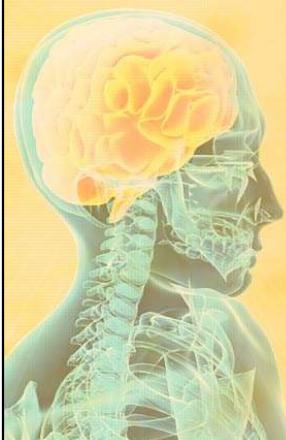


INFECTIONS OF THE CENTRAL NERVOUS SYSTEM PART 1

- Integrated Team Teaching
- Bringing Clinical Aspects and Basic Science together in one lecture series





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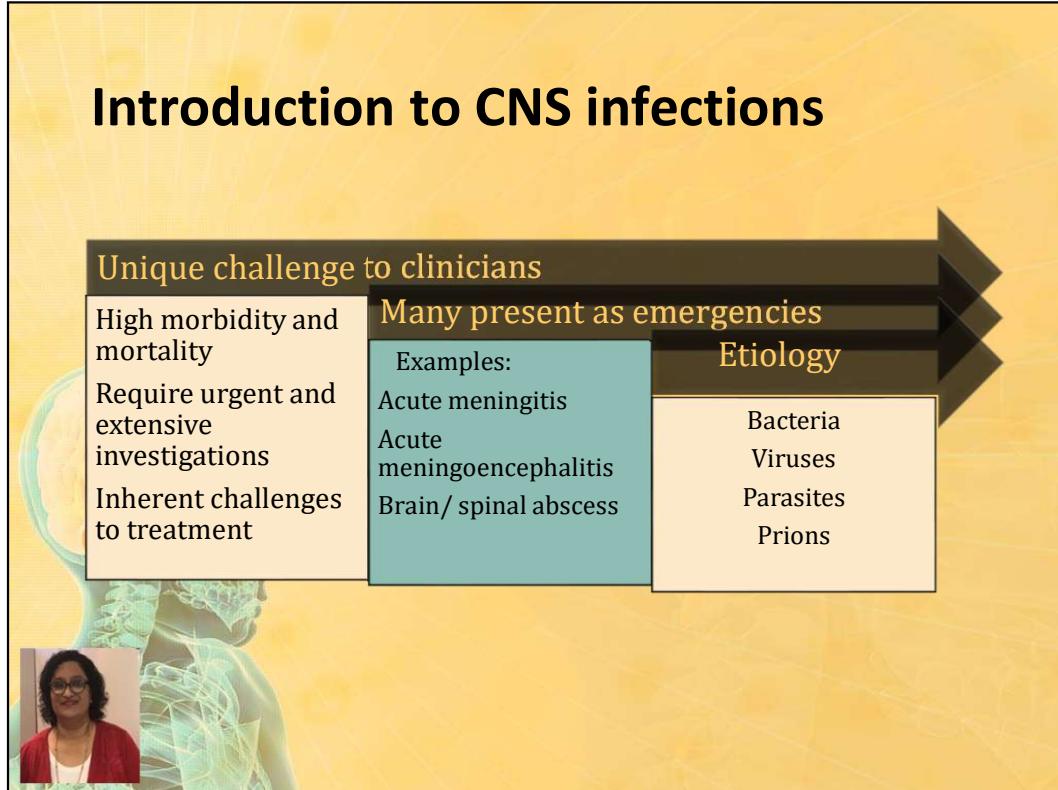
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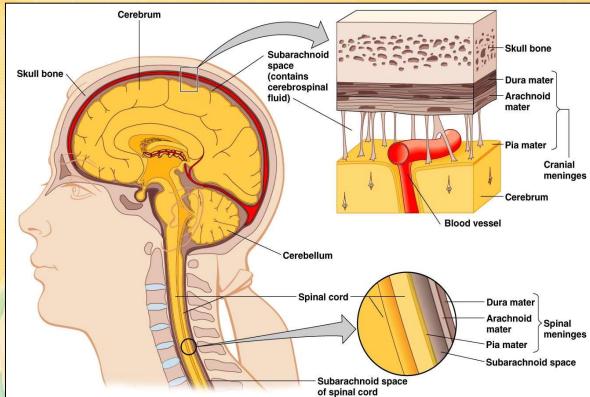
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Introduction to CNS infections



way it manifests is devastating - many are acute
timely, emergent situations
inherent challenges - BBB

Why are CNS infections not very common?



CNS infections are not very common due to the presence of coverings around the brain and spinal cord.

Protection by :

- Bone
- Meninges
- CSF (cerebrospinal fluid)
- Blood-Brain barrier (BBB)

- **The Blood-Brain Barrier** limits the permeability of CNS capillaries and confers a protective effect.
- Restricts the entry of immuno-globulins, complements and antibiotics except those that pass through the BBB.

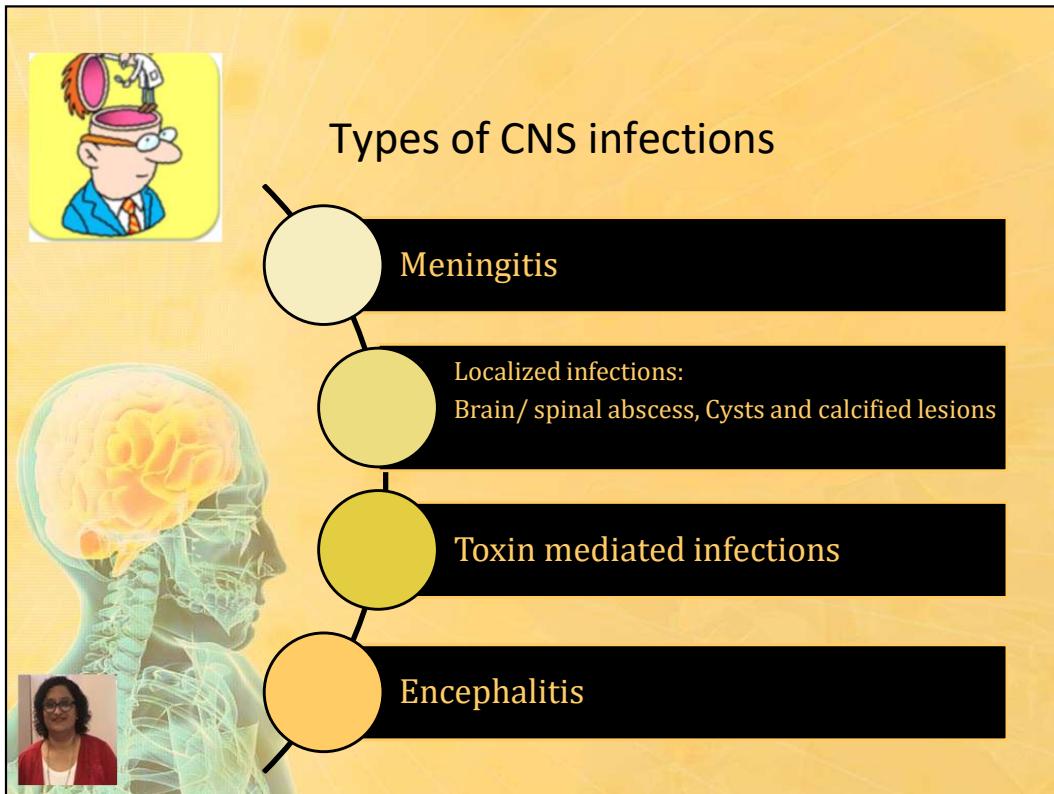


Learning Objectives

1. Enumerate the different types of CNS infections and list the important pathogens involved in these infections.
2. Identify the underlying conditions and routes leading to CNS infections.
3. Classify different types of meningitis based on presentation, causal organisms and age group affected. (Pyogenic or septic; Aseptic; Chronic; Nosocomial meningitis)
4. Recognize different etiologic agents causing acute and chronic meningitis.



Learning Objectives-complete list



LO: Enumerate the different types of CNS infections and list the important pathogens involved in these infections

Meningitis-Inflammation of the meningeal coverings of the brain and spinal cord

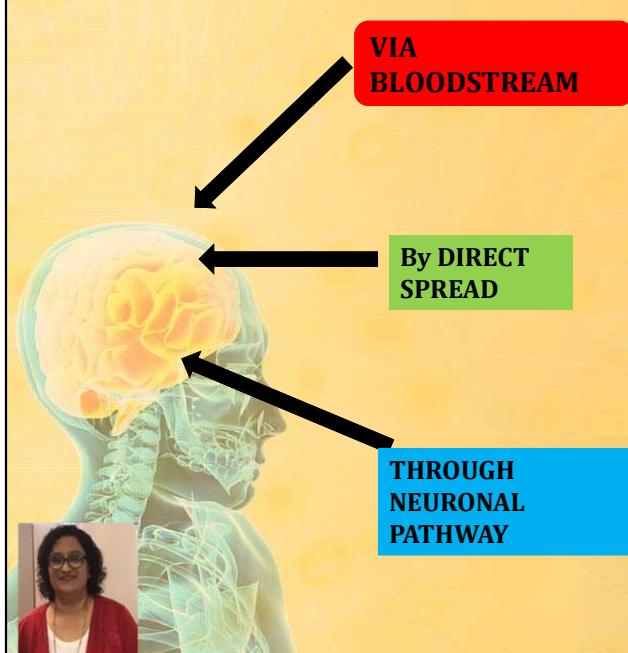
Encephalitis- Inflammation of the brain tissue

Meningoencephalitis-Inflammation of both the brain and meninges

Many of the localized lesions present as intracranial space occupying lesions

[ICSOL - intracranial space occupying lesion](#)

Routes of Infection



Hematogenous spread from

- Nasopharyngeal carriage
- Otitis media, Sinusitis
- Pneumonia
- Skin abscess or cellulitis
- Endocarditis
- GIT infection

Local extension from adjacent structures

- Otitis media, Sinusitis
- Trauma
- Iatrogenic (Surgery/ Shunts)
- Passage through infected birth canal

Invasion via peripheral nerves

- Tetanus
- Botulism
- Reactivation of HSV

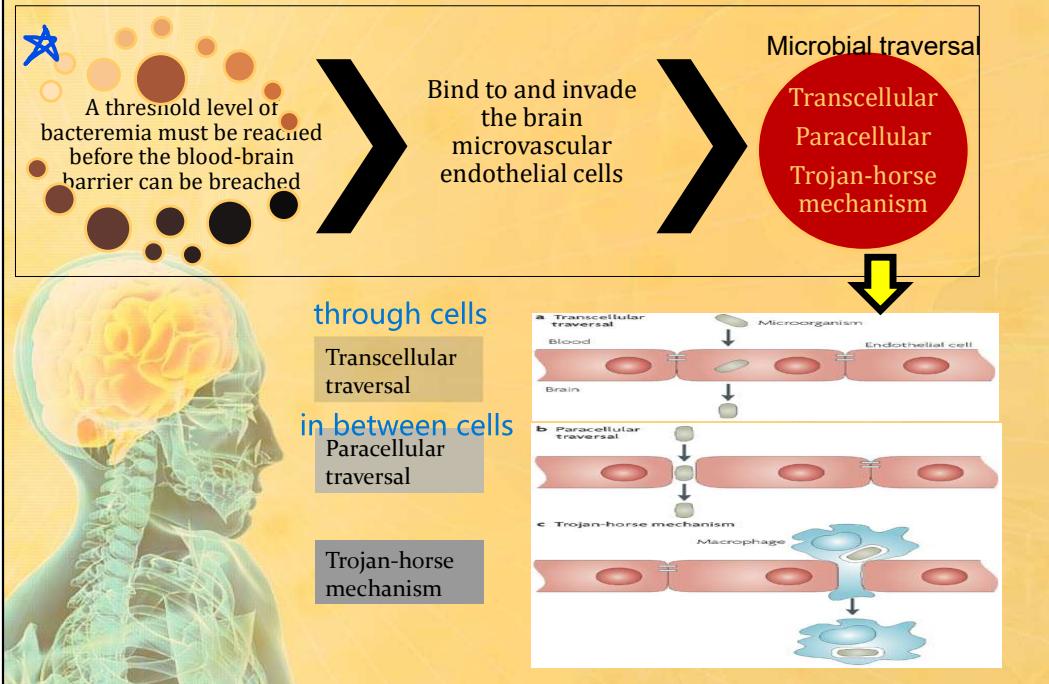
listeria

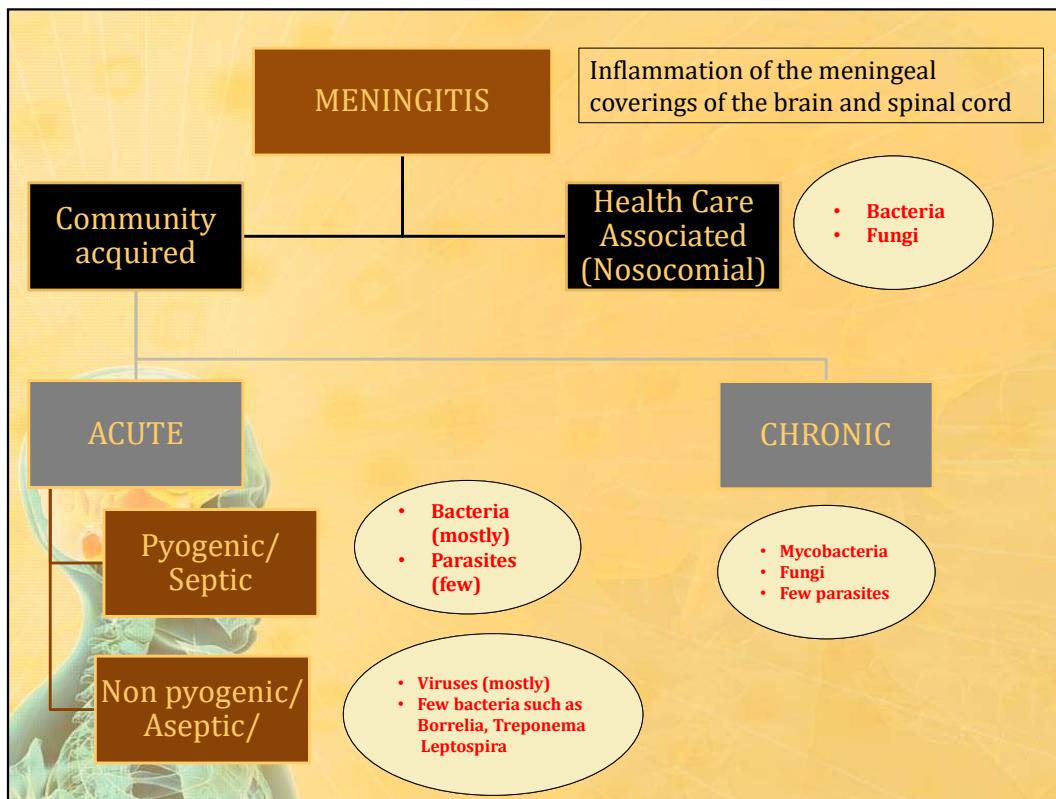
fracture at base of skull

LO: Identify the underlying conditions and routes leading to CNS infections.



Microbial traversal of the blood-brain barrier





LO: Classify different types of meningitis based on presentation, causal organisms and age group affected. (Pyogenic or septic; Aseptic; Chronic; Nosocomial meningitis)

Recognize different etiologic agents causing acute and chronic meningitis.

bacteria that can also cause BLT: Borrelia - lyme, Treponema, Leptospira

many more
that can
cause
infections
among the
age groups

★ Bacterial Meningitis - Most Common Pathogens

Rates of community-acquired infection with specific pathogens are strongly influenced by age

Newborns 1. <i>Streptococcus agalactiae</i> 2. <i>Escherichia coli</i> 3. <i>Listeria monocytogenes</i>	Children 1. <i>Streptococcus pneumoniae</i> 2. <i>Neisseria meningitidis</i> 3. <i>Haemophilus influenzae type b</i>	Adolescents and young adults 1. <i>N. meningitidis</i> 2. <i>S. pneumoniae</i>	Older adults 1. <i>S. pneumoniae</i> 2. <i>N. meningitidis</i> 3. <i>L. monocytogenes</i> 4. <i>Haemophilus influenzae</i>
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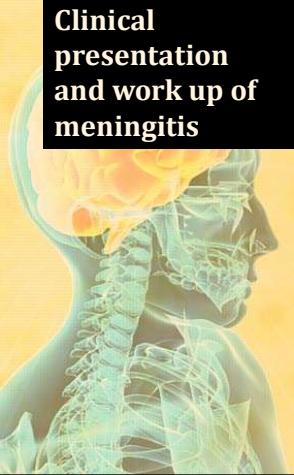
LO: Causal organisms and age group affected.

The agents of neonatal meningitis are usually the pathogens acquired from the mother's vaginal/ GI flora.

In children, the incidence of *H.influenzae* infections has drastically reduced after the introduction of the Hib and pneumococcal conjugate vaccines to the routine childhood immunization schedule in the US. However *H.influenzae* infections continue to be seen in countries where the Hib vaccine is not administered routinely.



Learning Objectives-contd..

- 
- 5. Identify and define the signs and symptoms of meningitis in infants, children and in adults
 - 6. Describe the physical exam findings associated with meningitis (Kernig sign, Brudzinski sign, Papilledema, Nuchal and Spinal rigidity)
 - 7. Formulate a work-up for CNS infections (including appropriate lab and radiographic studies)
 - 8. Name the contraindications for performing a lumbar puncture and possible complications of a lumbar puncture.
 - 9. Differentiate bacterial, viral and tuberculous meningitis based on the CSF examination results

age important bc diff types of organisms

Gather relevant history

1. AGE

2. ONSET

- Sudden onset/Fulminant onset <24 hours (Viral/ Some bacterial)
- Gradual onset and slowly progressive (Fungal/TB)
- Respiratory illness precedes onset by <7 days (50%)

3. SYMPTOMS

Classic Triad (41% cases of bacterial meningitis in adults)

- Neck stiffness
- Altered mental status
- Fever

95% cases presents with 2/4:

- Headache (84%) 100.4
- Fever (74%)
- Neck stiffness (74%)
- Altered mental status (71%)

Other common:

- Nausea (62%)

Symptoms of Meningitis

- Central**
 - Headache
 - Altered mental status
- Ears**
 - Phonophobia
- Eyes**
 - Photophobia
- Neck**
 - Stiffness
- Systemic**
 - High fever
- Trunk, mucus membranes, extremities**
 - (if meningo-coccal infection)
 - Petechiae

men B vaccine - 16 y.o. right before college

some come with rashes

tachycardia infection - septic sign

bacterial looks more sick when they come in

LO: Identify and define the signs and symptoms of meningitis in infants, children and in adults



- For a patient presenting with bacterial meningitis the typical cc may be:
 1. Fever X 1 day
 2. Headache X 2 days
 3. Stiff neck X 1 day
 4. Altered mental status
 5. Tachycardia



Using the information obtained from the history as well as the positive signs from the physical exam, create a problem list (be specific)

neck stiffness - irritation and it swells so get a headache but babies still have fontanelles - fever and irritated and bulging fontanelle is late sign

The infographic features a central image of a baby sitting, with various symptoms listed around it. A small portrait of a woman is in the top right corner.

Meningitis Baby Watch

Symptoms

- Fever
- Irritability
- Lethargy
- Refusal to feed etc.

Signs

- Seizures
- **Bulging Fontanelle**
(late sign in 1/3 neonates)

13

Labels pointing to the baby's body:

- Tense or bulging soft spot
- High temperature
- Very sleepy/staring expression/too sleepy to wake up
- Breathing fast/difficulty breathing
- Extreme shivering
- 'Pin prick' rash/marks or purple bruises anywhere on the body
- Sometimes diarrhoea
- Vomiting/refusing to feed
Irritable when picked up, with a high pitched or moaning cry
- Blotchy skin, getting paler or turning blue
- A stiff body with jerky movements, or else floppy and lifeless
- Cold hands and feet

Is your baby getting worse fast?
Babies can get ill very quickly, so check often.

Kids are different from adults anatomically, physiologically as well as developmentally. So they may present very differently as compared to adults. Also unlike adults, they are unable to tell that they have a headache or stiffness in their neck.

Sign of bulging of the softy spot or fontanelle can be really concerning as a grave sign. It is a late sign of raised intracranial pressure.

It is important to keep in mind that meningitis in very young and very old individuals does not present with these classic symptoms and signs. In elderly people, the onset of meningitis is often more insidious. The earliest symptoms are usually fever and alterations in mental status. Meningeal signs are less commonly reported, and many elderly patients have neck stiffness as a consequence of osteoarthritis, an old cerebrovascular accident, or Parkinson disease. The physician must have a high index of suspicion and must aggressively exclude the possibility of bacterial meningitis in an elderly patient with fever and confusion. In very young patients, neonatal and infant meningitis presents simply as fever and irritability. No history is obtainable, and as a consequence, lumbar puncture should be included in the fever workup of the very young patient. Much fewer - obvious symptoms

- Newborns and Infants
 - Temperature Instability (Hypothermia or Fever)
 - Listlessness
 - Lethargy
 - Irritability
 - High pitched crying
 - Refusal to eat
 - Weak sucking response
 - Diarrhea
 - Vomiting
 - Respiratory distress
 - **Bulging Fontanelle** (late sign in 1/3 neonates)
 - Seizures(40%)
 - Petechiae

don't need to memorize exact age but gets more classic as get older



Signs and Symptoms of Bacterial Meningitis by Age

Table 108-3. Signs and Symptoms of Bacterial Meningitis According to Age

Neonates and Young Infants (0 to 3 Months of Age)	Older Infants (3–24 Months of Age)	Children and Adolescents (2 to 18 Years of Age)
Fever (40% may not have fever, but more have temperature instability)	Fever	Fever (44% may not have fever if older than 6 years)
Lethargy	Lethargy or altered level of consciousness	Lethargy, confusion, coma
Vomiting or poor feeding	Vomiting	Vomiting
Seizure	Seizure	Seizure
Irritability	Irritability	Headache and photophobia
Respiratory distress	Respiratory symptoms (in up to one third)	Respiratory symptoms (in up to one third)
Apnea		Focal neurologic signs (hemiparesis and cranial nerve palsies)
Bulging fontanelle and splitting of the coronal sutures		Papilledema (rarely)
Neck stiffness (rare and late finding, 15% at most)	Neck stiffness	Neck stiffness (~50%)
Petechiae or decreased capillary refill	Petechiae or decreased capillary refill	Kernig/Brudzinski signs +(~50%)
Jaundice in newborns		

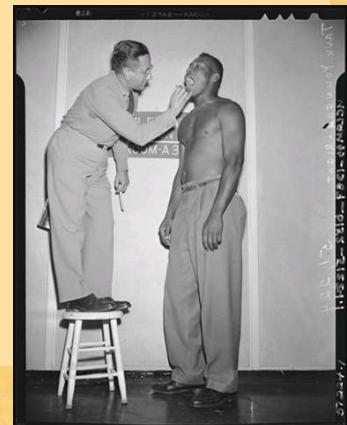


14



Physical Exam

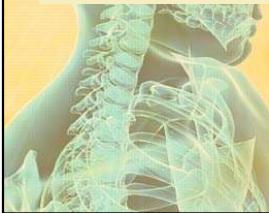
- Physical Exam (collecting signs more specific for CNS Infections)
 - **Full Neurologic Exam** (cranial nerves, mini mental status, tone, DTRs, strength)
 - **Nuchal Rigidity**
 - **Spinal Rigidity**
 - **Kernig's Sign**
 - **Brudzinski's Sign**
 - **Papilledema**
- **Rashes** associated with meningitis





Nuchal rigidity

- Early sign of **meningeal irritation**
- Neck stiffness that prevents flexion
- Attempt to passively flex the patient's neck and **touch their chin to their chest**
 - Triggers pain and muscle spasms
- DDx: subarachnoid hemorrhage, meningitis, late sign of cervical arthritis



Spinal rigidity

- Also, a sign of **meningeal irritation**
- Erector spinae muscle spasm limits spine movement
- Opisthotonus (rigid arched back) may occur



adults: can you flex your neck?

kids: can help them out



Kernig's Sign

- Technique
 - Patient supine
 - **Flex hip and knee to 90 degrees**
 - Hold hip immobile and **extend distal lower extremity**
- Positive Test suggests Meningeal Irritation
 - **Resistance to knee extension**
 - **Pain in hamstrings**



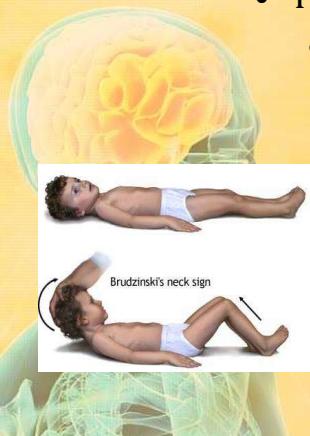


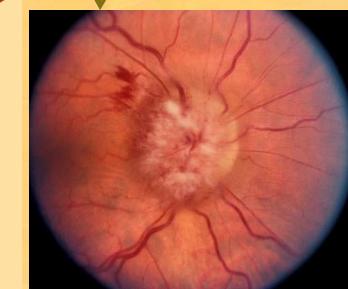
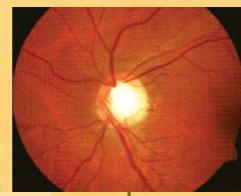
17



Brudzinski's Sign

- Technique
 - Patient supine
 - Immobilize trunk against bed
 - **Flex neck bringing chin to chest**
- Positive Test suggests Meningeal Irritation
 - **Involuntary hip flexion**





increased
intracranial
pressure

Papilledema

Swelling of the optic disk due to
increased intracranial pressure

Causes include:

- Brain tumor or abscess
- Cerebral trauma or hemorrhage
- Meningitis
- Arachnoidal adhesions
- Cavernous or dural sinus thrombosis
- Encephalitis
- Pseudotumor cerebri

19

Very important to assess for papilledema because increased intracranial pressure may alter your decision to do a lumbar puncture.
Usually sharp margins of the disc get blurred with papilledema.



Rashes Associated with Meningitis

- Rash is nonspecific for meningitis
- Petechia and Purpura
 - Meningococcal meningitis



maculopapular - Neisseria
vesicles - hsv



Symptomatic Comparison

	Bacterial Meningitis	Viral Meningitis	Encephalitis
Onset	Rapid (usually 24 hrs)	Can be slower (over 3-4 days)	Rapid
High Fever	Usually	Not always	Usually
Altered Mental Status	Sometimes	Rarely	Usually
Headache	Usually	Usually	Usually
Neck Pain	Usually	Usually	Usually

21



Work-Up for CNS Infections



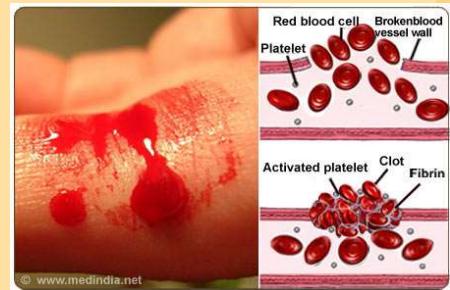
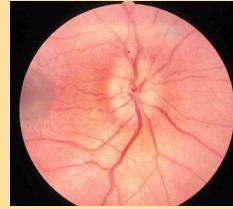
- **Lumbar Puncture with CSF analysis – best initial diagnostic test**
- **CSF culture , PCR**
- **Blood Culture**
- **CBC, CMP (serum glucose), coagulation studies**
- **\pm CT of head**
 - signs of elevated ICP, then CT before LP

22



Lumbar Puncture Contraindications

- **Local infection** at lumbar puncture site
- Suspicion/evidence of **increased ICP**
- Uncorrected **Bleeding Disorder**, severe **thrombocytopenia**, ongoing anticoagulation therapy
- Acute spinal trauma



can also have them sit on a chair and hug a pillow and kneel down to open lower spine

LP Technique

- Patient positioning
- Location
- Spinal needle insertion
- Misdirected Needle hits bone
- Causes difficult lumbar puncture

Cerebrospinal fluid drawn from between two vertebrae

Cerebrospinal fluid is collected from the thecal sac that surrounds the spinal cord

L3 vertebra
L4 vertebra

Needle

24

Spinal cord usually terminates at L1 or L1/L2 in adults (~95% of adults)

- Thecal sac terminates at ~S2
- Intercristal line is an imaginary line that connects the superior border of the iliac crests
- L4/5 interspace is the first interspace caudal to the intercristal line

L3/L4 or L4/L5 where conus medullaris ends to not puncture spinal point needle toward belly button to angle under the SP local lidocaine

make
sure
don't
have
high ICP

LP Complications

- *Relatively common*
 - Post LP **headache**
 - Post LP **back pain**
 - <1/3 of patients, due to local soft tissue trauma
- *Rare*
 - Infection
 - Spinal abscess, meningitis (estimated at 0.2%)
 - Spinal subdural / epidural hematoma
 - Nerve root or spinal cord injury/irritation
 - Transtentorial or cerebellar herniation
 - Complications secondary to low intracranial pressure
 - Hearing loss, CN VI paresis
 - Intracranial subdural hygroma / hematoma



25



Laboratory Diagnosis



Standard CSF Orders



CSF is collected in 4
sterile tubes

Tube 1

CSF Cell Count with Differential

Tube 2

CSF Glucose
CSF Protein

Tube 3

Gram Stain
Culture and sensitivity

Tube 4

Hold for special studies (HSV PCR, California
encephalitis panel, etc)

CSF Cell Count with Differential

26

pressure as get through dura and feel a pop then know when in space bc fluid v
tube 3 to get culture bc going skin to in so to not get skin flora

	White cell count		Biochemistry	
	Neutrophils	Lymphocytes	Protein	Glucose
Bacterial Meningitis	Elevated*	Lower than Neutrophils	Elevated*	Low*
Partially Treated Bacterial Meningitis	Slightly Elevated*	Lower than Neutrophils	Elevated	Low
Viral Meningitis	Slightly Elevated (less than Bacterial Meningitis)*	Elevated*	Usually normal/mod high	Usually normal
Fungal or TB Meningitis	Slightly Elevated (less than Bacterial Meningitis)*	Elevated*	Elevated*	Low*
There should never be RBC in the CSF - a high predominance of RBC without report of a "traumatic tap" and without clearing, is suspicious for HSV encephalitis - Acyclovir should be started in these cases, and the CSF sent for an HSV PCR				27 

bacteria like to eat the glucose and you poop out the protein



Microbiological diagnosis

- Gram stain
- CSF and Blood Culture and Sensitivity
- PCR

Let's learn more about the microbial pathogens that cause meningitis.



gram stain will usually yield nothing



Learning Objectives

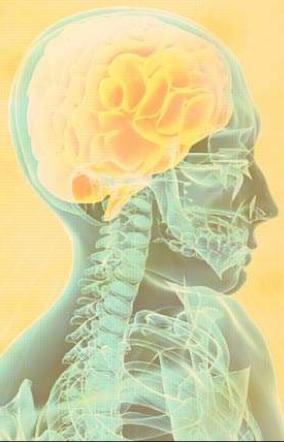


10. For specific pathogens causing meningitis, describe the **morphology, cultural characteristics and identification tests**.
11. Elaborate the **epidemiology, virulence factors and the pathogenesis** involved
12. Describe the **laboratory diagnosis** of meningitis.
13. Enumerate the **antibiotics** for treating these infections.
14. Formulate an appropriate **treatment plan** for meningitis (bacterial and viral)
15. Select the appropriate **preventive measures** against the specific pathogens.



Case studies

- Case 1: Pyogenic meningitis in a neonate
- Case 2: Meningitis in the elderly
- Case 3: Meningitis in a university student
- Case 4: Meningitis in an HIV positive patient



Please correlate the presentation of pyogenic meningitis, the CSF lab test results pointing towards the possibility of pyogenic or septic meningitis (versus aseptic) and features of the microorganisms if described.



Case 1

- A **10-day** infant is brought to the emergency department with the chief complaint of **fever and lethargy**. Mother reports that the infant developed fever a day prior.
- Over the last 2 days, the infant had not been feeding as well as usual, and had not had a wet diaper in over 20 hours. This morning the mother found the infant in bed, very difficult to arouse.
- She carried him limp to the emergency department where the initial vital signs were: **T 103.5F, P 170, RR 70, BP unable to attain**

31

Low urinary output-dehydration

Case 1 contd. Laboratory work up and results



- Blood and CSF samples were sent to the lab.

Blood work up results:

- White blood cell count -**21,600/mm³**. (raised)
- Differential counts: **71% PMNs**, 19% bands, 10% Lymphocytes. (neutrophils increased)

CSF analysis results:

- CSF counts: WBCs- 2340/mm³
- CSF **glucose 15 mg/ dL** and **protein -180mg/dL**. (Glucose \downarrow , Proteins \uparrow)
- CSF culture results:
 - a. Gram stain- **Many inflammatory (pus) cells with few Gram positive cocci in chains**
 - b. CSF culture: Small, **beta hemolytic colonies on Blood agar**, Catalase negative, Bacitracin resistant, CAMP test- positive.

Identification- ***Streptococcus agalactiae*** (*group B beta hemolytic Strep*)

Final Diagnosis: Acute pyogenic meningitis due to Streptococcus agalactiae

- Antibiotic Sensitivity Test- sensitive to ampicillin and gentamicin.

bacitracin thinking group a pyogenes but this is grc
found in sheep too

What type of meningitis was this?



NEONATAL MENINGITIS

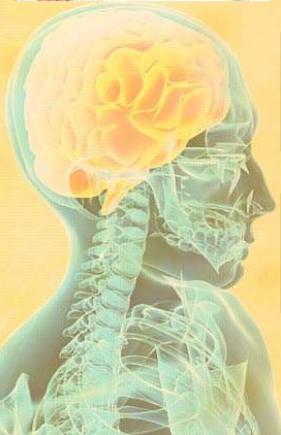


Top 3 etiologic agents

Streptococcus agalactiae



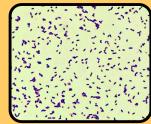
Aka Group B beta hemolytic strep (GBS)



Escherichia coli



Listeria monocytogenes



33

Streptococcus agalactiae

(Group B Streptococcus/ GBS)

#1 cause of neonatal meningitis and septicemia

GPC in short chains

- Group B, β -hemolytic Group B Lancefield antigen
- Catalase (-)
- Bacitracin resistant
- CAMP (+) , Hydrolyzes hippurate

Gram positive cocci in short chains

GpA is sensitive
Gp B is Bacitracin resistant

S. agalactiae *S. aureus* *S. pyogenes*

GBS produce a diffusible heat-stable protein (CAMP factor) that enhances β -hemolysis of *Staphylococcus aureus*

Hippurate hydrolysis- positive
Hippuricase hydrolyses substrate to produce color change

Normal flora of gastrointestinal tract
 ⇒ secondary spread to other sites – vagina

For specific pathogens causing meningitis, describe the morphology, cultural characteristics and identification tests.

Neonatal meningitis – *Escherichia coli*

Imp. features:

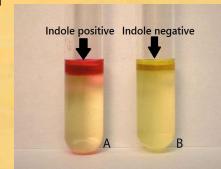
- GNR
- Enterobacteriaceae family
- Lactose fermenter
- Indole (+)
- Motile



Gram negative bacilli



Growth on MacConkey agar shows pink colonies due to lactose fermentation



Normal flora of gastrointestinal tract
⇒ secondary spread to other sites – vagina

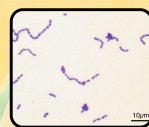


Neonatal Meningitis

Virulence factors and Pathogenesis



Transmission



From colonized mother

- Transmission during birth
- Prolonged labor after membrane rupture associated with ↑ risk of *S. agalactiae* meningitis

Nosocomial transmission

- Contact with hospital staff



Streptococcus agalactiae (GBS)

- Polysaccharide capsule - antiphagocytic
- Hydrolytic enzymes – cell and tissue destruction and systemic spread

Escherichia coli

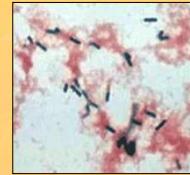
- Mostly due to strains containing the K1 polysaccharide capsule more virulent
- Pili adherence to brain microvascular endothelial cells
- Cytotoxins
- LPS



Listeria monocytogenes



- Small gram-positive bacilli or cocco-bacilli
- Non-sporing, facultative intracellular pathogens
- ★ Grow at 4°C (cold enrichment) -35°C
- Show characteristic tumbling motility at 25 °C.
- Weak beta hemolysis on Blood agar, Catalase positive



Gram positive bacilli

Susceptible populations



65 years and older;
renal transplant patients

- Reservoir: Animal gut/ genital tract
- Source of infection: Unpasteurized milk, deli meats, coleslaw, cheese, refrigerated foods.
- Several outbreaks reported.
- Modes of transmission:
 - Foodborne- pregnant women get infected by this route
 - Vertical: Across the placenta- fetus gets infected
 - Perinatal transmission- new-born gets infected

What foods are risky?

When it comes to *Listeria*, some foods are more risky than others. Meet some of the other foods where *Listeria* is known to hide.



Raw Sprouts



Raw Milk
(unpasteurized)

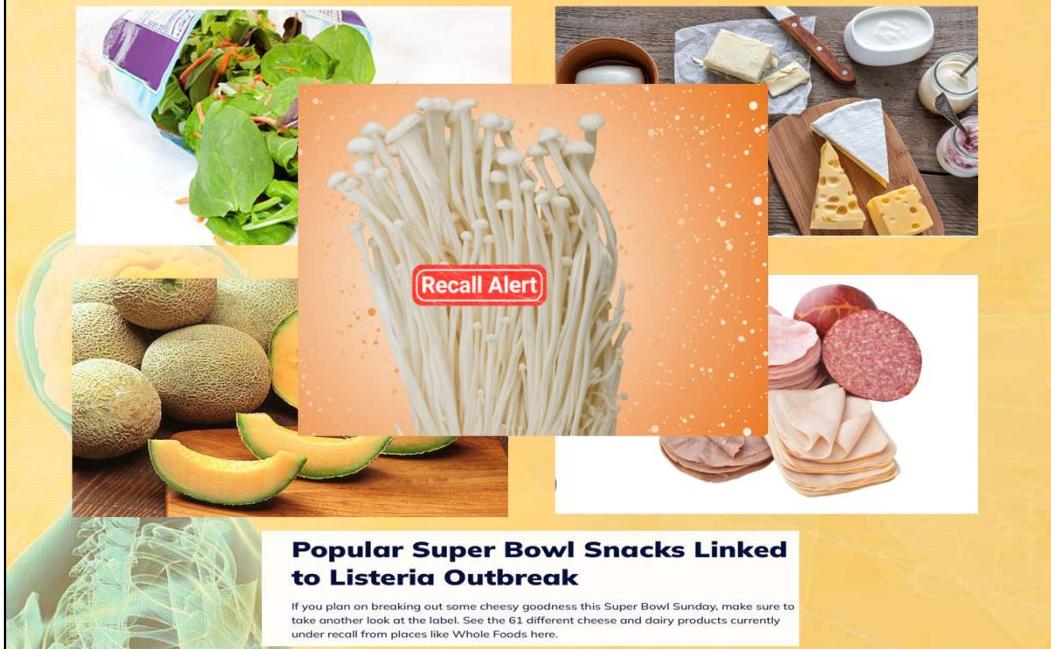


Soft Cheeses

Deli Meats and Hot Dogs
(cold, not heated)

Smoked Seafood

Per the CDC, outbreaks have been linked to greens, sprouts, unpasteurized cheese, milk, deli meats, cantaloupes, enochi mushrooms!



Listeria monocytogenes: Clinical presentation



Pregnant woman with Listeriosis (fever and chills)



Neonatal
disease



Early onset disease-within one week of exposure
Granulomatosis infantiseptica: Disseminated granulomas, severe infection resulting in death



OR

Late onset-2-3 weeks after birth due to fecal exposure: **Neonatal sepsis, Neonatal meningitis**

In immunocompromised patients:

- Septicemia and meningitis
- **Most common cause of meningitis in renal transplant patients**



L. monocytogenes - Pathogenesis and Virulence

Attach to host cell receptors like Enterocytes, M cells, phagocytes etc.



1. Internalins

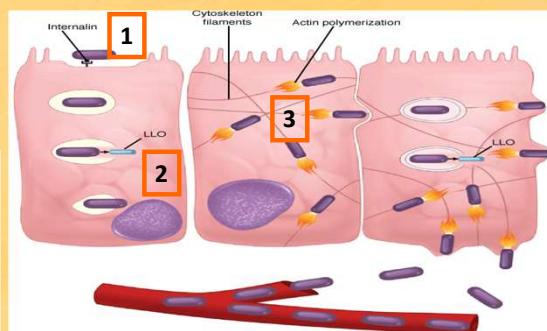
attachment and entry into nonphagocytic cells

2. Listeriolysin O

β -hemolysin (pore-forming exotoxin) allowing escape from phagosome into cytoplasm

3. ActA

actin polymerization \rightarrow motile, leaves comet tails (moves from one cell to another and avoids antibody-mediated immune response)



Source: Ryan KJ, Ray CG; Sherrie's Medical Microbiology, 5th Edition; www.ncbi.nlm.nih.gov
Copyright © 2004, Lippincott Williams & Wilkins Company, Inc. All rights reserved.
Listeriosis, cellular view. (Left) *Listeria monocytogenes* internalin mediates attachment to an enterocyte and enters in an endocytotic vacuole. Listeriolysin O (LLO) lyses the vacuole and the organism escapes to the cytoplasm. (Middle) The cytoskeleton of the host cell is hijacked by ActA, which triggers actin polymerization and forms comet tails that allow the bacterium to move from one cell to another. (Right) The bacterium invades a neighboring cell and forms a new endocytotic vacuole, which LLO again lyses. The process continues with escape to the submucosa and bloodstream invasion.

CMI is needed for resolution of Listeria infection





Neonatal meningitis – laboratory Diagnosis

- **CSF analysis** - decreased CSF glucose, elevated CSF protein, and pleocytosis
- **CSF grams stain and culture and blood cultures**- positive for the suspected pathogen.

E.coli/ Gp B strep/ Listeria identified

- **Antibiotic susceptibility test**
- **Bacterial cultures from mother's vaginal/ rectal swabs for GBS**

Rapid tests:

Latex particle agglutination

- identification of GBS antigen in urine or in CSF/ E.coli in CSF

Rapid screening should supplement, **not replace**, gram stain and culture

PCR

sensitive and specific

Neonatal Bacterial Meningitis Treatment & Prevention

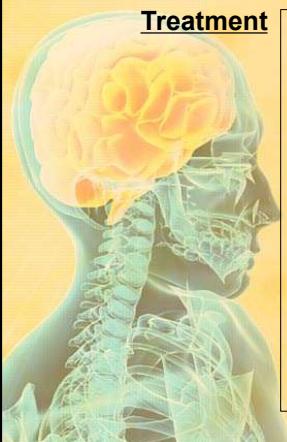


Prevention



- Screen the mother for GBS at 35-37 weeks
- If swab cultures are positive, intrapartum prophylaxis with IV Penicillin G/ Ampicillin if positive
- Pregnant women should avoid deli meats and unpasteurized milk and cheese etc.

Treatment



Rapidly progressive, hence empiric antibiotics therapy initiated immediately. Later adjusted based on culture results, if needed. Duration of therapy- 14-21 days.

Coverage for mainly GBS, E.coli, Listeria

Ampicillin(covers *GBS and Listeria*) +
Cefotaxime(for *E.coli or other gram- negative bacteria*) or
Ampicillin +Gentamicin(effective against GNB)
* For late onset meningitis(8-28days), add
Vancomycin(if MRSA is a concern in the nosocomial setting)

42

Note: Cefotaxime is often preferred over Gentamicin for meningitis because of its better penetration into the cerebrospinal fluid (CSF).

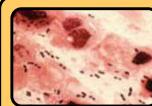
Vancomycin (added if MRSA is a concern or in healthcare-associated infections)

Supportive Care

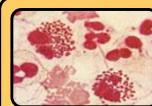
- **Monitoring:** Regular monitoring of renal function, blood counts, and serum drug levels (especially for Gentamicin and Vancomycin) to avoid toxicity.
- **Adjuvant Therapy:** Use of corticosteroids is not generally recommended in neonatal meningitis due to lack of clear benefit in this age group.

Source: UpToDate

Important causes of pyogenic meningitis (children and adults and elderly)



Streptococcus pneumoniae



Neisseria meningitidis



Haemophilus influenzae



Listeria-in pregnant/ elderly
and immunocompromised

Community-acquired disease is associated with four major pathogens:

S. pneumoniae is the most common. Meningitis follows bacteremia from ear, sinus, or lung infection. Also associated with chronic leaks of CSF.

N. meningitidis begins with colonization of the nasopharynx. Sporadic cases are often associated with terminal complement defects.

Epidemics occur in crowded environments such as dormitories and military training camps.

L. monocytogenes occurs in neonates, pregnant women, and immunocompromised patients. It is contracted by eating contaminated refrigerated foods.

H. influenzae was the most common form of meningitis in children. Following widespread administration of the *H. influenzae* B vaccine, it is now rare.



Case 2

- A 70-yr old man living at an old age home developed fever and headache of two days duration. He was rushed to the ER as he vomited 5 times and became weak and drowsy.
- Significant history: Chronic smoker, had a discharging ear infection earlier in the week.
- On physical examination , temperature - 40 °C (104 °F) , respiratory rate -20/min, Heart rate-140 beats/ min and blood pressure - 140/100 mm Hg.
- Neck was stiff with both Kernig and Brudzinski signs positive. Coarse diffuse rhonchi were evident through out the chest. No skin lesions were seen.
- Neurological examination: No cranial nerve abnormalities, symmetrical reflexes, all limbs could be moved.
- Lab work up: Peripheral WBC count: 19,500/mm³, 75% polymorphs, 15% lymphocytes
- LP done for CSF analysis: WBC count- 9500/mm³,protein 970 mg/dl, glucose 25mg/dl.
- Gram stain and the culture report awaited..

What is your diagnosis?

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What is your diagnosis?

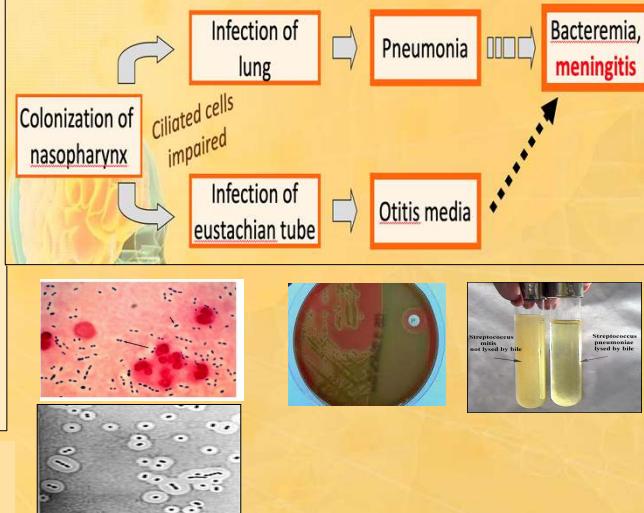
Streptococcus pneumoniae-

★ characteristics and pathogenesis



- Microscopy: Gram positive cocci in pairs.
- Culture: α hemolytic, Optochin sensitive and Bile soluble.
- Virulence factors:
 - Capsule- antiphagocytic
 - IgA protease – facilitates mucosal colonization and invasion
 - Pneumolysin- forms pores and causes cytolysis
 - Teichoic acid, peptidoglycan-induce inflammation

The outcome of colonization depends on the virulence of the specific serotype and on the host immune system



recap from IS-CVRR- RTI lecture

Demonstration

By Quellung reaction, India Ink.

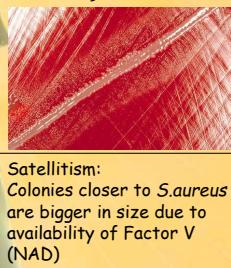
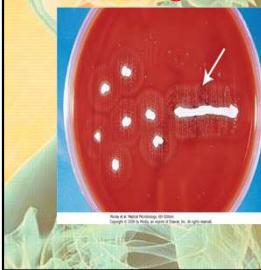
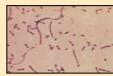
By Rapid test-CSF: Latex particle agglutination for capsular antigen

Haemophilus influenzae



recap from IS-CVRR- RTI lecture

- Encapsulated Gram negative pleomorphic bacilli.
- Typing based on capsule polysaccharide : a-f
- Type b (Hib) [with PRP/polyribitol phosphate] is clinically most virulent
- Others: nontypeable strains : NTHi
- Growth on Chocolate agar or Blood agar with *S. aureus*
- Satellitism: dependency on factor V and X demonstrated by growth on Blood agar with *S.aureus*)



Satellitism:
Colonies closer to *S.aureus* are bigger in size due to availability of Factor V (NAD)

Virulence factors:

- Pili – binding to epithelial cells
- IgA protease – mucosal colonization
- Polysaccharide capsule type-b = polyribitol phosphate (PRP), anti-phagocytic
- Endotoxin (LPS) – inflammation

Colonization of nasopharynx

↓
Invasion into deeper tissues

↓
Bacteremia

↓
Spread to CNS

H. Influenzae need X(Haemin) and V(NAD) for their growth. Chocolate agar provides both Factors X and V. Blood agar has X factor but not V factor as this needs to be released from the intact RBCs.

S.aureus on Blood agar releases Factor V and hence enhances growth of H.influenzae streaked in the vicinity.



H. influenzae type-b – Epidemiology, Diagnosis and Prevention



People at risk:

- unvaccinated young children(3 mo-2 yrs)
- Sickle cell anemics/Splenectomized patients
- HIV (+) patients
- Elderly
- Alaska natives

Diagnosis:

- Capsular antigen detection by latex particle agglutination
- CSF Microscopy and culture
- PCR

- In the prevaccine era, *H.influenzae* was the commonest cause of meningitis in children.
- Now seen in unvaccinated children (3mo-2yrs)
- Newborns are protected via maternal antibodies
- Unvaccinated children eventually acquire natural immunity

Prevention

- Conjugated polysaccharide-protein vaccine
- Rifampin to close contacts prevents nasopharyngeal colonization

- see Bacterial Respiratory Infections lecture -

Prior to the routine use of Hib conjugate vaccines in infants, invasive Hib was the leading cause of bacterial meningitis in children; 85 percent of these infections occurred in children under five years of age



Case 3

- A 23-yr-old college student from Temple University, apparently in a good state of health, woke up with a severe, throbbing headache and fever.
- His dorm partner found him toxic and drowsy but well oriented. He rushed him to the nearby health center where the attending physician came up with the following findings on a detailed examination:
- His temperature was 39.2°C (102.5°F), heart rate was 130 beats / min and B.P was 100/58 mmHg.
- There was a purpuric rash on the trunk, legs and wrists. This did not blanch on pressure. He had prominent neck rigidity.
- A lumbar puncture was performed, and the CSF analysis showed an increase in neutrophil counts and decreased CSF glucose and an increase in the CSF proteins.

Lab findings:

- CSF analysis- Elevated leukocyte count(mostly polymorphs)
- CSF glucose-lowered
- CSF proteins-increased
- Gram stain- pus cells with Gram negative diplococci.
- Culture- Gram negative cocci isolated, Oxidase positive, oxidize glucose and maltose
- Identification- *Neisseria meningitidis*



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- There was a **purpuric rash** on the trunk, legs and wrists. This **did not blanch on pressure**. He had **prominent neck rigidity**.
- A lumbar puncture was performed, and the CSF analysis , culture and sensitivity tests were ordered.

Lab findings:

- **CSF analysis-** Elevated leukocyte count(mostly polymorphs)
- **CSF glucose-lowered**
- **CSF proteins-increased**
- **Gram stain-** pus cells with Gram negative diplococci.
- **Culture-** Gram negative cocci isolated, Oxidase positive, oxidize glucose and maltose
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Outbreak News Today

BREAKING Karachi: 11 Naegleria fowleri deaths in 2019 through July according to Pakistan media

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Yale student hospitalized with probable meningococcal meningitis

by ROBERT HERRIMAN

February 7, 2015 | [US News](#) | 3 Comments

GET A FREE ESTIMATE

The New Haven, CT school is the latest institution of higher learning in recent weeks to report on a student being treated for meningitis. According to Yale University, a Yale College student was admitted to Yale-New Haven Hospital with probable bacterial meningitis (meningococcal disease).

In November 2013, in response to an outbreak of B-serotype meningitis on the campus of Princeton University, the head of CDC authorized emergency use of Bexsero (being used in Europe) and this was given FDA approval in 2015.



Meningococcal Meningitis-Epidemiology

Outbreaks in university dormitories, military barracks(crowded conditions)

North America

- Leading cause of meningitis(2-18 years)
- Most infections are by serogroups B, C and Y.
- Serogroup B -most dangerous.
- Usual vaccine ACWY does not protect against meningitis B. Vaccine against Men B became available from 2015 in the US.



Global epidemiology

- Highest incidence is in Sub-Saharan Africa
- The Meningitis Belt of Africa: Senegal to Ethiopia
- Saudi Arabia requires international Haj and Umrah pilgrims to take these vaccines.



Peak incidence in first year of life, second peak in adolescents and young adults (15-25 yrs.)

Carriage rate increases in winter and spring.

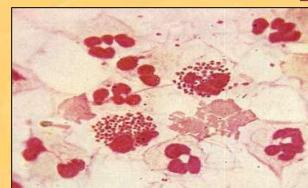
Although the Meningococcal polysaccharide (MPSV4) and conjugate vaccines(MCV4) were introduced much earlier in 1978 and 2005 respectively, the Serogroup B vaccines(Trumenba and Bexsero) were introduced only in 2015!

***Neisseria meningitidis*-characteristics**



Morphology and Growth

- Gram negative diplococci arranged in pairs, intracellular, non-motile and non-sporing.
- Polysaccharide capsule: Anti-phagocytic and is the basis for grouping into several sero-groups such as A, B, C, W-135, Y)
- Outer membrane contains lipo-oligosaccharide (LOS) instead of lipo-polysaccharide(LPS)
- Adhesins : PILI, Outer Membrane Proteins



CSF grams stain showing inflammatory cells with Gram negative diplococci

Fastidious, grow on enriched media/ selective media with added CO₂. Chocolate agar, Thayer Martin agar.

Biochemical reactions:

- a. Catalase positive
- b. Oxidase test +
- c. Oxidize sugars like Glucose and Maltose with acid only(*N. gonorrhoeae* are only glucose utilizers)



Chocolate agar/ Thayer Martin medium with colonies of meningococci



Virulence factors and Pathogenesis

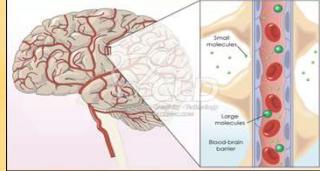
Inhalation of droplet nuclei containing *N. meningitidis*



Attachment to and interaction with the nasopharyngeal epithelium via adhesins like pili

Penetrates the cribriform fossa and enters CNS or Passes through the mucosa and entry into bloodstream and enter CNS

Bacterial meningitis



Meningococcemia and meningococcal sepsis



Imp. Virulence factors

★ Pili
Endotoxin
Lipoooligosaccharides (LOS) produce diffuse vascular endothelium damage, vessel wall inflammation → leaky capillaries



Terminal complement deficiency of C5-9 predisposes for infection and for recurrent attacks

A case of purpura fulminans

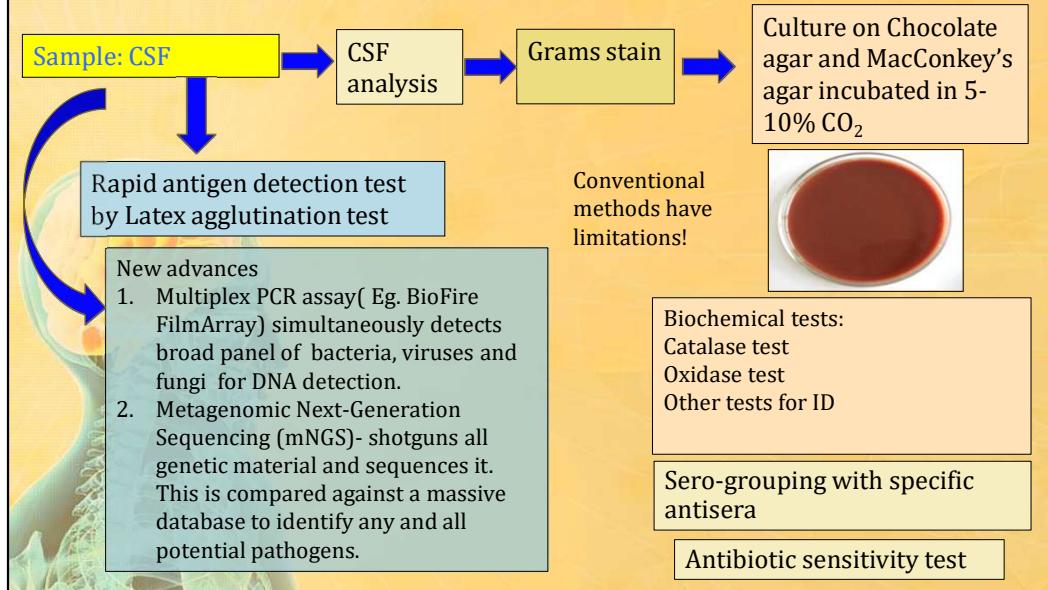
Complication of severe infection = Waterhouse-Friderichsen syndrome (DIC, shock, adrenal gland destruction due to hemorrhagic adrenalitis)



A comparison of CSF findings in different types of meningitis

	Cells/ul	Pressure (mm H ₂ O)	Macroscopy / appearance	Glucose (mg/dl)	Proteins (mg/dl)	Microscopy
Normal CSF	< 5 lymphocytes	70-180	Clear	40-80	15-45	Few cells, no organisms
Pyogenic meningitis	200-20000 Mainly Neutrophils	High >180	Turbid	Low <45	High	Many inflammatory cells, Bacteria+ Culture +
Aseptic meningitis	100-1000 Mainly mononuclear	Slightly High	Clear	Normal	Moderately High	Cells + No organisms seen
Chronic meningitis	100-1000 Mainly lymphocytes	Moderately High	Sometimes, Cob -web appearance in TB meningitis	Low	High	Cells+ AFB+ or India Ink +

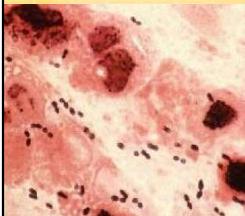
Laboratory Diagnosis-steps



- mNGS-unlike PCR panels that look for a pre-defined list of pathogens, mNGS "shotguns" all genetic material in a sample (CSF, for example) and then sequences it. mNGS can detect rare or unexpected pathogens, providing an "unbiased" approach to diagnosis. It has been shown to identify pathogens that were missed by conventional testing, leading to improved outcomes in some challenging/ perplexing cases.
- Future directions: potential role of AI in analyzing complex sequencing data from mNGS to quickly identify pathogens and predict antimicrobial resistance.

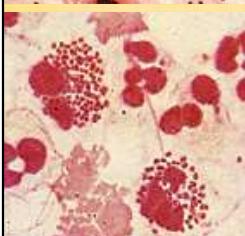


Gram stain and culture of CSF



S. pneumoniae

- GPC in pairs or chain + neutrophils
 - α -hemolytic on blood agar
 - optimal growth with 5% CO₂



N. meningitidis

- GNDC outside and within neutrophils
 - growth on chocolate agar
 - optimal growth with 5% CO₂



H. influenzae type-b

- GNCB + neutrophils
 - chocolate agar – provides both X & V factors
 - optimal growth with 5% CO₂



GNDC= Gram negative diplococci

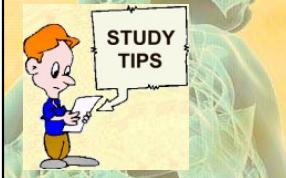
GNCB= Gram negative coccobacilli



Virulence Factor Comparison

Meningitis pathogens in children and young adults
Colonizing nasopharynx, spread by respiratory droplets

Factor	<i>S. pneumoniae</i>	<i>N. meningitidis</i>	<i>H. Influenzae b</i>
IgA protease	✓	✓	✓
Capsule	✓	✓	✓
LPS/ LOS	---	✓	✓
Pneumolysin	✓	---	---



58

Treatment of Meningitis – ASAP!



Prognosis worsens with delay in treatment.

Can lead to mortality and morbidity in 10-20% of the cases of bacterial meningitis.

- Case fatality rate (esp. if there is meningococcaemia/ sepsis)
- Intellectual disability, Learning disabilities
- Hearing loss

Lumbar puncture + blood culture STAT



Empiric therapy + dexamethasone ASAP

If suspect increased ICP,
Get blood cultures STAT -->
empiric therapy +dexamethasone ASAP --> CT scan --> Lumbar puncture

- Bacterial meningitis = **rapidly progressive**
- Requires **immediate** initiation of appropriate antibiotics.
- Choice of drugs is based upon ability to penetrate the Blood-Brain Barrier.
- Which bacteria are we worried about in adults?
 - **S. pneumo, N. meningitidis, H. flu**
 - **Vancomycin & 3rd generation cephalosporin (Ceftriaxone)**

59

Approximately 50 to 90 percent of patients with bacterial meningitis have positive blood cultures

Bacterial Meningitis Prevention

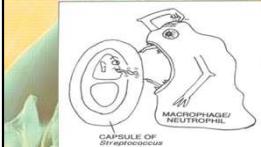
Immediate Prophylaxis-antimicrobial chemoprophylaxis
for close contacts: **Rifampin**




Immunization	Children	Adults
Pneumococcal meningitis	<5yrs: 15 or 20 valent Pneumococcal Conjugate Vaccine(PCV)	> 50 y: 20 or 21-valent Pneumococcal Conjugate Vaccine(PCV)
Meningococcal meningitis	MEN ACWY(4-valent) conjugate vaccine(11-12 y) and Monovalent serogroup B vaccine(16 y)	4-valent polysaccharide vaccine and Men B OR Men ABCWY Vaccine recommended for high-risk individuals
	Pentavalent Men ABCWY Vaccines	
Haemophilus meningitis	Infants (2-15 mo): HiB conjugate vaccine	HiB conjugate vaccine in high-risk individuals

High risk for septicemia and meningitis and hence need vaccination:

- Patients with asplenia/ undergoing elective splenectomy/ sickle cell anemia/HIV/ complement deficiency
- Those undergoing chemotherapy or hematopoietic stem cell transplant



Extra notes for reference:

- For immediate prophylaxis, close contacts should receive chemoprophylaxis-Rifampicin/ Ciprofloxacin. Cipro is not recommended in areas where cipro resistance is known.
- Immunization: Guidelines for pneumococcal vaccines are based on current **CDC/ACIP-recommendations in the U.S.**

Pneumococcal Conjugate Vaccine(PCV) are now recommended for children as well as adults. Conjugate vaccines contain polysaccharide+ protein

Ref: <https://www.cdc.gov/acip-recs/hcp/vaccine-specific/pneumococcal.html>

This information is more relevant during clinical rotations:

For children, routine immunization: A 4-dose series of a **pneumococcal conjugate vaccine (PCV)**—either **PCV15** or **PCV20**—given at:

2 months, 4 months, 6 months, and 12–15 months of age

For adults, PCV 20 or PCV 21 is recommended. For more information on vaccination guidelines visit <https://www.cdc.gov/acip-recs/hcp/vaccine-specific/pneumococcal.html>

- Two serogroup B meningococcal vaccines (Trumenba, MenB-FHbp and Bexsero, MenB-4C) were approved in late 2014 and early 2015 for use in individuals 10 through 25 years of age

Currently MEN ACWY(4-valent) conjugate vaccine(11-12 y) and Monovalent serogroup B vaccine(16 y) are recommended for adolescents. Pentavalent Men ABCWY Vaccines(10-25 y) is also available combining all the important serotypes.

Emerging Infant Option

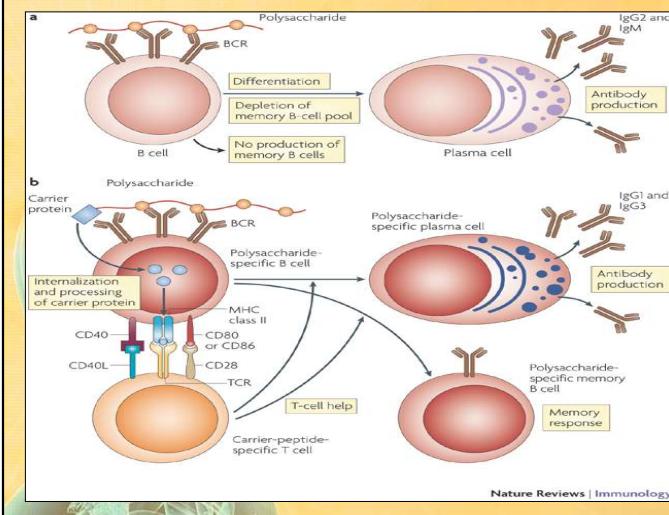
- In **May 2025**, the **FDA approved** Sanofi's **MenQuadfi** for use in infants **as young as 6 weeks**, though this is **not yet part of routine CDC recommendations**

A comparison between the immunological effects of a polysaccharide vaccine VS a polysaccharide-protein conjugate vaccine



What is the advantage of Conjugated vaccines?

Conjugate vaccines (Polysaccharide+ Protein) make the antigens T dependent requiring T cell help. Results in,
Class switching in antibody formation
Memory B cells generated



Nature Reviews | Immunology

Note: Bacterial capsular polysaccharides share the common immunological property of T-independent B-cell activation, which is associated with poor or absent immunogenicity in infants and a failure to induce immunological memory at any age. Purified capsular polysaccharide vaccines are generally not satisfactory in early childhood where the burden of disease is highest. Protein–polysaccharide conjugation has provided a solution to the problems of polysaccharide immunogenicity in childhood by recruiting T cells to the immune response.



CHRONIC Meningitis

CNS Tuberculosis: *Mycobacterium tuberculosis*

Primary Infection:

Lungs

→ Active or Reactivation:
Blood
(miliary TB)



CNS

Chronic Meningitis
Intracranial Tuberculoma
Granulomatous foci

See *Mycobacterium tuberculosis* in
Bacterial Respiratory Infections lecture

Microbiology of
M.tb will not
be tested in
exam

Pott's Disease
Spinal TB

Clinical Presentation and Diagnosis

- ✓ Important cause of meningitis in AIDS patients
- ✓ Gradual onset over a few weeks
- ✓ CSF picture: increased proteins, decreased sugar, lymphocytosis.
- ✓ Acid fast stain positive, growth on Lowenstein-Jensen agar
- ✓ PCR

62

Miliary TB = hematogenous spread of *M. tuberculosis*

Most often seen in regions of the world where incidence of TB is high



Tuberculous meningitis

Treatment

- Isoniazid
- Rifampin
- Pyrazinamide
- Streptomycin / Ethambutol
 - 2 months
- Isoniazid
- Rifampin
 - 7-10 months
- + corticosteroids

Enter CSF readily
in presence of meningeal inflammation
& Bactericidal



*TB meningitis is often advanced
before treatment begins, as its
slow progression makes it
difficult to diagnose*

63



Aseptic Meningitis



Milder than bacterial pyogenic meningitis
Headache, fever and photophobia, less neck stiffness
CSF picture is different.(Lymphocytic predominance)
Commonly caused by [viruses](#)- refer Dr. Hermel's material
Few bacteria cause aseptic meningitis:
✓ *Leptospira interrogans*
✓ *Treponema pallidum*
✓ *Borrelia burgdorferi*



Aseptic meningitis

Chronic Bacterial Meningoencephalitis

- **Neurosypphilis**

- *Treponema pallidum* (*details will be taught in IS-GERD- STI*)
 - Spirochete
 - Late stage of syphilis occurring in ~ 10% of untreated patients

- **Neuroborreliosis**

- *Borrelia burgdorferi* (*taught in IS-FOM- Systemic infections-Lyme disease*)
 - Spirochete
 - Lyme disease

Leptospirosis *taught in IS-FOM- Systemic infections-Lyme disease)*

Zoonotic infection

Leptospira interrogans, L. canicola



Will not be
tested in exam

65



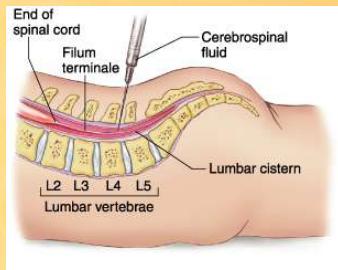
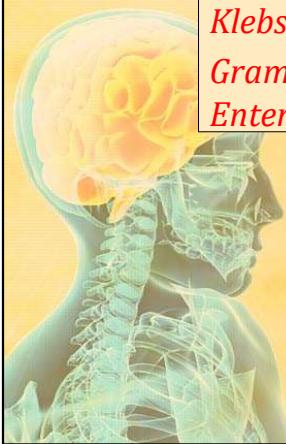
Nosocomial Meningitis

Iatrogenic infections following:

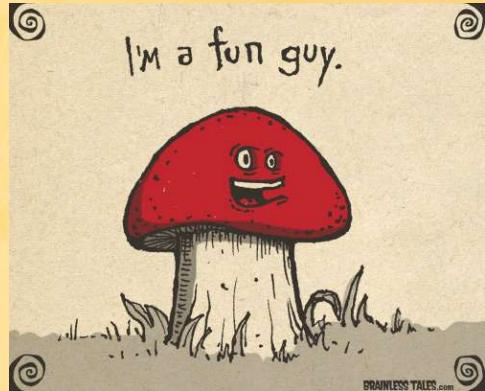
Lumbar puncture and Ventriculo-Peritoneal shunts:

Gram negative bacteria: Pseudomonas, E.coli, Klebsiella etc.

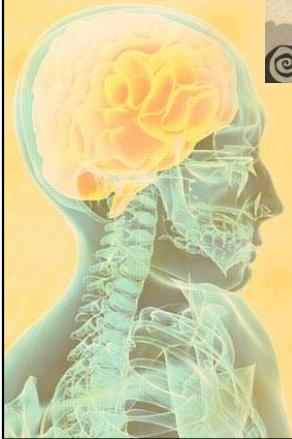
Gram positive: S.aureus, S. epidermidis, Enterococci



Lumbar puncture



FUNGAL MENINGITIS



Cryptococcus neoformans

Coccidioides immitis

67

CASE 4



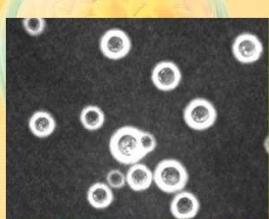
- A 48-year-old man was brought by his partner to the emergency department of a hospital because of fever, severe headache, nausea, vomiting, and mental status changes that had been progressive over the course of the past two weeks.
- The patient had been diagnosed with HIV infection 2 years before and was not currently on antiretroviral therapy.



Physical examination:

Vital signs- T 38.5 deg C, P 106/min, BP 110/68 mmHg.

PE: Patient was lethargic and disoriented. On exam, nuchal rigidity was noted with a positive Kernig sign.



CSF India ink preparation showing capsulated yeasts

Lab studies: WBC count- 3100/ μ l

CSF examination- 32 % PMNs and 66% lymphocytes, protein 68mg/dl, glucose 46 mg/dl.

CD4 + count-42/ μ l

Serum chemistries- normal

Chest X ray- normal, Head CT-normal

CSF grams stain- Gram positive yeasts seen

India ink preparation- Positive for capsulated budding yeasts

SDA- culture positive for ***Cryptococcus neoformans***

Patient received IV Amphotericin B and gradually recovered. He was given flucanazole to prevent relapses



Cryptococcus neoformans

- A pure yeast causing systemic infections like pneumonitis and meningitis
- Encapsulated monomorphous yeast (no pseudohyphae)
- Marked tropism for CNS. Most common cause of fungal meningitis in patients with depressed cell-mediated immunity (AIDS)

■ Clinical presentation

- slow onset – weeks
- headache, visual disturbances, abnormal mental status and seizures
- Can present as meningitis, brain abscess/ cysts leading to space occupying lesions and calcifications

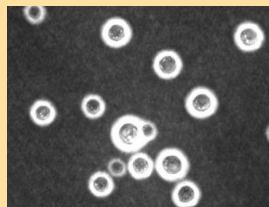
Epidemiology and Pathogenesis

Natural habitat = soil enriched with **pigeon droppings**



Virulence factor

Antiphagocytic polysaccharide capsule



CSF India Ink stain showing capsules

Pathogenesis

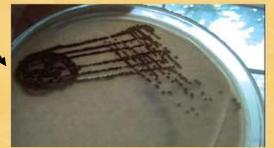
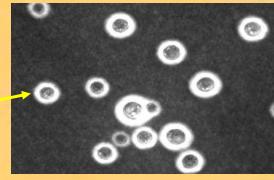
Inhalation of aerosolized yeast
↓
Hematogenous dissemination
↓
Meningitis/ abscesses/ pseudocysts



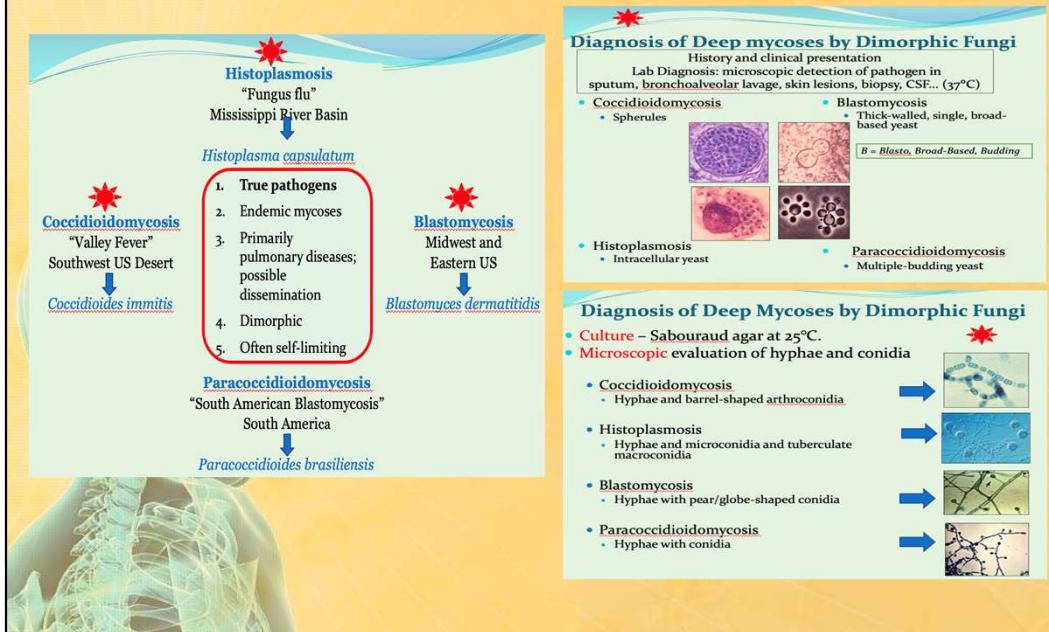
Cryptococcus neoformans –Lab Diagnosis



- CSF analysis
 - Chemistry-high protein and low glucose
 - Cytology: increased lymphocytes
 - **India-ink stain shows encapsulated yeast**
 - Culture – Mucoid colonies on Sabouraud agar. Black colonies on Bird seed or Niger seed
 - **Identification test: Urease ++**
- CSF latex agglutination test: Positive for Capsular antigen
- CSF PCR +



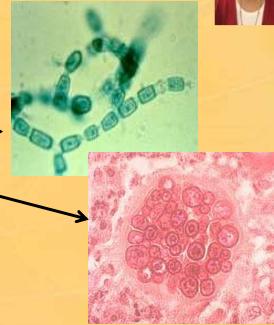
Recap from Resp System : Systemic mycoses can all cause disseminated infections and hence meningitis



Coccidioides immitis



- Dimorphic Fungus
 - environmental form: hyphae form **arthroconidia**
 - tissue form: spherules filled with **endospores**
- Habitat: soil – **desert sand** (southwestern US)
- Systemic infection in **AIDS**, immunocompromised, **3rd trimester of pregnancy**



Infection of lungs via inhalation

Arthroconidia → Spherules
(resistant to phagocytoses)

↓

Blood
(Disseminated coccidioidomycosis)

↓

Brain
Meningitis (rare)

- Diagnosis

- demonstrating **antibodies in the serum**
- rarely visible in CSF
- culture usually negative
- CSF: lymphocytes, high protein and low glucose

- RECAP-see Fungal Respiratory Infections lecture

San Francisco Chronicle

BAY AREA // HEALTH

Valley fever: Why the fungal disease is spreading into Northern California

Gabe Castro-Root
Aug. 13, 2023 | Updated: Aug. 13, 2023 8:16 a.m.

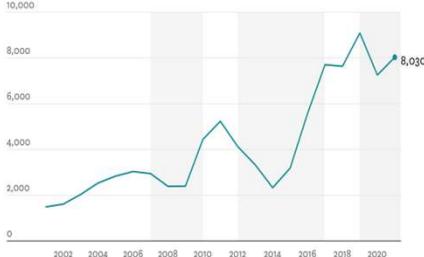


Valley fever, a respiratory disease caused by fungal spores that grow in soil, has long been found mostly in the Arizona desert and California's lower San Joaquin Valley. Research suggests the disease is now moving north, to areas such as Contra Costa County, due to climate change.
Bronia Witten/The Chronicle

The effects of climate change in California, from harsher heat waves to more volatile rainstorms, are well established. Lesser known is what those crises can help fuel: the northern migration of infectious diseases.

Annual cases of valley fever in California rose from fewer than 1,500 in 2001 to a high of more than 9,000 in 2019, according to the state's public health department. In 2021, the last year with available data, the state recorded more than 8,000 cases.

Valley fever cases in California
Drought years highlighted in gray



Year	Cases
2002	~1,500
2004	~2,000
2006	~2,500
2008	~2,000
2010	~4,500
2012	~3,500
2014	~2,000
2016	~6,000
2018	~7,500
2020	~7,000
2021	8,030

Chart: Sriharsha Devulapalli / The Chronicle - Source: California Department of Public Health



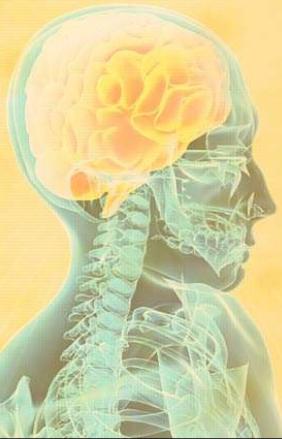
Diagnosis, Treatment & Prevention

- Fungal infections typically **progress slowly**
- **Difficult to diagnose**
 - Slow growing, if they show up at all on cultures
 - Often the only clue is that the patient continues to get worse on empiric antibiotics & antivirals
 - May have eosinophilia (>5%)
 - Can test for specific IgM
- Tx = **antifungals** (amphotericin B – known for its severe & potentially lethal side effects – nephro & hepatotoxic)
- **Prevention = good hygiene;** no vaccines available

75



PARASITES causing Meningitis/ Meningoencephalitis



Naegleria fowleri

Acanthamoeba spp.

Angiostrongylus cantonensis

Baylisascaris procyonis

LIFESTYLE

Child likely died of brain-eating amoeba infection after swimming in river

By Ben Cost
Published Aug. 18, 2022 | Updated Aug. 18, 2022, 3:08 p.m. ET

5 Comments

NAEGLERIA FOWLERI SYMPTOMS
SOURCE: CDC



- HEADACHE, FEVER & NAUSEA
- STIFF NECK, CONFUSION & SEIZURES
- DEATH USUALLY WITHIN 5 DAYS OF SYMPTOMS

FOX 46
6:03 93°

A child has likely died from a rare brain-eating amoeba they possibly contracted while swimming in a Nebraska river, according to local health officials.

Current Happenings Across STEM Magazine

Bingham Browne & Nichols STEM Magazine: Spring 2024 Issue

Contributor Information | Ongoing Research | School Happenings | About

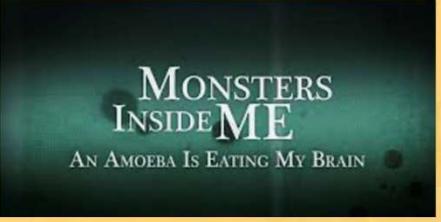
[Naegleria Fowleri: The "Brain-Eating Amoeba"](#)

[Previous](#) [Next](#) [Kate Coulter](#) [March 8, 2024](#) [Water Disease](#)



A more informed courtesy of disease with a 98.8% fatality rate. Should we be worried?

It's a beautiful day for swimming at the lake; the sun is shining, the breeze is blowing, and the water is clear. You're having a great time until you notice a slight headache and some small pains around your sinuses but think nothing of it. The next day, you notice a cluster of small aches and pains, followed by stiffness in your neck, confusion, and seizures. Headaches, high fevers, and seizures set in. You go to the doctor, who performs a spinal tap and biopsy the olfactory bulb through your nose. In your cerebrospinal fluid, they see it. Naegleria



Case 6



- In August, an 11-year-old boy was brought to the ER for a 2-day history of **headache and emesis; he was febrile and lethargic without focal neurologic deficits.**
- CSF analysis revealed **decreased sugar, increased proteins and leukocytosis.**
- The patient was started on intravenous antibiotics for suspected bacterial meningitis.
- Within several hours of admission, he had spontaneous non-purposeful movements, was unable to follow verbal commands, and was transferred to a children's hospital intensive care unit (ICU).
- A CT scan of the head on admission showed edema of the midbrain, and cranial MRI demonstrated areas of meningeal enhancement in the brainstem **suggestive of meningitis.**
- Follow-up lumbar puncture later that same day **revealed motile amebae** in a centrifuged CSF specimen.
- Patient was treated with IV amphotericin B and oral ketoconazole but worsened and died on Day 4.
- Autopsy findings showed PAME caused by *N. fowleri* identified by immunofluorescence testing with an *N. fowleri*-specific antibody.**

Guiding questions:

- Why did this patient's condition progress so rapidly ?
Primary Amebic Meningo-Encephalitis
- What is PAME?
Primary Amebic Meningo-Encephalitis
- What caused this infection? condition?
***Naegleria fowleri* trophozoites**
- What predisposed this patient to the infection?
Four days before onset of illness, the patient had attended a social event and had swum in a freshwater river with a group of friends in southern Georgia.

Free Living Amoebae



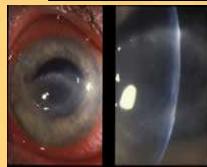
Naegleria fowleri

- Habitat – warm fresh water (lakes)
- Mode of infection- swimming in contaminated water /inhaling contaminated dust.
- Affects healthy children and young adults
- Causes primary amoebic meningoencephalitis which can be acute and fatal(severe prefrontal headache, nausea, fever, altered sense of smell.



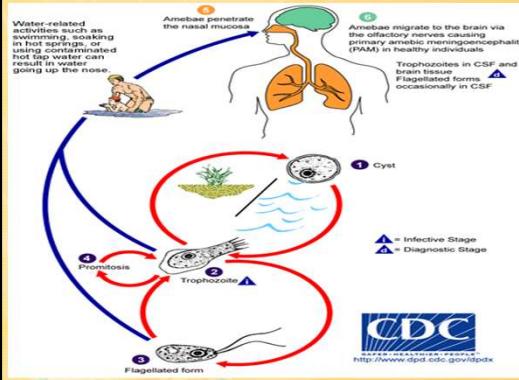
Acanthamoeba spp

- Habitat Soil; fresh, brackish, and sea water; sewage; swimming pools; contact lens equipment.
- Mostly affects immunocompromised hosts(meningitis) and rarely contact lens users(keratitis).
- Causes granulomatous amebic encephalitis- gradually progressive and can be fatal. Rarely, corneal ulcers/ keratitis in contact lens wearers)



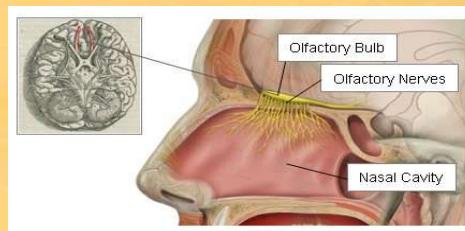
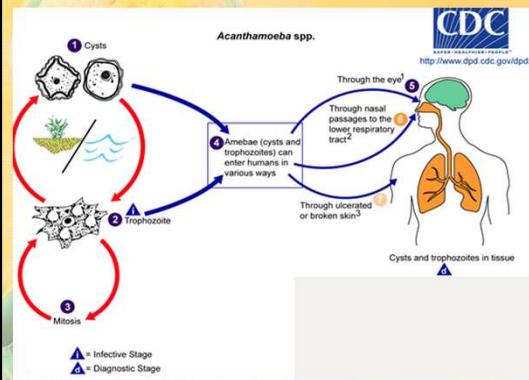
Eye of patient with *Acanthamoeba* keratitis.
(Photo courtesy of Dan B. Jones, M.D. -from CDC)

Free living amoebae found in nature include *Naegleria spp*, *Acanthamoeba spp*. and *Balamuthia mandrillaris*



Naegleria fowleri

- Morphological forms:
Trophozoite, Cyst and Flagellate forms.
- Infective form
 - TROPHOZOITE in *Naegleria*.
 - Trophozoite/ Cyst in *Acanthameba*
- Enter though nasal mucosa and migrate via olfactory neuroepithelium to the CNS.



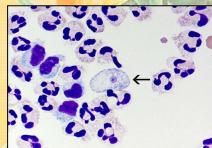
- Acanthameba can also enter directly through the eyes/skin

Free living amebae

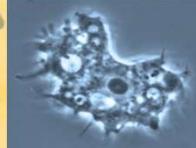


LABORATORY DIAGNOSIS

1. CSF findings-**bloody**, purulent (many neutrophils), ↑protein, ↓glucose
2. **CSF** Microscopy(Wet mount/ Giemsa stain/ Immunofluorescence stain) for **Trophozoites(Naegleria)/ Troph and Cysts (Acanthameba)**
3. CSF culture on plates seeded with gram negative bacteria. Look for tracks of amoeba on culture plate.



Trophozoites of Naegleria in CSF (CDC web site)



Trophozoites of Acanthameba with acanthopodia

TREATMENT

- For Naegleria-Amphotericin B; steroids to reduce cerebral edema
- Other drugs: miltefosine/ rifampin/ fluconazole/azithromycin
- For Acanthamoeba- multi drug regime- Flucanazole+miltefosine+penta -midine

PREVENTION



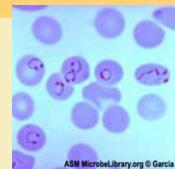
Other Parasitic CNS Diseases

Will not be tested in exams



- **Protozoal Encephalitis**

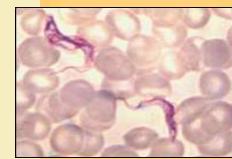
- *Plasmodium falciparum* – Cerebral malaria



ASM MicrobeLibrary.org © Garcia

- *Trypanosoma brucei* – Sleeping sickness in Africa

- Hemoflagellate transmitted by the tsetse fly



Eosinophilic meningitis

- *Baylisascaris procyonis* (found in raccoons)
- *Angiostrongylus cantonensis and costaricensis* (rats, snails, shrimps, crabs)

No content from this slide will be tested in the exam.

Here is some interesting information,

Baylisascaris: Ascarid worm found in Racoons. Humans ingest eggs in environment, most often young children. Larva emerge from egg and migrate. Tropism for neural tissue causing Neural Larva Migrans (NLM). They cause bleeding, eosinophilic granulomas and necrosis.

Eosinophilic meningitis. Diagnosis- ELISA for antibodies. Treatment: Albendazole/

Diethylcarbamazine. Prevention- Children's play area to be monitored. Racoons not to be allowed in the vicinity/ as pets.

Angiostrongylus cantonensis, which is also known as the rat lungworm, causes eosinophilic meningitis and is prevalent in Southeast Asia and tropical Pacific islands. The recognized distribution of the parasite has been increasing over time and infections have been identified in other areas, including Africa, the Caribbean, and the United States. Ingestion of raw or undercooked snails, slugs, or possibly transport hosts (such as frogs, fresh water shrimp or land crabs) in those areas can cause infection. CSF shows high eosinophilic counts. No specific test available

- **Pathology of bacterial meningitis**
To be continued in Part-2

