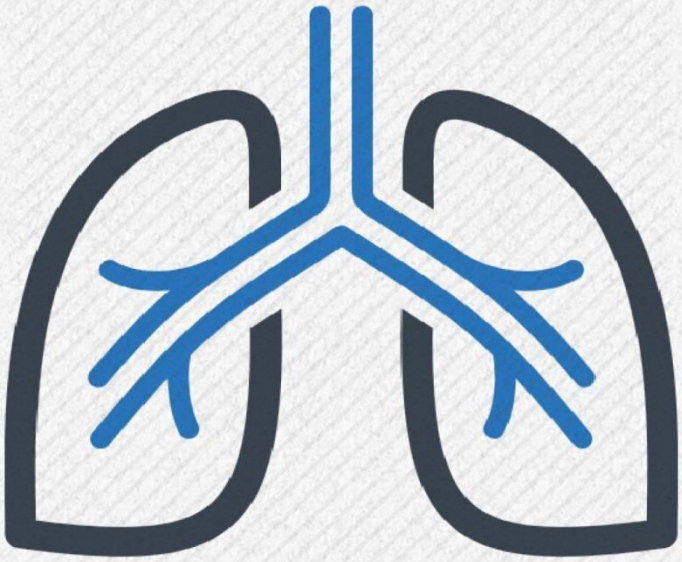

Respiratory system

Microbiology

sheet | handout | slides

Number	1
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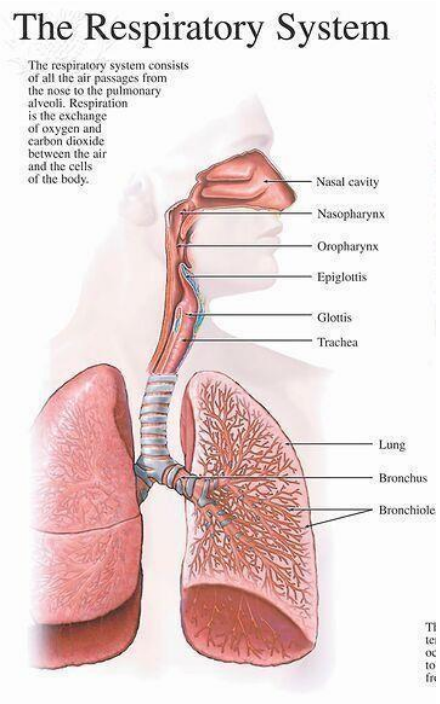
Today's lecture will be about **viral upper respiratory tract infections**. Those include: common cold, sinusitis, otitis, etc.

Infections in the **upper respiratory tract** (URT) are very common, resulting in large number of clinic visits and absences from work. The vast majority of infections are viral and self-limited. However, some might require hospitalization especially in children and neonates. Whereas **lower respiratory tract** (LRT) infections (the topic of next lecture) are an important cause of morbidity and mortality. LRT infections include pneumonia.



The infection-borne structures of the respiratory tract:

Any part of the respiratory tract is susceptible to viral infections, starting at the nose (rhinitis), nasal sinuses (sinusitis), pharynx (pharyngitis), larynx (laryngitis) and ending with the lung parenchyma.

Viral Infections of the Upper Respiratory Tract

Viruses are considered the most common cause of URT infections. Other causes include bacteria and fungi.

Infection of the nasal cavity is termed **rhinitis**, **coryza** or **common cold**. It is sometimes accompanied by sinus involvement. ENT specialists call it ***rhinosinusitis*** rather than rhinitis because the paranasal sinuses are usually involved.

Viral URT infections are usually mild, self-limited but the problem here is that they predispose affected individuals to secondary bacterial infections. This is because viruses can cause:

- **Disruption of the epithelial barrier**
- **Upregulation of adhesion molecules** as a result of inflammation
- Production of viral factors that **expose the bacterial receptors** on the surface of URT cells. Influenza virus for example has neuraminidase on its surface that exposes receptors for bacteria
- **dysfunction of the immune system components.**

❖ Viral Rhinitis (common cold)

- Common cold is the conventional term of mild URT illness. The **hallmark symptoms** are nasal stuffiness, nasal discharge (rhinorrhea), sneezing, sore throat, and cough.

- Although the term tends to imply that there is a simple cause for the illness, common cold is actually a **heterogenous group of diseases** that have the same symptoms but are caused by numerous viruses.

- It is **usually a self-limited illness** confined to the URT. However, the viral infection in some patients can spread to adjacent organs. For example, nasal infection might be accompanied with the involvement of sinuses, pharynx, or even the lower respiratory tract. This will result in different clinial manifestations.

- Occasionally, common cold predisposes the individual to a **secondary bacterial infection**. We already mentioned the factors that contribute to this predisposition (important!).

- Despite the usually benign nature of the illnes, common cold is an enormous economic burden. This is because people stay at home and thus work hours are reduced.

- **Etiology:**

Viral cause of the common cold

Virus	Estimated annual proportion of cases
Rhinoviruses	30–50%
Coronaviruses	10–15%
Influenza viruses	5–15%
Respiratory syncytial virus	5%
Parainfluenza viruses	5%
Adenoviruses	<5%
Enteroviruses	<5%
Metapneumovirus	Unknown
Unknown	20–30%

This table shows the relative proportions of different viruses that cause common cold. The relative proportions vary depending on several factors such as age, sampling and detection method, the season.

- Different age groups have different proportions of the underlying viral cause of common cold.
- Seasonality: some viruses spread more during summer and others during winter. For example, enteroviruses spread more in summer and are considered among the most common causes aseptic meningitis.

Regardless of these factors (age, detection method, season, etc...), the most common cause of common cold is ***rhinoviruses*** (~50% of cases). It most commonly affects the nasal mucosa (from its name).

Rhinoviruses are followed by ***coronaviruses*** or ***influenza viruses***. Other causes include: respiratory syncytial virus, parainfluenza viruses, adenoviruses, and metapneumovirus. Metapneumovirus (a paramyxovirus) was discovered in the 2000's.

The rest 20-30% of cases are of unknown cause. Most probably, these are due to undescribed infectious agents that cause rhinitis. Metapneumovirus for example was described before less than 20 years although people in the 60's thought they described all viral etiologies of rhinitis . So in the next years, there may be characterization of other infectious agents involved in URT infections.

These viruses are not limited to certain areas in the respiratory tract. For example, people previously thought that rhinoviruses only replicate in areas where the temperature is lower than the core temperature of the body (like the nose). But it was recently found that it can replicate in 37^{o}C like the lower respiratory tract. So, rhinoviruses can cause LRTI like bronchiolitis in infants.

Differences between flu and common cold:

Flu is also an URT infection. In flu, there is fever and the symptoms are more severe and persist for longer time. It also has systemic involvement (fever, myalgia…) due to cytokines released from the strong inflammatory response.

In common cold, the infection is most commonly superficial with no systemic involvement.

The table in the next page is a summary of common cold and their viral causes. Everything in the table is included.

Virus	Types involved	Attachment mechanism	Disease
Rhinoviruses (>100 types)	Several at any given time in the community	Capsid protein binds to ICAM-1 type molecule on cell	Common cold
Coxsackie virus A (24 types)	Especially A21	Capsid protein binds to ICAM-1 type molecule on cell	Common cold; also oropharyngeal vesicles (herpangina) and hand, foot and mouth disease (A16)
Influenza virus	Several	Hemagglutinin binds to neuraminic acid-containing glycoprotein on cell tract	May also invade lower respiratory tract
Parainfluenza virus (4 types)	1,2,3,4	Viral envelope protein binds to glycoside on cell	May also invade larynx
Respiratory syncytial virus	2 types	G protein on virus attaches to receptor on cell	May also invade lower respiratory tract
Coronaviruses (several types)	All	Viral envelope protein binds to glycoprotein receptors on cell	Common cold; severe acute respiratory syndrome
Adenovirus (41 types)	5–10 types	Penton fibre binds to cell receptor	Mainly pharyngitis; also conjunctivitis, bronchitis
Echovirus (34 types)	4,9,11,20,25		Common cold

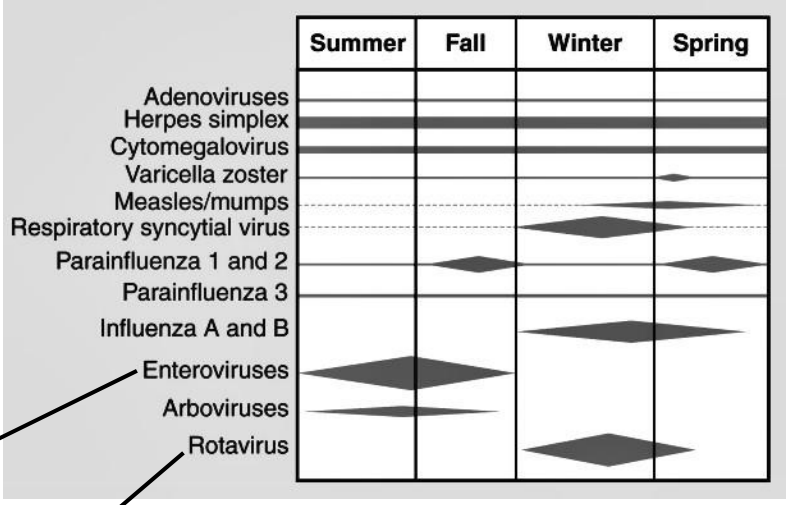
Student's question: Why do I care about knowing all this about common cold despite the fact that it has no treatment?

Common cold has no treatment, we only give symptomatic treatment. However, we must be able to diagnose it and differentiate between common cold and other diseases because a patient might have similar symptoms but a different underlying cause and his disease is serious. It is important to be safe doctors. For example, allergic rhinitis has similar symptoms to common cold. Since we can decrease the suffering of a patient with allergic rhinitis, we must know how to differentiate between them.

Seasonality: Many common viruses exhibit seasonal variations like influenza, respiratory syncytial virus and parainfluenza 1 and 2 which circulate every winter.

*Why are respiratory viruses more common in winter?

- No one knows the definitive cause. But the speculation is that in winter people stay inside their homes and don't go out that much; in conditions that are more crowded, so infection is more.

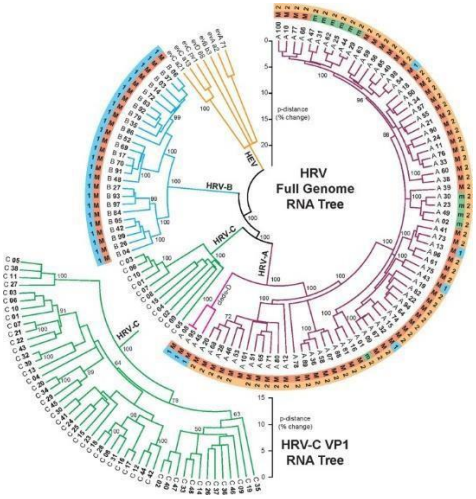


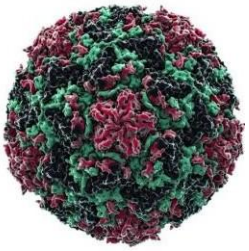
Aseptic meningitis caused by enteroviruses is more common during summer and the beginning of fall.

Rotavirus (a GI virus) is more common in winter.

Viral Rhinitis –Etiology

1. **Rhinovirus:**
   - Rhinoviruses are divided to more than one species (A, B, and C). Every species has different serotypes. The sum of all types of rhinoviruses is more than 150 (until now).
   - The figure on the right is a phylogenetic tree. It is constructed by comparing the whole genome (or segments of amino acid sequences of proteins) for different virus types. Those which are similar to each other are clustered together and those which are different are away from each other in the tree. This tree is important is classification of viruses because the virus' genotype might affect its pathogenicity (virulence). A certain strain (with similar genetic makeup) might be more virulent than others so it would be worth if we develop a vaccine against it or treat infections with this particular strain.





   - Rhinoviruses are **naked** (1). They are part of the ***picornaviridae*** family. It is a +ve sense single-stranded RNA virus (2).
   - Species A and B of rhinoviruses use **ICAM-1** (an adhesion molecule) as its receptor. They can utilize other receptors such as LDL receptor. The receptor for species C was discovered recently (not important to know).
   - In general, the symptoms might be the result of direct pathogenicity of the virus or the associated immune response or both. In rhinovirus infections, the related lack of pathology and small number of infected cells suggests that the immune response is responsible for the symptoms more than the direct pathogenicity.

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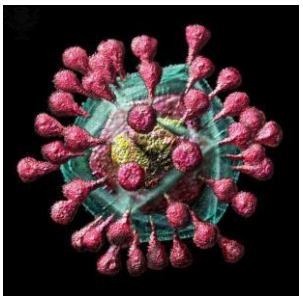
(1) Remember: Enveloped viruses are easier to be removed by disinfectants.
(2) +ve sense RNA can act as a mRNA and when we transfer the genome alone (without the capsid) it can be directly translated to proteins.

- **Transmission**: by aerosols or direct contact with infected fomites.
- Environmental factors and predisposing conditions that contribute in the severity of the infection (more severe infection):
    - Immunodeficiency
    - Cigarette smoking: it can affect the innate immune system leading to more severe symptoms. It also predisposes to secondary bacterial infections.
    - Pollution
    - Anything that affects the innate defences in the respiratory tract.



2. Coronavirus:

- The second most common cause of URT infection.
- It is an **enveloped** +ve sense single-stranded RNA virus. Its nucleocapsid is of helical symmetry.
- It got its name from its spikes described around the viral particle.

All RNA viruses are single stranded except for viridae families of viruses; they're double stranded. Known example is the **rotavirus** from the reoviridae family.

- Coronaviruses have different types. Some cause URT infections and others cause SARS (Severe Acute Respiratory Syndrome), each has its own receptors. The most important strains we need to know are **229E** and **OC43**, these use aminopeptidase N as host receptor. While SARS coronavirus use **ACE-2** as a receptor (SARS will be discussed in more detail later on).
- Most coronaviruses spread to susceptible hosts by the respiratory route with the replication first occurring in the epithelial cells.
- Outbreaks occur primary in winter.

For your info.
Why do you think that every 2-3 years we hear about an emerging infection?
This could be attributed to human, viral and environmental factors.

The End