Viral Respiratory Tract Infections (B)

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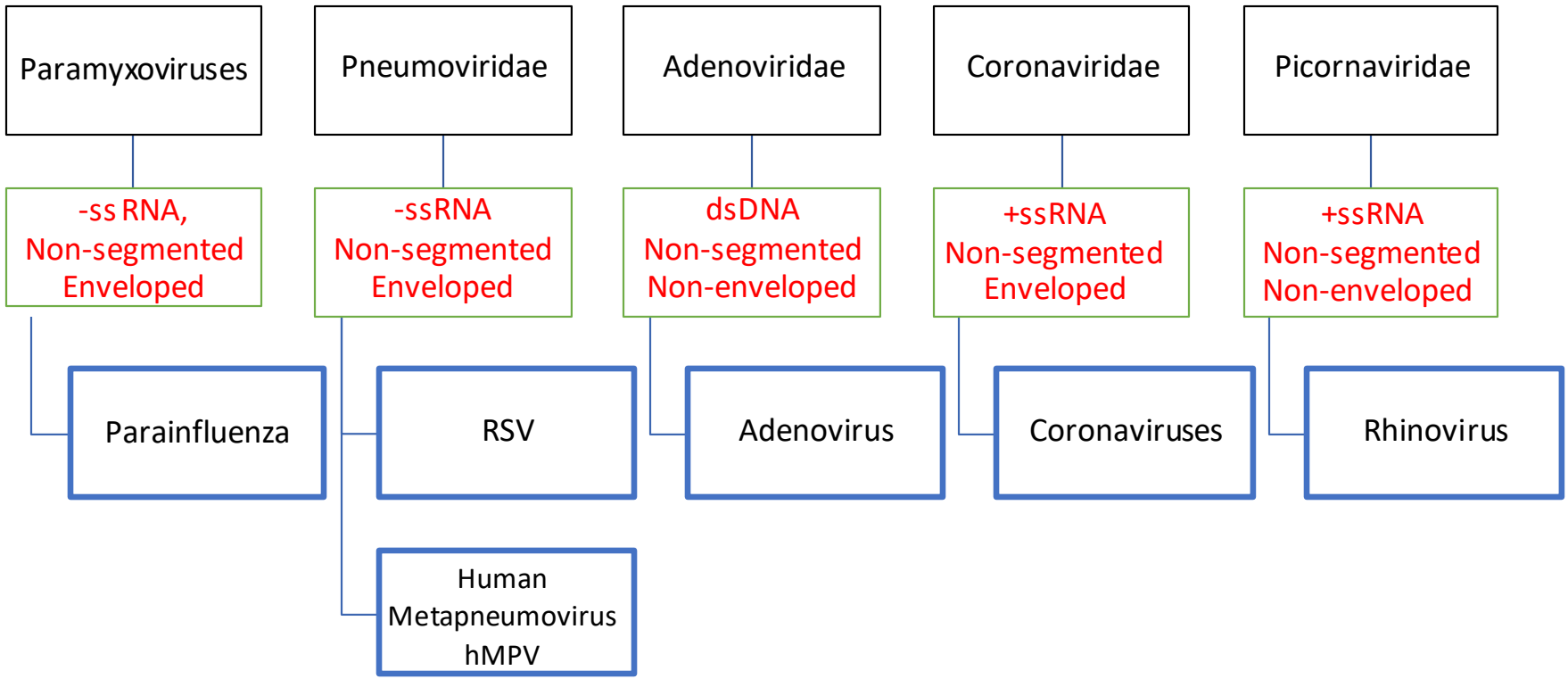
Paramyxoviruses and other respiratory viruses



Paramyxoviruses

- Family: Paramyxoviridae
- -ss RNA enveloped viruses.
- Have RNA dependent RNA polymerase.
- Includes Parainfluenza, mumps, measles, and Newcastle disease virus (NDV)
- Parainfluenza viruses are distributed within two genera, Respiroviroses and
- Rubularviruses
  - Respiroviroses → Parainfluenza viruses types 1, 3
  - Rubularviruses → Parainfluenza viruses types 2, 4a, 4b
- The envelop has HA, NA or a fusion protein.

Parainfluenza viruses

- Heat Labile, but survive on surfaces for several hours
- Highly infectious
- Susceptible to destruction by soap and water, disinfectants.
- Four serotypes 1-4
- Reinfections occur throughout life
- Many remain asymptomatic but infective
- Viral shedding lasts for about 1 week after infection
- Prolonged viral shedding in immunocompromised

Parainfluenza viruses / pathogenesis

- Hemagglutinin → binds to the sialic acid sugar on the surface of epithelial cells
- After binding
  - The Fusion (F protein) facilitates the fusion of the virus to fuse with the epithelial cell membrane and release the nucleocapsid into the cystoplasm
- After transcription and translation and assembly
  - The virus leaves the cell by using Neuraminidase → cleaves the sialic acid sugar
- Transmitted via resp. secretions leading to a wide spectrum from asymptomatic, common cold to severe Lower resp. Tract infections (LRTI).

Parainfluenza viruses - Clinically

❖ **Diseases**

1. Common cold: sore throat, hoarseness, cough and sometimes mild fever.
2. Croup (acute laryngotracheobronchitis):
   - Age: typically <6 years of age including infants
   - Involvement of the larynx, subglottic area and trachea
   - Clinical features: fever, cough, hoarseness, inspiratory stridor
   - May cause cyanosis and respiratory distress mandating tracheostomy.
3. Bronchiolitis: Common in young children.
4. Pneumonia: Common in young children and immunocompromised.

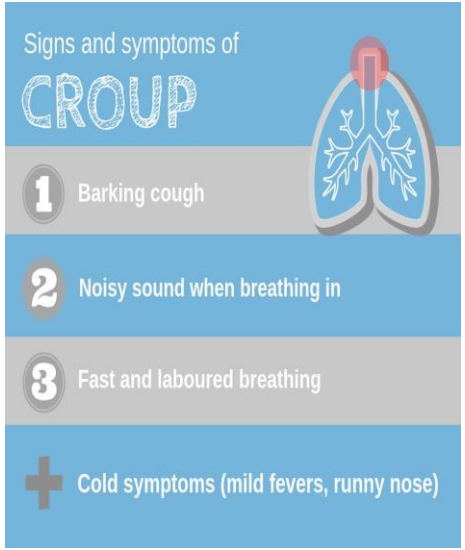
❖ **Diagnosis**

- Direct detection of the virus antigen (Serology) or RNA by PCR.
- Culture: less used.

❖ **Treatment**: supportive.

Croup

- Infection of the Larynx (Laryngitis), Trachea (Tracheitis) and bronchi (bronchitis)
- Almost all cases are caused by viruses esp. Parainfluenza viruses (most common).
- In rare cases: Staphylococcus aureus.
- Children have smaller airways and nonexpendable rings of trachea, so edema is more likely to cause narrowing of the lumen.
- Typically, mild upper R.T symptoms such as nasal discharge and dry cough are present days before signs of airway obstruction followed by sudden onset of barking cough (seal barking) and difficult respiration.
- **Treatment**:
  - It is a self-limited infection resolve after 5 to 7 days
  - Corticosteroids and inhaled aerosolized epinephrine can be used.
  - No specific antiviral drug.



Common cold

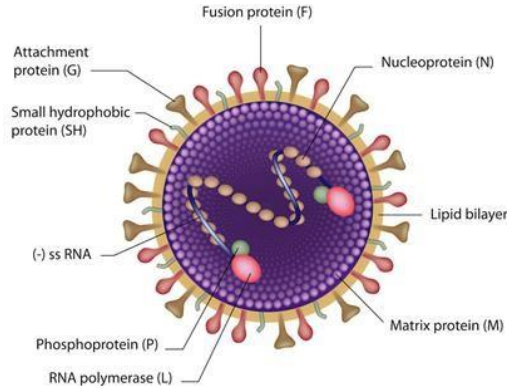
- Common cold (rhinitis) is a viral infection of the upper respiratory tract (nose, nasopharynx and throat).
- Over 100 viruses can cause common cold.
- Preschool children are at greatest risk of frequent colds.
- Children have an average of 8 colds per year, adults 3 per year.
- Most people recover from common cold within a week or two.
- Symptoms of common cold: Sore throat, runny nose, nasal congestion, sneezing, conjunctivitis (sometimes), myalgia, fatigue. (no fever)
- Complications: Secondary bacterial infection (otitis media and sinusitis).

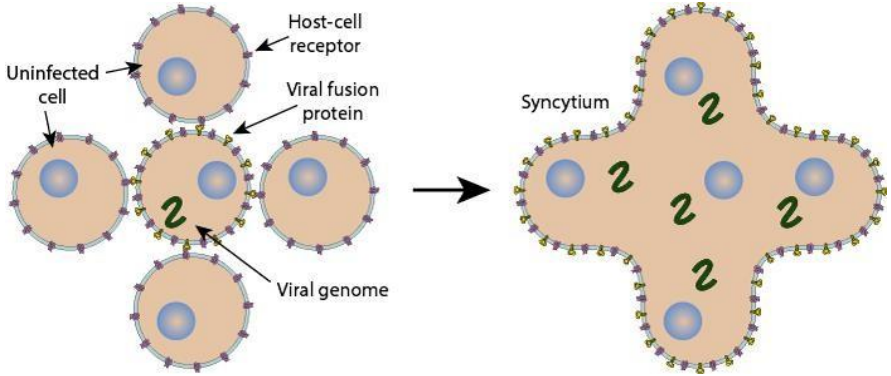
Respiratory syncytial virus (RSV)

- **Family**: Pneumoviridae (Previously, Pneumovirdae was part of the Paramyxovirus family, but in 2016, Pneumoviridae was reclassified as a separate family.)
- Enveloped virus.
- Envelope Glycoproteins: F and G proteins.
- Two antigenic subgroups ‘A’ and ‘B’ based on variations in G protein
- Entry through mucosa of nose and eyes.
- Cell to cell spread within respiratory tract, Syncytium formation with multinucleated giant cells.

Respiratory syncytial virus (RSV)

- G protein (mutates often) → Attachment
  - Glycoprotein G allows the virus to attach to respiratory epithelial cells; its ability to frequently mutate helps the virus evade the host immunity and permits reinfections throughout an individual's life.
- F protein (typically conserved) → Induces syncytia formation giant cell with multiple nuclei
  - The RSV vaccine targets the RSV fusion (F) protein, as it rarely mutates.



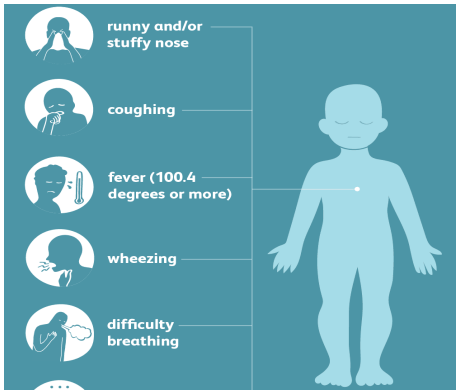


Respiratory syncytial virus (RSV)

- The incubation period is 2–8 days.
- Transmitted via direct contact with respiratory droplets and indirect contact with contaminated surfaces
  - RSV can survive on the hands for ≥ 30 minutes and on contaminated surfaces for several hours.
- Viral shedding typically lasts 3–8 days.
  - RSV viral shedding can be prolonged (≥ 3 weeks) in infants and immunocompromised individuals.

Clinical features

1. URTI:
   - Fever, Rhinitis, Pharyngitis, Otitis media, Croup.
2. LRTI: Bronchiolitis, Pneumonia.
   - Common in infants and in those with lung or heart diseases.
   - Cough, Poor feeding, lethargy, Hypoxemia
   - Respiratory Distress (tachypnea, retractions)
   - Apnea, wheezes.



Respiratory syncytial virus (RSV) – Dx

- Viral isolation/Culture
- Antigen detection - >90 % sensitivity and specificity
  - ELISA
  - RIA, IF
- PCR.
- CXR: Lung hyperinflation.

Respiratory syncytial virus (RSV) –Tx

1. Supportive (Antipyretics, fluid intake, nasal suctioning)
2. Antiviral Agents
   - Ribavirin, a synthetic guanosine analogue (inhibits the RNA-dependent RNA polymerase), given as an aerosol, approved for premature and immunocompromised infants.
3. Vaccine
   - RSV vaccine → a bivalent vaccine based on the prefusion form of the RSV fusion (F) protein
4. RSV prophylaxis (Two RSV monoclonal antibodies are now available)
   - Nirsevimab (preferred) → long-acting RSV monoclonal antibody
   - Palivizumab → short-acting RSV monoclonal antibody

Human metapneumovirus

- Human metapneumovirus was first identified in the Netherlands in 2001
- Single-stranded RNA
- Belongs to the Pneumoviridae family
- Transmitted through close contact with an infected person or a contaminated surface
- Diagnosis: RT-PCR.
- Treatment: No specific antiviral yet.

Adenovirus/structure & characteristics

- Non-enveloped ds DNA virus.
- Infects mucoepithelial cells of respiratory, GI and GU tracts
- Enter via epithelium, replicate and spread to lymphoid tissue.
- Viremia occurs with secondary involvement of viscera.
- Stable in the environment and in GI tract.
- Relatively resistant to disinfection (nonenveloped)
- Persists for long time in adenoids, tonsils & kidneys (latent?). Also, viral shedding in faeces may persist for years.
- Sub-grouped into 6 groups A-F (according to DNA sequence), with 51 serotypes in all the groups.
- Certain serotypes are associated with certain infections e.g types 1-4, 7, 14 and 21 are associated with respiratory infections, types 40 & 41 associated with Gut infection, types 8, 19 and 37 associated with epidemic keratoconjunctivitis

Adenovirus

Epidemiology	Adenovirus infections re-endemic in many parts of the world however, outbreaks are also common in Military recruits, swimming pool users, hospitals, residential institutions and nursing homes i.e crowded areas.
Incubation P	~ 2-14 Days.
Transmission	• Aerosols droplets • Fecal-oral route • direct inoculation of the conjunctiva
Clinically	**Many infections are sub-clinical** **Diseases** • **Respiratory** • **Eye** (conjunctivitis, keratoconjunctivitis). • **Genitourinary** (hemorrhagic cystitis). • **Gastrointestinal** (gastroenteritis and non bloody diarrhea especially in young children, bowel intussusceotion). • **Others**: Myocarditis, Pericarditis, Meningitis/Encephalitis, Hepatitis and Rash.

Adenovirus

Respiratory infections	1. Subclinical. 2. Mild upper respiratory tract infections (URTI): • Fever, runny nose wheezy chest and cough. • Pharyngitis, tonsillitis and conjunctivitis. • Majority are due to types 1-7. • Usually mild but may progress to a serious Lower resp. Tract infections. 3. Lower resp. Tract infections (LRTI): • Fever, shortness of breath (SOB), cough and wheezing. • Can be fatal particularly in children. • can be associated with increased WBC count and C-reactive protein (CRP).
Diagnosis	○ **Electron microscope**: Can not detect the serotype. ○ **Virus antigen detection** in nasopharyngeal aspirates or stool using ELISA. ○ **Culture**: speed of isolation can provide a pointer to the clinical significant, if > days, then unlikely to be significant. ○ **Serology**: detection of 4 fold increase in the antibodies. ○ **PCR**: Sensitive, single or part of a multiplex PCR for most respiratory viruses.

Adenovirus

Treatment	○ Infections are usually not life threatening in immunocompetent and no treatment required apart from symptomatic treatment. ○ No antiviral available or licensed
Prevention	○ Vaccine is not usually necessary as most infections are not serious, Nevertheless; ○ A vaccine is available for military people and not the civilians. ○ The vaccine is given orally and it contains 3 serotypes, 4, 7 and 21.

Coronaviruses

- Family: Coronaviridae
- Large, enveloped, positive-sense single-stranded RNA genomes.
- Genus: Betacoronavirus this genus include
  - SARS-CoV (responsible for the 2002-2003 SARS outbreak) and
  - MERS-CoV (responsible for Middle East Respiratory Syndrome)
  - SARS-CoV-2 (the virus responsible for COVID-19)

Rhinovirus

Clinically	• Common in preschool children and adults. • It causes nearly one third of all common colds • Found all over the year but more in Winter. • Signs and symptoms (S & S): ‘common cold • S&S may stay for 1-2 weeks • Complications as sinusitis and otitis media
Diagnosis	Not usually attempted but can be carried out by culture or PCR (single or Multiplex)
Treatment	No specific treatment
Prevention	No specific vaccine: many serotypes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❖Regarding SARS-CoV-2 and COVID-19 infection, all are true EXCEPT?

a. Symptoms of COVID-19 may appear as quickly as 2 days or as long as 14 days after exposure
b. SARS-CoV—Z bind to angiotensin-converting enzyme 2
c. Coronaviruses have single-stranded, positive-polarity RNA genome
d. SARS-CoV—Z S1 subunit of the spike protein is responsible for the fusion of the viral envelop with the host cell membrane
e. Bat might be the original host for SARS-CoV—Z

Answer : D

❖Which of the following is the main histologic finding in the organizing phase of diffuse alveolar damage in COVID-19 infection?

a. Alveolar hemorrhage.
b. Hyaline membrane formation.
c. Fibroblastic proliferation.
d. Dense collagenous fibrosis.
e. Fibrinoid necrosis of small vessels.

Answer : C

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- SARS COV2 belongs to the Coronaviruses family, one is WRONG:
  a. It is diagnosed by RT-PCR
  b. It carries spike proteins on its surface that are immunogenic
  c. Non-enveloped

  - Answer : C

- A man presented with a seal barking sound which is a feature of:
  a. Croup
  b. Bronchitis
  c. Rhinitis
  d. Pneumonia

  - Answer: A

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❖All of the following are features of common cold except:

a. Sore throat
b. Runny nose
c. Sneezing
d. Loss of appetite
e. Headache

Answer: D

❖Each of the following statements concerning rhinoviruses is correct EXCEPT?

a. The cell surface receptor for rhinoviruses is ICAM-1
b. Rhinoviruses grow better at 37°C than at 33°C
c. They are naked nucleocapsid viruses with single-stranded, positive-polarity RNA
d. Rhinoviruses are members of the picornaviruses family
e. Rhinoviruses are the most common cause of the common cold

Answer : A

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❖ Regarding Coronaviruses, all are true EXCEPT?

a. Remdesivir, a protease inhibitor as well as Lopinavir-ritonavir, polymerase inhibitor can be used in treatment of COVID-19 infection
b. It may persist on hard and soft surfaces for hours or up to several days
c. SARS originated in China in 2002
d. Excessive production of pro-inflammatory cytokines is an underlying cause of disease severity
e. MERS-CoV is a beta coronavirus of subfamily Coronavirinae

Answer : A

❖ Wrong about parainfluenza:

- Susceptible to water, soap, and disinfectant


Thank YOU
Dr . Reef alqaissi
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