CNS Infections

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Objectives

- To identify causes of CNS infections
- To identify presentations of CNS infections
- To identify treatment options of CNS infections

CNS Infections

Diffuse infection

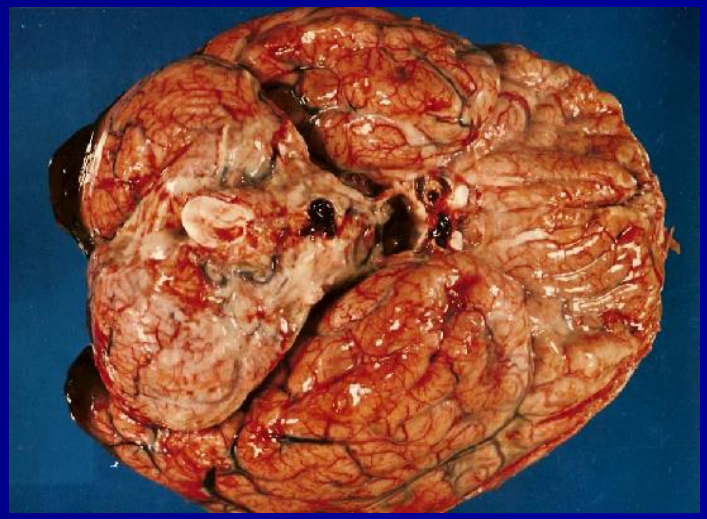
- Meningitis
  - Acute
  - Subacute/chronic
- Encephalitis
  - Acute
  - Chronic

Space lesions

- Brain abscess
- Epidural abscess
- Subdural empyema
- Encephalomyelitis
  - Acute
  - Chronic

Meningitis

- Inflammation involving the arachnoid, pia mater & the interposed CSF in the subarachnoid space
- Extends throughout the subarachnoid space around the brain, spinal cord & ventricles

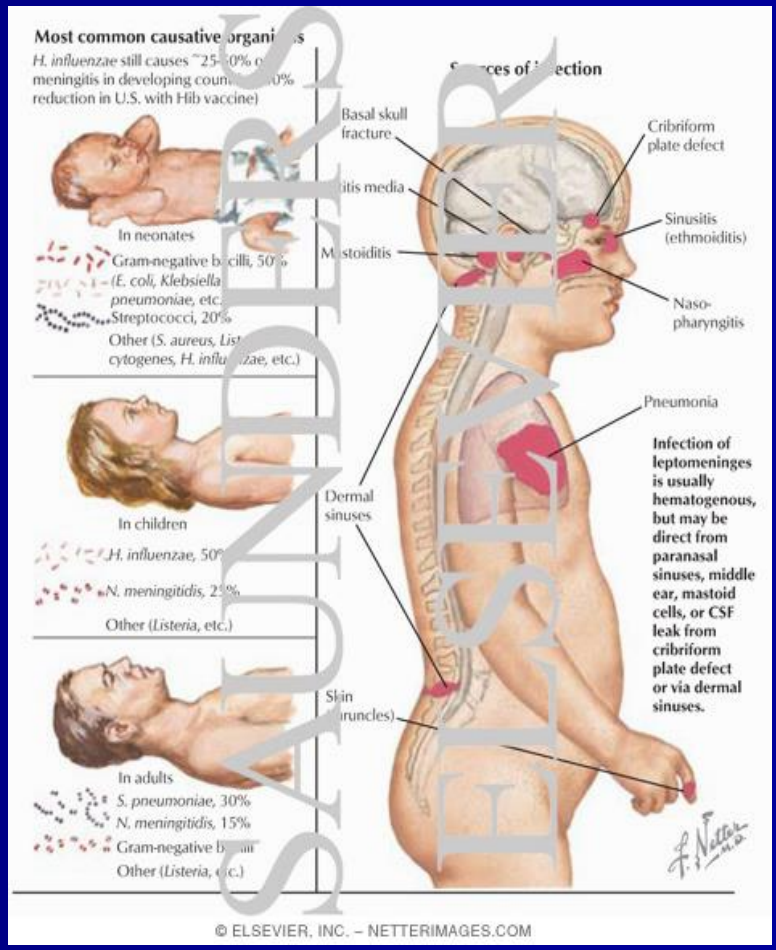


Acute Bacterial Meningitis Risk Factors

- Extremes of age
- Crowded conditions
- Terminal complement deficiency
- Splenectomy
- Sickle cell disease
- Alcoholism
- Cirrhosis
- CSF leak
- CSF shunt
- Sinusitis, otitis media, brain abscess
- Recent neurosurgical procedure

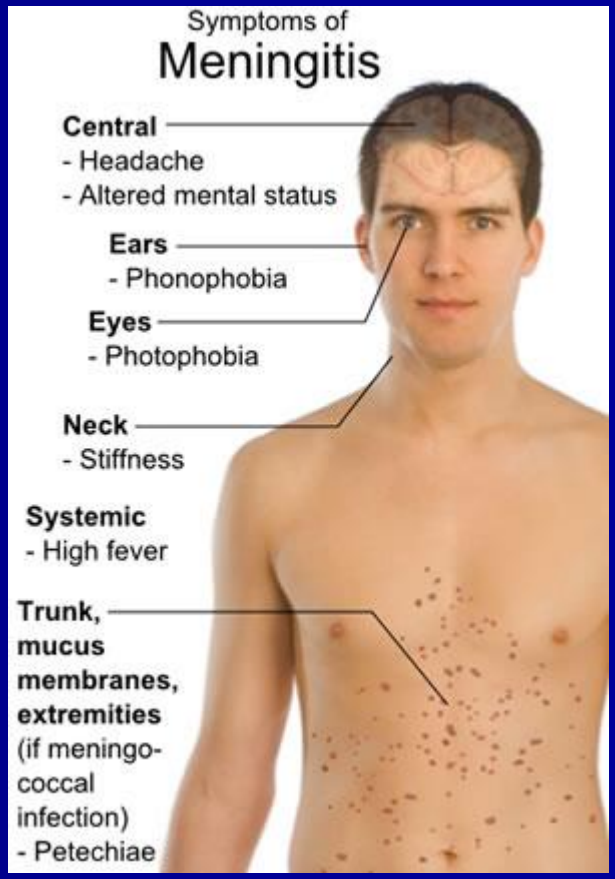
Pathophysiology

- Pathogens reach the CNS either by hematogenous spread or direct extension
- Virulence factors:
  - IgA proteases allow bacteria to adhere to nasopharyngeal mucosa
  - Capsule inhibits phagocytosis & comple- mediated bactericidal activity
- Once bacteria reach CSF they multiply quickly due to lack of host defenses



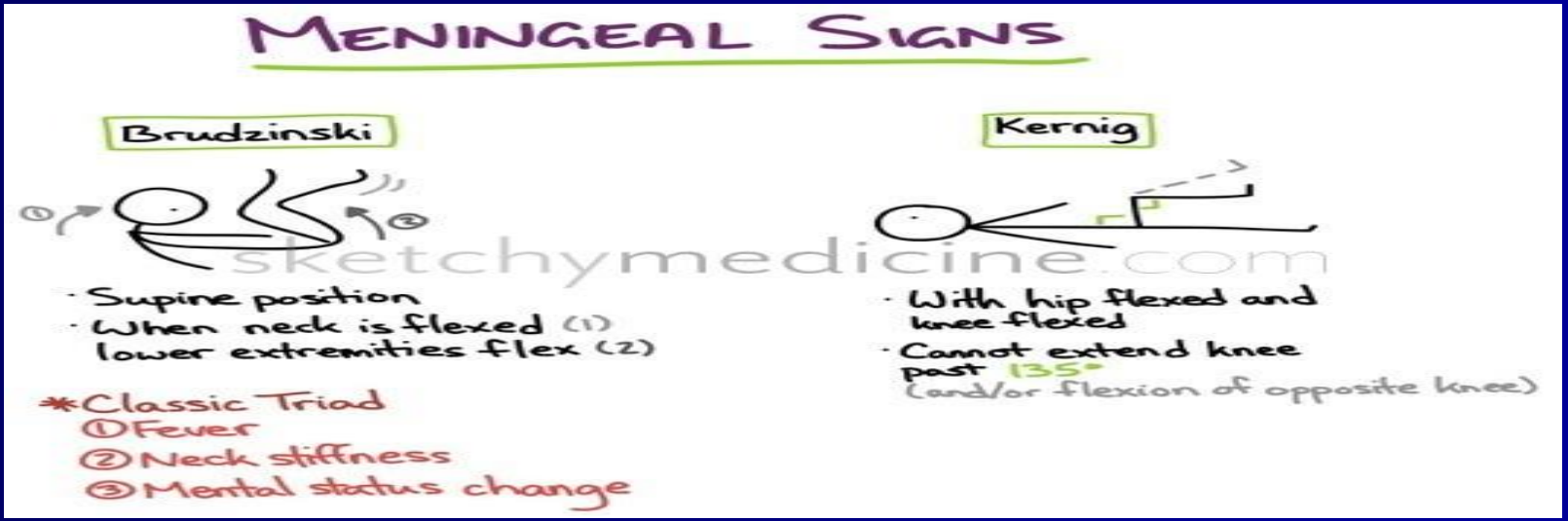
Acute Bacterial Meningitis Clinical Manifestations

- Headache, fever, meningismus, + altered mental status
- Elderly may present with lethargy only
  - May have nuchal rigidity w/o meninigitis
- Patterns of presentation
  - Insidious development of symptoms
  - Acute, fulminant disease
- Purpura, petechiae associated with *N. meningitidis*
- Seizures occur in 20-30%



Physical Examination

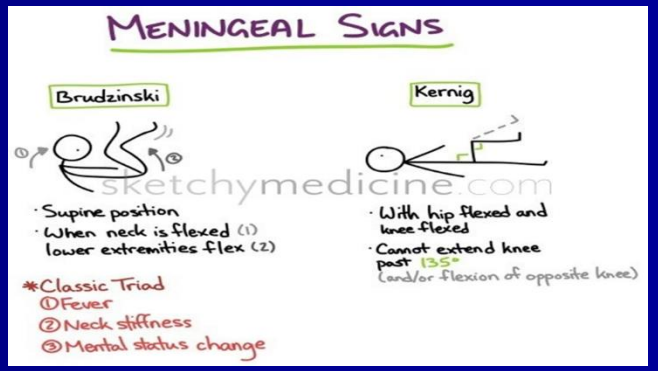
- Vital signs, brief MSE
- Assess neck stiffness
- Kernig & Brudzinski signs
- Neuro exam
- General exam - include skin, ears, sinus,



Clinical Examination

If fever, neck stiffness, & altered mental status are ALL absent, the diagnosis of bacterial meningitis is virtually eliminated

Kernig & Brudzinski signs have low sensitivity but high specificity



Lumbar Puncture

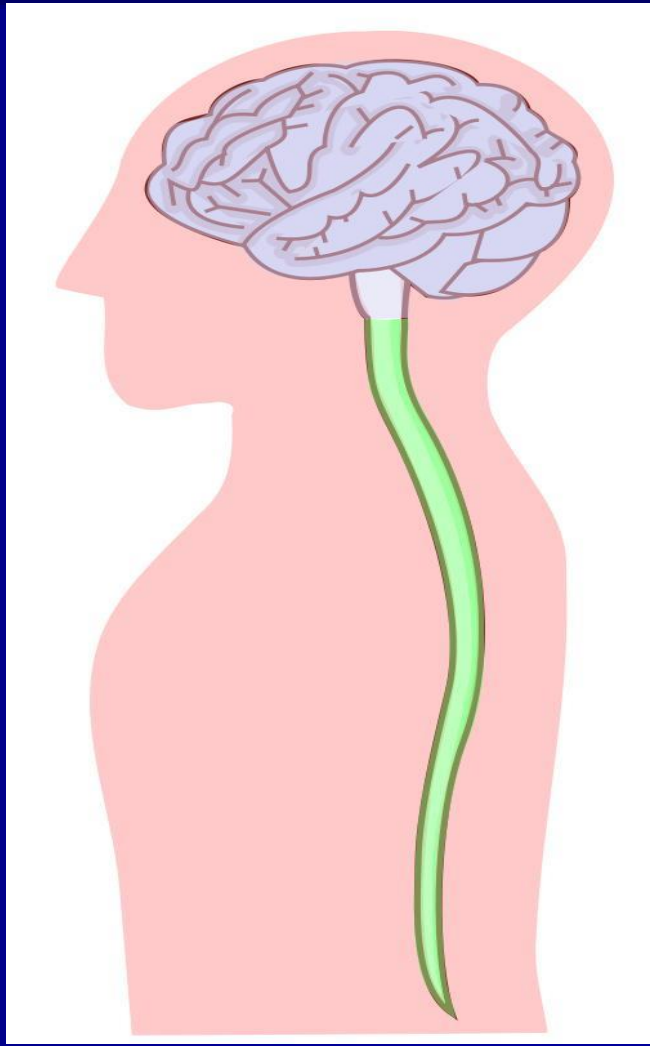
- If acute bacterial meningitis is suspected, obtain CSF & blood cultures before neuroimaging
- If diagnosis is uncertain, a repeat spinal tap should be repeated in 8-12 hours
- Pts with neurologic findings or papilledema usually have diseases other than acute bacterial meningitis;
  LP should be not be performed until imaging is performed
- With brain abscess, subdural empyema,
  subdural hematoma or cerebral hemorrhage, LP may be catastrophic
- LP relative contraindications: infection of the underlying skin,
  significant bleeding disorder

LP Complications

- Brain herniation– Risk greatly increased with space occupying lesion
- Spinal hematoma with cord compression in patients with coagulopathy
- Infection
- Post-LP headache - occurs in ~30%

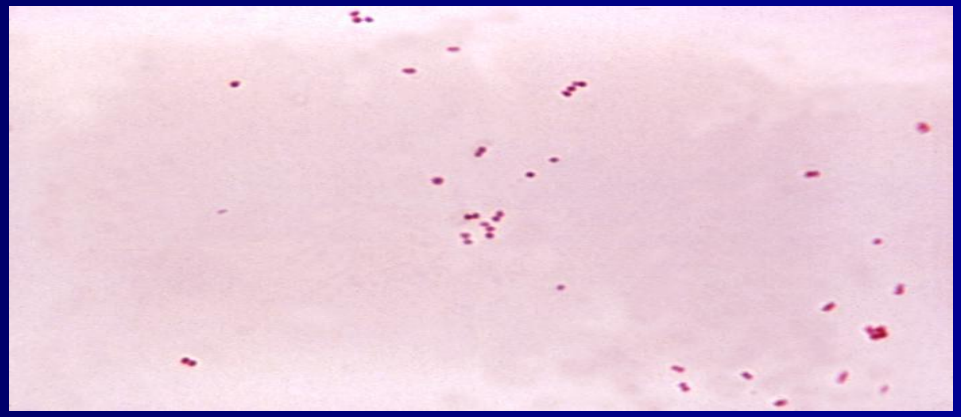
CSF Opening Pressure

- Must be measured in the lateral decubitus position with legs & neck in a neutral position
- Normal opening pressure = 5 – 19.5 cm CSF



Acute Bacterial Meningitis CSF Microbiology

- Gram stain (+) in 60-90%
  - In pts who received an antibiotic: 40-60% (+)
- Culture (+) in 70-85%
  - <50% (+) in those partially treated
- False-negatives may occur in patients who are partially treated



CSF Findings in Meningitis

	Normal	Bacterial	Viral	Fungal/ TB	Parameningeal Focus/Abscess
WBC	0-5	>1,000	100-1,000	100-500	10-1,000
%PMNs	0-15	90	<50	<50	<50
Glucose	45-65	<40	45-65	30-45	45-65
CSF:Blood glucose	0.6	<0.4	0.6	<0.4	0.6
Protein*	20-45	>150	50-100	100-500	50->150

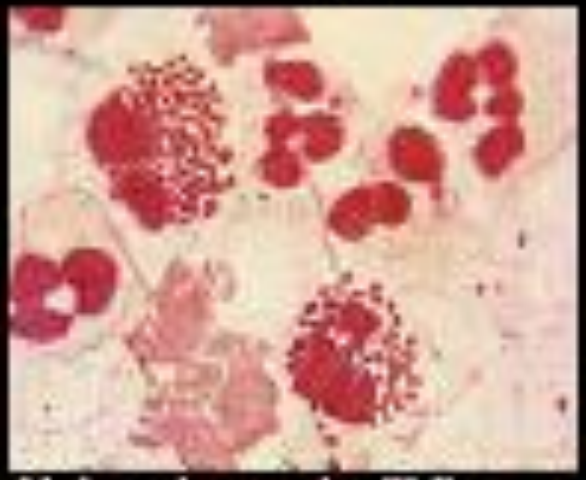
If LP is traumatic subtract 1 mg/dL protein for every 1,000 RBCs

Acute Bacterial Meningitis

CSF Microbiology: Gram Stain

Listeria monocytogenes

Haemophilus influenzae



Neisseria meningitidis

Streptococcus pneumoniae

Meningitis

- DIC
- Shock
- Subdural abscess
- Intracerebral abscess
- Epidural abscess
- Cerebral thrombosis

Acute Bacterial Meningitis

Treatment

- Antibiotics should be started within 30 minutes of presentation
- If LP must be delayed, obtain blood cultures and immediately start antibiotics
- Therapy should usually cover *S. pneumoniae, H. influenzae, N. meningitidis, L. monocytogenes*
  - Vancomycin + ceftriaxone ± ampicillin
- If there is significant immunosuppression, h/o CSF leak, recent neurosurgery, head trauma, potential line sepsis, therapy should also cover gram(-) rods & *S. aureus*
- LP typically only repeated when pt fails to improve

Acute Bacterial Meningitis
Definitive Antimicrobial Therapy

Pathogen	Antibiotics		Duration
	1st Line	PCN allergy	
N. meningitidis	Ceftriaxone	Moxifloxacin	7d
H. influenzae	Ceftriaxone	TMP/ SMX	14-21d
S. pneumoniae			10d
--PCN (S)	PCN G	Vanco	
--PCN (I)	Ceftriaxone	Vanco	
--PCN (R)	Vanco + Ceftriaxone + Rifampin	Vanco + Rifampin	
Listeria	Amp ± gent	TMP/SMX	14-21d

Steroids for Meningitis in Adults

- Meta-analysis of 5 trials, n=623
- Mortality:
  - Dexamethasone group: 12%
  - Control group: 22%
  - RR = 0.6

  Van de Beek D et al. Lancet Infect Dis 2004;4:139-143.
- Must be given shortly before or with first dose of antibiotics
  - Dexamethasone 0.15 mg/kg IV every 6 hours x 2-4 days
  - Dexamethasone decreases vanco levels in the CSF; if vanco used, add rifampin
- Steroids should be given if *S. pneumoniae* suspected

Acute Bacterial Meningitis

Mortality by Pathogen

Organism	Mortality (%)
N. meningitidis	3
H. influenzae	6
Group B strep	7
Listeria monocytogenes	15
Streptococcus pneumoniae	21

Schuchat A et al. New Engl J Med 1997;337:970-976.

„Covered syndrome”

(pretreated/masked form of purulent meningitis)

Clinical picture

headache, intermittent febrile state, but
no prominent meningeal signs
antibiotic therapy in the recent history

CSF

- no more than 1000 cells, granulocytes/mixed
- protein elevated >1 g/l
- sugar: decreased
- negative culture result

Diagnosis based on CSF findings

Therapy should be the same as in acute purulent meningitis (combined antibiotics)

Acute aseptic meningitis

Pathogens:
- virus
  HERPES (HSV, HZV, EBV, CMV),
  ENTERO (echo, coxaci, polio, etc.),
  ARBO (tick-bite encephalitis virus),
  ADENO, LCMV, HIV, etc.
- spirochete (leptospira, borrelia, treponema)

Clinical picture
Incubation 7-10 day, "dromedary" course

CSF:
- cell count 50-1000/ul, lymphocytes
- protein level moderately elevated (0.4-lg/1)
- sugar: normal
- microbiol. culture: negative **Dg**: serology (repeated)

Others:
EEG, neuroimaging: usually normal

Therapy: supportive

Subacute/chronic meningitis

Pathogens:
- mycobacterium, mycoplasma
- fungus (candida, cryptococcus, aspergillus)
- spirochete (leptospira, borrelia)
- virus (LCMV)
- toxoplasma
- non-infective (leukemia, SLE, tumour cells)

Clinical picture (weeks-months)
intermittent febrile states
slowly progressive mental changes, mild (or absent) meningeal signs, progressive cranial nerve palsies

CSF:
- 50-100/ul cells, lymphocytes
- high protein level - 1-3 g/1 (severe BBB damage)
- low sugar level (>2 mmol/l)

Dg: need special culture technique, serology

Therapy: for tbc: Isonicid, Rifampycin, Dexamethason. for fungus: Amphotericin B

Brain abscess

Etiol.: direct or haematogenic spreading

Clinical picture: focal signs, seizures, rised intracranial pressure

Dg: CT, MRI

TH: antibiotics, surgical

ENCEPHALITIS

Pathology:

Blood-brain barrier damage
+
Central nervous system damage

Clinically: "Encephalitis syndrome"

meningeal syndrome +
neurological signs (focal signs of motor-, sensory, autonomic systems, sings of inreased intracranial pressure)
seizures
altered mental state

EEG, MRI, CSF alterations

Herpes simplex encephalitis

- Clinical: primary [subclinical] infection with HSV-1, endogenous reactivation,
- flu-like phase followed by encephalitis located to temporal lobe (aphasia, paresis, seizures, psychoorganic syndrome).
- Dg: CSF, EEG, MRI, biopsy (PCR), serology.
- Treatment with Acyclovir 30mg/bwkg a day for weeks

Lyssa, rabies

Clinical: transmitted by bite of an rabid animal {small predators}, week to months of incubation period,

Stages: 1. Prodrome (fever, fatigue) 2. Excitation (restlessness, hyperirritability, convulsions, 3. Paralytic phase (widespread paresis, death)

Dg. Pathology (Negri-body in hippocampus), CSF, preventive immunization)

Leukoencephalitis

Pathology: immune demyelination
Clinical picture: acute/subacute, monophasic disease with widespread white matter lesion, typical CSF (BBB damage +OB)

- **parainfectious encephalomyelitis** (measles, rubella, varicella, smallpox, mumps, infectious mononucleosis)

- **postvaccination encephalomyelitis** (vaccination against smallpox, measles, rabies, tetanus)

Panencephalitis

(„slow virus" diseases, progressive course)

- **SSPE** (subacute sclerotising panencephalitis)
- **CJD** (Kreutzfeld-Jakob disease)
- **PML** (progressive multifocal leuko-encephalopathy)

CJD

Etiology:

Prion (sporadic, iatrogenic, familial)

Clinical picture

Onset: 35-65 y, personality changes, progressive dementia within few months, extrapyramidal signs, ataxia, dysarthria, myoclonus, death within a years

EEG: triphasic slow complexes, 1-2 cps

CSF: unremarcable

Dg: clinical picture, (brain biopsy)

Th: symptomatic

PML

(progressive multifocal leukoencephalopathy)

Immunsuppression (HIV, cytostatics, leukemia, malignancies)

Mechanism: JC papova virus causes oligodendroglia degeneration

Clinical picture: subacute onset, changing in personality, pramidal signs, ataxia, dementia, death within a few months

CSF: unremarkable

MRI: demyelination (confluent, no enhancement)

Dg: brain biopsy

Th: stop immunsuppression, symptomatic

Neurosyphilis

Pathogen: treponema pallidum

Primer genital infection followed by hematogenous spreading

Forms:

1. Luetic meningitis (early)
2. Meningovascular syphilis (months)
3. Paralysis progressiva (dementia, psychosis, several years)
4. Tabes dorsalis (spinal ataxia)

Dg: CSF, serology, MRI

Th: penicillin

Meninigitis

- Serious Infectious Disease
- Minutes Count
- Empiric Therapy is usually the first choice so need to know the risk groups
- Confirm with cultures and special tests
- Modify is necessary antimicrobial Rx

Thank You