A Diagnostic and treatment approach to Central Nervous System (CNS) Infections

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Objectives: What we will cover today?

- Major clinical syndromes of central nervous system infection- most common and the most dangerous (associated with morbidity and mortality)
  - Acute community acquired bacterial meningitis
  - Acute community acquired viral meningitis
  - Acute hospital acquired/post-neurosurgical meningitis
  - Brain abscess, Epidural abscess, Subdural empyema
  - Encephalitis

How would you approach this patient

52 yo woman who has a
headache fever & altered mental status
On exam has neck stiffness & photophobia.

Infectious Diseases diagnosis has two components:
Syndromic or Anatomic diagnosis: Where is the infection?
Microbiologic Diagnosis: What is causing the infection?

Antibiotics should get in to where the infection is and kill the organism causing the infection

Antimicrobial therapy

- **Empiric therapy-** clinical syndrome-guess the bugs

↓

- **Empiric therapy-** gram stain/ organism with out ABX susceptibilities

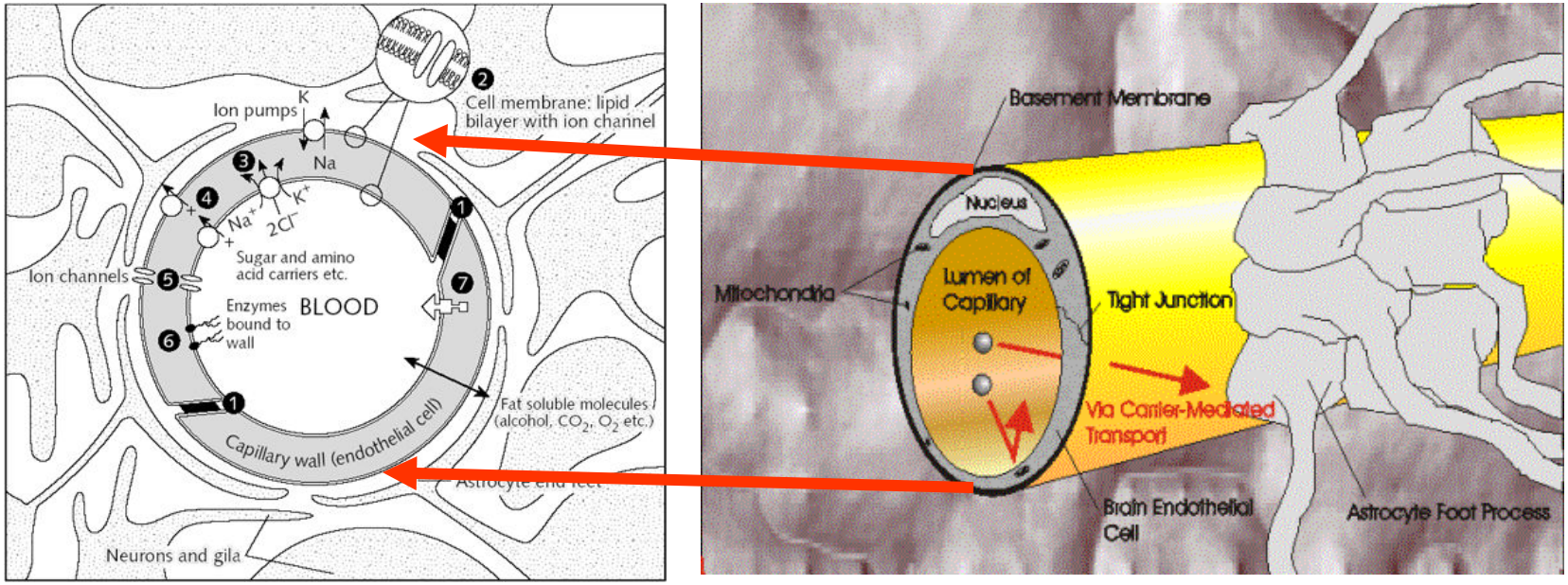
↓

- **Definitive/ directed therapy-** Abx susceptibilities

Antimicrobial Treatment Principles in CNS infection:

- CNS is an area of impaired host resistance
- Treatment requires bactericidal therapy
- CSF or CNS penetration
  - Levels are 10-20% of serum levels for most drugs

Blood CSF/ Brain Barrier

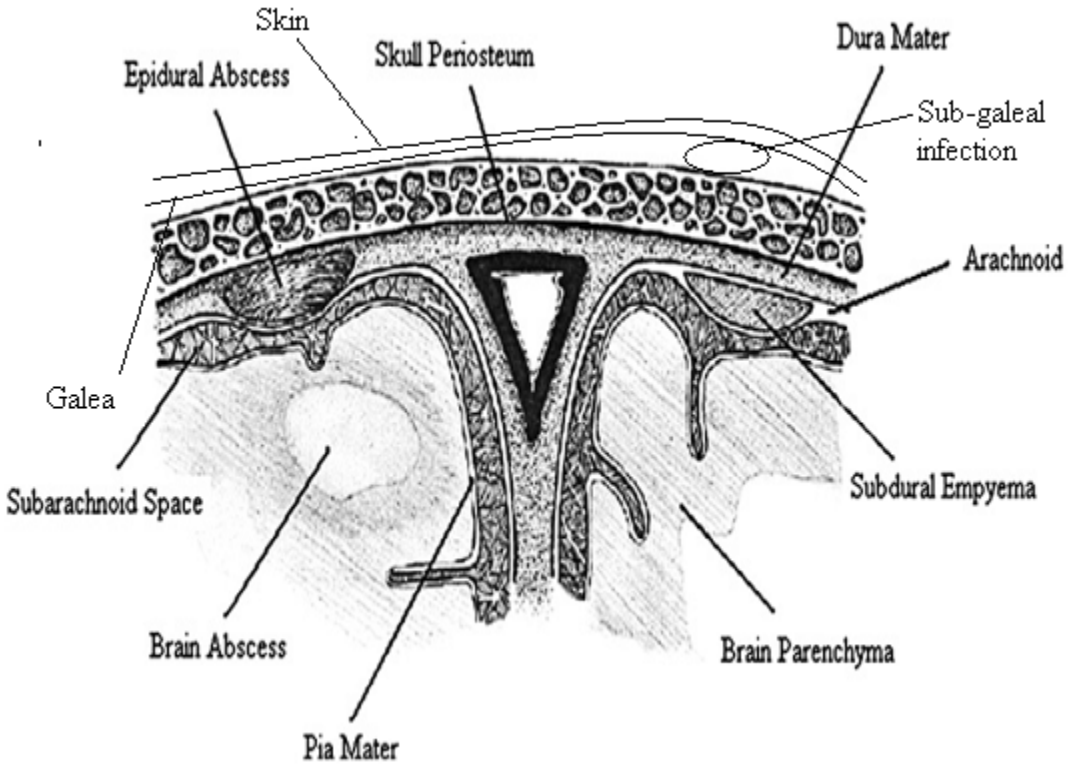


4 questions we should ask, as a clinician, in a patient with a suspected CNS infection

1. Where is the infection (Anatomic location in the CNS)?
2. How long has it been going on?
3. What is the clinical setting and what is the "exposure history"?
4. Is the patient a "normal host" or has a "compromised immune system"?

WHY ASK THESE QUESTIONS?

Question 1:
Where is the infection (Anatomic location in the CNS)?



(Outside→inside)

Skin and subcutaneous infection

Sub-galeal infection

Skull –osteomyelitis

Epidural abscess

Subdural empyema

Encephalitis

Brain abscess

Modified picture from Lewin JJ, LaPointe M, Ziai WC. Central nervous system infections in the critically ill. Journal of Pharmacy Practice 2005;18(1):25–41

Question 2:

How long has it been going on for?

Some organisms cause acute infections & some cause sub-acute & chronic infections

- Acute- hours/days
- Sub-acute- weeks
- Chronic –months

If chronic- is it a single prolonged episode or recurrent “acute” infections?

Question 3:
What is the clinical setting and what is the "exposure history"?

- Community acquired
  - Pneumococcal & meningicoccal meningitis
- Hospital acquired/ post neurosurgical
  - MRSA & *Pseudomonas* meningitis
- Age of the patient (Different pathogens at different ages)
- Time of the year
  - Summer/fall- West Nile Encephalitis

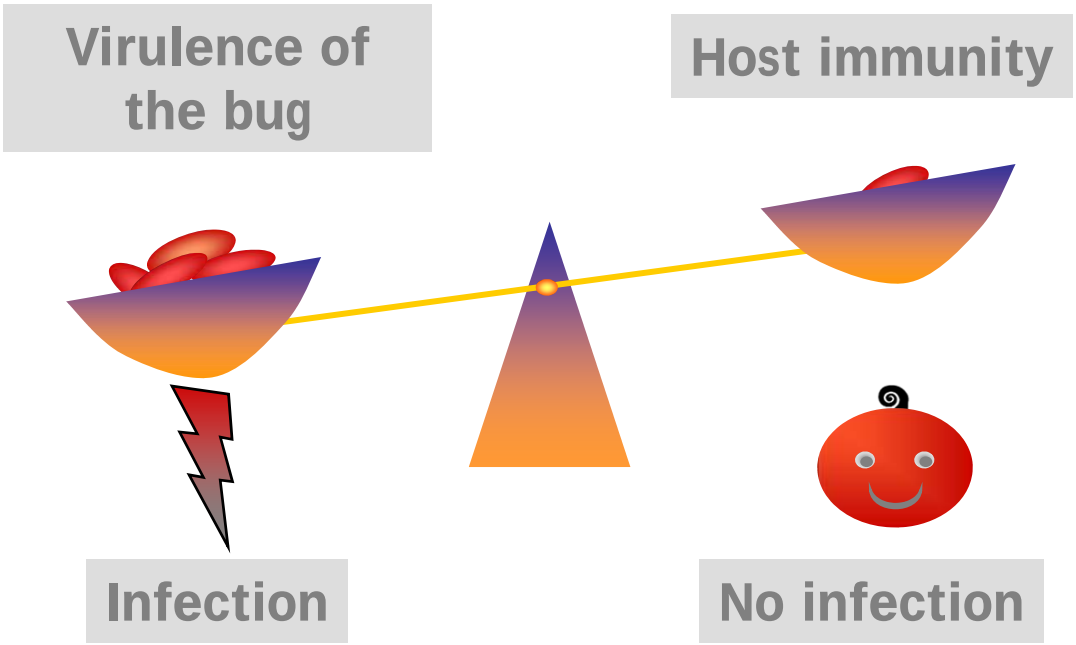
Question 3:
What is the clinical setting and what is the "exposure history"?

- **Travel:** e.g. Arizona- Coccidoides; Africa-cerebral malaria
- **Insect bites:** e.g. Tick bites-lyme disease; Mosquitoes-west Nile virus
- **Animal bites, close contact with certain animals**: e.g. Raccoon bites-Rabies encephalitis;
- **"Sick contacts":** e.g. close contacts in closed environments like dorms-meningococcus
- **Sexual history:** e.g. unprotected sexual intercourse- HIV-acute retroviral syndrome with meningitis; Neuro-syphilis

Question 4:

Is the patient a “normal host” or has a “compromised immune system”?

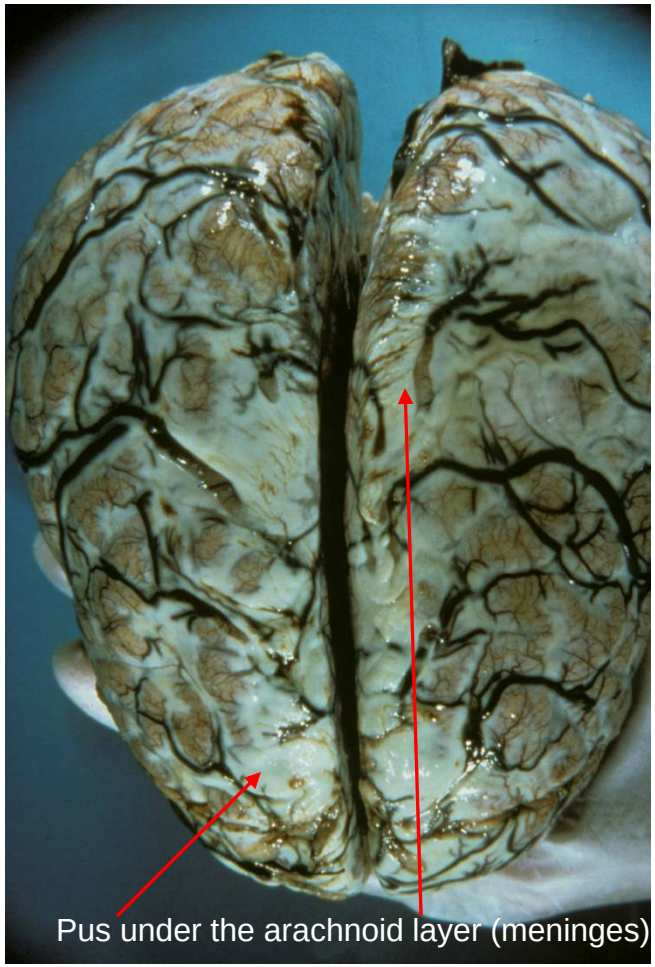
Infection- Balance between organism virulence (infectivity) & host immune capacity



In the right setting any organism (bug) can be a pathogen- In patients with defective immune systems organisms that usually don’t cause infections can cause infections – e.g. Toxoplasmosis in AIDS

Meningitis:
Inflammation of the arachnoid and pia (inner meninges)

- Acute bacterial meningitis (hours-days)
  - 1. Community acquired
  - 2. Hospital acquired/ post neurosurgical
- Acute viral meningitis (hours-days)
- Chronic persistent meningitis (weeks-months-single continuous episode)
- Chronic recurrent meningitis (multiple acute episodes over months-years)



Courtesy: Richard Prayson, MD

Acute community acquired bacterial meningitis

- Acute community acquired viral meningitis
- Acute hospital acquired/post-neurosurgical meningitis
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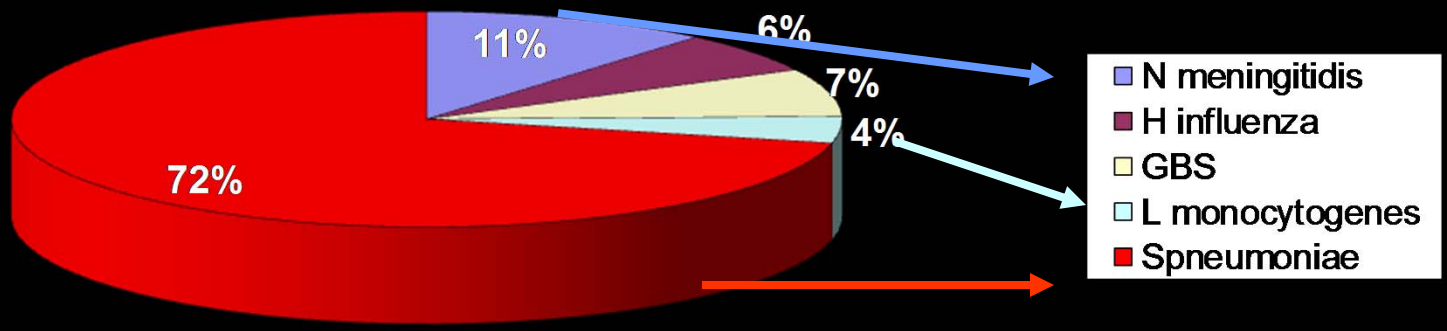
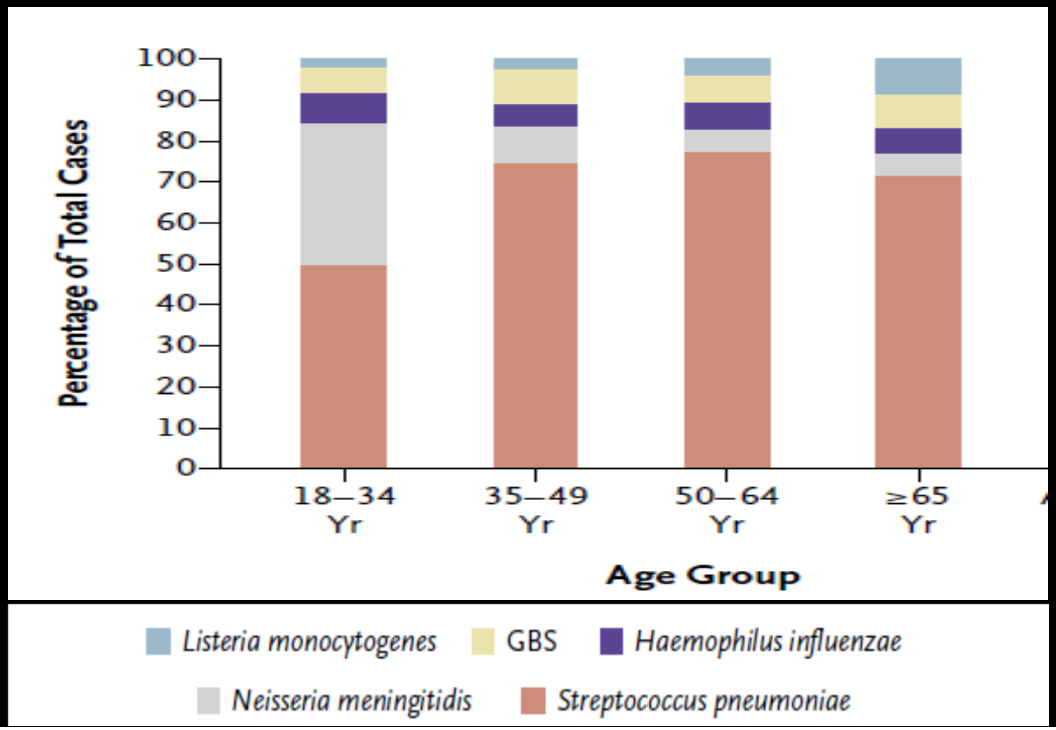
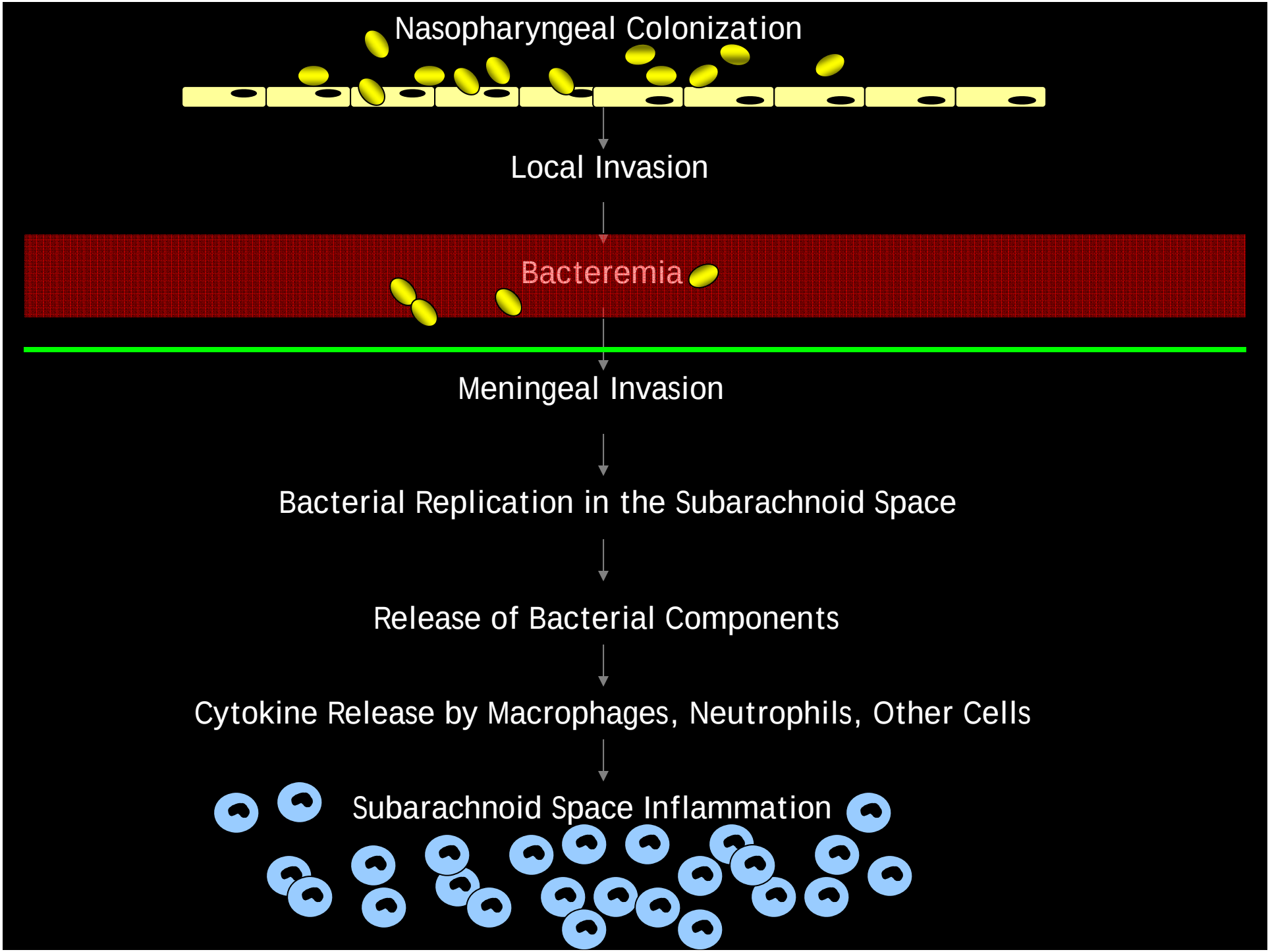
Bacterial Meningitis in the US 1998-2007






Nasopharyngeal Colonization
Local Invasion
Bacteremia
Meningeal Invasion
Bacterial Replication in the Subarachnoid Space
Release of Bacterial Components
Cytokine Release by Macrophages, Neutrophils, Other Cells
Subarachnoid Space Inflammation

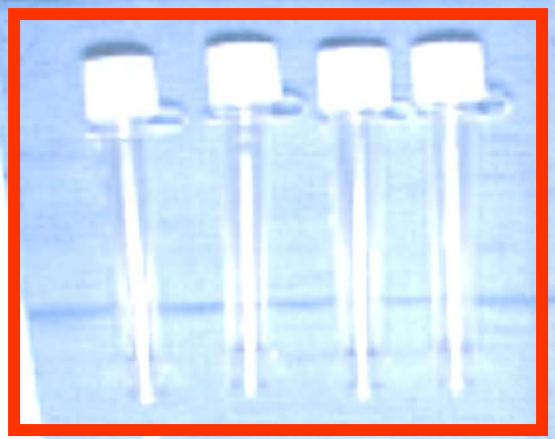
Acute community acquired bacterial meningitis
Symptoms & Signs - *Sick" & "septic"*

Classic triad of signs: 46% but at least one Sx in 99-100%

Findings	Sensitivity (%)
Headache	50
Fever	85
Neck stiffness	70
Altered mental status	67
Nausea &Vomiting	30

JAMA, July 14, 1999—Vol 281, No. 2

Community acquired bacterial meningitis diagnosis: Lumbar puncture →CSF studies



Tube 1: Cell count and differential

Tube 2: Micro-gram's stain and cultures

Tube 3: Chemistry-glucose, protein

Tube 4: Special tests or cytology & RPT cell counts

CSF parameters: Acute meningitis

CSF Parameter	Normal	Bacterial	Viral
Opening pressure (mm H_2O)	60-180	200-500	≤250
WBC (/mm^3)	<5	500-5000	50-1000
WBC differential	-	Neutrophils	Lymphocytes
Glucose (mg/dL)	45-80	<40	>40
CSF: Blood glucose ratio	>0.6	<0.4	>0.6
Protein (mg/dL)		100-500	<200

Community acquired bacterial meningitis in adults: Steroids + antibiotics

Age	**Antimicrobial Therapy**
2-50 years	Vancomycin + a third generation cephalosporin[a]
Older than 50 years	Vancomycin + ampicillin + a third generation cephalosporin[a]

[a]cefotaxime or ceftriaxone

Tunkel AR, Hartman BJ, Kaplan SL, et al: Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis* 39. 1267-1284.2004;

-Acute community acquired bacterial meningitis

Acute community acquired viral meningitis

–Acute hospital acquired/post-neurosurgical meningitis

–Brain abscess, Epidural abscess, Subdural empyema

–Encephalitis

Acute community acquired viral meningitis:

- Symptoms: same as bacterial
  - ”less sick”
  - not septic

- Causative organisms:
  - Enteroviruses- *most common*
  - Adenovirus
  - Arbovirus
  - Herpes Simplex virus
  - Varicella Zoster virus

- Diagnosis: LP – CSF studies (next slide)
  - CSF ;PCR for viruses- especially enterovirus- *results back in hours*

- Treatment & Prognosis:
  - No specific treatment
  - Short duration of symptoms
  - Generally get better by themselves

CSF parameters: Acute meningitis

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-Acute community acquired bacterial meningitis
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Acute hospital acquired/ post-neurosurgical meningitis

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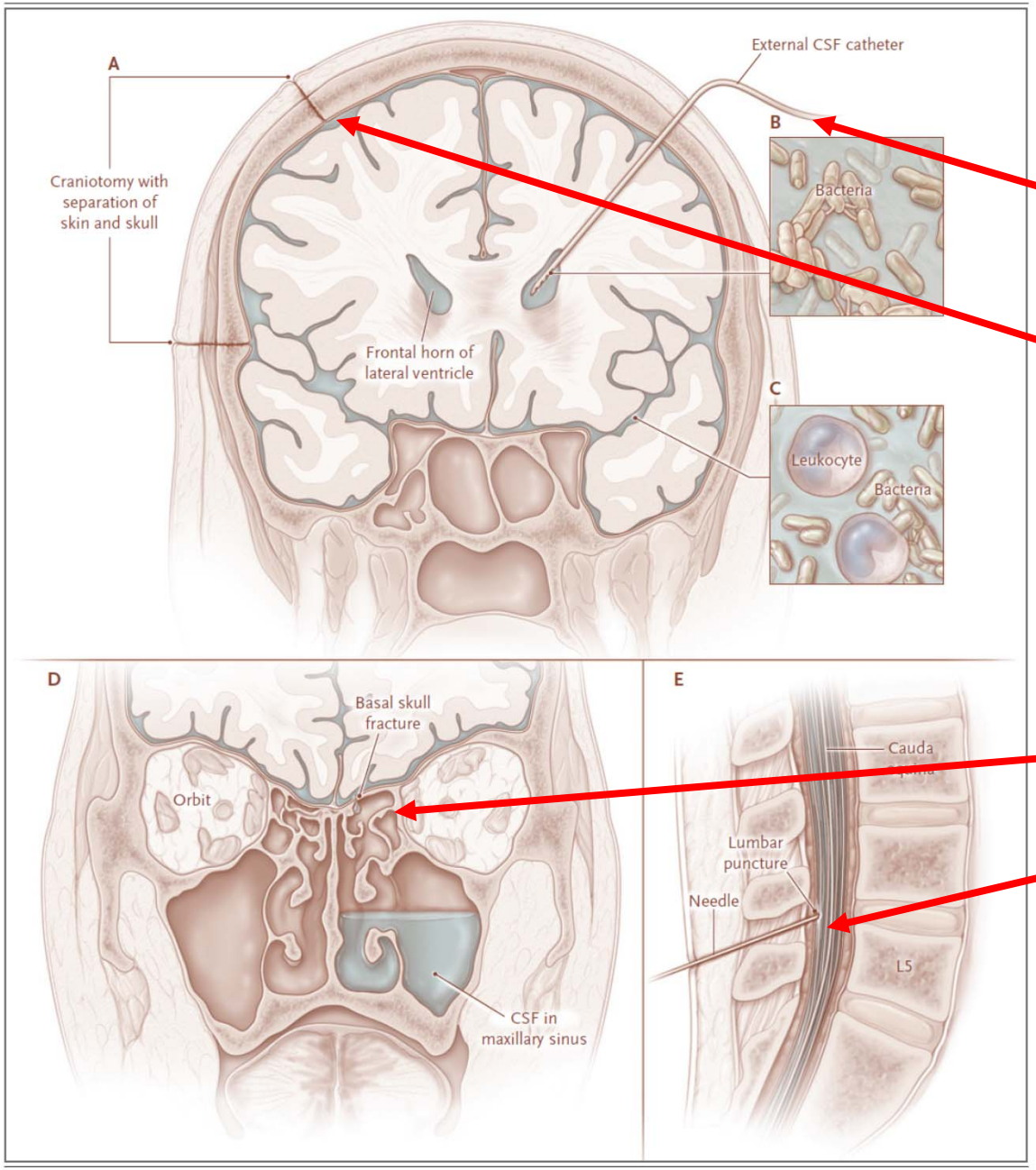
Acute hospital acquired/ post neuro-surgical bacterial meningitis

- Direct spread from the skin through surgical incision site/ neuro-trauma site or introduced intra-op or peri-op
- Can occur days to months after surgery
- Etiology/ clinical presentation:
  - Skin commensals *(Staphylococcus epidermidis* and *Propionobacter acnes*)→ indolent & subtle presentation without fevers or a septic picture
  - Hospital acquired multi-drug resistant bacteria- MRSA, Gram negatives including *Pseudomonas*- Fulminant or septic picture
- CSF: may not be remarkable- only a few WBC's and high protein with a normal glucose
- CSF microbiology: aseptic precautions while collecting form EVD's to avoid contamination. Send aerobic and anaerobic (propionobacter is an anaerobe) cultures

Acute health care acquired/post-neurosurgical meningitis/ ventriculitis



VP shunt related ventriculitis
EVD/LD associated meningitis/ventriculitis

Post craniotomy meningitis

Post traumatic meningitis

Post-LP/LD meningitis

N ENGL J MED 362;2 NEJM.ORG JANUARY 14, 2010

Antimicrobial recommendations for hospital acquired bacterial meningitis

adapted from CID 2004:39

Predisposing Factor	Common pathogens	Treatment
Head Trauma		
Basilar Skull Fracture	Pneumococcus, *H. influenzae*, GAS	Vancomycin + 3rd gen CSPN
Penetrating trauma	*S. aureus*, CNS, aerobic GNR	Vancomycin + cefepime, ceftazidime, or meropenem
Post neurosurgery	*S. aureus,* CNS, aerobic GNR	Vancomycin + cefepime, ceftazidime, or meropenem
CSF Shunt/ drain	CNS, *S. aureus*, aerobic GNR, *P. acnes*	Vancomycin + cefepime, ceftazidime, or meropenem

-Acute community acquired bacterial meningitis
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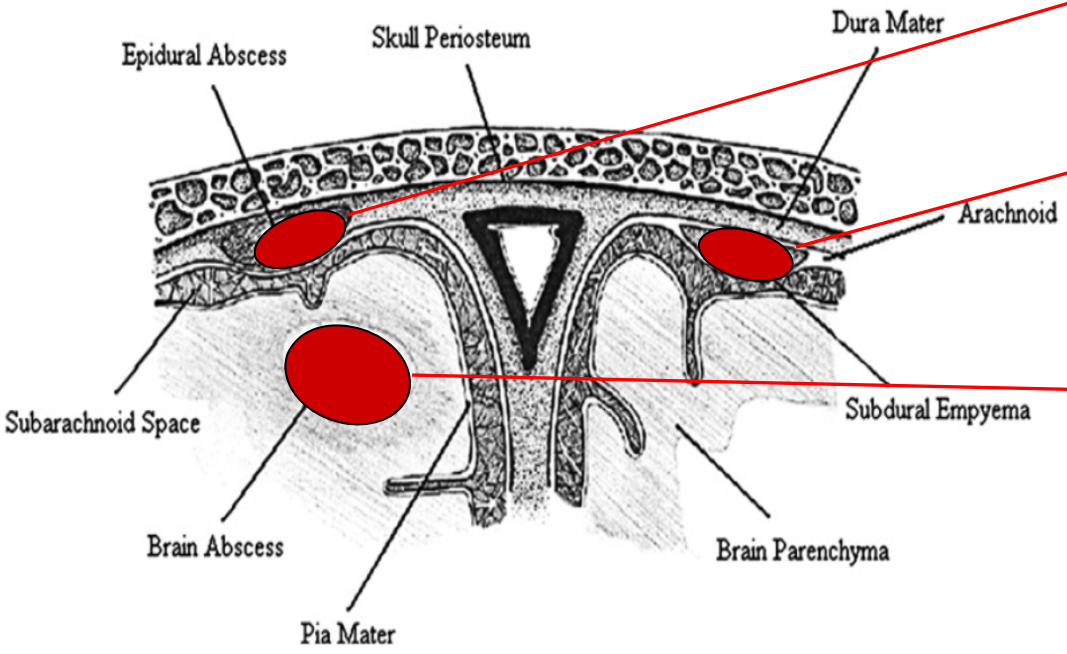
Brain abscess, epidural and subdural empyema

-Encephalitis

Focal infections of the brain parenchyma (pus collections)

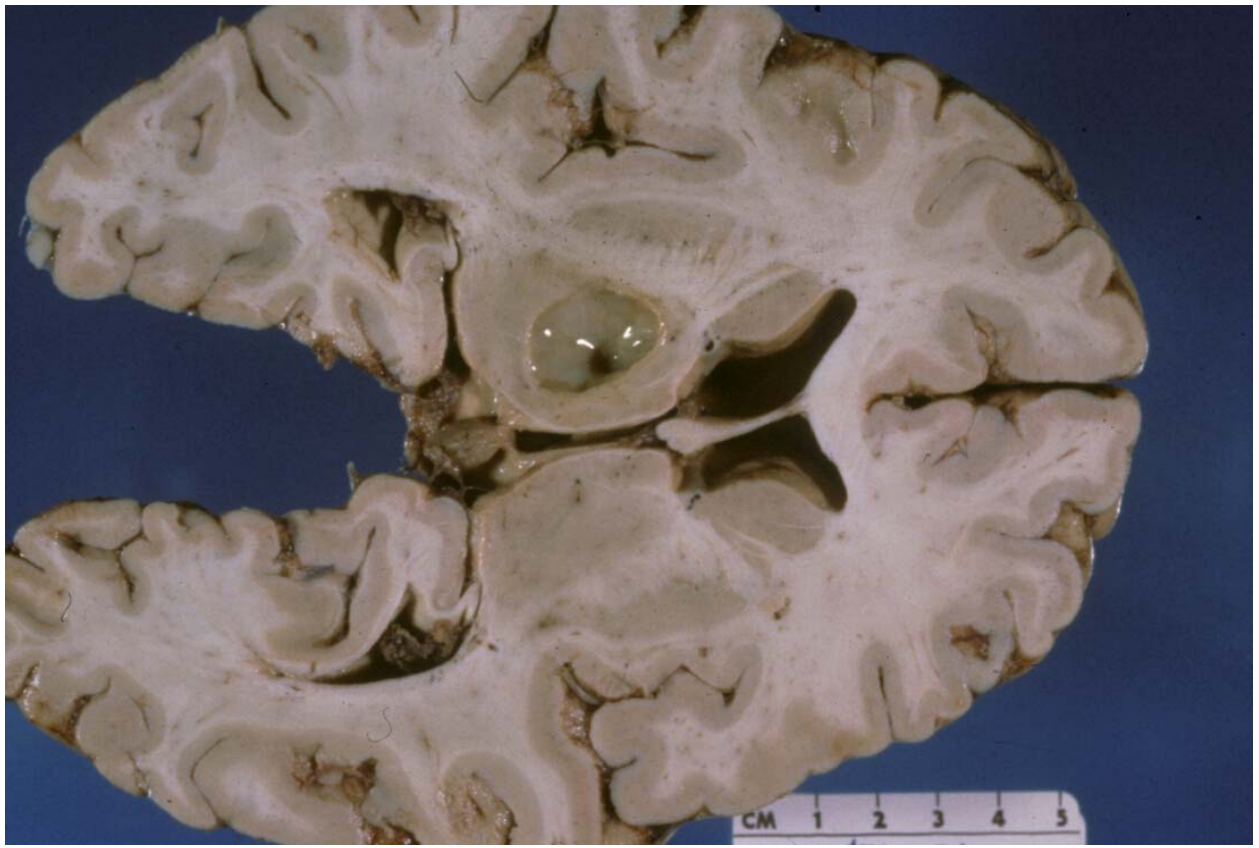


- Epidural abscess
- Subdural empyema (abscess)
- Brain abscess

Focal infections of the brain parenchyma (pus collections)

- Spread from contiguous structures/post op incision sites –direct and via valve-less veins (face, sinuses, ear infections)
- "Focal neurologic" symptoms & signs: paralysis, gait disturbances- depending on the area of the brain involved
- **Diagnostic imaging:** MRI brain with & without contrast-better than CT brain
- **Treatment:** Often need surgical drainage + antibiotics
- Start antibiotics after drainage and collection of tissue for stains & culture
- Empiric antibiotics: Vancomycin + ceftriaxone (ceftazidime in post neurosurg patiets to cover Pesudomonas)+ metronidazole (anaerobes)

Brain abscess



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-Acute community acquired bacterial meningitis
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-Acute hospital acquired/post-neurosurgical meningitis
-Brain, epidural and subdural empyma

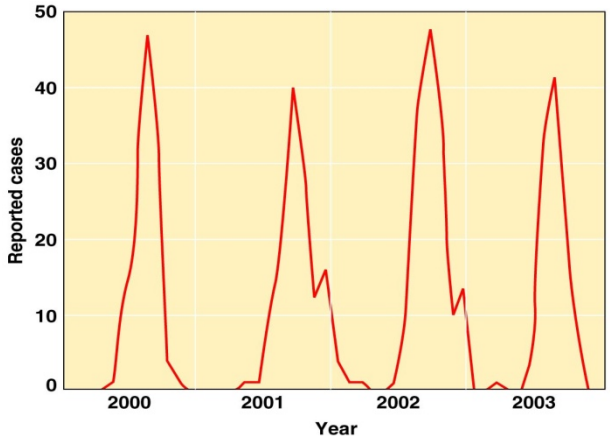
Encephalitis

Encephalitis-infection of the brain parenchyma

- Mostly viral etiology
  - HSV1 (herpes simplex 1) -Most common viral encephalitis
  - Other causes arboviruses

- Arboviruses are arthropod-borne viruses that belong to several families
  - Mosquito borne

  - June to November (seasonal)



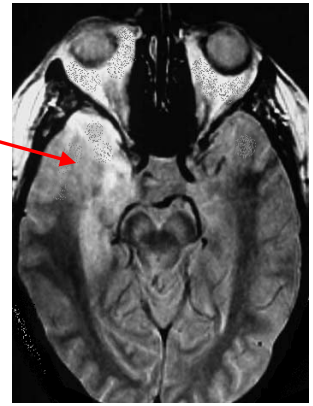
  - Most common arboviral infection in the US:West Nile virus

Arboviral Encephalitis

Encephalitis	Reservoir	Mosquito vector	U.S. distribution
Western equine	**Birds, horses**	*Culex*	
Eastern equine	**Birds, horses**	*Aedes*, *Culiseta*	
St. Louis	**Birds**	*Culex*	
California	**Small mammals**	*Aedes*	
West Nile	**Birds, mammals**	*Culex*, *Aedes*	

HSV Encephalitis

- Most common viral encephalits
- Occurs through out the year- no seasonal predilection
- Clinical presentation: Confusion, personality changes and olfactory hallucinations.
- CSF: RBC's- Due to temporal lobe damage/ hemorrhage
- Typical MRI/CT finding- Temporal lobe involvement
- CSF Polymerase Chain Reaction
  - Sensitivity 98%
  - Specificity 94%
- Only viral encephalitis with an effective treatment- Acyclovir 10 mg/kg IV q8hrs is the antiviral agent of choice x 14-21 days



Questions & Discussion