

Respiratory system

Microbiology



sheet



handout



slides

Number

4

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In this lecture we will continue talking about the viral infections of the respiratory tract, a few about the upper respiratory tract infections and then continue talking about the lower respiratory tract infections.

➤ Pharyngitis (Sore Throat) and Tonsillitis:

- ✓ Caused by bacteria or viruses, but the most common cause is viruses (2/3 of cases).
- ✓ Manifestations are either due to direct infection of the mucosa by the virus or the immune response in the lymphoid tissues.
- ✓ Findings that suggest viral rather than bacterial infections include: involvement of the conjunctiva (adenoviruses), the nasal mucosa “coryza” (rhinoviruses), the GI tract “diarrhea” (enteroviruses) or “hoarseness” (parainfluenza).
- ✓ We can also differentiate using serology: antistreptolysin O in case of infection by group A β -hemolytic Streptococci.
- ✓ Why is it so important to differentiate between viral and bacterial infections and treat the bacterial infection?
 - Inappropriate use of antibiotics leads to **antibiotic resistance** due to selective pressure on normal commensals that do not normally cause infection
 - We treat bacterial infections to avoid **non-suppurative complications** such as rheumatic fever and Poststreptococcal Glomerulonephritis. “Group A β -hemolytic Streptococci”
- ✓ Most common cause is the adenovirus which is a double stranded DNA virus.
- ✓ Other causes include EBV, CMV both multiply locally, Herpes, and Coxsackie (painful lesions).
- ✓ **Transmission:** person to person contact and fomites (indirect)
- ✓ **Treatment:** symptomatic: analgesics, fluids in case of dehydration and antipyretics.

- All the DNA viruses are double stranded except the Parvoviruses
- All DNA viruses are considered human pathogens
- All RNA viruses are single stranded except the reoviridae

➤ Herpangina:

- ✓ Febrile illness of a sudden onset with fever and sore throat.
- ✓ There is a predilection for the young.
- ✓ Characteristic lesions, usually vesicular lesions “Herp” on the soft palate, uvula, tonsils, and posterior pharynx.
- ✓ The disease is usually self-limited and disappears within a few days.
- ✓ Side note: [Viral diseases of the upper respiratory tract are very much alike, so we

use molecular testing to differentiate between them. These viruses have a panel that includes parainfluenza...etc. We take a single swab for example a nasopharyngeal swab and the tests are made usually one of them is detected if there is viral infection.]

- ✓ Because it is caused by a Coxsackie virus which is an enterovirus there might be CNS involvement ultimately causing aseptic meningitis.

➤ **Hand-foot-mouth disease:**

- ✓ Enteroviral respiratory tract infection caused by Coxsackievirus **A16** and **A10**.

➤ **Infectious mononucleosis:**

- ✓ Triad of **clinical manifestations**:

- Fever.
- Pharyngitis.
- Lymphadenopathy.

(Spleen is enlarged to a palpable degree in physical examination of the abdomen in only 20%-60% of cases so it not considered in the triad.

Enlargement of the spleen is detected by physical examination (palpation) or ultrasound)

- ✓ EBV (Epstein Barr virus) and CMV (cytomegalovirus) mainly cause the disease and other parasites such as toxoplasma may cause similar manifestations.
- ✓ **Seroprevalence** (the proportion of the population that is affected by the disease, as measured in blood serum): How many individuals in the population have antibodies against the virus (i.e. they had a previous infection.) In the developed countries, adults in their twenties have a prevalence of 95%. It may have infected them, and it was asymptomatic.
- ✓ **Transmission**: Through saliva “kissing disease” and sexual way of transmission.
- ✓ Why there is splenomegaly and lymphadenopathy?
 - There is B-cell involvement and it uses **CD21 receptor** to enter, CD21 is also called complement receptor 2.
- ✓ Vaginal ulcers may be present.
- ✓ Why is it important to differentiate EBV infection From other clinical conditions that resemble it clinically?
 - There are other conditions which have similar clinical manifestations, most importantly “Lymphomas”.
 - In both diseases the lymphocyte count is increased so it is necessary to do lab

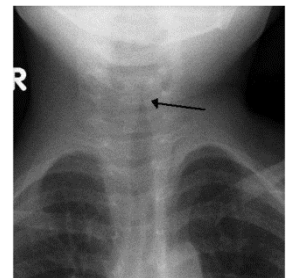
investigations which include CBC, differential and blood films.

- In the blood film there is atypical lymphocytes; those are associated with EBV more than 10% Out of all WBCs.

- ✓ **Serologic diagnosis:** there are heterophile antibodies that cross react with the sheep or horse RBCs. The test is called "*monospot test*" but it is not specific or sensitive.
- ✓ The definitive diagnosis is done by detecting IgM antibodies for antigens on the virus such as viral capsid antigens, Epstein-Barr nuclear antigen (EBNA). We look for IgM antibodies because it is a recent infection.

➤ **Croup:**

- ✓ Inflammation of the larynx, trachea and large bronchi; Laryngotracheobronchitis.
- ✓ **Key findings:** hoarse voice, barking cough which indicate involvement of the larynx.
- ✓ Symptoms may begin in a subtle fashion: nasal irritation, congestion.
- ✓ Most common cause of infectious upper airway obstruction in children.
- ✓ The **most common cause** is viral: influenza "10% of cases" esp. type A, RSV and parainfluenza 1. Parainfluenza is the most common cause.
- ✓ Diagnosis is made clinically, and the radiograph will show characteristic steeple sign. Demonstrates narrowing of the subglottic airway. "Steeple: a church tower and spire."
- ✓ Children with severe croup will have severe symptoms with nasal flaring, suprasternal and intercostal retractions all of which are indicative of airway obstruction.
- ✓ These children will have lethargy, agitation, inspiratory stridor, tachycardia, tachypnea, and hypoxemia. Those are indications of worse prognosis. The child might not be able to maintain adequate oral intake and become dehydrated.
- ✓ Patients with moderate to severe symptoms may be given corticosteroids as there is no antiviral therapy for croup until now.



➤ **Otitis media:**

- ✓ Inflammation of the middle ear. Can be caused by viruses or bacteria. Could be acute or chronic. Any process that leads to Eustachian tube obstruction could lead to fluid retention and concomitant infection in the middle ear.
- ✓ Most common **predisposing factors** are upper respiratory tract infections.

- ✓ Mainly in children under 3 years of age because the Eustachian tube is small and easily obstructed.
- ✓ Patient present with ear pain, pressure often accompanied by upper respiratory tract infections. May also complain of decreased hearing and fever and the tympanic membrane may be erythematous.
- ✓ Among the **viruses** the most common is RSV, corona and rhino.

➤ **Laryngitis:**

- ✓ Inflammation of the vocal cords and larynx.
- ✓ **Most common cause** is the parainfluenza virus. Other viruses include Rhino, RSV, influenza, adeno and corona viruses.
- ✓ Why are they called parainfluenza viruses?
 - The diseases are influenza like.
 - It is medium sized, negative sense enveloped RNA virus, *but* its genome is not segmented unlike Influenza.
- ✓ **Transmission** is either direct or indirect (fomites) contact. It cannot persist for a long time in the environment as it is enveloped.

Now we will discuss LRTI:

➤ **Acute bronchitis:**

- ✓ It is inflammation of trachea and bronchi sparing the alveoli.
- ✓ It is usually **caused by** viral agents like: Influenza A and B, parainfluenza viruses, adeno and RSV are the common ones. Other viruses include coxsackie A, B and echoviruses [Note from me: both are enteroviruses and remember enteroviruses cause aseptic meningitis].
- ✓ **Manifestations:** cough that can become mucopurulent if there are subsequent bacterial infections. X-ray will show no infiltrates and can be used to differentiate pneumonia and acute bronchitis.
- ✓ Bronchitis in healthy persons is almost always self-limited and the management is supportive therapy.

➤ **Bronchiolitis:**

- ✓ Important in pediatrics, inflammation in the bronchial tree as low as the bronchioles with alveolar sparing. The infants have narrower airways. "Infants are

up to a year” and “older than a year are toddlers”.

[Note: we can see viruses infecting more than one area and disease manifestations in more than a single area. The best example is croup it mainly involves the larynx but may also involve the Trachea and bronchi; this is because the epithelium changes gradually.]

- ✓ **Most common causes** are RSV and other causes include: metapneumoviruses, parainfluenza and adeno.
- ✓ Early symptoms are like the upper respiratory tract infections: mild rhinorrhea, low grade fever, cough.
- ✓ In children it may reach the lower respiratory tract causing paroxysmal cough, dyspnea and other symptoms include: tachypnea, tachycardia, diffuse wheezing “usually associated with lower respiratory tract complications” and respiratory crackles That can be detected by auscultation. Those indicate worse prognosis.
- ✓ **Diagnosis:** clinical manifestations, chest radiograph and antigen testing for RSV as it is the most common (sample is taken by nasal wash usually).
- ✓ **Management:** oxygen and fluid supply. There is a monoclonal antibody “palivizumab” that can be used in the case of RSV bronchiolitis.

➤ **Viral Pneumonia:**

- ✓ The most obvious example for the lower respiratory infections. Infection of the wall of the alveolar sacs.
- ✓ Pneumonia in general is caused by viruses, bacteria, fungi, atypical bacteria. It is hard to differentiate between them without radiography and lab tests.
- ✓ The avian flu (H5N1), swine flu and emerging respiratory viral infections (e.g. SARS) reemphasize the importance of viruses in causing severe pneumonia.
- ✓ Despite the technology advances as in the suspicion of an RNA virus we use reverse transcriptase PCR, DNA viruses we use PCR, and these have higher accuracy compared to conventional methods.
- ✓ The **most common cause** of viral community acquired pneumonia in **children** is **RSV**, influenza, parainfluenza and adeno viruses. While in the **adults** it is **influenza**.

❖ **Emerging severe viral infections:** common viral pathogens that have not resulted from cross species jump are usually milder, Just for clarification, almost all viral infections circulating among humans today are the result of cross species transmission. However, they have already been established within the human population for a very long time, hence these viruses became less virulent compared to the strains that cross the species barrier recently. When discussing these reemergent

viral infections, they mainly came from other species which they are adapted to for example an animal such as birds and then they attacked humans. The humans themselves do not have herd immunity and the virus is adapted to another species and the human virulence is high with the resulting strong immune reaction which will result in the severe symptoms. ~**not included**

These viruses cause cytokine storms while the normal circulating viruses do not because they are not adapted to humans and that all the pathogens do not have an interest in killing the host in order to survive and be transmitted. When cross species jump happens the host is not capable of fighting the virus as it has no memory to fight the infections without complications. ~**not included**

Thus, we **conclude**: These emerging infections happen due to the fact that the virus itself is not adapted to live within the host without causing this massive immune reaction. Also, there is no herd immunity in population itself. ~**not included**

Another to point to clarify things is the Viruses, particularly RNA viruses have a high mutation rate, thus they continuously mutate resulting in a large group of variants coexisting within the host and suppose that 100 one is transmitted. 99 of those will cause severe diseases and death while that one copy did not kill the host and it has been transmitted. ~**not included**

➤ **Avian flu (H5N1):**

- ✓ Since 2003 it has caused more than hundreds and thousands of human infections with case fatality of 60%.
- ✓ Multi-organ failure develops within a week. Lymphopenia, thrombocytopenia, raised concentrations of amino transferases and creatinine indicating deteriorating liver and renal functions. Why lymphocytopenia?
 - There is systemic involvement and cytokine storm that is why we have lymphopenia. The patients may also have other predisposing conditions for the comorbidities such as liver disease and diabetes with their effects.
- ✓ The virus is novel and there is no herd immunity to it and there are no antibodies against it.
- ✓ Human influenza is transmitted by inhalation of infected droplets, direct or indirect contact.
- ✓ Studies on isolated avian flu indicate that the virulence factors include: highly cleavable hemagglutinin that can be cleaved by multiple cellular proteases. Specific substitution in PB2 (polymerase basic protein 2) causes enhanced replication and substitutions in structural proteins to make them fight interferons and TNF-alpha and this will cause increasing pathogenicity.

➤ **Pandemic flu (H1N1):**

- ✓ Associated geographical spread “across geographic borders” as the name suggests. It has resulted in several pandemics in the previous century such as the Spanish flu 1918, caused by the same strain **and** the secondary bacterial infection back then by *Streptococcus pneumoniae* contributed in the huge mortality.
- ✓ The first pandemic of the virus was in 2009 the first pandemic of the century first reported in the USA and Mexico.
- ✓ Most likely it resulted from a pig which was infected with avian and human viruses, then assortment happened.

➤ **Emerging Viral Respiratory Infections SARS & MERS:**

- ✓ Corona viruses and they cause lower respiratory tract infections.
- ✓ This century has seen the global spread of 2 unknown previously coronaviruses.
- ✓ SARS (severe acute respiratory syndrome) was reported earlier than MERS in China (2002) another one in 2003 and it has spread over the world (Canada, Vietnam...) but now it is contained. **Cross-species transmission** happened from civets.
- ✓ MERS (Middle East respiratory syndrome): the first report is in 2012 in Saudi Arabia and there were cases in Jordan. There were other countries like Qatar and Oman. It is not yet declared eradicated.
- ✓ (Important) The animal in which the **cross-species transmission** happened from is **camels**.
- ✓ The risk is on health care professionals is high as it is a nosocomial infection transmitted in health care settings. Then the infected individuals travel to other places across the world.
- ✓ (Important) The original reservoir is **Bats for SARS and MERS**. This is important as we can look in the bats for potential human pathogens!
- ✓ For further reading refer to:
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1539106/> This is not part of the exam
- ✓ There is human to human transmission, again through nosocomial settings.
- ✓ **Clinical course** is similar; the incubation period is 5-6 days, with systemic manifestations such as fever and local to the lower respiratory tract such as cough. Other less common symptoms are diarrhea, nausea and vomiting. Upper

respiratory symptoms are rare.

- ✓ **Diagnosis:** molecular detection in respiratory tract samples “nasopharyngeal swabs will not result in diagnosis because they represent the upper respiratory tract”.
- ✓ **Risk factors:** patients with diabetes, hypertension, heart disease, renal disease, lung disease and cancer, which result in poor prognosis.
- ✓ Immune response is essential in the resolution of the viruses but can result in immunopathogenesis.
- ✓ Effective antiviral agents are experimental now such as ribavirin as well as interferons and supportive therapy is the one relied on.

THE END