NEUROLOGICAL INFECTIONS

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LEARNING OBJECTIVES

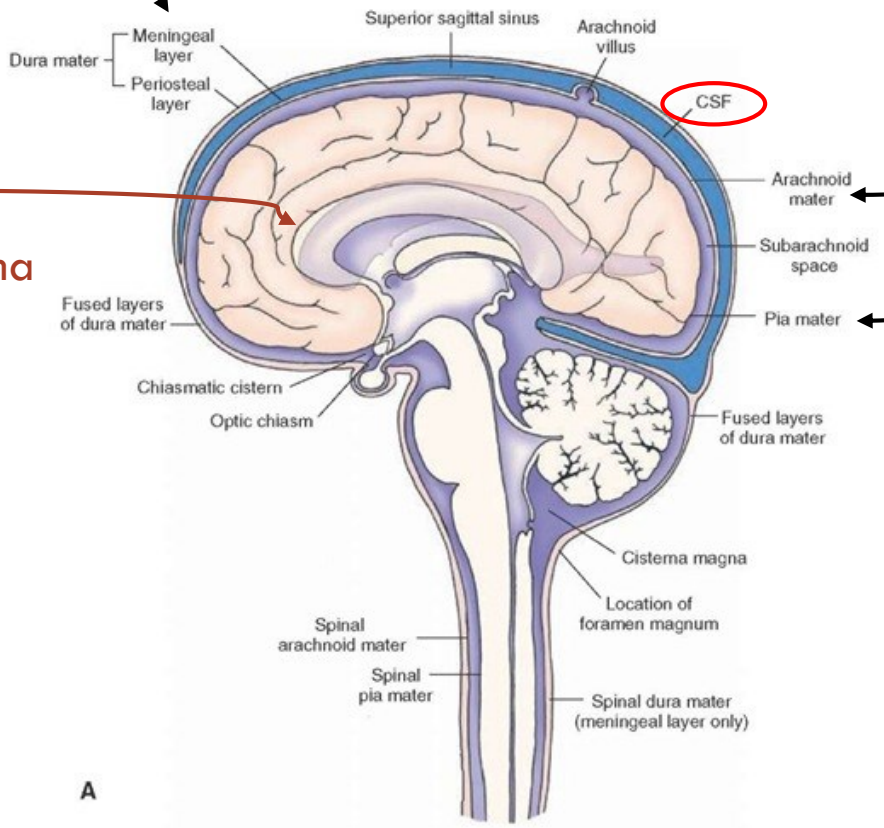
1. Understand that infections of the central nervous system is a medical emergency
2. Know the different types of CNS infections
3. Appreciate the different routes of acquiring CNS infections
4. Describe the principles in interpreting the CSF findings in meningitis/meningoencephalitis
5. Know the principle of treatment for meningitis/meningoencephalitis

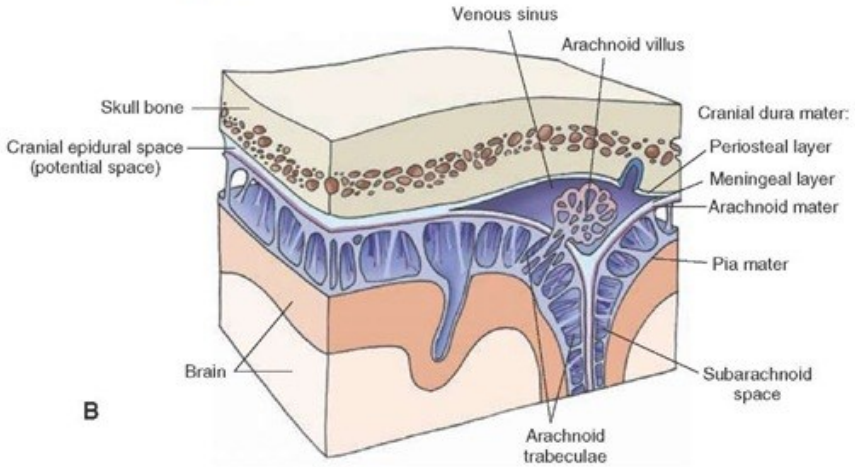
ANATOMY OF NEUROLOGICAL SYSTEM

- Central nervous system (CNS)
  - Brain
  - Spinal cord
- Peripheral nervous system (PNS)
  - Peripheral nerves

Meninges + Subarachnoid space

Brain parenchyma





IMPORTANT MESSAGE

- Infection involving CNS is one of the few medical emergencies relating to infectious diseases
- Often life-threatening and can have severe sequelae
  - Coma
  - Decreased mental capacity
  - Seizure, evolving to epilepsy
  - Persistent neurological deficit

TYPES OF INFECTIONS

Name	Definition
Meningitis	Infection within subarachnoid space and/or throughout the leptomeninges
Encephalitis	Inflammation of brain parenchyma
Meningoencephalitis	Concomitant meningitis with encephalitis
Brain abscess	Localized collections of pus in brain

ROUTES OF INFECTION

Haematogenous spread	Through choroid plexus or other blood vessels of brain to subarachnoid space *The most common route of CNS infections
Direct spread from adjacent infected site	Otitis media Sinusitis Mastoiditis
Anatomic defects allowing microbes to get access to CNS	Surgery Trauma Congenital abnormalities
Travel along nerves to the brain	Rabies HSV *The least common route of CNS infection

MENINGITIS

CLINICAL PRESENTATION

- Fever
- Headache
- Neck stiffness

- Altered mental status
- Photophobia
- Vomiting

- Seizure
- Focal neurological deficits

- Disseminated disease due to causative agents

CLINICAL PRESENTATION

- Depending on:
  - Speed of onset of initial presentation
  - Rate of progression of the illness
  - CSF findings
- Classified into:
  - Acute (progress in hours to days)
  - Subacute or chronic (progress in days to weeks)

Types of meningitis	Causative agents	CSF finding				
		Opening pressure (mmH_2O)	WBC/mm^3	Predominant cell type	Protein (mg/dL)	Glucose (CSF/Blood ratio)
Normal	Nil	<200	0-5	None	15-50	>0.6
Acute bacterial	(Refer to next table)	Increased	5-20,000 (mean 800)	PMN	>100	<0.6
Acute viral	Enteroviruses HSV-2 VZV Arbovirus Mumps	Slight increase	2-2000 (mean 80)	Lym	50-100 or normal	Normal
Subacute /chronic	MTB *Cryptococcus* *Histoplasma* *Coccidioides*	Increased	5-2000 (mean 100)	Lym	>50	<0.6

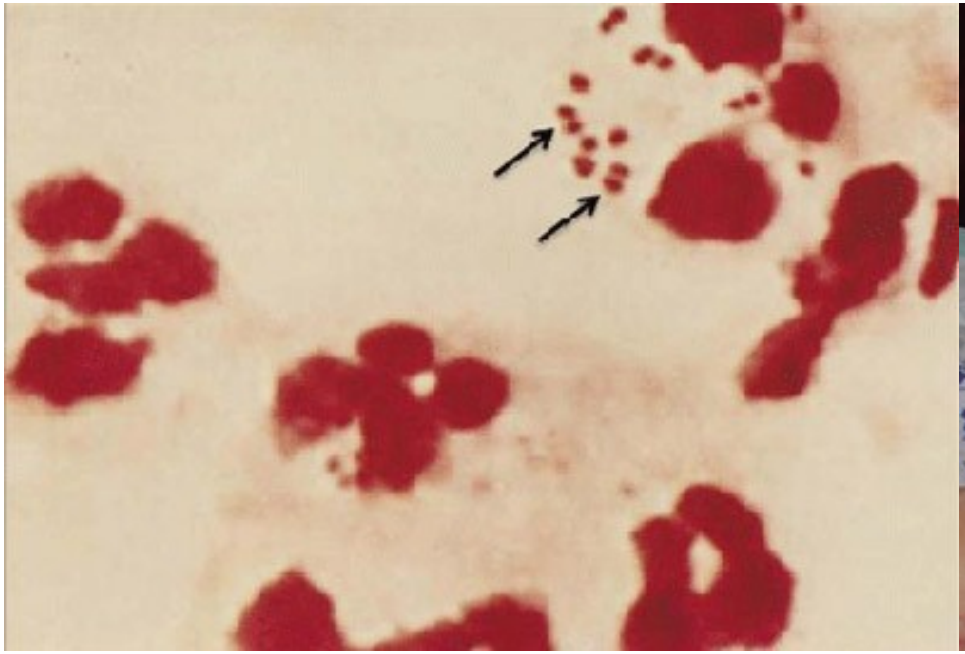
Table 1. Common Bacterial Pathogens

Age/Predisposing Factor	Pathogens
<1 mo	GBS, *E coli*, *L monocytogenes*
1-3 mo	GBS, *E coli*, *L monocytogenes*, *S pneumoniae*, *N meningitidis*, Hib
>3 mo	*S pneumoniae*, *N meningitidis*
>50 y	*S pneumoniae*, *N meningitidis*, *L monocytogenes*, gram-negative bacilli
Immunocompromised state	*S pneumoniae*, *N meningitidis*, *L monocytogenes*, gram-negative bacilli (including *P aeruginosa*)
Post neurosurgical procedure, head trauma	*S aureus*, coagulase-negative staphylococci, gram-negative bacilli (including *P aeruginosa*)
CSF shunt	Coagulase-negative staphylococci (*S epidermidis*), *S aureus*, gram-negative bacilli (including *P aeruginosa*)

CSF: cerebrospinal fluid; E coli: Escherichia coli; *GBS: group B streptococcus; Hib:* Haemophilus influenzae *type b;* L monocytogenes: Listeria monocytogenes; N meningitidis: Neisseria meningitidis; P aeruginosa: Pseudomonas aeruginosa; S aureus: Staphylococcus aureus; S epidermidis: Staphylococcus epidermidis; S pneumoniae: Streptococcus pneumoniae.

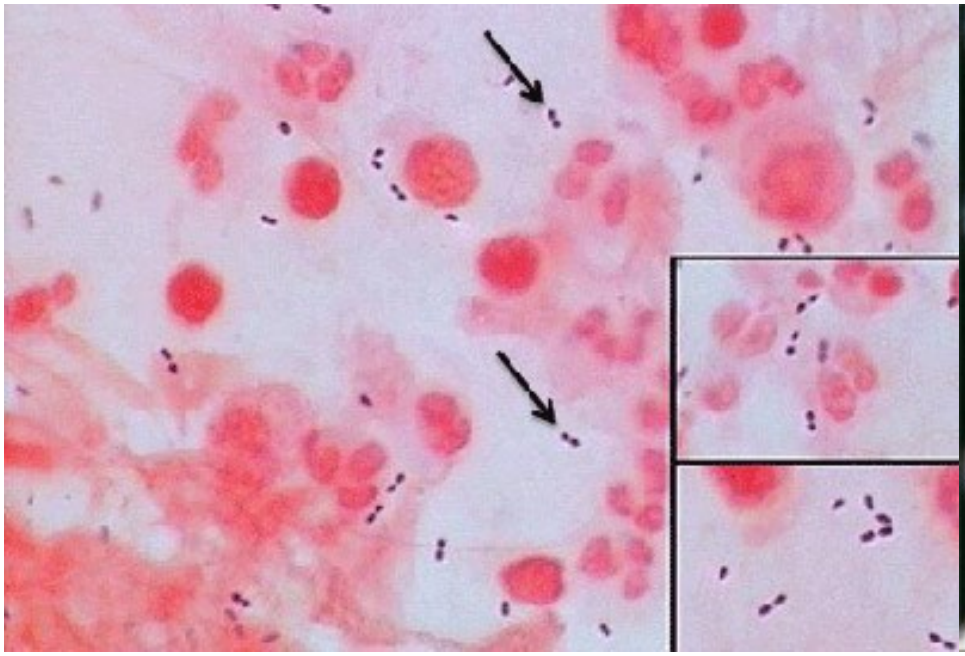
DIAGNOSIS

- Lumbar puncture to get CSF
  - Opening pressure
  - Cell count
  - Protein
  - Glucose
- Gram stain, India ink test
- Polymerase chain reaction (PCR) assay
- Antigen detection assay
- Serologic tests for specific antibody
- Culture

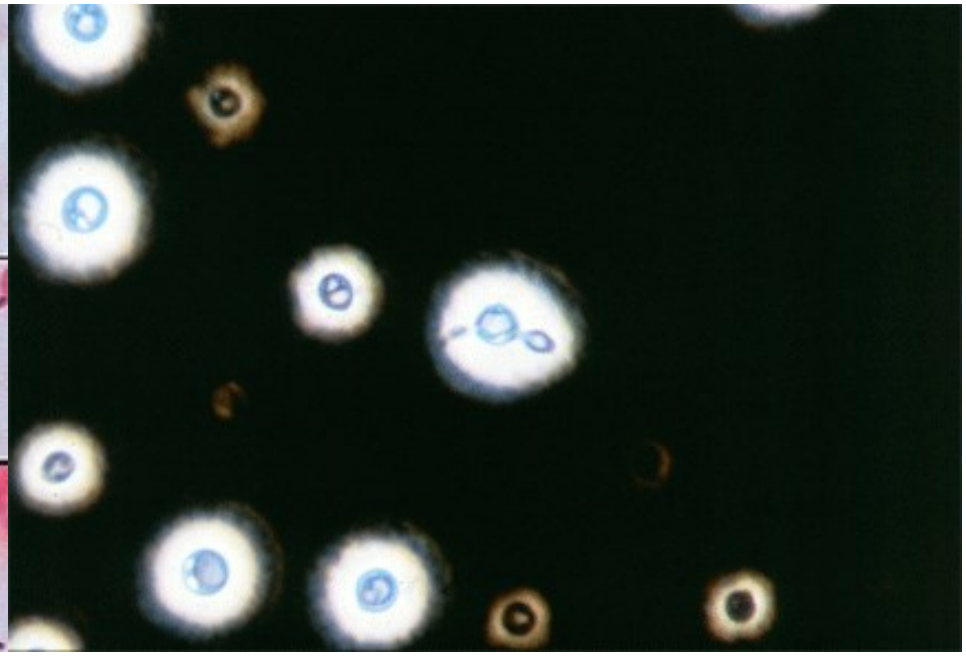


Gram stain of *N. meningitidis* in CSF with associated PMNs.
N. meningitidis may occur intracellularly or extracellularly in PMN leukocytes and will appear as gram-negative, coffee-bean shaped diplococci.

Purpura fulminans caused by *N. meningitidis*



Gram stain of *S. pneumoniae* with WBCs. *S. pneumoniae* may occur intracellularly or extracellularly and will appear as gram-positive diplococci, sometimes occurring in short chains.



India ink preparation for *Cryptococcus* spp. The presence of capsules will produce a halo around the yeast cells against the dark background.

TREATMENT

- Empirical treatment should be started immediately after collection of CSF
- Antibiotics of choice:
  - Good penetration into CSF
  - Bactericidal
  - Prolonged course (at least 2 weeks)

PREVENTION

- Vaccination
  - *S. pneumoniae*
  - *H. influenzae*
  - *N. meningitidis*
- Chemoprophylaxis
  - Group B streptococcus-carrying pregnant women

ENCEPHALITIS

CLINICAL PRESENTATION

- Fever
- Headache
- Altered mental status

- Seizures
- Focal neurologic deficits
- Coma

CAUSATIVE AGENTS

Predisposing factors	Organisms
Neonate	HSV-2
Child over age of 1 year and adult	HSV-1 VZV
Mosquito bites	Japanese encephalitis
Animal bites (dog, cat, bat, raccoon)	Rabies
Travelling history	Arboviruses (West Nile virus, Eastern and Western equine encephalitis)
Post-infection/immunization encephalitis	VZV Measles Influenza

DIAGNOSIS

- CSF
  - Cell count, protein and glucose may all be normal
  - PCR-based testing to look for viral agents
  - Viral-specific antibody
- Imaging esp. MRI
- EEG
- Rabies:
  - PCR of CSF/saliva/brain tissue
  - Nuchal biopsy with fluorescent antibody staining

TREATMENT

- Supportive
- If available, antiviral agents targeting the causative agents
  - Acyclovir - VZV, HSV
  - Oseltamivir - Influenza

PREVENTION

- Targeted population and Pathogens-specific
- E.g.
  - Pre- and post-exposure vaccination against rabies
  - Caesarian section for pregnant women with active HSV lesions

BRAIN ABSCESS

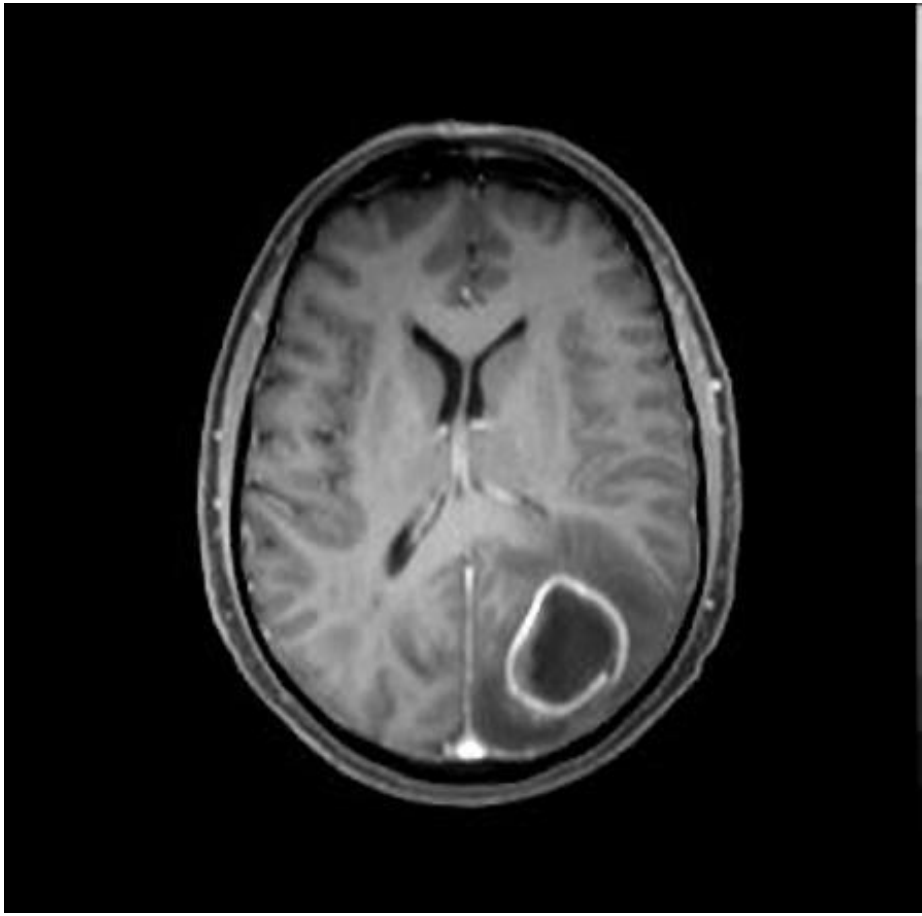
CLINICAL PRESENTATION

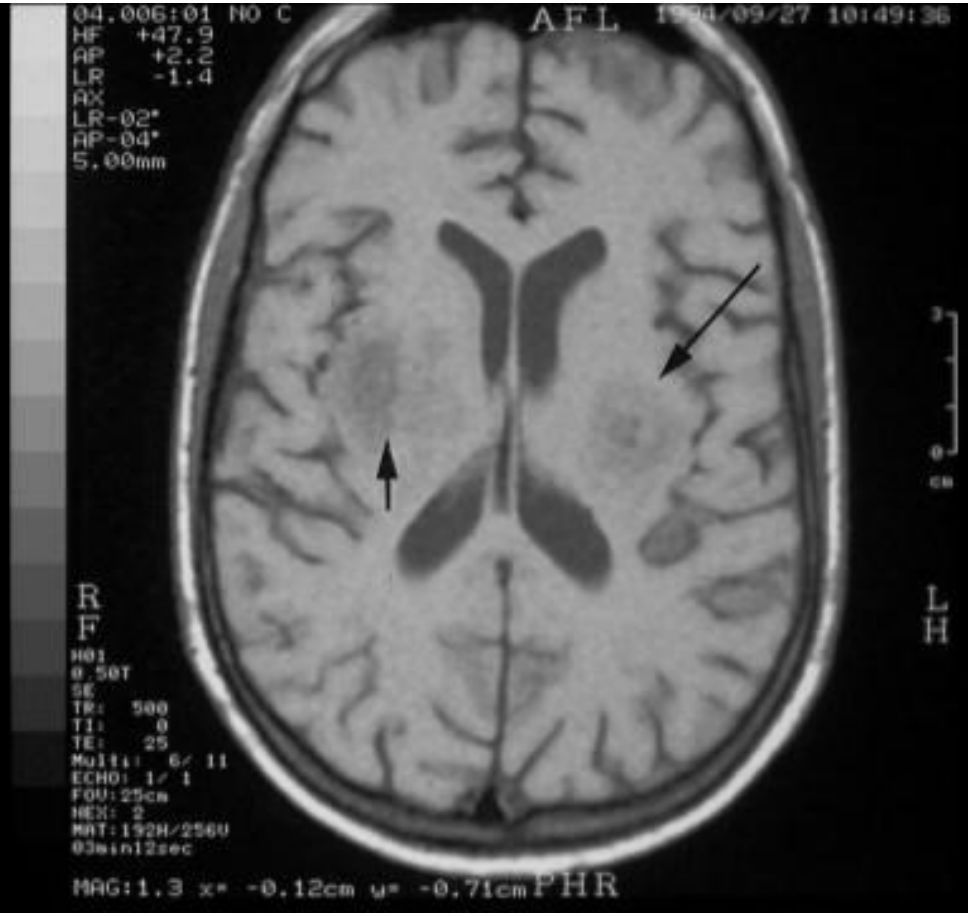
- Headache
- Fever
- Papilloedema
- Nausea
- Vomiting
- Behavioural changes
- Focal neurological deficits
- Seizures

Bacteria	Otitis media or sinusitis	*S. pneumoniae*, anaerobic streptococci, gram-negative anaerobes such as *Bacteroides, Prevotella* and *Fusobacterium*
	Dental infection	Viridans streptococci, anaerobic streptococci, gram-negative anaerobes, *Actinomyces*
	Trauma or neurosurgery	*S. aureus*, *S. epidermidis*, aerobic and anaerobic streptococci
	Neutropenia	Aerobic gram-negative rods *(Enterobacteriaceae*)
	HIV	*Listeria*, *Nocardia*, *Mycobacterium*
	Endocarditis	*S. aureus*, viridans streptococci
Fungi	Immunocompromised	Moulds (*Aspergillus*, *Mucor*, *Rhizopus*), *Cryptococcus*
Parasites	HIV	*Toxoplasma gondii*
	Ingestion of feaces-contaminated raw vegetables	Cysticercosis by cysts of *Taenia solium*

DIAGNOSIS

- Lumbar puncture is absolutely contraindicated
- Imaging
  - CT brain or MRI brain for any rim-enhancing lesions in brain parenchyma
- Drained pus for microscopy and culture
- Serology





MRI brain of a 40-year-old man with brain abscess caused by *Streptococcus salivarius*. The image shows hypointense lesions in the region of occipital lobe.

MRI brain of a 24-year-old man with HIV infection. The image shows hypointense lesions in the region of the thalami (arrows) caused by toxoplasmosis.

TREATMENT

- Surgical drainage is usually needed
  - Reduce bacterial load in the lesion
  - Difficult for antimicrobial agents to penetrate into the abscess
  - High acidity inside the abscess may render the antimicrobial agents ineffective
- Appropriate antimicrobial agents

SUMMARY

1. CNS infection is a serious infection and a medical emergency that needs to be managed promptly.

2. CNS infections include meningitis, encephalitis, meningoencephalitis and brain abscess.

3. People may acquire CNS infections by haematogenous spread, direct spread from adjacent infections sites, access from anatomic defects in the CNS, and retrograde spread from peripheral nerves.

4. The differential white cell counts, the protein and glucose level in CSF provide clues on the possible cause for meningitis/meningoencephalitis.

5. Empirical antimicrobial agents should be started once CSF has been collected for investigations in cases of meningitis/meningoencephalitis.

REFERENCES

- Levinson W. Review of Medical Microbiology and Immunology. 14th edition. McGraw-Hill Education, 2016.
- Tille P. Bailey and Scott's Diagnostic Microbiology. 13th edition. Elsevier Mosby, 2014.