

# Development of a Department of Defense Regional Viral Respiratory Surveillance Program

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**ABSTRACT** A continuous viral respiratory surveillance program was established throughout the U.S. Department of Defense beneficiary population living in Europe with a few specimens coming from the Middle East. This program provided influenza rapid antigen test kits, specimen collection kits, detailed instructions, and a questionnaire. Training on specimen collection and testing was provided to health care providers and lab staff. We received 1875 patient specimens (39% active duty, 13% adult beneficiary, and 48% pediatric beneficiary) collected from 36 medical treatment facilities in 10 European and Middle Eastern countries over a 52-week period. Nine hundred and twenty-two questionnaires were received. The greatest activity of viral respiratory infections occurred between weeks 7 to 13. We found the sensitivity of rapid antigen testing compared poorly to both viral culture and PCR; however, the information provided by the rapid testing was utilized locally for guiding patient treatment. Additionally, although 91% of the active duty population received the influenza vaccine, we calculated the vaccine efficacy to be 52%.

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## INTRODUCTION

Influenza viruses, respiratory syncytial virus (RSV), adenoviruses, and parainfluenza viruses (PIV) are significant viral pathogens that cause respiratory tract infections during the winter and early spring months. These viruses are responsible for the majority of pneumonia related hospital admissions during these seasons.<sup>1,2</sup> RSV and PIV, although able to infect any age group, are most active and severe in infants and sometimes the elderly. Influenza on the other hand can affect between 5 and 20% of the entire U.S. population each year and is responsible for ~36,000 deaths annually.<sup>3</sup> The influenza virus has a segmented RNA genome and can change its genetic composition rapidly both because of a high rate of mutation during RNA synthesis (genetic drift) and also the ability of influenza to rearrange and incorporate genetic material from circulating strains, either not currently circulating in or not found in humans (genetic shift). Current circulating human influenza strains are Influenza A (containing hemagglutinins H1 and H3), Influenza B, and Influenza C. Influenza A is the predominant pathogen of the influenza virus group and the most likely to rapidly develop into a pandemic strain. Influenza B and Influenza C tend to be less pathogenic viruses, but remain significant pathogens in children.<sup>4</sup> The military also recovers a large number of adenoviral infections from basic training sites because of the numerous recruits attending basic training annually.<sup>5</sup>

Laboratories currently have several diagnostic tools available to detect respiratory viruses.<sup>6</sup> Rapid and accurate detection of viral infections leads to better patient care and reduction in overall costs.<sup>7</sup> Among the many benefits are reductions in testing and hospitalization costs for the institution and the patient, better antibiotic stewardship, and more

accurate care.<sup>8-10</sup> Rapid and accurate diagnosis leads to the best patient management.<sup>3,11</sup> One of the most common and simplest diagnostic tests is the rapid antigen test, which takes <30 minutes to perform and does not require technically trained staff. Rapid antigen testing is, however, not very sensitive when compared to traditional viral isolation using tissue culture.<sup>8,11,12</sup> Tissue culture is a much more sensitive technique, but requires a patient specimen that contains viable virus and can require up to 14 days to yield results.<sup>1</sup> Proper specimen handling and transport are crucial for successful tissue culture as enveloped RNA viruses such as RSV and influenza are quite liable. Real-time PCR that can identify viral nucleic acids in patient specimens is rapidly enhancing, and in many cases, replacing traditional virology culture methods.<sup>13-16</sup> Several real-time PCR assays have been developed that are highly sensitive, specific, and rapid. At this time, the majority of real-time PCR assays are currently performed only by laboratories capable of performing high-complexity testing.

We received funding from the U.S. Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS) to establish increased viral surveillance in our area of responsibility. Our goal was to establish an operating respiratory viral surveillance program and provide data in real-time both to the DoD tracking mechanisms as well as the European Influenza Surveillance Scheme (EISS). Additionally, we wished to compare and contrast the methods to determine the optimal approach for respiratory viral disease diagnosis at remote locations.

## MATERIALS AND METHODS

### *Project Planning and Recruitment*

Before the start of the traditional viral respiratory season (October–May), the Center for Health Promotion and Preventive Medicine in Europe (CHPPM-EUR) provided triservices

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This manuscript was received for review in February 2008. The revised manuscript was accepted for publication in September 2008.

public health emergency officer (PHEO) training concerning the prevention, detection, and response to a pandemic influenza outbreak. During this training period, and in subsequent PHEO training conferences, we provided information on the proposed surveillance project and the importance of participation. Additionally, we provided site assistance visits (SAVs) for several clinical facilities in person or by proxy through trained trainers. During these meetings, we briefed the provider staff on patient symptom criteria, introduced a paper copy of the patient questionnaire developed by AFIOH (Air Force Institute of Operational Health, Brooks City Base, Texas) (<https://afioh.brooks.af.mil/pestilence/Influenza/questionnaire.cfm>), and instructed personnel on specimen collection procedures. We trained and competency assessed clinic laboratory staff on correct testing procedures using the selected influenza rapid antigen test kit and provided shipping instructions for submission of viral culture specimens. We also worked with regional Composite Health Care System (CHCS) laboratory staff to ensure interoperability between all sites so that viral cultures completed and resulted at Landstuhl Regional Medical Center (LRMC) would be visible by the original ordering clinic staff. In doing so, we developed a standardized order set so that the rapid antigen and viral culture results could be linked together.

### **Patient Specimens**

Patient specimens were collected from U.S. military service members or their dependents throughout Europe with a few specimens arriving from the Middle East. Health care providers were instructed to collect respiratory specimens from patients presenting with influenza-like illness (ILI) case definition of fever ( $\geq 100.5^{\circ}\text{F}/38^{\circ}\text{C}$ , oral or equivalent, and cough or sore throat (<72 hours duration). Rapid antigen testing was performed locally at the medical treatment facility where the specimen was collected to aid in treatment decisions. After rapid testing, specimens were shipped to Landstuhl Regional Medical Center for viral culture and real-time PCR testing. All specimens were shipped and stored at 2–8°C before reference testing. Receipt of specimens at LRMC varied from 1 day up to 7 days according to location because of regularly scheduled lab shipments.

### **Specimen Collection**

Specimen collection kits were assembled for distribution consisting of two nylon flocked nasopharyngeal swabs (Copan), a tube of viral transport media, and instructions for specimen collection. All health care providers were instructed before the beginning of the season on the proper collection method. One swab was used for local rapid antigen testing at the medical treatment facility and the other placed in viral transport medium (VTM), either commercially available or provided by our lab [Hank's buffered salt solution (HBSS) with 0.5% (w/v) gelatin, and 0.5% (w/v) sucrose, and 0.001% (w/v) gentamicin]. Specimens were then shipped at 2–8°C to Landstuhl Regional Medical Center for viral culture and PCR testing.

### **Rapid Antigen Testing**

BinaxNow Influenza A & B test kits (Binax) were used for local rapid influenza antigen testing. The BinaxNow tests utilized for rapid antigen testing did not detect Influenza C viruses. All lab staff were trained and competency assessed on the proper test performance. RSV rapid antigen testing was also performed at LRMC for pediatric patients (typically <age 2) using the BD Directigen RSV (Becton Dickinson) test kits. These kits were able to detect RSV A and B virus types. All rapid antigen tests were performed according to the manufacturer's instructions.

### **Cell Culture**

Four cell lines were used for viral culture. LLCMK2 and MDCK cell lines were used for detection of ortho- and paramyxoviruses and A549 and MRC-5 cell lines were used to detect other viruses. During viral isolation LLCMK2 and MDCK cells were incubated with Eagle's minimum essential medium (EMEM) without serum and 0.002  $\mu\text{g}/\text{ml}$  trypsin. A549 and MRC-5 cells were incubated in EMEM with 2% fetal calf serum. All cell lines were incubated at 35–37°C and screened Monday–Friday for cytopathic effects (CPEs). If cultures showed a cytopathic effect, an immunofluorescent antibody (IFA) screen was performed by fixing cells onto a glass microscope slide after drying, using acetone at  $-20^{\circ}\text{C}$  for 10 minutes. Cell cultures that demonstrated no CPE after 14 days were also tested by IFA. Immunofluorescent antibodies specific for respiratory viruses (respiratory screen, Chemicon) were incubated on the fixed samples in accordance with manufacturer's instructions. Our screening antibodies could detect adenoviruses, Influenza A/B, Parainfluenza 1/2/3, and RSV infection. Mounting medium and a cover slip were added to the slides and cells were examined for fluorescent signal. If the screen was positive, an additional respiratory immunofluorescent panel (Chemicon) was used to identify the virus.

### **Viral Nucleic Acid Extraction**

A 200- $\mu\text{L}$  aliquot was taken from the VTM specimen for nucleic acid extraction using a MagNA Pure Compact Instrument (Roche) with the MagNA Pure Compact Nucleic Acid Isolation Kit I (Roche). The Total\_NA\_Plasma\_protocol was utilized according to the manufacturer with a final elution volume of 50  $\mu\text{L}$ .

### **RT-PCR**

All real-time PCR testing for influenza virus RNA was performed using either a Roche LightCycler or Cepheid SmartCycler instrument using identical protocols as described previously<sup>17</sup> with minor modifications. The primer concentration for the outer sense primer set was 1  $\mu\text{M}$  and the outer antisense primer set, 2  $\mu\text{M}$ . The reverse transcriptase step was performed by holding 55°C for 20 minutes. Initial denaturation at 95°C for 30 seconds was followed by 40 cycles of 5 seconds at 95°C, 10 seconds at 55°C, and 44 seconds at 72°C.

A melting curve analysis followed amplification. Amplified specimens were diluted 1:10 with molecular-grade water and 0.5 µL used for a second PCR reaction or “nested run” using primer concentrations at 2 µM. Initial denaturation at 95°C for 10 minutes was followed by 25 cycles of 10 seconds at 95°C, 10 seconds at 56°C, and 25 seconds at 72°C. A melting curve analysis again followed amplification. The amplification reagents used for PCR were Roche LightCycler RNA Amplification SYBR Green I for the reverse transcription and initial amplification and Roche LightCycler FastStart DNA Master SYBR Green I for the nested PCR. RSV reverse transcription-PCR primers were described previously.<sup>18</sup> The RSV primer pair for the one-step SYBR Green I RT-PCR detected both A and B subtypes. The reaction volume was 20 µL with primer concentrations of 1 µM each, a final MgCl<sub>2</sub> concentration of 4 mM and 5 µL extracted nucleic acid. Reverse transcription lasted 20 minutes at 55°C. Initial denaturation at 95°C for 30 seconds was followed by 40 cycles of 1 second at 95°C, 10 seconds at 55°C, and 34 seconds at 72°C and a melting curve. Amplified material was diluted 1:10 with molecular-grade water and 0.5 µL of this dilution was used in a nested PCR reaction. Primer concentrations were 1 µM each and the MgCl<sub>2</sub> concentration was 5 mM. Initial denaturation of 10 minutes at 95°C was followed by 20 cycles of 5 seconds at 95°C, 5 seconds at 50°C, and 10 seconds at 72°C. A melting curve analysis followed the amplification. The amplification reagents used for PCR were Roche LightCycler RNA Amplification SYBR Green I for the reverse transcription and initial amplification and Roche LightCycler FastStart DNA Master SYBR Green I for the nested PCR. Primer sequences were as follows (all primers shown are 5'-3'): Influenza type B, (HA gene)-outer sense (OS) GTGACTGGTGTGA TACCACT, outer antisense (OAS)TGTTTTTACCCATATTG GGC, inner sense (IS)CATTTTTGCAAATCTCAAAGC, inner antisense (IAS)TGGAGGCAATCTGCTTCACC; Influenza type A(H1N1)-(OS)CAGATGCAGACACAATATGT,(OAS)AAACC GGCAATGGCTCCAAA,(IS)ATAGGCTACCATGCGAACAA,(IAS)CTTAGTCCTGTAACCATCCT; Influenza type A(H3N2)-(OS)CAGATTGAAGTGACTAATGC,(OAS)GTTTCTCTGGT ACATTCCGC,(IS)AGCAAAGCTTTCAGCIAACTG,(IAS)GCT TCCATTTGGAGTGATGC; Influenza type C-(OS)ACACTTCC

AACCCAATTTGG,(OAS)CCTGACAGCAACTCCCTCAC,(IS)GTGCAAACACTGCATCTTGTGG,(IAS)TCATTTCTTGA TCTCCATG;RSV type A/B-(OS)GTCTTACAGCCGTGATT AGG,(OAS)GGGCTTTCTTTGGTTACTTCA, RSV type A (IS)GATGTTACGGTGGGGAGTCT,(IAS)GTACACTGTAG TTAATCACA,RSV type B-(IS)AATGCTAAGATGGGGAG TTC,(IAS)GAAATTGAGTTAATGACAGC.

**Statistical Analysis**

Calculation of sensitivity, specificity, positive predictive value, and negative predictive value were calculated using the following formulas with PCR as the “gold standard”: (We have previously demonstrated that this testing methodology is superior to viral cell culture.)<sup>17,18</sup> Sensitivity = TP/(TP + FN), specificity = TN/(FP + TN), PPV = TP/(T + FP), NPV = TN/(TN + FN), where TP stands for true positive (both testing methodologies positive); FN, false negative (“gold standard,” positive; compared methodology, negative); TN, true negative (both testing methodologies negative); FP, false positive (“gold standard,” negative; compared methodology, positive).

**RESULTS/DISCUSSION**

**Program Establishment**

To stand up an increased influenza surveillance program in EUCOM, we first initiated contact with public health officials both in the military (CHPPM-EUR, AFIOH) and our host nation (Germany, Robert Koch Institute). We discussed the project and established contacts and channels to share information in so that the host nation, military preventive medicine community, and command (EUCOM) were aware of influenza surveillance results in real-time. The geographic distribution of ~43 medical treatment facilities in 10 countries throughout the region posed a challenge in coordinating this triservice effort. We were able to coordinate specific service agreements by working through the Army, Navy, and Air Force European service commands. The initial effort was focused on Germany and Italy where the bulk of service members are stationed. Specimen collection kits and rapid antigen kits (Binax) were procured and distributed to all participating medical treatment facilities. A Summary or the data gathered (by virus and week) is shown in Figure 1.

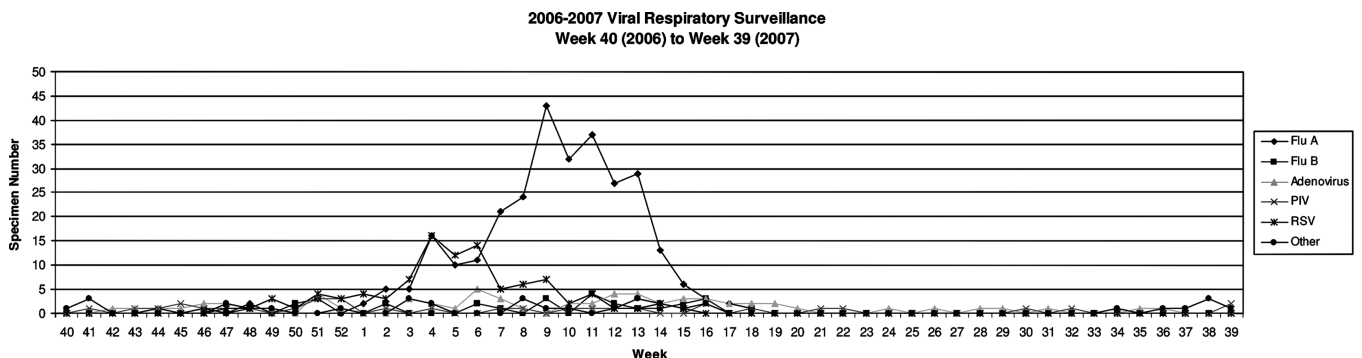


FIGURE 1. Week-by-week isolation of viral respiratory pathogens starting from week 40 (October 2006) and ending at week 39 (September 2007).

**TABLE I.** Participating Medical Clinics by Country, Service, and Number of Specimens Submitted

Unit	Country	Service	Specimens
Aviano	Italy	Air Force	20
Bamberg	Germany	Army	8
Baumholder	Germany	Army	261
Brussels	Belgium	Army	14
Bitburg	Germany	Air Force	48
Dexheim	Germany	Army	14
Darmstadt	Germany	Army	33
Friedberg	Germany	Army	1
Grafenwoehr	Germany	Army	6
Geilenkirchen	Germany	Air Force	13
Heidelberg	Germany	Army	91
Hoehnfels	Germany	Army	4
Hanau	Germany	Army	1
Illesheim	Germany	Army	5
Incirlik	Turkey	Air Force	33
Kaiserslautern	Germany	Army	30
Kosovo	Kosovo	Air Force	1
Katterbach	Germany	Army	3
Kuwait	Kuwait	Air Force	1
Landstuhl	Germany	Army	776
Lajes Field	Portugal	Air Force	25
Lakenheath	United Kingdom	Air Force	90
Livorno	Italy	Army	5
Mannheim	Germany	Army	18
Stuttgart	Germany	Army	10
Qatar	Qatar	Air Force	4
Rota	Spain	Navy	204
Ramstein	Germany	Air Force	42
Sembach	Germany	Air Force	13
Sigonella	Italy	Navy	12
SHAPE	Belgium	Army	8
Upwood	United Kingdom	Air Force	1
Vicenza	Italy	Army	21
Vilseck	Germany	Army	2
Wiesbaden	Germany	Army	46
Wurzburg	Germany	Army	11

**Program Participation**

We collected 1875 respiratory specimens over a 52-week period beginning in October 2006 and ending in September 2007. This amounted to a threefold increase over previous years' averages. The specimens were received from 36 submitting locations throughout Europe and the Middle East, with the largest concentrations of specimens coming from installations throughout Germany and Italy (Table I). Military beneficiaries in general and specifically overseas beneficiary populations are typically younger than the population at large, with 20–40 year olds and children <10 years old comprising the majority. The average age of all patients was 20.9 years split between 45% female and 55% male patients. The breakdown of patient category by age group and service affiliation is presented in Table II. Influenza A was the most common respiratory viral infection among this population with an overall prevalence rate of 15.7%. The other common viral agents isolated with prevalence rates included influenza B (1.5%), RSV (5.2%), adenovirus (3.5%), and

**TABLE II.** Distribution of Patient Specimens by Service and Patient Category

Service	Pediatric <sup>a</sup>	Beneficiary <sup>b</sup>	Active Duty	Total
Army	639	183	547	1369
Air Force	254	47	151	452
Navy	16	10	28	54

Questionnaire

Service	Pediatric	Beneficiary	Active Duty	Total
Army	231	84	215	530
Air Force	147	47	144	338
Navy	16	10	28	54

<sup>a</sup>Pediatric patients include beneficiaries under age 18. <sup>b</sup>Beneficiary patients represent all adult patients without the family member prefix<sup>20</sup> indicating active duty status.

PIV (1.7%). The breakdown of positive isolates by age and gender is noted in Table III. Influenza A mainly affected the pediatric population and 21–40 age group, whereas RSV, adenovirus, and PIV commonly affected the infant population (<2).

**Questionnaire Data**

We received 922 (49%) completed patient questionnaires. They provided additional patient information regarding specific symptoms, age, gender, fever temperatures, travel and vaccination history, and onset of symptoms. Additionally, we searched through patient records to obtain prescription data from these clinic visits. We determined that the top three symptoms in pediatric patients differed from those of adult patients. Pediatric patients presented with the classical cough, fever, and runny nose, whereas the adults typically noted fatigue, body ache, and headache. This is not surprising as much of the pediatric population was too young to communicate effectively and objective signs were documented where adults tended to report the symptoms they were suffering from. Fever was, however, a common symptom between both groups. Many patients did travel before presentation to the clinic to places mainly throughout Europe, the Middle East, and the continental U.S. No trends were noted from travel histories. Patients reported symptoms on average 2.5 days before presenting to the clinic. In most cases (67%), no prescriptions were given, whereas the commonly prescribed agent was azithromycin (13%) followed by amoxicillin (6%). Antibiotics were provided to patients presenting on average 2.8 days after onset of symptoms. Antiviral medication, (oseltamivir) was prescribed carefully for patients with early presentation (≤1 day) with mostly positive rapid antigen results. Influenza rapid antigen testing kits have historically not performed as well as the manufacturer's claims.<sup>11,14,19</sup> Typically, manufacturer-supported studies publish data using a large sampling size from an institution with a very high prevalence rate and very controlled conditions. Binax's overall claim is 80% sensitivity against both culture and PCR. However, our results indicated a sensitivity of only 54% against both culture

**TABLE III.** Age Distribution of the Positive Patient Cultures with Gender Breakdown (Male/Female)

Age Distribution	Influenza A	Influenza B	RSV	Adenovirus	PIV
<2 years	20 (11/9)	1 (1/0)	71 (44/27)	37 (27/10)	17 (5/12)
2–5 years	46 (23/23)	3 (3/0)	22 (11/11)	10 (6/4)	5 (2/3)
6–10 years	37 (17/20)	9 (9/0)	0	10 (9/1)	1 (0/1)
11–20 years	38 (26/12)	1 (1/0)	2 (2/0)	4 (3/1)	2 (2/0)
21–40 years	124 (64/60)	8 (2/6)	2 (1/1)	4 (2/2)	6 (2/4)
41–60 years	29 (17/12)	6 (3/3)	1 (0/1)	1 (0/1)	1 (0/1)
Totals	294 (158/136)	28 (19/9)	97 (58/29)	66 (47/19)	32 (13/19)

**TABLE IV.** Comparison of Rapid Antigen, PCR, and Viral Culture Results

	Sensitivity (%)	Specificity (%)	PPV	NPV
2006–2007 (19% prevalence <sup>a</sup> )				
Rapid flu vs. PCR	54	97	73	81
Rapid flu vs. culture	54	97	73	85
Culture vs. PCR	97	98	92	94
2006–2007 (24% Prevalence <sup>b</sup> )				
Rapid RSV vs. PCR	29	98	81	80
Rapid RSV vs. culture	41	97	72	89
Culture vs. PCR	60	99	94	88

<sup>a</sup>Prevalence is based on PCR results as the “gold standard” compared to other testing methodologies. <sup>b</sup>RSV prevalence population was defined as pediatric population <6 years old.

and PCR. These data are shown in Table IV. Of the 1875 specimens collected, 175 specimens were not included in this data pool because they were either not tested using all three methodologies or were rejected specimens where no testing was performed. Influenza and RSV prevalence in this data set based solely on PCR results was 19% and 24%, respectively.

We were surprised at how poorly rapid antigen testing performed in our study compared to the manufacturer’s claims and existing literature.<sup>11,14,19</sup> Some factors possibly contributing to these lower sensitivities include sampling method, age of population, time of collection, and specimen quality. We began using flocked nasopharyngeal swabs (Copan) instead of nasopharyngeal aspirates/washes because the literature indicated that a greater amount of specimen can be collected and released from the “new” generation of swab, making this method equivalent to NP wash/aspirate.<sup>20</sup> Our health care providers and technicians strongly preferred collecting a swab specimen vs. a nasal wash because of its ease of use, especially in the pediatric population. Additionally, swab collection minimizes the potential exposure of the health care worker from aerosolized particle droplets that may occur while collecting a nasal wash.

Comparing RSV rapid antigen sensitivity and specificity from 2005–2006 (nasopharyngeal aspirate) to 2006–2007 (Copan nasopharyngeal swab), our rapid antigen testing sensitivities remained constant, supporting the conclusion that flocked swabs for specimen sampling are comparable to NP wash/aspirates. Also, calculating sensitivity, specificity,

positive and negative predictive values (see “Materials and Methods”) by population breakdown showed very little differences between pediatric (56%, 96%, 76%, 90%), beneficiary (55%, 94%, 73%, 88%), and active duty populations (54%, 91%, 56%, 91%). With the exception of the positive predictive value difference in active duty status, all other percentages remained relatively equal. Time of collection affects antigen load, which may be very low at onset of symptoms or may begin to wane after a delay before presentation to a health care provider. However, reviewing questionnaire data subsets did not detect any differences at either end of the collection timing window. Lastly, specimen quality may have had an effect on testing sensitivity.

For us, two basic questions remain: Are rapid antigen tests worth the cost and why didn’t the rapid antigen tests work very well? Rapid antigen testing has the benefit of rapid diagnosis oftentimes providing results before patients leave the medical facility so that interventional therapeutics can be provided. Although LRMC performed the reference testing for most of the military clinics throughout Europe, several specimens required transport of 1–7 days following collection as opposed to local testing of patients within the facility. Local LRMC testing allowed for same-day antigen and in several cases same-day PCR resulting. Therefore, it may not be required to perform rapid antigen testing when such rapid and more sensitive PCR tests are readily available. However, testing at outlying health clinics with only a rapid antigen result may be important for proper therapy, particularly during the peak of the respiratory virus season. Although the cost of these tests is high (~\$15.00 per patient specimen) and the sensitivity is very low compared to other diagnostic methods, our health care providers are hesitant to eliminate this testing. Therefore, rapid antigen testing will continue at remote and local clinics with confirmatory testing being performed at LRMC.

Why did these rapid antigen tests not work as well as described? There is a specific threshold amount of antigen required for a positive result, which in some cases may be too low because of the timing of collection, the method of collection, and most importantly, the quality of the specimen.<sup>21</sup> When performing a direct fluorescent antibody screening, specimen quality can be deemed adequate or inadequate on the basis of the number of intact epithelial cells present in the specimen. There are no such controls for determining specimen quality for a rapid antigen test. In addition, it has been

demonstrated that these rapid tests have their highest sensitivity during the peak of the season to give a very high predictive value.<sup>11</sup> Our results confirm this phenomenon, where we observed an increased sensitivity during the height of the season for both influenza and RSV.

This study enhances previously published data that indicate rapid antigen testing kits are less sensitive than manufacturer claims. By collecting a larger specimen pool from a geographically diverse region, we found that increasing the number of testing sites decreases the sensitivity of these tests even further than that seen in previous studies. We feel that this significant decrease in rapid testing sensitivity is likely because of the dramatic increase in the number of personnel collecting specimens and performing the rapid testing. The rapid test kit utilized is clinical laboratory improvement amendment (CLIA) waived and can be performed in either the health care provider's location or at the laboratory. Previous studies have evaluated these rapid tests in a more or less fixed pool of collecting and testing personnel. In our area of responsibility the vast geographic differences and 35% annual personnel turnover can reduce competency and can increase errors in collecting specimens and performing testing.

### **Vaccine Effectiveness**

Public Health records indicate that 91% of the active duty military service members throughout EUCOM received flu vaccine. We determined vaccine effectiveness by comparing the attack rate of influenza between immunized and unimmunized service members. There were only 13 cases among the 9096 unimmunized, for a rate of 1.43 per 1000. In comparison, there were 80 cases among the 117,320 immunized service members for a rate of 0.68 per 1000. Using the calculation (attack rate unvaccinated – attack rate vaccinated)/attack rate unvaccinated,  $[(13/9096)-(80/117320)]/(13/9096) = 52.28\%$  vaccine effectiveness for active duty service members was ~52% for the season. No tracking mechanisms were in place to determine beneficiary vaccine effectiveness. Although the vaccine effectiveness may seem low at first glance, it may be confusing as many previous studies use different models to determine effectiveness.<sup>22</sup>

### **Lessons Learned**

We felt that this project was successful in many ways. Compared to data from previous years' surveillance from the surrounding community and some of the Army outlying health clinics, we nearly tripled the number of patient specimens tested by broadening our scope. Obviously, a large proportion of the testing came locally from LRMC clinics within the Kaiserslautern Military Community because we were able to provide constant encouragement to clinics with the help from preventive medicine and public health channels. We developed a tremendous working relationship with CHPPM-EUR

by performing complementary tasks. CHPPM-EUR provided PHEO training and worked with providers to increase surveillance and we trained both provider and laboratory personnel in testing procedures. Obviously, when starting a new program, there were many difficulties that were encountered including:

- Local vendors were unable to meet the timeline for providing required materials.
- There were occasional customs concerns in receiving/shipping materials.
- Bringing all of the services into agreement on how the program would work and coordinate testing/training at specific sites required extensive dialogue and command influence.
- Time constraints resulted in the inability to personally train staff at each submitting location.
- Several Air Force clinics had to switch from an established program "Project Gargle" to support the effort.
- Verification of CHCS interoperability at all locations took longer than expected.

The increased influenza surveillance for 2006–2007 was well received by the health care providers and various medical commands in EUCOM. It was able to provide increased surveillance, important for characterizing circulating strains for inclusion into the annual influenza vaccine, and turn influenza results around rapidly to the health care providers. This rapid viral diagnosis improves antibiotic stewardship allowing providers to make informed decisions on whether to prescribe antibiotic therapy, or, if prescribed, an opportunity to withdrawal inappropriate antibiotic treatment. These outcomes can play a central role in reducing acquired bacterial resistance that is often encountered in our patients.

Increasing viral surveillance in the region provides our combatant commanders and local public health officials with real-time information regarding circulating viruses in our service members and health care beneficiaries. This enhanced surveillance also increases the capability to detect and respond to novel viruses, particularly the emergence of a pandemic strain of influenza. LRMC participates in the CDC's Laboratory Response Network and is able to detect and confirm H5N1 avian influenza in addition to detection and characterization of other novel strains of influenza through genetic sequencing. This increase in surveillance and capabilities has increased EUCOM's ability to respond in the event of a pandemic virus.

### **ACKNOWLEDGMENTS**

Department of Defense, Global Emerging Infections Surveillance (GEIS), Europe Regional Medical Command (ERMC) funding sources.

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