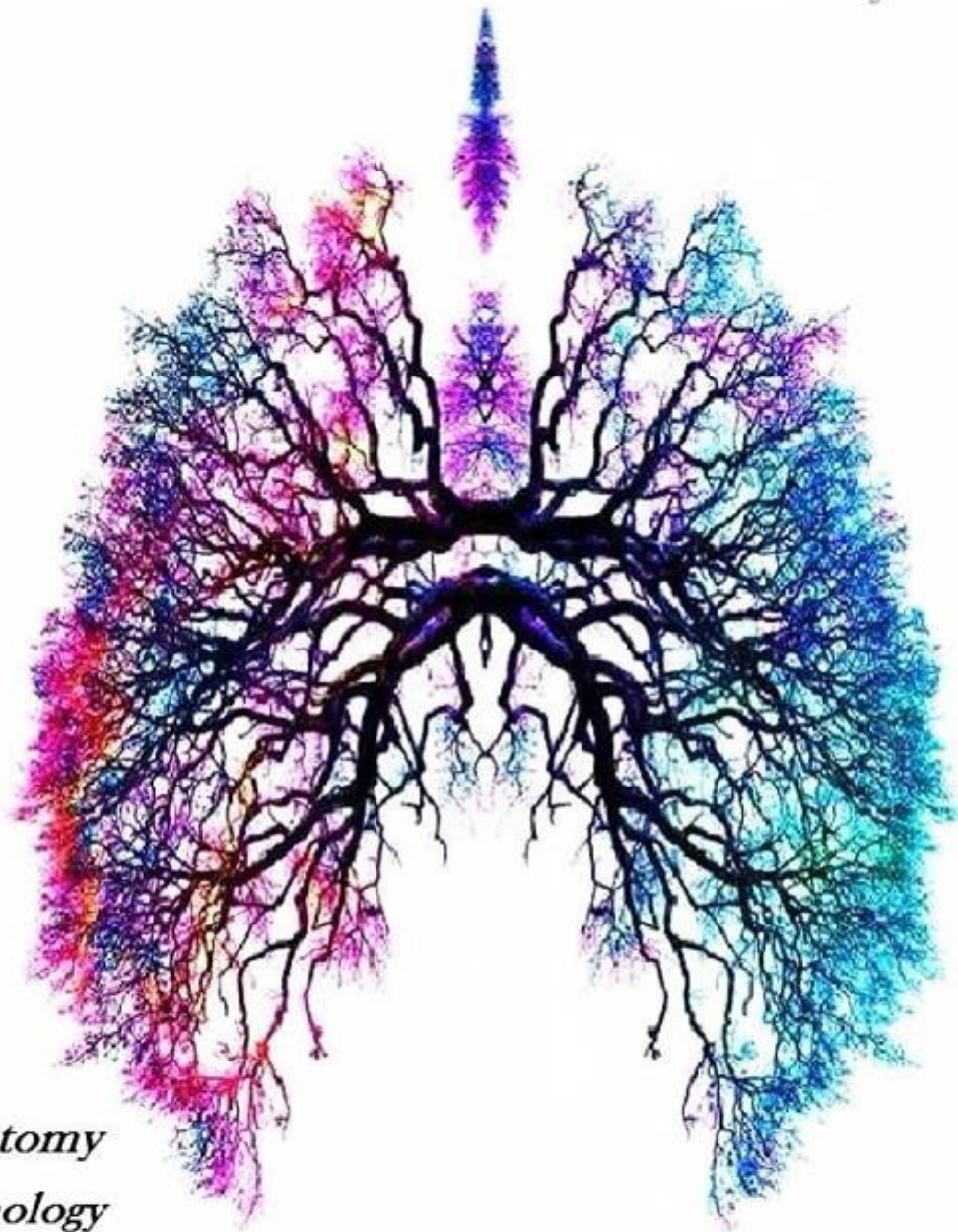


# RESPIRATORY SYSTEM

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- Anatomy*
- Pathology*
- Physiology*
- Pharmacology*
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- PBL*

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*Lecture #* 2

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## Acute Pharyngitis

Pharyngitis is an inflammation of the pharynx secondary to an infectious agent; mainly viruses (85-90%) in adults and children, bacteria cause the remaining 10-15%.

- ✧ The most common cause of bacterial pharyngitis is group A  $\beta$ -hemolytic streptococci (*S. pyogenes*).
- ➔ Today we're going to talk about the different viruses that cause infection of pharynx and tonsils & we're going to differentiate in terms of clinical presentation and clinical examination between viral and bacterial tonsillitis or pharyngitis. In addition to that, we're going to talk about diagnosis and treatment of pharyngitis.
- ✧ Pharyngitis often coexists with tonsillitis.
- ✧ Viral Causes: Rhinoviruses and Corona viruses.  
Remember: common cold is mainly caused by **Rhinovirus**, **Coronavirus** & some other viruses to a lower degree. Symptoms start as sneezing, coughing, rhinorrhea followed by sore throat, headache and myalgia as well.
- ✧ After 2-3 days of common cold or even 1-2 days of having URT infections, the patient may start complaining of pharyngitis.

Other causes of pharyngitis include: **Adenovirus** (sometimes associated with conjunctivitis > pharyngoconjunctival... this is significant for adenovirus – it may be associated with acute respiratory illness as well), **CMV**, **Para-influenza**, **EBV**, **herpes simplex type 1 virus**, enteroviruses such as **Coxsackie A virus** & **enterovirus71** (herpes simplex type 1 and these two enteroviruses



are characterized by vesicular lesions which ulcerate in the palate or surrounding the pharynx and the tonsils).

About **HIV**: it has an acute phase, then a long incubation period and after that the full picture of HIV which is the aids. In the acute phase, the patient is present with flu-like symptoms; pharyngitis may be present among these symptoms.

Bacterial causes include: **S.pyogenes** (mainly), **Mycoplasma**, **Arcanobacterium** & others.

### History

Classic symptoms of pharyngitis: fever, throat pain and dysphagia (difficulty in swallowing).

❖ Fever is more pronounced with bacterial pharyngitis. Whereas, it is usually mild or absent in viral pharyngitis.

➤ **VIRAL**: Most likely concurrent URI symptoms of rhinorrhea, cough, hoarseness, conjunctivitis & ulcerative lesions.

- Conjunctivitis → in adenovirus

- Ulcerative lesions → in herpes simplex type 1 virus and Picorona viruses or enteroviruses such as: coxackievirus and enterovirus 71.

➤ **STREPTOCOCCAL**: Look for associated headache, and/or abdominal pain (especially in children). Fever and throat pain are usually cute in onset.



## Physical examination

### ➤ VIRAL

**EBV** is present with white exudate covering erythematous pharynx and tonsils & cervical adenopathy (cervical lymph nodes enlargement).

❖ White exudate is usually associated with bacterial infections, but certain viral infections may also be associated with white exudate such as: EBV & Adenovirus. Why? Because infections then replication of the virus occur locally at this location so there is an injury at this location that results in exudate formation (injury of endothelial cells).

- Subacute/chronic symptoms (fatigue/myalgia).

- Spread via infected saliva.

### ➤ BACTERIAL

- Spread by contact with respiratory secretions; either by aerosols or by direct contact with secretions of infective patients on fomites.

In the case of viral pharyngitis, the child/adult is infectious for a longer period of time (3-5 days) → as long as the virus is there, the cell is replicating and shedding occurs into secretions ... the patient is contagious to others

- More common in winter & spring.
- Usually observed in school age children (5-15y).
- Communicability is highest during acute infection.
- Patient is no longer contagious after 24 hours of antibiotics in the case of strep. pneumonia ... the child once diagnosed should not go to school for 24 hours.

-If hospitalized, droplet precautions needed until no longer contagious.



✧ **Look for white exudate covering pharynx & tonsils.**

- Tender anterior **cervical adenopathy**.
- Palatal/uvular **petechiae** (small reddish dots representing bleeding in mucous membranes).
- Scarlatiniform **rash** covering torso and upper arms.

✧ Macular rash is associated with scarlet fever (streptococcus A beta hemolytic group).

- Spread via respiratory particle droplets.

✧ **Absence of viral symptoms (rhinorrhea, cough, hoarseness).**

A general rule ☺

If you see URT symptoms such as cough, sneezing and rhinorrhea... you should think of a viral infection more than bacterial! بس مو شرط!

## Differential diagnosis of pharyngitis



pharyngeal exudates →  
seen in cases of: **S. pyogenes, C. diphtheriae, EBV, Adenovirus and Oral Candidiasis**

- C. diphtheria doesn't really form an exudate; it rather forms a grey-white fibrinous **pseudomembrane**. Our immune system tries to attack the bacteria, which results in necrosis of pharyngeal cells forming a pseudomembrane that includes the debris & inflammatory cells.



- Oral Candidiasis -in immunocompromised patients- can be present with a whitish coat or an oral thrush covering the tongue, the throat & the pharynx.

✧ Coxsackie A virus is usually present with Gingivostomatitis.

✧ Hepatosplenomegally, rash, fatigue & Cervical lymphadenitis are observed with **EBV**



skin rash → you should think of:

**S. pyogenes (scarlet fever) , HIV or EBV**



conjunctivitis accompanied with pharyngitis → most probably caused by **Adenovirus.**

- As we said yesterday, if you suspect bacterial pharyngitis, **start antibiotics treatment immediately.** Otherwise you will end up with bad consequences -especially in children- represented by suppurative & nonsuppurative complications.

➤ **The nonsuppurative complications:**

- 1- Acute rheumatic fever; follows only streptococcal pharyngitis (not group A strep skin infections).



↪ In the case of acute rheumatic fever, what occurs is **hypersensitivity type 2** in which there is similarity in structure between certain streptococcal antigens and heart proteins (molecular symmetry). Antibodies are generated against bacterial antigens, but due to this similarity they are going to attack the cardiac valves most probably.

2- Acute glomerulonephritis; May follow pharyngitis or skin infections (pyoderma) and is associated with nephritogenic strains.

↪ This is considered as **hypersensitivity type 3**; bacterial antigens bind to their specific antibodies generated by our immune system forming immune complexes. These complexes will deposit in the kidney activating the complement system; complement system will attack the immune complexes causing kidney damage.

If you treat the patient with antibiotics within 8-9 days of bacterial infection you can prevent rheumatic fever, but antibiotic treatment is not protective against glomerulonephritis.



**infectious mononucleosis caused by EBV. Notice the white exudate on pharynx & tonsils.**



**Herpangina caused by  
Coxsackie A virus & is  
associated with vesicular  
lesions which ulcerate  
(lesions are present with  
dysphagia and severe pain).**



**Petechiae (small red dots) →  
more common in bacterial  
infections.**

When there is rash, the differential diagnosis would be streptococcal, EBV, or HIV infections.

### Clinical manifestations

**Bacterial pharyngitis** is characterized by: rapid onset (starts with high fever and sore throat directly; not rhinorrhea, sneezing and cough like in viral), headache, GI symptoms, sore throat, erythema, exudates, palatine petechiae, enlarged tonsils, anterior cervical adenopathy and tender red & swollen uvula.

**Viral pharyngitis** is characterized by: Gradual onset, rhinorrhea, cough, diarrhea and fever (mild fever or absent).

→ As we said previously, viral pharyngitis is self-limited within 5-7 days and usually not associated with complications. So, it is not that important to differentiate between viral agents as long as you're





going on the same path for diagnosis (based on clinical picture) and treatment (symptomatic).

→ You only need to differentiate between viral and bacterial pharyngitis & start antibiotics immediately if diagnosed as bacterial.

## Diagnosis

For strep.: **throat culture** is the gold standard and we have **rapid strep. antigen kits** as well.

For Mycoplasma: we have **cold agglutination test**.

For Infectious Mononucleosis: we have **CBC** (atypical lymphocytes) and **spot test** (positive slide agglutination).

For viral pharyngitis, you don't need to send samples to specialized virology labs. **You diagnose based on clinical manifestations.**

## Treatment

- ✓ In strep. pneumonia **Penicillin** is the drug of choice. We can also use Azithromycin & Erythromycin (macrolites).

Remember... you have to treat to prevent acute rheumatic fever, but acute glomerulonephritis can't be prevented with treatment. In addition, treatment helps reduce symptoms & prevent local suppurative complications.

- ✓ In viral pharyngitis, we only give **supportive care**: analgesics, antipyretics or fluids.



→ In the case of infectious mononucleosis or infection associated with EBV, we said that it causes hepatosplenomegaly. As a result of sports, splenic ruptures may occur... patient must avoid sports 😊

## Specific viruses involved in causing pharyngitis

### Parainfluenza virus (HPIVs)

Negative-sense, ssRNA / enveloped / 4 serotypes: 1, 2, 3, 4 / Paramyxoviridae family

- viral proteins → **F-protein** for fusion to target cells & **HN-tetramer** (hemagglutinin-neuraminidase glycoprotein "spikes") on their surface for attachment and entry.

✧ Pathogenesis → HPIVs infections in the RS lead to secretions of high levels of inflammatory cytokines such as interferons and interleukins. The peak duration of secretion is 7-10 days after initial exposure. Increasing levels of certain chemokines such as RANTES (regulated upon activation, normal Tcell expressed and secreted), macrophage inflammatory protein (MIP)-K are detected in the nasal secretion of paediatric patients.

✧ It has 4 serotypes:

Type 1 is associated with acute croup and pharyngitis.

Type 2 is associated with acute laryngotracheobronchitis.

Type 3 is associated with Lower Respiratory infections in children.

Type 4 is associated with Upper Respiratory infections >>> least common / **types 1&3 are the most common.**



✧ Clinical manifestations:

→ **Croup** = laryngotracheobronchitis (involves larynx, trachea & bronchus) ... the most common manifestation of HPIVs infection.

Seen mostly in children (< 7years).

Present with harsh barking cough and gasping for air.

✓ Common in fall & winter months.

✓ **Symptomatic treatment**, there is no specific antiviral drug for HPIVs.

✓ In severe cases, you may need to give oxygen & you should start steroid therapy for a short period of time (7-10 days) in order to decrease the level of infection in larynx and trachea and you need to do tapering of steroid (تخفيف الجرعة تدريجياً).

→ Other conditions that may be caused by HPIVs: bronchiolitis, pneumonia or LRT infections.

✧ NO VACCINE available.

### Respiratory Syncytial Virus (RSV)

ssRNA / enveloped / belong to the genus Pneumovirus of the Paramyxovirus family.

▪ From its name “syncytial” → due to syncytial formation as a cytopathic effect on affected cells.

Microscopically, syncytia or multinucleated giant cells present as giant cells with multi-nuclei.

✓ Considerable strain variation exists, may be classified into subgroups A and B . Both subgroups circulate in the community at any one time.



- ✓ **A strain is predominant.** The two strains circulate at the same time.
- ✓ Causes a sizable epidemic each year.
- ✓ Present worldwide, yearly epidemics especially during winter months & persist till April or May.
- ✓ Strain variation does not significantly affect the clinical severity.
  - ✓ Peak incidence 2-5 months (mostly infects children or infants).
  - ✓ Causes **LRT** infections (bronchiolitis & bronchopneumonia). It may start as URT infection, but 50-60% eventually end up with LRT infections.
  - ✓ May cause croup > not common.
  - ✓ More severe in : Boys & socioeconomic classes.

✧ Reinfection throughout life is common, but with each infection symptoms are less severe due to presence of antibodies.

They found that antibodies aren't protective against further infection, but the symptoms become milder.

**In older children and adults, the symptoms are milder.**

- ✓ Long incubation period :2-8 days.

Transmission: Ocular, nasal contact with infected secretions.

- ✧ Mechanism: this is an enveloped virus, it enters the cell leaving the envelope with its spikes (glycoproteins) to become part of cell membrane. The nearby cells have receptors, so interaction occurs between these receptors & glycoproteins > fusion of the two membranes happens > cell with two nuclei. If multiple nearby cells are infected



with the virus, they're all going to fuse together giving a multinucleated giant cell.

- ✧ Immunity against RSV is not well understood, but they found that: higher levels of maternal Abs are associated with lower infection rates & prophylactic Abs reduce but do not eliminate severe disease. No level of serum Abs provides protection.
- Seroconversion is the state of presence of Ab against a certain antigen or certain virus.
  - If there is seroconversion of RSV, this means that this person has been previously exposed to this virus, so he has Ab against it.
- ✧ It's most harmful when seen in patients with: pre-existing lung disease, pre-existing heart disease or immuno-compromised patients >> mortality rate is higher & may reach up to 15%.
- ✧ Usual mortality for an immune-competent person is around 1%.

Diagnosis: season (winter), typical history (cough, wheezing and respiratory distress), physical examination & hyperexpansion of the lungs clinically. Hyper-inflated lungs on chest x-ray & increased interstitial markings.

**In severe cases, you may need to take sample from a nasal wash or bronchoalveolar lavage & send it to a virology lab for culturing and isolation.**

- ✓ RSV grows in multiple cell lines.
- ✓ Typical pattern: syncytial & giant cell formation. Syncytial pattern is indicative for RSV but not necessarily, there are other viruses with the same pattern.



### Treatment & Prevention

Adequate oxygenation, ventilatory support and close observation for bacterial superinfection. **Antiviral drug is available: Ribavirin (aerosol).**

✧ NO VACCINE available.

RSV immunoglobulin (against F protein) can be used to protect infants at risk of severe RSV disease, but they are expensive.

### Adenovirus

DNA virus / naked / icosahedral / has antenna like projections that comes from penton structures on the helix / replication occurs in the nucleus / >100 serotypes, around 50-55% cause infection in humans.

✧ Where did the name 'Adenovirus' come from?  
It is due to isolation of the virus from children adenoids (structures lay next to tonsils).

✧ The virus was isolated from asymptomatic individuals, so Adenovirus can cause acute infection and then they remain in the body >>replicate very slowly & still shed the virus while the patient is asymptomatic. Is it considered as latency (like that found in EBV or HSV)?  
NO, because in latency the virus is dormant.

- Adenovirus has tropism for cells of epithelial origin. >>> reaches many sites of the body.
- Proteins: Important antigens (hexon, pentonbase, fiber) are associated with the major outer capsid proteins.
- Virion has unique "spike" or fiber associated with each penton base of the capsid.



- Replicative cycle is sharply divided into EARLY & LATE events. Once the virus enters the late stage, early stage of protein synthesis stops.
- Clinical syndromes caused by Adenovirus:  
**Pharyngitis, Pharyngoconjunctivitis, acute respiratory disease of recruits, pneumonia, conjunctivitis, haemorrhagic cystitis, gastroenteritis & meningitis.**
- Serotypes associated with pharyngitis → 1,2,3,5 & 7  
serotypes associated with conjunctivitis → 3 & 7
- It mainly infects children & they found that early military recruits are more prone to infections of adenovirus and usually associated with LRT infections rather than URT infections.
  - ✧ association with conjunctivitis is usually preceded by contact with the virus -in swimming pools for example-
- **NO VACCINE** available for the public, but they designed a vaccine for early military recruits.
- Good hygiene can break the replication cycle of Adenovirus. This is seen in many viruses especially respiratory viruses, so make sure to wash your hands in between patients in the hospital.

THANK YOU :)

Dedicated to my loved ones: Sura Mubarak, Munya Salti, Heba Hajjaj, Dana Khlaifat and Elaf Bataineh <3