Bacterial Respiratory Infection
(3rd Year Medicine)

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Introduction

- The respiratory tract is the most common site of body acquired infection by pathogens and opportunistic pathogens.
- This site becomes infected frequently because it comes into direct contact with the physical environment and is exposed continuously to many microorganisms in the air.
- The human respiratory tract is exposed to many potential pathogens via close contact with human healthy carriers via air droplets, hand & mouth contacts, smoke and dust particles.
- It has been calculated that the average individual inhaled & ingests at least to 8 microbial cells per minute or 10,000 per day.
2/

Before a **Respiratory Disease** is developed via exogenous source, the following conditions need to be met:

- There must be a sufficient cell numbers "dose" of infectious agent inhaled.
- The infectious particles must be airborne.
- The infectious organism must remain alive and viable while in the air.
- The organism must be deposited on susceptible tissue in the host & attached.
- The patients can’t resist the infection process by his immune system. **The role of respiratory normal flora in preventing infection**
Normal Bacterial Respiratory Flora

- Most of the surfaces of the upper respiratory tract (including nasal and oral passages, nasopharynx, oropharynx, and trachea) are colonized by normal flora. These organisms are usually normal inhabitants of these surfaces and rarely cause disease (Fig. 1):

  - **Common bacteria >10%:** Viridans Streptococci (S. mutans, S. mitis), Neisseria (N. flava, N. sicca), Haemophilus - Parahaemophilus, Corynebacteria spp., Anaerobic Bacteria (Bacteroides fragilis, Spirochities).

  - **Less Common <10:** Group A streptococci & others, H. influenzae, S. pneumoniae, N. meningitidis., Candida Various Gram-ve bacilli
Most infections are mixed Viruses plus Bacteria

Common Cold - Rhinoviruses, Coronaviruses, Adenoviruses, Myxoviruses, Echoviruses, Coxsackie A and B, Echoviruses, M. pneumoniae, C. pneumoniae

Dental caries - S. mutans
Thrush - C. albicans
Trench mouth - Treponema vincentii, Fusobacterium fusiforme
Stomatitis - Herpes Simplex Virus

Pharyngitis - Adenovirus, Herpes Simplex Virus, Coxsackieviruses, S. pyogenes, C. diphtheriae

Otitis Media - S. pneumoniae, H. influenzae, M. catarrhalis
Otitis Externa - P. aeruginosa

Sinusitis - S. pneumoniae, H. influenzae

Croup - Parainfluenza viruses, Respiratory Syncytial virus
Epiglottitis - H. influenzae

Whooping Cough
Bordetella pertussis

Bronchitis - Parainfluenza viruses, Respiratory Syncytial virus, Influenza viruses, M. pneumoniae, C. pneumoniae

Bronchiolitis
Respiratory Syncytial Virus
Common Bacteria Agents cause of Upper Respiratory Infections

- **Haemophilus influenzae** type b: Capsule, Lipooligosaccharides, invasive. Highly susceptible to cold & room and high temperatures. Autolysis rapidly.

**Clinical Features:** Rare Sore Throat. Common Otitis – Sinusitis, Conjunctivitis. Blood sepsis/ Meningitis. Children (6 months-5 years). Less Adults.

- **Hib-vaccine** polysaccharide-protein conjugate vaccine combined with diphtheria-tetanus-pertussis vaccine. Starting after the age of 6 weeks.

- **Staphylococcus aureus**: Gr-positive cocci. Infect All ages. Sinusitis, Pneumonia, Conjunctivitis, Rare Sore Throat. Blood sepsis. Rare Meningitis.

Staphylococcal pneumonia is a frequent complication following influenza infection. Infants, Elderly patients, immunosuppressed.
Fig. 2 Haemophilus influenzae
Gram-stain: G-ve coccobacilli + fimentes

- meningitis (type b)
- otitis media (nontypable)
- sinusitis (nontypable)
- epiglottitis (type b)
- tracheobronchitis (nontypable)
- bacteremia (type b)
- pneumonia (nontypable)
Streptococcus infections

- The genus *Streptococcus* consists of gram-positive cocci. Human commensals & opportunistic pathogens. Respiratory Tract. *Beta-H-streptococci group, Viridans Streptococci group*

- Definitive identification of hemolytic pyogenic streptococci based on the serologic reactivity of cell wall polysaccharide antigens (*Lancefield groups*).

- The most important groups are A, B, C, D, G, F.

- *Groups A & B streptococci* are common human comensals & opportunistic pathogens. Always produce *beta hemolytic reaction* on blood agar in vitro.
**S. pyogenes (Group A Hemolytic Streptococcus)**-1

- **Group A Hemolytic Streptococcus** causes in 10-30% Pharyngitis-Tonsillitis/Sore Throat less Otitis—Sinusitis, Skin in all Children..Virulence factors

- **Complication:** Post-streptococcal diseases

- **Group A** is one of the most frequent pathogens of humans. It is estimated that between 5-15% of normal individuals carry this bacterium, usually in the respiratory tract, without signs of disease as normal flora.. **Healthy Carriers**

- Endogenous Infection occurs when the organism is able to penetrate the host defenses..mostly children

- Causes localized or systemic infections.. Its virulence is related to cell structures, enzymes & toxins
Fig.3-Beta-Hemolytic Streptococci
Fig. 4- Streptococcus pyogenes

- Extracellular substance
- Capsule (hyaluronic acid)
- Cell membrane
- Peptidoglycan (cell wall): (group carbohydrate antigen: rhamnose, N-acetylglucosamine)
- Pili M protein type antigen; lipoteichoic acid; R and T proteins

- Streptolysins
- NADase
- Hyaluronidase
- Streptokinases
- Streptodornases
- Pyrogenic exotoxins
Pathogenesis of Group A Streptococcus-2

- It has ability to colonize and rapidly multiply and spread in its host while resist phagocytosis due to the cell surface T, R, M-proteins.. About 100 serotypes
- Resistance & Immunity to infection developed by presence of specific M-protein antibodies
- Respiratory Infection.. Via droplets.. Mostly occurs in Children < 12 years.. begin as acute Pharyngitis-Tonsillitis.. Repeat Streptococcal Throat infection is common in young children.. each few weeks-months.
- Infection may spread to other body sites.. sinusitis, otitis media, blood sepsis, wound-Skin.. rarely pneumonia & meningitis
Fig. 5 - Infections of Streptococcus pyogenes

1. Entry
2. Spread
3. Disease
   - Meningitis
   - Otitis
   - Sinusitis
   - Tonsilitis and pharyngitis
   - Adenitis
   - Pneumonia
   - Endocarditis
   - Skin:
     - Impetigo
     - Erysipelas
     - Scarlet fever
     - Puerperal fever
     - Myositis
     - Fasciitis
4. Exit

Sequelae (nonsuppurative)
- Rheumatic fever
- Glomerulonephritis

Uterus
Group A *Streptococcus* Skin infection-3

- **Scarlet fever.** In children, begins as pharyngitis caused by certain *lysogenic S. pyogenes* Strains producing pyrogenic/erythrogenic exotoxins (A,B,C). Causes diffuse erythematous rash in oral mucous membranes. Red Tong & Skin rash. Infection results in lifelong immunity.

- **Impetigo** manifested as superficial skin blisters associated with massive brawny edema.

- **Cellulitis.** Skin infection rapidly spread to subcutaneous tissues. Wound highly communicable in children. May cause glomeronephritis; but rarely Rheumatic fever.

- **Erysipelas.** Complication of cellulitis involving Lymphatics.

- **Streptococcal Toxic Shock Syndrome** are systemic responses to increased circulating pyrogenic toxins A, excreted from some *GAH Streptococcus strains*. High fever, sepsis, Diarrhea, can be fatal.
Scarlet Fever
Necrotizing fasciitis .. **Wound infections** .... Rapid and extensive necrosis subcutaneous tissues & fascia.. associated with Bacteriamia, Endocarditis, Heart failure.. High fatality without antibiotics treatment.

Blood sepsis.. meningitis .. endocarditis.. Rare Puerperal fever.. infected uterus after delivery.. blood sepsis

**Post streptococcal diseases:**

**Rheumatic fever** & **Glomerulonephritis**, followed repeat infection with Group A streptococcus.. Mostly Sore Throat .. developed in 1-3% of untreated infections.

Both diseases and their pathology are not due to dissemination of bacteria, but to immunological reactions to **Group A streptococcal antigens**.. mainly Cell wall antigens & M-protein.
Diagnosis & Treatment

- **Lab Diagnosis**: Culture. Throat, Nose, Blood, Vagina, CSF. Definitive identification type of Hemolytic Strept. accomplished by using specific **antistrepococcal sera** by slide agglutination test.

- **Detection Specific Antibodies**: 2-4 weeks after throat or skin infection. **Antistreptolysin 0 (ASO)** titer: > 240 IU, positive **Streptokinase**, **Anti-M Protein**

- **Treatment**: Clinical cases. healthy Carrier. **Penicillin G / V.** Monthly injection in repeat infection

- Group A is still highly susceptible to **Penicillins**. Less to Cephalosporins & Macrolides and other antibiotics

- No Vaccine is available
Corynebacterium diphtheriae


- Lab Diagnosis: Throat swab, Direct Smear not significant, Culture for C. diphtheria. Selective Tellurite Blood agar + blood agar. Toxigenesity test.

Gingivitis
Neisseria meningitidis


- Prompt diagnosis + antibiotic treatment. Contacts Prophylaxis

- Lab Diagnosis: 1-Direct gram-negative CSF. Culture Throat swabs, blood, CSF. Blood + Chocolate agar.

  2- Biochemical + Haematological investigation of CSF. increased protein-decreased sugar levels. numerous neutrophiles

  3- Detection *N. meningitidis* antigens in CSF
Lower Bacterial Respiratory Infection

- Mostly endogenous source of Infection.. Opportunitic Organisms spread from the upper respiratory tract .. less commonly hematogenous spread to the lung parenchyma.

- A combination of factors .. including virulence of the infecting organism, status of the local defenses, and overall health of the patient may lead to bacterial pneumonia.

- The patient become more susceptible to infection by presence chronic lung disease.. Infant, Old age .. dysfunction of immune defense mechanisms.. Viral Respiratory infection..
Whooping cough & Bronchitis

*Bordetella pertussis* /B. parapertussis, Gram-ve bacilli, difficult to culture.. Release Endotoxin, Cytotoxins, Obstruction ciliated epithelium small Bronchi.. Pertussis toxin causes Lyphocytosis..

- **Clinical Features:** 1-Catarrhal stage..Mild Cough, Mild inflammation pharynx-Larynx, Low fever.. Few days.. 2-Paroxysmal cough.. Prolonged irritating Cough & mucus secretion, Fever, Cyanosis, Lung collapse, Convulsions, No Blood invasion.. Most infection Young Children.. Rare Adults..Community Outbreaks & single cases.

- Clinical Diagnosis..PCR detection bacterial DNA in nasopharyngeal swab, blood & Urine.. Specific antibodies..Prevention by vaccination.
Bacteria attached to Ciliated epithelium cells
Acute/Chronic bronchitis

- A clinical syndrome caused by inflammation of the trachea, swelling & irritation of bronchi & bronchioles, Persistent cough.. Few sputum.. often associated with viral respiratory tract infection. Acute bronchitis is rarely a primary bacterial infection in healthy children.

- Adults Chronic bronchitis followed viral infections.. Associated with secondary *Strept. pneumoniae, H. influenzae*, Group A *Strept.*, *S. aureus*. Complications: Asthma.. Rare Pneumonia
Pneumonia

- **Pneumonia** is an inflammation of the lungs. Sputum.
  Many different opportunistic organisms including **Bacteria, Viruses, Fungi**.

- **Pneumonia** is a common illness that affects millions of people each year worldwide. Associated with high fatality. Intensive Care. Use Respiratory Equipments.

- The symptoms of pneumonia range **mild-severe-fatal**. The severity depends on the type of organism, Patient's Age, Health condition & general immunity.

- **Severe pneumonia**: Lung Inflammation, fluid buildup, Purulent sputum. containing pus / blood. High Fever, Malaise, Nausea, Vomiting, Rapid respiration/Breath shortness. Increased heart beats, Mental confusion.
Bacterial Causes of Pneumonia

- Pneumonia may be further categorized into community-acquired pneumonia (CAP), or hospital-acquired pneumonia (HAP). Respiratory Equipment.

- CAP caused mostly by *Strep. pneumoniae* and followed viral infection in children. Elderly patients.

- HAP. Caused by Gram-ve *P. aeruginosa*, *Klebsiella pneumonia*, *Acinetobacter baumannii*. Less by *Haemophilus influenzae type b*, *Staphylococcus aureus* or others. May associated with blood sepsis.

Streptococcus pneumoniae

- **90 Capsular Serotypes**: Common Healthy Carriers.. normally found in the nasopharynx of **5-10% of healthy adults**.. **20-40% of healthy children**

- **Several virulence factors**: polysaccharide Capsule & Pneumolysins (invasion) .. Both resist phagosytosis & host's immune system.. inhibit activation of complement.. **IgA1** .. Proteases destroy mucosa secretory IgA

- **Strept. Pneumoniae** begins as **intrapulmonary abscess**.. Lung necrosis.. Can be associated with **Empyem** (inflammatory fluid and bacterial debris accumulate in the pleural cavity).

- **Strept. Pneumoniae** often causes blood sepsis, Meningitis, Sinusitis, Otitis Media in young children.
Strept. pneumoniae & Viridans
Streptococci Group
Lab Diagnosis

- *S. pneumoniae* can be differentiated from *S. viridans*, which is also alpha hemolytic, using an Optochin/bile solubility test on Blood agar. Gram-positive diplococcus.

- Up to 80% *S. pneumoniae* are R-Penicillin in Jordan & other countries.

- Treatment: Amoxicillin-clavulanate, Macrolides (Azithromycin, clarithromycin), Fluoroquinolones (Levofloxacin, ciprofloxacin). For Bacteremia + meningitis, vancomycin, ceftriaxone/cefotaxime.

- Prevention: (Pneumovax) Polysaccharide vaccine. 23-valent strains. 85% protection in those under 55 years of age. Five years or longer. Less for older. For children, there is 7-valent strains vaccine up 80% protection.
Atypical Pneumonia


- Causing mostly milder forms of pneumonia. Characterized by slow development of symptoms unlike other forms of pneumonia which can develop more quickly. More severe early symptoms.

Mycoplasma


- Severe forms of M pneumonia have been described in all age groups.

- Lab Diagnosis: Special culture medium. PCR. Sputum, Pleural fluid, Blood. Serological Cold-Agglutination Test. Increased antibody titers.

- Treatment: Levofloxacin, Moxifloxacin, Macrolides/Azithromycin. No Vaccine
Chlamydia species

- **Chlamydia**. Attached human mucosal membrane... obligate intracellular... intracytoplasmic inclusions... Rapidly killed outside body, dryness & high temperature > 4°C.

- **Live cycle**: Infectious elementary bodies attached to the host mucosa and promoting its entry... Cytoplasm phagosome... producing reticulate bodies in inclusion... released elementary bodies.

- **Chlamydia trachomatis**. **Serotypes C, K**: Common cause of sexually transmitted disease (STD). Nonspecific urethritis... mother to newborn babies... maternal fluid... Atypical pneumonia... Eye infection... **Opthalmia neonatorum**

- About half of all newborns with Chlamydial pneumonia develop inclusion conjunctivitis... 1-2 weeks starts mild - severe eyes redness, swollen eyelids, inflammation & yellow thick discharge eyes.

- A & C serotypes of endemic *Ch. trachomatis* cause **Trachoma**... conjunctival scarring, damage eyelids & Cornea... blindness.
Chlamydia Life Cycle

- Infectious Elementary Body
- Lysosome (Cell Organelle)
- Cell Nucleus

1. Ingestion and Establishment of Phagosome
2. Release of Progeny
3. Metabolically Active RB Inside Phagosome
4. Condensation to Elementary Bodies
5. Replication of Reticulate Bodies
Chlamydial Pneumonia

- **C. pneumoniae**: droplets infection. Infants/children often develops gradually. Several weeks mild respiratory symptoms, dry irritating prolonged cough, nasal congestion, with/without fever. Few weeks. No blood sepsis.

- **C. pneumoniae** infections in adults: often asymptomatic, mild. May include sore throat, headache, fever, dry cough.

- Clusters of infection have been reported more common in Children than Adults.

**Diagnosis & treatment**: Sputum, throat-nasal swab. MaCoy Cell Culture, ELSA Specific antibodies, PCR.

**Treatment**: Tetracyclines, Macrolides, levofloxacin, moxifloxacin. No Vaccine
**Chlamydia Psittaci**

- *C. psittaci* causes Zoonotic diseases... Human infection followed contact with *birds* (parrots, pigeons, turkeys, and ducks)... A rare human disease called *psittacosis* (*ornithosis*).

- Humans respiratory tract can be infected via inhalation bacteria shed from feathers, secretions, and droppings localized inflammation in Bronchi & lung tissues.

- **Signs Symptoms**: Starts mild..flu-like & ended with severe disease including fatal *pneumonia*, associated high fever, dry cough, headache.

- **Diagnosis &Treatment** similar to other Chlamydia.
Legionella pneumophila

- **Legionella** carry flagella, Pathogenic-Nonpathogenic spp. often found in natural aquatic bodies and wet soil. Facultative Anaerobes Growth in Cold/Hot (4-80°C) Water..Transmitted, Inhalation via Air Condition, Wet Soil.. Cause outbreak of disease.

- Lung Mucosa..multiply intracellular within the macrophages.. High Fever .. Incub. period 2-10 days .. Nonproductive /Productive dry cough.. Shortness of breath, Chest pain, Muscle aches, Joint pain, Diarrhea, Renal Failure, higher mortality rate. Legionnaires' disease is not contagious

- Risk factors include heavy cigarette smoking, old age underlying diseases such as renal failure, cancer, diabetes, or chronic obstructive pulmonary, suppressed immune systems, corticosteroid.

- **Diagnosis & treatment**: Special Culture Media, blood/urine specimen for detection Specific antibodies or Antigens by PCR, or ELSA .. Macrolides (azithromycin), levofloxacin, moxifloxacin .. No Vaccine.