Bacterial Meningitis

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Objectives

- Describe the pathophysiology and epidemiology of bacterial meningitis.
- Recognize the common signs and symptoms of meningitis.
- Discuss the importance of obtaining initial blood cultures, CSF fluid and cultures prior to antimicrobial therapy.
- Identify the most common pathogens in bacterial meningitis by patient age and appropriate empiric therapy.
- Recognize multiple ways to narrow empiric antimicrobial therapy.
- Choose targeted antimicrobial therapy based upon CSF and blood culture results.
- Utilizing a patient case, recognize key issues and develop an appropriate treatment plan.

Pathophysiology

- Defined as inflammation of the meninges, lining of the brain and spinal cord
  - Bacterial
  - Viral
  - Fungal
- Factors involved in development of meningitis
  - Mucosal colonization
  - Systemic invasion
  - Intravascular bacterial survival and meningeal invasion
  - Bacterial survival in subarachnoid space
  - Increased intracranial pressure (ICP)
  - Alterations in cerebral blood flow and neuronal injury

Tunkel AR, Harman BJ, Kaplan SL, etc. Practice guidelines for the management of bacterial meningitis. IDSA Guidelines. Clinical Infectious Disease. 2004;39:1267-84.
Nudelman Y, Tunkel AR. Bacterial Meningitis: Epidemiology, Pathogenesis and Management Update. *Drugs* 2009; 69 (18): 2577-2596.

Epidemiology

- Historically, the 3 most common pathogens were:
  - *H. influenzae*
  - *N. meningitidis*
  - *S. pneumoniae*

- *H. influenzae*
  - Originally isolated from 45-48% of cases in the U.S. with most patients being <6 yo
  - Now isolated from ~7% of cases secondary to the development of Hib vaccine

Nudelman Y, Tunkel AR. Bacterial Meningitis: Epidemiology, Pathogenesis and Management Update. Drugs 2009; 69 (18): 2577-2596.

Epidemiology (cont.)

- *N. meningitidis*
  - Most commonly seen in children/young adults
  - Mortality rate of 3-13%
  - Prevalence of nasopharyngeal colonization
    - 5-10% in non-epidemic populations
    - 40-90% in closed populations (eg. military, college dorms)

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Epidemiology (cont.)

- *S. pneumoniae*
  - Now most common pathogen in bacterial meningitis → 61% of cases (2009)
  - Mortality rate 19-26%
  - Most common agent in patients who have a history of:
    - Basilar skull fracture with CSF leak
  - Remote head injury with CSF leak = main factor in recurrent bacterial meningitis
  - With vaccine, mortality rates have been reported to have decreased ~33%
    - Greatest reduction seen in children

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Common Presentation

Headaches

Fever

Photosensitivity

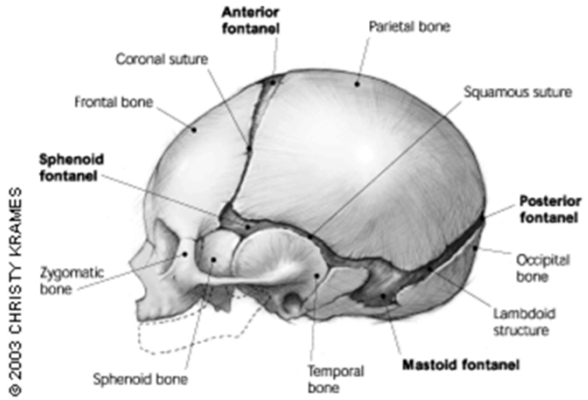
Nuchal rigidity

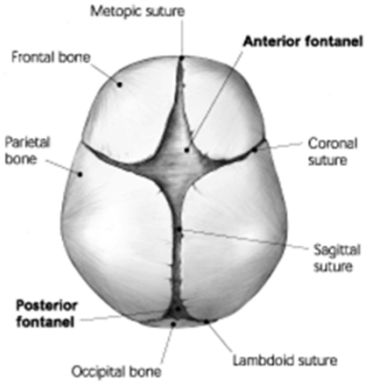
Seizures

Vomiting

AMS

Infants – bulging anterior fontanel





Dipiro JT. Pharmacotherapy: A Pathophysiologic Approach. 8th ed.
http://www.aafp.org/afp/2003/0615/p2547.html

Important Initial Treatment

- KEY: EARLY RECOGNITION
- Once meningitis is suspected:
  - Blood cultures
  - Lumbar Puncture (Spinal Tap)
  - Empiric Antibiotics - based on age, other presenting conditions
- Delaying antibiotics can increase morbidity/mortality

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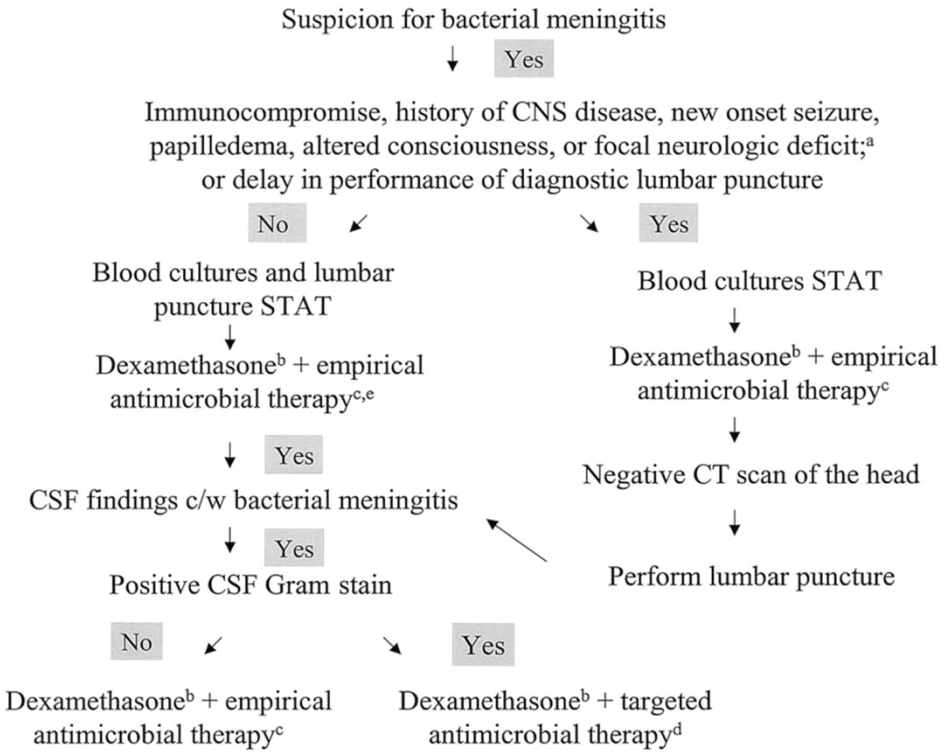
Adult Management Algorithm



Tunkel A R et al. Clin Infect Dis. 2004;39:1267-1284.

Analyzing CSF Results

Characteristics	Bacterial	Viral
Appearance	Cloudy	
WBCs	1000-5000 cells/mm^3	< 500 cells/mm^3
Neutrophils	80% - 95%	
Protein	> 250	< 100
Glucose	< 40 mg/dL	Normal
CSF:serum glucose	≤ 0.4	

Tunkel AR, Harman BJ, Kaplan SL, etc. Practice guidelines for the management of bacterial meningitis. IDSA Guidelines. Clinical Infectious Disease. 2004;39:1267-84.
Pentima, CD. UpToDate. Viral Meningitis: Clinical features and diagnosis in children.
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Narrowing Treatment Therapy

- CSF cultures are positive in 70-85% of patients who did not receive antibiotics prior to the LP
  - May take several days for definitive answer
- Other options to help narrow empiric treatment
  - CSF gram stain
  - Rapid diagnostic tests
  - PCR

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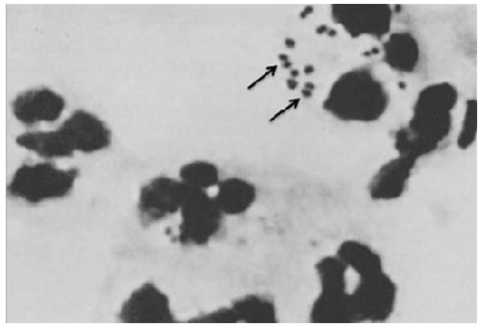
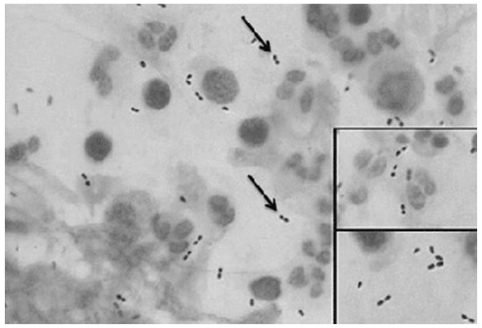
CSF Gram Stain





- Negative (but bacterial meningitis clinically suspected)
  - Empiric antibiotics
- Positive
  - Tailor therapy based on results
  - Specificity ≥ 97%
  - Probability of positive result by bacteria:
    - 90% *S. pneumoniae*
    - 86% *H. influenza*
    - 75% *N. meningitidis*
    - 50% gram-negative bacilli
    - ~33% *L. monocytogenes*

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http://www.cdc.gov/meningitis/lab-manual/chpt06-culture-id.html

Rapid Diagnostic Tests

- Latex Agglutination
  - Rapid results (<15 min)
  - Good sensitivity for more common pathogens
  - Detect antigens for *H. influenzae* type B, *S. pneumoniae*, *N. meningitidis* and *E. coli* K1 and group B streptococci
  - HOWEVER → routine use not recommended
    - False positives
    - Results don't affect decision to administer antibiotics

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PCR

- May play role in excluding diagnosis of meningitis and determining the length of antibiotic treatment
- One study has shown:
  - Sensitivity – 100%
  - Specificity – 98.2%
  - Positive predictive value – 98.2%
  - Negative predictive value – 100%
- KEY: most useful in patients who received antibiotics before cultures drawn and are likely to have negative CSF results

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Common Pathogens By Age

Age	Pathogens
< 1 months	*S. agalactiae, E. coli, L. monocytogenes, Klebsiella* species
1- 23 months	*S. pneumoniae, N. meningitidis, S. agalactiae, H. influenzae, E. coli*
2 – 50 years	*N. meningitidis, S. pneumoniae*
> 50 years	*S. pneumoniae, N. meningitidis, L. monocytogenes*, aerobic gram-negative bacilli

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Common Pathogens by Predisposing Condition

Predisposing Conditions	Pathogens
Head Trauma	
Basilar skull fracture	*S. pneumoniae*, *H. influenzae*, group A ß-hemolytic strepococci
Penetrating trauma	*S. aureus*, coagulase-negative staphylococci (*S. epidermidis*), aerobic gram-negative bacilli (*P. aeruginosa*)
Postneurosurgery	Aerobic gram-negative bacilli (*P. aeruginosa*), *S. aureus*, coagulase-negative staphylococci
CSF shunt	Coagulase-negative staphyococci, *S. aureus*, aerobic gram-negative bacilli (*P. aureginosa*), *Propionibacterium acnes*

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Treatment: Empiric Antibiotics

Predisposing Factor	Antibiotics
Age	
< 1 mo	Ampicillin + Claforan OR Ampicillin + AMG
1-23 mo	Vancomycin + 3rd gen Cephalosporin
2-50 yo	Vancomycin + 3rd gen Cephalosporin
> 50 yo	Vancomycin + Ampicillin + 3rd gen Cephalosporin
Basilar Skull Fracture	Vancomycin + 3rd gen Cephalosporin
Head Trauma; postneurosurgery	Vancomycin + Fortaz OR Maxipime OR Merrem

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Treatment: Targeted Therapy

Pathogen	Antibiotics
H. Influenzae type B	3rd gen Cephalosporin
N. meningitidis	3rd gen Cephalosporin
S. pneumoniae	Vancomycin + 3rd gen Cephalosporin
L. monocytogenes	Ampicillin or benzylpenicillin
S. agalactiae	Ampicillin or benzylpenicillin
E. coli	3rd gen Cephalosporin

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Duration of Therapy

Pathogen	Duration (days)
N. meningitidis	7
H. Influenzae	7
S. pneumoniae	10-14
S. agalactiae	14-21
Aerobic gram-negative bacilli	21
L. monocytogenes	≥ 21

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Dexamethasone Controversy

- Inflammation secondary to antibiotic induced bacterial lysis → major factor contributing to morbidity/mortality
- Recommended in children with *H. influenzae*
  - Reduced morbidity – decrease in sensorineural hearing loss
- Adults – study in the Netherlands
  - Adjunct dexamethasone = decreased mortality and unfavorable outcomes
  - Particularly in pneumococcal meningitis, moderate to severe disease
- Other studies show no benefit – especially in low income countries
- Another concern: PCN or Cephalosporin resistant strains of pneumococcal meningitis
  - Will have to use Vancomycin – less penetration into BBB if inflammation decreased

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Dexamethasone Dosing

- Recommended in pneumococcal meningitis
- Dose: 0.15 mg/kg IV Q6 hrs x 4 days

- MUST be given before or with first dose of antibiotics
  - If antibiotics already administered, dexamethasone should not be started

- If CSF culture results are negative for *S. pneumoniae*
  - Dexamethasone should be discontinued

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Patient Case

- LD is a 63 yo F who presented to Memorial on 12/3 with a CC of AMS
- HPI: Headaches, fever over past few days, n/v for last 24 hrs. Hx of pneumococcal meningitis in 01/2014. Upon arrival in ED patient was lucid. During ED stay, began having fevers and became somnolent/lethargic. Labs all WNL. Sent for LP given hx of meningitis this year.
- PMH:
  - Hx pneumococcal meningitis 01/2014
  - Recurrent sinusitis – sees Dr. Greer as outpatient
  - Hx of MVA during her 20s with facial fractures that required multiple surgeries
  - Bilateral knee replacements

Patient Case – LP Results

CSF Characteristics	Results
Appearance	Cloudy
WBCs	11545
Lymph	1
Mono	0
Segs	99
Glucose	< 1
CSF:serum glucose	<1:156 = <0.4
Protein	556.2

- CSF examination significant for bacterial meningitis based on:
  - WBC
  - Glucose
  - Protein

Patient Case (cont.)

- Blood cx and CSF gram stain and cx obtained prior to antibiotics
- CT scan positive for sphenoid air fluid levels consistent with sinusitis
- Suspected pneumococcal meningitis
  - Hx of meningitis in January
  - Latex agglutination test was positive for *S. pneumoniae*, negative for *N. meningitidis*, influenza B
- Gram stain - negative
- LD was transferred to CCU
  - AMS
  - Potential impending respiratory failure requiring intubation

Treatment Course

- LD was given the following in the ED:
  - Vancomycin
  - Rocephin
  - Ampicillin
  - Dexamethasone

- Based on high suspicion for pneumococcal meningitis – Ampicllin was discontinued
- LD required intubation the night she came into the ED
- Blood cx and CSF culture results = *S. pneumoniae*
  - Resistant only to Erythromycin

Treatment Course (cont.)

- At this point, what questions do you have?

- Developed AKI – secondary to Rocephin?
- CT 12/9 – showed deformity of the maxillary sinus and medial orbital wall consistent with old trauma to the face. Also showed small defect in the posterior wall of the frontal sinus which could explain communication with epidural space intracranially
- 12/15 – taken to OR by Dr. Greer
- Medication Course:
  - Currently still receiving Vancomycin – Total 12 days (break from 12/5-12/8)
  - Received 4 days of dexamethasone
  - Received 5 total days of Rocephin
  - Received 2 days of PenG

Prevention

- *H. influenzae* type B (Hib) vaccine
  - 2 mo, 4 mo, 6 mo (depending on vaccine used), booster dose at 12-15 mo
- Meningicoccal vaccine (Menomune, Menactra)
  - Menactra – single dose at 11-12 yo with booster at 16 yo
- Pneumococcal vaccine (PCV13, PPSV23)
  - PCV13 is recommended for all children < 5 yo, adults ≥ 65 yo, patients > 6 yo with certain medical conditions
  - PPSV23 is recommended in all adults ≥ 65 yo and patients > 2 yo at high risk for pneumococcal disease (sickle cell disease, HIV, other immunocompromising conditions), adults 19-64 yo who smoke or have asthma

http://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

Summary

- Over the last 20 years, common pathogen involvement in bacterial meningitis has changed dramatically with the development of vaccines.
- Obtaining blood cultures and performing an LP prior to antibiotics is significantly important in appropriately treating bacterial meningitis.
- Prior to receiving culture results, patient should receive empiric antimicrobial therapy based on age and predisposing conditions.
- Once culture results are published, antimicrobial therapy should be targeted to treat the specific pathogen represented.
- Vaccines have become incredibly important in reducing the prevalence of *H. influenza*, meningococcal and pneumococcal meningitis.

Questions??