



# GEIS Respiratory Disease Surveillance Newsletter

DoD Center for Deployment Health Research  
Naval Health Research Center, San Diego



Issue 5

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Sponsored by the DoD Global Emerging Infections System (GEIS), the Naval Health Research Center (NHRC) collaborates with numerous federal and non-federal institutions to conduct surveillance for several respiratory pathogens, including adenovirus, influenza, respiratory syncytial virus (RSV), parainfluenza, *Streptococcus pyogenes*, and invasive *Streptococcus pneumoniae*. Please visit our website at <http://www.nhrc.navy.mil/geis> for additional information

## Current Study Updates

### Pneumococcal Vaccine Trial

In collaboration with Centers for Disease Control and Prevention, the Mayo Clinic and Foundation, and Wyeth-Lederle vaccines, NHRC and 4 recruit training sites are conducting a double blind, placebo-controlled trial of a 23-valent pneumococcal vaccine to assess the vaccine's clinical effectiveness among the military trainee population. The study is currently underway at Fort Jackson, Fort Leonard Wood, NRTC Great Lakes, and MCRD Parris Island. The study will eventually enroll over 191,000 trainees. The participants will be actively followed during recruit training for pneumonia and passively followed (by tracking inpatient and outpatient military medical databases) for pneumonia and acute respiratory disease after recruit training until the end of the study period (up to 3 years) for pneumonia and acute respiratory disease. To date, study site personnel have enrolled more than 84,000 recruits with a better than 70% enrollment rate.

### Evaluation of PCR Testing

#### Using Room Temperature Specimens

One of the biggest challenges the Febrile Respiratory Illness (FRI) sites face is keeping viral specimens frozen at ultra-low temperatures for long periods before and during shipping. A new sub-study at Fort Jackson will evaluate the performance of room temperature specimens in comparison with frozen viral cultures. The study, in collaboration with researchers at the Armed Forces Institute of Pathology, will use PCR techniques to test for adenovirus and influenza. If these tests prove successful, the specimen collection portion of FRI surveillance could be simplified and the surveillance expanded to regions where freezing specimens is not feasible. Specimen collection has just concluded and lab analysis is underway.

### Febrile Respiratory Illness (FRI) in a Mexican population

In collaboration with the Mexican Institute of Public Health Services, a one-year FRI surveillance project has begun at a

community clinic in Ensenada, Mexico. The purpose of this pilot study is to determine the etiology of viral pathogens causing FRI among clinic attendees. A total of 200 throat swab specimens will be collected and tested using conventional viral culture techniques. The first specimens we collected in January 2002 and preliminary lab results indicate that both flu and adenovirus are present in the population.

## Febrile Respiratory Illness Surveillance



**Current Progress** – Febrile Respiratory Illness surveillance is currently being conducted at eight military training sites. Specimens from trainees presenting with symptoms matching the definition of FRI are tested for adenovirus, influenza A and B, respiratory syncytial virus (RSV), and parainfluenza 1, 2 and 3. The specific trends observed for each of these viruses are described in the following sections.

**Geographic Trends** – Since January 1, 2001, six of the eight surveillance sites have reported FRI rates above the epidemic threshold, which is defined as 1.5 cases per 100 trainees per week (Figures 1, 2). The distribution of viral test results by site demonstrates the geographic variance in FRI etiology (Figure 3).

**Temporal Trends** – In 2001, epidemic level FRI rates peaked between February and April, and again in August at several sites, in contrast to historically described peaks during the winter months for FRI-like illnesses. This change in seasonal trends was also observed during the year 2000, as FRI rates above the epidemic threshold were observed during each month of that year.

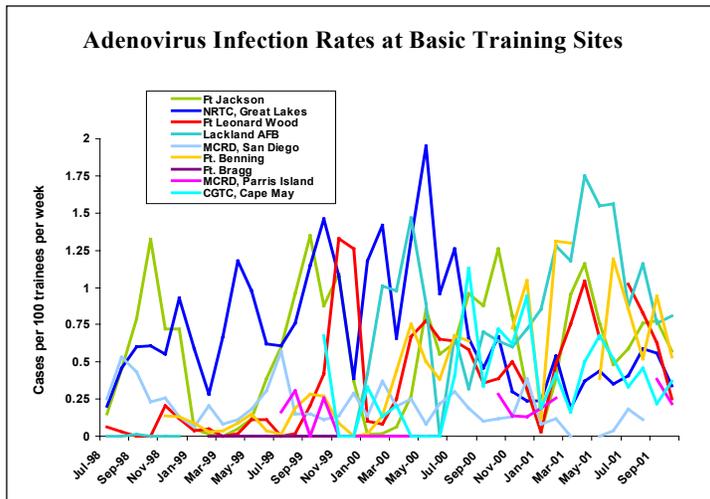
## FRI Specimens Tested per Site June 1998 – February 2002

<u>SITE</u>	<u>SPECIMENS TESTED</u>
Fort Benning	1282
Fort Jackson	2777
Fort Leonard Wood	1340
NRTC, Great Lakes	1239
MCRD, San Diego	604
MCRD, Parris Island	297
CGTC Cape May	437
Lackland AFB	748

### Adenovirus

**Current Progress** – In the absence of vaccine, adenovirus remains the leading cause of FRI among trainees. More than 61% of the 8787 throat cultures collected for the FRI study between June 1998 and February 2002 tested positive for adenovirus. Approximately 97% of the adenovirus isolates collected to date have been type 4.

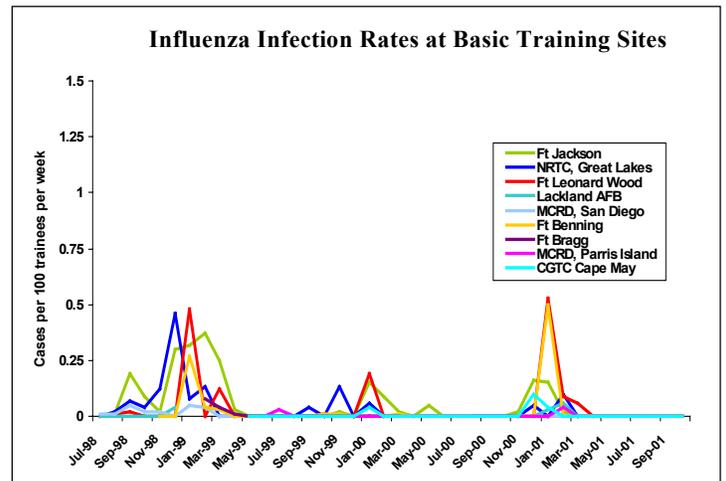
**Geographic Trends** – From January 1, 2001 to February 10, 2002, the amount of FRI morbidity caused by adenovirus remained high at all sites, ranging from 48.6% at MCRD Parris Island, to 75.6% at CGTC Cape May. Please see accompanying charts for adenovirus infection rates by site.



to Mar 2002), and have seen some isolates from January 2002 test positive for influenza.

**Geographic Trends** – Our surveillance data demonstrate that morbidity among trainees caused by infection with influenza A or B varies by training site location. Please see accompanying chart for influenza infection rates by basic training site location.

**Temporal Trends** – Influenza infection rates were highest at the recruit camps during the 1998-99 flu season, followed by high rates during last year's 2000-2001 flu season. In contrast, the 1999-2000 flu season demonstrated low infection rates as compared to the other two seasons surveyed. Testing for the 2001-2002 flu season is currently underway.



### Other FRI Study Pathogens

Of the 8787 throat cultures tested thus far under the FRI study, 21 (0.2%) have been positive for RSV and 75 (0.9%) have been positive for parainfluenza 1, 2, or 3.

### Influenza

**Current Progress** – From the start of this study in June 1998 to February 2002, 409 (4.7%) of the 8787 FRI specimens tested thus far have been positive for influenza, with 3.4% identified as type A and 1.3% as type B. During this period, trainees who were not vaccinated against influenza were almost 5 times more likely to be influenza-positive (OR= 4.7, 95% CI, 3.7-5.9) than those who did receive the vaccine. We have begun processing specimens from the 2001 - 2002 flu season (Nov 2001

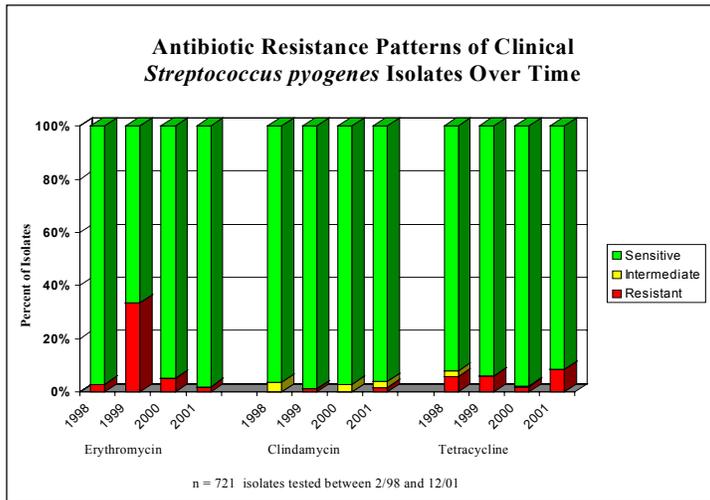
### Streptococcus pyogenes Surveillance



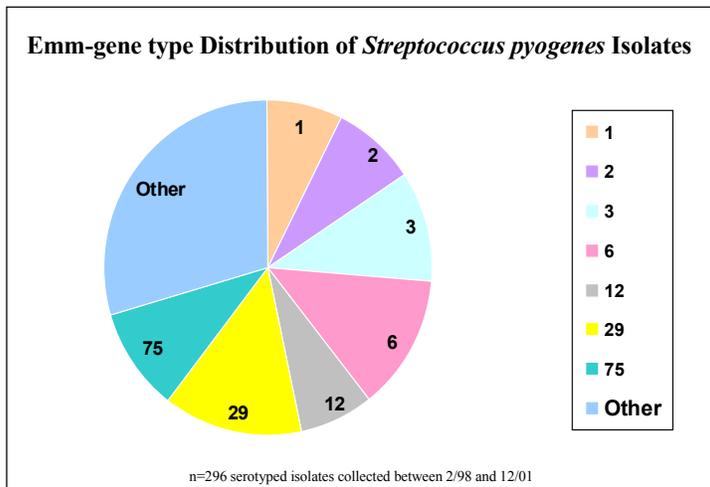
**Current Progress** – *Streptococcus pyogenes* (Group A streptococcus) continues to be a threat to the health of military trainees. Between February 1998 and February

2002, 721 clinical isolates were collected from trainees at 8 military sites.

**Antibiotic Resistance** – Among the specimens tested, *S. pyogenes* maintains 100% susceptibility to the antibiotics penicillin, levofloxacin, and vancomycin. Forty-seven (6.5%) of the 721 isolates collected exhibited full or partial resistance to erythromycin, 43 (6%) to tetracycline, and 23 (3.2%) to clindamycin (Figure 4). Ten (1.4%) of the isolates were resistant to both erythromycin and tetracycline. Isolates from female trainees showed a similar proportion of erythromycin resistance as compared to male trainees (6.2% and 8.5%, respectively). Temporal trends in antibiotic resistance among *S. pyogenes* isolates collected to date demonstrate no discernible pattern, as shown in the following chart.



**Emm-gene Types** – As of February 2002, 296 *Streptococcus pyogenes* specimens had been emm-gene typed. Among these, the most common emm-gene types among military trainees were 29 (13.5%), 6 (12.8%), 3 (10.5%), 75 (9.8%), 2 (8.4%), 1 (7.4%), and 12 (7.4%). These seven emm-gene types made up more than 69% of all the typed isolates.



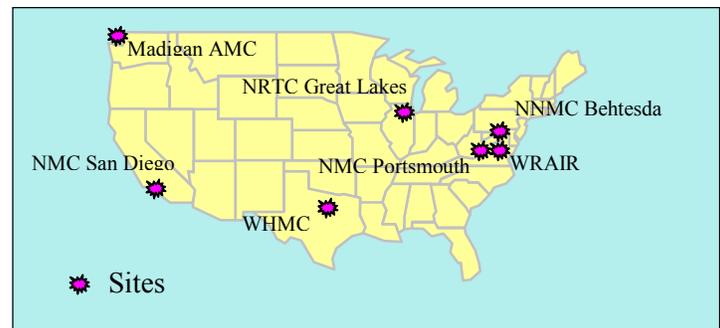
**Resistance by Emm-gene type** – Erythromycin resistance varied by emm-gene type. Type 75 exhibited the most erythromycin resistance of all emm-gene typed isolates, with 76% of type 75 isolates demonstrating full resistance.

**Geographic Trends** – *S. pyogenes* isolates from military trainees currently maintain high susceptibility to many commonly prescribed antibiotics, including tetracycline, erythromycin and clindamycin; and 100% susceptibility to penicillin, levofloxacin, and vancomycin. However, we continue to observe an unequal geographic distribution of erythromycin resistance at the sites. Resistance to erythromycin differed between sites, the highest resistance rate was Lackland AFB (29.1%). One hundred percent of the erythromycin resistant isolates from Lackland AFB, were fully resistant.

***S. pyogenes* Isolates Received per Site February 1998 to February 2002**

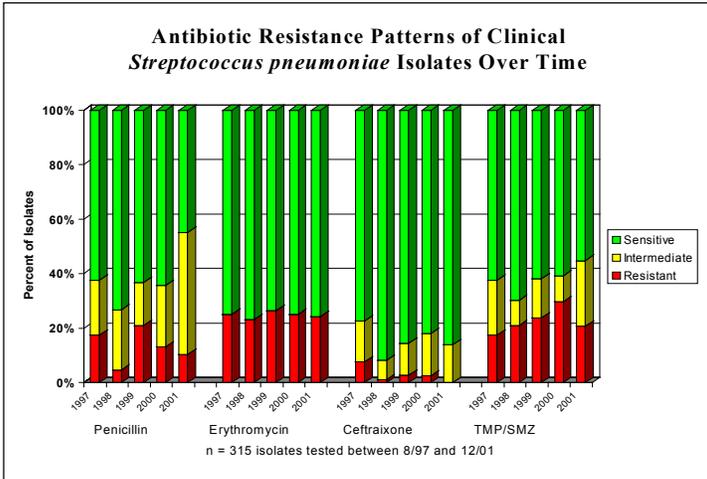
<u>SITE</u>	<u>ISOLATES RECEIVED</u>
NRTC, Great Lakes	277
MCRD, Parris Island	253
MCRD, San Diego	3
Fort Jackson	4
Fort Knox	23
Fort Leonard Wood	39
Fort Sill	19
Lackland, AFB	103

***Streptococcus pneumoniae* Surveillance**



**Current Progress** – Testing is complete for 321 invasive clinical isolates collected between August 1997 and February 2002 from military healthcare beneficiaries at 7 military medical centers.

**Geographic Trends** – We observed an unequal geographic distribution of penicillin resistance among the collection sites. Among the sites with an adequate number of specimens, penicillin resistance was relatively stable, ranging from 33% at Madigan AMC to 45% at Walter Reed AIR.



**Antibiotic Resistance** – One-hundred and thirteen (35.2%) of the 321 isolates collected demonstrated full or partial resistance to penicillin, and 74 isolates (23.1%) exhibited multiple resistance to three or more antibiotics (Figure 5). The patterns of penicillin resistance between males (36.9% resistant) and females (32.8% resistant) were similar. As shown in the chart below, temporal trends in antibiotic resistance among *S. pneumoniae* isolates collected to date do not demonstrate a discernible pattern.

***S. pneumoniae* Serotypes** – Of the 258 typed isolates, the most common serotypes were 14 (27.1%), 6 (15.5%), 9 (14%), 19 (13.6%), 23 (9.3%), and 4 (9.3%), all of which are included in the 23-valent pneumococcal vaccine. These seven serotypes made up more than 88% of all typed isolates.

**Resistance by Serotype** – Penicillin resistance differed by serotype, with types 19 (54.3%), 9 (50%), and 23 (37.5%) demonstrating the most resistance. These three serotypes accounted for more than 59% of all penicillin resistance among the serotyped isolates, though they only comprised 37% of the total number of serotyped isolates.

***S. pneumoniae* Isolates Received per Site  
August 1997 to February 2002**

<u>SITE</u>	<u>ISOLATES RECEIVED</u>
NRTC Great Lakes	4
NMC, San Diego	93
NMC, Portsmouth	2
NNMC, Bethesda	12
Walter Reed AIR	30
Wilford Hall MC	65
Madigan AMC	112

***Bordetella pertussis* Surveillance**

**Current Progress** – Surveillance of *Bordetella pertussis* is currently underway at four military recruit training sites: MCRD-San Diego, Ft. Benning, Ft. Leonard Wood, and NRTC Great Lakes. Site personnel have enrolled 246 subjects to date. Of these, 130 specimen sets have been complete, and have been tested using conventional culture methods. These specimens were collected from recruits meeting the case definition for pertussis, which is more than seven days of coughing as well as symptoms consistent with a respiratory infection. Preliminary results indicate that at least one (1.3%) of the specimens tested positive by PCR and culture techniques for the pathogen. Additionally, 35 specimens have been tested by PCR, and of those tested, 9 (7%) were positive for *B. pertussis*. Testing of sera specimens has begun, and at least 2 (2.6%) have tested positive for pertussis infection thus far.

***B. pertussis* Specimens Received per Site  
June 2000 to February 2002**

<u>SITE</u>	<u>SPECIMENS RECEIVED</u>
MCRD San Diego	148
Fort Leonard Wood	49
Fort Benning	33
NRTC Great Lakes	17

**New Protocols**

**Association between adenovirus infections among military personnel and the development of obesity** – This case control study, which began in October 2001, investigates if an association exists between weight control problems (obesity) and adenovirus-36 exposure in a population of active duty Navy personnel. The study is being conducted at the at the Clinical Trials Center in San Diego and is currently enrolling cases (individuals with a Body Mass Index (BMI) of >30) and controls (BMI <25).

**Adenovirus serology** – This study may use beginning- and end-of-training paired sera to measure the incidence of adenovirus infection during recruit training.

**Shipboard FRI surveillance** – NHRC may begin to monitor ships on deployment in a manner similar to the current FRI surveillance at basic training sites. This study may include viral culture testing and the calculation of FRI rates.

**Restriction enzyme analysis and sequencing of type 4 adenovirus** – NHRC will examine the subtypes of adenovirus type 4 isolates accumulated over the past 5 years to look for geographic and/or temporal changes.

## Center News

### **Presentations and/or Posters at Recent Conferences**

**IV International Symposium on Respiratory Viral Infections**, November 29-December 2, 2001, Curacao, Netherlands

- ◆ Ryan M, et al. **Adenoviral respiratory infections in young adults in US military training.**

**42<sup>nd</sup> Navy Occupational Health and Preventive Medicine Workshop**, March 14-22, Chesapeake, VA

- ◆ McDonough E, et al. **National Department of Defense surveillance for *Streptococcus pneumoniae*: update on antibiotic resistance and serotype distribution.**
- ◆ Baker C, et al. **Implementation of a large, double-blind, placebo-controlled trial of the 23-valent pneumococcal vaccine in healthy young adults.**
- ◆ Hawksworth A, et al. **Interlab agreement of respiratory viral culture results between two Department of Defense laboratories.**
- ◆ Ryan M, et al. **Febrile respiratory illness surveillance in the military: an update.**
- ◆ Russell K, et al. **The pneumococcal vaccine trial: progress.**

**International Conference on Emerging Infectious Diseases**, March 24-27, Atlanta, GA

- ◆ Cameon C, et al. **National Department of Defense surveillance for *Streptococcus pneumoniae*: update on antibiotic resistance and serotype distribution.**
- ◆ Sammons J, et al. **Bordetella pertussis infection in military recruit populations.**
- ◆ Russell K, et al. **Implementation of a large, double-blind, placebo-controlled trial of the 23-valent pneumococcal vaccine in healthy young adults.**

**DARPA Sponsored Conference on TIGER, A PCR / Mass Spectrometer High Throughput Technique of Pathogen Identification**, April 1-4, New York City, NY

- ◆ Russell K, et al. **DoD center for deployment health research respiratory disease laboratory.**

### **Upcoming Conferences**

- ◆ **Recruit Healthcare Symposium 2002**, April 15-18, Towson, MD
- ◆ **International Symposium of Pneumococcal Illness**, May 5-9, Anchorage, AL
- ◆ **9th ASM Undergraduate Microbiology Education Conference**, May 19-23, Salt Lake City, UT

### **New Publications**

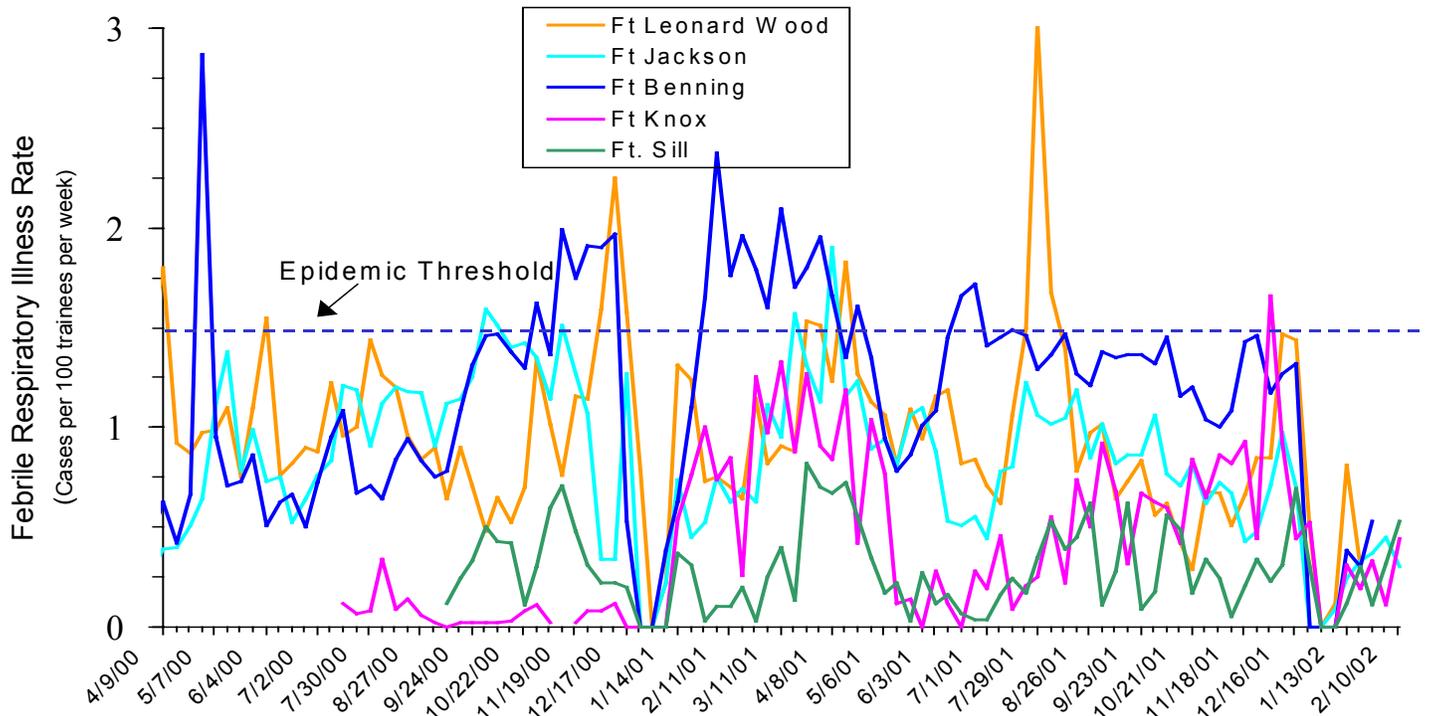
- ◆ **Pneumococcal vaccine to counter emerging infectious disease threat in the military.** McKeehan J, et al. *Mil Med*, 2001; 166:1087-90.
- ◆ **Large epidemic of respiratory illness from adenovirus types 7 and 3 in healthy young adults.** Ryan M, et al. *Clin Infect Dis*, 2002;34(3):577-82.
- ◆ **An outbreak of pneumococcal pneumonia among military personnel at high risk: Control by low-dose azithromycin post-exposure chemoprophylaxis.** Craig SC, et al. *Mil Med*, in press.
- ◆ **Molecular epidemiology of adenovirus type 7 in the United States (1996-2000).** Erdman D. et al. *Emerg Infect Dis*, 2002;8(3):269-77.

*Please contact the newsletter staff with any comments or suggestions regarding the information in this issue.*

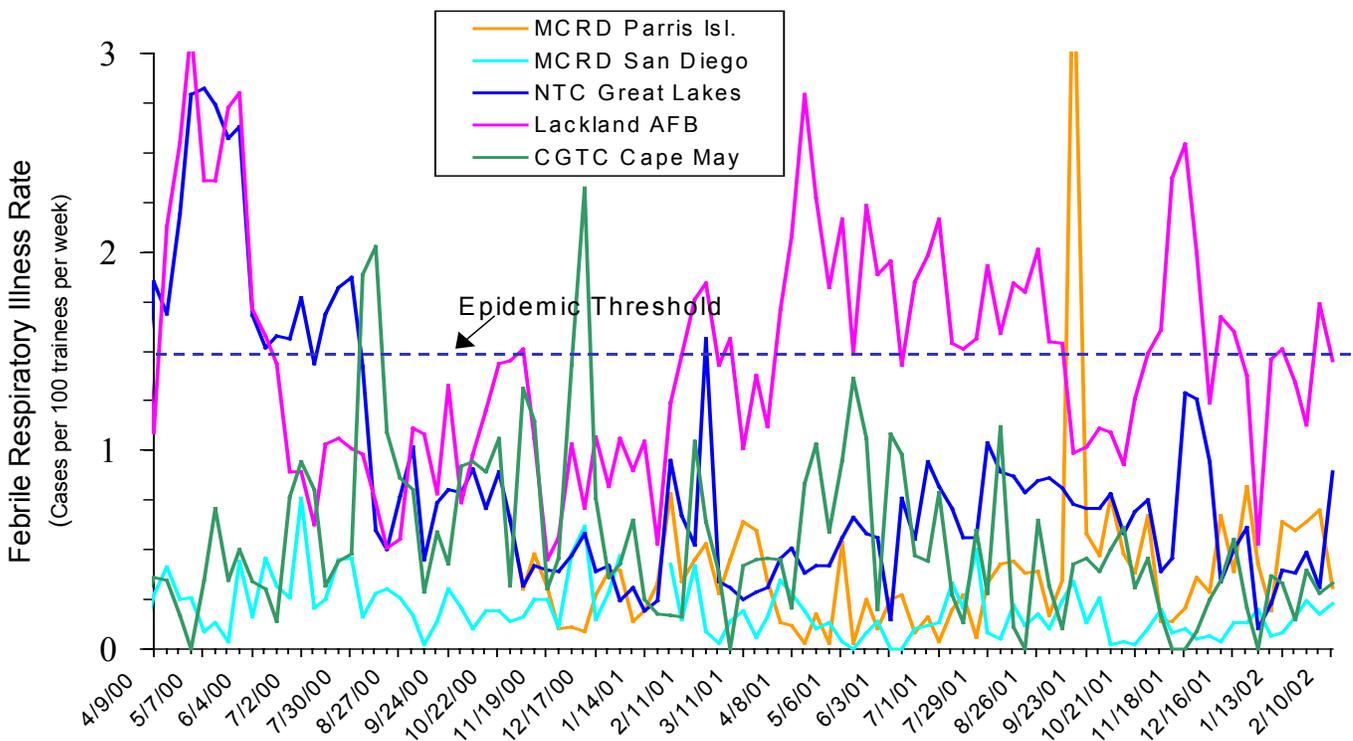
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*These studies would not be possible without the hard work and dedication to excellence of the staff at our collaborating institutions. Thank you!*

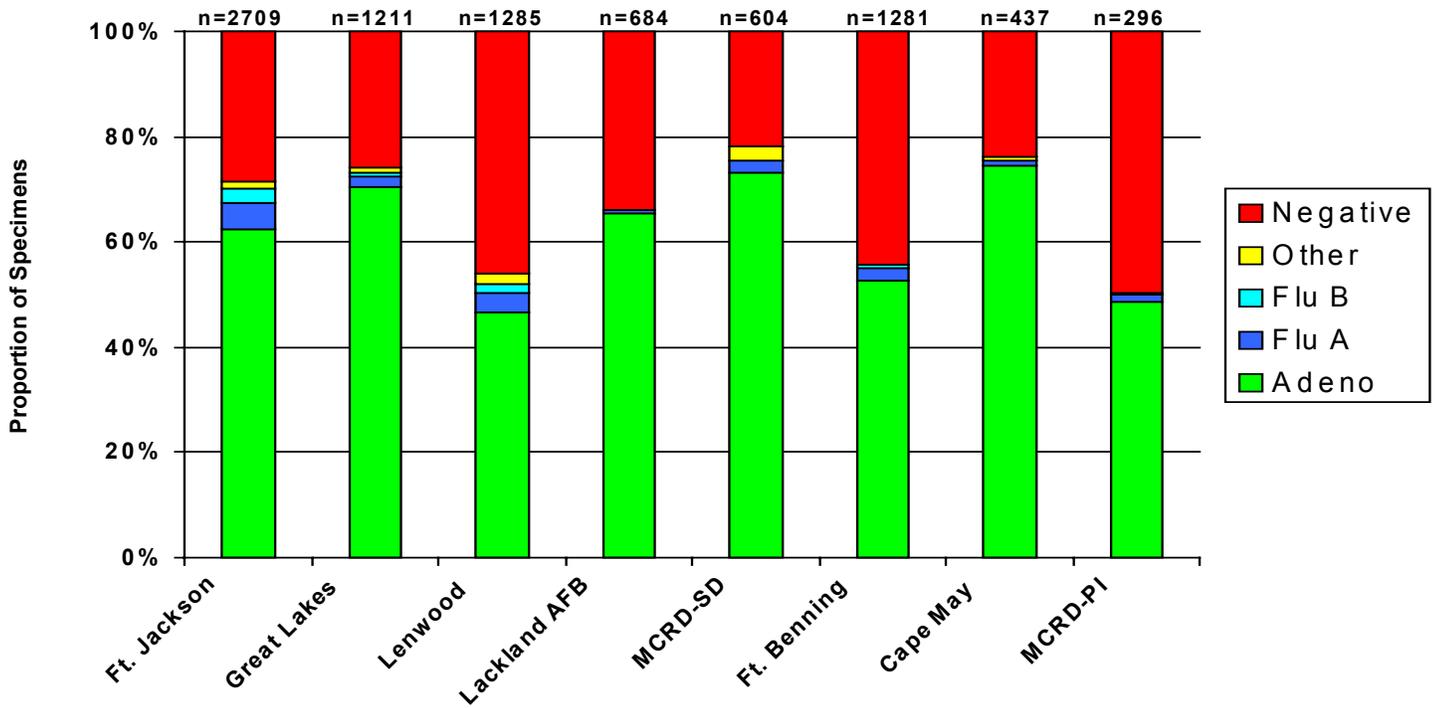
# Febrile Respiratory Illness Rates at US Army Training Installations



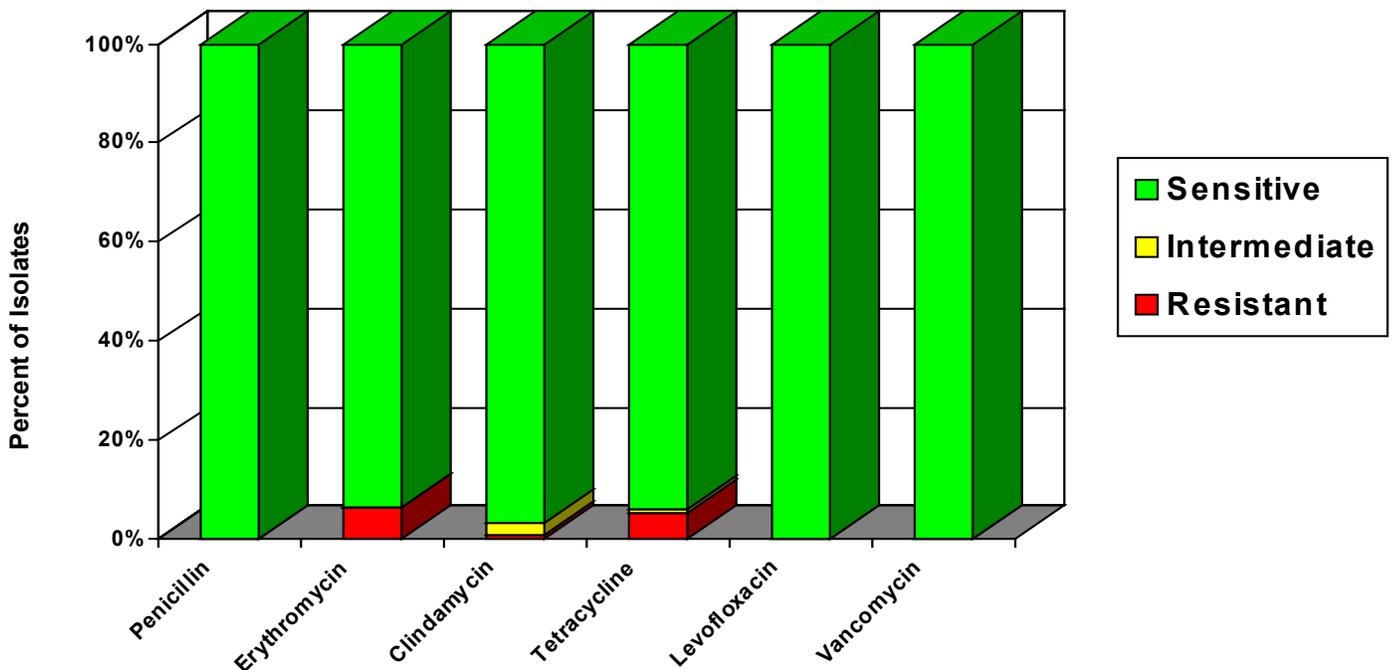
# Febrile Respiratory Illness Rates at US Navy/Marine/Air Force/Coast Guard Training Installations



## Distribution of Viral Test Results by Site June 1998 - October 2001 n=8507

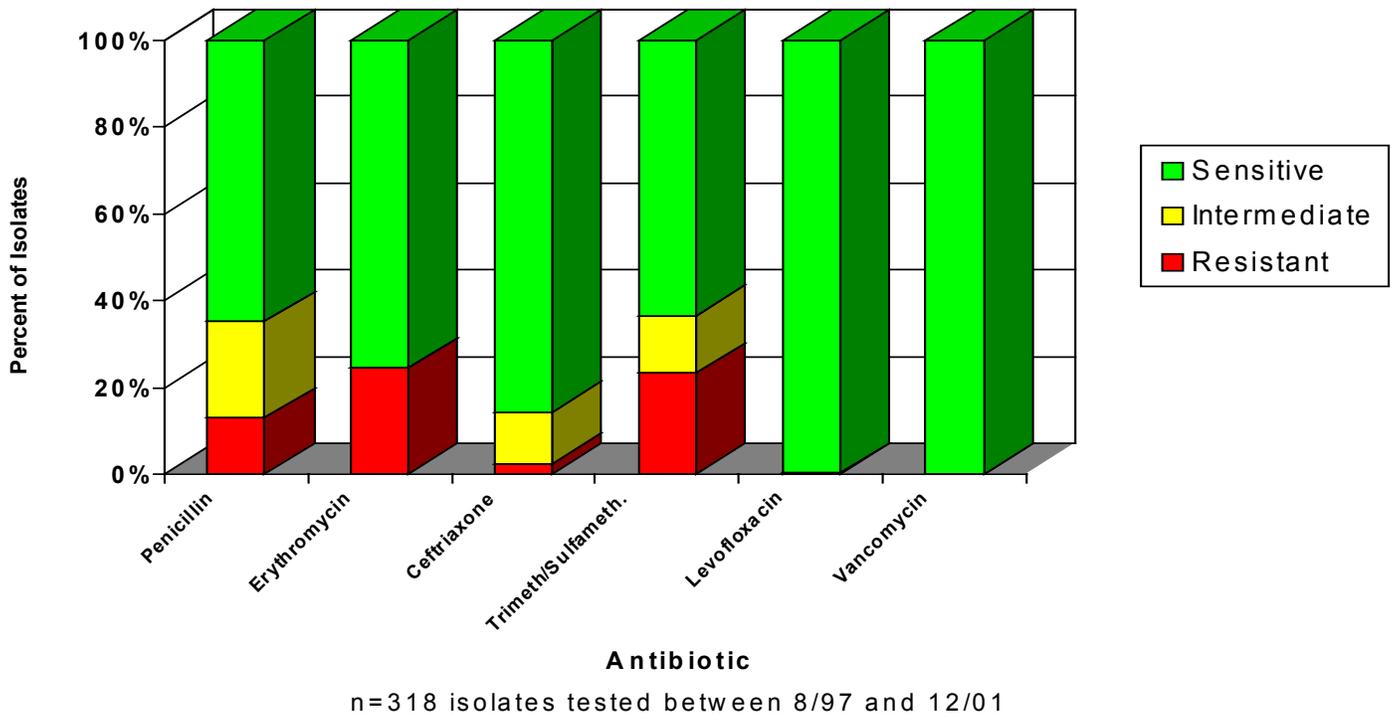


## Antibiotic Resistance Patterns of Clinical *Streptococcus pyogenes* Isolates from Military Trainees



n=721 isolates tested between 2/98 and 12/01

## Antibiotic Resistance Patterns of Sterile Site *Streptococcus pneumoniae* Isolates From Military Medical Facilities



## Serotype Distribution of Sterile Site *Streptococcus pneumoniae* Isolates

