**د. سرى سلمان عجام Respiratory diseases**

**Pulmonary Infections**

Respiratory tract infections are more frequent than infections of any other organ and account for the largest number of workdays lost in the general population. The vast majority are upper respiratory tract infections caused by viruses (common cold, pharyngitis), but bacterial, viral, mycoplasmal, and fungal infections of the lung (pneumonia) still account for an enormous amount of morbidity

***Pneumonia can be very broadly defined as any infection of the lung parenchyma.***

Pneumonia can result whenever the local defense mechanisms are impaired or the systemic resistance of the host is lowered. Factors that affect resistance in general include chronic diseases, immunological deficiency, treatment with immunosuppressive agents, and leukopenia.

The local defense mechanisms of the lung can be interfered with by many factors, such as the following:

• Loss or suppression of the cough reflex, as a result of coma, anesthesia, neuromuscular disorders, drugs, or chest pain (may lead to aspiration of gastric contents)

• Injury to the mucociliary apparatus, by either impairment of ciliary function or destruction of ciliated epithelium, due to cigarette smoke, inhalation of hot or corrosive gases, viral diseases, or genetic defects of ciliary function (e.g., the immotile cilia syndrome)

• Accumulation of secretions in conditions such as cystic fibrosis and bronchial obstruction

• Interference with the phagocytic or bactericidal action of alveolar macrophages by alcohol, tobacco smoke, anoxia, or oxygen intoxication

• Pulmonary congestion and edema

The Pneumonia Syndromes

COMMUNITY-ACQUIRED ACUTE PNEUMONIA

Streptococcus pneumoniae

Haemophilus influenzae

Moraxella catarrhalis

Staphylococcus aureus

Legionella pneumophila

Enterobacteriaceae (Klebsiella pneumoniae) and Pseudomonas spp.

COMMUNITY-ACQUIRED ATYPICAL PNEUMONIA

Mycoplasma pneumoniae

Chlamydia spp. (C. pneumoniae, C. psittaci, C. trachomatis)

Coxiella burnetii (Q fever)

Viruses: respiratory syncytial virus, parainfluenza virus (children); influenza A and B (adults); adenovirus (military recruits); SARS virus

HOSPITAL-ACQUIRED PNEUMONIA

Gram-negative rods, Enterobacteriaceae (Klebsiella spp., Serratia marcescens, Escherichia coli) and Pseudomonas spp.

Staphylococcus aureus (usually penicillin resistant)

ASPIRATION PNEUMONIA

Anaerobic oral flora (Bacteroides, Prevotella, Fusobacterium, Peptostreptococcus), admixed with aerobic bacteria (Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, and Pseudomonas aeruginosa)

CHRONIC PNEUMONIA

Nocardia

Actinomyces

Granulomatous: Mycobacterium tuberculosis and atypical mycobacteria, Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis

NECROTIZING PNEUMONIA AND LUNG ABSCESS

Anaerobic bacteria (extremely common), with or without mixed aerobic infection

Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pyogenes, and type 3 pneumococcus (uncommon)

PNEUMONIA IN THE IMMUNOCOMPROMISED HOST

Cytomegalovirus

Pneumocystis jiroveci

Mycobacterium avium-intracellulare

Invasive aspergillosis

Invasive candidiasis

SARS, severe acute respiratory syndrome

***Streptococcus pneumoniae***

*Streptococcus pneumoniae*, or *pneumococcus*, is the most common cause of community-acquired acute pneumonia. Examination of Gram-stained sputum is an important step in the diagnosis of acute pneumonia. The presence of numerous neutrophils containing the typical gram-positive, lancet-shaped diplococci supports the diagnosis of pneumococcal pneumonia, but it must be remembered that *S. pneumoniae* is a part of the endogenous flora in 20% of adults, and therefore false-positive results may be obtained. Isolation of pneumococcifrom blood cultures is more specific but less sensitive (in the early phase of illness, only 20% to 30% of patients have positive blood cultures). Pneumococcal vaccines containing capsular polysaccharides from the common serotypes are used in patients at high risk.

Clinical Features :-

The onset is usually abrupt, with high fever , shaking chills , pleuritic chest pain, and productive mucopurulent cough . occasional patients may have heamoptysis

***Morphology:-***

There are 2 morphological pattern:-

a- labor pneumonia .

b- Bronchopneumonia. (is much more prevalent at extremes age) .

Regardless the morphologic pattern , the lower lobes or the right middle lobe are most frequently involved.

***a- lobar pneumonia*** which is most frequent is caused by streptococcus Pneumoniae, It involve the entire lobe. Consolidation can be seen by X-ray *.*

***Microscopically + grossly***

in preantibiotic era, it evolved through 4 stages:-

1-congestion: - The affected lobe is heavy, red and baggy .

histologically: - vascular congestion can be seen, with proteinaceous Fluid, scattered neutrophils and many bacteria in the alveoli

2-Red hepatization: - in which the lung has a liver like consistency, the alveolar spaces are packed with neutrophils, red cells and fibrin and the pleura shows fibrino or fibrinopurulent exudate

*3-Grey hepatization; - the lung is dry, gray and firm because the red cells become lysed while fibrinous exudate persists within alveoli .*

*4- resolution: follows in uncomplicated cases, as exudates within the alveoli are enzymatically digested and either resorbed or expectorated leaving basic architecture intact. the pleural reaction, leaving fibrous thickening or permanent adhesion*

***bronchopneumonia*** *are consolidated areas of acute suppurative inflammation. The consolidation may be patchy through one lobe but is more often multilobar and frequently bilateral and basal because of the tendency of secretions to gravitate into the lower lobes*

***Histologically*** *: the reaction consist of focal Suppurative exudate that fills the bronchi, bronchioles and adjacent alveolar spaces.With appropriate therapy, complete restitution of lung is the rule for both forms of pneumonia.*

*COMMUNITY-ACQUIRED ATYPICAL (VIRAL AND MYCOPLASMAL) PNEUMONIAS*

***Definition***

The term primary **atypical pneumonia was initially applied to an acute febrile respiratory disease characterized by patchy inflammatory changes in the lungs, largely confined to the alveolar septa and pulmonary interstitium.**

The **term atypical** (denotes the moderate amount of sputum, no physical findings of consolidation, only moderate elevation of white cell count, and lack of alveolar exudate.)

**Causative agents**

The pneumonitis is caused by a variety of organisms,

1- the most common being Mycoplasma pneumoniae. Mycoplasma infections are particularly common among children and young adults. They occur sporadically or as local epidemics in closed communities (schools, military camps, and prisons).

2- viruses, including influenza virus types A and B, the respiratory syncytial viruses, human metapneumovirus, adenovirus, rhinoviruses, rubeola, and varicella viruses;

3-Chlamydia pneumoniae; and Coxiella burnetii (Q fever).

Any one of these agents can cause merely an upper respiratory tract infection, recognized as the common cold, or a more severe lower respiratory tract infection.

Factors that favor such extension of the infection include

**extremes of age,**

**malnutrition,**

**alcoholism,**

**underlying debilitating illnesses.**

**The common pathogenetic mechanism**

is attachment of the organisms to the upper respiratory tract epithelium followed by necrosis of the cells and an inflammatory response. When the process extends to the alveoli there is usually interstitial inflammation, but there may also be some outpouring of fluid into alveolar spaces, so that on chest x-ray the changes may mimic bacterial pneumonia. Damage to and denudation of the respiratory epithelium inhibit mucociliary clearance and predispose to secondary bacterial infection

**Morphology.** All causal agents produce essentially similar morphologic patterns. The lung involvement may be quite patchy or may involve whole lobes bilaterally or unilaterally. The affected areas are red-blue and congested. The pleura is smooth, and pleuritis or pleural effusions are infrequent.

The histologic pattern depends on the severity of the disease. **Predominant is the interstitial nature of the inflammatory reaction, virtually localized within the walls of the alveoli**. The alveolar septa are widened and edematous and usually have a mononuclear inflammatory infiltrate of lymphocytes, macrophages, and occasionally plasma cells. In acute cases neutrophils may also be present. The alveoli may be free from exudate, but in many patients there is intra-alveolar proteinaceous material and a cellular exudate. When complicated by ARDS, characteristically pink hyaline membranes lining the alveolar walls are present Eradication of the infection is followed by reconstitution of the normal architecture of the lung.

***ClinicalCourse.***

The clinical course is extremely varied. Many cases masquerade as severe upper respiratory tract infections or as *chest colds*. Even individuals with well developed atypical pneumonia have few localizing symptoms. Cough may be absent, and the major manifestations may consist only of fever, headache, muscle aches, and pains in the legs.

***Tuberculosis (TB)***

TB is a communicable chronic granulomatous disease caused by Mycobacterium tuberculosis it usually involves the lungs but may affect any organ or tissue  *.*

***((Immune Mechanisms in pathogenesis of TB.)):***

a- the organism are ingested by macrophages which process the bacterial antigens for presentation to CD4 TH1 T cells in the context of class II MHC molecules

b- The CD4+ T cells proliferate and secrete cytokines , attracting lymphocytes and macrophages.

IFN- γ released by CD4 + T cell is critical in activating macrophages

c- Activated Macrophages release a variety of mediators:

1-TNF is responsible for recruitment of monocytes which in turn undergo activation and differentiation into epithelioid histiocytes

2- IFN- γ in conjunction with TNF result in increased level of nitric oxide at site of infection , Nitric oxide is a powerful oxidizing agent and results in generation of free radicals capable of destruction of several Mycobacterial constituents.

d- CD4 T cells facilitate the development of CD8 cytotoxic T cells and kill TB infected macrophages.

e- Delayed hypersensitivity is marked by a positive tuberculin skin test result. The test result is positive in both primary and secondary infect on represents hypersensitivity and relative immunity and usually remains positive throughout life.

***Types of TB:***

***1° (Primary) TB***

is the form of disease that develops in a previously unexposed, Elderly and profoundly immunosuppressed persons may lose their sensitivity to tubercles and so may develop tuberculosis more than once.

With primary TB source of organism is exogenous, 5% only develop significant disease

***Morphology:-***

*Gross:-*

primary TB almost always begins in lungs. Typically the inhaled bacilli in distal airways of lower part of upper lobes or upper part of lower lobes. Gray white consolidation emerges which called Ghon focus, this focus undergoes caseous necrosis. The TB bacilli either free or within phagocytes drain to regional LN which is also caseate → Ghon focus + Regional LN complex = (Ghon complex). Which is a characteristic of primary TB.

Ghon complex undergoes fibrosis + calcification that can be detected by X-ray (Ranke complex)

Microscopically

granulomatous inflammatory reaction that forms both caseating and non caseating tubercles the granulomas are usually enclosed within a fibroblastic rim punctuated by lymphocytes

Multinucleated giant cells are present in granuloma *.*

***Fate of primary TB***

1- induce hypersensitivity and increased resistance

2- The foci of scarring may harbor viable bacilli for years perhaps for life.

3- Uncommonly the disease may progress without interruption into so called progressive TB because of well-defined disease such as AIDS.

Diagnosis of PPTB in adult is difficult. PPTB resembles pneumonia

lymphatohaematogenous dissemination may develop → TB meningitis and miliary TB

***2- Secondary TB (reactivation TB)***

Is the pattern of disease that arises in previously sensitized host, it may follow shortly after 1°TB, but more commonly it arises from reactivation of dormant 1° lesions many decades after initial infection when host resistance is weakened or it may results from exogenous reinfection.

2° TB is classically localized to the apex of one or both upper lobes , this is may be due to high oxygen tension

because of preexisting hypersensitivity, the bacilli excite a prompt and marked tissue response that tends to wall off the focus so there's no LN involvement

Cavitation occurs resulting in dissemination along airways in neglected 2° TB . So the erosion along the airway is an important source of infectivity because the patient raises sputum containing bacilli*.*

***Morphology:-***

*a*- localized lesions usually in the apical or posterior segments of upper lobes.

b- Tubercle formation:-The lesions frequently coalesce and rupture into the bronchi

The Caseous content may liquefy and be expelled resulting in cavitory lesions . Cavitations is a characteristic of 2° TB (not 1° TB).

c- Scarring and calcification

**Spread of disease of 2nd TB:-**

1-Miliary TB: - which is seeding of distal organs with innumerable small millet seed like lesions by lymphatic and haematogenous routes, this is may be pulmonary miliary TB or systemic.

2- Endobronchial, endotracheal and laryngeal TB develop either by spread of infective material through lymphatic channels or from expectorated infectious material.

3-Isolated organ TB:-

This is occur by haematogenous spread to any organ and may the presenting feature, most common sites meninges, kidneys, adrenals, bone, Para spinal abscess or Pott disease, and fallopian tube.

4- Lymphadenitis especially cervical LN

lymph adenopathy is unifocal and the patient don't have the ongoing disease.

5-Intestinal TB:-

due to ingestion of contaminated milk or secondary to swallowing of coughed up infective materials in 2° TB .Typically the organisms are trapped in mucosal lymphoid aggregations of the small and large bowel which undergo inflammatory enlargement and ulceration especially in the ileum

**Clinical Features**

Localized secondary TB may be asymptomatic when manifestation appear they are usually insidious. There are :

1- systemic symptoms related to (TNF and IL1)

Malaise, anorexia, weight loss and fever (remittent low grade) and night sweat.

2- localized symptoms (with progressive pulmonary TB)

- increase amount of sputum first mucoid then purulent.

- Haemoptysis (in 1/2 of patients).

- Pleuritic chest pain

in extrapulmonary TB the symptoms depend on the organ that is involved

E.g.: Fallopian tube → infertility

meninges → neurologic deficit.