

UNITED STATES AIR FORCE IERA

DoD Global Influenza Surveillance Program Season Summary, 2001 - 2002

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INTRODUCTION

Influenza poses a significant threat to military readiness. This was first recognized during the 1918 influenza pandemic, which took the lives of 43,000 U.S. military personnel. More recent outbreaks have underscored influenza's continued impact on military training and operational missions. In an effort to monitor and prevent outbreaks of influenza attributable to newly emerging strains, the U.S. Air Force has conducted global influenza surveillance of U.S. military forces and their families since 1976 in a program called Project Gargle. In 1997, Project Gargle, incorporating data derived from the U.S. Navy's Febrile Respiratory Illness Surveillance Study, expanded into the Department of Defense (DoD) Global Influenza Surveillance Program. The tri-service program is managed from Brooks Air Force Base (AFB), Texas and is largely funded by the DoD Global Emerging Infections Surveillance and Response System (DoD-GEIS).

METHOD

There are two components of the DoD Global Influenza Surveillance Program: population-based and etiology-based surveillance. The Naval Health Research Center (NHRC) in San Diego, California manages the population-based component. Eight military training sites perform population-based febrile respiratory illness (FRI) surveillance. Febrile respiratory illness incidence rates are calculated and reported from these data. For more information on FRI surveillance, refer to http://www.nhrc.navy.mil/geis/studies/febrile_respiratory_illness_surveillance.htm.

The U.S. Air Force manages the etiology-based component of the DoD Global Influenza Surveillance Program. Nineteen U.S. Air Force, U.S. Army, and U.S. Navy installations around the world formally participated as sentinel sites for the 2001–2002 influenza surveillance season (refer to Table A1). Sentinel sites are reviewed annually and are selected using criteria relating to military mission and geographic location. Traditionally, military training sites, international military ports, and overseas installations have been chosen as sentinel sites.

Health care providers at the sentinel sites collected throat swabs from individuals presenting with a fever and either a cough or sore throat, or evidence of acute non-bacterial pneumonia. These swabs were sent to the Epidemiology Surveillance Division (AFIERA/SDE) at Brooks AFB, Texas for viral isolation and identification. Sentinel sites were requested to submit a minimum of six specimens per week during the Northern Hemisphere influenza season (October–April). Throat swab specimens also arrived from Peru and Ecuador through the Naval Medical Research Institute Detachment (NMRID) and other military installations when laboratory support was desired or needed.

AFIERA/SDE provided viral transport media to the sentinel sites, overseas research labs, and other military medical facilities that requested these supplies. Providers strived to obtain throat swabs within 72 hours of illness onset as the number of viral particles in the throat decreases rapidly as the illness progresses. Early sampling increases the likelihood of viral isolation by the laboratory. All military health care beneficiaries from all installations and nationals of specific foreign locations were considered eligible participants in this public health surveillance program provided they met the case definition.

Once received by AFIERA/SDE, specimens were cultured and examined for the presence of viruses. The most likely isolates were influenza A and B, adenovirus, parainfluenza, enterovirus, and herpes simplex virus (HSV). Positive influenza isolates were typed and most isolates received from overseas installations and representative samples of isolates received from domestic installations were subtyped.

Selected influenza isolates also underwent molecular characterization. Genetic sequencing of the hemagglutinin and neuraminidase surface proteins was performed to detect variations from the vaccine component strains. Results were shared with the Centers for Disease Control and Prevention (CDC).

RESULTS

During the 2001–2002 influenza season, AFIERA/SDE processed 3049 throat swab specimens as part of the influenza surveillance program. Nineteen percent (567) of those were positive for influenza. Specimens were received from 18 sentinel sites and 45 non-sentinel sites worldwide. While U.S. Navy and U.S. Army data are presented in this summary, their data were not complete at the time of this report and therefore were not incorporated into the findings of this section (refer to NHRC and MEDCENS section).

Influenza A peaked in Week 4 (20–26 Jan 02) while influenza B peaked in Week 13 (24–30 Mar 02). Unlike last year, when influenza B predominated throughout the season, influenza B

made a late appearance and accounted for only 10 percent of influenza isolates identified by the DoD program during 2001–2002. As shown in Figure 1, influenza B was observed more frequently than influenza A from Week 13 through the end of the surveillance season. The CDC’s preliminary national influenza surveillance data showed a similar occurrence.¹

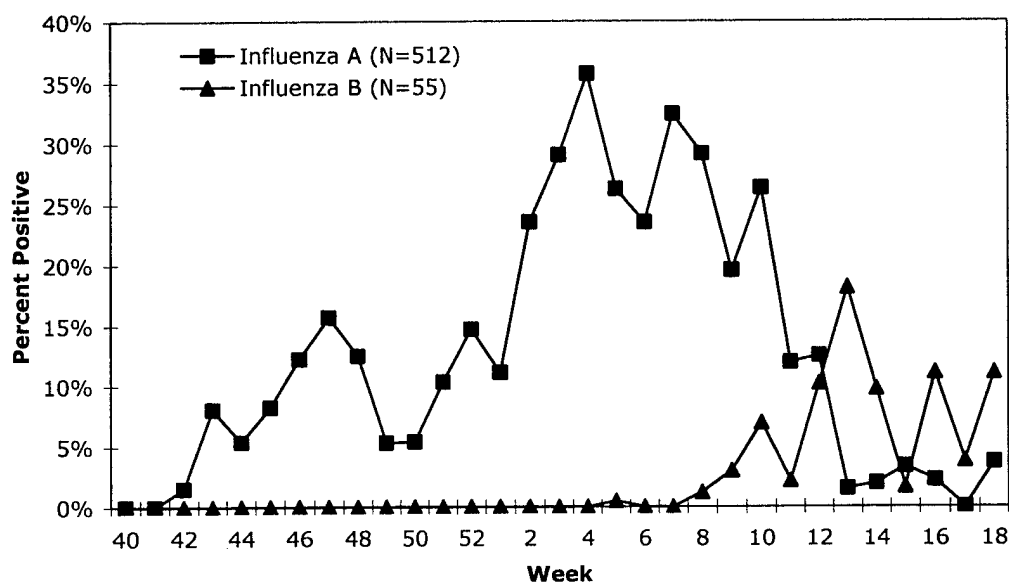


Figure 1. Influenza isolates by type and week (N=567)

Sentinel v. Non-Sentinel Site Specimens

Of the 3049 specimens processed by AFIERA/SDE, 66 percent (2007) were received from sentinel sites. Twenty percent (393/2007) of the specimens received from sentinel sites and 16 percent (174/1042) received from non-sentinel sites were positive for influenza viruses. A larger proportion of specimens collected at sentinel sites were negative for any respiratory virus compared to those collected at non-sentinel sites (refer to Figure 2). The reason for this is not clear, but could potentially have been due to selection bias. Non-sentinel sites may have been more likely to submit specimens based on clinical suspicion compared to sentinel sites that were encouraged to submit a minimum number of specimens. The inclusion of a large number of specimens from training sites that experienced a high incidence of respiratory illness due to adenovirus may have increased the overall pathogen recovery from non-sentinel sites. Improper collection and/or transport of the specimens may have accounted for the high number of total negatives. Another explanation may have been that the causative organism was non-viral, hence not identified using viral techniques.

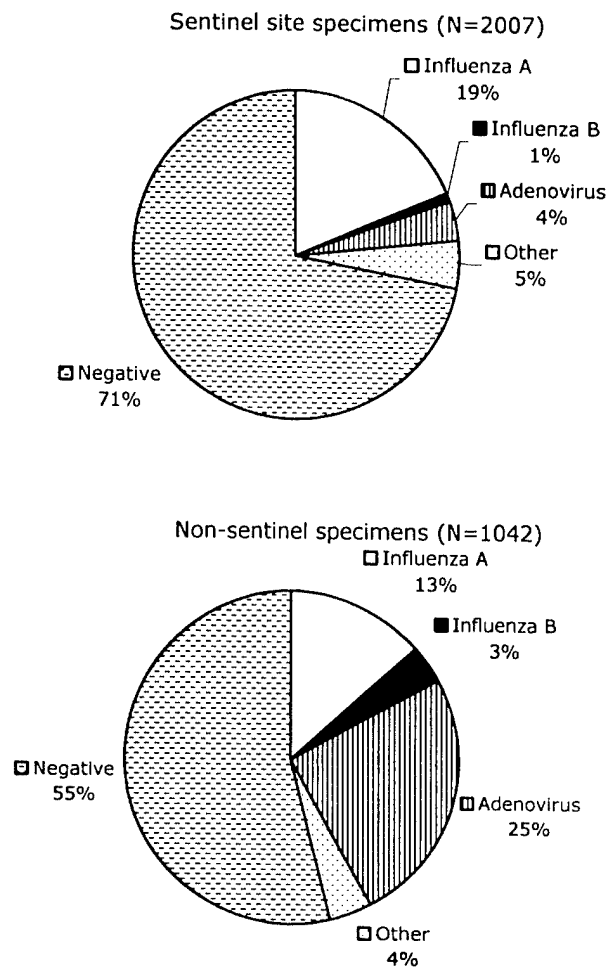


Figure 2. Sentinel v. non-sentinel site specimens

Sentinel Site Specimens

Specimens were submitted from 18 of the 19 sentinel sites—no specimens were received from Madigan Army Medical Center at Fort Lewis, Washington. Respiratory viruses were isolated from specimens collected at each submitting sentinel site with the exception of Incirlik AB, Turkey (refer to Figure 3). Influenza A isolates were collected from 17 sentinel sites and influenza B isolates from 10 sentinel sites. Kunsan AB, South Korea had the largest proportion (100 percent) of influenza A isolates while the U.S. Air Force Academy had the largest proportion (13 percent) of influenza B isolates.

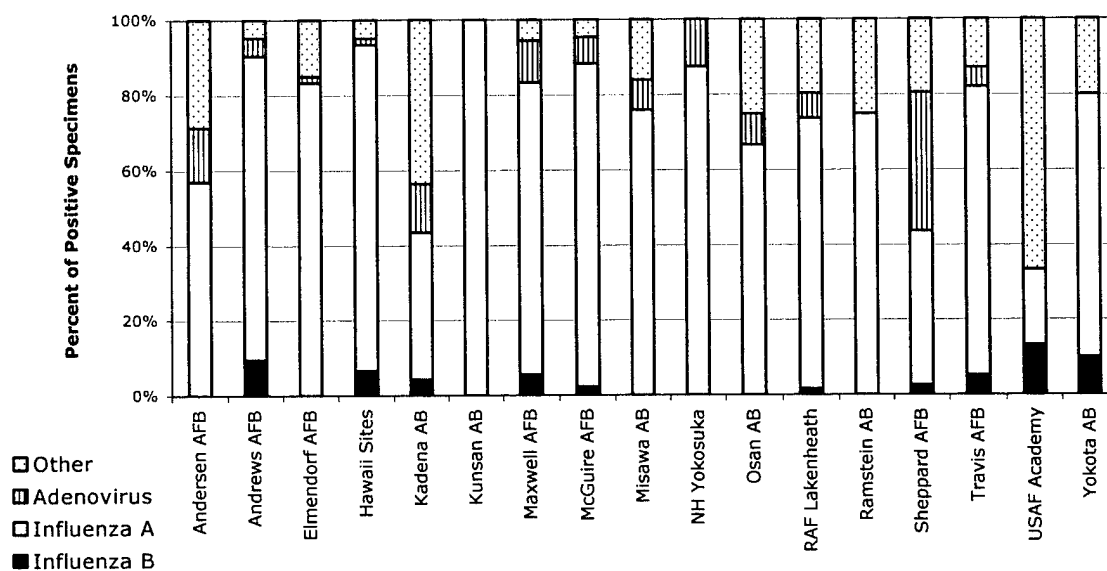


Figure 3. Distribution of positive respiratory viruses by sentinel site (N=564)

Positive Respiratory Isolates—All Locations

Of the 1043 positive specimens, 49 percent (512) were influenza A, 5 percent (55) were influenza B, and 33 percent (340) were adenovirus (refer to Figure 4). The majority of adenovirus specimens were collected from basic trainees at Lackland AFB, Texas and technical training students at Sheppard AFB, Texas. The remaining 13 percent (136) were enterovirus, parainfluenza, respiratory syncytial virus (RSV), or HSV.

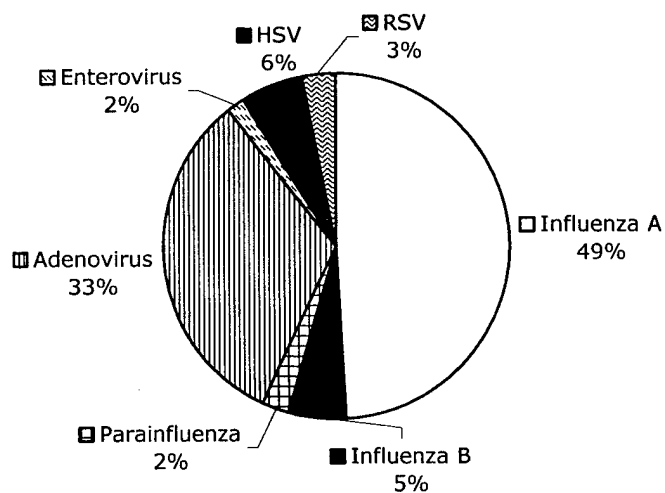


Figure 4. Distribution of positive respiratory viruses (N=1043)

Influenza Isolates

Of the 567 influenza isolates, 90 percent (512) were influenza A and 10 percent (55) were influenza B. This was identical to the CDC's preliminary national data confirming 90 percent of the influenza isolates were influenza A and 10 percent were influenza B.² Of the 139 selected influenza A isolates that were subtyped by AFIERA/SDE, ninety-four percent (131) were A (H3N2) and 6 percent (8) were A (H1N1).

The hemagglutinin gene of 58 H3N2 and 16 H1N1 influenza A viruses (preliminary data; may not be reflected in numbers reported elsewhere in this report) were sequenced during the 2001-2002 season and shared with the CDC. Additionally, molecular surveillance efforts were increased to include the molecular characterization of neuraminidase in light of the appearance of the influenza A (H1N2) reassortment strain. Sequence data of the genes encoding these two proteins were compared with vaccine component strains to determine the level of homology at the genetic level. Certain mutations that cause amino acid changes in antibody binding sites on the hemagglutinin and neuraminidase proteins can greatly alter viral pathogenesis and compromise vaccine efficacy. All of the isolates characterized this season were genetically similar to the current vaccine strains. One of the H3N2 influenza isolates from Osan AB, South Korea contained an amino acid signature characteristic of typical U.S. strains and represents the first appearance of this lineage outside the U.S.

The proportion of influenza B isolates recovered by the DoD program dramatically decreased from 56 percent for the 2000-2001 season to 10 percent for the current season (refer to Figure 5). The CDC reported a similar decrease in the proportion of influenza B from 46 percent to 10 percent.³ Compared to last season, when influenza B appeared within the first weeks of DoD surveillance, the first influenza B virus of the 2001-2002 season was isolated mid-season during Week 5 (27 Jan-2 Feb 02). This specimen was received from Aviano AB, Italy.

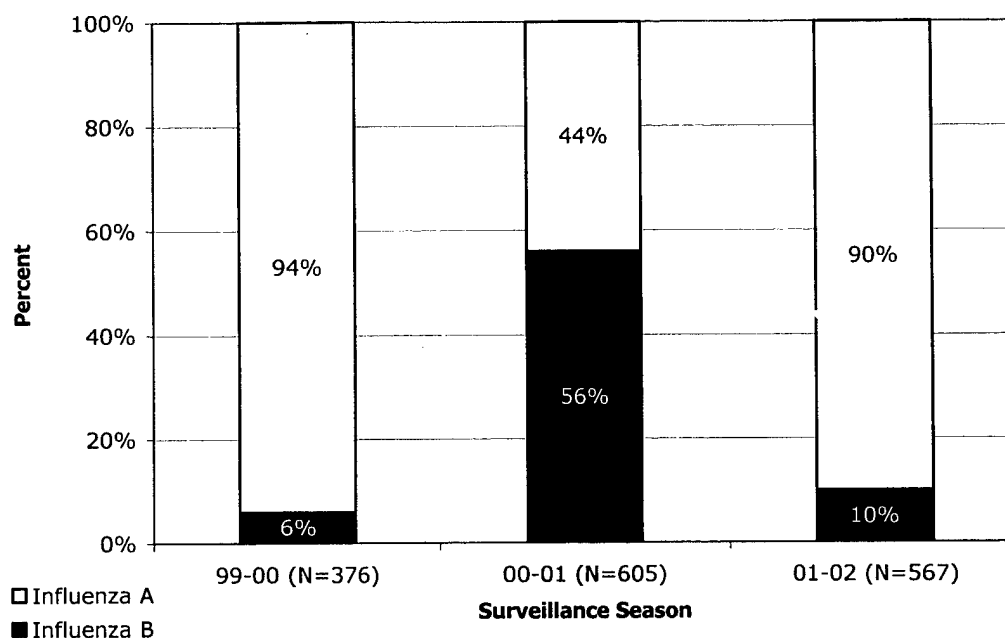


Figure 5. Influenza isolates by type and season

Demographics-Age

Age was available for 99 percent (562) of the influenza cases. The age for all positive influenza cases ranged from less than one year to 91 years with a median age of 21 years, reflecting the generally young DoD beneficiary population. Among the influenza cases identified by the DoD program during 2001-2002, almost half (48 percent) were in the 18 to 49 age group (refer to Figure 6).

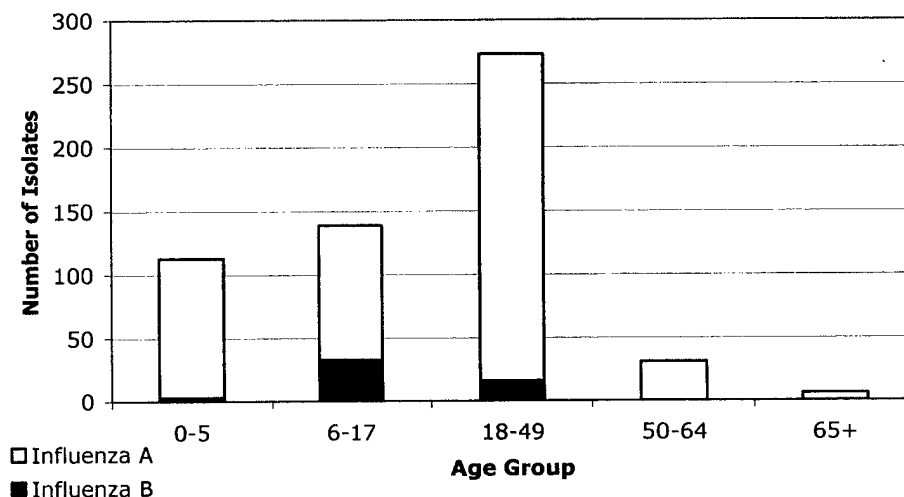


Figure 6. Influenza isolates by type and age group

Demographics–Military Status

Of the 567 influenza cases, 33 percent (187) were classified as military sponsors, 65 percent (371) were classified as family members, and 2 percent (9) were classified as "Other". Figure 7 illustrates the break down of military sponsor status (the status of four sponsors was not available).

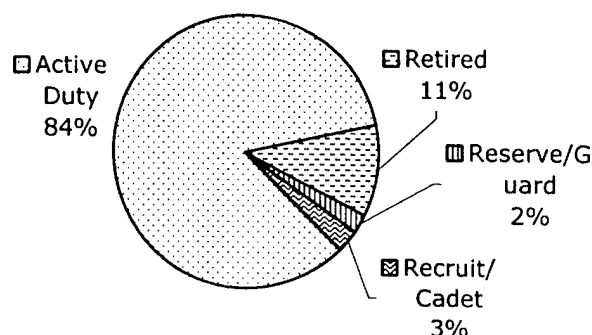


Figure 7. Military status of influenza cases (N=183)

Geographic Distribution of Isolates

Sixty percent (341) of the influenza isolates were submitted by continental United States (CONUS) installations, 31 percent (173) by installations in the Pacific, and 9 percent (53) by installations in Europe. Of the 341 CONUS influenza isolates, 37 percent (125) were received from the South Central region of the U.S., 35 percent (121) from the Atlantic region, 11 percent (39) from the Mountain region, 10 percent (33) from the Pacific region, and 7 percent (23) from the North Central region.

Vaccination Status

The vaccination status for influenza cases identified within the U.S. Air Force was found in the Complete Immunizations Tracking Application (CITA), formerly the Military Immunization Tracking System (MITS), or taken from the individual's Air Force Reportable Events Surveillance System (AFRESS) entry. For members of the U.S. Army and U.S. Navy, vaccination information was taken from the individual's questionnaire submitted with the specimen.

Twenty-six percent (148) of the 567 influenza cases had an influenza vaccination record for the 2001–2002 season and 53 percent (302) did not. The vaccination status of 21 percent (117) of the cases could not be verified. The majority (82 percent) of the vaccinated cases were active duty (AD) personnel.

Vaccine Efficacy

Development of influenza in vaccinated individuals may occur for a number of reasons. First, overall vaccine effectiveness depends upon the similarity between the influenza vaccine strains and the circulating influenza viruses. Secondly, vaccine efficacy varies with individual age and health status. The vaccine is 70 to 90 percent effective in preventing illness in healthy young adults during seasons when there is a good match between the vaccine and circulating viruses.⁴ Finally, it can take up to 14 days to build immunity to the influenza virus once vaccinated. An individual exposed to the virus prior to developing full vaccine-associated immunity may develop influenza.

Eighty-five percent (103/121) of the vaccinated AD cases received the 2001–2002 influenza vaccine at least 14 days prior to specimen collection. The mean number of days between vaccination and specimen collection was 90 days, with a range of 16 to 164 days. Eighty-four percent (96/114) of vaccinated AD influenza A cases and 100 percent (7/7) of vaccinated AD influenza B cases received the vaccine at least 14 days prior to the collection of their throat swabs.

The fact that such a large proportion of vaccinated AD individuals developed influenza may seem surprising, but this is a highly vaccinated population. For example, 89 percent of all U.S. Air Force personnel were vaccinated with the 2001–2002 influenza vaccine. If the vaccine is anticipated to fail in 10 to 30 percent of those vaccinated, and all 360,000 ADAF members were properly vaccinated, 72,000 cases of influenza would not be unexpected even in a year when there is a good match between vaccine strains and circulating viruses. Please note that it is not possible to calculate vaccine efficacy from these data, because there was no systematic sampling. It may be possible that vaccinated symptomatic individuals were preferentially cultured in search of a pathogen.

Specimen Transit Time

The elapsed time between date of collection and receipt by AFIERA/SDE for all specimens ranged from zero to 63 days with a median of two days. Of the 1398 specimens with a transit time greater than two days, 45 percent (636) were submitted by Pacific and European installations.

NHRC and MEDCENS Data

According to data provided by the NHRC, 507 specimens were submitted (through Mar 2002) for viral isolation and identification by the eight training sites participating in its FRI surveillance study between October 2001 and March 2002. Five percent (26) were positive for influenza. All of the influenza isolates were sub-typed as A (H3N2). The remaining positive specimens (277) were adenovirus (refer to Figure 8).

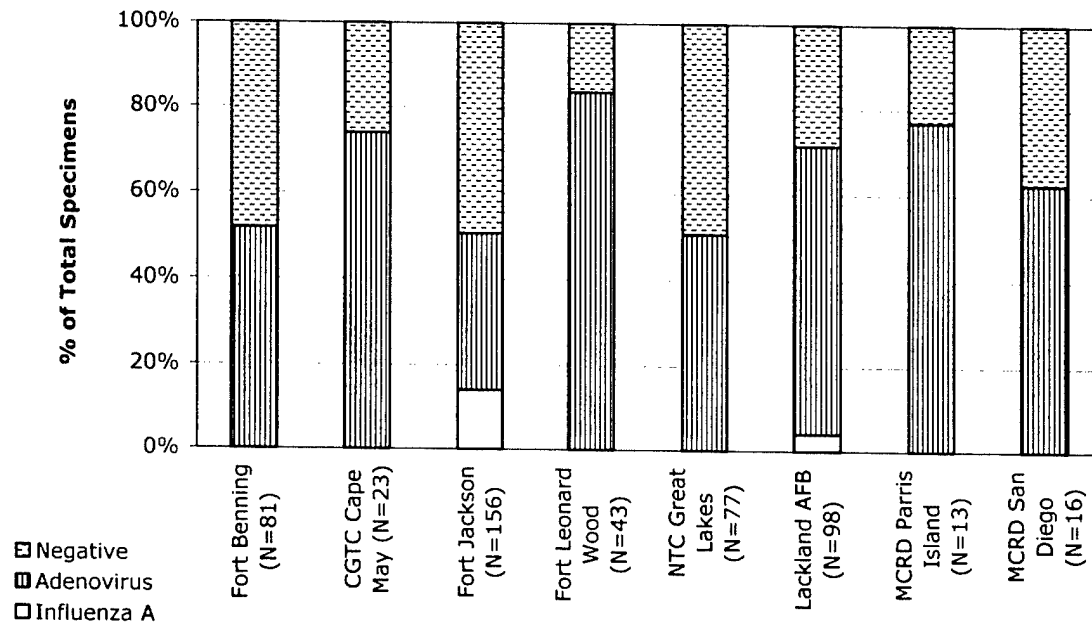


Figure 8. Distribution of NHRC respiratory specimens by site (N=507)

In addition to the data collected from AFIERA/SDE and the NHRC, U.S. Army medical centers (MEDCENS) provided the Epidemiology Services Branch (AFIERA/RSRH) with clinical virology results for inclusion into the 2001–2002 influenza surveillance season summary. Of the 2361 specimens cultured, four percent (100) were positive for influenza viruses. Of those, 86 percent were influenza A and 14 percent were influenza B.

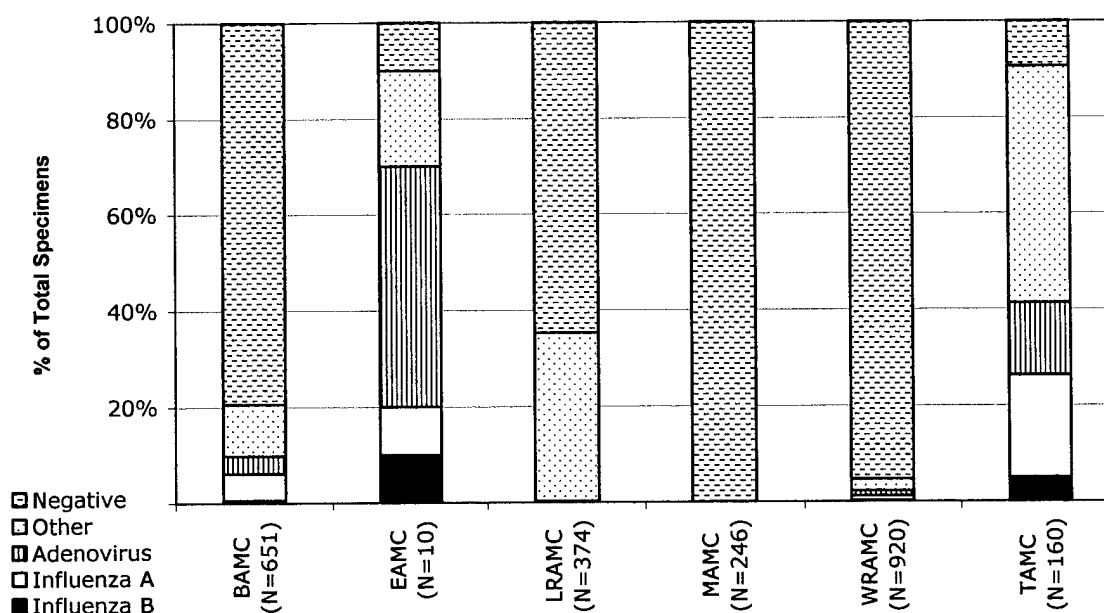


Figure 9. Distribution of U.S. Army respiratory specimens by MEDCEN (N=2361)

Reporting

AFIERA/SDE sent clinical results back to the submitting laboratory as a patient report and to AFIERA/RSRH, which notified the installation public health/preventive medicine office of confirmed positive influenza cases.

Due to the anticipated vaccine delay for the 2001–2002 Northern Hemisphere influenza season, AFIERA/RSRH continued the reporting policy established last season of posting surveillance data to its website twice a week. The web-based reports not only allowed interested personnel convenient access to the data, but also assisted public health and medical professionals to track the activity of influenza and other respiratory viral pathogens on a more “real-time” basis. [Please note that website access is restricted to .gov and .mil users.]

Additionally, AFIERA/RSRH summarized weekly surveillance data into a report of influenza activity within DoD, the U.S., and throughout the world. This weekly update was distributed to all participating sites and posted on the website each Thursday.

Air Force Reportable Events Surveillance System (AFRESS)

The public health office at U.S. Air Force installations was required to enter all confirmed cases of influenza into AFRESS as an urgent "epi-event" within 24 hours of notification. This policy was continued from last season in light of the predicted vaccine delay. At the time of this report, 90 percent (399/442) of influenza cases at U.S. Air Force installations identified by the DoD program had been entered into AFRESS.

CONCLUSIONS

During the 2001-2002 influenza surveillance season, overall influenza activity peaked in Week 4 (20-26 Jan 02) when nearly 36 percent of total specimens were positive for influenza viruses. Influenza A peaked during this same week, however, influenza B peaked later in the season in Week 13 (24-30 Mar 02). Compared to last season when influenza B predominated throughout the season, influenza B accounted for only 10 percent of all influenza isolates identified during the 2001-2002 season. It was first isolated by the DoD program in Week 5 (27 Jan-2 Feb 02) and was observed more frequently than influenza A during the last weeks of the surveillance season. The CDC's preliminary data showed similar patterns. With the exception of the Osan AB, South Korea A (H3N2) isolate, the DoD Global Influenza Surveillance Program noted no unusual strains.

DISCUSSION

The primary goal of the DoD Global Influenza Surveillance Program is to prevent influenza outbreaks in military personnel due to emerging strains. Intermediate objectives include the identification and characterization of circulating strains of influenza, the detection of variant strains of influenza due to antigenic changes (i.e. antigenic drift and shift), and the evaluation of influenza vaccine effectiveness.

Each year the U.S. Food and Drug Administration Vaccines and Related Biological Products Advisory Committee (VRBPAC) recommends modifications to the influenza vaccine based on the viral strains that circulated during the preceding season. VRBPAC's decision relies in part on data provided by the DoD Global Influenza Surveillance Program.

The data are particularly important for two other reasons. First, program specimens are received from areas of the world where novel influenza strains have historically emerged. Secondly, the DoD program has made possible influenza surveillance in geographic regions where very little is known about influenza activity. It must be emphasized that this etiology-based program does not collect population data and therefore cannot provide influenza incidence rates. The program's contribution to the VRBPAC is valued, as it impacts not only the health of the military, but of the entire nation.

The success of the DoD Global Influenza Surveillance Program requires cooperation between clinical, laboratory, and public health/preventive medicine staff of all military branches. Continued awareness and participation is key to worldwide surveillance efforts and determination of the annual influenza vaccine composition.

VACCINE INFORMATION FOR THE 2002-2003 NORTHERN HEMISPHERE INFLUENZA VACCINE

The World Health Organization (WHO) has recommended that the 2002-2003 Northern Hemisphere influenza vaccine include A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Hong Kong/330/2001-like viruses. For the A/Moscow/10/99 (H3N2)-like virus, U.S. vaccine manufacturers will use the antigenically similar A/Panama/2007/99 vaccine strain. The final report of the WHO Consultation on Influenza Vaccine Composition for the Northern Hemisphere is available at <http://oms2.b3e.jussieu.fr/flunet/docs.html>.

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- ¹⁻³ CDC. Influenza Summary Update for the Week Ending May 4, 2002–Week 18.
<http://www.cdc.gov/ncidod/diseases/flu/weeklyarchives/weekly18.htm>
- ⁴ CDC. Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2002; 51[No. RR-3]: 1-31.
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APPENDIX A

Table A1. DoD Global Influenza Surveillance Program Sentinel Sites

Installation	Location
Andersen AFB	Guam
Andrews AFB	Maryland
Elmendorf AFB	Alaska
Hickam AFB, Pearl Harbor NS, Tripler AMC, and Pacific naval ships	Hawaii
Incirlik AB	Turkey
Kadena AB	Japan
Kunsan AB	South Korea
RAF Lakenheath	United Kingdom
Madigan AMC/Fort Lewis	Washington
Maxwell AFB	Alabama
McGuire AFB /Fort Dix	New Jersey
Misawa AB	Japan
Osan AB	South Korea
Ramstein AB	Germany
Sheppard AFB	Texas
Travis AFB	California
United States Air Force Academy	Colorado
Yokosuka Naval Station	Japan
Yokota AB	Japan

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