BACTERIAL LOBAR PNEUMONIA

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INTRODUCTION

- Based on area of lungs involved, and type of cough produced, bacterial pneumonia is traditionally classified into two groups:
 - > Typical (lobar) pneumonia
 - > Atypical or (interstitial) pneumonia.



- **Lobar or typical pneumonia:** Infection of the lung parenchyma and its alveoli.
- Characterized by consolidation (gives a dull note on percussion) and productive cough with purulent sputum - caused by:
 - Streptococcus pneumoniae
 - Haemophilus influenzae
 - Staphylococcus aureus



- Interstitial or atypical pneumonia occurs in the interstitial space of lungs.
- Cough is characteristically non-productive.
- Mostly caused by bacteria Mycoplasma, Chlamydia, Legionella species, etc.



Clinical features - found in both types of pneumonia include:

- Fever, with chills and/or sweats, tachycardia
- Increased respiratory rate (tachypnea),increased use of accessory muscles.
- Dyspnea (shortness of breath)
- Pleuritic chest pain
- Gastrointestinal symptoms: nausea, vomiting, and/or diarrhea
- Fatigue, headache, myalgia, and arthralgia

Severely ill-patients - septic shock and multiorgan failure.



PNEUMOCOCCAL PNEUMONIA



PNEUMOCOCCAL PNEUMONIA

- Streptococcus pneumoniae (commonly referred to as pneumococcus) leading cause of lobar pneumonia, otitis media in children and meningitis in all ages.
- They are α-hemolytic present as commensals in human upper respiratory tract



DIFFERENCES BETWEEN STREPTOCOCCUS PNEUMONIAE AND VIRIDANS STREPTOCOCCI

Features	S. pneumoniae	Viridans streptococci
Arrangement	Gram-positive cocci in pairs	Gram-positive cocci in long
		chains
Morphology	Lanceolate shaped	Round/oval
Capsule	Present	Absent
On blood agar	Draughtsman or carrom coin colony	Minute colony
Bile solubility	Soluble in bile	Insoluble in bile
Inulin	Fermented	Not fermented
Optochin	Sensitive	Resistant



VIRULENCE FACTORS AND PATHOGENESIS

- Capsular polysaccharide: Principal virulence factor protects the cocci from phagocytosis. Typing of pneumococci - based on capsular polysaccharide.
- C-carbohydrate antigen (C-polysaccharide): Precipitates with Creactive protein (CRP) - marker of acute inflammation, raised in many acute inflammatory conditions.



VIRULENCE FACTORS AND PATHOGENESIS (CONT..)

- Pneumolysin: Inhibits neutrophil chemotaxis and phagocytosis.
- Autolysin: Amidase enzyme that cleaves its own peptidoglycan autolysis of cells responsible for bile solubility and draughtsman appearance.
- Other virulence factors: Pneumococcal surface proteins (PspA, PspC), IgA protease, neuraminidase and pneumococcal surface adhesin A (PsaA).



CLINICAL MANIFESTATIONS

- Colonize human nasopharynx spread either via bloodstream to distant sites (e.g. brain, joint, bones & peritoneal cavity) or spread locally to cause otitis media or pneumonia.
 - Lobar pneumonia
 - Empyema and parapneumonic effusion
 - Invasive pneumococcal disease (IPD)



CLINICAL MANIFESTATIONS (CONT..)

Invasive pneumococcal disease (IPD):

- Infection confirmed by isolation of pneumococci from normally sterile site
- Blood stream infection
- Pyogenic meningitis cause of meningitis in all ages (except in neonates)
- Others Osteomyelitis, septic arthritis, endocarditis, pericarditis, primary peritonitis, rarely, brain abscess & hemolytic-uremic syndrome.



EPIDEMIOLOGY

- **Source** upper respiratory tract of carriers (less often patients)
- Carrier rate Up to the age of 5 years, 70—90% of children nasopharynx
- **Mode of transmission –** inhalation of droplet nuclei
- Infection usually leads to colonization and carrier state.
- Disease results only when the host resistance is lowered presence of



RISK FACTORS

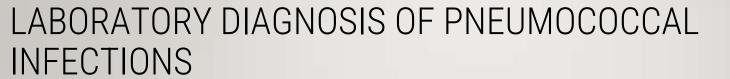
- Children (<2 years)</p>
- Splenectomy, sickle cell disease & other hemoglobinopathies
- Underlying comorbid diseases chronic lung, heart, kidney and liver disease, cochlear implants, diabetes mellitus &immunosuppression
- **Viral URTI**



RISK FACTORS (CONT..)

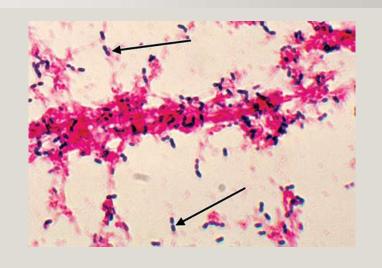
■ Nature of infecting serotypes:

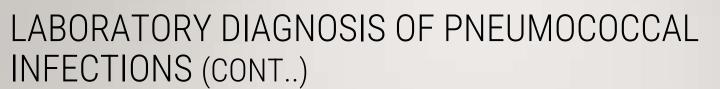
- Most common: 6 and 19 F universally. In India 1, 6, 19A and 19F
- ➤ **Age:** In children, seven serotypes (1, 5, 6A, 6B, 14, 19F and 23F) 60% of IPD cases.





- Specimen collection: Sputum, CSF, pleural fluid
- Direct smear microscopy: Reveals pus cells and lanceolate shaped grampositive diplococci, surrounded by a clear halo (due to capsule)



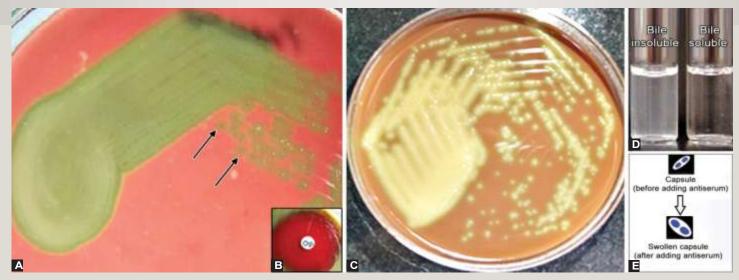




- **Capsular antigen detection in CSF:** By latex agglutination
- **C-antigen detection** in urine and CSF by ICT
- **Culture:**
 - > Blood agar: It forms draughtsman or carrom coin shaped colonies
 - Chocolate agar: It produces greenish discoloration (bleaching effect)







A. α-hemolytic draughtsman-shaped colonies on blood agar; **B.** Sensitive to optochin;

C. Bleaching effect on chocolate agar; **D.** Bile solubility test (left-viridans streptococci, not soluble in bile; right pneumococcus, soluble in bile); **E.** Quellung reaction.



LABORATORY DIAGNOSIS OF PNEUMOCOCCAL INFECTIONS (CONT..)

- **Culture smear:** Reveals lanceolate-shaped gram-positive diplococci
- Identification:
 - Biochemical identification: It is bile soluble, optochin sensitive, inulin fermenter
 - Automation methods such as MALDI-TOF and VITEK



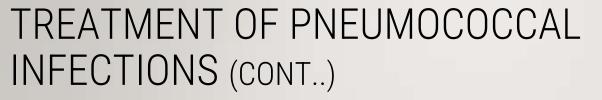
LABORATORY DIAGNOSIS OF PNEUMOCOCCAL INFECTIONS (CONT..)

- **Serotyping:** By Quellung reaction or latex agglutination test
- Molecular methods: Such as multiplex PCR
- Non-specific findings: ↑ acute phase reactant proteins, e.g. C-reactive protein, procalcitonin
- Antimicrobial susceptibility testing.

TREATMENT OF PNEUMOCOCCAL INFECTIONS



- Pneumonia: Oral therapy with amoxicillin for five days standard treatment. Alternative drugs IV penicillin or ceftriaxone, oral quinolone (levofloxacin or moxifloxacin), clindamycin or azithromycin
- Meningitis: As mortality is very high (~ 20%), treatment initiated as early as possible. Ceftriaxone/cefotaxime ± vancomycin for 10-14 days





Other invasive infections:

- For stable children penicillin, cefotaxime or ceftriaxone.
- In critically ill children treatment same as that of meningitis
- Otitis media: Oral amoxicillin for 7-10 days



DRUG RESISTANCE IN PNEUMOCOCCUS

- **Penicillin Resistance -** Alteration of PBP to PBP2a
- MDR Pneumococcus Resistant to penicillin, erythromycin, tetracycline, clindamycin, sulfonamides.
- Serotype 19A most common serotype to exhibit multidrug resistance
- Some serotypes can undergo capsule switching



TYPES OF PNEUMOCOCCAL VACCINES

	PPSV23	PCV13
Name	23-valent pneumococcal	Pneumococcal conjugate vaccine
	polysaccharide vaccine	
Brand	Pneumovax 23	Prevnar13
Serotypes included	Contains 23 serotypes of S.	Contains 13 serotypes of
	pneumoniae	S. pneumoniae
	1, 2, 3, 4, 5, 6B, 7F, 8, 9N,	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14,
	9V, 10A, 11A, 12F, 14,	18C, 19A, 19F, & 23F.
	15B, 17F, 18C, 19A, 19F,	Conjugated with
	20, 22F, 23F, and 33F	diphtheria toxoid





	PPSV23	PCV13
Coverage	Covers 70-80% of invasive	Covers only 30-40% of invasive serotypes in
	serotypes in adults	adults, however it covers most of the
		serotypes infecting children
Immuno- genicity	Less immunogenic: Capsular	More immunogenic:
	antigen being T cell independent	The protein conjugate acts as adjuvant and
	antigen, is less immunogenic to	increases the immunogenicity of capsular
	children, hence not given to children	antigen. Hence, PCV is effective against
	<2 years age	children <2 years age





	PPSV23	PCV13
Duration	Provides short-term immunity (3–5	Provides longer immunity
	years)	
Herd	Promotes herd immunity	Does not promote herd immunity
Effect on carriers	Does not provide mucosal immunity,	Provides mucosal immunity; hence, it can
	hence no effect on carriers	eradicate carriage from nasopharynx
Cost	Less expensive	More expensive
Indication	Adults ≥65 years Adults 19-64 years	Indications in adults same as PPSV23
	age with underlying risk factors	Children (as primary
		immunization)



HAEMOPHILUS INFLUENZAE PNEUMONIA



INTRODUCTION

- Haemophilus species oxidase positive, capsulated pleomorphic gramnegative bacilli.
- Require special growth factors present in blood factor X and V (Haemo means blood, philus means loving).



- Important species are:
 - H. influenzae: Ccauses pneumonia and meningitis in children
 - H. ducreyi: Causes a sexually transmitted disease chancroid
 - > H. aegyptius: Causes conjunctivitis and rashes



- ➤ H. haemolyticus and H. parahaemolyticus : Commensals in throat or mouth
- H. aphrophilus and H. paraphrophilus (renamed as Aggregatibacter aphrophilus and A.paraphrophilus): Infective endocarditis
- > H. parainfluenzae: Cause infective endocarditis



HISTORY

- Also called Pfeiffer's bacillus discovered by Pfeiffer (1892). The
- Species name coined wrongly, thinking that it would cause human influenza which is actually a viral disease caused by influenza virus.



VIRULENCE FACTORS

- Capsular polysaccharide most important virulence factor, acts by inhibiting phagocytosis
- Other virulence factors include—(i) bacterial endotoxin, (ii) outer member proteins, (iii) IgAI proteases, and (iv) pili and other adhesion proteins.



SEROTYPING

- Based on the capsular polysaccharide of H.influenzae, it can be typed into six serotypes (a to f).
- H. influenzae serotype b (Hib) most virulent among all types and accounts for most of the invasive infections



SEROTYPING (CONT..)

- Hib capsule unique chemical structure, made up of polyribosyl ribitol phosphate (PRP) antigen. It is
- Strongly immunogenic induces IgG, IgM and IgA antibodies bactericidal, opsonic and protective.
- PRP antigen is used for vaccination



CLINICAL MANIFESTATIONS - H. INFLUENZAE TYPE B (HIB)

- Central nervous system infections
- Epiglottitis
- Community acquired bacterial pneumonia
- Parameningeal focus



CLINICAL MANIFESTATIONS - H. INFLUENZAE TYPE B (HIB) (CONT..)

Less common invasive conditions include:

- Cellulitis of neck and head region
- Osteomyelitis, septic arthritis
- Pericarditis
- Empyema and bronchiectasis
- Orbital cellulitis, endophthalmitis
- Urinary tract infection

CLINICAL MANIFESTATIONS - NONTYPEABLE H. INFLUENZAE



- Childhood otitis media
- Exacerbations of COPD MC cause
- Pneumonia in adults with underlying COPD or AIDS
- Puerperal sepsis and neonatal bacteremia
- Sinusitis in adults and children
- Invasive infections rarely



DIFFERENCES BETWEEN TYPE B AND NONTYPEABLE HAEMOPHILUS STRAINS

Features	Type b strains	Nontypeable strains
Capsule	Made up of poly ribosyl	Noncapsulated
	ribitol phosphate (PRP)	
Manifestations	Invasive-meningitis,	Noninvasive—otitis media
	epiglottitis, pneumonia,	(in children) and pneumonia
	bacteremia	(in adults)
Commonly affect	Children	Adults
Spread	Hematogenous spread	Contiguous spread
Vaccine	Hib vaccine is available	Not available



EPIDEMIOLOGY

- **Host:** H.influenzae human pathogen
- Mode of transmission respiratory route -droplet inhalation
- **Age:** < 5 years of age and >65 years
- **Risk factors** household contact, day care centre, asplenia, socioeconomic conditions, and genetic differences

LABORATORY DIAGNOSIS OF H. INFLUENZAE INFECTIONS

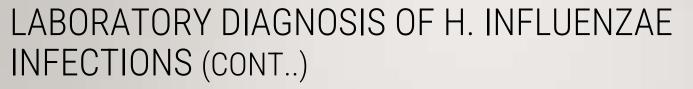
- Specimens: Sputum, blood, CSF
 - Processed immediately, should never be refrigerated

Direct examination:

- > Pleomorphic gram-negative coccobacilli
- Capsule detection: By Quellung reaction
- > Antigen detection: By latex agglutination test, direct-



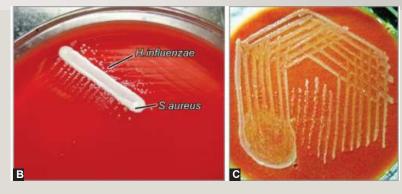
Gram-stained smear showing pleomorphic gram-negative bacilli



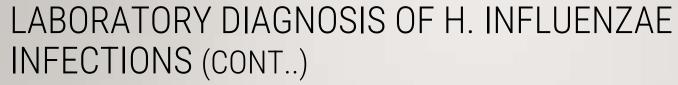


Culture:

- Blood agar with S. aureus streak line shows satellitism
- Others: Chocolate agar, Fildes agar and Levinthal's agar



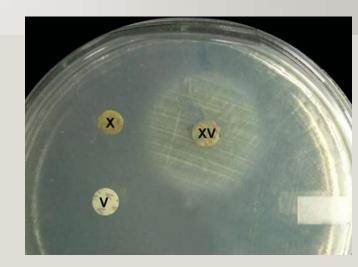
B. Satellitism of H. influenzae around S. aureus streak line; **C**. Colonies of H. influenzae on chocolate agar.





Identification:

- Biochemical tests such as disk test for X and V factor
- Automated systems such as MALDI-TOF or VITEK



Typing methods such as biotyping and

serotyping (using specific antisera)

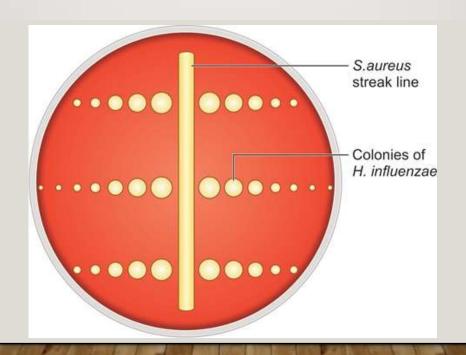


LABORATORY DIAGNOSIS OF H. INFLUENZAE INFECTIONS (CONT..)

- Molecular method: Multiplex PCR (BioFire FilmArray), detecting common agents of pyogenic meningitis in CSF
- Antimicrobial susceptibility testing

SATELLITISM OF HAEMOPHILUS INFLUENZAE





TREATMENT OF H. INFLUENZAE INFECTIONS



- For invasive infections due to H. influenzae type b ceftriaxone, cefotaxime (for I−2 weeks) drug of choice.
- Alternatively ampicillin + chloramphenicol may be used

TREATMENT OF H. INFLUENZAE INFECTIONS (CONT..)



- Nontypeable strains of H. influenzae resistant to β-lactams [due to β-lactamase production (20–35% of strains) or rarely by expressing altered penicillin binding protein-3].
- Those strains usually susceptible to quinolones (levofloxacin) and macrolides (azithromycin).



PROPHYLAXIS - HIB CONJUGATE VACCINE

- Polyribosyl ribitol phosphate (PRP) capsular antigen of H. influenzae type b
 used for vaccination.
- Capsular antigens poorly immunogenic to children conjugated with adjuvants - diphtheria toxoid, tetanus toxoid and N. meningitidis outer membrane proteins
- Reduce the rate of pharyngeal colonization with Hib



PROPHYLAXIS - HIB CONJUGATE VACCINE (CONT..)

- Schedule: Under national immunization program, Hib vaccine given in combination with DPT, hepatitis B (pentavalent vaccine) at 6, 10 and 14 weeks of birth IM route, at anterolateral side of mid-thigh
- Protection: >95% of infants develop protective antibody levels after 2 or 3 doses



PROPHYLAXIS - CHEMOPROPHYLAXIS

- Oral rifampin drug of choice. It is indicated to:
 - Household contacts or
 - Health care workers (if two or more cases occur in the hospital within 60 days).



STAPHYLOCOCCAL PNEUMONIA



STAPHYLOCOCCAL PNEUMONIA

- **Infant pneumonia:** Leading cause of pneumonia in newborns and infants;
 - > Presents with dyspnea, fever, and respiratory failure
 - Chest X-ray pneumatocele (shaggy, thin-walled cavities)
 - > Complications pneumothorax and empyema
- VAP in adults
- Post-viral CAP





GRAM-NEGATIVE BACILLI PNEUMONIA



GRAM-NEGATIVE BACILLI PNEUMONIA

- Gram-negative bacilli increasingly associated to cause lobar pneumonia -VAP in the healthcare facility.
- Most of these agents are multidrug resistant (MDR) pathogens found in the hospital environment.



GRAM-NEGATIVE BACILLI PNEUMONIA (CONT...)

- Non-fermenters Pseudomonas aeruginosa, Acinetobacter, Burkholderia cepacia major cause of VAP.
- Enterobacteriaceae: Escherichia coli, Klebsiella pneumoniae, Enterobacter species and Serratia marcescens.



1. KLEBSIELLA PNEUMONIAE

- Klebsiella found as commensals in human intestine and as saprophytes in soil.
- Has three species—K. pneumoniae, K. oxytoca, and K. granulomatis
- K. pneumoniae further comprises of three subspecies—pneumoniae, ozaenae and rhinoscleromatis.
- **K. pneumoniae subspecies pneumoniae** most pathogenic among all.



1. KLEBSIELLA PNEUMONIAE (CONT..)

- Responsible for severe lobar pneumonia, urinary tract infections, meningitis (neonates), septicemia and pyogenic infections - abscesses and wound infections.
- Frequently colonizes the oropharynx of the hospitalized patients common cause of nosocomial infections.





Hypervirulence:

- hvKp more virulent than classical K. pneumoniae; possesses several virulence factors siderophore, increased capsule production, etc.
- Two capsular serotypes KI (more common) and K2



HYPERVIRULENT STRAINS OF K. PNEUMONIAE (HVKP) (CONT..)

- **Manifestations:** Causes various community-acquired infections:
 - Pyogenic liver abscess (most common)
 - Metastasize from liver to distant sites eye, lung and CNS
 - Cause primary extrahepatic infections including bacteremia, pneumonia and soft tissue infections



HYPERVIRULENT STRAINS OF K. PNEUMONIAE (HVKP) (CONT..)

Identification: hvKp strains are hypermucoid— a viscous string is formed when a loop is used to stretch the colony on an agar plate





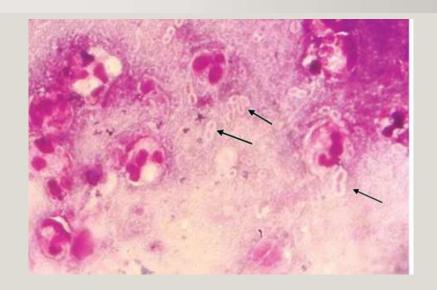


- Lactose fermenters, non-motile and capsulated (possess capsular polysaccharide).
- Specimens sputum, endotracheal aspirate, urine, blood, exudate specimen.





Gram staining: Short, plump, straight capsulated gramnegative rods







Culture: On MacConkey agar, it produces large dome-shaped mucoid (due to capsule) sticky, pink color, lactose fermenting colonies





LABORATORY DIAGNOSIS OF KLEBSIELLA PNEUMONIAE (CONT..)

- Identification: MALDI-TOF or VITEK or by conventional biochemical tests:
 - Catalase positive and oxidase negative
 - ➤ ICUT tests: Indole test (negative), citrate test (positive), urease test (positive) and TSI (triple sugar iron agar) test shows acid/acid, gas present, H2S absent.



TREATMENT OF KLEBSIELLA INFECTIONS

- In healthcare facilities with high prevalence of MDR K. pneumoniae, empirical treatment - started with higher spectrum antimicrobial - therapy can be tailored based on the susceptibility report
- \blacksquare Carbapenems, amikacin or β-lactam/β-lactamase inhibitor combinations (BL/BLIs) for hospital acquired MDR infections.
- Polymyxins or tigecycline for carbapenem resistant





- Intrinsically resistant ampicillin and ticarcillin
- **MDR:** Resistant to cephalosporins, quinolones, co-trimoxazole, etc.
- **ESBL:** In India (2019), 40–90% of strains of *K. pneumoniae* are ESBL (extended spectrum β-lactamases) producers.





- Carbapenem resistance: In India 28–56%; out of which 37% are colistin resistant. Carbapenem resistance due to production of carbapenamases such as:
 - New Delhi β-lactamase (NDM)
 - ➤ K. pneumoniae carbapenamase (KPC).



2. ENTEROBACTER SPECIES

- E. aerogenes and E. cloacae most commonly isolated species from the clinical specimens.
- E. aerogenes recently renamed as Klebsiella aerogenes
- Opportunistic pathogens in infected wounds, urinary and respiratory tract infections (pneumonia) and occasionally - septicemia and meningitis



2. ENTEROBACTER SPECIES (CONT..)

- E. sakazaki (recently named as Cronobacter sakazakii) bacteremia and meningitis in neonates and is associated with consumption of powdered milk
- Enterobacter intrinsically resistant to amoxicillinclavulanate and ampicillinsulbactam.
- Treatment same as that for E. coli and Klebsiella



3. SERRATIA MARCESCENS

Pigmented Group:

- Produce red non-diffusible pigment prodigiosin.
- Saprophytes found in water, soil and food.
- Grow in sputum after collection and make the sputum red (due to pigment production) -





3. SERRATIA MARCESCENS (CONT..)

Non-pigmented Group:

Reported in various healthcare-associated infections - lobar pneumonia, meningitis, endocarditis, septicemia, urinary, and wound infections.



TREATMENT OF SERRATIA INFECTIONS

- \blacksquare Hospital strains multiple drug resistant (produce AmpC β-lactamases).
- Guideline for treatment same as E. coli and Klebsiella.
- Intrinsically resistant to ampicillin, first and second generation cephalosporins, amoxicillin-clavulanate, ampicillin-sulbactam, nitrofurantoin and polymyxins.



RARE CAUSES OF BACTERIAL PNEUMONIA



PULMONARY ANTHRAX

- Also called Wool Sorter's disease caused by Bacillus anthracis.
- Transmission inhalation of spores during exposure to contaminated animal products.
- **Bioterrorism**: Most common form of anthrax -associated with bioterrorism
- Incubation period I-7 days, but up to 6 weeks or longer is reported



PULMONARY ANTHRAX (CONT..)

- Hemorrhagic pneumonia: Prodromal stage of fever, myalgia and lethargy, followed by abrupt onset of hemorrhagic pneumonia respiratory failure
- Spread: By lymphatics or blood, leading to—severe sepsis, hemorrhagic mediastinitis and hemorrhagic meningitis
- Chest X-ray mediastinal widening and/or pleural effusions



TREATMENT OF PULMONARY ANTHRAX

- Antibiotic regimen + anthrax immunoglobulin.
- **Antibiotic regimen** induction and maintenance therapy
- Induction therapy:
 - If meningitis is suspected: Ciprofloxacin + meropenem + linezolid for 2–3 weeks
 - ➤ If meningitis is excluded: Ciprofloxacin + clindamycin or linezolid for 2





- Maintenance therapy: Oral ciprofloxacin or doxycycline 60 days course
- Anthrax immunoglobulin: Raxibacumab and Obiltoxaximab monoclonal antibodies that neutralizes anthrax toxin (protective antigen).



PNEUMONIC PLAGUE

- Caused by a zoonotic pathogen Yersinia pestis.
- Human plague occurs in three clinical forms—(1) bubonic (most common form), (2) pneumonic, and (3) septicemic.
- **Transmission:** Inhalation of bacilli in droplets expelled from another person or an animal with plague pneumonia



PNEUMONIC PLAGUE (CONT..)

- **Incubation period** shorter than bubonic plague I—3 days
- Manifestations: Onset is sudden fever, headache and respiratory symptoms— productive cough or hemoptysis, dyspnea, and chest pain.
- Agent of bioterrorism
- **Treatment:** Gentamicin or streptomycin



OTHER BACTERIAL AGENTS THAT CAN OCCASIONALLY CAUSE PNEUMONIA

- Nocardia
- Actinomyces
- Streptococcus pyogenes
- Streptococcus agalactiae
- Corynebacterium diphtheriae



OTHER BACTERIAL AGENTS THAT CAN OCCASIONALLY CAUSE PNEUMONIA (CONT..)

- Nontyphoidal salmonellae
- Aeromonas hydrophila
- Rhodococcus equi
- Moraxella catarrhalis



QUESTIONS:

- Q1. Which of the following agent of meningitis can grow on chocolate agar but not on blood agar:
- a. Neisseria meningitides
- b. Haemophilus influenza
- c. Moraxella catarrhalis
- d. Escherichia coli



QUESTIONS:

- Q2. Polyribosyl ribitol phosphate (PRP) antigen is present in the capsule of H. influenzae:
- a. Serotype a
- b. Serotype b
- c. Serotype c
- d. Serotype d



QUESTIONS:

- Q3. Wool Sorter's disease is caused by:
- a. Bacillus anthracis
- b. Staphylococcus aureus
- c. Yersinia pestis
- d. Rhodococcus equi