RESPIRATORY SYSTEM
MICROBIOLOGY

Title: Sheets 7+8 – viral respiratory infections

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This sheet's topics going from the nose down:

Rhinosinusitis (common cold), Pharyngitis, Laryngitis/Croup, Bronchiolitis, and Pneumonia.

و نتفق من اولها انه اي اشي اسمه كورونا فايروس قصدنا فيه الكورونا القديم اللي ما حدا كان مهتم فيه مش كوفيد-19, until stated otherwise.

Common cold/ Coryza/ Acute rhinosinusitis:

It's an acute, self-limited infection of the nasal mucosa and adjacent tissues, usually the sinuses. (others include: middle ear, pharynx).

Signs and symptoms:

- are usually localized to the nasal mucosa.
- Sneezing, coughing, nasal discharge and congestion are common.
- Fever and other systemic symptoms are NOT common in adults. Fever may indicate infection with influenza virus more commonly or the involvement of the lower respiratory tract.
- Bouts of infections and severity (may include fever) are both higher in children.

Keep in mind:

a. We may have similar symptoms to common cold but with different causes, e.g. allergic rhinitis.
b. These symptoms can be the prodrome of a more serious infection, e.g. pneumonia.
c. The viruses involved in common cold can cause the other respiratory infections as well.

This table shows the characteristics of viral colds in adults and children.

Characteristic	Adults	Children <6 Years
Frequency	2–4 per year	One per month, September–April
Fever	Rare	Common during first 3 days
Nasal manifestations	Congestion	Colored nasal discharge
Duration of illness	5–7 days	14 days

Some notes:

1. The frequency of infection is higher in children , because they don't have immunity to many viral agents yet.
2. The duration of illness refers to the major symptoms (cough may persist for weeks).

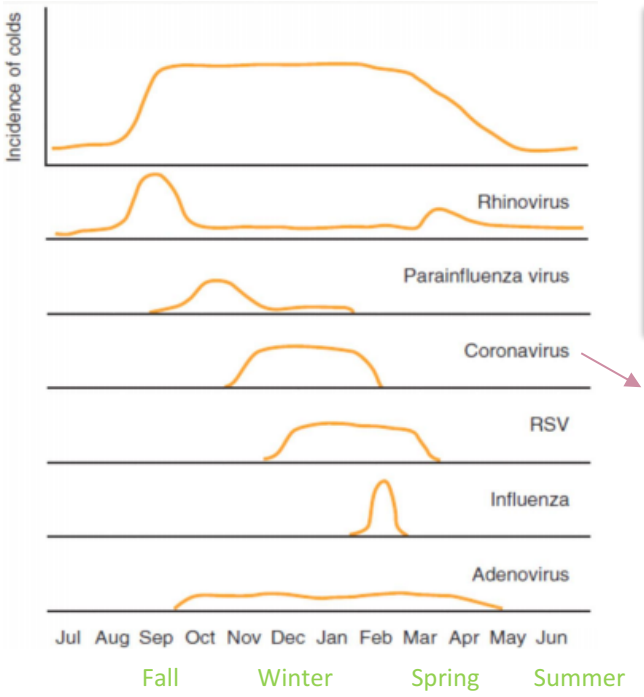
Etiology:

Virus	Percentage of cases (%)
Rhinovirus	30–50
Coronavirus	10–15
Influenza virus	5–15
Respiratory syncytial virus	5
Parainfluenza virus	5
Adenovirus	<5
Metapneumovirus	±2
Undiscovered virus	20–30

Some more notes:

- The most common cause of (common cold) is **always Rhinoviruses** accounting for 30-50% of cases.
- Adenovirus is the most common cause of pharyngitis and pneumonia (and other non-respiratory infections).
- This order (excluding Rhinovirus) can differ depending on many many variants.
- As we said before, these agents can cause respiratory infections other than common cold, but with a predilection of each virus to a certain illness.
  for example, rhino and corona are commonly associated with common cold but that doesn't mean they can't cause pneumonia. Adeno is associated with pharyngitis more commonly than common cold, and the list goes on and on.

Epidemiology of common cold and the others as well



The epidemiology is variable according to the time of year and the geographic area, So if we're talking about temperate regions, common cold happens all year round, but with different causes according to the season. Now take a look at the graph and pay attention to the seasonality of each virus.

This doesn't include covid-19 for many reasons so please don't go out saying hot weather kills the virus.

	Mode of transmission	Incubation period
Rhinovirus	Airborne Large particle aerosol	2-7 days
Coronavirus	Possibly airborne	2-4 days
Influenza	Airborne Small-particle aerosol	1-4 days
Respiratory syncytial virus	Large-particle aerosol Direct contact with self-inoculation	4-5 days
Parainfluenza virus	Large-particle aerosol Direct contact with self-inoculation	3-10 days
Adenovirus	Airborne Direct contact with self-inoculation	4-14 days

Extra info for the sake of understanding microbiology and not just memorizing:

Droplet transmission is infection spread through exposure to virus-containing respiratory droplets (i.e., larger and smaller droplets and particles) exhaled by an infectious person.

Airborne transmission is infection spread through exposure to virus-containing respiratory droplets that can remain suspended in the air over long periods of time.

Aerosol transmission is infection through smaller particles that can travel longer distances than droplets.

Pathophysiology of common cold:

Host response to the virus plays a greater role than direct viral destruction of nasal mucosa, so the symptoms are the result of an immune response with an influx of polymorphonuclear leukocytes, cytokine release, and vascular leak.

Immunity to common cold viruses:

When you get infected with a certain type of virus, you only get immunity for the serotype you got infected with. That means there are other serotypes your immune system doesn't know.

Now based on this, we can sort common cold viruses into two categories:

Virus	No. of Serotypes
LONG-LASTING IMMUNITY NOT PRODUCED BY INFECTION[a]	
Respiratory syncytial virus (RSV)	1
Parainfluenza virus	4
Human coronavirus	2
IMMUNITY PRODUCED BY INFECTION[b]	
Rhinovirus	>100
Adenovirus	≥33
Influenza	3[c]
Echovirus	31
Coxsackievirus group A	3
Coxsackievirus group B	6

[a]Repeated infection with the same serotype is usual.
[b]Reinfection with the same serotype is uncommon.
[c]Type A subtypes change.

a. Viruses that don't confer long-lasting immunity (i.e. a few years) but have a low number of serotypes. Therefore, reinfection with the same serotype is common.
b. Viruses that do confer long-lasting immunity but have so many serotypes. That's why reinfection with the same serotype is uncommon.

Remember that influenza viruses undergo antigenic shifts and drifts, explaining the recurrent infections with this virus despite giving you a long-lasting immunity.

Diagnosis:

The clinical picture is never enough to distinguish between these viruses. The exception to that is when there's an ongoing epidemic. At first ,many tests are done even for patients presented with the same clinical profile until a certain virus is proved to be the

cause of all of them (e.g. H1N1), then we start declaring all similar cases to be caused by that agent by strong probability.

For a definitive diagnosis, we take a sample from the respiratory tract, usually it's a nasopharyngeal swap or a bronchoalveolar lavage (has a high sensitivity for COVID 19 for example), the sample is sent to a lab → then molecular testing for the virus is done.

Throat swaps can be done too, but they have decreased sensitivity towards the diagnosis, meaning they result in a lot of false negatives.

What can I test for?

Each manufacturer can create their own panel with the viruses their test can be used to detect. They can even detect some bacterial respiratory infectors along with the viruses.

In slides 14 and 15 you can find 2 different panels, one of them includes bacterial agents, here are some notes about the viruses in the panel of slide 14:

- Boca virus: a single stranded DNA virus, similar to parvo virus, associated with respiratory tract infections in humans.
- How did we contain SARS CoV and MERS CoV?
  - This is probably because there are no asymptomatic cases, and the high severity of the disease →leading to hospitalization→ fast detection of cases
- VZV can be complicated by pneumonia.
- Multiplex qPCR is the test used
  - Multiplex: because it contains multiple primers to specific respiratory viruses.

Adenovirus*
Coronavirus HKU1*
Coronavirus NL63*
Coronavirus 229E*
Coronavirus OC43*
Human metapneumovirus*
Rhinovirus*
Enterovirus*
Enterovirus D68*
Influenza A (Pan)*
Influenza A/H1-2009*
Influenza A/H3*
Influenza B (Pan)*
Parainfluenza 1*
Parainfluenza 2*
Parainfluenza 3*
Parainfluenza 4*
Respiratory Syncytial Virus A*
Respiratory Syncytial Virus B*
Bocavirus*
Epstein-Barr virus (EBV)*
SARS-CoV
MERS-CoV
Mumps
Measles
Cytomegalovirus*
Human herpesvirus 6 (HHV-6)*
Varicella zoster virus (VZV)*
Parechovirus

Management:

supportive treatment is the way to go, we only try to fix the symptoms by giving fluids, decongestants, analgesics for pain, antipyretics for fever, etc.

Pharyngitis: التهاب الحلق

- Same viruses that cause common cold can cause pharyngitis, but the most common cause of pharyngitis are **adenoviruses**.

Some viruses that cause pharyngitis cause what's known as Mononucleosis Like Syndrome, where fever and cervical lymphadenopathy accompany the pharyngitis.

- The most common causative agent of mononucleosis is Epstein-barr virus.

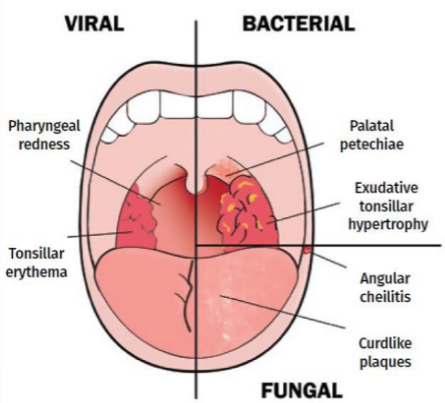
Etiology:

CMV, herpes simplex virus, HIV, Rhinoviruses, adenoviruses, coxackieviruses ,coronaviruses, respiratory syncytial virus, parainfluenza, EBV, orthomyxoviruses.

We must Consider mononucleosis like syndrome especially in teenagers that present with pharyngitis AND cervical lymph adenopathy.

How to distinguish viral from bacterial pharyngitis?

Distinguishing is important so that antibiotics are given when needed but not otherwise.



Gross evaluation:

- Viral→ pharyngeal and tonsillar erythema
- Bacterial → Erythema + Tonsillar Hypertrophy + exudates + petechiae sometimes
  - Most common cause of bacterial pharyngitis: streptococcus pyogenes .

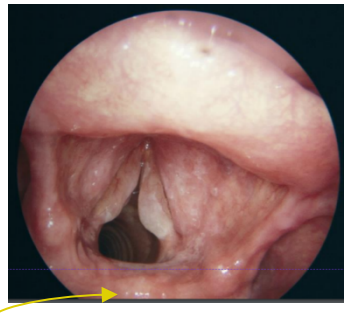
Tests:

- Bacterial culture of throat swabs.
- If the infection was there for a long time we might go to serology and test for the anti-streptolysin o titre.

If we're suspecting a case of mononucleosis caused by EBV, we have to check the serologic panel for the EBV .

Diseases	VCA IgM	VCA IgG	VCA IgA	EA (D) IgG	EA (R) IgG	EA IgA	EBNA1 IgG
Choronic active infection	+/-	++	+/-	+	++	-	+/-
Burkitt's lymphoma	-	++	-	+/-	++	-	+
Nasopharingeal carcinoma	-	++	+	++	+/-	+	+
Hodgkin's lymphoma	-	++	-	+	-	-	+
Reactivation	+/-	++	+/-	+	+/-	+/-	+/-

- First, we can use a Monospot test to detect heterophilic antibodies which indicate mononucleosis / it's a 'rapid test' but with very low specificity and sensitivity(false positive and false negative results).
- Or we can use serologic testing:
  - Viral capsid antigen antibody (VCA IgM)→ more used to detect **acute infection.**
  - VCA IgG → to confirm past infection .
  - Early antigenic (diffuse and restrictive portions) and EB nuclear antigen IgG.
  - When we do the VCA IgM, the monospot result could be either positive or negative.
    VCA IgG and EBNA increase after a while.



Laryngitis and croup

- Croup is basically laryngeo-tracheo-bronchitis
- It is called croup because the patient's breathing sounds like frogs' sound, it's caused by swelling in the vocal cords.
- Laryngitis is strongly associated with parainfluenza .

A smell of clinical practice:

Differential diagnosis of stridor:
Viral croup is the most common underlining etiology, so it should be first on your list.
Less commonly it's bacterial acute epiglottitis (caused by *Haemophilus influenza*) which causes obstruction of the larynx and tracheitis [these are more dangerous]
Other less common causes to check for are: Abscesses, foreign bodies, allergic reactions, etc.

Level of severity of croup by clinical features → It's divided to help in treatment and management into: Mild①, moderate②, severe③ and impending respiratory failure④ which means the state is so bad respiratory failure is nearly unavoidable. (slides 25,26)

Bronchiolitis

It affects infants most commonly and is one of the main causes of hospitalization in infants because their bronchioles are easily obstructed by respiratory secretions, accompanying infections just like **(Respiratory Syncytial Virus**) which might cause wheezing. These infants might need to be isolated in the hospital, so they don't spread it to others.

↳ for *treatment:* **ribavirin** might be used among other anti-virals.

Viral Pneumonia

Is an inflammation of the alveolar sacs, associated with viral infections.

Common Viral etiologies: Influenza, adenovirus

Chest x ray findings → diffuse infiltrates

For treatment of viral pneumonia a collection of antivirals can be used as follows: (slide 29)

- Influenza: **Oseltamivir, zanamivir**
- Varicella chicken pox complicated by pneumonitis: **acyclovir**
- CMV pneumonitis in immune compromised patients: **ganciclovir**
- Adenovirus: **Cidofovir**

COVID 19:

You all heard about it, virologists are people who talk about it the least.

Profile: It belongs to the corona-viridae, is enveloped and has a large genome.

Proteins it contains: as proteins are the antigens we use in vaccines and detection. For example: **RNA dependent RNA polymerase**. This is the most important and most conserved part of a virus to be molecularly detected.

COVID 19 is an RNA virus , the RNA has a high probability of mutations, these mutations create variants that might be fixed in the population if they give the virus an advantage, higher viral load and transmissibility for example.

Signs and symptoms:

- Headache, generalized weakness, fever.
- 20-30% of patients show no symptoms.
- Lower respiratory involvement, which might end with Respiratory distress and failure shows as shortness of breath, dyspnea with a decreased oxygen saturation, This is where it starts getting dangerous.

Of all Symptomatic cases:

- 80% are mild
- 15% are severe
- <5% are critical cases with multi organ failure