

Emerging Illness Update

Newsletter for Emerging Illness Studies at Naval Health Research Center, San Diego

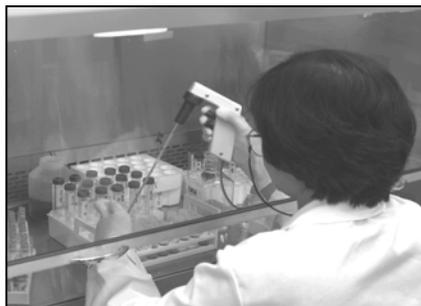
Emerging Illness Surveillance and Research Expands at Naval Health Research Center

Introduction

Scientists at Naval Health Research Center (NHRC), San Diego, are conducting 3 projects involving surveillance for emerging respiratory pathogens. Studies of adenovirus, *Streptococcus pneumoniae*, and *Streptococcus pyogenes* are underway at 13 military sites throughout the United States. This newsletter will update you on the progress of these studies and will describe other exciting projects that are on the horizon.

Adenovirus

Before the implementation of a vaccine, adenovirus infected up to 10% of military recruits and caused up to 90% of recruit pneumonia. Vaccines against types 4 and 7 adenovirus have been successfully used in military training populations for nearly 30 years; however, an impending loss of the vaccine (due to the manufacturer ceasing production) could result in epidemics such as those seen in the pre-vaccine era.



NHRC virologist hard at work culturing and typing adenovirus.

Surveillance was established at 5 training centers (see site map, p. 4) between October 1996 and April 1997. Study personnel at each site monitor their "sick call" clinics and obtain throat swab specimens from trainees who have fever and respiratory disease symptoms. The swabs are placed in viral transport media, frozen, and shipped to NHRC every 4 weeks. More than 3,000 specimens have been received to date. Our heartfelt thanks go out to the on-site study personnel; their hard work and dedication make the study a success!

Virologists at NHRC utilize a microneutralization technique (described in a previous newsletter) to isolate, identify, and type adenovirus. Preliminary data suggest that the vaccines are very effective in preventing infection with types 4 and 7 adenovirus. A closer look at the data appears on pages 2-3.

Streptococcus pneumoniae Surveillance Underway at 7 Military Hospitals

S. pneumoniae has long been a leading cause of morbidity and mortality in the United States. In the past, *S. pneumoniae* has been susceptible to antibiotics such as penicillin and erythromycin. However, antibiotic resistance of *S. pneumoniae* has steadily increased in the last decade, with some areas of the U.S. now reporting that 30-40% of isolates are resistant to

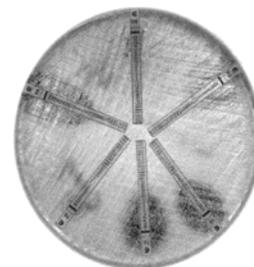
penicillin. Resistant strains of *S. pneumoniae* may not be eradicated by empiric antibiotic therapy, thereby increasing the costs of treating such infections and increasing the potential for more serious disease.

This study's primary objective is to measure the prevalence of antibiotic resistance among sterile site (e.g., blood) *S. pneumoniae* isolates from patients at 7 military medical facilities (see site map, p. 4). Isolates will also be serotyped by our collaborator at the University of Alabama, Birmingham, to determine the proportional distribution of serotypes causing invasive disease. Unlike our other studies that collect specimens from active-duty personnel only, any patient who receives health care at these military medical centers (active-duty, dependent, retiree) is eligible for this study. Each center preserves all such clinical isolates and ships them to NHRC monthly.

Surveillance began in December 1997 and more than 50 isolates have been received to date. A summary of the current data can be found on pages 2-3.

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Antibiotic gradient strips are used to determine the minimum inhibitory concentrations (MICs) of antibiotics against *S. pneumoniae* and *S. pyogenes*.

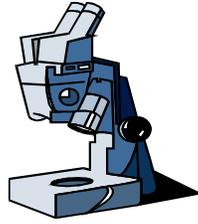
Clinical Isolates Now Included in *Streptococcus pyogenes* Surveillance

Similarly to pneumococci, *S. pyogenes*, or Group A streptococci (GAS), has shown increasing antibiotic resistance in the last decade. Although still exquisitely sensitive to penicillin, a proportion of GAS isolates are now resistant to the macrolides erythromycin and clindamycin. This has clinical significance because erythromycin is often prescribed to treat GAS infection in patients who are allergic to penicillin.

NHRC has begun collecting a systematic 50% sample of clinical GAS isolates from trainees at 8 military training centers (see site map, p. 4). The sites will preserve these isolates and ship them to NHRC monthly. The isolates will be tested for resistance to 6 antibiotics and will be typed by our collaborator at the University of Alabama, Birmingham. The 8 sites began saving these isolates in February 1998. The first group of specimens arrived at NHRC in March.

The original (and continued) focus of this study is to identify risk factors for invasive *S. pyogenes* infection. Invasive infection, which has also increased in the last decade, can lead to severe diseases such as cellulitis, necrotizing fasciitis, and streptococcal toxic shock syndrome (STSS). If your facility has a patient with invasive *S. pyogenes* infection or STSS, please contact NHRC and we will include your patient in the study and provide you with unique test results. We would like to remind everyone that a positive blood culture is not necessary to meet the case definitions for this study. A positive culture from a nonsterile site (throat, skin, etc.), in combination with toxic shock syndrome, also meets the case definition.

We have received excellent cooperation from our 8 surveillance sites in tracking invasive disease. As we begin to collect clinical GAS isolates in addition to the invasive data, we are relying on their efforts to an even greater degree. NHRC would like to thank the on-site personnel for their work on behalf of this study; any successes are due in large part to their efforts.



Current Findings

Adenovirus: As of March 1998, 245 (30%) of the 806 specimens tested have been positive for adenovirus. The isolation rates varied from 8% (Ft. Leonard Wood) to 41% (Ft. Jackson). The serotype distribution patterns were markedly different between those who received the vaccines and those who did not (Fig. 1). Statistically, those who did not receive the vaccines were 11 times more likely to have a positive adenovirus culture (OR=11.2; 95% CI 7.2-17.4) and were 41 times more likely to culture positive for adenovirus types 4 or 7 (OR=41.7, 95% CI 17.1-131.7) as compared to their vaccinated peers.

***S. pneumoniae*:** Eighteen (43%) of the 42 isolates tested to date have shown full or partial resistance to penicillin. Fifteen (83%) of those 18 isolates also had resistance to 2 or more other antibiotics. Penicillin resistance patterns were similar irrespective of age or gender. Resistance patterns to all 6 antibiotics tested are shown in Figure 2. Although the data is preliminary, it suggests that antibiotic resistance of *S. pneumoniae* may still be on the rise.

Capsular serotyping of the isolates will begin in April.

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New Studies Being Developed at NHRC

Pneumococcal Vaccine Trial

The 23-valent pneumococcal vaccine is not routinely used in military training camps. An exception is Camp Pendleton, a Marine training post north of San Diego. Trainees at Camp Pendleton have 38 times the risk of hospitalization for pneumonia as compared to the rest of the Navy and in 1989 experienced the largest military epidemic of pneumococcal pneumonia since the advent of antibiotics (128 cases).

We have proposed an ambitious clinical trial to evaluate the efficacy of the pneumococcal vaccine in trainees at Camp Pendleton. The study has a double-blind, placebo-controlled design and will enroll 60,000 Marine trainees over a 3 year period.

Respiratory Disease at the United States Naval Academy

In August 1997, an epidemic of acute respiratory illness was observed at the United States Naval Academy (USNA) in Annapolis, Maryland. Several hundred Midshipmen became ill with symptoms that included fever, sore throat, cough, and chills, and several of the patients required hospitalization. Although diagnoses of tonsillitis and pneumonitis were made, specific etiologic agents were not identified. Epidemics such as this are highly disruptive to the mission of the USNA.

NHRC has initiated a protocol that will follow a cohort of freshman, or "plebe", Midshipmen during their first year to determine the incidence and etiology of respiratory disease at the USNA. Data from this study will be used by public health officials to make policy decisions regarding vaccine interventions and appropriate empirical therapies.

Influenza: NHRC has been proposed as a center of laboratory excellence in the DoD's Global Emerging Infectious Disease Surveillance (GEIS) for influenza. NHRC's role would be to conduct population-based epidemiological surveillance at locations in the U.S. and abroad.

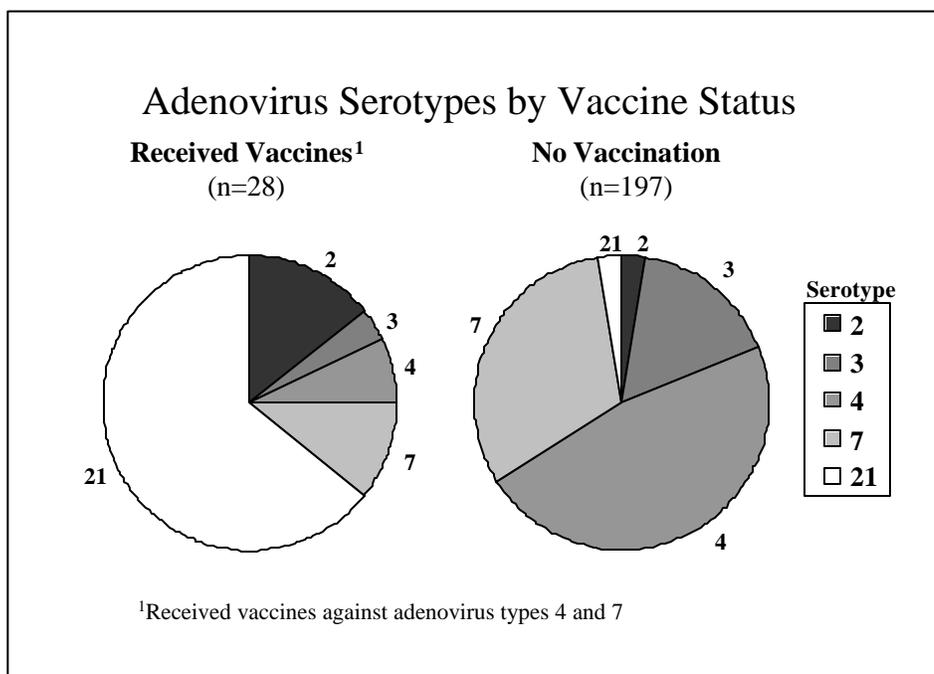


Figure 1

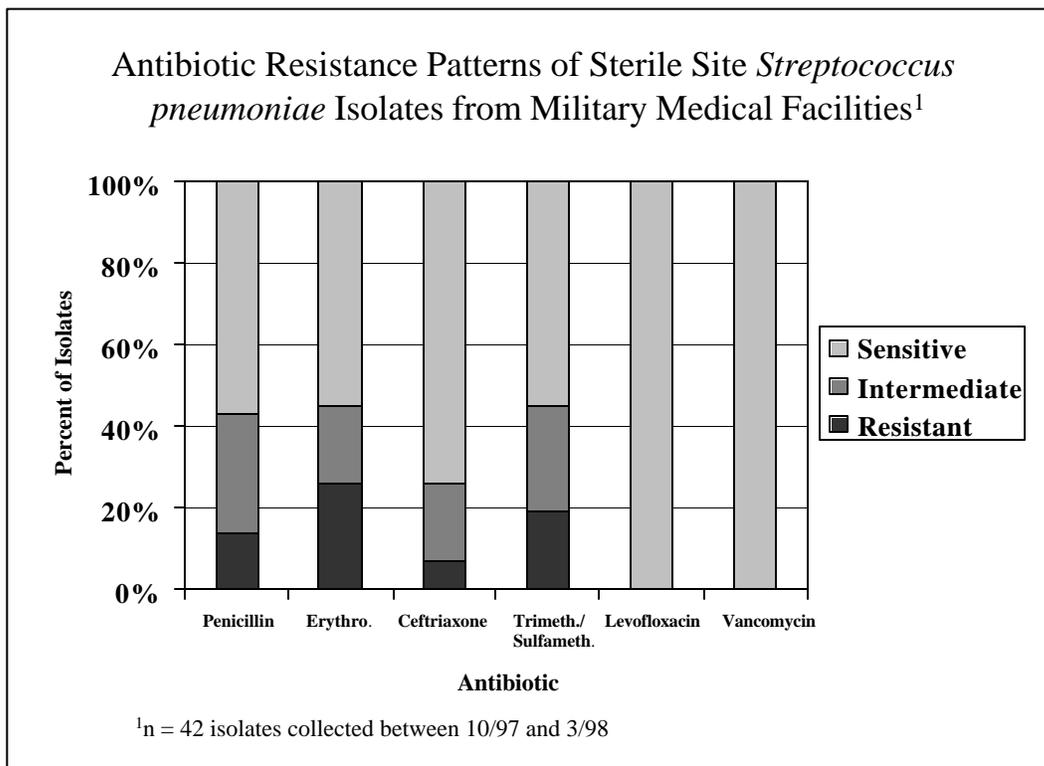


Figure 2

Surveillance Sites for Emerging Illness Studies

