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

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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 malaria

• Elegant transmission studies conducted in the 1940s
  – Demonstrated predominance of person-to-person transmission
  – Nasal carriage individuals more infectious than pharyngeal carriage individuals
  – Carriage common; contributions of sick call exposures to transmission

• Antibiotic era ensued
  – Sulfonamides, then penicillins were tested
  – Near complete control of illness, dramatic reduction in sequelae, and reduced carrier state (pens) demonstrated

• 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.

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History

• Thomas and colleagues recommended streptococcal surveillance programs continue\(^1\)
  – 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 chemoprophylaxis\(^2\)
  – History repeating itself
    • NTC San Diego; mass prophylaxis until 1980, discontinued; 1986-1987, 10 cases of ARF, 3 cases carditis, 6 cases GAS pneumonia\(^3\)
    • 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 GAS\(^4\)
  – IMPORTANT PARAGIGM SHIFT: BPG indicated to decrease rates of GAS pharyngitis, despite rarity of sequelae

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– History repeating itself (CONT)

• Despite year-round and 2X per training prophylaxis, 2002 outbreak of 127 GAS pneumonias in Marine recruits in San Diego
  – 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 mg

• Azithromycin is also highly efficacious with potentially better compliance

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

Use of Bicillin for incoming recruits

Use of Bicillin for late-training recruits
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


- “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.”
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

PCN Supply

Mode
Abx Given
PCN Allergic

Fort Benning
Mode
Primary abx
PCN Allergic
Targeted Prophylaxis per Surveillance Data

Fort Jackson
Mode
Primary abx
PCN Allergic
Targeted Prophylaxis per Surveillance Data

Fort Knox
Mode
Primary abx
PCN Allergic

Fort Leonard Wood
Mode
Primary abx
PCN Allergic

Fort Sill
Mode
Primary abx
PCN Allergic

NSTC Great Lakes
Mode
Primary abx
PCN Allergic

Lackland AFB
Mode
Primary abx
PCN Allergic

MCRD Parris Island
Mode
Primary abx
PCN Allergic

MCRD San Diego
Mode
Primary abx
PCN Allergic

Prophylaxis Mode
- Automatic Accesion Dose
- Automatic Second Dose
- Surveilance

Prophylaxis Drug
- Bicillin
- Bicillin or Azithromycin
- Oral PCN
- Azithromycin
- Erythromycin
- Levaquin
- None

Prophylaxis Year
NSTC Great Lakes Data

Strep Pharyngitis per 1,000 Recruits

Calendar Weeks

Data retrieved from NHCGGL Weekly Recruit & Student Health Surveillance Report – Nov 10 2006
Army Data

Data retrieved from USACHPPM Acute Respiratory Disease Surveillance System Weekly Summary Report – Nov 2006
Army Data (cont.)

Data retrieved from USACHPPM Acute Respiratory Disease Surveillance System Weekly Summary Report – Nov 2006
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

- Madigan Army MC
- NMC San Diego
- Wilford Hall
- Great Lakes
- Portsmouth
- Bethesda
- MCRD Parris Island
- Ft Sill
- Ft Knox
- Ft Leonard Wood
- Ft Jackson
- Ft Benning
- Cape May

Pathogens:
- **Viral pathogens**
- **S. pyogenes**
- **S. pneumoniae**
- **Pneumo vaccine**
- **Pertussis**
- **RSV**

- 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 *emm*75 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

Recruit Camp

- Great Lakes: n = 316
- MCRD-SD: n = 32
- MCRD-PI: n = 655
- Ft. Jackson: n = 4
- Ft. Knox: n = 23
- Ft. L. Wood: n = 463
- Ft. Sill: n = 354
- Lackland: n = 159
- Ft. Benning: n = 71

n=2077 isolates collected between Feb 1998 and Nov 2006
Emm Type Distribution of GAS Isolates Received by Site 1998-2005

- Ft. Benning: n = 20
- Ft. Jackson: n = 4
- Ft. Knox: n = 22
- Ft. Len Wood: n = 120
- Ft. Sill: n = 103
- Great Lakes: n = 284
- Lackland: n = 115
- MCRD P: n = 394
- MCRD SD: n = 18

Legend:
- Other
- 75
- 6
- 5
- 44/61
- 3
- 29
- 2
- 12
- 1
GAS Isolates MCRD-PI
with Antibiotic Sensitivities
GAS Isolates LAFB
with Antibiotic Sensitivities
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
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)