

Note: This sheet contains everything mentioned in the lecture, in addition to the slides. There is no need to refer to the slides after studying this sheet as it includes everything. Information from the slides, and not mentioned by Dr. Asem during the lecture will be marked (S).

- The respiratory tract is the most common site of body exposed for infection by pathogens and opportunistic pathogens. (S)
- RT site becomes infected frequently because it comes into direct contact with the physical environment and is exposed continuously to many microorganisms & their spores in the air.. Smoke, dust & human air droplets
- Air is full of pathogenic organisms that are carried and transmitted to infect human beings.
- A certain percentage of individuals in each community are called asymptomatic carriers; they carry the pathogen and transmit it to others without having the clinical signs of the disease.
- There are large numbers of spores from fungi that might lodge in the lungs of certain individuals. These spores cause infections in immunocompromised patients.
- A couple of years ago, a study conducted in China concluded that we inhale 8-10 pathogens per minute. Some of those might cause infections.
- Our respiratory tract is highly resistant to the attachment and adherence of such organisms. In fact, individuals rarely get infections, unless they are susceptible (either due to mucosal damage or underlying disease)
- The organism will produce clinically apparent symptoms when it is able to overcome the patient's immune system. As a matter of fact, not all individuals develop the same degree of illness. According to a recent study, only 15% of children infected by Streptococcus Group A require antimicrobial treatment.

Slide No. 3:

- Before a Respiratory Disease is developed, the following conditions need to be met
 - o There must be a sufficient number or "dose" of infectious agent inhaled.
 - o The infectious organism must remain alive and viable while in the air.
 - o The organism must be deposited on susceptible respiratory mucosa & attached.
 - o The infectious agent must overcome the host immune system.
 - o The importance role of normal flora
- There are two important classes of organisms that cause problems ONLY under suitable conditions:
 - o Opportunistic pathogens
 - o Obligate pathogens
- Our respiratory flora is important for two reasons (They occupy nasopharynx, oropharynx, and laryngopharynx) (S):
 - o Occupy a place and prevent other bacteria from settling
 - o Release certain enzymes which prevent the attachment of other organisms. ex: streptococcus veridans secrete enzymes that cause lyses of the newly introduced organisms

- Viruses might be present as part of the normal flora for a short period of time. However, under certain conditions, the pathogen is activated. We see cases either as sporadic cases or as community outbreaks.
- Many infections that affect the human body are caused by multiple pathogens. For example, tonsillitis can be caused by: H. influenza, N. meningitides, and Streptococcus group B.
- When there are two or more pathogens causing the disease, one of them must be prevalent over the others.
- In order to say that strep A is the causative agent of sore throat, it must be isolated in large numbers from the respiratory tract.
- Pseudomonas Aeruginosa and Klebsiella Pneumonia both can cause pneumonia. This is why we need to know which one is the causative agent in order to be able to give the proper antibiotic treatment.
- Common respiratory tract bacteria include:
 - o Streptococcus (of different variations)
 - o N. meningitides
 - o Certain Haemophilus strains other than H. influenza: such as egypticus.

The aforementioned organisms are susceptible to most antibiotics. Thus, we should use antibiotics cautiously. With the abuse of antibiotics, many multiresistant strains have emerged.

- **Common normal flora (S):**
 - o Viridans Streptococci (S. mutans, S. mitis)
 - o Neisseria (N. flava, N. sicca)
 - o Haemophilus /Parahaemophilus
 - o Corynebacteria
 - o Anaerobic Bacteria (Bacteroides fragilis, Spirochetes)
- **Less common normal flora (S):**
 - o Group A streptococci
 - o H. influenza
 - o S. pneumonia
 - o Candida
 - o Gram-negative bacilli
- Staph. aureus and Haemophilus influenza are rarely associated with sore throat, but, in certain cases, like immunocompromised patients and those who are treated with cytotoxic drugs, they reside in the respiratory tract and are associated with systemic infections.
- These infections include patients of all ages especially hospitalized patients. They are associated with H. influenza, especially type B, which is more virulent.

- There have not been many cases of H. influenza meningitis in the past years; this is largely due to the vaccination program.
- This decrease in H. influenza B numbers lead to the evolution of a new strain which is slowly replacing the former.
- Streptococcus fecalis, which is already highly resistant to aminoglycosides and cephalosporines, is becoming more resistant and is acquiring more virulence factors. There is a horizontal transfer of certain factors such as hemolysin and endocarditis antigen.
- Hemophilus can be associated with any part of the body. It might produce a multitude of infections such as: pneumonia in adults, eye infections and lung infections.
- H. influenza is usually associated with streptococcus and physicians usually overlook the presence of two organisms as infectious agents.
- **H. influenza B features (S)**
 - **Capsules made of lipooligopolysaccharides**
 - **Invasive**
 - **Highly susceptible to all temperatures (autolysis)**
 - **Rarely causes sore throat**
 - **Common cause of:**
 - **Otitis media**
 - **Sinusitis**
 - **Conjunctivitis**
 - **Blood sepsis**
 - **Meningitis**
 - **Hib-Vaccine available (polysaccharide protein conjugate vaccine). Taken with DTP vaccine.**
- **Staphylococcus aureus (S):**
 - **Affects all ages**
 - **Causes sinusitis, conjunctivitis, but rarely causes sore throat, sepsis, or meningitis.**
 - **Staphylococcal pneumonia is a frequent complication following influenza infection**
 - **Most susceptible patients are: infants, elderly, and immunocompromised**
- Streptococcus group A (beta hemolytic) is an important pathogen of the respiratory tract. This is due to the fact that it secretes many extracellular enzymes.
- It is a gram positive, catalase negative cocci. Part of the normal flora of the respiratory tract (S)
- The classification and definite identification of the type of bacterium (Groups A through F) or what is known as the Lancfield classification is based on the polysaccharide chain. (S)
- 5-15% of the population carries this organism asymptotically. (S)
- Streptococcal infections are most common in children less than 12 years old. (S)
- Only 1-3% develop poststreptococcal disease. (S)
- This organism can infect any part of the body:
 - Respiratory tract

- Sinuses (sinusitis)
 - Middle ear (otitis media)
 - Lungs
 - Blood (bacteremia)
 - Meninges (meningitis)
 - Uterus (causing puerperal fever in 5% of the patients)
- The problem with this organism is the release of antigens and extracellular products which cause post streptococcal disease. It is associated with localized and invasive infections.
- **The structure:**
- **Cell wall:**
 - The capsule is made of hyaluronic acid and (the only type of organism with this type of capsule.)
 - The peptidoglycan layers have a special polysaccharide, and it is specific for each type of group A streptococci; there are about 100 serotypes.
 - The presence of certain specific proteins which are considered as specific virulent proteins (They might become superantigens or help in the etiology of certain autoimmunity diseases)
 - **Pili:**
 - Unlike the gram negative pili, which are used for conjugation, are related to the cell wall surface and are called M protein.
 - This M protein is important in the invasiveness of the organism.
 - It is (M protein) a major factor for developing post streptococcal disease.
 - It makes the bacterium resistant to phagocytosis. In addition to preventing phagocytosis, this protein destroys macrophages producing a more complex antigen which leads to a more complicated infection.
 - Not all strains of streptococcus produce the same amount of M protein.
 - The body produces antibodies against it, and these antibodies are assessed to evaluate the immune response of the affected patient; the results are indicative for the risk of post streptococcal disease.
 - RMP protein is also a virulence factor.
 - T and R proteins are also present (S)
- Some streptococcus group A strains are lysogenic and produce erythrogenic and pyrogenic toxins.
- These toxins produce skin manifestations such as scarlet fever
- **Scarlet fever:**
- Begins as pharyngitis
 - Diffuse erythematous rash in oral mucosal membranes (red tongue) and on the skin.
 - Results in lifelong immunity
- Some strains might cause erysipelas which is a superficial skin infection that can be easily confused with pyoderma (impetigo). Features of impetigo and erysipelas are not easily differentiable in the first few days. Impetigo can be caused by strep A, and might

be present without brown edema. However, erysipelas might involve lymphatics and subcutaneous layers; it might develop into glomerular nephritis and death if not treated.

- Streptococcal infections are highly communicable.
- Another highly dangerous toxin is the recently discovered “toxic shock syndrome toxin”, which is related to erythrogenic toxins. It produces the same clinical features as the staphylococcal toxic shock syndrome toxin
- Necrotizing fasciitis is a recently discovered fatal infection caused by a supertoxin secreted by a few streptococcal strains. Once the infection reaches the subcutaneous layers (in less than 24 hours), you will be able to recognize liquefaction, damage, and necrosis of the tissues. It is a deadly disease

- Repeated infection with streptococcus leads to poststreptococcal diseases such as glomerular nephritis and rheumatic fever. In order to prevent re-infection, the patient is put on a course of penicillin (the drug of choice, except for those who have allergies towards it).

- Macrolides are not enough to eradicate the infection completely
- Cotrimoxazole (sulfamethaxole and trimethprim combination) proved to be superior.
- There is no vaccine available due to the large number of varieties.
- Lab diagnosis includes identifying the number, serotype and M protein type. There are certain M protein strains that are more dangerous than others. In modern clinical practice, M protein identification has become of a huge importance.
- The culture is made on sheep blood agar (S)
- Serotype is confirmed via slide agglutination test. (S)
- Serology: (detection of antibodies starts after 2-4 weeks (S))
 - o It is not easy to isolate the causative with patients who have received partial antimicrobial treatment.
 - o Antistreptolysin 0 (ASO) is associated with more immunological reactions; patients who are positive (240 + titer (S)) are at a higher risk for developing poststreptococcal diseases.
 - o Streptokinase
 - o Anti-M proteins.

These tests are particularly important with children who suffer from recurrent infections.

- **Corynebacterium:** (Read slide 18, the Dr. did not read/explain anything from that slide)
 - o Not all strains of corynebacterium are toxic.
 - o Since 1980, we haven't had any important cases of diphtheria.
 - o About 100% of the population is covered with the triple vaccine.
 - o Due to high immigration rates from neighboring countries, Corynebacterium has become an issue of increasing concern.
 - o Some people are not totally immune against this bacterium, so they might get a mild form of the infection.
 - o Certain strains might produce an increased amount of toxins which might be associated with severe localized throat infection but not damage to other organs such as the heart.

- **Vincet Angina or Trench Mouth** :
 - Mixed infection caused by oral normal flora such as Borrelia, Treponema vincenti, and Fusobacterium
 - The disease causes:
 - Oral mucosa Lesions such as Gingivitis (gum swelling)
 - Angina related to oral mucosa