Bacterial Meningitis
From Presentation to Prevention

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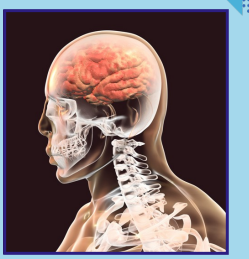

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Objectives

- 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.

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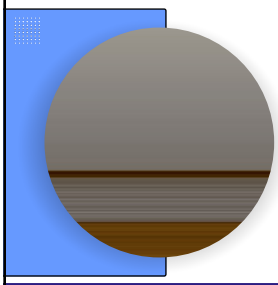

Meningitis

- 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.

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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

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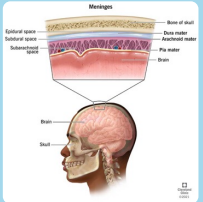

Picture Source: https://my.clevelandclinic.org/health/articles/22266-meninges

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

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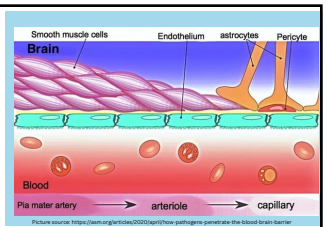
Blood-Brain Barrier

- 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://aem.org/articles/2020/april/how-pathogens-penetrate-the-blood-brain-barrier

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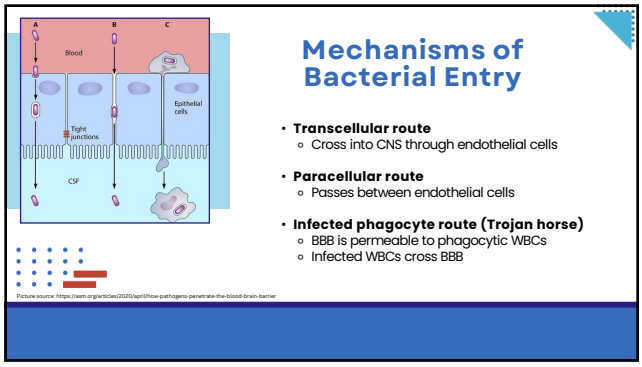
A
B
C
Blood
Epithelial cells
Tight junctions
CSF
Mechanisms of Bacterial Entry
Transcellular route
Cross into CNS through endothelial cells
Paracellular route
Passes between endothelial cells
Infected phagocyte route (Trojan horse)
BBB is permeable to phagocytic WBCs
Infected WBCs cross BBB
Picture source: https://aem.org/articles/2020/april/how-pathogens-penetrate-the-blood-brain-barrier

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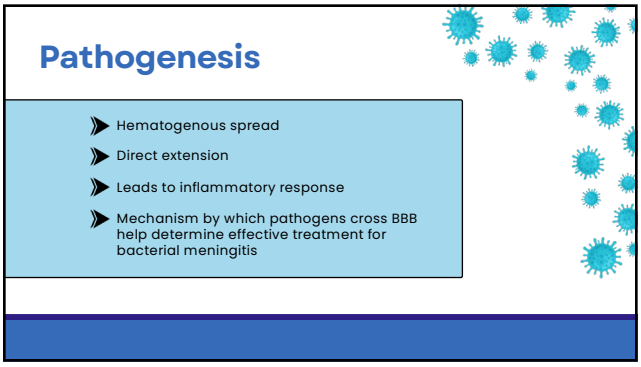
Pathogenesis
Hematogenous spread
Direct extension
Leads to inflammatory response
Mechanism by which pathogens cross BBB help determine effective treatment for bacterial meningitis

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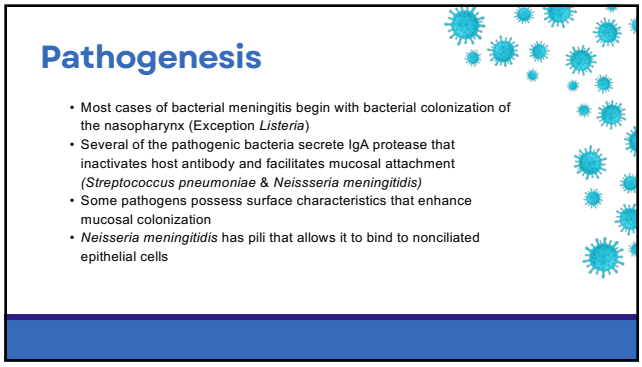
Pathogenesis
Most cases of bacterial meningitis begin with bacterial colonization of the nasopharynx (Exception Listeria)
Several of the pathogenic bacteria secrete IgA protease that inactivates host antibody and facilitates mucosal attachment (Streptococcus pneumoniae & Neissseria meningitidis)
Some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

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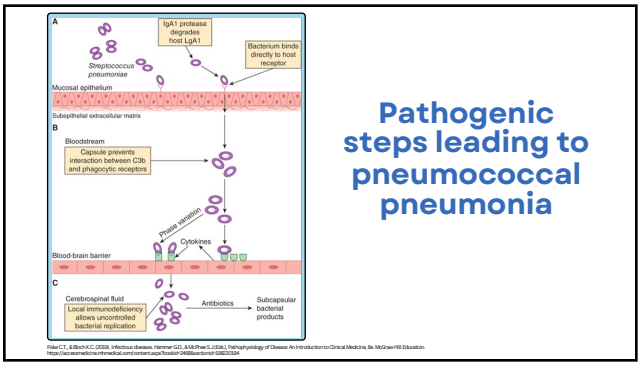
A
IgA1 protease degrades host LgA1
Streptococcus pneumoniae
Bacterium binds directly to host receptor
Mucosal epithelium
Subepithelial extracellular matrix
B
Bloodstream
Capsule prevents interaction between C3b and phagocytic receptors
Phase variation
Cytokines
Blood-brain barrier
C
Cerebrospinal fluid
Local immunodeficiency allows uncontrolled bacterial replication
Antibiotics
Subcapsular bacterial products
Pathogenic steps leading to pneumococcal pneumonia

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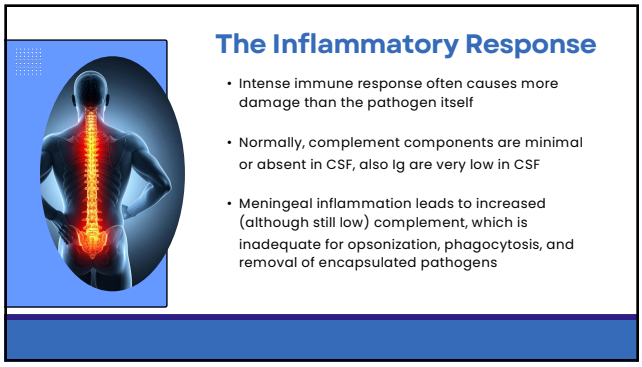
The Inflammatory Response
Intense immune response often causes more damage than the pathogen itself
Normally, complement components are minimal or absent in CSF, also Ig are very low in CSF
Meningeal inflammation leads to increased (although still low) complement, which is inadequate for opsonization,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

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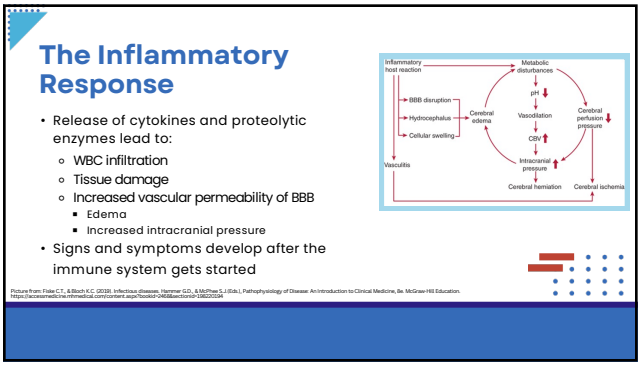
The Inflammatory Response
Release of cytokines and proteolytic enzymes lead to:
WBC infiltration
Tissue damage
Increased vascular permeability of BBB
Edema
Increased intracranial pressure
Signs and symptoms develop after the immune system gets started
Inflammatory host reaction
Metabolic disturbances
pH
BBB disruption
Hydrocephalus
Cellular swelling
Cerebral edema
Vasodilation
Cerebral perfusion pressure
CBV
Intracranial pressure
Vasculitis
Cerebral herniation
Cerebral ischemia

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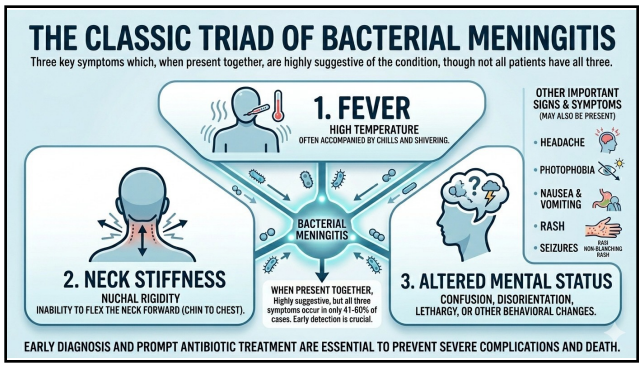

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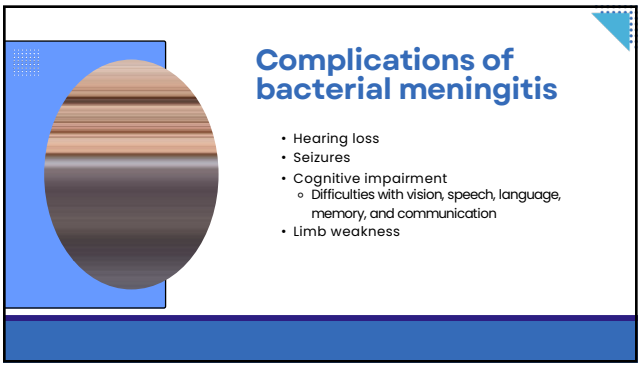

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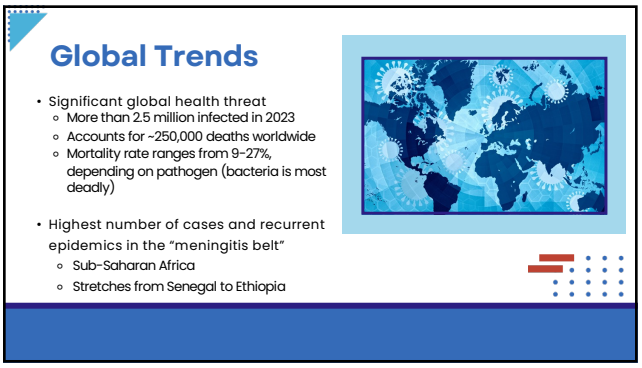

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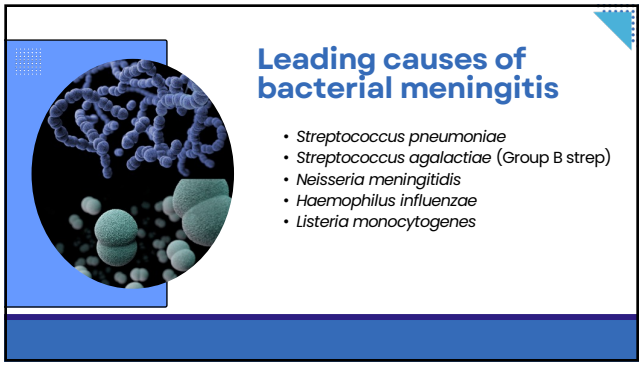

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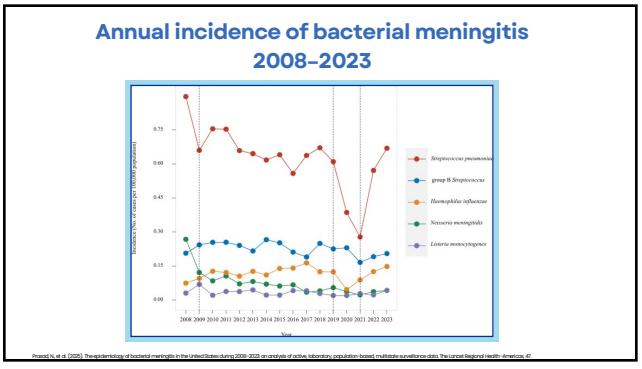

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Other causative agents

- 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*

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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

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

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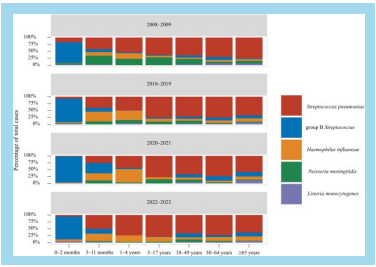
Proportion of bacterial meningitis cases, stratified by epidemiologic period and age group



Prezzati 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.

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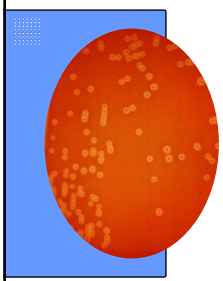

Group B streptococcus (GBS)

- *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

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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.

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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

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Listeria monocytogenes

<u>High risk for meningitis:</u>

- 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

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E. coli K1

- Gram-negative bacilus
- 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

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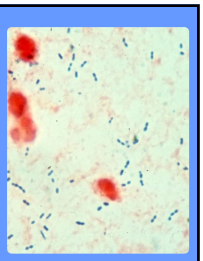
Steptococcus pneumoniae

- 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



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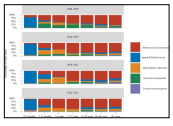
Steptococcus pneumoniae

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



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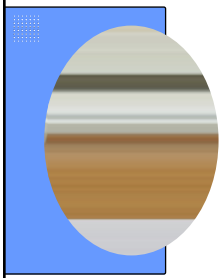
Haemophilus influenzae

- 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



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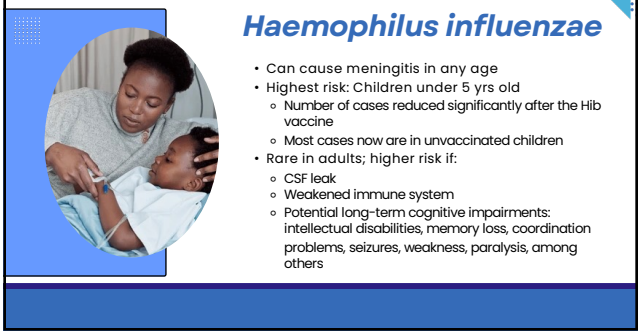

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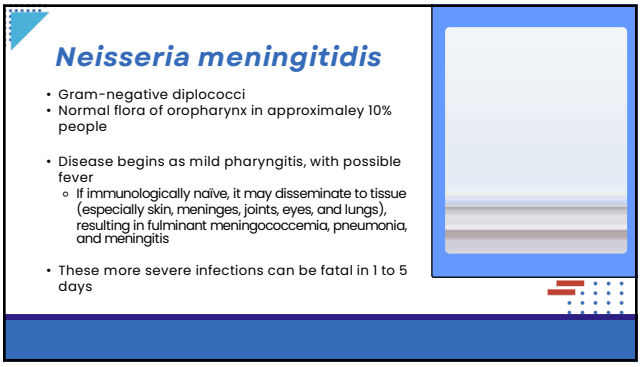

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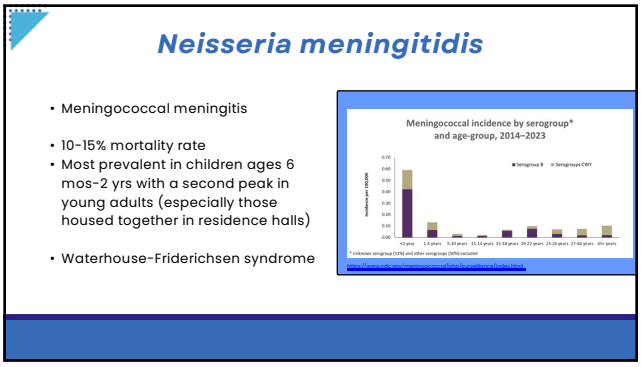

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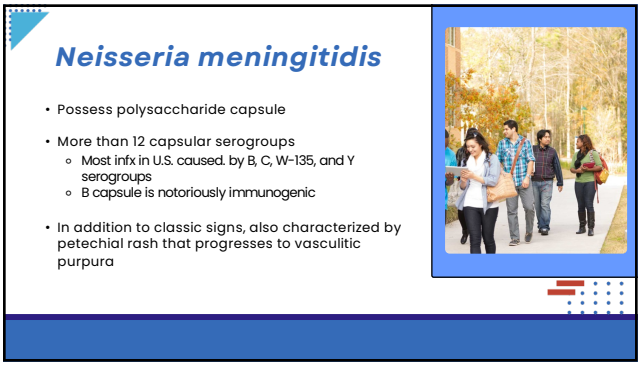

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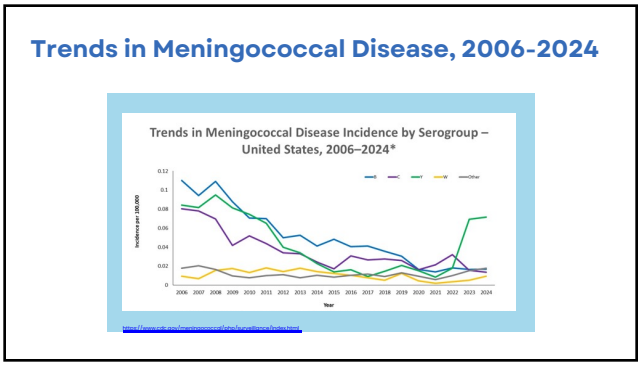

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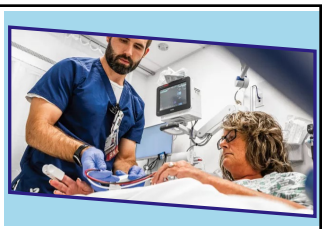
Early detection is imperative

- 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%



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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 but of variability, especially with age
- IMPORTANT: Any patient who presents with symptoms of meningitis should undergo lumbar puncture (LP) for evaluation of CSF

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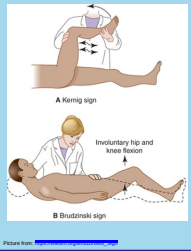
Clinical Signs of Meningitis



- **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

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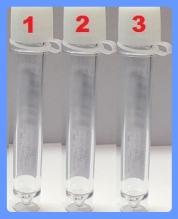
CSF Collection & Transport

- 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!



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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

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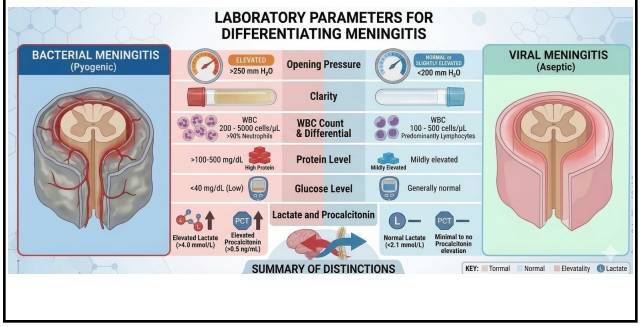

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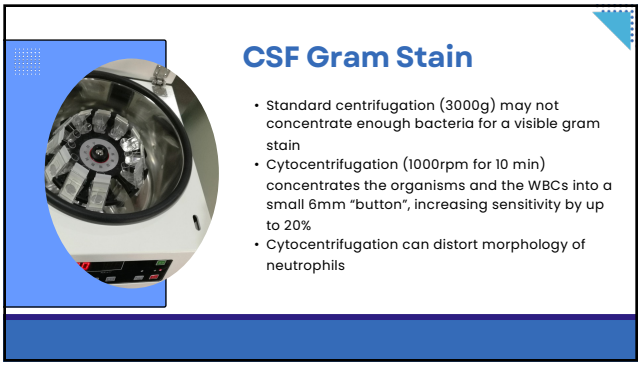

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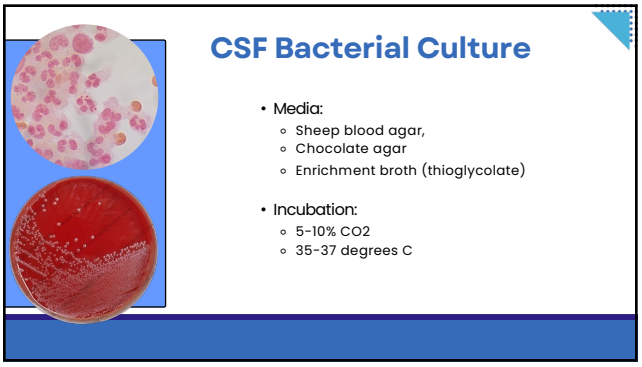

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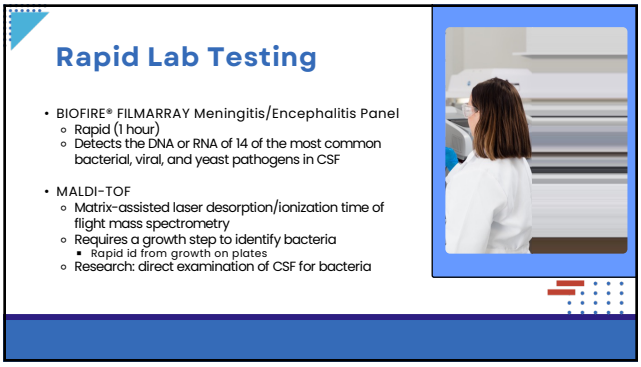

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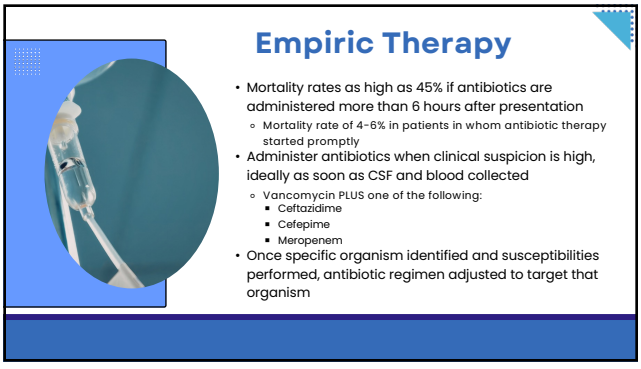

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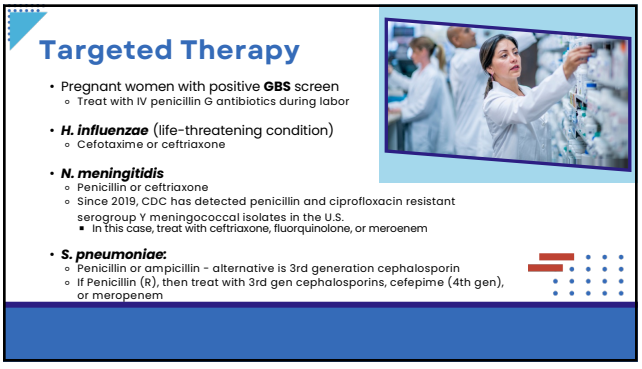

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Chemoprophylaxis

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 menginococcal infection
  - Contact with oral secretions with someone with menginococcal infection

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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

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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

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Conjugate Vaccine

- *H. influenze* 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

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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

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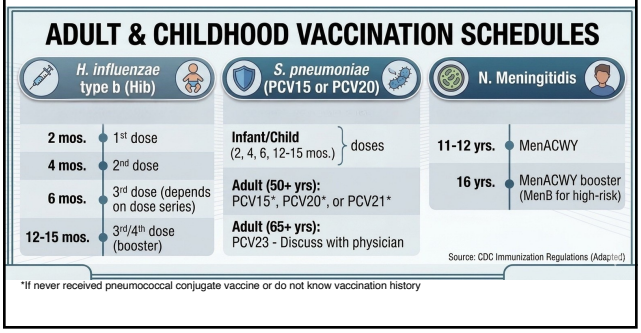

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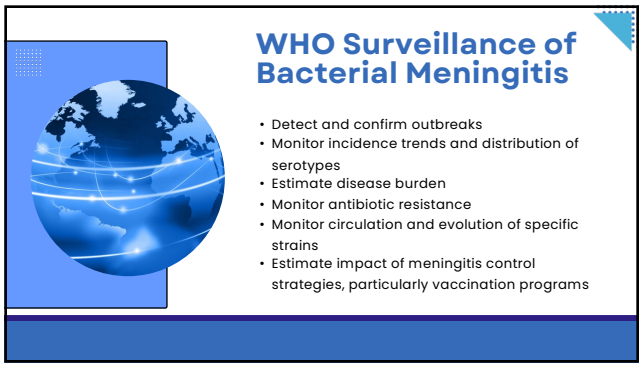
WHO Surveillance of Bacterial Meningitis
• Detect and confirm outbreaks
• Monitor incidence trends and distribution of serotypes
• Estimate disease burden
• Monitor antibiotic resistance
• Monitor circulation and evolution of specific strains
• Estimate impact of meningitis control strategies, particularly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

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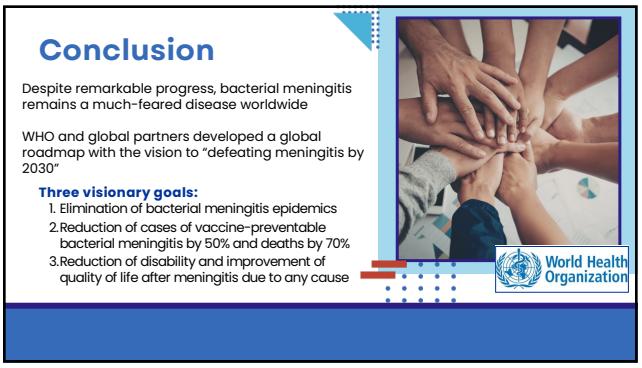
Conclusion
Despite remarkable progress, bacterial meningitis remains a much-feared disease worldwide
WHO and global partners developed a global roadmap with the vision to "defeating meningitis by 2030"
Three visionary goals:
1. Elimination of bacterial meningitis epidemics
2. Reduction of cases of vaccine-preventable bacterial meningitis by 50% and deaths by 70%
3. Reduction of disability and improvement of quality of life after meningitis due to any cause
World Health Organization

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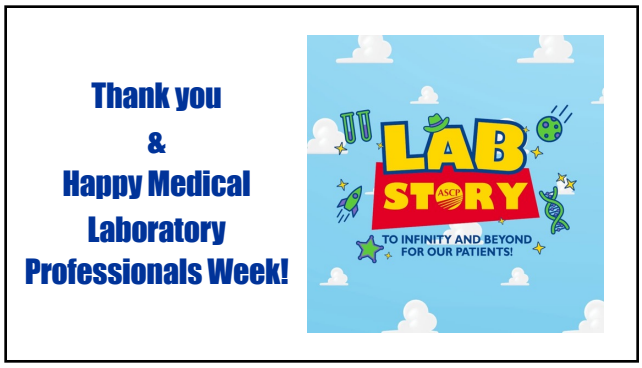
Thank you
&
Happy Medical Laboratory Professionals Week!
LAB STORY
TO INFINITY AND BEYOND FOR OUR PATIENTS!

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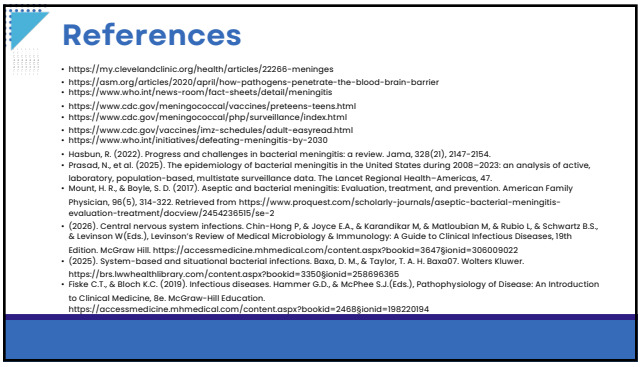
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