>
</tr>
<tr>
<td>H3N2 NA</td>
<td>37</td>
<td>A/Switzerland/9715293/2013</td>
<td>97.9-98.6%</td>
</tr>
</tbody>
</table>

Summary of Influenza A (H3N2) N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity. Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server http://www.cbs.dtu.dk/services/NetNGlyc/

<table>
<thead>
<tr>
<th>A/H3N2 Segment</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>K160T</td>
<td>S47P N122D T128A N144S N158K N158H T160K T160I</td>
</tr>
<tr>
<td>NA</td>
<td>S245N N329I S331R</td>
<td>S247T N329S N329T</td>
</tr>
</tbody>
</table>

Phylogenetic Comparison of Influenza B (Victoria and Yamagata) HA and NA Protein Sequences

- 52 analyzed Influenza B HA sequences were derived from MDCK isolates. 27 isolates belonged to the V1A clade of the Victoria Lineage and 25 belonged to the Y3 clade of the Yamagata lineage.
- 53 analyzed Influenza B NA sequences were derived from MDCK isolates. 27 isolates belonged to the V1A clade of the Victoria Lineage and 26 belonged to the Y3 clade of the Yamagata lineage.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown (both HA and NA sequences) are with respect to previous vaccine strains B/Ohio/01/2005-like virus for B/Victoria specimens and B/Florida/04/2006-like virus for B/Yamagata specimens.

Summary of Influenza B Protein Homology When Compared to 2015-2016 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. Isolates</th>
<th>2015-2016 Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/Victoria HA</td>
<td>27</td>
<td>B/Brissone/60/2008</td>
<td>99.1-99.5%</td>
</tr>
<tr>
<td>B/Victoria NA</td>
<td>27</td>
<td>B/Brissone/60/2008</td>
<td>98.3-98.54%</td>
</tr>
<tr>
<td>B/Yamagata HA</td>
<td>25</td>
<td>B/Phuket/3073/2013</td>
<td>99.1-99.5%</td>
</tr>
<tr>
<td>B/Yamagata NA</td>
<td>26</td>
<td>B/Phuket/3073/2013</td>
<td>98.7-100.0%</td>
</tr>
</tbody>
</table>

Summary of Influenza B N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity. Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server. [http://www.cbs.dtu.dk/services/NetNGlyc/](http://www.cbs.dtu.dk/services/NetNGlyc/)

<table>
<thead>
<tr>
<th>INF B Segment</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>A198T</td>
<td>N196D T198N</td>
</tr>
<tr>
<td>NA</td>
<td>D463N, S295N</td>
<td></td>
</tr>
</tbody>
</table>

Summary of Influenza A/pH1N1, A/H3N2 and Influenza B Hemagglutinin (HA) Genetic Groups

Influenza A/pH1N1
- 6B.1, 6B.4, 9%
- 6B.1, 43, 91%

Influenza A/H3N2
- H3N2 3C.3a 50%
- H3N2 3C.2a 50%

Influenza B
- B/Vic (1A), 27, 52%
- B/Yam (Y3), 25, 48%
Evolutionary Relationships
Among Influenza A (pH1N1) Hemagglutinin (HA) Genes
2015-2016 Influenza Season

Vaccine Strain
Reference Strain
2013-2014 consensus*

December 2015
January 2016
February 2016
March 2016
April 2016
May 2016

LOSS GLY1: predicted loss of glycosylation
ADD GLY1: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border Inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit
Ship: Shipboard

*No pH1N1 sequencing data available
for 2014-2015 season
Evolutionary Relationships Among Influenza A (pH1N1) Neuraminidase (NA) Genes 2015-2016 Influenza Season

Vaccine Strain
Reference Strain

2013-2014 consensus*

December 2015
January 2016
February 2016
March 2016
April 2016

May 2016

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border Inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit
Ship: Shipboard

*No pH1N1 sequencing data available for 2014-2015 season
Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2015-2016 Influenza Season

Vaccine Strain

Reference Strain

December 2015
January 2016
February 2016
March 2016
April 2016
May 2016
July 2016

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border outpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit
Ship: Shipboard
*: clinical specimen

A/California/19/2015
A/California/NIHRC_BRD41174N/2016 [P79S]
A/California/NHCRC_BRD21326N/2016
A/California/NHCRC_BRD27582/2016
A/California/NHCRC_BRD27575/2015
A/California/NHCRC_SAR2052S/2015
A/NewYork/57/2015
A/California/NHCRC_BRD41207N/2016
A/California/NHCRC_SAR41418N/2016 [E64K]
A/NewJersey/NHCRC_93398/2016*
A/NewJersey/NHCRC_93400/2016*
A/NewJersey/NHCRC_93408/2016*
A/NewJersey/NHCRC_93416/2016*
A/California/NHCRC_BRD41199N/2016
A/Canberra/82/2014
A/Switzerland/9715293/2013
A/Nebraska/04/2014 [P79S]
A/Victoria/361/2011 [E358K, N329T (LOSS GLY)]
A/Texas/50/2012 [R150H]
A/HongKong/146/2013

A/Perth/16/2009
A/Norway/1186/2011

Amino Acid Substitution per 100 residues
Evolutionary Relationships Among Influenza B Hemagglutinin (HA) Genes 2015-2016 Influenza Season

Vaccine Strain

Reference Strain 2013-2014 consensus December 2015

January 2016
February 2016
March 2016
April 2016
May 2016

July 2016

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit
Ship: Shipboard

Amino Acid Substitution per 100 residues

Yamagata Lineage

Victoria Lineage

B/Washington/3871/2014 [H2N1M]
B/Sydney/7/2014
B/Brisbane/09/2014 [T198N LOSS GLY]
B/NewYork/3871/2014 [G251M]
B/Massachusetts/02/2012 [N196D LOSS GLY]
B/Florida/4/2006
B/Phuket/3073/2013 [N196D]
B/Wisconsin/01/2010

1.7

B/California/NHRC_27794/2016
B/Illinois/NHRC_FDX51712/2016
B/Illinois/NHRC_FDX41383N/2016
B/Illinois/NHRC_FDX21851/2016
B/Illinois/NHRC_FDX40802/2016
B/California/NHRC_BRD142149N/2016
B/California/NHRC_BRD1414N/2016
B/California/NHRC_BRD1407N/2016
B/California/NHRC_SAR1407N/2016
B/California/NHRC_BRD14354N/2016
B/California/NHRC_BRD14250N/2016
B/California/NHRC_BRD14274N/2016
B/California/NHRC_BRD14295N/2016
B/California/NHRC_SAR14381N/2016
B/California/NHRC_BRD12013N/2016
B/California/NHRC_BRD142123N/2016
B/California/NHRC_BRD14219N/2016

Y3

Y2

1A

1B

B/Ohio/01/2005
B/Washington/63/2016 [V252M]
B/Washington/83/2016 [N299D, V146I]
B/Colorado/36891/2016 [T199N LOSS GLY]
B/Wellington/24/2015
B/Louisiana/180/2015
B/California/NHRC_BRD12120N/2010
B/Washington/63/2016 [V252M]
B/Washington/83/2016 [N299D, V146I]
B/Louisiana/180/2015

B/Georgia/NHRC_68492/2016
B/Georgia/NHRC_68447/2016
B/Georgia/NHRC_68429/2016
B/Illinois/NHRC_FDX51734/2016
B/Illinois/NHRC_FDX51735/2016
B/Missouri/NHRC_36910/2016
B/California/NHRC_BRD60552N/2016
B/Illinois/NHRC_FDX51689/2016
B/Missouri/NHRC_36897/2016
B/Texas/NHRC_55426/2016
B/Georgia/NHRC_68410/2016
B/Georgia/NHRC_68417/2016
B/California/NHRC_BRD12149N/2016 [D562G]
B/California/NHRC_BRD12149N/2016 [A276G]
B/California/NHRC_FDX11042/2016
B/California/NHRC_BRD60517N/2016
B/California/NHRC_BRD60549N/2016
B/California/NHRC_FDX30430/2016
B/NewJersey/NHRC_93380/2016
B/California/NHRC_FDX21822/2016
B/NewJersey/NHRC_93327/2016
B/NewJersey/NHRC_93327/2016
B/NewJersey/NHRC_93327/2016

B/Ohio/01/2005
B/Washington/63/2016 [V252M]
B/Louisiana/180/2015
B/California/NHRC_BRD12120N/2010
B/Ohio/01/2005
B/Washington/63/2016 [V252M]
B/Louisiana/180/2015
B/California/NHRC_BRD12120N/2010

1.6

Amino Acid Substitution per 100 residues

0
Evolutionary Relationships Among Influenza B Neuraminidase (NA) Genes

2015-2016 Influenza Season

Vaccine Strain

Reference Strain

2013-2014 consensus

December 2015
January 2016
February 2016
March 2016
April 2016
May 2016

July 2016

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Yamagata Lineage

W

Victoria Lineage