Bacterial infections of the Respiratory tract 2

By : Nader Alaridah MD , PhD

STREPTOCOCCUS PNEUMONIAE

- Pneumococci are gram-positive lancet-shaped cocci arranged in pairs (diplococci) or short chains (The term lancet-shaped means that the diplococci are oval with somewhat pointed ends rather than being round.
- All virulent strains have surface capsules, composed of high-molecular-weight polysaccharide polymers.
- On blood agar, they produce α-hemolysis, In contrast to viridans streptococci, they are lysed by bile or deoxycholate, and they are sensitive to optochin.
- Pneumolysin forms pores after release by autolysins

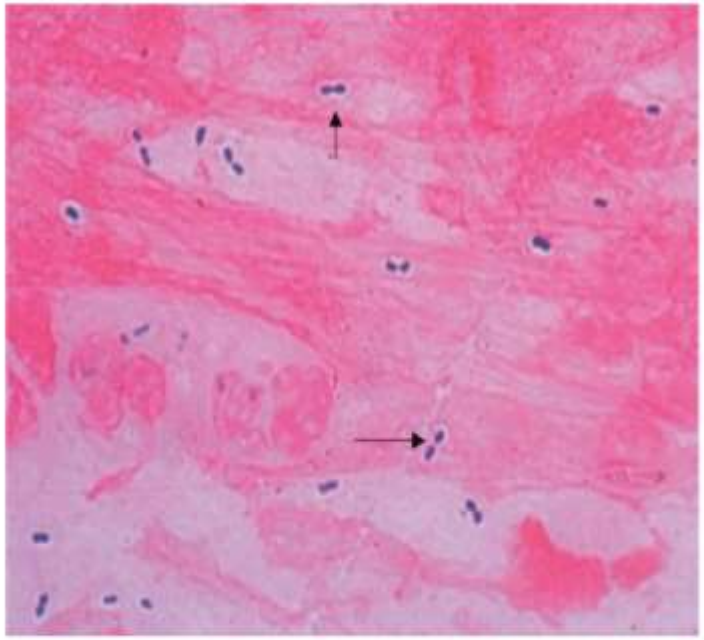


FIGURE 15–15 *Streptococcus pneumoniae*—Gram stain. Arrows point to typical gram-positive diplococci. Note that the clear area around the organism is the capsule. (Used with permission from Professor Shirley Lowe, University of California, San Francisco School of Medicine.)

Pathogenesis, virulence factors:

- The most important virulence factor is the capsular polysaccharide, and anticapsular antibody is protective.
- Lipoteichoic acid: complement activator, it induces inflammatory cytokine production contributes to the inflammatory response and to the septic shock syndrome that occurs in some immunocompromised patients (a bit similar to protein A in LPS in Gram negatives).
- Pneumolysin, the hemolysin that causes α-hemolysis, may also contribute to pathogenesis.
- Pneumococci produce IgA protease that enhances the organism's ability to colonize the mucosa of the upper respiratory tract.

- Factors that lower resistance and predispose persons to pneumococcal infection include (factors that reduce mucus clearing or factors that decrease immune reaction)
- (1) anything that can depress the cough reflux : alcohol or drug intoxication or other cerebral impairment(geriatrics ,CVA, mental impairment) , all contribute to an increase **aspiration** of secretions (and thus pneumonia)
- (2) abnormality of the respiratory tract (e.g., viral infections), pooling of mucus, bronchial obstruction, and respiratory tract injury caused by irritants (which disturb the integrity and movement of the mucociliary blanket) all prevent clearing of mucus and predispose to community acquired pneumonia caused by pneumococcus.
- (3) abnormal circulatory dynamics (e.g., pulmonary congestion and heart failure)- will congest the blood in the lung, increase pulmonary secretions→ pnumococcus
- (4) splenectomy (capsule, reduces immunity) and certain chronic diseases such as sickle cell anemia and nephrosis, patients with sickle cell anemia autoinfarct their spleen, become functionally asplenic, and are predisposed to pneumococcal sepsis.
- Trauma to the head that causes leakage of spinal fluid through the nose predisposes to pneumococcal meningitis.

Transmission

- Humans are the natural hosts for pneumococci; there is no animal reservoir.
- Because a proportion (5%–50%) of the healthy population harbors virulent organisms in the oropharynx, pneumococcal infections are not considered to be highly communicable (often it happens from your own flora).
- Resistance is high in healthy young people, and disease results most often when predisposing factors are present.

- Diseases
- Streptococcus pneumoniae (pneumococcus) causes 1) pneumonia 2) bacteremia 3) meningitis, and 4) URTI (upper respiratory tract infections)- such as otitis media, mastoiditis, and sinusitis.
- Pneumococci are the **most common cause** of community-acquired pneumonia, meningitis, sepsis in splenectomized individuals(?), otitis media, and sinusitis.
- They are a common cause of conjunctivitis, especially in children.

Pneumonia

- *Str. pneumoniae* **is the most frequent cause of pneumonia** with an estimated annual incidence of 1–3 per 1000 of the population, **with a 5% case fatality rate.**
- Pneumococcal pneumonia usually follows aspiration (!) with subsequent migration of through the bronchial mucosa to involve the surrounding lymphatics.
- The inflammatory reaction is **focused primarily within the alveolus of a single lobule or lobe, although multilobar disease can also occur**.
- Contiguous spread commonly results in inflammatory involvement of the pleura; this may progress to empyema.
- Pericarditis is an uncommon but well recognized complication.

http://www.chestx-ray.com/index.php/education/normal-cxr-module-train-your-eye

- Occasionally, lung necrosis and intrapulmonary abscess formation occur with the more virulent pneumococcal serotypes.
- Bacteraemia may complicate pneumococcal pneumonia in up to 15% of patients.
- This can result in metastatic involvement of the meninges, joints and, rarely, the endocardium.
- The mortality rate from pneumococcal pneumonia in those admitted to hospital in the UK is approximately 15%.
- It is increased by age, underlying disease, bloodstream involvement, metastatic infection and certain types of pneumococci with large capsules (e.g. serotype 3).

Otitis media and sinusitis

- Middle ear infections (otitis media) affect approximately half of all children between the ages of 6 months and 3 years; approximately one-third of cases are caused by *S. pneumoniae*.
- Disease occurs after acquisition of **a new strain to which** there is no pre- existing immunity.
- The prevalence is highest among children attending kindergarten or primary school,
- where there is a constant exchange of pneumococcal strains.

Meningitis

- *Str. pneumoniae* is among the three leading causes of bacterial meningitis. It is assumed that invasion arises from the pharynx to the meninges via the blood- stream, as bacteraemia usually coexists. Meningitis may occasionally complicate pneumococcal infection at other sites, such as the lung and middle ear.
- The incidence of pneumococcal meningitis is bimodal and affects children less than 3 years of age and adults of 45 years and above.
- **The fatality rates are 20% and 30%,** respectively, considerably higher than those associated with other types of bacterial meningitis

Clinical Findings

- Pneumonia:
- sudden chill, fever, cough, and pleuritic pain (chest pain that increases with chest movement-breathing).
- Sputum is a red or brown “rusty” color.
- Bacteremia occurs in 15% to 25% of cases.
- Spontaneous recovery may begin in 5 to 10 days and is accompanied by development of anticapsular antibodies.
- Pneumococci are a prominent cause of otitis media, sinusitis, mastoiditis, conjunctivitis, purulent bronchitis, pericarditis, bacterial meningitis, and sepsis.
- Pneumococci are the **leading cause of sepsis in patients** without a functional spleen.

Laboratory Diagnosis

- In sputum: lancet-shaped gram-positive diplococci in Gram-stained smears.
- Can be detected by using the quellung reaction with multitype antiserum.
- On blood agar, pneumococci form small **α-hemolytic colonies**.
- The colonies are bile-soluble (i.e., are lysed by bile), and growth is inhibited by optochin.
- Blood cultures are positive in 15% to 25% of pneumococcal infections.

Left Side

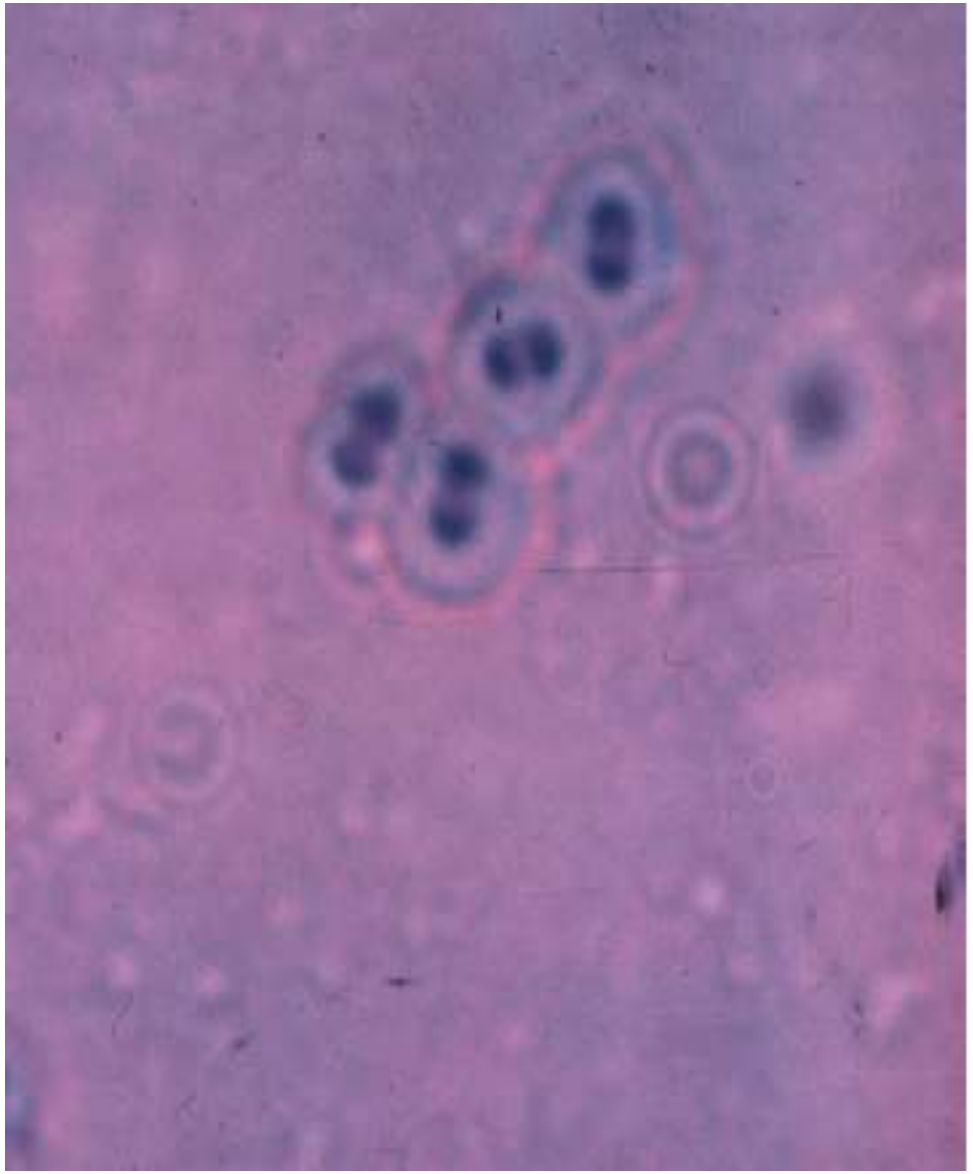
S. mitis

Resistant to optochin

Right Side

S. pneumoniae

Susceptible to optochin



Quellung reaction

Treatment

- Most pneumococci are susceptible to penicillins and erythromycin, although significant resistance to penicillins has emerged
- In severe pneumococcal infections, penicillin G is the drug of choice, whereas in mild pneumococcal infections, oral penicillin V can be used.
- A fluoroquinolone with good antipneumococcal activity, such as levofloxacin, can also be used.
- In penicillin-allergic patients, erythromycin or one of its long-acting derivatives (e.g., azithromycin) can be used.
- An increasing percentage of isolates, ranging from 15% to 35% depending on location, show high-level resistance, which is attributed to multiple changes in penicillin binding proteins.
- They do not produce β-lactamase. Vancomycin is the drug of choice for the penicillin-resistant pneumococci, especially for severely ill patients.
- Ceftriaxone or levofloxacin can be used for less severely ill patients.

Prevention

- Despite the efficacy of antimicrobial drug treatment, the mortality rate of pneumococcal infections is high in **immunocompromised** (especially splenectomized) patients **and children under the age of 5 years** Such persons should be immunized with the 13-valent pneumococcal conjugate vaccine (Prevnar 13) (must be given booster doses every 5 years).
- The immunogen in this vaccine is the pneumococcal polysaccharide of the 13 most prevalent serotypes conjugated (coupled) to a carrier protein (diphtheria toxoid). The unconjugated 23-valent pneumococcal vaccine (Pneumovax 23) should be given to healthy individuals **age 50 years or older (booster doses at 65)**.
- These vaccines are safe and effective and provide long-lasting (at least 5 years) protection.

HAEMOPHILUS important Properties

- *H. influenzae* G-ve ROD encapsulated with a polysaccharide capsule.
- one of the three important encapsulated pyogens (pneumococcus and the meningococcus).
- Using serologic methods against the antigen of the polysaccharide capsule, six serotypes are detected, with serotype B (group B) being the most significant one.
- Serotype B is the one most responsible for the more serious illnesses (meningitis, epiglottitis, sepsis)
- The type B capsule is composed of polyribitol phosphate, promotes anti-phagocytosis and invasiveness .
- Unencapsulated strains are less invasive but can cause disease usually limited to the upper respiratory tract (sinusitis and otitis media).
- Growth of the organism on laboratory media requires the addition of two components, heme (factor X) and NAD (factor V), for adequate energy production.

HAEMOPHILUS

- Diseases *H. influenzae* used to be the leading cause of meningitis in young children
- Note we have 1 representative from each Gram reaction and shape that is a respiratory organism, the three capsulated ones are causative of meningitis and have vaccines made against the capsule:
- Pneumococcus G+ve coccus = capsulated respiratory organism causes mengitis and URTI
- Meningiococcus G-ve coccus also capsulated which can colonize the respiratory epithelium
- and now the Gram negative ROD, Haemophilus is also a respiratory capsulated organism that is the third most common cause of meningitis.

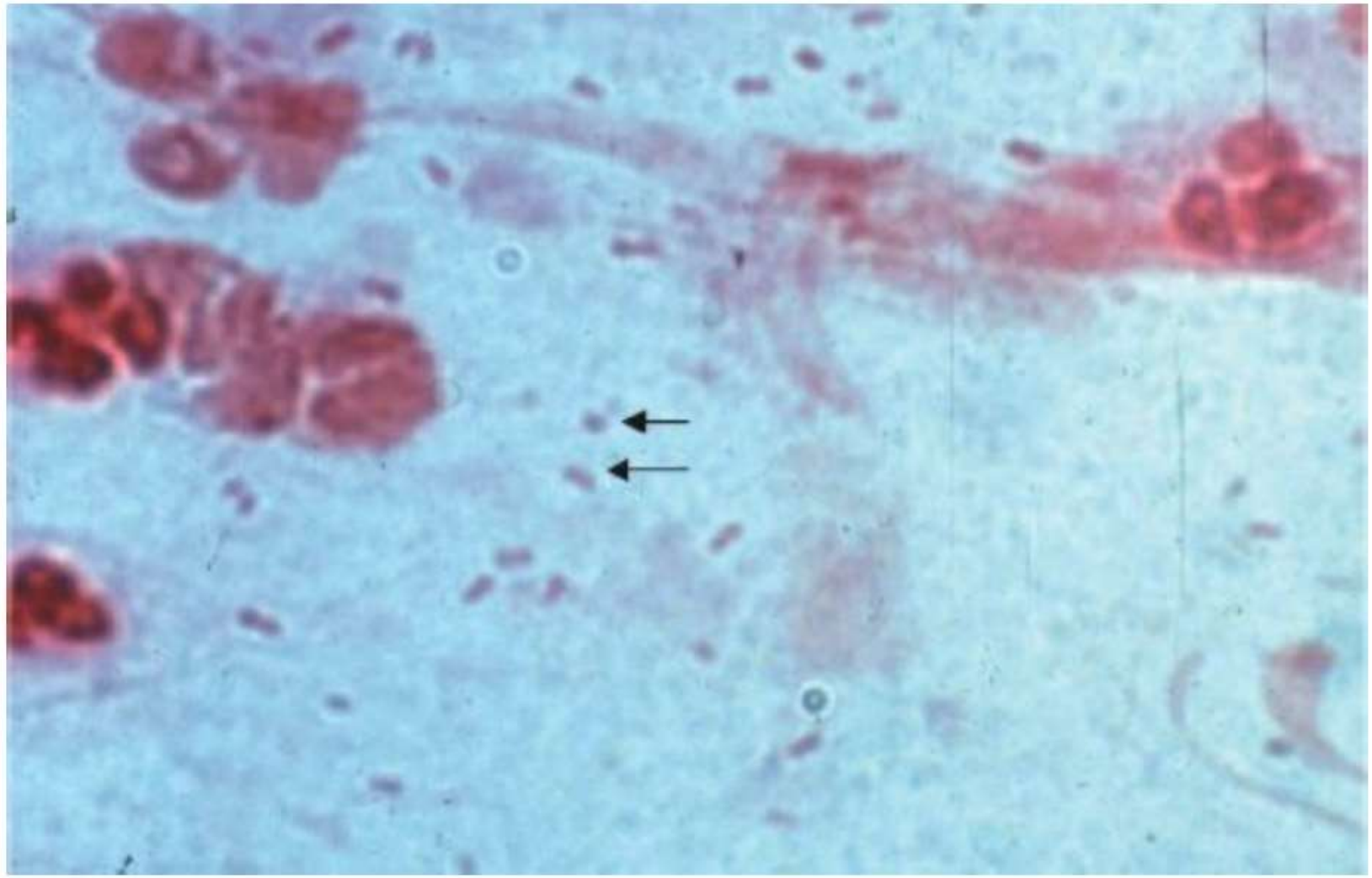


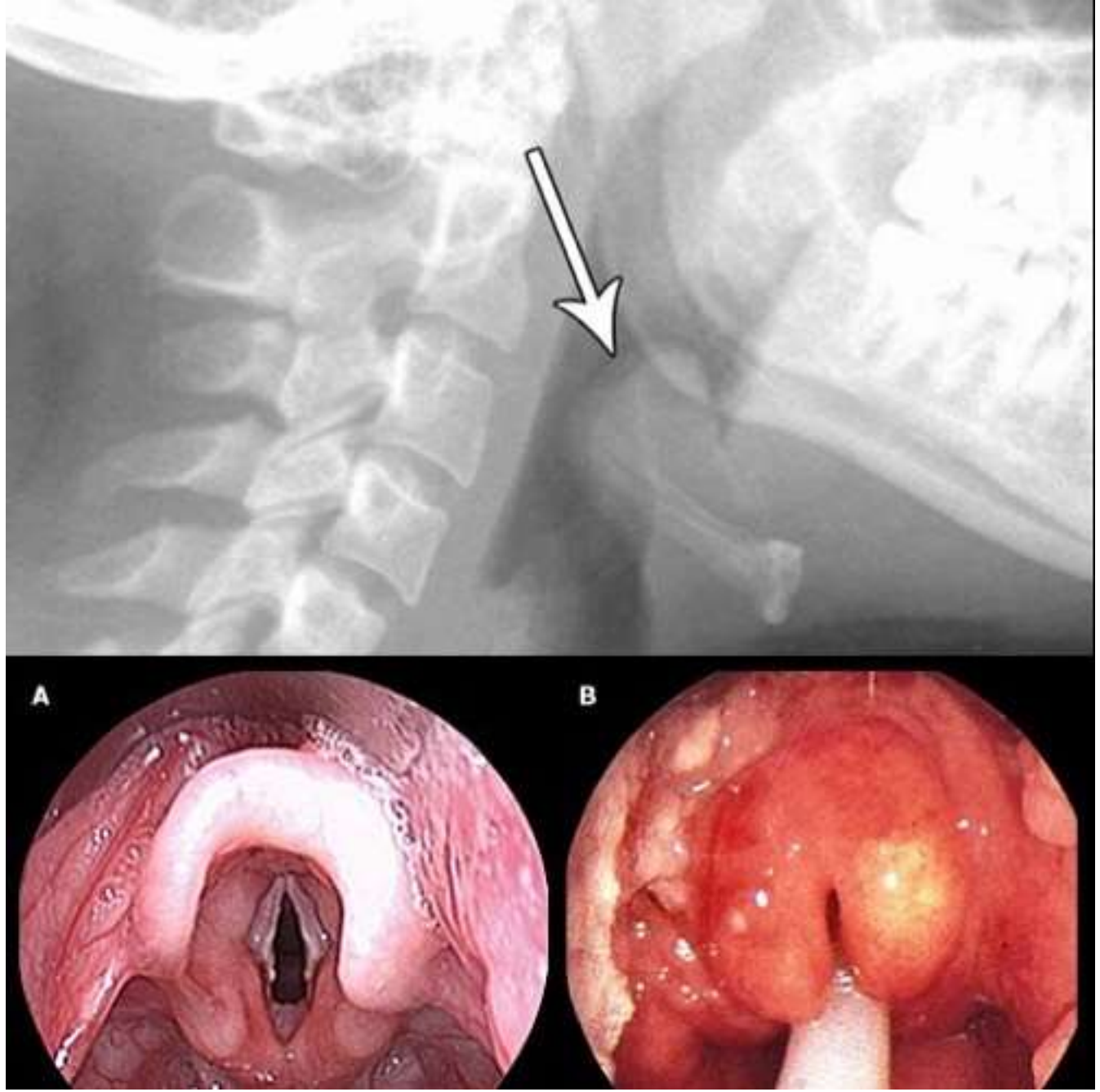
FIGURE 19–1 *Haemophilus influenzae*—Gram stain. Arrows point to two small "coccobacillary" gram-negative rods. (Used with permission from Professor Shirley Lowe, University of California, San Francisco School of Medicine.)

Pathogenesis & Epidemiology

- *H. influenzae* **infects only humans with no animal reservoir.**
- Similar to other respiratory pathogens, it is transmitted by the inhalation of airborne droplets into the respiratory tract, this can result in **a**symptomatic colonization or infection (otitis media, sinusitis, pneumonia).
- Also like all respiratory pathogens, to be able to survive in this environment, the organism produces an **IgA protease** that degrades secretory IgA which would otherwise inhibit its attachment to the mucosa.
- After becoming established in the upper respiratory tract, the organism can enter the **bloodstream (bacteremia) and spread to the meninges**.
- As mentioned, capsulated strains cause meningitis (they have to have antiphagocytic capability to survive the trip through the blood to reach the meninges, this is true *for Pneumococcus and Meningiococcus*)
- meningitis caused by capsular type b has been greatly reduced by vaccine contains the type b polysaccharide as the immunogen.
- Similar to pneumococcus and meningococcus, the pathogenesis of H. infleunzae is pyogenic with no exotoxin production (capsule and endotoxin based)

Clinical Findings

- Meningitis caused by *H. influenzae* produces a clinical picture that is almost identical pneumococcal or meningococcal meningitis.
- Meningitis → The rapid onset of fever, headache, **stiff neck**, (neurological symptoms; drowsiness), is typical.
- URTI → Sinusitis and otitis media cause pain in the affected area, opacification of the infected sinus, and redness with bulging of the tympanic membrane.
- *H. influenzae* is second only to the pneumococcus as a cause of these two infections.
- Other serious infections : septic arthritis, cellulitis, and sepsis(more in asplenic patients, due to the fact that this is a capsulated organism).
- **Epiglottitis** →rare, but can obstruct the airway and CAN BE FATAL. Upon inspection, a swollen "cherry-red" epiglottis is seen. This life-threatening disease of young children is caused almost exclusively by *H. influenzae*. Symptoms include, drooling, stridor (high pitched breathing noise) and comfort on sitting up.
- Pneumonia in elderly adults, especially those with chronic respiratory disease, can be caused by untypeable strains of *H. influenzae*



http://www.pictame.com/tag/epiglottitis

Laboratory Diagnosis

- Need to isolate the organism to make the Dx, inactivated blood must be used (chocolate agar, to remove inhibitors of growth in the blood) **enriched** with two growth factors required for bacterial respiration (chocolate agar +factor x and factor V).
- An organism that grows on Chocolate+Factors X and V is assumed to be *H. influenzae*; other species of *Haemophilus*, such as *Haemophilus parainfluenzae*, do not require both factors.
- Quelling reaction (Antibody against the capsule which shows swelling of the capsule if contained the antigen for the provided antibody) can be used, also biochemical tests.
- Additional means of identifying encapsulated strains include fluorescentantibody staining of the organism and counter immunoelectrophoresis or latex agglutination tests, which detect the capsular polysaccharide.

Treatment

- For **meningitis and serious systemic infections** (remember these are more invasive and aggressive) caused by *H. influenzae* the treatment of choice is ceftriaxone (3rd gen).
- From 20% to 30% of *H. influenzae* type b isolates produce a β-lactamase that degrades penicillinase-sensitive β-lactams such as ampicillin but not ceftriaxone.
- It is important to institute antibiotic treatment promptly, because the incidence of neurologic sequelae (subdural empyema) is high.
- Untreated *H. influenzae* meningitis has a fatality rate of approximately 90%.
- *H. influenzae* upper respiratory tract infections (such strains as mentioned are less aggressive and less invasive), that cause otitis media and sinusitis, are treated with either amoxicillin-clavulanate or trimethoprim-sulfamethoxazole.

Prevention

- Capsule= vaccine, so the vaccine contains the capsular polysaccharide of *H. influenzae* type **b** conjugated to diphtheria toxoid or other carrier protein.
- Depending on the carrier protein, it is given some time between the ages of **2 and 15 months**.
- This vaccine is much more effective in young children than the unconjugated vaccine and has reduced the incidence of meningitis caused by this organism by approximately 90% **in immunized children**.
- Meningitis in close contacts of the patient can be prevented by rifampin.
- Rifampin is used because it is secreted in the saliva to a greater extent than ampicillin. Rifampin decreases respiratory carriage of the organism, thereby reducing transmission

The End