

# Community Acquired Bacterial Meningitis

**Alan Taege, M.D.**  
Director HIV Care  
Infectious Disease  
Medicine

07 1130

## Meningitis Syndromes: Definitions

### Acute Meningitis

- Onset of meningeal symptoms over hours to several days

### Chronic Meningitis

- Onset over weeks to months, abnormal CSF for at least 4 weeks

### Encephalitis

- Decreased mentation early in the clinical course with minimal meningeal signs



## Question

*Which of the following is true regarding the EPIDEMIOLOGY of bacterial meningitis?*

- a. occurs mainly in infants and young children
- b. The majority of patients with pneumococcal bacteremia will go on to develop pneumococcal meningitis
- c. Most persons with meningitis from *N. meningitidis* will have a defect in terminal complement
- d. A and B
- e. All above are false

## Question

*Which of the following is true regarding the EPIDEMIOLOGY of bacterial meningitis?*

- a. occurs mainly in infants and young children
- b. The majority of patients with pneumococcal bacteremia will go on to develop pneumococcal meningitis
- c. Most persons with meningitis from *N. meningitidis* will have a defect in terminal complement
- d. A and B
-  e. All above are false

## Epidemiology

- Worldwide, 1.2 million cases/year
  - 135,000 deaths/yr
- The age of the patient is a major factor determining the specific bacterial cause
- Frequency of meningitis after invasive disease also varies between organisms
  - **Most cases of invasive infection do NOT lead to meningitis**
  - 4% of invasive pneumococcal infections lead to meningitis
  - 48% of invasive meningococcal infection, 30% of invasive listeriosis, 4% of invasive gp B strep

## Epidemiology Trends

- “PAST”
  - Mainly a disease of infants and children
  - *Streptococcus pneumoniae* and *Haemophilus influenzae* were the major pathogens
- “CURRENT”
  - Major decline in H. influenzae meningitis
  - **Mainly a disease of adults**
    - Average age: 15 months (1986) to 25 years (1995) to 39 years (2003)
  - Emergence of **antibiotic-resistant** *S. pneumoniae*
  - Post-neurosurgical or device infections increasing

## Question

*Which of the following is true regarding the microbiology of the organisms?*

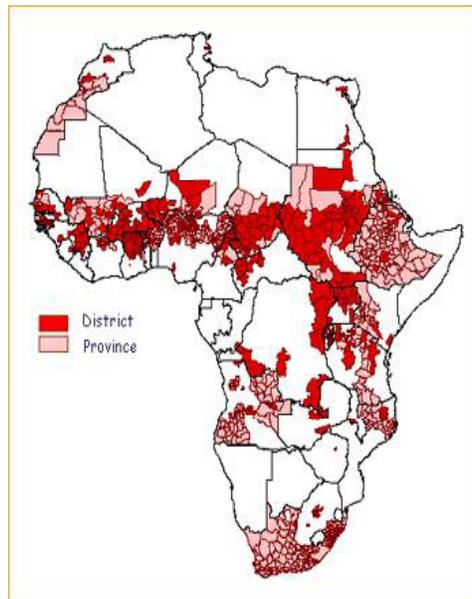
- Meningococcus is the main pathogen that is associated with outbreaks
- Staphylococcus aureus* and *Streptococcus pneumoniae* are the most common pathogens in nosocomial or device related meningitis
- Propionibacterium acnes* is usually considered a contaminant in neurosurgical device infections
- All the above are true

## Question

Which of the following is true regarding the microbiology of the organisms?

- a. Meningococcus is the main pathogen that is associated with outbreaks
- b. *Staphylococcus aureus* and *Streptococcus pneumoniae* are the most common pathogens in nosocomial or device related meningitis
- c. *Propionibacterium acnes* is usually considered a contaminant in neurosurgical device infections
- d. All the above are true

## “Meningitis Belt: Meningococcus”



## Epidemiology: Community Acquired Meningitis

	Age <60 years	Age > 60 years
<b><i>S. pneumoniae</i></b>	<b>60%</b>	<b>70%</b>
<i>N. meningitidis</i>	20%	3%
<i>H. Influenzae</i>	10%	3-4%
<i>Listeria monocytogenes</i>	6%	20%
Group B strep	4%	4%

## Questions to Ask

- Recent exposure to someone with meningitis?
  - Suggests meningococcus
- Recent infection?
  - Sinusitis, pneumonia or other respiratory infection
- Recent travel?
  - International travel, sub-Saharan Africa
- Injection drug use?
- Recent head or facial trauma (MVA)?
  - Pneumococcus
- Otorrhea or rhinorrhea?

HOST PROBLEM	ORGANISM	Frequency of DEFECT leading to meningitis
Opsonization	S. Pneumoniae H. Flu	Common all age groups, and young children
Asplenia, hypogammaglob	S. Pneumoniae N. Meningitidis	Rare Very rare
Complement	N. Meningitidis	Very rare
Corticosteroids	L. Monocytogenes Cryptococcus	Rare Rare
HIV	Cryptococcus S. Pneumoniae	5% HIV Common
Bacteremia or endocarditis	S. Aureus Gram-negative bacilli	Rare
Fracture of cribiform plate	S. Pneumoniae or nasopharyngeal flora	Very rare

## Several Mechanisms

- Colonization of nasopharynx → bacteremia → CNS invasion
- “Contiguous infection”
  - Sinusitis, mastoiditis → CNS
- Post-traumatic (fracture of cribiform plate)
- Post-neurosurgery or device-related
- Bacteremia (endocarditis, UTI, etc) → CNS (rare)

## Question: CLINICAL

Which of the following is true?

- a. The majority of patients with bacterial meningitis still maintain a normal MS, despite fever and stiff neck
- b. Kernig's and Brudzinski's signs are sensitive but not specific
- c. Seizures are the most common in Listeria meningitis
- d. CN palsies are present in about 30%, the highest in Listeria

## The Classic Triad

CLASSIC TRIAD = fever, nuchal rigidity, altered mental status

- FEVER
  - Most have T > 38, some hypothermic
  - In several series, almost NO patients had a normal temp
- NUCHAL RIGIDITY (by EXAM, not by history!)
  - 88% on presentation, can persist > 1 week
- Altered MS
  - 80% on presentation
  - mainly confusion but 22% only responsive to pain and 6% completely unresponsive

## Other Manifestations

- Headache: very common, generalized and severe
- Photophobia
- Seizures: 15% or more, depending on age
- CN palsies
  - 20-30%
  - particularly with Listeria
- Cutaneous signs

## The Classic Triad

*Although one or more of the classic findings may be absent, nearly all patients with bacterial meningitis have at least one of the findings*

*If all 3 are absent, bacterial meningitis is virtually excluded (sensitivity 99-100%)*

## Tests for Nuchal Rigidity

- How good are these tests?
  - Large prospective study of suspected meningitis
  - Sensitivity very low
    - 5% for Kernig, 5% Brudzinski, 30% nuchal rigidity
  - Specificity high
    - > 95% for Kernig and Brudzinski
    - 68% nuchal rigidity
  - Did not matter even in severe case (> 1000 WBCs in CSF)
- Jolt Accentuation of headache
  - May be more sensitive meningitis
  - Rotate head horizontally 2-3x/second
  - Sensitivity 97%; specificity 60%

## Distinguishing Bacterial from Aseptic Meningitis in Adults: Clues at the Bedside

### Aseptic Meningitis

- Summer months
- Normal mentation, nonfocal exam
- Immunocompetent

## Distinguishing Bacterial from Aseptic Meningitis in Adults : Clues at the Bedside

### Bacterial Meningitis

- Altered mentation
- Focal neurologic findings
- Hemodynamic compromise
- Seizures
- Immunocompromised
- Anatomic focus
- Petechial rash
- Head trauma
- Recent neurosurgery
- CSF shunt
- Splenectomized or functionally asplenic
- Looks sick

## Question: CLINICAL

Which of the following is true?

- a. The majority of patients with bacterial meningitis still maintain a normal MS, despite fever and stiff neck
- b. Kernig's and Brudzinski's signs are sensitive but not specific
- c. Seizures are the most common in Listeria meningitis
-  d. CN palsies are present in about 30%, the highest in Listeria

## Role of Head CT Prior To LP

### Guidelines by IDSA 2004 (Clin Inf Dis 2004:39)

- Obtain head CT if:
  - History of CNS disease (e.g. mass lesion, stroke, prior focal infection)
  - Immunocompromised pt
  - Seizure < 1 week PTA
  - Certain neuro findings (abnormal level of consciousness, an inability to answer 2 consecutive questions correctly or to follow 2 consecutive commands, gaze palsy, abnormal visual fields, facial palsy, arm or leg drift, abnormal language)
- Otherwise, can do LP without CT
- **If awaiting CT, obtain BC and start antibiotics prior to LP**

## Question

*Which of the following is true regarding CSF findings in meningitis?*

- a. Gram stain will show an organism in > 65% of cases of bacterial meningitis
- b. Very low CSF glucose can be seen in bacterial meningitis or leptomenigeal carcinomatosis
- c. Enteroviral meningitis can present with nearly all PMNs in the CSF
- d. All are true
- e. All are false

## Question

Which of the following is true regarding CSF findings in meningitis?

- a. Gram stain will show an organism in > 65% of cases of bacterial meningitis
- b. Very low CSF glucose can be seen in bacterial meningitis or leptomeningeal carcinomatosis
- c. Enteroviral meningitis can present with nearly all PMNs in the CSF
- d. All are true
- e. All are false

## Typical CSF Findings in Meningitis

	Normal	Bacterial	Viral	Fungal/TB	Paramening
WBC	0-5	>1000	$10^2$ - $10^3$	100-500	10-1000
%PMNs <50	0-15	90	<50	<50	
Glucose	45-65	<40	45-65	30-45	45-65
CSF:blood glucose ratio	0.6	<0.4	0.6	<0.4	0.6
Protein	20-45	>150	50-100	100-500	50->150

Segretti, ID Clin N Am 1996;10:797

## “Atypical” CSF Findings

- Wide range of CSF profiles with overlap
- Bacterial meningitis
  - CSF WBCs can range < 100 cells/mm<sup>3</sup> to > 10,000
  - 10% can present with mainly lymphocytes
  - When CSF-WBCS 100-1000 range can be either viral or bacterial
- Viral meningitis can occasionally present with neutrophilic predominance
  - Enteroviral meningitis
- CSF glucose < 10 typical of bacterial meningitis
  - Also mumps, TB, fungi, LCM, leptomenigeal carcinoma

## Sensitivity CSF Gram Stain - Bacterial Meningitis

Organism	Gram Stain (% Positive)
<b>Pneumococcus</b>	<b>90</b>
<i>H. influenzae</i>	<b>86</b>
<b>Meningococcus</b>	<b>75</b>
<b>Gram negative bacilli</b>	<b>50</b>
<b>Listeria</b>	<b>&lt;50</b>

Gray, Clin Microbiol Rev 1992;5:130

## Latex Agglutination



- Antisera against capsular polysaccharides
- LA, CIE, coagglutination
- LA simple and 15 minutes
- Good sensitivity, about 70-100%
- Negative test does not rule out meningitis
- May not alter management
- IDSA: NOT routinely recommended, but may be useful for pt pretreated with atbx with negative GS and culture

## PCR

- Newer studies with broad range bacterial primers
- “real time” PCR—LightCycler methodologies and others
- **Considerable variation in methodology**
- Best reports of 100% sensitivity, 98% specificity, PPV 98%, PNV 100%
- IDSA: PCR is “promising” but needs “further refinements”
- PCR for enterovirus; becoming widely available

## Bacterial vs. Viral Meningitis

- No test definitive for or against bacterial meningitis
- Combination of tests may permit accurate prediction
- One study, N=422, predictors of bacterial (vs. viral) meningitis were
  - CSF glucose < 34 mg/dL
  - CSF/blood glucose < 0.23
  - CSF protein > 220 mg/dl
  - CSF WBCs > 2000/mm<sup>3</sup>
  - CSF neutrophil > 1180 neutrophils/mm<sup>3</sup>
- If any one of these present, predicted bacterial meningitis over viral meningitis with > 99% certainty
- Validated by others retrospectively, but NOT prospectively

## Question

Which of the following is true regarding the treatment of meningitis?

- a. Meningitis caused by *S. pneumoniae* resistant to penicillin (MIC > 2 ug/ml) should be treated with BOTH vancomycin and ceftriaxone
- b. Meningitis caused by *S. pneumoniae* with intermediate resistance to penicillin (MIC > 1-2 ug/ml) should be treated with vancomycin
- c. Ceftriaxone 2 g iv q 24 hours is the cephalosporin of choice against Listeria
- d. All above are true

## Question

Which of the following is true regarding the treatment of meningitis?

-  a. Meningitis caused by *S. pneumoniae* resistant to penicillin (MIC > 2 ug/ml) should be treated with BOTH vancomycin and ceftriaxone
- b. Meningitis caused by *S. pneumoniae* with intermediate resistance to penicillin (MIC > 1-2 ug/ml) should be treated with vancomycin
- c. Ceftriaxone 2 g iv q 24 hours is the cephalosporin of choice against Listeria
- d. All above are true

## *S. pneumoniae*

- Penicillin (parenteral, non-meningitis):  $\leq 2 = S$ ;  $4 = I$  and  $\geq 8 = R$
-  • **Penicillin (parenteral, meningitis):  $\leq 0.06 = S$ ;  $\geq 0.12 = R$**
- Penicillin (Oral PenV):  $\leq 0.06 = S$ ;  $0.12 - 1 = I$ ;  $> 2 = R$
- Amoxicillin (nonmeningitis):  $\leq 2 = S$ ;  $4 = I$  and  $> 8 = R$
- Amox/clav (nonmeningitis):  $\leq 2/1 = S$ ;  $4/2 = I$  and  $> 8/4 = R$
-  • **Ceftriaxone (meningitis):  $\leq 0.5 = S$ ;  $1 = I$  and  $\geq 2 = R$**
- Ceftriaxone (nonmeningitis):  $\leq 1 = S$ ;  $2 = R$ ;  $\geq 4 = S$

## Therapy

- Initiate antibiotics immediately
- Bactericidal antibiotics
- CSF concentrations are a small fraction of serum concentrations
- Important issue is the development of penicillin (and cephalosporin) resistance in *S. pneumoniae*
  - Susceptible, intermediate, resistant to PCNG

**Table 3. Recommendations for antimicrobial therapy in adult patients with presumptive pathogen identification by positive Gram stain.**

Microorganism	Recommended therapy	Alternative therapies
<i>Streptococcus pneumoniae</i>	Vancomycin plus a third-generation cephalosporin <sup>a,b</sup>	Meropenem (C-III), fluoroquinolone <sup>c</sup> (B-II)
<i>Neisseria meningitidis</i>	Third-generation cephalosporin <sup>a</sup>	Penicillin G, ampicillin, chloramphenicol, fluoroquinolone, aztreonam
<i>Listeria monocytogenes</i>	Ampicillin <sup>d</sup> or penicillin G <sup>d</sup>	Trimethoprim-sulfamethoxazole, meropenem (B-III)
<i>Streptococcus agalactiae</i>	Ampicillin <sup>d</sup> or penicillin G <sup>d</sup>	Third-generation cephalosporin <sup>a</sup> (B-III)
<i>Haemophilus influenzae</i>	Third-generation cephalosporin <sup>a</sup> (A-I)	Chloramphenicol, cefepime (A-I), meropenem (A-I), fluoroquinolone
<i>Escherichia coli</i>	Third-generation cephalosporin <sup>a</sup> (A-II)	Cefepime, meropenem, aztreonam, fluoroquinolone, trimethoprim-sulfamethoxazole

**NOTE.** All recommendations are A-II, unless otherwise indicated. In children, ampicillin is added to the standard therapeutic regimen of cefotaxime or ceftriaxone plus vancomycin when *L. monocytogenes* is considered and to an aminoglycoside if a gram-negative enteric pathogen is of concern.

<sup>a</sup> Ceftriaxone or cefotaxime.

<sup>b</sup> Some experts would add rifampin if dexamethasone is also given (B-III).

<sup>c</sup> Gatifloxacin or moxifloxacin.

<sup>d</sup> Addition of an aminoglycoside should be considered.

**Clinical Infectious Diseases 2004; 39:1267–84**

**Table 4. Recommendations for empirical antimicrobial therapy for purulent meningitis based on patient age and specific predisposing condition (A-III).**

Predisposing factor	Common bacterial pathogens	Antimicrobial therapy
<b>Age</b>		
<1 month	<i>Streptococcus agalactiae</i> , <i>Escherichia coli</i> , <i>Listeria monocytogenes</i> , <i>Klebsiella</i> species	Ampicillin plus cefotaxime or ampicillin plus an aminoglycoside
1–23 months	<i>Streptococcus pneumoniae</i> , <i>Neisseria meningitidis</i> , <i>S. agalactiae</i> , <i>Haemophilus influenzae</i> , <i>E. coli</i>	Vancomycin plus a third-generation cephalosporin <sup>a,b</sup>
2–50 years	<i>N. meningitidis</i> , <i>S. pneumoniae</i>	Vancomycin plus a third-generation cephalosporin <sup>a,b</sup>
>50 years	<i>S. pneumoniae</i> , <i>N. meningitidis</i> , <i>L. monocytogenes</i> , aerobic gram-negative bacilli	Vancomycin plus ampicillin plus a third-generation cephalosporin <sup>a,b</sup>
<b>Head trauma</b>		
Basilar skull fracture	<i>S. pneumoniae</i> , <i>H. influenzae</i> , group A $\beta$ -hemolytic streptococci	Vancomycin plus a third-generation cephalosporin <sup>a</sup>
Penetrating trauma	<i>Staphylococcus aureus</i> , coagulase-negative staphylococci (especially <i>Staphylococcus epidermidis</i> ), aerobic gram-negative bacilli (including <i>Pseudomonas aeruginosa</i> )	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
Postneurosurgery	Aerobic gram-negative bacilli (including <i>P. aeruginosa</i> ), <i>S. aureus</i> , coagulase-negative staphylococci (especially <i>S. epidermidis</i> )	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
CSF shunt	Coagulase-negative staphylococci (especially <i>S. epidermidis</i> ), <i>S. aureus</i> , aerobic gram-negative bacilli (including <i>P. aeruginosa</i> ), <i>Propionibacterium acnes</i>	Vancomycin plus cefepime, <sup>c</sup> vancomycin plus ceftazidime, <sup>c</sup> or vancomycin plus meropenem <sup>c</sup>

<sup>a</sup> Ceftriaxone or cefotaxime.

<sup>b</sup> Some experts would add rifampin if dexamethasone is also given.

<sup>c</sup> In infants and children, vancomycin alone is reasonable unless Gram stains reveal the presence of gram-negative bacilli.

## Scale Back

**Table 5. Recommendations for specific antimicrobial therapy in bacterial meningitis based on isolated pathogen and susceptibility testing.**

Microorganism, susceptibility	Standard therapy	Alternative therapies
<i>Streptococcus pneumoniae</i>		
Penicillin MIC		
<0.1 $\mu$ g/mL	Penicillin G or ampicillin	Third-generation cephalosporin, <sup>a</sup> chloramphenicol
0.1–1.0 $\mu$ g/mL <sup>b</sup>	Third-generation cephalosporin <sup>a</sup>	Cefepime (B-II), meropenem (B-II)
$\geq$ 2.0 $\mu$ g/mL	Vancomycin plus a third-generation cephalosporin <sup>a,c</sup>	Fluoroquinolone <sup>d</sup> (B-II)
Cefotaxime or ceftriaxone MIC $\geq$ 1.0 $\mu$ g/mL	Vancomycin plus a third-generation cephalosporin <sup>a,c</sup>	Fluoroquinolone <sup>d</sup> (B-II)
<i>Neisseria meningitidis</i>		
Penicillin MIC		
<0.1 $\mu$ g/mL	Penicillin G or ampicillin	Third-generation cephalosporin, <sup>a</sup> chloramphenicol
0.1–1.0 $\mu$ g/mL	Third-generation cephalosporin <sup>a</sup>	Chloramphenicol, fluoroquinolone, meropenem
<i>Listeria monocytogenes</i>	Ampicillin or penicillin G <sup>e</sup>	Trimethoprim-sulfamethoxazole, meropenem (B-III)
<i>Streptococcus agalactiae</i>	Ampicillin or penicillin G <sup>e</sup>	Third-generation cephalosporin <sup>a</sup> (B-II)

**Clinical Infectious Diseases 2004; 39:1267–84**

<i>Escherichia coli</i> and other Enterobacteriaceae <sup>a</sup>	Third-generation cephalosporin (A-II)	Aztreonam, fluoroquinolone, meropenem, trimethoprim-sulfamethoxazole, ampicillin
<i>Pseudomonas aeruginosa</i> <sup>a</sup>	Cefepime <sup>a</sup> or ceftazidime <sup>a</sup> (A-II)	Aztreonam, <sup>a</sup> ciprofloxacin, <sup>a</sup> meropenem <sup>a</sup>
<i>Haemophilus influenzae</i>		
β-Lactamase negative	Ampicillin	Third-generation cephalosporin, <sup>a</sup> cefepime, chloramphenicol, fluoroquinolone
β-Lactamase positive	Third-generation cephalosporin (A-I)	Cefepime (A-I), chloramphenicol, fluoroquinolone
<i>Staphylococcus aureus</i>		
Methicillin susceptible	Nafcillin or oxacillin	Vancomycin, meropenem (B-III)
Methicillin resistant	Vancomycin <sup>f</sup>	Trimethoprim-sulfamethoxazole, linezolid (B-III)
<i>Staphylococcus epidermidis</i>	Vancomycin <sup>f</sup>	Linezolid (B-III)
<i>Enterococcus</i> species		
Ampicillin susceptible	Ampicillin plus gentamicin	...
Ampicillin resistant	Vancomycin plus gentamicin	...
Ampicillin and vancomycin resistant	Linezolid (B-III)	...

**NOTE.** All recommendations are A-III, unless otherwise indicated.

<sup>a</sup> Ceftriaxone or cefotaxime.

<sup>b</sup> Ceftriaxone/cefotaxime-susceptible isolates.

<sup>c</sup> Consider addition of rifampin if the MIC of ceftriaxone is >2 µg/mL.

<sup>d</sup> Gatifloxacin or moxifloxacin.

<sup>e</sup> Addition of an aminoglycoside should be considered.

<sup>f</sup> Consider addition of rifampin.

<sup>g</sup> Choice of a specific antimicrobial agent must be guided by in vitro susceptibility test results.

**Clinical Infectious Diseases 2004; 39:1267–84**

## Duration

**Table 8. Duration of antimicrobial therapy for bacterial meningitis based on isolated pathogen (A-III).**

Microorganism	Duration of therapy, days
<i>Neisseria meningitidis</i>	7
<i>Haemophilus influenzae</i>	7
<i>Streptococcus pneumoniae</i>	10–14
<i>Streptococcus agalactiae</i>	14–21
Aerobic gram-negative bacilli <sup>a</sup>	21
<i>Listeria monocytogenes</i>	≥21

<sup>a</sup> Duration in the neonate is 2 weeks beyond the first sterile CSF culture or ≥3 weeks, whichever is longer.

## Adjunctive Steroids

- IDSA: give adjunctive dexamethasone with known or suspected pneumococcal meningitis (regardless of GCS)
- IDSA: do not give dexamethasone to those who have already received antibiotics, “unlikely to improve outcome”
- Inadequate data to recommend dexamethasone if other pathogens known or suspected, although some recommend it to be given for all adults, since the etiology is often unknown initially

Resistant Pneumococci? (steroid decreases inflammatory response = less CNS penetration of antibiotic)

- IDSA feels this question will be unanswered for a long time
- Recommends giving dexamethasone even if pneumococcal isolates are PCN-resistant or cephalosporin-resistant
- IDSA: consider adding rifampin (to vanco and 3<sup>rd</sup> generation cephalosporin) even prior to culture results

## Chemoprophylaxis of Meningococcal Meningitis : Regimens

### Adults

- Rifampin 600 mg po bid x 2 days ... or
- Ceftriaxone 250 mg im x 1 ... or
- Ofloxacin 400 mg or Cipro 500 mg po x 1

### Children

- Rifampin 10 mg/kg po bid x 2 days... or
- Ceftriaxone 125 mg im x 1

## Meningococcal Vaccines

- Meningococcal polysaccharide vaccine
- Meningococcal polysaccharide CONJUGATE vaccine (MCV-4); single dose
  - Menactra
  - Serogroups W-135, A, C, Y
  - No vaccine for serogroup B
- Major groups: 11-12 y.o. routinely; high school or 15 y.o., college students - dorms, those who received polysaccharide vaccine, complement deficiency, asplenia etc

## Meningococcal Vaccines

- ADULTS: military recruits, microbiologists exposed, asplenics, complement deficiency, certain travelers; previously immunized with polysaccharide vaccine at risk
- Any college student upon request
  - Not cost effective for entire adult population
  - Possibly HIV, efficacy unknown
  - Possibly outbreaks - reduce secondary cases (if covered)
- Relation with Gillian Barre? Registry



**Cleveland Clinic**

Every life deserves world class care.