

MICROBIOLOGY OF OTITIS, SINUSITIS, AND MENINGITIS

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- **diseases and their agents that afflict various parts of the head**
- **middle ear (otitis media)**
- **sinuses (sinusitis)**
- **central nervous system (meningitis)**

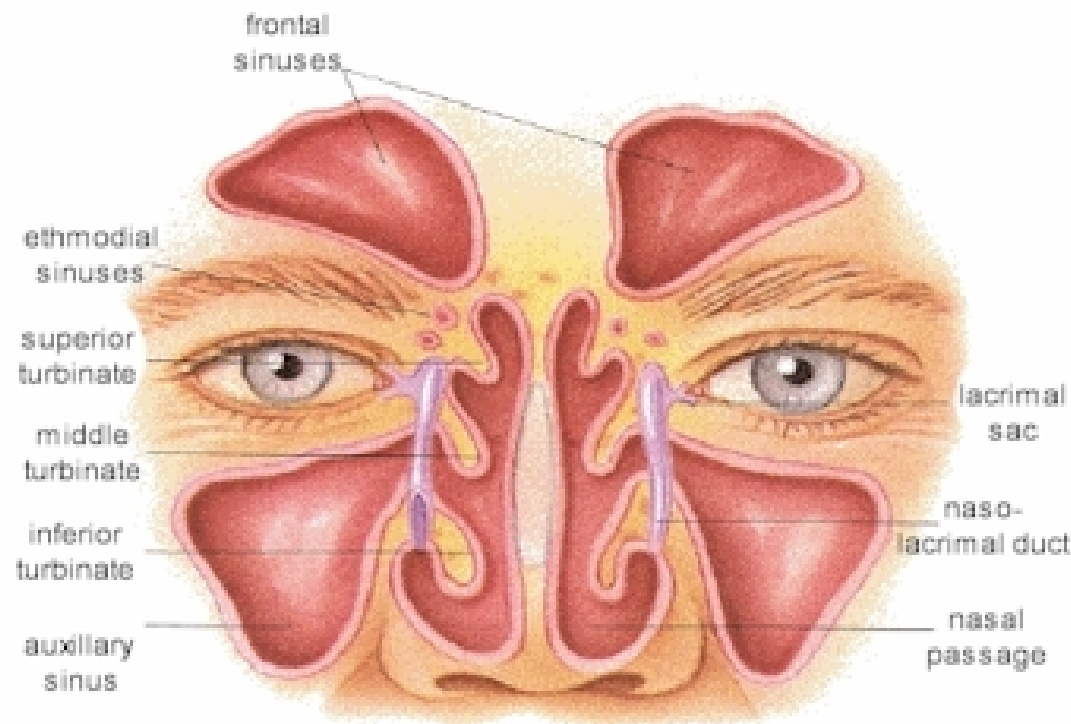
- **Upper respiratory tract**
 - **lack of cellular and humoral defenses**
 - **normal flora**

- **almost all of these diseases begin with infection of the nasopharynx and/or nasal cavities**

A 35 year-old male experiences an unremarkable cold during the fall. After a course of rhinorrhea, cough, and post-nasal URT congestion, his nasal drainage becomes more **purulent, thick, and greenish**. He relies on OTC decongestants. However, the nasal congestion continues to worsen with increased **pressure in the sinuses** upon bending over. Then the pressure and pain in the sinuses reach a crescendo forcing a phone call to the physician's office resulting in a prescription for antibiotics. Patient promptly initiates therapy. However, later in the day extreme burning pain radiates from the sinuses upward to the **orbit** without relief from OTC anesthetics, forcing a visit to the Shands ER. Attending physician makes diagnosis without radiology, prescribes potent pain-killers, stronger antibiotics, and non-steroidal anti-inflammatory agents. Symptoms gradually subside over next two days with copious nasal drainage.

SINUSITIS - infection and inflammation of the sinuses - primarily in adults, rarely in infants

The **sinuses** open to the **nasal cavity**. They normally are **sterile, air-filled mucosal-lined cavities** but can become **infected with bacteria from the URT**. Consider the **predisposing** factors in the initial blockage - URT infection, mechanical (polyps, enlarged lymph nodes, tumor), allergy, etc.



Symptoms

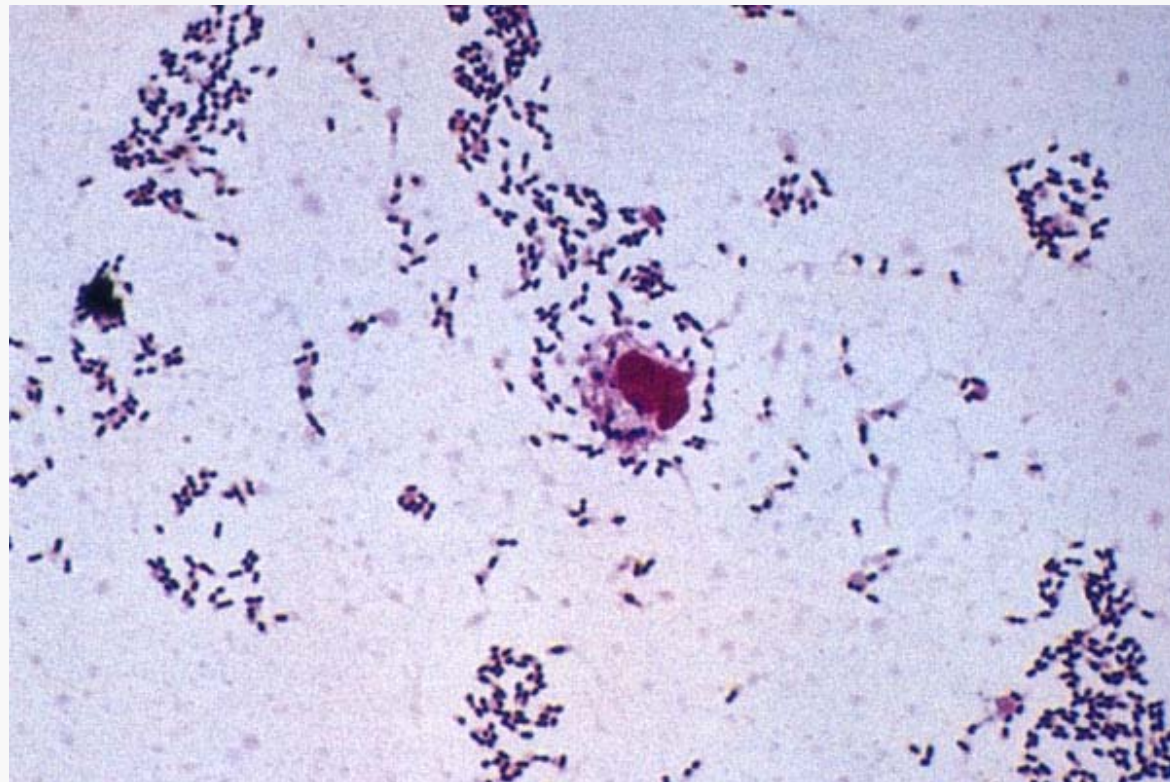
- **fever**
- **cough**
- **nasal discharge**
- **fetid breath**
- **pain over sinuses**
- **headache**
- **tenderness over sinuses**

Agents

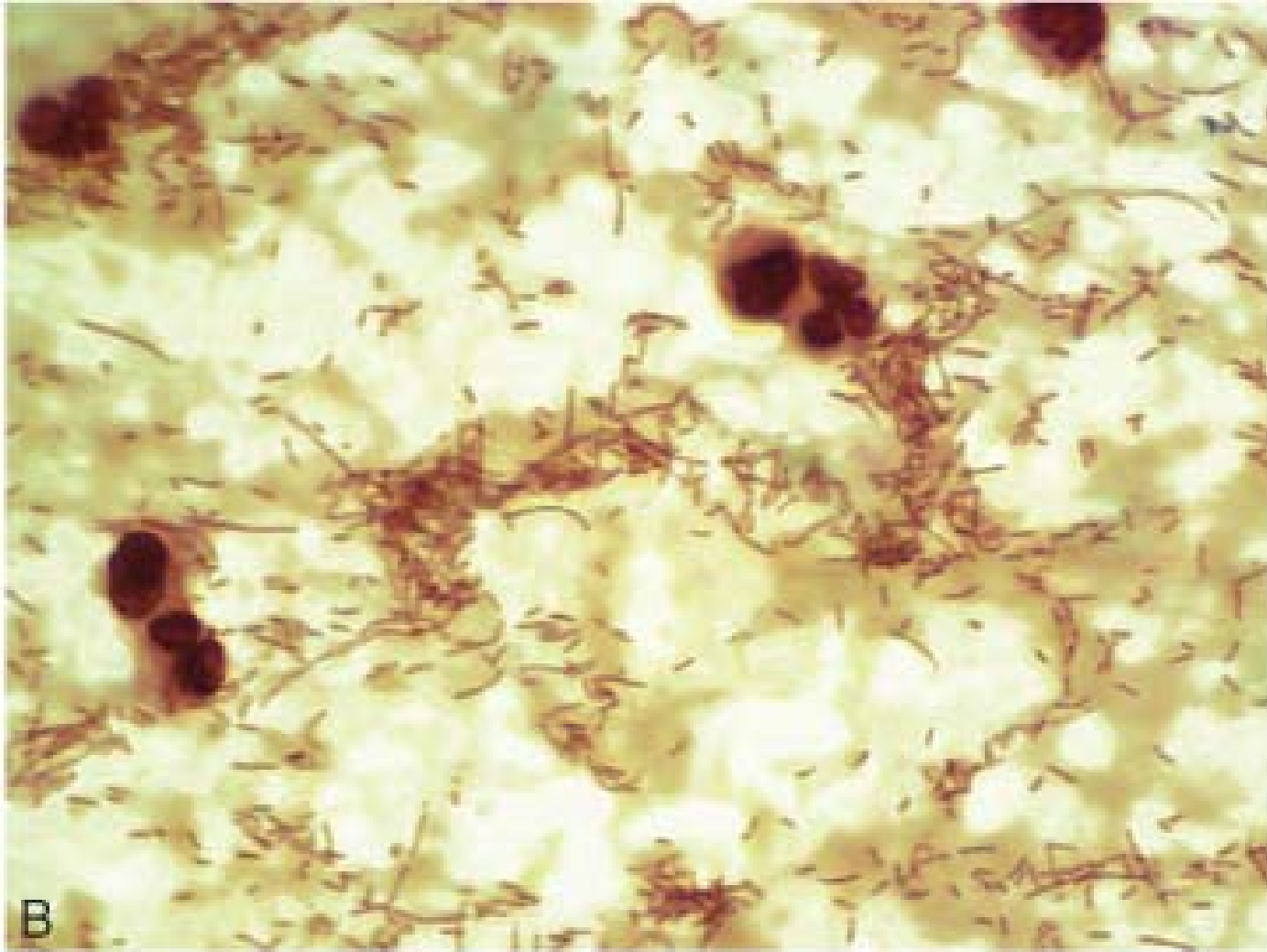
acute sinusitis

- **normal flora** of the upper respiratory tract with the potential to cause disease

Streptococcus pneumoniae



non-typeable *Haemophilus influenzae*
- gram-negative coccobacillus, fastidious



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Moraxella catarrhalis

- gram-negative diplococcus



chronic sinusitis

same as for acute + gram-negative enterics,
anaerobes

mixed infections

PATHOGENESIS

1. ENCOUNTER

- **endogenous** infection from URT flora
- human only

2. ENTRY

- sinuses from the URT (nasopharynx and nasal cavity).
- **Drainage of the sinuses is obstructed**, usually by a viral URI.
- Enabling growth of bacteria at that site.

3. SPREAD

- **none needed**
- organisms can remain at the mucosal surface
- invasion through tissues
- invasive disease (e.g., adjacent tissues; bacteremia and meningitis)

PATHOGENESIS

4. **EVADE DEFENSES**

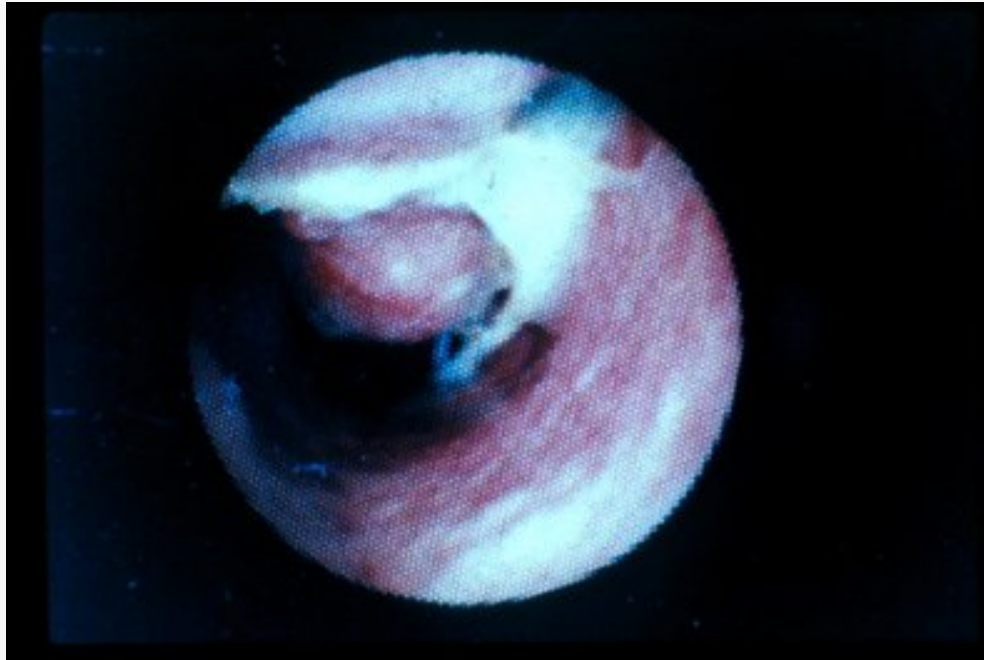
- mucus drainage
- non-immune host there are **none**
- Inflammation - phagocytes
- **EXTRACELLULAR** pathogens; sIgA could help.

5. **MULTIPLY**

- discharge is a good growth environment
- blockage - anaerobic, especially with mixed infections

6. DAMAGE

- **inflammation** and **discharge**



- swelling and blockage
- cyclic pattern of damage
- discomfort - pressure and blocked nasal passages

7. Outcome:

- **usually self limiting**
- **spread to new hosts - droplet/saliva**

DIAGNOSIS

- **radiology** of sinuses



- **clinical** presentation
- Defer to clinical lecture
- (the Parker Small snot test?)

TREATMENT

antibiotics

anti-inflammatory agents

decongestants, fluids

Two-year-old son of patient from case 1 experiences **unremarkable cold** with minor, clear nasal drainage and no fever. Two days later as cold is subsiding, the boy experiences a low grade **fever of 38°C**, is **irritable**, and pulls at his right ear. At pediatrician's office using an othothermometer, pediatrician notes fever and elicited pain and crying during taking of temperature in right ear! He then bends child's legs to chest and then bends child's neck forward during physical examination. Otoscopic examination of left ear is unremarkable; however right tympanic membrane is **red, inflamed, and dull in appearance**. Tympanometry reveals **lack of acoustic impedance**. Child is placed on antibiotics, and 10 day follow-up examine is scheduled. Child begins recovery within one day of treatment.

OTITIS MEDIA

infection of the **middle ear**, primarily in **infants and young children**

three manifestations

- **acute otitis media**
- **chronic otitis media**
- **otitis media with effusion**

Symptoms

- **fever**
- **pain in the ear**
- **dulled hearing**

DIAGNOSIS –

1. **clinical presentation** of fever and pain, especially following an URT infection such as a cold
2. **otoscopic examination** to see inflammation and/or fluid (pus); also loss of mobility with air pressure



3. **tympanometry** to detect impaired tympanic membrane function

Agents

1. **Acute** (normal flora of the URT)
 - ***Streptococcus pneumoniae***
 - **nontypeable *Haemophilus influenzae***
 - ***Moraxella catarrhalis***
 - lesser importance: *Streptococcus pyogenes*,
Staphylococcus aureus
2. **chronic**
mixed infections with various URT flora
anaerobes, and enterics, possibly viruses

PATHOGENESIS

1. **ENCOUNTER - endogenous** infection; human only

2. **ENTRY**

- middle ear - **eustachian tube** URT (nasopharynx)
- infants and very young children, predisposed
- **URT flora** communicate into the middle ear
- inhibited **drainage** by inflammation, infection, or physical barrier (just as for sinusitis), the bacteria can initiate an infection that cannot be mechanically cleared.

3. **SPREAD - none** needed; mucosal surface only

Infection can spread to mastoid air cells and rarely CNS

PATHOGENESIS

4. EVADE DEFENSES

- mucus drainage
- non-immune host there are **none**
- inflammation – phagocytes; **EXTRACELLULAR**
- **sIgA** could help

5. **MULTIPLY** - the discharge is a good growth environment

6. DAMAGE –

- **INFLAMMATION** and fluid exudation/edema (effusion)
- severe/chronic infection - damage to middle ear
- prolonged **hearing** impairment - learning development

7. OUTCOME

- Self limiting, possible severe sequelae
- Spread to new hosts - droplet/saliva

TREATMENT - HIGHLY CONTROVERSIAL !!!!

depends on the form of otitis media

I always defer to ENT docs

1. **antibiotics**
2. for recurrent cases - **surgery** (remove **adenoids**) to remove bacterial reservoir and blockage
3. **Myringotomy tubes** - a tube placed through the tympanic membrane to enable ventilation, thereby decreasing subsequent infection.

One week after arriving at boot camp, Pvt. A experiences a precipitous onset of fever (40C) and headache. Within hours he felt pain in his neck upon movement of his head. He reported to the medical unit. Lumbar puncture was performed after determining that pressure was only slightly elevated (220 mm H₂O). CSF was cloudy and contained 5,000 leukocytes/ul (75% PMNs), no RBCs, glucose - 15 mg/dl, protein - 150 mg/dl. A gram stain revealed gram-negative diplococci with kidney bean appearance. Patient was initiated on i.v. antibiotics. Three days later, Pvt. B experienced similar course of illness and prompt treatment based on diagnosis of Pvt. A. Other contacts within their unit were then placed on prophylactic antibiotics to halt the epidemic.

ACUTE BACTERIAL MENINGITIS

infection and inflammation of the meninges

infection of other parts of the **CNS**

SYMPTOMS

(meningeal symptoms)

- high fever
- headache
- stiff neck
- irritability (children)
- neurologic dysfunction
 - lethargy
 - confusion
- uncharacteristic sleepiness
- vomiting

Agents: - vary depending on the **age** of the patient

1. newborns/neonates

- **Group B streptococci**
- ***E. coli* K1**
- ***Listeria monocytogenes***

2. infants and children up to 24 months old

- ***Streptococcus pneumoniae***
- ***Neisseria meningitidis***
- **(*Haemophilus influenzae* type b – vaccine; self study)**

3. Adults

- ***Streptococcus pneumoniae***
- ***Neisseria meningitidis***

Meningitis and sepsis of newborns:

Group B streptococci (GBS)

- gram-positive cocci
- type-specific carbohydrate capsules
 - prevent phagocytosis



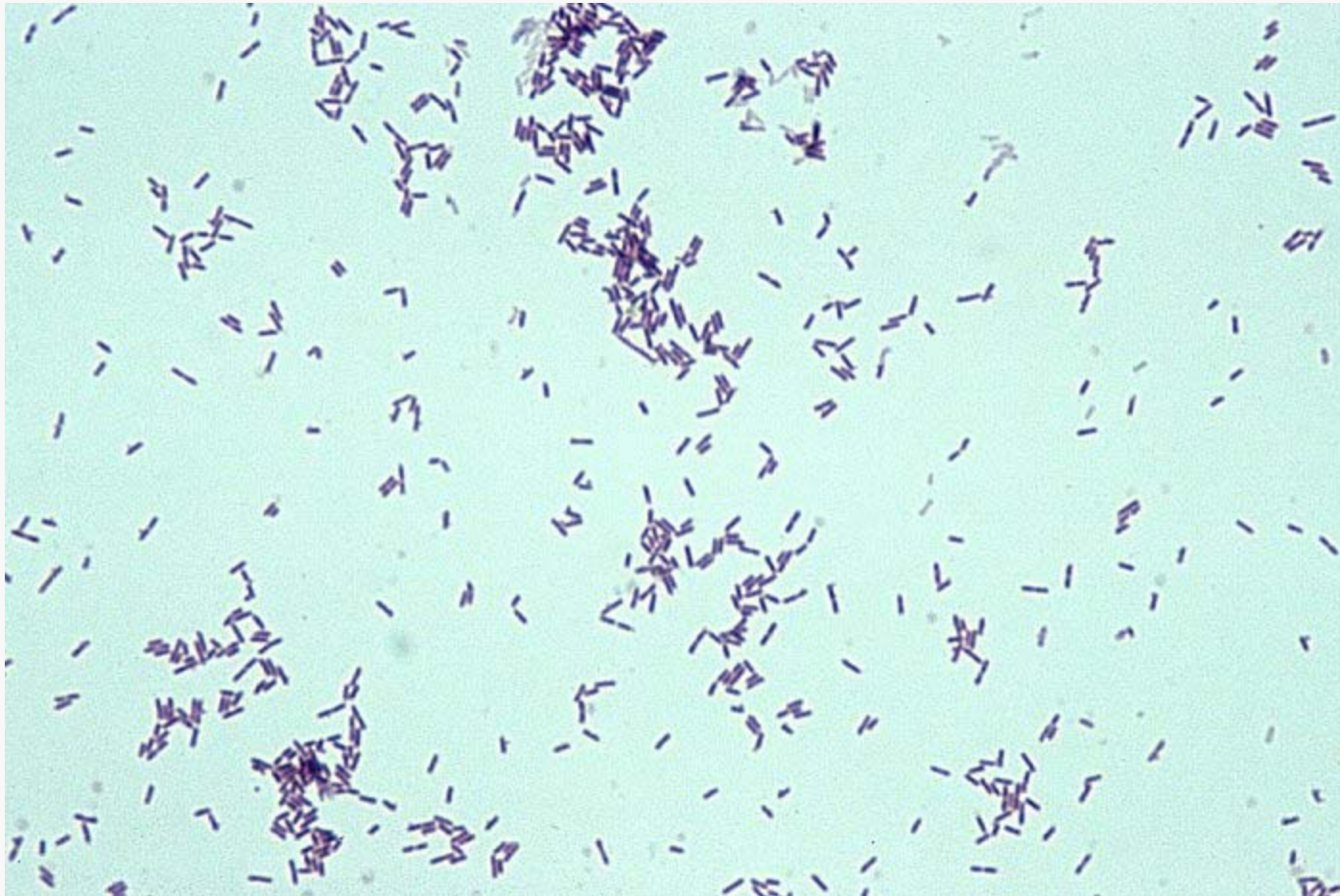
E. coli K1

- gram-negative rod
- polysialic acid capsule



Listeria monocytogenes

- gram-positive rod
- non-spore forming



PATHOGENESIS

1. ENCOUNTER

- **genital tract of the mother** is colonized

2. ENTRY

- newborn infected during birth via the **upper respiratory tract or gastrointestinal tract**

3. SPREAD

- from the **URT**, the bacteria **invade through the mucosal surface** into the **bloodstream**
- crossing the **blood/brain barrier** by unknown mechanisms
- **inflammation** can contribute to leakiness

PATHOGENESIS

4. EVADE DEFENSES

- **GBS and *E. coli* K1 – EXTRACELLULAR**
- **CAPSULES**
- **GBS secretes a C5a peptidase**

***L. monocytogenes* – INTRACELLULAR**

- **invade non-phagocytes**
- **infect **macrophages****
- **lyse the phagosome**
- **escape into the **cytoplasm****
- **use host actin to spread from cell-to-cell**

5. DAMAGE

INFLAMMATION

- triggered by either peptidoglycan and/or LPS

fluid accumulation

- increased intracranial pressure, hydrocephalus, and brain damage

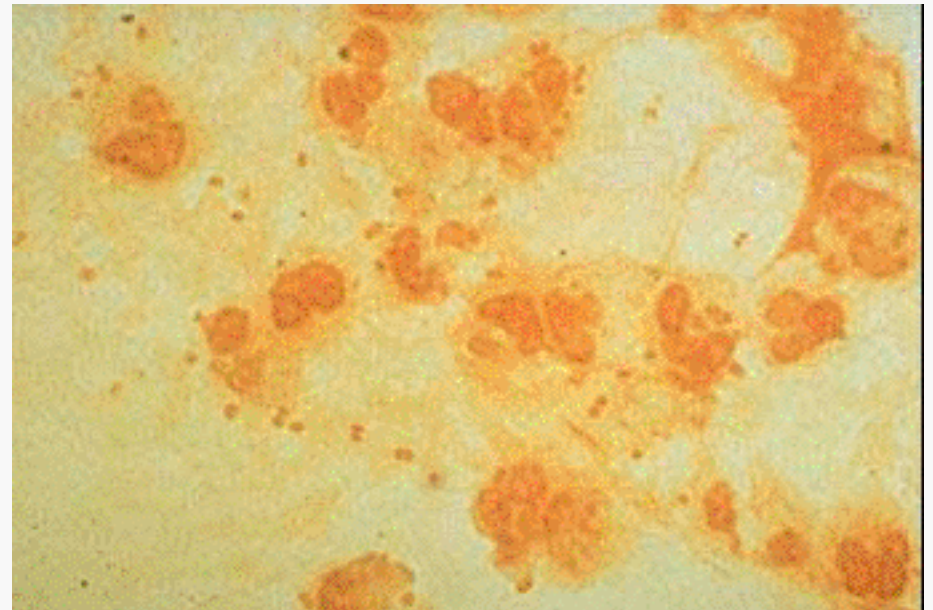
INFECTIONS OF **CHILDREN**: PRIMARILY **MENINGITIS**

Streptococcus pneumoniae

- gram-positive diplococcus
- encapsulated

Neisseria meningitidis

- gram-negative diplococcus
- encapsulated
 - antigenic group
 - group B is polysialic acid



***Haemophilus influenzae* type b (Hib)** gram negative rod, encapsulated (type b antigen)

- non-typeable and types a,c,d,e,f - less disease
- **Hib was the primary cause of meningitis in children ages 6 months to 2 years; vaccine** all but eliminated **Hib meningitis** and invasive disease

Self study

Pathogenesis

1. **ENCOUNTER** – **human only**, respiratory droplet or saliva, can be endogenous
2. **ENTRY - URT** (nasopharynx), adherence factors pili for Hib and meningococcus
3. **SPREAD** - invade from URT into blood, cross blood-brain barrier then to CNS
4. **MULTIPLICATION** - Hib is fastidious, requires chocolate agar [X factor - hemin, V factor - NAD]; *N. meningitidis* - chocolate agar or Thayer-Martin agar
5. **EVADE DEFENSES – EXTRACELLULAR; CAPSULES; IgAse**
6. **DAMAGE - INFLAMMATION** - peptidoglycan and/or LPS
7. **OUTCOME:**
 - a. death, neurological sequelae
 - b. Spread to new host - droplet/saliva

HIB VACCINE

- humoral **IgG** to capsule prevents systemic infection by **opsonization**
- composed of type b carbohydrate coupled to protein
- drastically reduced meningitis by Hib
- single serologic type of capsule associated with systemic disease makes single vaccine sufficient
- part of the standard infant/childhood regimen

Infections of adults - meningitis and sepsis

Agents

- a. *Streptococcus pneumoniae*
- b. *Neisseria meningitidis*

Pathogenesis - same as children:

URT -> blood -> CNS -> inflammation

***N. meningitidis* can also severe sepsis - meningococemia with petechial rash and hemorrhagic adrenal damage (Waterhouse- Friderichsen syndrome)**

meningococcal meningitis - epidemic spread in stressed and crowded populations (e.g., military boot camp)

PREVENTION - polyvalent polysaccharide vaccines are available for *S. pneumoniae* and *N. meningitidis*. They are given to populations at risk.

new protein conjugate vaccine for *S. pneumoniae* - 13 capsular carbohydrates coupled to genetically modified diphtheria toxin (also a 7 type form); also might be used in children to prevent otitis media?

N. meningitidis has a capsular type composed of polysialic acid (antigenic mimicry)

DIAGNOSIS of bacterial meningitis

1. **cerebrospinal fluid analysis** - Gram stain, presence of or elevated leukocytes, with predominant PMN, decreased glucose, elevated protein
2. **blood culture**
3. possibly detecting capsular antigen in CSF, blood, or urine by antigenic test

TREATMENT - Prompt antibiotic therapy; possibly anti-inflammatory agents; reducing intracranial pressure