Viral Respiratory Tract Infections 1

TEAM 439
MICROBIOLOGY

VERSION 1

Objectives

- Introduction to respiratory viral infections
- Characteristics of respiratory viruses (Orthomyxoviridae, Paramyxoviridae)
- Mode of transmission
- Clinical features
- Lab diagnosis
- Treatment & prevention

Colour index:

Red: Important & Doctor's notes.

Grey: Extra info & explanation.

Green: Lecture Notes.

Any future corrections will be in the editing file, so please check it frequently.

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Respiratory Tract Infections

- The most common human infections and cause large amounts of morbidity and loss of time at work (sick leave).
- Are common in both children and adults.
- Mostly caused by viruses.
- Mostly are mild and confined to the upper respiratory tract (URT).
- Mostly are self-limiting disease
  (**only** influenza virus and RSV can be treated)
- URT-infection may spread to other organs causing more severe infection and death.

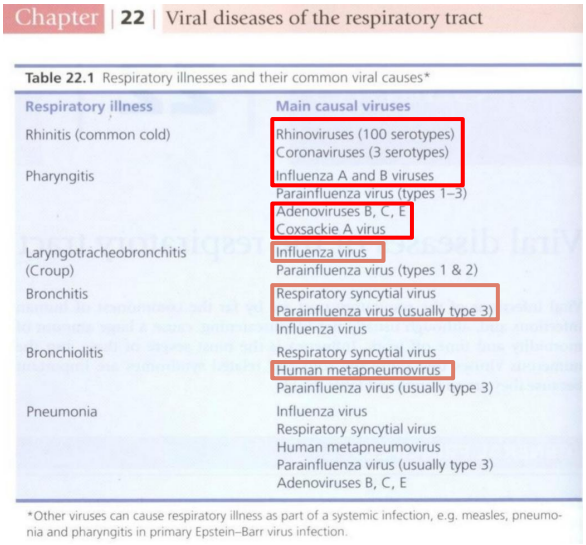
Clinical Manifestations

Common in Upper respiratory tract

- Common cold (rhinitis).
- Pharyngitis.
- Sinusitis & otitis media.
- Tonsillitis

Common in Lower respiratory tract

- Croup (acute laryngotracheobronchitis)
- Viral pneumonia.
- Acute bronchitis.
- Acute bronchiolitis.



Chapter | 22 | Viral diseases of the respiratory tract

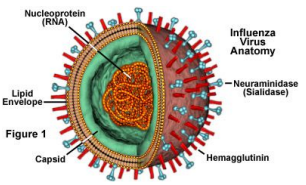
Table 22.1 Respiratory illnesses and their common viral causes*

Respiratory illness	Main causal viruses
Rhinitis (common cold)	Rhinoviruses (100 serotypes) Coronaviruses (3 serotypes)
Pharyngitis	Influenza A and B viruses Parainfluenza virus (types 1–3) Adenoviruses B, C, E Coxsackie A virus
Laryngotracheobronchitis (Croup)	Influenza virus Parainfluenza virus (types 1 & 2)
Bronchitis	Respiratory syncytial virus Parainfluenza virus (usually type 3) Influenza virus
Bronchiolitis	Respiratory syncytial virus Human metapneumovirus Parainfluenza virus (usually type 3)
Pneumonia	Influenza virus Respiratory syncytial virus Human metapneumovirus Parainfluenza virus (usually type 3) Adenoviruses B, C, E

*Other viruses can cause respiratory illness as part of a systemic infection, e.g. measles, pneumonia and pharyngitis in primary Epstein–Barr virus infection.

* The most important URT infections
* The most important LRT infections

Influenza Virus



Family	Orthomyxovirus. A family of RNA viruses.
Structural features *Explained more in the next page.	❖ Enveloped virus. ❖ Has 2 projecting glycoprotein spikes (found on the surface of influenza viruses) Which are: 1- Haemagglutinin (H) serves as an **attachment** factor and membrane fusion protein. 2- Neuraminidase (N) helps in **releasing** viral particles from the plasma membrane of infected cells
Genome	❖ 8 Segmented (Seperated) Negative polarity single stranded RNA. (It is the only 8 segmented virus) Note that all viruses in this lecture are RNA viruses :) ❖ This virus is highly susceptible to mutations and rearrangements (because RNA viruses don't have a proofreading mechanism) within the infected host. That's why we take a different vaccine against it each year.
Pathogenesis	❖ The virus infects the epithelial cells of the nose, throat, bronchi. ❖ Occasionally it infects the lungs. (if the host is immunocompromised)
Transmission	**Inhalation** of infectious aerosol droplets, or close contact with an infected individual.
I.P	Incubation period is 1-4 days (incubation period: time when a person is infected and when symptoms begin to appear)
Symptoms	**Fever**, malaise, headache, cough, chills, sore throat, and generalized pain.
Prognosis	Usually self-limiting disease. (Patient will recover without medical intervention).
Complications	❖ Primary influenza pneumonia The virus is deposits & attaches to ciliated epithelial cells. Local host defenses such as mucociliary clearance can remove viral particles. However, if its impaired as in smokers / older patients, infection continues unabated, leading to primary pneumonia. ❖ Secondary bacterial pneumonia 2-3 days after viral pneumonia, patient might develop bacterial pneumonia too . ❖ Reye's syndrome [fatty degeneration of CNS & Liver (Aspirin)] Acute brain disease & fatty degenerative liver failure, typically occurs after viral infection and is associated with the use of **aspirin** during the illness (this is why it is better to give children Paracetamol for fever not aspirin).
Lab diagnosis	**1- Routine testing:** by direct detection of influenza A or B virus from sputum, **Nasopharyngeal swab / aspirate** (NPA) or Respiratory secretion, and then doing a direct immunofluorescence assay (IFA) IFA: a test that utilizes fluorescent dyes to identify the presence of antibodies bound to specific antigens. **2- Other detection methods:** Cell culture, PCR. Usually done after the routine testing to further differentiate & specify the virus among influenza A for example.
Treatment	★ Amantadine & Rimantadine is effective against influenza A virus only.(rarely used nowadays, because many viruses are resistant to it) ★ Oseltamivir (Tamiflu), Zanamivir (Relenza) are effective against both influenza A & B viruses & can be used as treatment/ prophylaxis.
Prevention **(Influenza Vaccine)**	**The flu shot vaccine:** Inactivated (killed vaccine). Given to people older than 6-months, including healthy people & those with chronic medical conditions **The nasal spray flu vaccine (Flu mist):** Live attenuated vaccine Approved for use in healthy (**immunocompetent**) people between 5-49 years of age. Dr: this vaccine is commonly used in USA, it is manufactured using egg-based technology بزرع في البيض. And because of this, there is a risk for people with allergies. Both vaccines are trivalent i.e contain two strains of the current circulating influenza A virus (H1N1 & H3N2) and the current circulating strain of influenza B virus. **(Vaccine should be given before the influenza season begins)**

Influenza Viral Proteins

Haemagglutinin (H)	Neuraminidase (N)
Responsible for attachment to the cell surface receptors. (Antibodies to the HA is responsible for immunity)	Responsible for release of the progeny viral particles from the infected cell.
There are 16 haemagglutinin antigenic types, H1–H16	There are 9 neuraminidase antigenic type, N1 – N9.
Human associated H antigenic types are H1, H2 & H3	Human associated N antigenic types are N1, N2.

Influenza Virus Divided into subtypes based on the haemagglutinin and neuraminidase proteins. The currently circulating strains are: H1N1 & H3N2.

Types of Influenza Virus

A

- ➔ Infects **human and animal**
- ➔ Causes epidemic & pandemic ممكن يعدي قارة كاملة
- ➔ Causes epizootic in animal
- ➔ **Antigenic drift = minor change = (Point Mutation)**
- ➔ **Antigenic shift = major change = (Reassortment)**

(Difference between drift & shift is explained with the picture)

B

- ➔ Infects **human only,** so it can be easily controlled.
- ➔ Causes outbreak
- ➔ **Antigenic drift only**

C

- ➔ Infects human only
- ➔ Causes mild illness

Girls Dr: Type c is NOT IMPORTANT

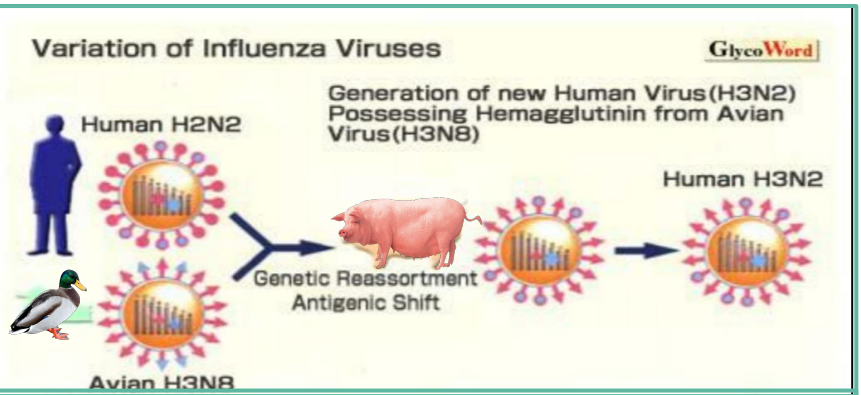
Antigenic shift: mixing of genes from Influenza viruses from different species.

شرح الدكتورة لتبسيط الفكرة:
بالصورة الـ hemagglutinin والـ neuraminidase عند الانسان زي ما تشوفون شكله دائري، وعند الطيور شكله مثلث ،

هذا يعني أن حتى لو عندي طيور مصابة بانفلونزا ماراح تجيني عدوى لأن ماعندي رسبتر للمثلثات والعكس بالنسبة للطيور ماراح اعديها لأن ماعندها رسبتر للدوائر.

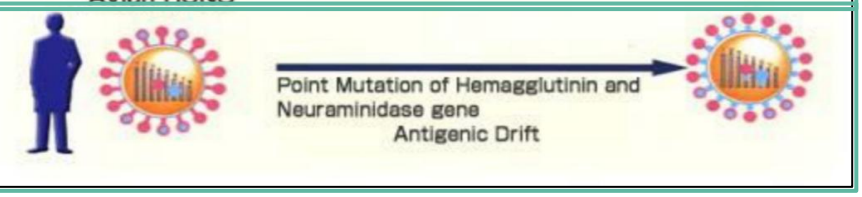
اللي صار بعدين أن فيه خنزير اصابته العدوى من الإنسان والطيور برضو لأنه مخلوق عنده كل أنواع الرسبترز، فصار عنده دوائر ومثلثات، وحصل جوا جسمه reassortment للجينات والنتيجة طلع لنا فايروس جديد فيه دوائر ومثلثات، وبيقدر يعدي الانسان والحيوان كلهم، يعني نتج لي Influenza type A

SHIFT / REASSORTMENT ONLY HAPPENS WITH **TYPE A**



Antigenic drift: the accumulation of a series of minor (small) genetic mutation.
غالبا يكون فيروس واحد صار له طفرة اكثر من مره ومع الزمن وكثرة الطفرات صار كأنه فيروس جديد مثلا تغير مكان أو ترتيب الرسبترز مو أكثر من كذا

DRIFT / MUTATIONS HAPPEN WITH BOTH **TYPE A & B**



Avian flu

إنفلونزا الطيور

Family	Typical orthomyxovirus.
Viral etiology	Avian **influenza type A** virus (**H5N1**).
Epidemiology	❖ Wild birds are the natural reservoir for the virus. ❖ They shed the virus in saliva, nasal secretion and feces. ❖ Avian influenza viruses **do not usually infect human easily.** ❖ All domestic poultry are susceptible to infection (They become infected, when they eat food contaminated with secretion or excretion from infected bird).
Risk group	- Those who working in poultry farms. مزارع الدواجن - Those who are in close contact with poultry. It was found that there are some receptors in the alveoli of the lung that might accept the virus from animals, so people who are always near poultry are in risk of infection & developing pneumonia.

The presence of a certain type of viral receptor throughout the mucosa of the bird respiratory tract

H5N1 strain infect birds more effectively than human due to:

In contrast ,human have this receptor only in **alveoli**, not in the upper respiratory tract.

- This explains why human are rarely infected with H5N1 but if human become infected will **have severe lower respiratory tract infection** and **pneumonia**.

Symptoms

-Ranges from typical flu to severe acute respiratory disease.
-Diarrhea, abdominal pain and bleeding from the nose have been reported.

Treatment

Should be initiated within 48 hours.
Oseltamivir and Zanamivir are used.

Lab diagnosis

PCR, detection of the viral RNA in throat swap.

Parainfluenza Virus

Family	Paramyxoviridae
Structural features	❖ Enveloped virus ❖ Negative polarity, single stranded RNA genome ❖ Has 5 serotypes.
Transmission	Inhalation of infectious aerosol droplets mainly in winter.

★ **Clinical Syndromes**

عند البالغين تأثيره بسيط جدًا common cold بس ، لكن المشكلة أكبر لما يصيب أطفال ورضّع

★ Infants & Young Children	Young Children	Adults
Croup or Acute laryngotracheobronchitis PIV Type-I, II. Inflammation of vocal cords. Fever, harsh (barking) cough, difficult inspiration (Can lead to airway obstruction which may require hospitalization and tracheostomy).	**Bronchiolitis and Pneumonia** PIV Type-III	**Common cold** No fever

1

Lab diagnosis:

Routine testing by Direct detection of the virus from sputum, **Nasopharyngeal swab, aspirate (NPA)** or respiratory secretion by **direct immunofluorescence assay (IFA).** (Just as in influenza)

Dr: If croup / acute laryngotracheobronchitis are is suspected, YOU NEVER TAKE A THROAT SWAB!!! Go for NPA

2

Other detection methods:

tissue culture, PCR.

3

Treatment and prevention:

Supportive treatment (reassurance), **No specific treatment or vaccine available**.

Respiratory Syncytial Virus (RSV) & Human metapneumovirus

Syncytial means fused cells

Family	Paramyxoviridae
Structural features	❖ Enveloped virus ❖ Negative polarity, single stranded RNA genome.
Transmission	Inhalation of infectious aerosol droplets mainly in winter.

★ **Clinical Syndromes**

نفس الكلام اللي قبل، عند البالغين الـ RSV مايسوي شي غير common cold لكنه خطر على الرضّع

infants especially under 6 month	infants	Adults
Bronchiolitis **Life-threatening** disease with respiratory distress and cyanosis can be fatal and can **lead to chronic lung disease in later life.**	**Pneumonia** Can be fatal	**Common cold** No fever

1

Lab diagnosis:

Routine testing by Direct detection of the virus from sputum, **Nasopharyngeal swab, aspirate (NPA)** or respiratory secretion by **direct immunofluorescence assay (IFA).** (Just as in influenza & Parainfluenza virus)

2

Other detection methods:

Isolation of virus by cell culture from N.P.A with multinucleated giant cell or syncytia as cytopathic effect (C.P.E); PCR.

3

Treatment and prevention:

★ **Ribavirin** administered by inhalation for infants with severe condition.

- **No vaccine** available, but passive immunization immunoglobulin can be given for infected premature infants.

Measles Virus

Family:	Paramyxoviridae
Structural features:	❖ Enveloped virus ❖ Negative polarity single stranded RNA genome.
Transmission	Inhalation of infectious aerosol droplets.
Epidemiology	❖ Measles virus infects human only. ❖ Most cases in preschool children, very infectious. ❖ Infection occurs mainly in winter and spring.
Pathogenesis	1- The virus infects first epithetical cells of upper respiratory tract (Dr: It is not really a respiratory infection, but its transmission is throuh URT) 2- Then the virus spreads to the blood **causing viremia** Viremia = Fever 3- Then it infect the endothelial cells of blood vessels. 4- Then the virus reaches the lymphoid tissue where it replicates further and disseminates to the skin causing **maculopapular rash.**
I.P	Incubation period is 7- 14 days. (Influenza was 1-4 days, Measles & mumps have a longer IP because they cause a systemic infection)
Clinical Features	Prodromal symptom: **Fever**, cough, conjunctivitis and running nose. ★ **Koplik's spot: Small red papules with white central dots appear mostly in buccal mucosa.** (buccal mucosa is the lining of the cheeks and the back of the lips, and inside the mouth).  ★ **Rash: Maculopapular rash** first on face, trunk, extremities. The rash is red, become confluent, last 4 or 5 days, then disappears leaving brownish discoloration of the skin and final desquamation (skin peeling). Recovery complete in normal children with **life long immunity.**
Complications	★ Encephalitis: Acute or subacute sclerosing panencephalitis (SSPE). **(VERY RARE)** A progressive demyelinating neurological disorder of children and young adults that affects the central nervous system (CNS), The first symptoms are usually poor school performance, forgetfulness, temper outbursts, distractibility, etc.. Read more about it here. ❖ Giant cell pneumonia: rare in **immunocompromised children** due to direct invasion of measles virus to the lung tissue.

1

Lab diagnosis:

Serology by detection of **IgM Ab** using **ELISA**, and in case of Subacute sclerosing panencephalitis **(SSPE)** detection of measles antibodies in **CSF** or detection of viral NA using PCR.

2

Treatment and prevention:

- **No specific treatment**, Prevention by giving the live attenuated vaccine **(MMR)** for Measles, Mumps and Rubella.
- MMR is given to all children 15 months & booster dose at school entry
- . Give excellent long last protection.

Mumps Virus

Definition	★ **An acute benign viral parotitis.** Parotitis: a painful inflammation & swelling of salivary gland, mainly parotid glands. A disease of children (5-15 years) Also can be seen in young adult, but with more complicated features.
Family	Paramyxoviridae
Structure features	❖ Enveloped virus with Negative polarity, single stranded RNA genome. ❖ The viral envelope is covered with two glycoprotein spikes, hemagglutinin and neuraminidase.
Transmission	**Inhalation** of infectious aerosol droplets during sneezing and coughing, or direct contact with **saliva**.
Epidemiology	★ **Mumps virus infects human only.** ▪ Highly infectious, peak in winter. ▪ Long incubation period 18-21 days.
Pathogenesis	1- Infection started in the epithelial cells of **upper respiratory tract.** 2- Then virus spread by **viremia** to parotid gland mainly. Viremia = viruses in blood, cause Fever 3- Also might spread to other organs such as testes, ovaries, pancreas and CNS.
Clinical Features	❖ Classic mumps starts with moderate **fever**, malaise, pain on chewing or swallowing, particularly acidic liquids. ❖ Sudden onset of fever and painful swelling of parotid gland (parotitis) ❖ Self-limiting disease resolve within one week. ❖ Solid and long life immunity developed. 
Complications	- Aseptic meningitis, Encephalitis, Pancreatitis, Thyroiditis. **After puberty:** المرض لو أصيب فيه شخص بالغ ممكن يسبب عقم ❖ Orchitis: inflammation of one or both testicles. usually unilateral, rarely leads to sterility. ❖ Oophoritis: inflammation of ovaries.

1

Lab diagnosis:

Serology by detection of **IgM Ab** using **ELISA**, cell culture and isolation of the virus from saliva or detection of viral NA using **PCR**.

2

Treatment and prevention:

- **No specific treatment**, Prevention by giving the live attenuated vaccine **(MMR)** for Measles, Mumps and Rubella,
- MMR is **live attenuated vaccine** given to all children 15 months old & a booster dose at school entry.
- Give excellent long last protection.

SAQ

SAQ1: A 2-year-old child presents to the pediatrician's office for a rash. Her mother is against vaccines, so the child had not received any childhood vaccines. On physical exam, she has a high fever as well as a confluent maculopapular rash. She also has blue-white spots on her buccal mucosa.
A) What do you think is the virus? B) How will you diagnose it? C) Treatment or prevention? D) What are possible complications?

SAQ2: 5-month-old girl was admitted to the emergency department of a secondary hospital for recurrent episodes of shortness of breath. She had been referred to the hospital by the general practitioner after 3 days of gradually worsening symptoms of difficult breathing, cough and expiratory wheeze. No medication had been given. Physical examination on admission showed a well-developed, well- nourished infant. There were no congenital abnormalities. The patient had a normal weight and length. Temperature: 38, BP: 90/65 mmHg Heart rate: 140/min Respiratory rate: 65/minute with nasal flaring and intercostal retractions, Pulse oximetry: 95% on room temperature.
A) What is your diagnosis? B) What virus could this be a complication of? C) How will you confirm it in the lab? D) Your choice of treatment? (E) Is there a vaccine for the causative virus?

SAQ3: 1-year-old boy who was brought to the clinic in January because he developed fever, chest congestion, rhinorrhea, decreased oral intake and a "barking" cough 3 days previously. His medical history was significant only for recurrent otitis media. On examination, his temperature was 38.40C. He was in acute distress and had audible obstructive upper airway sounds. His throat was erythematous. On lung examination, upper airway sounds were prominent and there was wheezing and subcostal retractions.
A) What is your diagnosis? B) What lab diagnostic method should be asked for? C) What are other complications that this virus may cause? D) What is your choice of treatment?

SAQ1: (A)Measles (B) Serology IgM, ELISA (C) No treatment, but MMR vaccine (D) Encephalitis & Giant cell pneumonia

SAQ2: (A) Bronchiolitis (B) RSV infection (C) Nasopharyngeal swab + IFA (D) Ribavirin (E) Nope

SAQ3: (A) Croup Aka. Acute laryngotracheobronchitis (B) Nasopharyngeal swab, aspirate (NPA) + IFA (C) Bronchiolitis and Pneumonia (D) Supportive treatment

MCQs

Q1: A 3-year-old boy is brought to the emergency department by his mother for fever and a change in his behavior over the past 4 days. The patient and his mother recently immigrated from Beijing and they have never had access to healthcare. She noticed he developed a rash and became more confused over the past several days. His temperature is 104°F (40.0°C), blood pressure is 74/54 mmHg, pulse is 140/min, respirations are 22/min, and oxygen saturation is 98% on room air. Physical examination shows a red, maculopapular rash on his forehead and face in addition to red-based lesions with blue-white centers in his mouth . The patient deteriorates and is admitted to the ICU. After 7 days in the ICU the patient is able to be discharged. Which of the following is a possible complication that lead to the patient's condition?			
A- Encephalitis	B- Glomerulonephritis	C- Mental retardation	D- Sensorineural deafness
Q2: The virus that is diagnosed with serology detection of the IgM using ELISA?			
A- Mumps Virus	B- RSV Virus	C- Measles Virus	D- A & C
Q3: which one of the following can treated by ribavirin ?			
A- Coronavirus	B- Respiratory syncytial virus	C- Parainfluenza virus	D- Influenza virus
Q4: Koplik's spot is characteristic of which virus?			
A- Influenza virus	B- Parainfluenza virus	C- Mumps virus	D- Measles virus
Q5: Which one of the following can cause parotitis?			
A- Measles virus	B- Mumps virus	C- RSV	D- Influenza virus
Q6: The antiviral that is effective against influenza A virus only is			
A- Oseltamivir	B-Amantadine	C- Zanamivir	D- Rimantadine
Q7: All are correct about influenza A virus except			
A- Infects human and animal	B- Causes epizootic in animal	C- Antigenic drift but no shift	D- Antigenic drift and shift
Q8: The virus that does not have an antiviral treatment, nor does it have a vaccine is			
A- Influenza A virus	B- Respiratory Syncytial Virus	C- Mumps virus	D- Parainfluenza virus
Q9: Which one of the following is ORTHOMYXOVIRUS ?			
A- RSV	B- Parainfluenza virus	C- Influenza virus	D- measles virus
Q10: Which type of PIV cause Croup or Acute laryngotracheobronchitis?			
A- PIV Type-I	B- PIV Type- II	C-PIV Type-III	D-PIV Type-I, II

Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
A	D	B	D	B	B	C	D	C	D

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