

GAS Surveillance at U.S. Military Basic Training Camps 1998-2006



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**CDR Kevin L. Russell, MC, USN
Mr. Tony Hawksworth
LCDR Dennis Faix
CDR Margaret Ryan**

**Naval Respiratory Disease Laboratory
DoD Center for Deployment Health Research
Naval Health Research Center**

Outline

- History of Group A Streptococcus in Military Populations
- Relevant Instructions
- Current Chemoprophylaxis Regimens at Recruit Training Centers
- Service-Specific Implemented Surveillance Initiatives
- GAS Surveillance Initiatives by the Naval Health Research Center Respiratory Disease Laboratory
 - Antibiotic resistance patterns—geographic and temporal distribution
 - Strain identification—geographic and temporal distribution
 - Associations between strain, antibiotic resistance, and site
- Recent GAS Outbreaks
- Recent Fatalities with Presumed GAS Etiology
- Conclusions

History

- Long recognized as an important pathogen contributing to morbidity within Armed Forces
 - WWII: 1,600 *recognized* cases of streptococcal illness for every 108 cases of malaria¹
- Elegant transmission studies conducted in the 1940s
 - Demonstrated predominance of person-to-person transmission^{1,2}
 - Nasal carriage individuals more infectious than pharyngeal carriage individuals³
 - Carriage common; contributions of sick call exposures to transmission¹
- Antibiotic era ensued
 - Sulfonamides, then penicillins were tested⁴
 - Near complete control of illness, dramatic reduction in sequelae, and reduced carrier state (pens) demonstrated⁴
- **HOWEVER**, treatment regimens still often proved ineffective because:
 - Spread from asymptomatic individuals or carriers
 - Avoidance of medical care; not presenting for treatment
- Mass chemoprophylaxis became widespread at Recruit Training Centers by the 1950s.

¹Coburn AFY, Donald C. *The Epidemiology of Hemolytic Streptococcus During World War II in the United States*. Baltimore, MD: Waverly Press Inc; 1949.

²Wannamaker LW. The epidemiology of streptococcal infections. In: McCarty M, ed. *Streptococcal Infections*. New York, NY: Columbia University Press; 1954.

³Hamburger M Jr, Lemon HM. The problem of the dangerous carrier of hemolytic streptococci. III. The chemotherapeutic control of nasal carriers. *JAMA*. 1946;130:836.

⁴Various: Denny FW, Wannamaker LW, Seal JR, Bernstein SH and others. 1951-1954.

History

- Thomas and colleagues recommended streptococcal surveillance programs continue¹
 - data generated should “influence prophylaxis decisions”
 - 1.2 M units of benzathine penicillin G IM regimen adopted
- Subsequent Decades demonstrated:
 - Mass prophylaxis was effective in decreasing infections and sequelae
 - When mass efforts stop, recurrences often occur
 - Individuals allergic to penicillin should receive alternate chemoprophylaxis²
 - History repeating itself
 - NTC San Diego; mass prophylaxis until 1980, discontinued; 1986-1987, 10 cases of ARF, 3 cases carditis, 6 cases GAS pneumonia³
 - Army: low incidence of ARF, discontinued mass prophylaxis in 1970s; 1980s, GAS-related illnesses identified: ARF, carditis, carriage >70%⁴
 - Gunzenhauser demonstrated that with institution of BPG prophylaxis, ARDs fell 64%...not all explainable by GAS. Suggesting effective against pathogens other than GAS⁴
 - IMPORTANT PARAGIGM SHIFT: BPG indicated to decrease rates of GAS pharyngitis, despite rarity of sequelae

¹Thomas RJ, Conwill DE, et al. Penicillin prophylaxis for streptococcal infections in the United States Navy and Marine Corps recruit camps, 1951-1985. *Rev Infect Dis.* 1988;10(1):125-130.

²Gray GC et al. Hyperendemic *Streptococcus pyogenes* infection despite prophylaxis with penicillin G benzathine. *N Engl J Med.* 1991;325(2):92-97.

³Wallace et al. The return of acute rheumatic fever in young adults. *JAMA.* 1989;262(18):2557-2561.

⁴Gunzenhauser JD et al. Broad and persistent effects of benzathine penicillin G in the prevention of febrile, acute respiratory disease. *J Infect Dis.* 1992;166(2):365-373.

History

– History repeating itself (CONT)

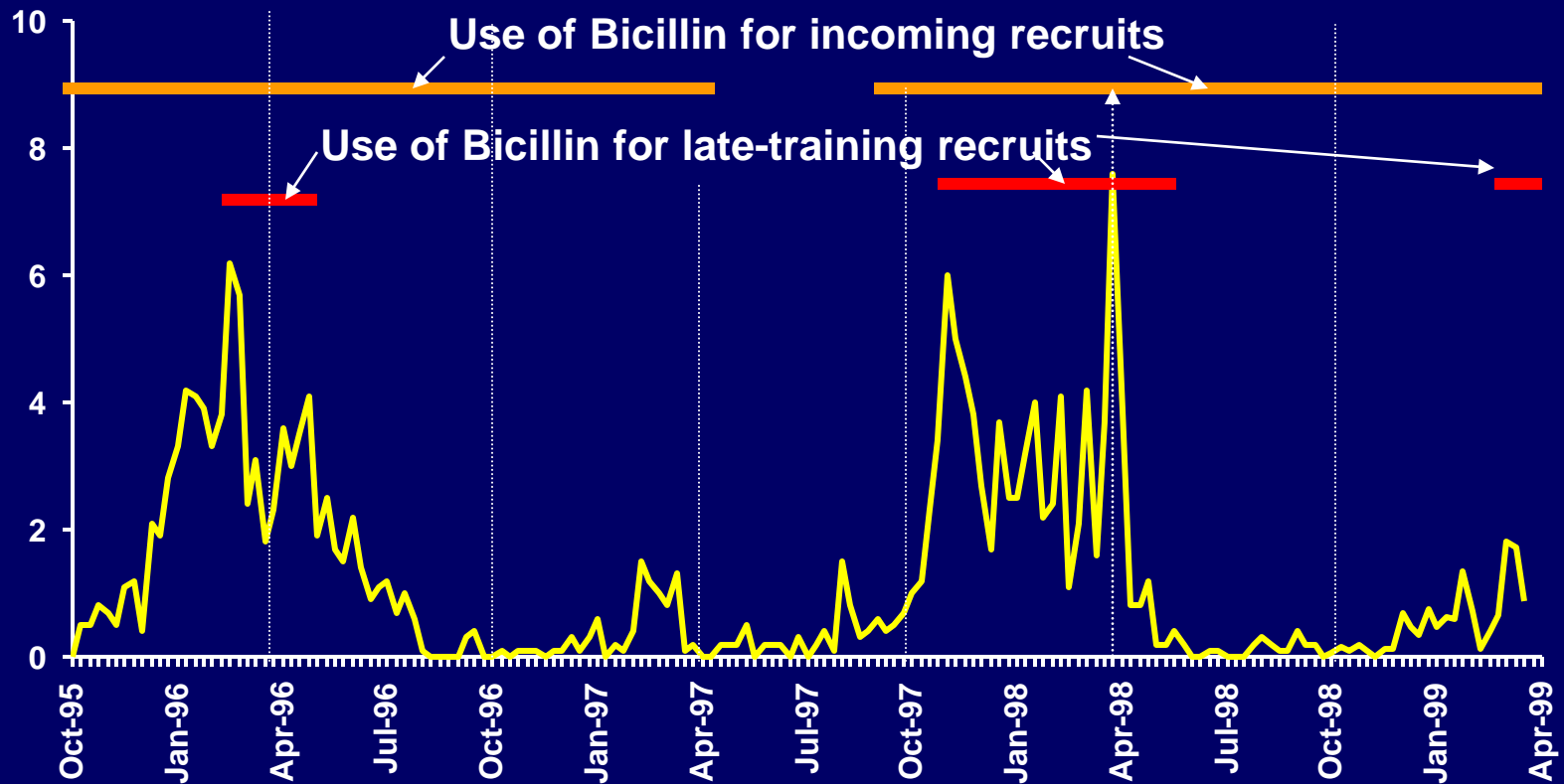
- Despite year-round and 2X per training prophylaxis, 2002 outbreak of 127 GAS pneumonias in Marine recruits in San Diego¹
 - 30% reported as “Pen allergic”; less than 20% compliance with Erythromycin alternate chemoprophylaxis
 - Illnesses began at around day 20-21 post BPG injection
- Erythromycin demonstrated effective in 2X daily dose of 250 mg²
- Azithromycin is also highly efficacious with potentially better compliance³

¹Crum NF, Russell KL, Kaplan EL et al. Pneumonia outbreak associated with group A streptococcus species at a military training facility. *Clin Infect Dis.* 2005;40(4):511-518.

²Fujikawa J et al. Oral erythromycin prophylaxis against *Streptococcus pyogenes* infection in penicillin-allergic military recruits: A randomized clinical trial. *J Infect Dis.* 1992;166(1):162-165.

³Gray GC et al. Weekly oral azithromycin as prophylaxis for agents causing acute respiratory disease. *Clin Infect Dis.* 1998;26(1):103-110.

Streptococcal Pharyngitis Rates in Navy Recruits (cases/1000 recruits/week)



Relevant Correspondences and Instructions

1. AFEB Memorandum of 19 Sept 1983

- ✓ Selective Streptococcal monitoring programs should be continued in the Navy and Marine Corps recruit facilities
- ✓ Tailored chemoprophylaxis
- ✓ Two areas should be studied:
 - ✓ Desirability of a second dose of bicillin four weeks after the first
 - ✓ Occurrence of streptococcal skin infections, particularly in the summer, as justification for bicillin prophylaxis

2. Army regulation 40-562/BUMEDINST 6230.15/Air Force Instruction 48-110(I)/CG COMDTINST M6230.4F: “Immunizations and Chemoprophylaxis”. Date: 20 Jan 1995, currently updated version at press.

- ✓ “it may be required to administer penicillin prophylactically to the entire group to terminate disease transmission”
- ✓ “Consider penicillin G benzathine (IM, also known as *Bicillin LA*)”
- ✓ “Customized approach.each Service will develop policies for surveillance and prophylaxis of streptococcal disease at training centers.”

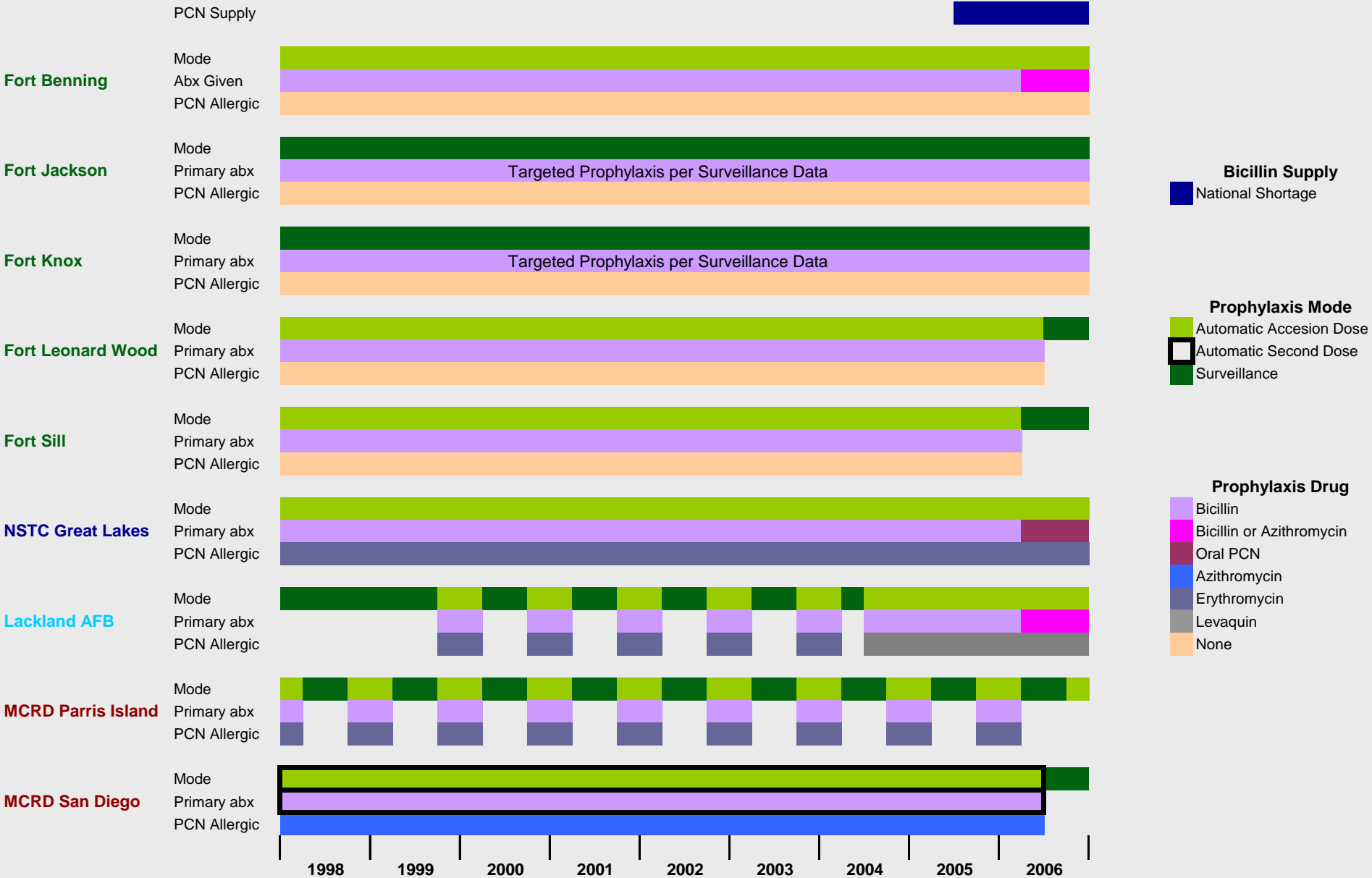
Relevant Correspondences and Instructions

3. BUMED Instruction 6220.8 (dated 3/16/91); Under BUMED review for revision

- Current guidance: Culture everyone with sore throat
 - Sites find this burdensome, and rarely comply
- Action point for decisions on antibiotic prophylaxis based on surveillance at 10 cases per 1,000 recruits per week.

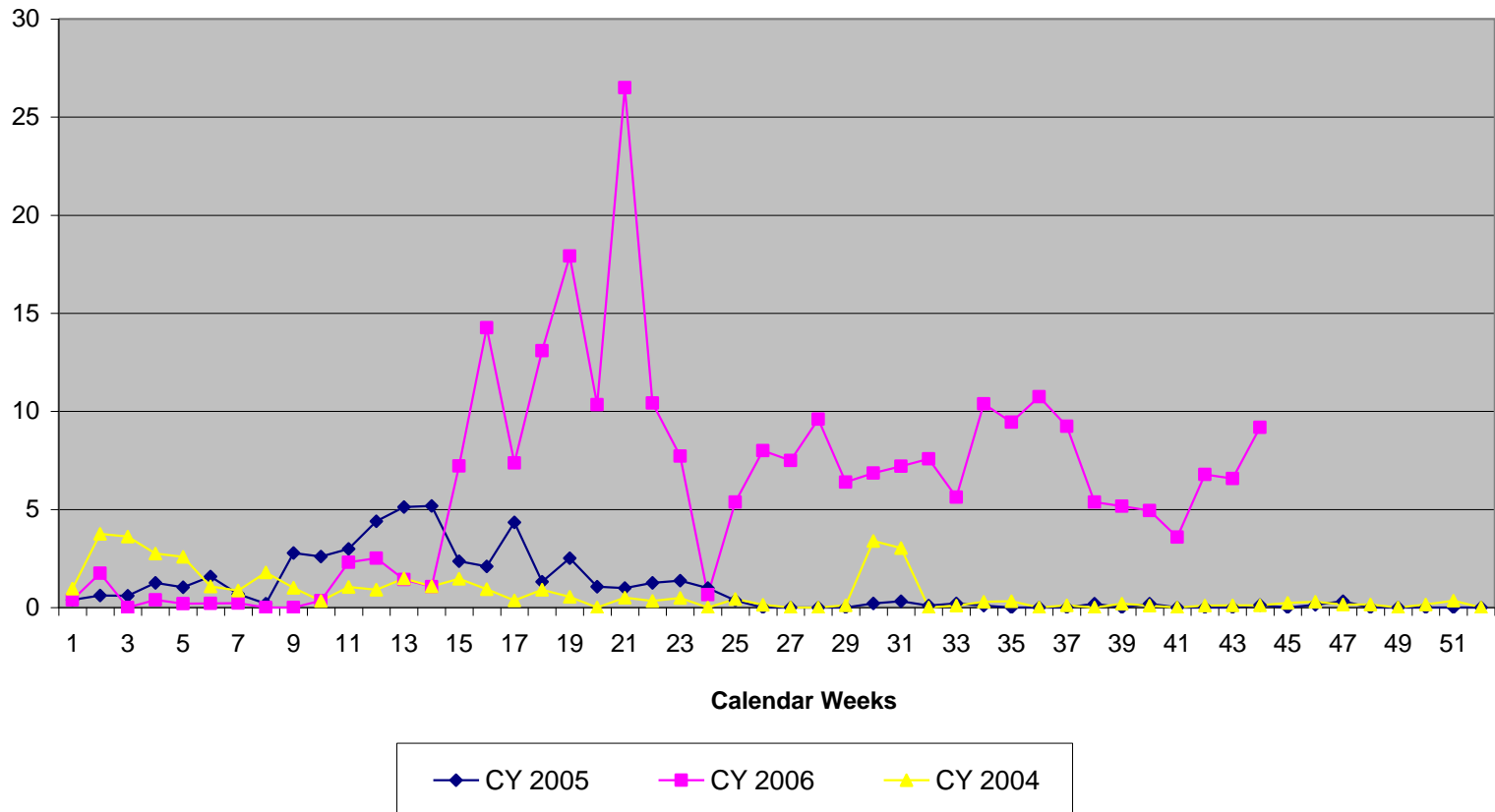
- **Suggested Revisions:**
 - Treat Navy and Marines differently, as “Marine Corps and Navy recruit training is significantly different”
 - Marines, calculate GABHS incidence rates by company, and administer only to those that meet criteria
 - At RTC, record rates for 2 groups: all recruits, and after the 4th week “second half recruits”
 - Follow a “validated clinical prediction scoring system” for culture and treatment, including following morphology—4 criteria
 - Fever >100.4
 - Absence of cough
 - Tender anterior cervical lymphadenopathy
 - Tonsillar swelling or exudates
 - Graded 1-4 pts.
 - 0-1 pts: tested and treated at investigator discretion
 - 2-3 pts: Rapid test recommended; also culture for monitoring of culture morphology
 - 4 pts: Cultured and empirically treated

GAS Prophylaxis Strategies at Recruit Training Sites



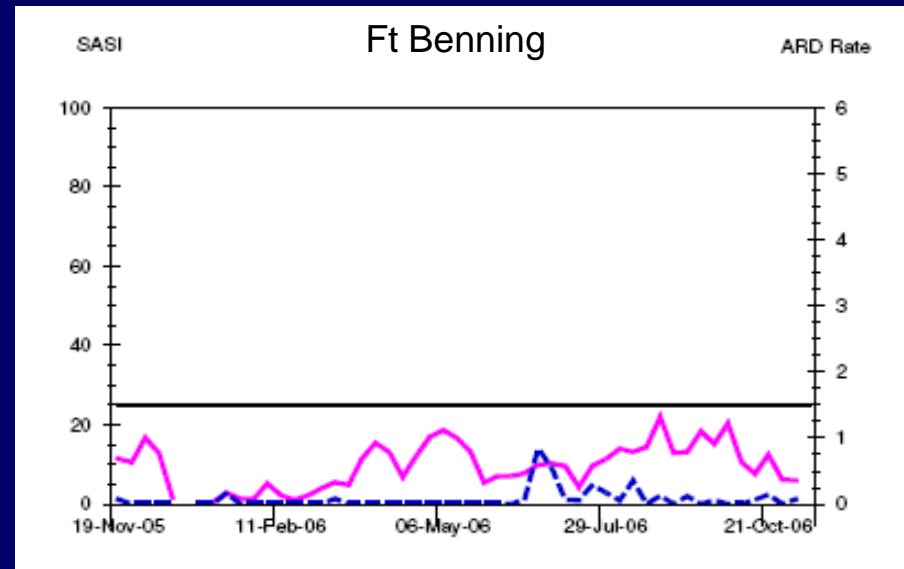
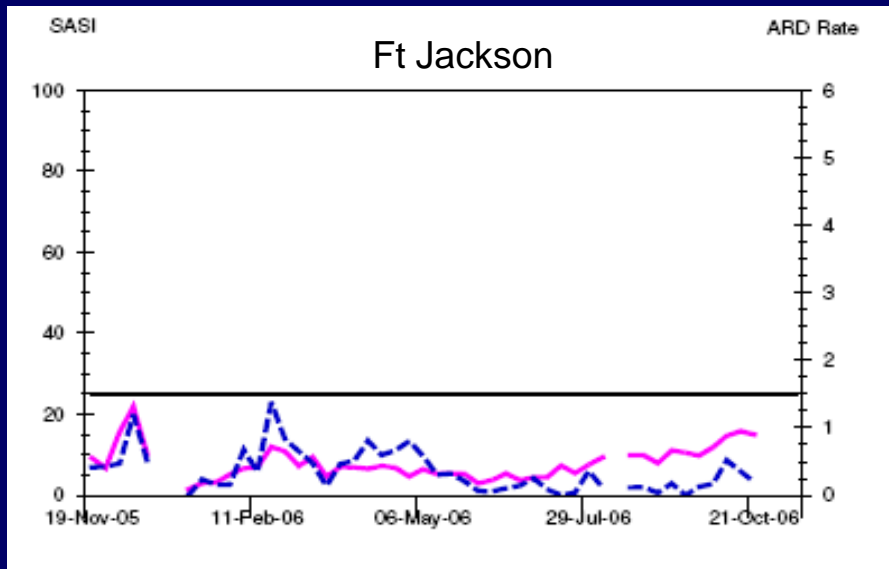
NSTC Great Lakes Data

Strep Pharyngitis per 1,000 Recruits



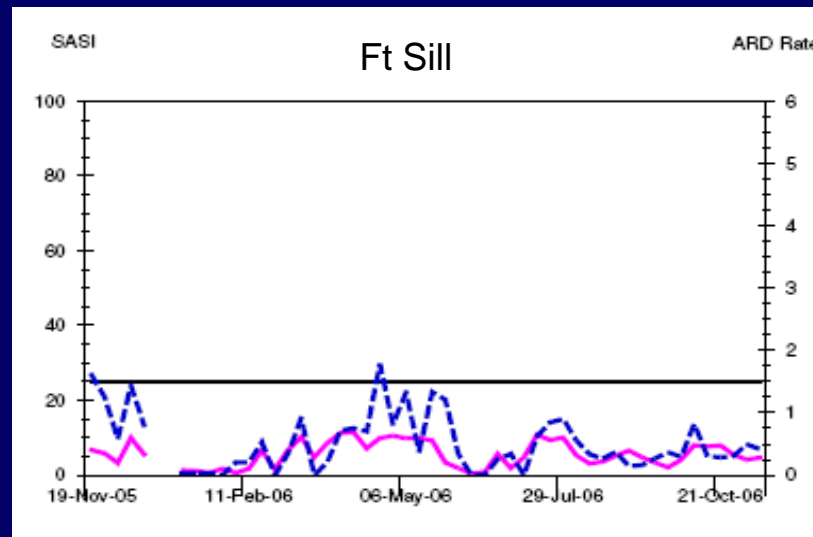
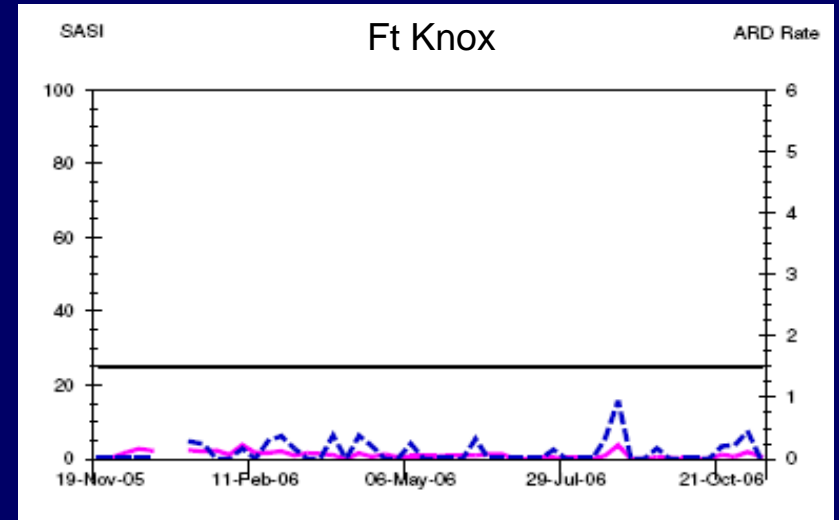
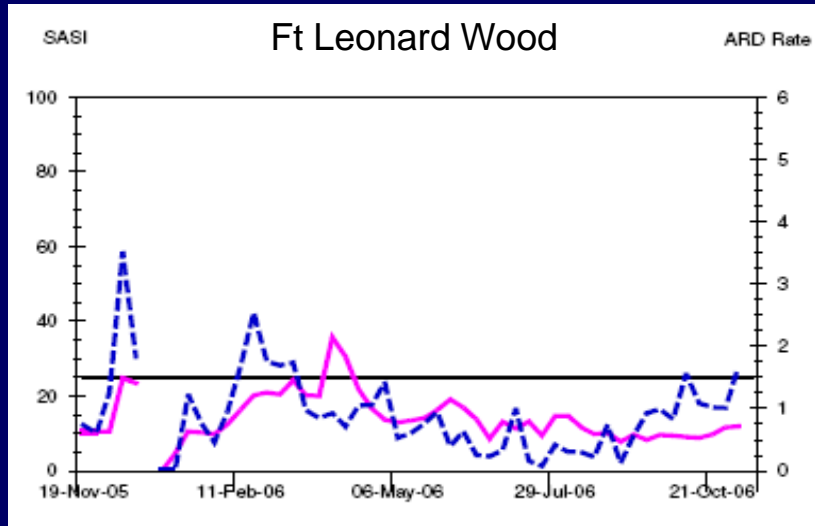
NSTC Great Lakes

Army Data



SASI --- ARD ---

Army Data (cont.)



SASI --- ARD ---

NHRC GAS Surveillance at U.S. Military Basic Training Camps

- NHRC instituted surveillance for GAS in 1998
- A systematic sample of GAS-positive clinical isolates are collected from laboratories at 9 military training sites
- Over 2,000 isolates collected to date
 - Antibiotic sensitivity testing is performed on all isolates
 - emm gene typing is performed on a subset of isolates
 - Implementation of Advanced Diagnostic Methodology helping with throughput
- NHRC also offers support for outbreak response and fatal case investigations

NHRC Respiratory Disease Surveillance Sites



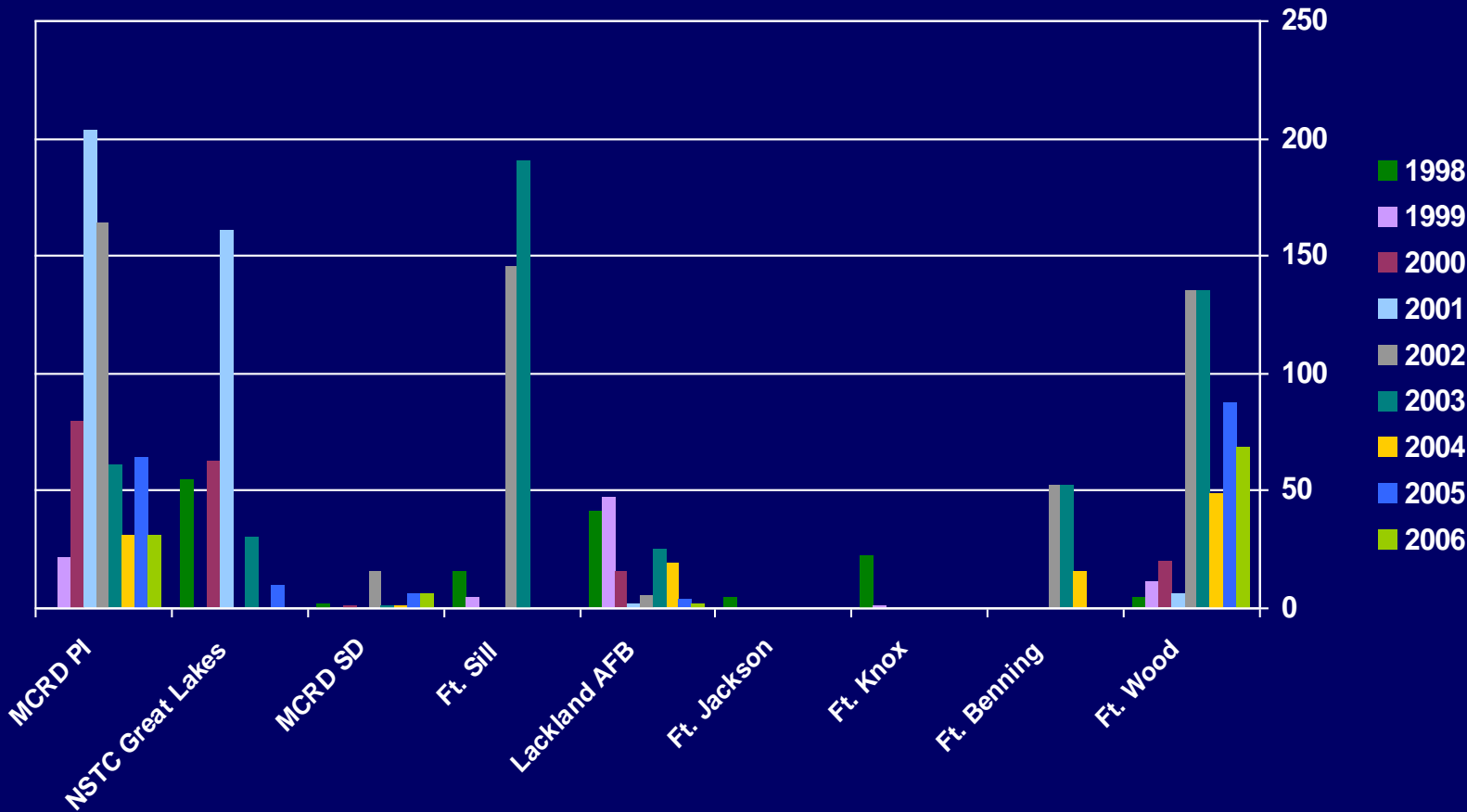
- ★ Viral pathogens
- *S. pyogenes*
- ▲ *S. pneumoniae*
- ★ Pneumo vaccine
- ★ Pertussis
- ☀ RSV

NHRC GAS Surveillance at U.S. Military Basic Training Camps

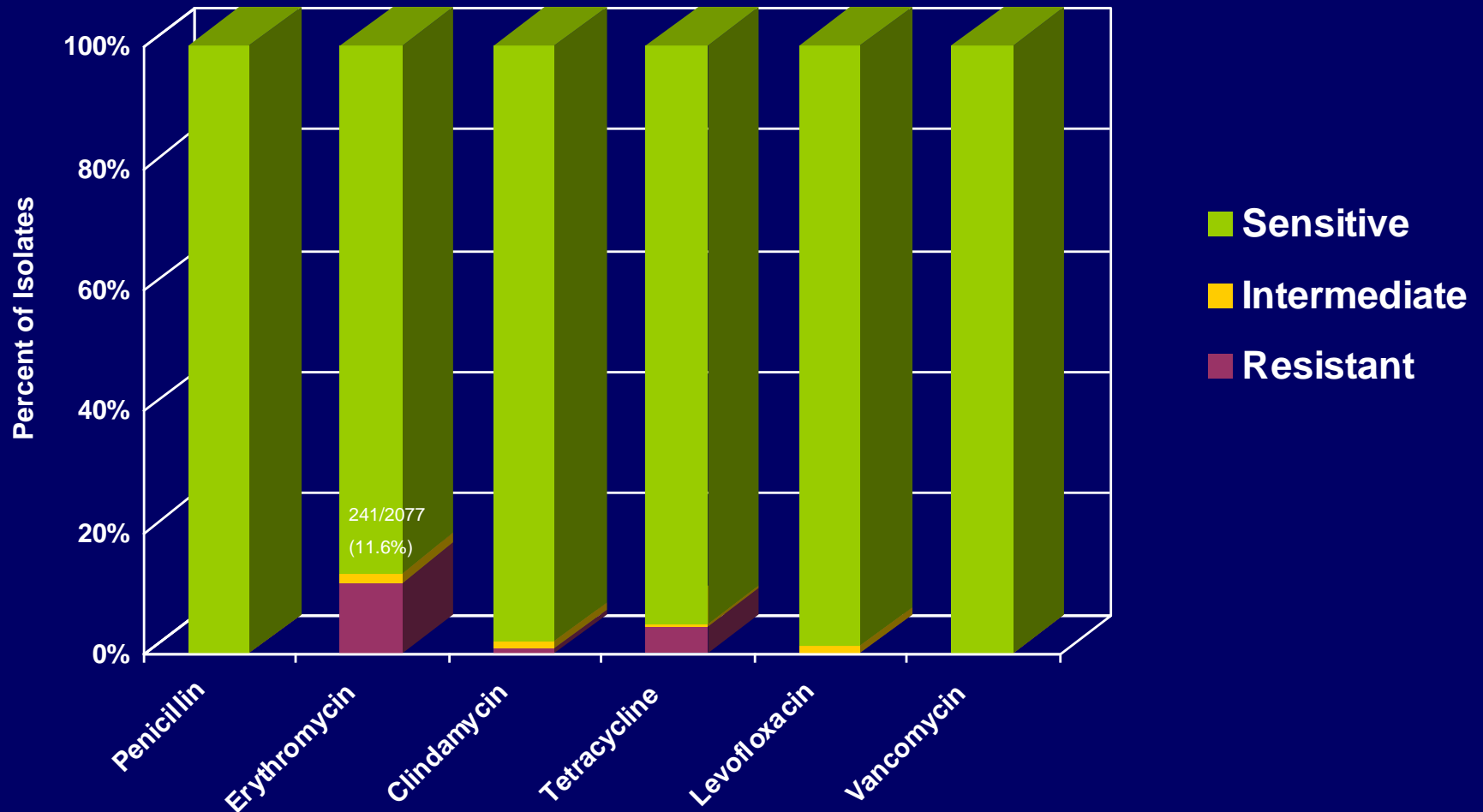
- Barrozo CP, Russell KL, Smith TC, Hawksworth AW, Ryan MA, Gray GC. National Department of Defense surveillance data for antibiotic resistance and emm gene types of clinical group A streptococcal isolates from eight basic training military sites. *J Clin Microbiol.* 2003 Oct;41(10):4808-11.
 - 1998-2001: analysis of 692 isolates:
 - 44/692 (6.4%) resistant to erythromycin; 34/692 (4.9%) resistant to tetracycline
 - Macrolide resistance was associated with geographic site—Lackland AFB
 - Erythromycin resistance strongly associated with *emm75* isolates ($p < 0.0001$)

GAS Isolates Received From Each Training Site 1998-2006

(n = 2077)

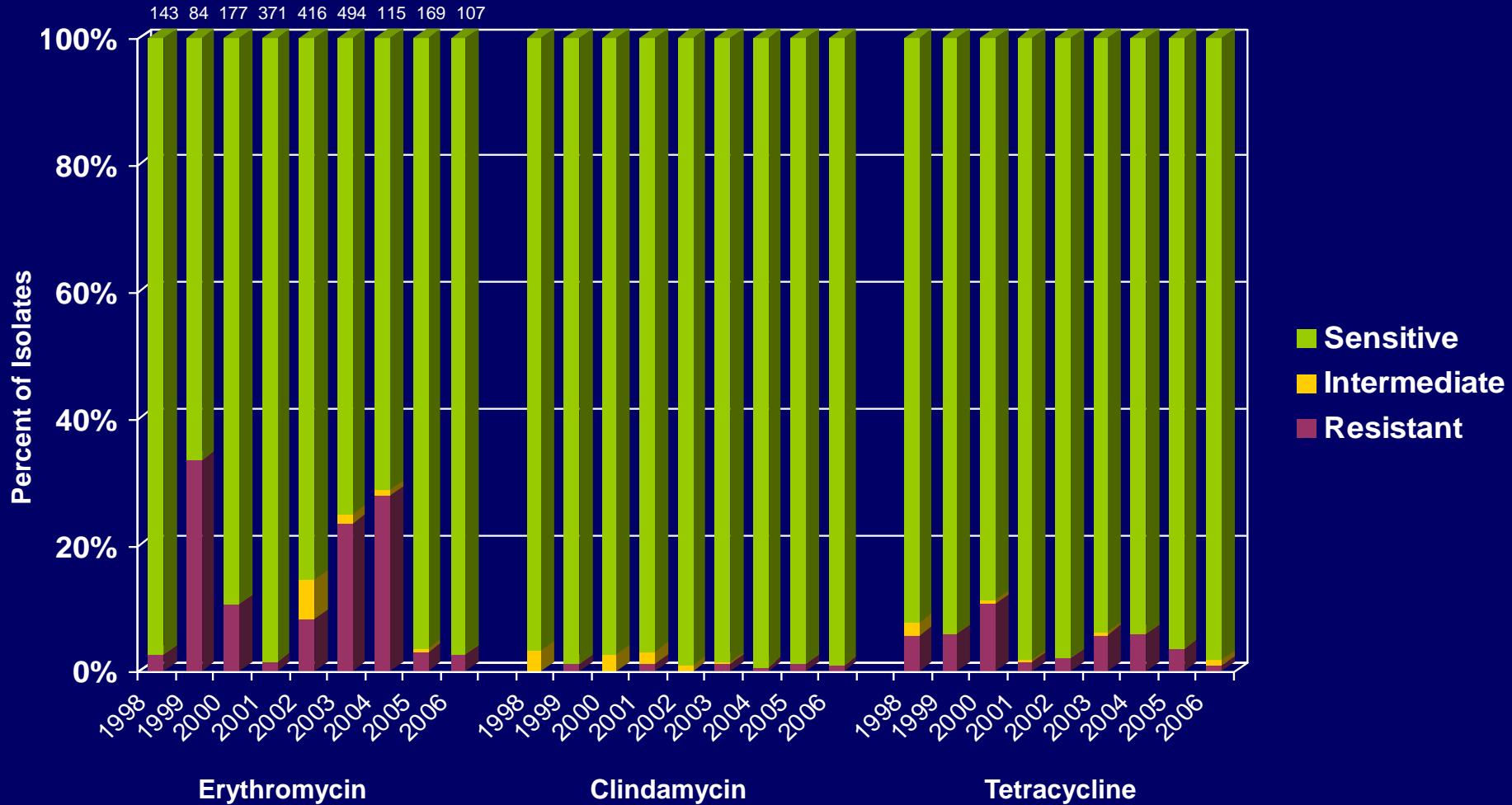


Antibiotic Resistance Patterns of Clinical *Streptococcus pyogenes* Isolates from Military Trainees



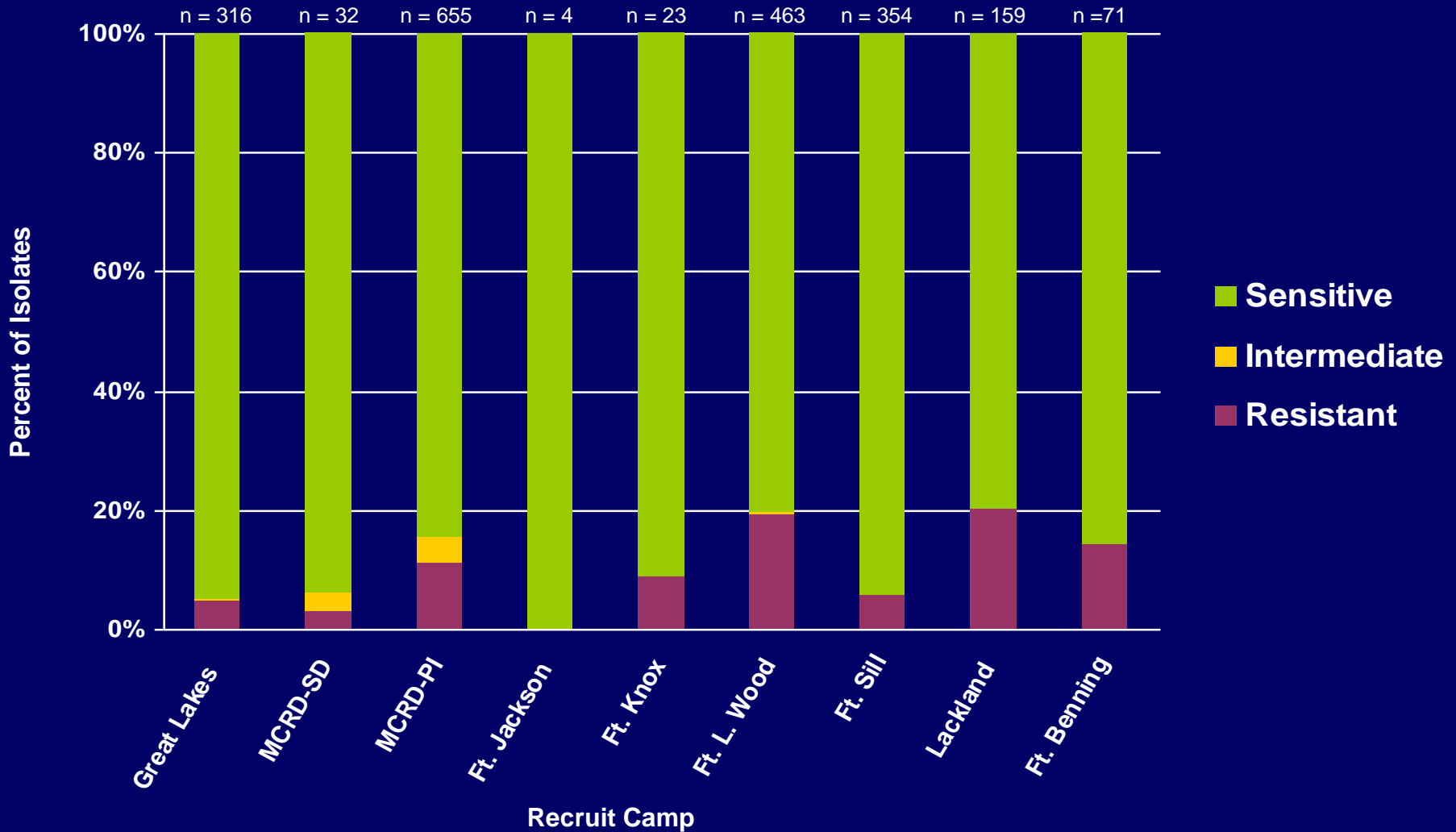
n=2077 isolates collected between Feb 1998 and Nov 2006

Antibiotic Resistance Patterns of Clinical *Streptococcus pyogenes* Isolates Over Time



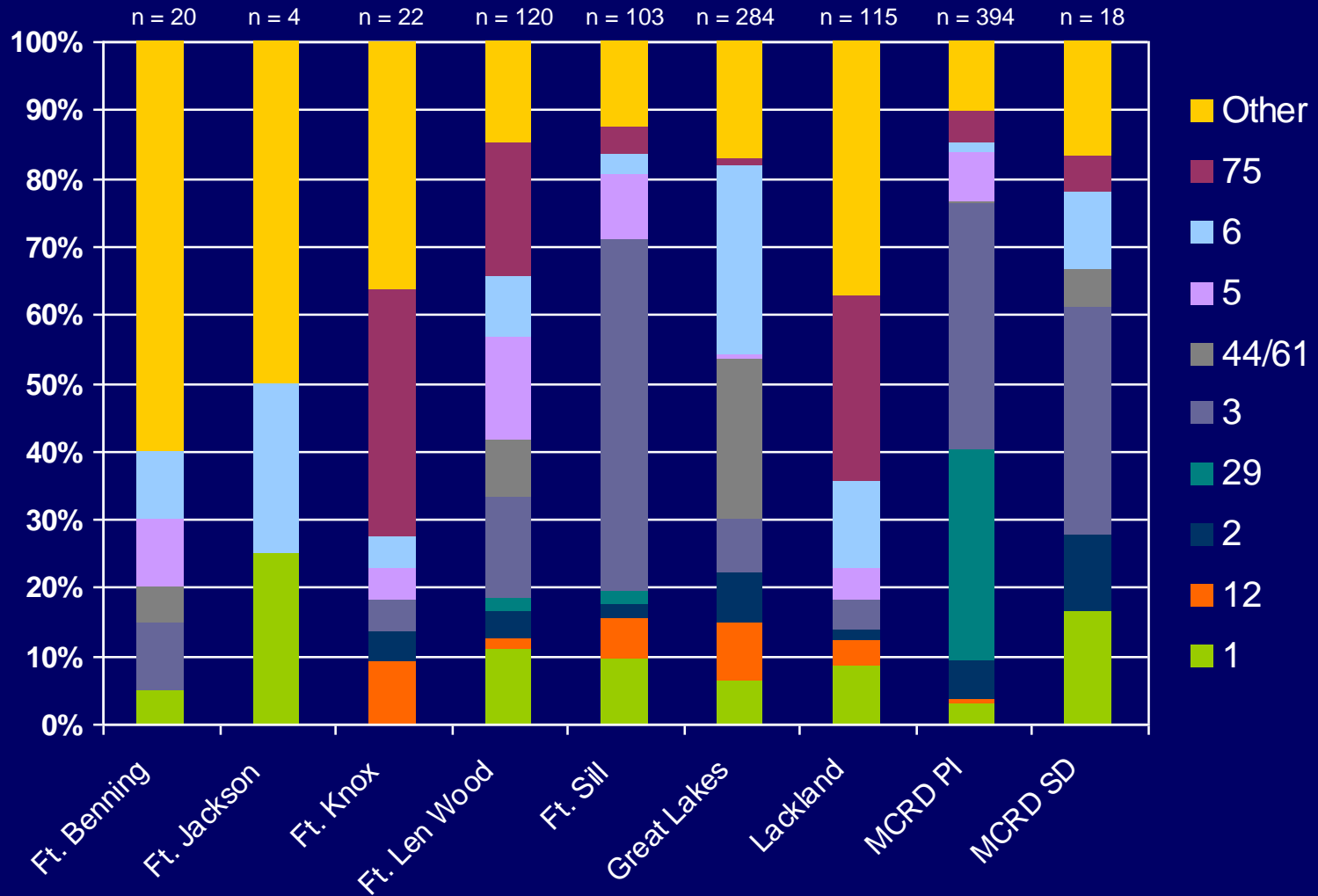
n=2077 isolates collected between Feb 1998 and Nov 2006

Erythromycin Resistance Patterns of *Streptococcus pyogenes* Isolates by Recruit Camp Location

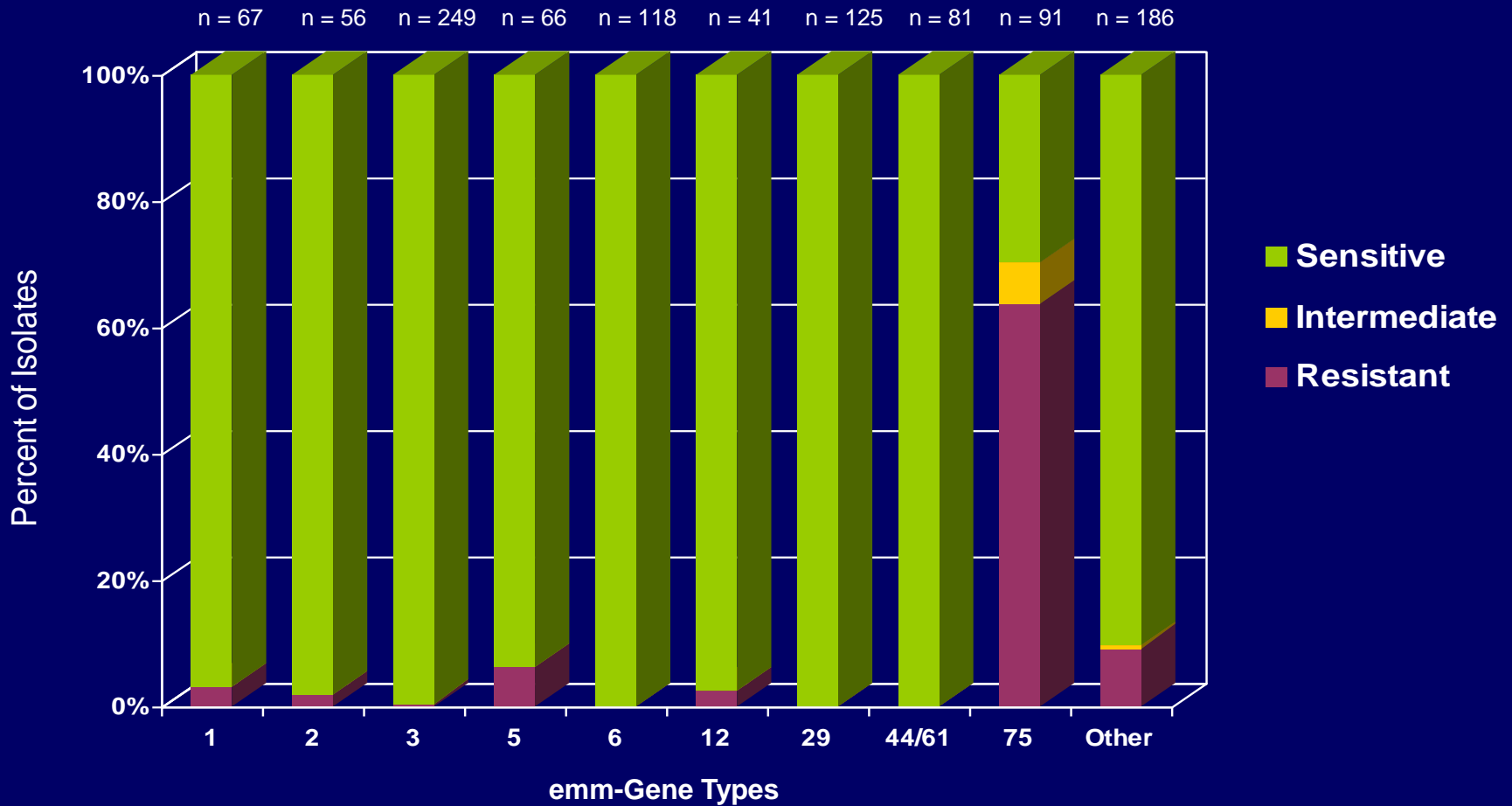


n=2077 isolates collected between Feb 1998 and Nov 2006

Emm Type Distribution of GAS Isolates Received by Site 1998-2005



Erythromycin Resistance of *Streptococcus pyogenes* by emm-gene Type



n=1080 emm-gene typed isolates collected between 2/98 and 12/05

Recent GAS Outbreaks

MCRD Parris Island: November 2006

- Five recruits with retropharyngeal abscesses
- Reported + GAS in two of these cases
 - One GAS isolate obtained by NHRC, emm Type 118

Fort Leonard Wood: October 2006

- Short on Bicillin since Summer 2005. No alternative chemoprophylaxis was given until this outbreak.
- Earliest invasive GAS (iGAS) case reported to the Reportable Medical Events System (RMES) on 12 Aug 2006.
- During the week of 2-9 Oct, 12 additional GAS+ cases were reported – Bicillin given
- Starting 28 Oct: All incoming recruits are given oral Pen VK
- 04 Nov: Began giving Bicillin to all current trainees on post
- Testing at NHRC revealed **emm Type 5** as most common type. Types 18, 77, and 101 also seen

Fort Knox: August 2006

- Sentinel event: 16 Aug 06, recruit admitted to Ireland Army Hospital (IRACH) for peritonsillar abscess
- Entire unit of index case cultured for GAS: 34% were found to be carriers of GAS
- Two additional GAS+ patients from different units as index case hospitalized during the week of 21 Aug
- Summary of intervention: targeted prophylaxis (Bicillin or Zithromax)
- Testing at NHRC revealed **emm Type 5** as most common type. Type 4 also seen

Fort Jackson:

- November 2005
- Testing at NHRC revealed **emm Type 5** as most common type

Fort Leonard Wood:

- October 2005 – February 2006
- Testing at NHRC revealed **emm Type 5** as most common type

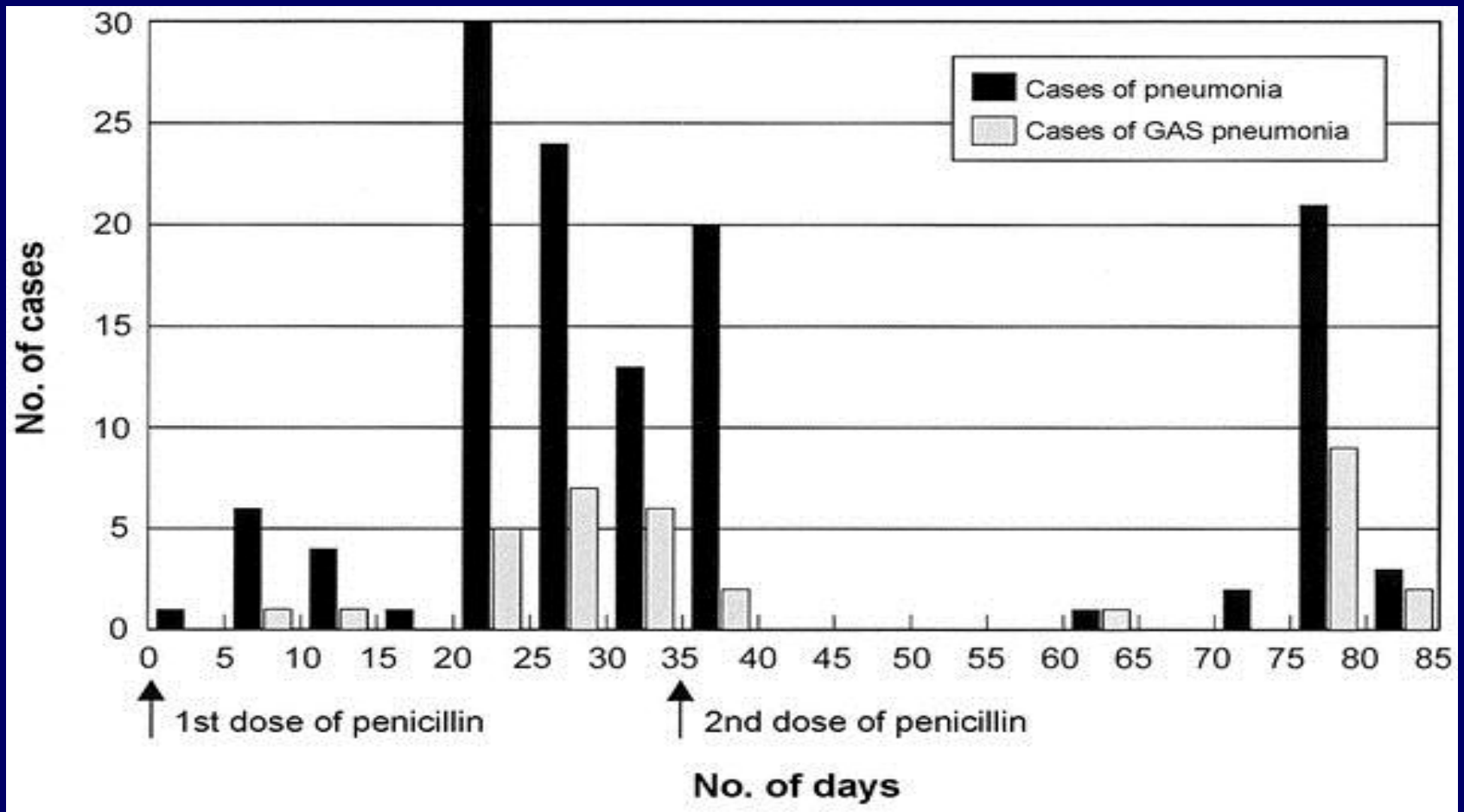
MCRD Parris Island:

- September - November 2005
- Testing at NHRC revealed **emm Type 5** as most common type

Recent GAS Outbreaks (Cont)

MCRD-SD, 2002

127 pneumonias, 44% with evidence of GAS



Recent GAS Fatal Cases

Camp Pendleton, CA:

- October 2006
- 1 death
- Testing at NHRC found *S. pyogenes* emm Type 77

Texas:

- March 2006
- 2 deaths
- Testing at NHRC found *S. pyogenes* emm **Type 5** in both cases

Advanced Diagnostics



- Currently certified T-5000 in our new “Advanced Diagnostics Laboratory”, providing high-throughput diagnostic support for:
 - Respiratory Panel
 - Adenovirus
 - Influenza (publication pending)
 - *****Streptococcus pyogenes* (PNAS, 2005 May 31;102(22):8012-7)**



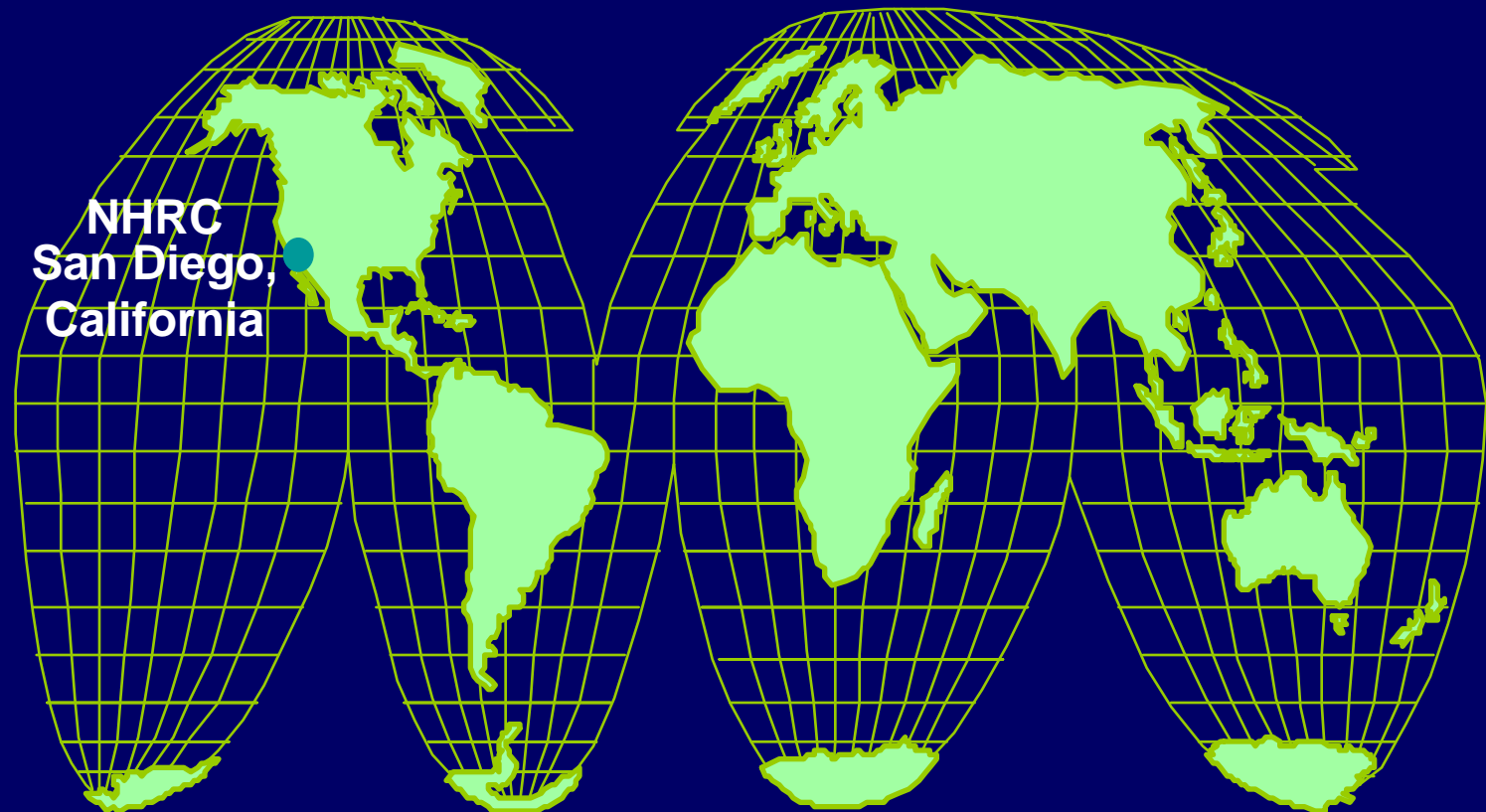
Conclusions

- Recent increase in GAS morbidity among trainees
 - at least partly due to shortage of bicillin and subsequent lack of prophylaxis
- Overall Macrolide (erythromycin) resistance of 11.6% (240/2077)
- High macrolide resistance seen in emm Type 75
 - decreasing prevalence of emm 75 in recent years
- No temporal or geographical trends in resistance
- Increasing prevalence of emm Type 5 associated with outbreaks, 2005-2006
 - associated with most recent outbreaks
 - remains largely sensitive to antibiotics
- NHRC passive surveillance of clinical GAS among trainees provides valuable data

**QUESTIONS?
COMMENTS?
SUGGESTIONS?**



**Navy Node for the DoD
Global Emerging Infections Surveillance and Response Systems
(GEIS)**

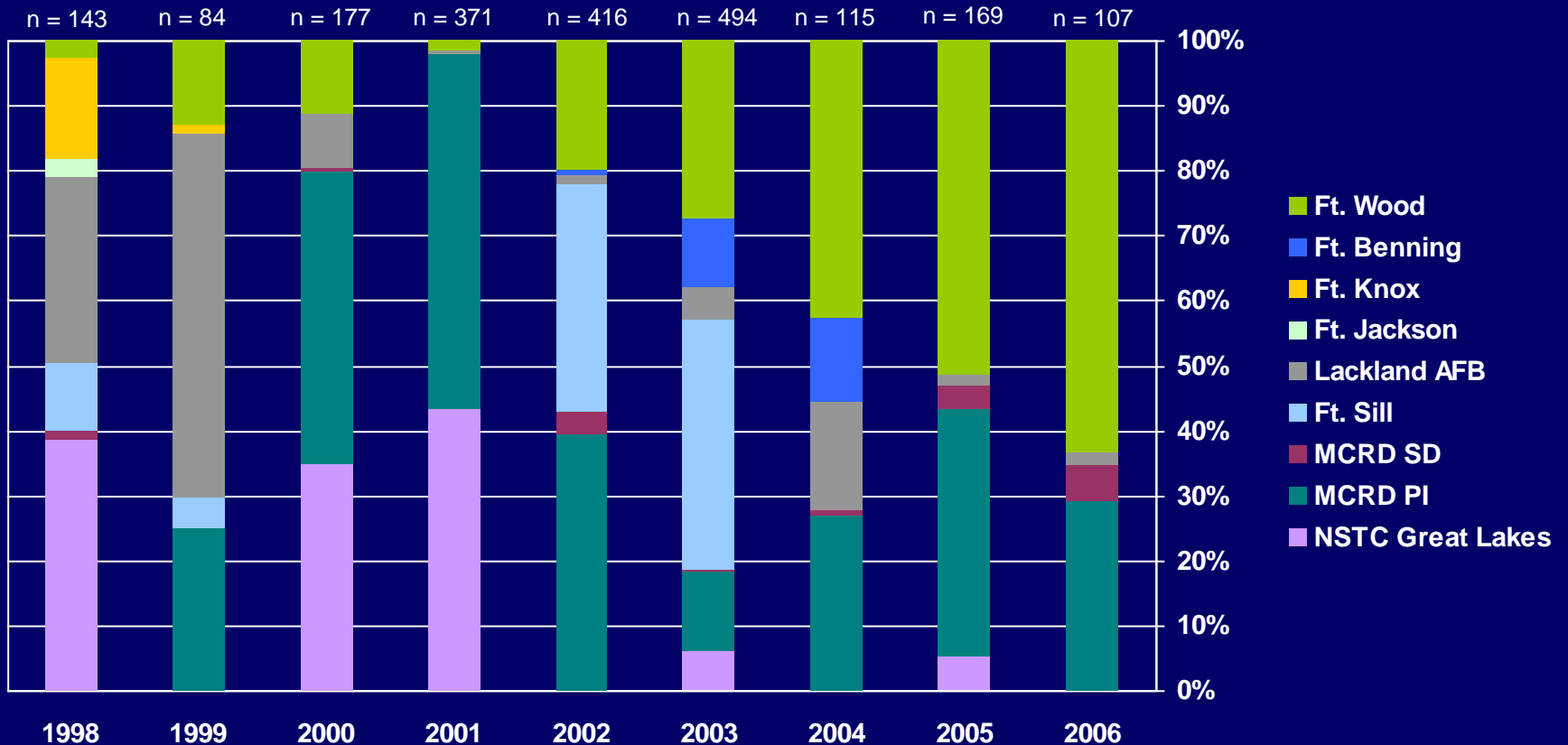


Naval Health Research Center Web Site
<http://www.nhrc.navy.mil/>

Back-Pocket Slides

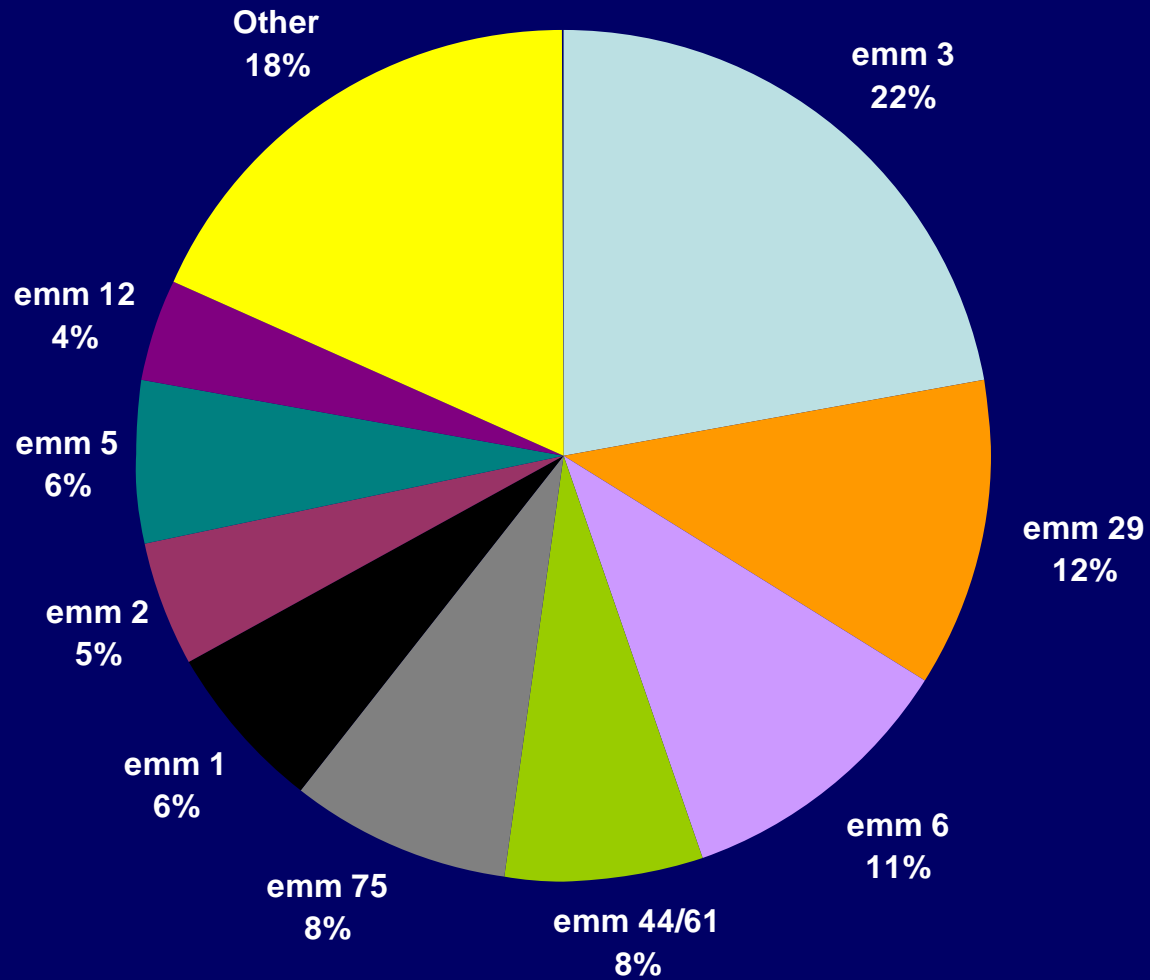
Proportion of GAS Isolates Received From Each Training Site, 1998-2006

(n = 2077)



Distribution of emm types among isolates collected from 1998-2005

(n = 1080)



Emm Type Distribution of GAS Isolates Received by Year 1998-2005

