

Bacterial Meningitis

From Presentation to Prevention


Stephanie Blackburn, EdD, MLS(ASCP)CM
LSU Health Shreveport



1

Objectives

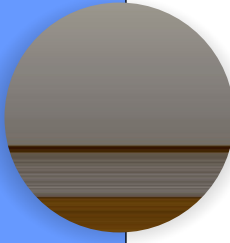
- Identify the most common bacterial pathogens associated with meningitis across different age groups and risk populations.
- Distinguish bacterial and viral meningitis.
- Discuss laboratory findings, treatment strategies, and prevention measures for bacterial meningitis.



2

Meningitis


- Inflammation of tissues surrounding the brain and spinal cord
- Classified as infectious or non-infectious
- May be associated with high-risk of death or long-term complications
- Caused by:
 - Infectious: Virus, bacteria, fungus
 - Non-infectious: cancer, inflammatory disease, etc.



3

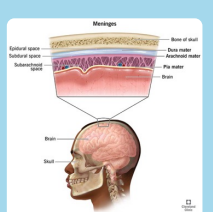
Meningitis

- Can affect anyone, anywhere, at any age
- Significant global health threat
- Pathogens vary, based on:
 - Age
 - Immune system
 - Level of exposure, which is influenced by:
 - Living conditions
 - Geography



4

Anatomy of the Meninges

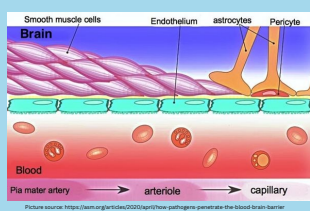


- **Three layers**
 - Dura mater: Outer layer, closest to skull
 - Arachnoid mater: Middle layer
 - Pia mater: Inner layer, closest to brain tissue
- **Three spaces:**
 - Epidural space
 - Subdural space
 - Subarachnoid space

Picture Source: <https://my.clevelandclinic.org/health/articles/22856/meninges>

5

Blood-Brain Barrier



- Found between:
 - Blood vessels and interstitial fluid in brain
 - Blood and CSF-producing cells
- Protective barrier around blood vessels in the brain
- Primary regulator of microorganisms and harmful substances entry into CNS
- BBB consist of multiple cell types
 - Endothelial cells
 - Pericytes
 - Astrocytes
 - Microglia

Picture source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2020202/figure/fig1>

6

Mechanisms of Bacterial Entry

- **Transcellular route**
 - Cross into CNS through endothelial cells
- **Paracellular route**
 - Passes between endothelial cells
- **Infected phagocyte route (Trojan horse)**
 - BBB is permeable to phagocytic WBCs
 - Infected WBCs cross BBB

Picture source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2020491/figure/fig1>

7

Pathogenesis

- Hematogenous spread
- Direct extension
- Leads to inflammatory response
- Mechanism by which pathogens cross BBB help determine effective treatment for bacterial meningitis

8

Pathogenesis

- Most cases of bacterial meningitis begin with bacterial colonization of the nasopharynx (Exception *Listeria*)
- Several of the pathogenic bacteria secrete IgA protease that inactivates host antibody and facilitates mucosal attachment (*Streptococcus pneumoniae* & *Neisseria meningitidis*)
- Some pathogens possess surface characteristics that enhance mucosal colonization
- *Neisseria meningitidis* has pili that allows it to bind to nonciliated epithelial cells

9

Pathogenic steps leading to pneumococcal pneumonia

Revised from Palmer C.T., & Blotnik K.C. (2015). Infectious diseases. Harman, G.D., & McPhee S.J. (Eds.). Pathophysiology of Disease: An Introduction to Clinical Medicine, 10th Edition. McGraw-Hill Education.

10

The Inflammatory Response

- Intense immune response often causes more damage than the pathogen itself
- Normally, complement components are minimal or absent in CSF, also Ig are very low in CSF
- Meningeal inflammation leads to increased (although still low) complement, which is inadequate for opsonization, phagocytosis, and removal of encapsulated pathogens

11

The Inflammatory Response

- Release of cytokines and proteolytic enzymes lead to:
 - WBC infiltration
 - Tissue damage
 - Increased vascular permeability of BBB
 - Edema
 - Increased intracranial pressure
- Signs and symptoms develop after the immune system gets started

Picture from Palmer C.T., & Blotnik K.C. (2015). Infectious diseases. Harman, G.D., & McPhee S.J. (Eds.). Pathophysiology of Disease: An Introduction to Clinical Medicine, 10th Edition. McGraw-Hill Education.

12

THE CLASSIC TRIAD OF BACTERIAL MENINGITIS

Three key symptoms which, when present together, are highly suggestive of the condition, though not all patients have all three.

1. FEVER

HIGH TEMPERATURE
OFTEN ACCOMPANIED BY CHILLS AND SHIVERING.

2. NECK STIFFNESS

NUCHAL RIGIDITY
INABILITY TO FLEX THE NECK FORWARD (CHIN TO CHEST).

3. ALTERED MENTAL STATUS

CONFUSION, DISORIENTATION,
LETHARGY, OR OTHER BEHAVIORAL CHANGES.

OTHER IMPORTANT SIGNS & SYMPTOMS (MAY ALSO BE PRESENT)

- HEADACHE
- PHOTOPHOBIA
- NAUSEA & VOMITING
- RASH
- SEIZURES

NON-BLANCHING RASH

WHEN PRESENT TOGETHER, Highly suggestive, but all three symptoms occur in only 41-60% of cases. Early detection is crucial.

EARLY DIAGNOSIS AND PROMPT ANTIBIOTIC TREATMENT ARE ESSENTIAL TO PREVENT SEVERE COMPLICATIONS AND DEATH.

13

Complications of bacterial meningitis

- Hearing loss
- Seizures
- Cognitive impairment
 - Difficulties with vision, speech, language, memory, and communication
- Limb weakness

14

Epidemiology & Pathogens

15

Global Trends

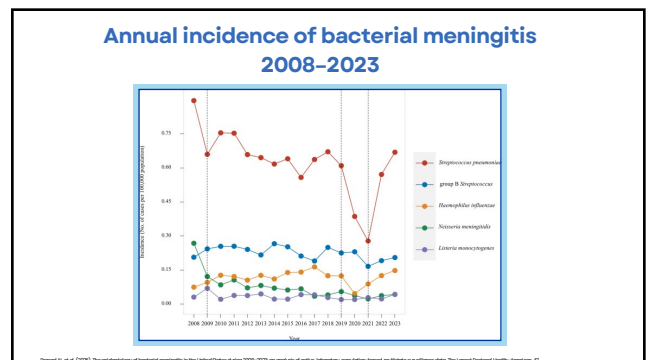
- Significant global health threat
 - More than 2.5 million infected in 2023
 - Accounts for ~250,000 deaths worldwide
 - Mortality rate ranges from 9-27%, depending on pathogen (bacteria is most deadly)
- Highest number of cases and recurrent epidemics in the "meningitis belt"
 - Sub-Saharan Africa
 - Stretches from Senegal to Ethiopia

16

Leading causes of bacterial meningitis

- *Streptococcus pneumoniae*
- *Streptococcus agalactiae* (Group B strep)
- *Neisseria meningitidis*
- *Haemophilus influenzae*
- *Listeria monocytogenes*

17



18


Other causative agents

- Post-neurosurgery patients
 - *S. aureus*, gram-negative bacilli, *P. aeruginosa*
- Patients with ventricular shunts
 - *S. epidermidis*, *S. aureus*, gram-negative bacilli
- Neutropenic patients
 - Gram-negative bacilli, including *P. aeruginosa*
- Subacute or chronic meningitis may be caused by
 - *M. tuberculosis*, fungi, and spirochetes such as *Treponema pallidum* or *Borrelia burgdorferi*

19

Risk factors

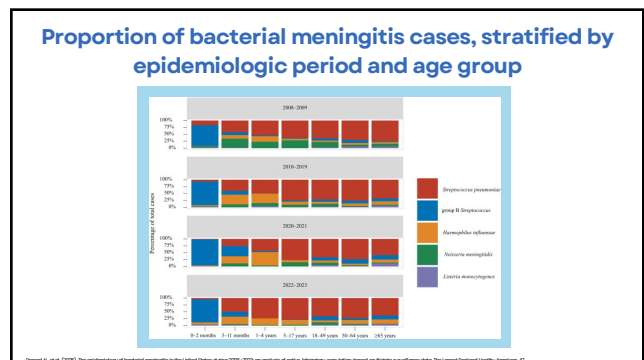
- Age – some pathogens are more likely to affect certain age groups
- Certain medical conditions
 - Immunocompromised
 - Asplenic
 - CSF leak
- Group setting
 - Large gatherings
 - People in close proximity
- Travel



20

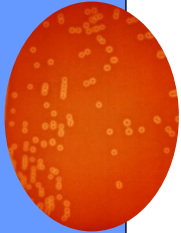
Age	Common Bacterial Pathogen
Newborns	Group B streptococcus <i>Listeria monocytogenes</i> <i>Escherichia coli</i> K1
Babies & young children	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Neisseria meningitidis</i>
Teens & young adults	<i>Streptococcus pneumoniae</i> <i>Neisseria meningitidis</i>
Older adults	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Listeria monocytogenes</i> <i>Neisseria meningitidis</i>

21



22


Group B streptococcus (GBS)



- *Streptococcus agalactiae*
- Beta hemolytic, Gram-positive cocci
- Possess Lancefield group B cell wall Ag
- Polysaccharide capsule that inhibits phagocytic uptake
- Normal flora of gastrointestinal tract and genital tract
 - Up to 40% females have colonization in rectal or genital tract

23

Group B streptococcus (GBS)




- Passed from mother to newborn during delivery
 - Newborn predisposed to respiratory infections and septicemia, which may progress to meningitis
- Causes >85% cases of bacterial meningitis in neonates under 2 mos.

24

Listeria monocytogenes

- Beta hemolytic, Gram-positive bacillus
 - Tumbling motility in broth
 - Psychrophile
 - Grows at 4°C
- Organism invades mononuclear phagocytes and epithelial cells
- Found in unpasteurized dairy, deli meats, soft cheeses made from unpasteurized milk, unheated hot dogs, and uncooked cabbage
- Tends to cause GI illness




25

Listeria monocytogenes

High risk for meningitis:


- Pregnant female
 - Placenta infection (usually presence of abscesses and granulomas)
 - Fecal contamination at birth (septicemia and meningitis)
- Immunocompromised people

• Prevention: limit exposure and consume pasteurized dairy



26

E. coli K1

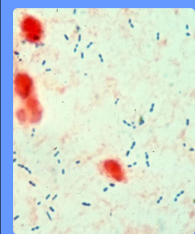


- Gram-negative bacillus
- Normal GI flora
- May colonize in lower urethra and vagina
- Encapsulated strains (K1) associated with meningitis in newborns
- Transmitted during birth causing neonatal sepsis and meningitis

27

Streptococcus pneumoniae

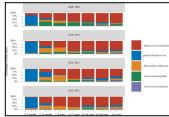
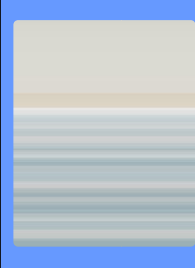
- Alpha hemolytic Gram-positive diplococci, lancet-shaped
- Easily colonizes in the upper respiratory tract due to its protein adhesins and IgA protease
- Spread through direct contact with respiratory secretions
- Has a polysaccharide capsule that inhibits phagocytic uptake (important virulence factor)
 - More than 100 serotypes based on capsule



28


Streptococcus pneumoniae

- Can invade the bloodstream and cross blood-brain barrier
- Leading cause (post-HiB) of bacterial meningitis amongst ALL AGES (except neonates)
- Pneumococcal meningitis

29


Haemophilus influenzae



- Fastidious, Gram-negative coccobacillus
- Normal upper respiratory flora
 - These strain generally do not have a capsule (nontypeable)
- Encapsulated virulent strains are serotyped
 - Types a-f
 - Type b is most virulent
 - Associated with meningitis and epiglottitis
- Transmitted via respiratory droplets
- More commonly associated with otitis media

30

Haemophilus influenzae



- Can cause meningitis in any age
- Highest risk: Children under 5 yrs old
 - Number of cases reduced significantly after the Hib vaccine
 - Most cases now are in unvaccinated children
- Rare in adults; higher risk if:
 - CSF leak
 - Weakened immune system
 - Potential long-term cognitive impairments: intellectual disabilities, memory loss, coordination problems, seizures, weakness, paralysis, among others

31

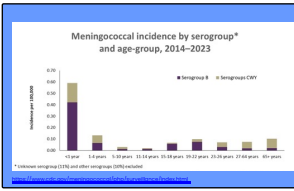
Neisseria meningitidis

- Gram-negative diplococci
- Normal flora of oropharynx in approximately 10% people
- Disease begins as mild pharyngitis, with possible fever
 - If immunologically naive, it may disseminate to tissue (especially skin, meninges, joints, eyes, and lungs), resulting in fulminant meningococemia, pneumonia, and meningitis
- These more severe infections can be fatal in 1 to 5 days

32

Neisseria meningitidis


- Meningococcal meningitis
- 10-15% mortality rate
- Most prevalent in children ages 6 mos-2 yrs with a second peak in young adults (especially those housed together in residence halls)
- Waterhouse-Friderichsen syndrome



33

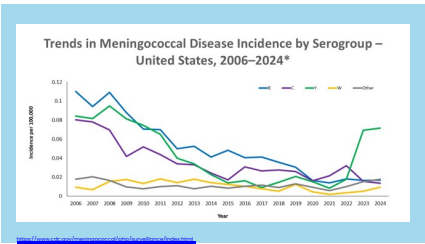
Neisseria meningitidis

- Possess polysaccharide capsule
- More than 12 capsular serogroups
 - Most infx in U.S. caused by B, C, W-135, and Y serogroups
 - B capsule is notoriously immunogenic
- In addition to classic signs, also characterized by petechial rash that progresses to vasculitic purpura



34

Trends in Meningococcal Disease, 2006-2024



35

Differential Diagnosis & Laboratory Testing



36

Early detection is imperative


- About 50% of patients with bacterial meningitis present within 24 hour of developing classic symptoms
- 50% of patients with meningococcal meningitis present with petechial or purpuric rash and DIC
- Delay in diagnosis is associated with:
 - Mortality rate up to 54%
 - Neurological complications up to 25%



37

Diagnosis of Meningitis

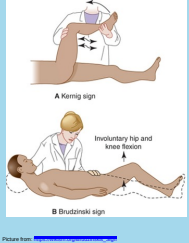
- Physical examination findings tend to show wide variability in their sensitivity and specificity
 - Not completely reliable to rule out bacterial meningitis
- Symptoms have a quite a bit of variability, especially with age
- IMPORTANT:** Any patient who presents with symptoms of meningitis should undergo lumbar puncture (LP) for evaluation of CSF



38

Clinical Signs of Meningitis


- Neck stiffness**
- Kernig's sign**
 - Flexing a patient's hip, then extending the knee causes pain at angles less than 135° with the popliteal fossa as the inner angle
- Brudzinski's sign**
 - After passive flexion of the patient's neck, there is flexion of the hips and knees



39

CSF Collection & Transport


- Tube 1: Chemistry/Immunology
- Tube 2: Microbiology
- Tube 3: Hematology
- If only 1 tube: Micro - Heme - Chemistry
- Must be transported to the lab immediately and analyzed within 1 hour
 - CSF glucose levels can drop by 2-3 mg/dL per hour if the sample is at room temperature due to ongoing glycolysis by cells and bacteria
- Do not refrigerate Micro samples!



40

CSF Appearance

- Turbidity, clots (fibrin), blood, and xanthochromia
- Traumatic tap correction
 - For every 1000 RBC introduced through traumatic tap, there is about one WBC and 1 mg/dL protein added
- Xanthochromia
 - If supernatant remains yellow after centrifugation, it indicates older blood (heme breakdown) rather than a fresh traumatic tap



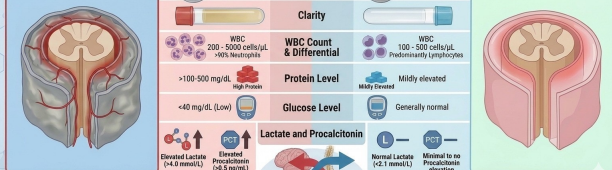
41

LABORATORY PARAMETERS FOR DIFFERENTIATING MENINGITIS

Parameter	BACTERIAL MENINGITIS (Pyogenic)	VIRAL MENINGITIS (Aseptic)
Opening Pressure	Elevated (>250 mm H ₂ O)	Normal (<200 mm H ₂ O)
Clarity	Turbid	Clear
WBC Count & Differential	WBC: 200 - 5000 cells/μL >90% Neutrophils	WBC: 100 - 500 cells/μL Predominantly Lymphocytes
Protein Level	>100-500 mg/dL High Protein	Mildly elevated Alkyl (low)
Glucose Level	<40 mg/dL (Low)	Generally normal
Lactate and Procalcitonin	Elevated Lactate (>4.0 mmol/L) Elevated Procalcitonin (>0.5 ng/mL)	Normal Lactate (<2.0 mmol/L) Minimal to no Procalcitonin elevation

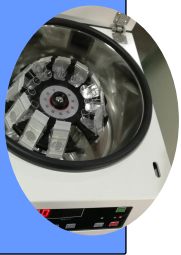
SUMMARY OF DISTINCTIONS

KEY: ◻ Normal ◻ Normal ◻ Elevated ◻ Lactate



42

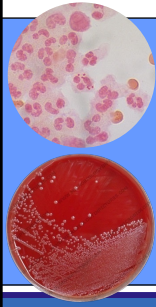
CSF Gram Stain



- Standard centrifugation (3000g) may not concentrate enough bacteria for a visible gram stain
- Cytocentrifugation (1000rpm for 10 min) concentrates the organisms and the WBCs into a small 6mm "button", increasing sensitivity by up to 20%
- Cytocentrifugation can distort morphology of neutrophils

43


CSF Bacterial Culture



- Media:
 - Sheep blood agar,
 - Chocolate agar
 - Enrichment broth (thioglycolate)
- Incubation:
 - 5-10% CO2
 - 35-37 degrees C

44

Rapid Lab Testing



- BIOFIRE® FILMARRAY Meningitis/Encephalitis Panel
 - Rapid (1 hour)
 - Detects the DNA or RNA of 14 of the most common bacterial, viral, and yeast pathogens in CSF
- MALDI-TOF
 - Matrix-assisted laser desorption/ionization time of flight mass spectrometry
 - Requires a growth step to identify bacteria
 - Rapid id from growth on plates
 - Research: direct examination of CSF for bacteria


45

Treatment & Prevention



46


Empiric Therapy



- Mortality rates as high as 45% if antibiotics are administered more than 6 hours after presentation
- Mortality rate of 4-6% in patients in whom antibiotic therapy started promptly
- Administer antibiotics when clinical suspicion is high, ideally as soon as CSF and blood collected
 - Vancomycin PLUS one of the following:
 - Cefazidime
 - Cefepime
 - Meropenem
- Once specific organism identified and susceptibilities performed, antibiotic regimen adjusted to target that organism

47


Targeted Therapy



- Pregnant women with positive **GBS** screen
 - Treat with IV penicillin G antibiotics during labor
- **H. influenzae** (life-threatening condition)
 - Cefotaxime or ceftriaxone
- **N. meningitidis**
 - Penicillin or ceftriaxone
 - Since 2019, CDC has detected penicillin and ciprofloxacin resistant serogroup Y meningococcal isolates in the U.S.
 - In this case, treat with ceftriaxone, fluorquinolone, or meropenem
- **S. pneumoniae:**
 - Penicillin or ampicillin - alternative is 3rd generation cephalosporin
 - If Penicillin (R), then treat with 3rd gen cephalosporins, cefepime (4th gen), or meropenem

48

Chemoprophylaxis




Post-exposure prophylaxis:

- Treatment given to close contacts
- Given within 24 hours of patient's diagnosis
- *H. influenzae* – Rifampin
 - Living in household with one or more unvaccinated or incompletely vaccinated children
- *N. meningitidis* – Ceftriaxone, Ciprofloxacin, or Rifampin
 - Close contact (more than 8 hours) with someone with meningococcal infection
 - Contact with oral secretions with someone with meningococcal infection

49

Chemoprophylaxis




Prevention of Group B strep:

- Screen pregnant females at 35-38 weeks
- If positive for GBS:
 - Treat with IV penicillin G during labor and delivery
- Untreated GBS is associated with:
 - High fatality rate in neonates, birth to 7 days, when mother untreated
 - Permanent neurological damage in neonates

50


Role of Dexamethasone



- Reduces inflammation in CSF caused by bacteriolytic antibiotics, such as 3rd gen cephalosporins and vancomycin
- Given 10-20 minutes prior to or simultaneously with antibiotics
- Associated with lower rates of:
 - Severe hearing loss in children with Hib meningitis
 - Any hearing loss in adults
 - Short-term neurological deficits in adults
 - Mortality in pneumococcal meningitis in adults

51


Conjugate Vaccine



- *H. influenzae* type b, *N. meningitidis*, and *S. pneumoniae*
 - Significant decrease in the incidence of meningitis caused by these pathogens
- Consists of pathogen's polysaccharide Ag bound to a carrier protein that stimulates T-cell dependent processing of the Ag
 - Reduces mucosal colonization by bacteria
 - Produce better T-cell immunity than vaccines that don't bind the polysaccharide Ag to a carrier protein
- Efficacy is affected by emergence or persistence of serotypes that are not included in the vaccine

52

Immunizations



- *S. pneumoniae*:
 - 13-valent polysaccharide-protein conjugate vaccine for infants
 - 23-valent polysaccharide-protein conjugate vaccine for adults >65
- *H. influenzae* type b (Hib)
 - Led to 60% reduction in Hib meningitis cases globally
 - Other serotypes can cause meningitis
- *N. meningitidis*
 - Meningococcal conjugate vaccine
 - Includes capsules from serotypes Y, W-135, C, and A, each conjugated with protein
 - Recombinant protein vaccines for serogroup B are available
 - Given to high-risk children ages 2-10, all children 11-12, and all military recruits and college students

53


ADULT & CHILDHOOD VACCINATION SCHEDULES

<i>H. influenzae</i> type b (Hib)	<i>S. pneumoniae</i> (PCV15 or PCV20)	<i>N. Meningitidis</i>
2 mos. • 1 st dose 4 mos. • 2 nd dose 6 mos. • 3 rd dose (depends on dose series) 12-15 mos. • 3 rd /4 th dose (booster)	Infant/Child (2, 4, 6, 12-15 mos.) } doses Adult (50+ yrs): PCV15*, PCV20*, or PCV21* Adult (65+ yrs): PCV23 - Discuss with physician	11-12 yrs. • MenACWY 16 yrs. • MenACWY booster (MenB for high-risk)

Source: CDC Immunization Regulations (Adapted)

*If never received pneumococcal conjugate vaccine or do not know vaccination history

54



WHO Surveillance of Bacterial Meningitis

- Detect and confirm outbreaks
- Monitor incidence trends and distribution of serotypes
- Estimate disease burden
- Monitor antibiotic resistance
- Monitor circulation and evolution of specific strains
- Estimate impact of meningitis control strategies, particularly vaccination programs

55



Conclusion

Despite remarkable progress, bacterial meningitis remains a much-feared disease worldwide

WHO and global partners developed a global roadmap with the vision to “defeating meningitis by 2030”


Three visionary goals:

1. Elimination of bacterial meningitis epidemics
2. Reduction of cases of vaccine-preventable bacterial meningitis by 50% and deaths by 70%
3. Reduction of disability and improvement of quality of life after meningitis due to any cause

56

**Thank you
&
Happy Medical
Laboratory
Professionals Week!**



TO INFINITY AND BEYOND
FOR OUR PATIENTS!

57

References

- <https://my.clevelandclinic.org/health/articles/22266-meninges>
- <https://asm.org/articles/2020/april/how-pathogens-penetrate-the-blood-brain-barrier>
- <https://www.who.int/news-room/fact-sheets/detail/meningitis>
- <https://www.cdc.gov/meningococcal/vaccines/pteteens-teens.html>
- <https://www.cdc.gov/meningococcal/php/surveillance/index.html>
- <https://www.cdc.gov/vaccines/imz-schedules/adult-easyread.html>
- <https://www.who.int/initiatives/defeating-meningitis-by-2030>
- Hasbun R. (2022). Progress and challenges in bacterial meningitis: a review. *Jama*, 328(2), 2147-2154.
- Prasad N, et al. (2025). The epidemiology of bacterial meningitis in the United States during 2008-2023: an analysis of active, laboratory, population-based, multistate surveillance data. *The Lancet Regional Health-Americas*, 47.
- Mount, H. R., & Boyle, S. D. (2017). Aseptic and bacterial meningitis: Evaluation, treatment, and prevention. *American Family Physician*, 96(5), 314-322. Retrieved from <https://www.proquest.com/scholarly-journals/aseptic-bacterial-meningitis-evaluation-treatment/docview/245423551?se=2>
- (2026). Central nervous system infections. Chin-Hong P, & Joyce E.A., & Karandikar M, & Matlobian M, & Rubio L, & Schwartz B.S., & Levinson W(Eds.), *Levinson's Review of Medical Microbiology & Immunology: A Guide to Clinical Infectious Diseases*, 19th Edition. McGraw Hill. <https://accessmedicine.mhmedical.com/content.aspx?bookid=3847&ionid=306009022>
- (2025). System-based and situational bacterial infections. Bana, D. M., & Taylor, T. A. H. Bana D. M., & Taylor T. A. H. Bana D. M., & Taylor T. A. H. *Walters Kluwer*.
- <https://brs.lwwhealthlibrary.com/content.aspx?bookid=3350&ionid=268696365>
- Fiske C.T., & Bloch K.C. (2018). *Infectious diseases*. Hammer G.D., & McPhee S.J.(Eds.), *Pathophysiology of Disease: An Introduction to Clinical Medicine*, 8e. McGraw-Hill Education. <https://accessmedicine.mhmedical.com/content.aspx?bookid=24658&ionid=198220194>

58