Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

<table>
<thead>
<tr>
<th>Site</th>
<th>Since last report*</th>
<th>Since Sept. 25, 2017</th>
<th>No. Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A/ Untyp. A/H3 A/H1 B</td>
<td>A/ Untyp. A/H3 A/H1 B</td>
<td></td>
</tr>
<tr>
<td>Ft. Benning</td>
<td>5</td>
<td>1</td>
<td>114</td>
</tr>
<tr>
<td>Ft. Jackson</td>
<td>16</td>
<td>4</td>
<td>186</td>
</tr>
<tr>
<td>Ft. Leonard Wood</td>
<td>2</td>
<td>5</td>
<td>106</td>
</tr>
<tr>
<td>NRTC Great Lakes</td>
<td>5</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Lackland AFB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCRD Parris Island</td>
<td>11</td>
<td>1</td>
<td>87</td>
</tr>
<tr>
<td>MCRD San Diego</td>
<td>29</td>
<td>2</td>
<td>215</td>
</tr>
<tr>
<td>CGTC Cape May</td>
<td>3</td>
<td>16</td>
<td>193</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Cases presented 26 April – 8 May and one case had been vaccinated more than 14 days prior to illness.

- 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.

**Items of Note**

- Elevated FRI rate at MCRD San Diego

- Eight *C. pneumoniae* cases at Fort Leonard Wood in March-May

- “Slow burn” of type 14 adenovirus cases at MCRD Parris Island, June 2017 to present

**Contact Information**

Address: Commanding Officer Attn: Code 166 Naval Health Research Center 140 Sylvester Rd. San Diego, CA 92106

Web: NHRC Operational Infectious Diseases

Email: NHRC FRI Surveillance Program

**Vaccination Status of Confirmed Influenza Cases Among US Military Basic Trainees, 2015-18**

**Other Items of Interest**

- 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**

- FRI rates and the proportion of FRI cases positive for adenovirus have decreased markedly since vaccine was reintroduced in late 2011.

**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 16 June 2018:

- **At or below expected value:**
  - Fort Benning
  - Fort Jackson
  - Fort Leonard Wood
  - Naval Recruit Training Command, Great Lakes (data through 16 September)
  - Marine Corps Recruit Depot, Parris Island
  - Lackland Air Force Base (data through 28 April)
  - Coast Guard Training Center, Cape May

- **Moderately elevated:**
  - Marine Corps Recruit Depot, San Diego

- **Substantially elevated:**
  - None
Ft. Benning FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Ft. Jackson FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)
Ft. Leonard Wood FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

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

Samples Received

<table>
<thead>
<tr>
<th>Year</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct</td>
<td>20</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>Nov</td>
<td>30</td>
<td>32</td>
<td>30</td>
</tr>
<tr>
<td>Dec</td>
<td>15</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Jan</td>
<td>8</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Feb</td>
<td>28</td>
<td>25</td>
<td>34</td>
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<tr>
<td>Mar</td>
<td>36</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Apr</td>
<td>3</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

Influenza Subtype

- B: 0% 0% 0% 0% 0% 0% 0% 0% 0% 0% 50% 100%
- A/H3: 100% 100% 100% 0% 100% 0% 100% 0% 0% 0% 100% 100%
- A/pH1: 0% 0% 0% 100% 0% 100% 0% 0% 0% 0% 0% 0%
- Untyped: 0% 0% 0% 0% 0% 0% 0% 0% 0% 0% 0% 0%

- Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)
Samples Received

<table>
<thead>
<tr>
<th>Year</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>Jun</th>
<th>Jul</th>
<th>Aug</th>
<th>Sep</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
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<td>21</td>
<td>18</td>
<td>45</td>
<td>40</td>
<td>37</td>
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<td>43</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>2017</td>
<td>25</td>
<td>25</td>
<td>24</td>
<td>8%</td>
<td>4%</td>
<td>8%</td>
<td>2%</td>
<td>2%</td>
<td>4%</td>
<td>5%</td>
<td>7%</td>
<td>3%</td>
<td>4%</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>2018</td>
<td>18</td>
<td>17</td>
<td>16</td>
<td>15</td>
<td>14</td>
<td>13</td>
<td>12</td>
<td>11</td>
<td>10</td>
<td>9%</td>
<td>10%</td>
<td>12%</td>
<td>14%</td>
<td>16%</td>
<td>18%</td>
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Influenza Subtype

<table>
<thead>
<tr>
<th>Subtype</th>
<th>A/H3</th>
<th>A/H1</th>
<th>B</th>
<th>Untyped</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td></td>
<td></td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2017</td>
<td></td>
<td></td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

MCRD SD FRI Rates and Diagnostic Test Results

Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Back to FRI Report

Samples Received

<table>
<thead>
<tr>
<th>Year</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>Jun</th>
<th>Jul</th>
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<td>5</td>
<td>4</td>
<td>6</td>
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<td>2017</td>
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<td>17</td>
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<td>21</td>
<td>50</td>
<td>40</td>
<td>35</td>
<td>39</td>
<td>44</td>
<td>43</td>
<td>40</td>
<td>48</td>
</tr>
<tr>
<td>2018</td>
<td>10</td>
<td>3%</td>
<td>32%</td>
<td>33%</td>
<td>43%</td>
<td>13%</td>
<td>18%</td>
<td>25%</td>
<td>55%</td>
<td>50%</td>
<td>25%</td>
<td>19%</td>
<td>33%</td>
<td>22%</td>
<td>80%</td>
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Influenza Subtype

<table>
<thead>
<tr>
<th>Subtype</th>
<th>A/H3</th>
<th>A/H1</th>
<th>B</th>
<th>Untyped</th>
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<tbody>
<tr>
<td>2016</td>
<td></td>
<td></td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2017</td>
<td></td>
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<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Back to FRI Report

- Observed FRI rate (expected rate = dashed line)
- Moderately elevated  
- Substantially elevated
- Pneumonia rate (incl. afebrile)
Observed FRI rate (expected rate = dashed line)

- Moderately elevated
- Substantially elevated

Pneumonia rate (incl. afebrile)
**DoD Beneficiary Surveillance**

- NHRC conducts FRI surveillance among DoD beneficiaries at 12 military facilities including Naval Medical Center San Diego (NMCSD), Naval Branch Health Clinic Kearny Mesa (NBHCKM), Naval Branch Health Clinic, Naval Training Center (NTC), Naval Hospital Camp Pendleton (NHCP), Branch Health Clinic Yuma (BHCY), James A. Lovell Federal Health Care Center (JALFHCC), United States Naval Hospital, Japan (PRSH), Naval Medical Center Portsmouth (NMCP), Boone Branch Health Clinic (BBHC), Oceana Branch Health Clinic (OBHC), Naval Hospital Lemoore (NHL), and Robert E. Bush Naval Hospital (RBNH).

- For questions regarding surveillance in this population, please contact the principal investigator (Chris Myers, christopher.a.myers48.civ@mail.mil) or the study coordinator (Michelle Ricketts, michelle.n.ricketts.ctr@mail.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 and Mexicali, Mexico (1).
Phylogenetic Comparison of Influenza A(H1N1)pdm09 HA and NA Protein Sequences

- 18 analyzed H3N2 HA and 19 NA sequences were derived from whole genome sequencing.
- This sequence belonged to the subclade 6B.1, defined by mutations S84N, S162T (ADD GLY) and I216T.
- 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.

Summary of Influenza A(H1N1)pdm09 Protein Homology When Compared with 2016-2017 Vaccine Strain and upcoming 2017-2018 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. Isolates</th>
<th>Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(H1N1)pdm09 HA</td>
<td>18</td>
<td>A/Michigan/45/2015 (2017-18)</td>
<td>98.5-99.3%</td>
</tr>
<tr>
<td>A(H1N1)pdm09 NA</td>
<td>19</td>
<td>A/Michigan/45/2015 (2017-18)</td>
<td>98.1-99.1%</td>
</tr>
</tbody>
</table>

Summary of Influenza A(H1N1)pdm09 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>Mutation</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>S164T</td>
<td>N/A</td>
</tr>
<tr>
<td>NA</td>
<td>N44S, S70N</td>
<td>N386K</td>
</tr>
</tbody>
</table>

Evolutionary Relationships
Among Influenza (H1N1)pdm09
Hemagglutinin (HA) Genes
2017-2018 Influenza Season

Vaccine Strain
Reference Strain

2016-2017 Consensus (1 strain)
Nov 2017 (1 strain)
Dec 2017 (7 strains)
Jan 2018 (7 strains)

February 2018 (3 strains)

A/California/NHRC_BRD41866N/2018 (3 strains)
A/California/NHRC_BRD41808N/2018 (2 strains)
A/South Carolina/NHRC_75742/2018
A/Arizona/NHRC_MAP6094A/2017
A/California/NHRC_28352/2017
A/California/NHRC_QV853/2018 [H273Y]
A/California/NHRC_28351/2017
A/California/NHRC_QV10858/2017
A/Japan_NHRC_FDX70322/2018
A/Japan_NHRC_FDX70303/2017
A/Japan/NHRC_FDX70298/2017
A/California/NHRC_BRD41800N/2018
A/California/NHRC_BRD41771N/2017
A/California/NHRC_SAR41891N/2017
A/California/NHRC_BRD80970N/2018

A/North Dakota/03/2016 [R205K]
A/Michigan/45/2015 [Q233R]
2016-2017 Group 6B.1 (1 whole genome strain)

A/Minnesota/32/2015
A/Darwin/11/2015
A/Norway/2417/2013 (Group 6B)
A/California/07/2009

Amino Acid Substitution per 100 residues
Evolutionary Relationships Among Influenza (H1N1)pdm09 Nauraminidase (NA) Genes 2017-2018 Influenza Season

**Vaccine Strain**

**Reference Strain**

**2016-2017 Consensus (1 strain)**

**Nov 2017 (1 strain)**

**Dec 2017 (8 strains)**

**Jan 2018 (7 strains)**

**February 2018 (3 strains)**

**A/Delaware/39/2015 [V394I, I443M]**

**A/Michigan/45/2015**

**A/California/80/2005 [I13V, I32V, V67I, S79L]**

**A/California/07/2009 [I241V, D248N, K369N]**
Phylogenetic Comparison of Influenza A (H3N2) HA and NA Protein Sequences

- **110** analyzed H3N2 HA and **111** NA sequences were derived from whole genome sequencing.
- **All sequences** were in subclade 3C.2a. Of those 3C.2a sequences, **17** were further classified as 3C.2a1, defined by the mutations N171K, I406V (HA2: I77V), and G484E (HA2: G155E).
- 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 **A/Texas/50/2012** for HA and **A/Perth/16/2009**
- for NA sequences

Summary of Influenza A (H3N2) Protein Homology When Compared with 2017-2018 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No.</th>
<th>Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3N2 HA</td>
<td>110</td>
<td>A/HongKong/4801/2014</td>
<td>97.3-98.9%</td>
</tr>
<tr>
<td>H3N2 NA</td>
<td>111</td>
<td>A/HongKong/4801/2014</td>
<td>97.0-98.7%</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/](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>NA</td>
<td>D93N, S245N, S329N</td>
<td>N70K, D329S, I331G</td>
</tr>
</tbody>
</table>

Evolutionary Relationships Among Influenza A (H3N2) Hemagglutinin (HA) Genes 2017-2018 Influenza Season

Vaccine Strain
WHO Recommended 2018-19 Vaccine Strain

Reference Strain
2016-2017 Consensus (75 strains)
Sept 2017 (2 strains)
Oct 2017 (8 strains)
Nov 2017 (21 strains)
Dec 2017 (42 strains)
Jan 2018 (36 strains)
Feb 2018 (1 strain)

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
FDA: DOD beneficiaries
JX or no prefix: US Recruiter
SEA: US Special Forces

Amino Acid Substitution per 100 residues

- 13 -
Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2017-2018 Influenza Season

WHO Recommended 2018-19 Vaccine Strain

Reference Strain
2016-2017 Consensus (9 whole genome strains)
- Sept 2017 (2 strains)
- Oct 2017 (8 strains)
- Nov 2017 (21 strains)
- Dec 2017 (42 strains)
- Jan 2018 (37 strains)
- Feb 2018 (1 strain)

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: JX prefix: US Recruit
SEA: US Special Forces
Shipboard Surveillance
Phylogenetic Comparison of Influenza B (Yamagata and Victoria) HA and NA Protein Sequences

- 28 HA sequence belonged to the Y3 clade of the Yamagata lineage and 57 HA sequences belonged to the V1A clade of the Victoria lineage.
- 27 NA sequence belonged to the Yamagata lineage and 57 NA sequences belonged to the Victoria lineage. All sequences were derived from whole genome sequencing.
- Of note, 46 Victoria sequences contained the double amino acid deletion at positions 162 and 163.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown with respect to B/Phuket/3073/2013 for B/Yamagata HA sequences, B/Wisconsin/01/2010 for B/Yamagata NA sequences, and B/Brisbane/60/2008 for both HA and NA Victoria sequences.

Summary of Influenza B Protein Homology When Compared with 2016-2017 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. Isolates</th>
<th>Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/Yamagata HA</td>
<td>28</td>
<td>B/Phuket/3073/2013</td>
<td>99.1-99.3%</td>
</tr>
<tr>
<td>B/Yamagata NA</td>
<td>27</td>
<td>B/Phuket/3073/2013</td>
<td>98.5-98.9%</td>
</tr>
<tr>
<td>B/Victoria HA</td>
<td>57</td>
<td>B/Brisbane/60/2008</td>
<td>98.1-99.1%</td>
</tr>
<tr>
<td>B/Victoria NA</td>
<td>57</td>
<td>B/Brisbane/60/2008</td>
<td>98.1-98.5%</td>
</tr>
</tbody>
</table>
Evolutionary Relationships Among Influenza B Hemagglutinin (HA) Genes 2017-2018 Influenza Season

Vaccine Strain
Reference Strain
2016-2017 Consensus (16 whole genome strains)
Oct 2017 (1 strain)
Nov 2017 (7 strains)
Dec 2017 (30 strains)
Jan 2018 (43 strains)
Feb 2018 (9 strains)

Yamagata Lineage

Victoria Lineage

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
SEA: US Special Forces
Shipboard Surveillance

D129G, K162 DEL, N163 DEL, I180V, R498K

Amino Acid Substitution per 100 residues

16 - 17

- 16 -
Evolutionary Relationships Among Influenza B Neuraminidase (NA) Genes 2017-2018 Influenza Season

Vaccine Strain
Reference Strain
2016-2017 Consensus (28 whole genome strains)
Oct 2017 (1 strain)
Nov 2017 (7 strains)
Dec 2017 (30 strains)
Jan 2018 (42 strains)
Feb 2018 (9 strains)

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
SEA: US Special Forces
Shipboard Surveillance

Yamagata Lineage

Victoria Lineage

Amino Acid Substitution per 100 residues

1.3