Virology for 2nd Year MD Students

(12) RNA Viruses: *Orthomyxoviridae, Coronaviridae, Paramyxoviridae*

University of Jordan

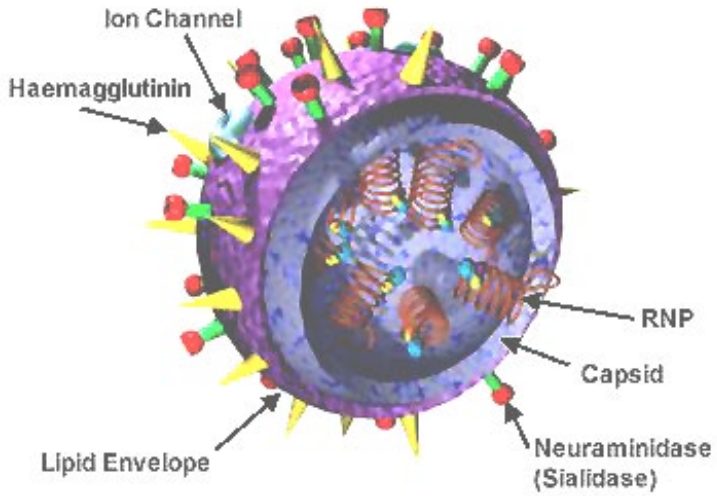
Malik Sallam, M.D., Ph.D.

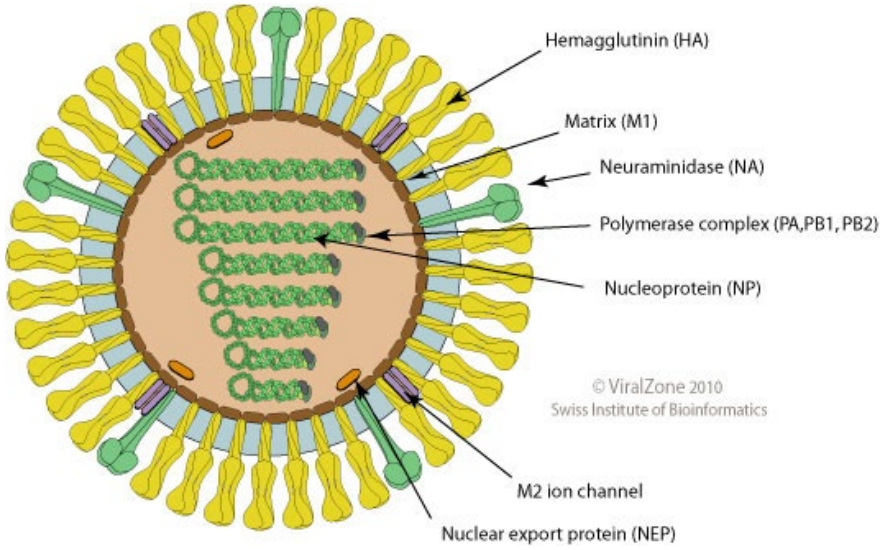
School of Medicine

Department of Pathology, Microbiology and Forensic Medicine

Orthomyxoviridae (influenza viruses)

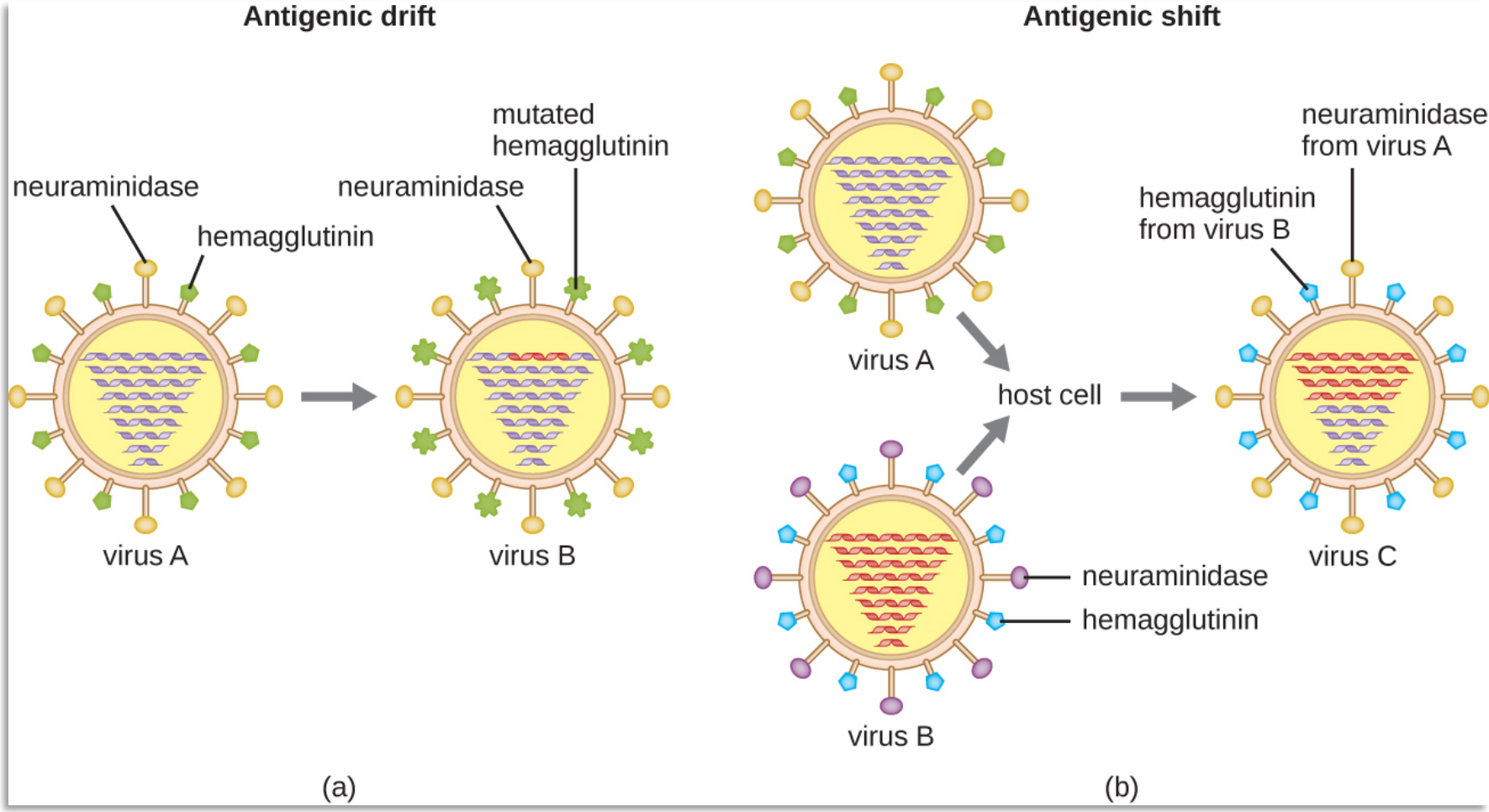
- Negative sense, single-stranded RNA, enveloped viruses with a **segmented genome** that replicate in the nucleus.
- Based on the differences in the nucleoprotein, influenza viruses are classified into types: type A, type B and type C.
- Based on the differences in the hemagglutinin protein (H) and neuraminidase protein (N), only Type A is classified into subtypes (e.g., subtype H1N1, subtype H5N1, subtype H3N2).





Orthomyxoviridae (influenza viruses)

- Type A can cause pandemics if exchange of influenza gene segments occurs between human and animal/bird strains (the result is antigenic shift).
- Type A and type B can cause outbreaks (epidemics), through mutations (antigenic drift)
- Type C causes common cold.



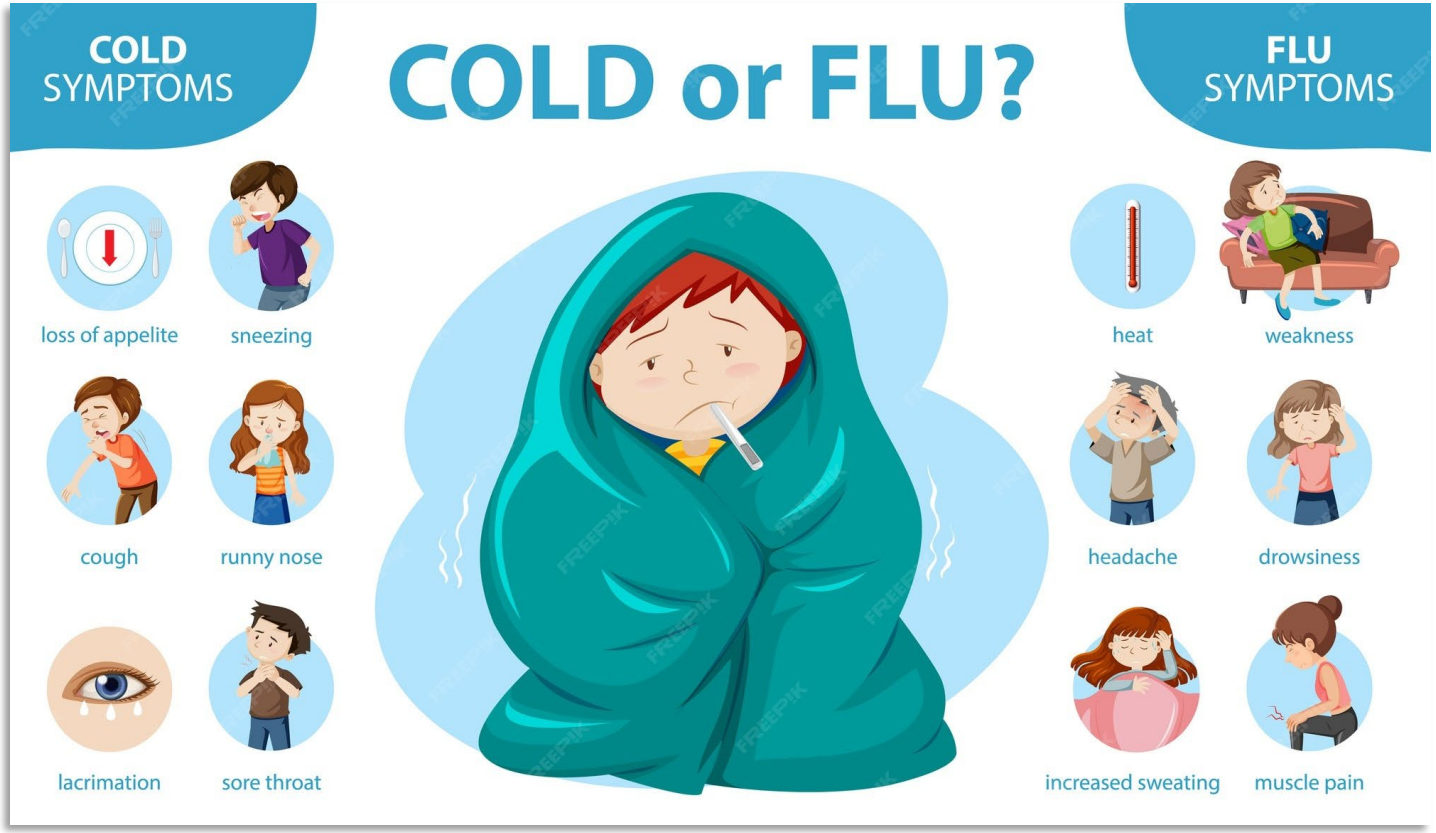
Orthomyxoviridae (influenza viruses)

Transmission: respiratory secretions, aerosols.

Tropism: epithelial cells of the RT.

Clinical features:

A. High fever and chills.
B. Frontal headache.
C. Generalized weakness.
D. Myalgia, arthralgia
E. Sore throat.
F. Dry cough.
G. Pneumonia (children, elderly, those with chronic disease). Secondary bacterial pneumonia can also occur (*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, Gram-negative bacilli).



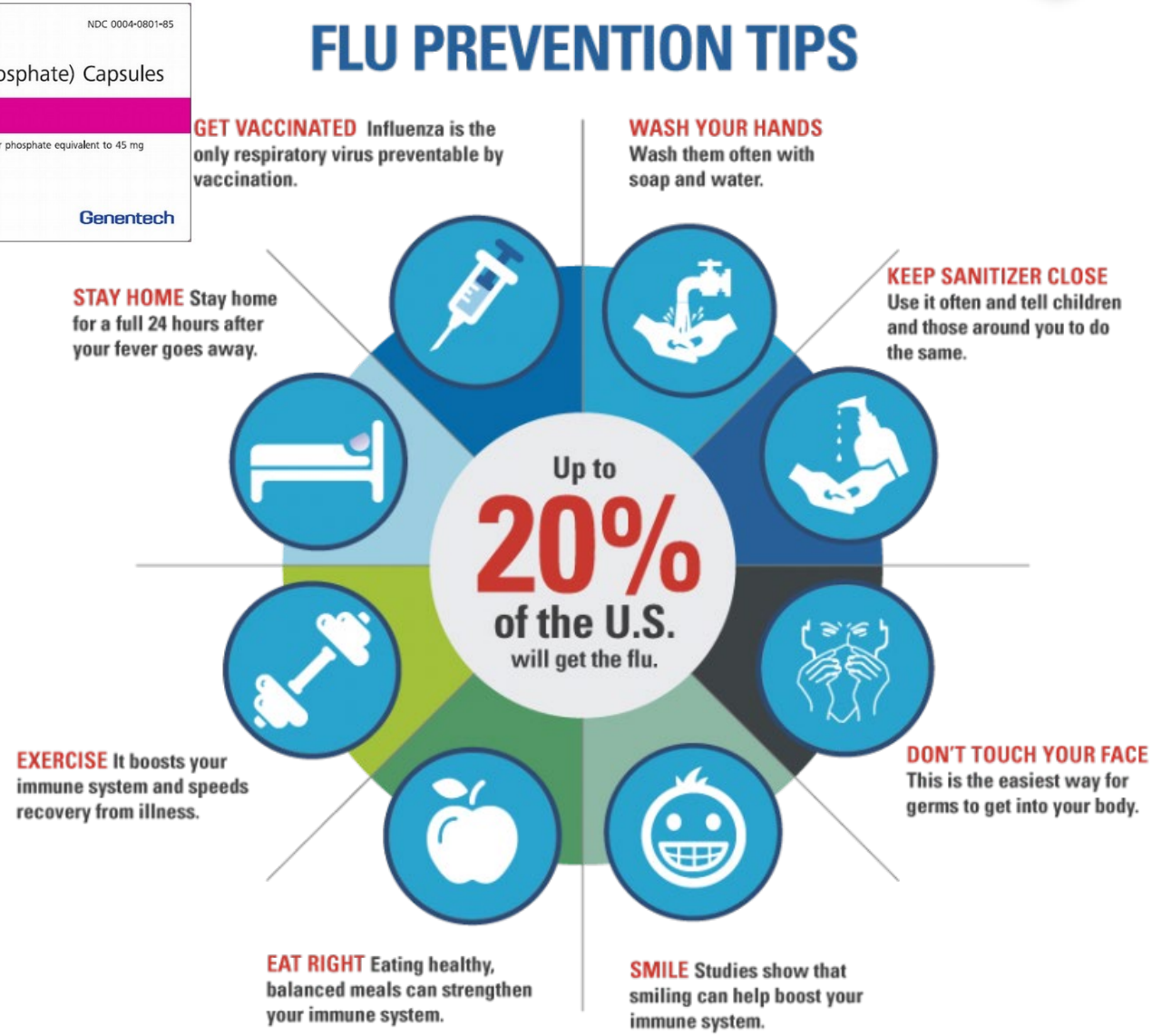
Orthomyxoviridae (influenza viruses)

Diagnosis: Rapid antigen detection; PCR.

Treatment: Supportive, antivirals (oseltamivir (Tamiflu), zanamivir (Relenza)).

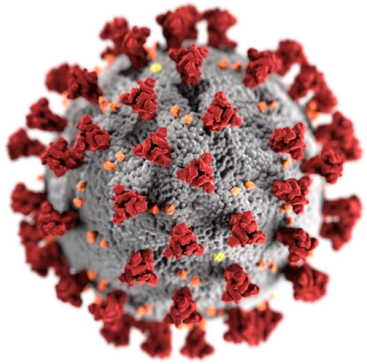
Prevention: Live attenuated, inactivated and recombinant vaccines are available. Trivalent (2 A strains and 1 B strain) or quadrivalent (2 A strains and 2 B strains) are available.

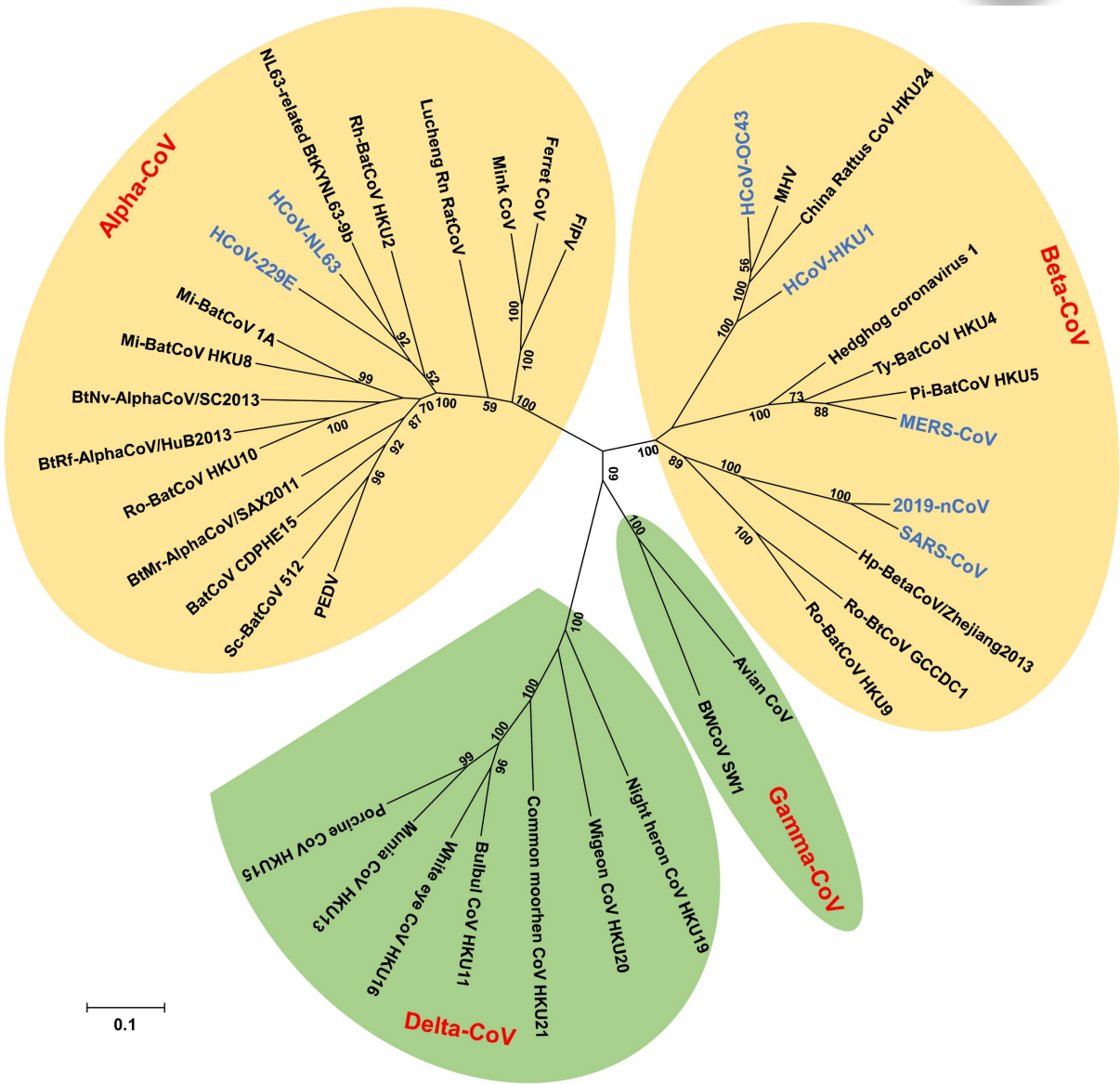
Epidemiology: Seasonal outbreaks occur in winter as a result of declining immunity and antigenic drift with types A and B as the causative agents. Pandemics occur only with type A as a result of antigenic shift.



Coronaviridae

- Enveloped, positive-sense, single-stranded RNA viruses
- Large RNA genome
- Replicate entirely in the cytoplasm
- Characteristic spike (S) glycoproteins protrude from the surface giving coronaviruses the crown-like appearance
- Human coronaviruses causing common cold:
  - HCoV-OC43
  - HCoV-HKU1
  - HCoV-229E
  - HCoV-NL63





Highly pathogenic human coronaviruses

❖**SARS-CoV-1**

Outbreak: 2002-2004

Case fatality rate ~10%

❖**MERS-CoV**

First identified: 2012

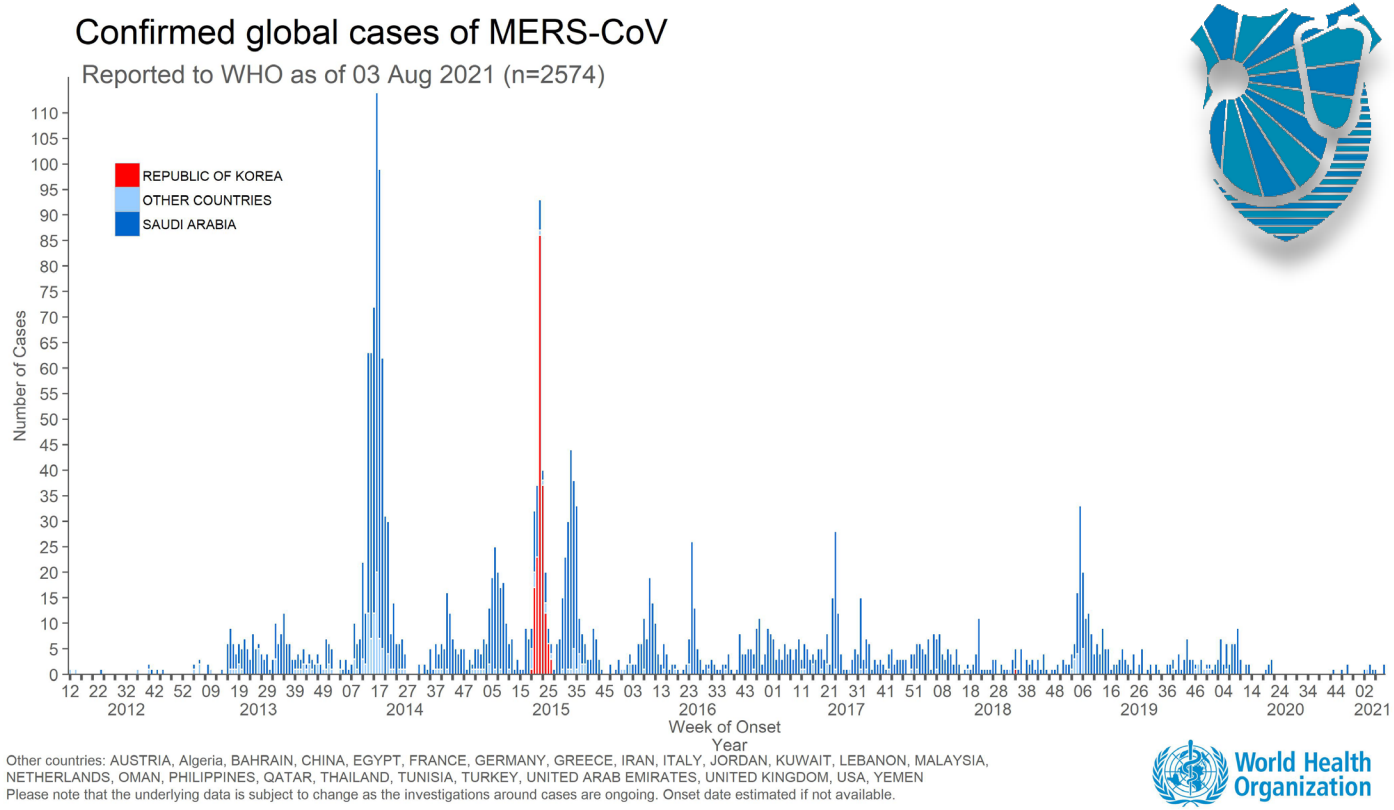
Case fatality rate 35-40%

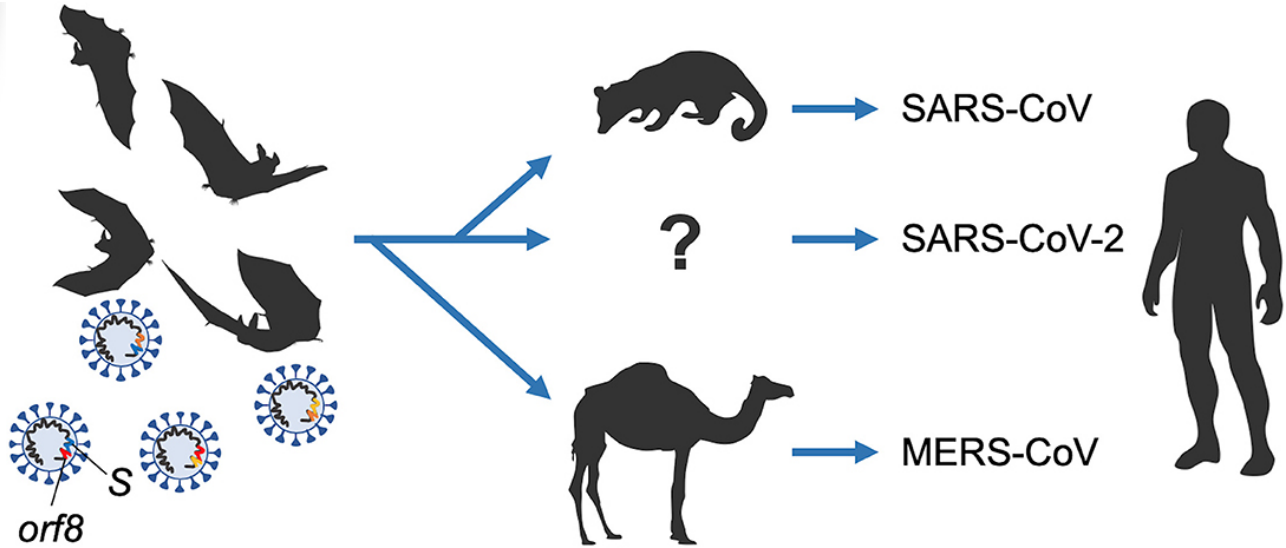
Zoonotic reservoir: camels

❖**SARS-CoV-2**

Emerged: 2019. Causes COVID-19. Overall infection fatality rate <1%, but markedly higher in elderly, comorbid, and unvaccinated.

Massive global impact due to high transmissibility





Coronaviridae: Diagnosis and Treatment

❖Diagnosis

- RT-PCR is highly sensitive and specific by detection of viral RNA
- Antigen detection tests: Rapid but have lower sensitivity compared to PCR. Most useful when the viral load is high (early infection).

❖Treatment

For most human coronaviruses, supportive care only. For severe disease (e.g., COVID-19) oxygen therapy, ventilatory support if needed. Antivirals and immunomodulators in selected patients (dexamethasone, nirmatrelvir-ritonavir, remdesivir).

Types of COVID-19 Tests — Homage

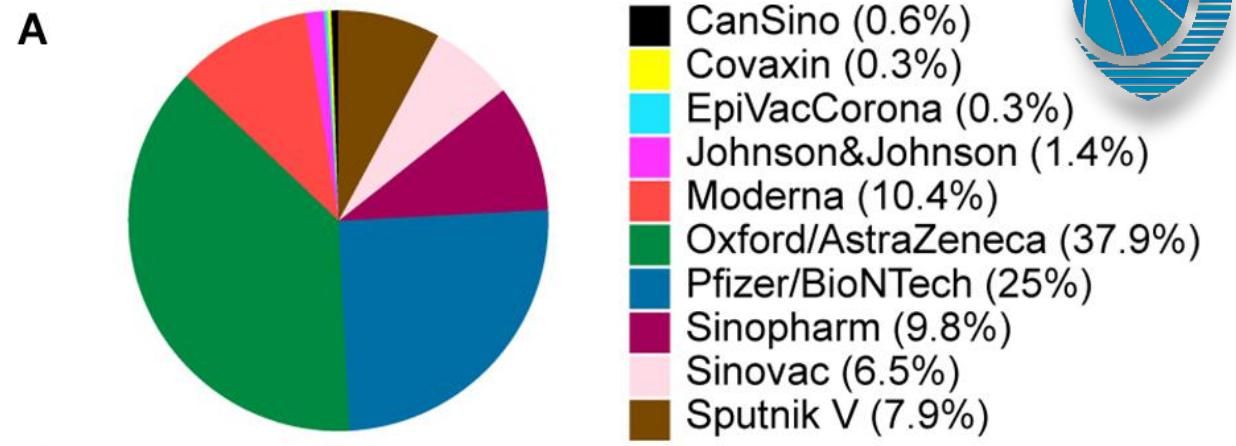
	Polymerase Chain Reaction (PCR) Test	Antigen Rapid Test (ART)	Antibody/Serology Test
Purpose of Test	Diagnosis of active SARS-CoV-2 infection (COVID-19)	Diagnosis of active SARS-CoV-2 infection (COVID-19)	Check for past SARS-CoV-2 infection (COVID-19)
Sample Type	The sample is taken with a swab from the nose or mouth	The sample is taken with a swab from the nose or mouth	The blood sample is taken with a finger prick or venous blood draw
Use of Test	• Symptomatic individuals • Stay-Home Notice (SHN) exit swab • Quarantine Order (QO) entry and exit swab • Rostered routine testing	• Screening for pre-event testing • Rostered routine testing	• Differentiate between acute and old infections in cases that test positive for COVID-19
Turnaround Time	As early as 24 hours after sample collection	As early as 30 minutes after sample collection	One to three weeks on average
Limitations	Unable to differentiate between acute and old infections	• Potentially high false-negative rate in individuals with low viral load • Higher false positive rate than PCR tests	Unable to rule out acute/early infection if the antibody test is negative

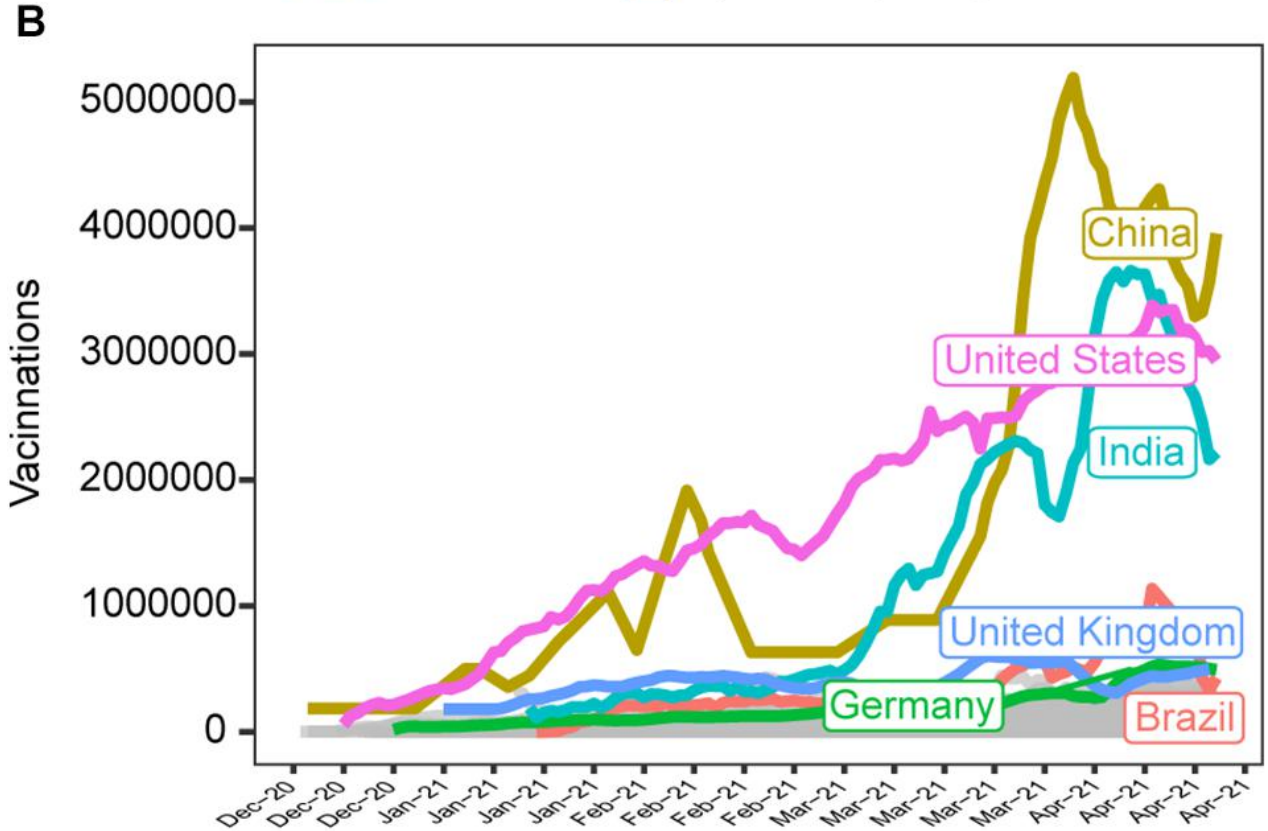
Coronaviridae: Vaccination

❖Vaccination

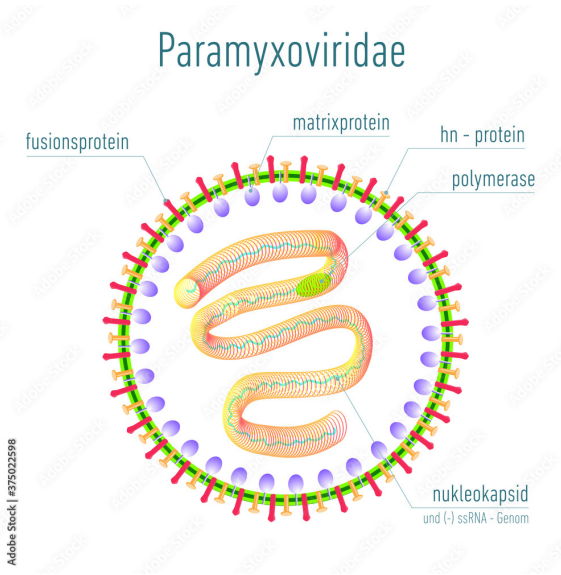
No licensed vaccines for endemic common cold coronaviruses, SARS-CoV-1, and MERS-CoV.

Effective vaccines available only for SARS-CoV-2. Reduce severe disease, hospitalization, and death. Do not fully prevent infection





Paramyxoviridae



- Enveloped, negative-sense, single-stranded RNA. Replicate in the cytoplasm. Characteristic ability to cause cell fusion (syncytia).

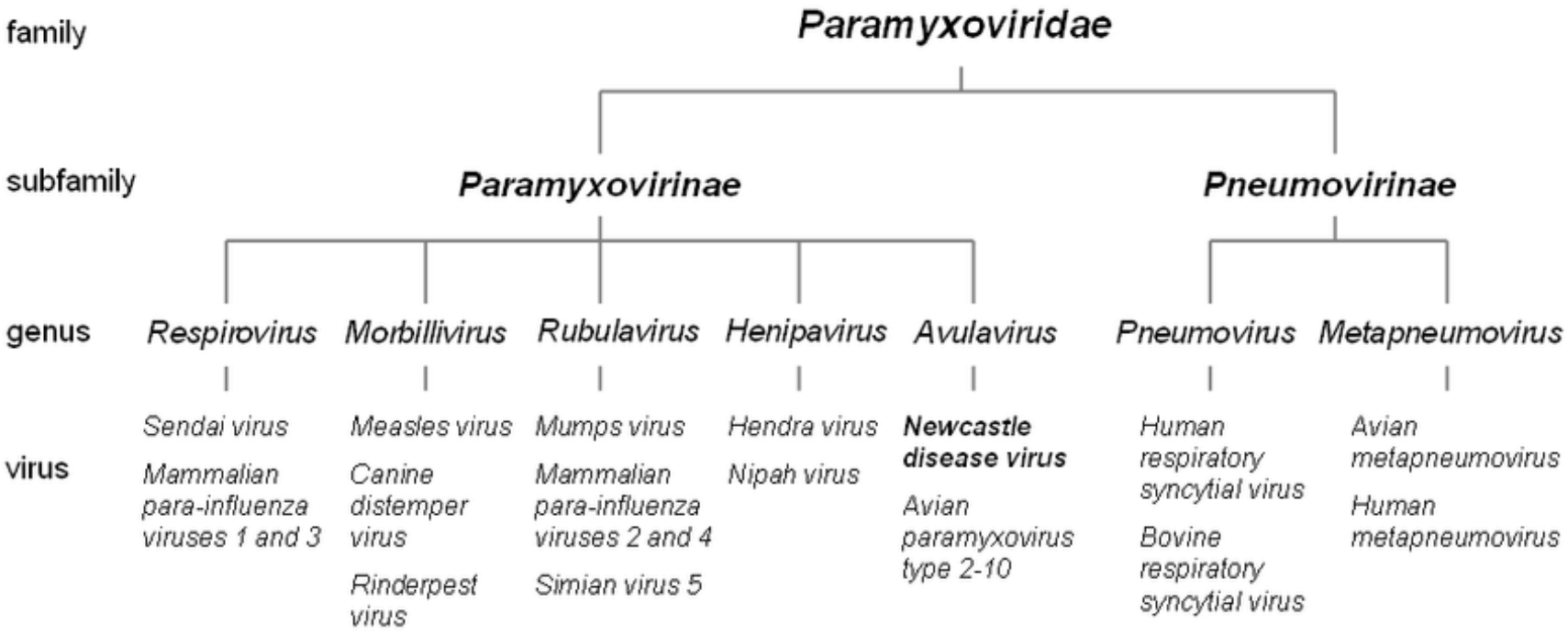
❖Parainfluenza viruses (PIV 1-4)

❖Respiratory syncytial virus (RSV)

❖Human metapneumovirus

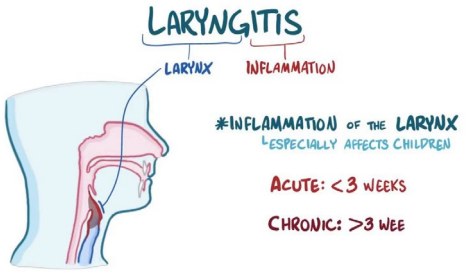
❖Measles virus

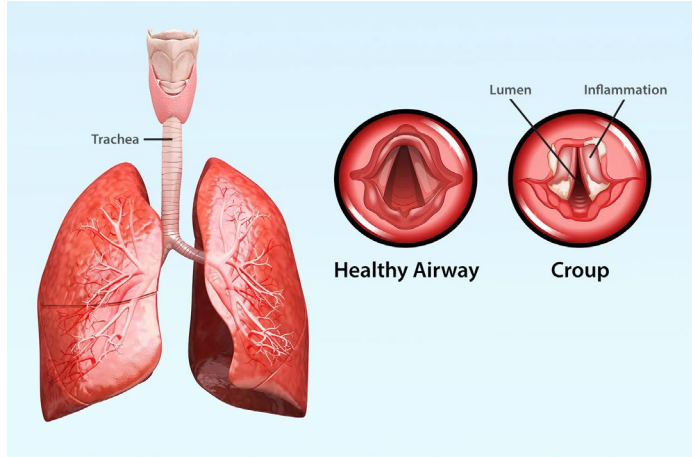
❖Mumps virus



Paramyxoviridae

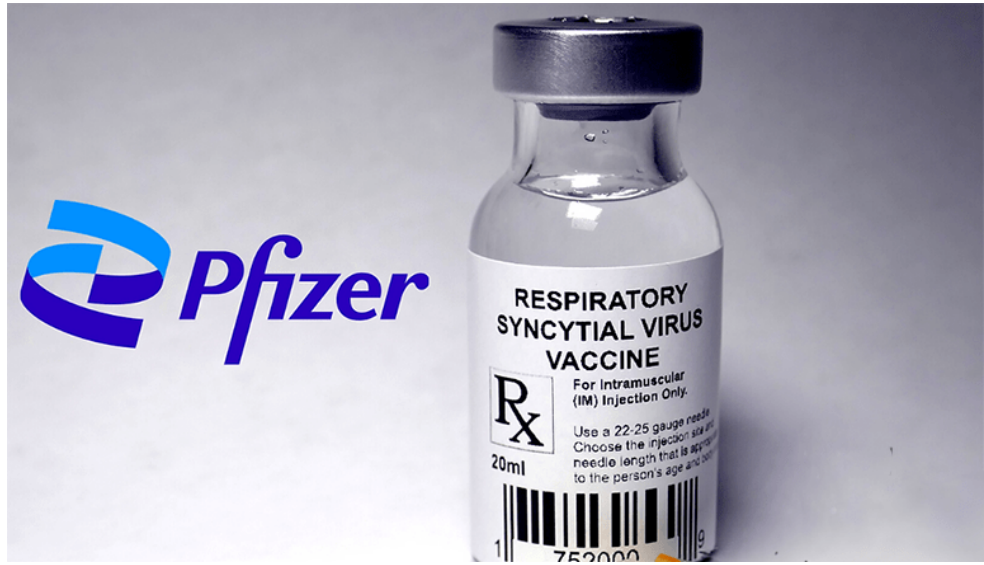
- Transmission: Respiratory droplet and aerosol spread. Highly contagious in close-contact settings. Tropism is in the epithelial cells of the respiratory tract. Some viruses (measles, mumps) later disseminate systemically
- Clinical manifestations:
  - Common cold: PIV, RSV, Human metapneumovirus
  - Laryngitis: PIV. Manifests in hoarseness and barking cough
  - Croup (laryngotracheobronchitis): PIV (the most common cause), RSV. Manifests in inspiratory stridor, barking cough.
  - Bronchiolitis: RSV is the most common cause in infants
  - Pneumonia: RSV (infants, elderly, immunocompromised)





Paramyxoviridae

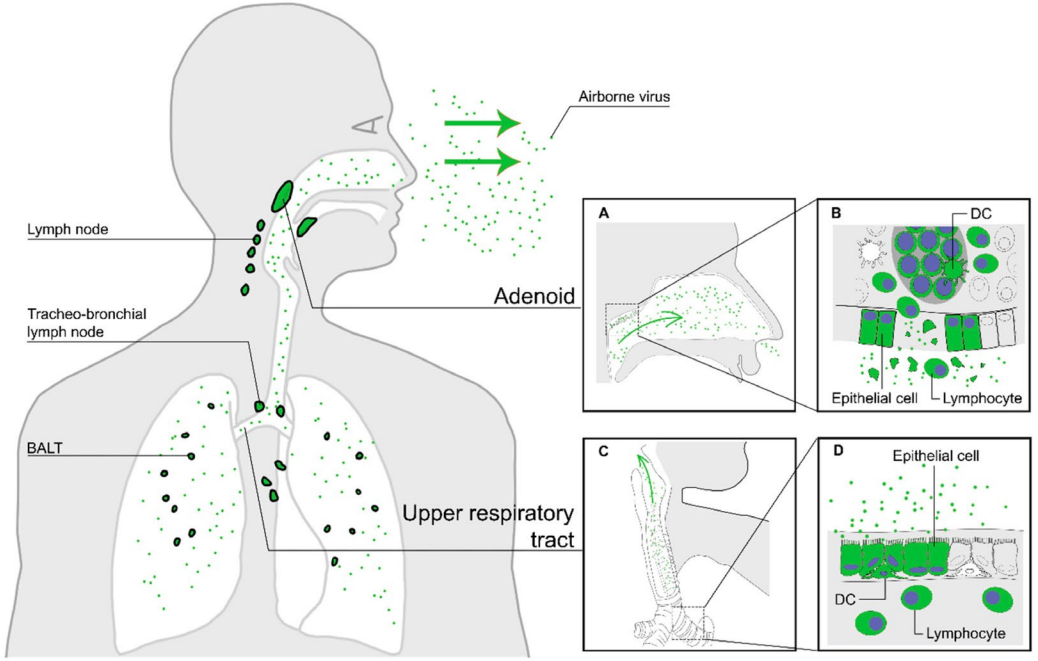
- Diagnosis: Rapid antigen detection which is useful in pediatrics but has a low sensitivity. PCR has higher sensitivity and specificity and detects RSV, PIVs, hMPV, flu, rhinoviruses simultaneously in multiplex panels.
- Mainstay Rx: Supportive care such as oxygen, hydration, respiratory support if needed.
- Prevention: Maternal RSV vaccination protects infants via transplacental antibodies. Elderly RSV vaccines reduce severe RSV disease in the elderly. Passive immunization: Nirsevimab, Palivizumab for high-risk infants.
- Immunity is incomplete and short-lived and re-infection is possible.



Measles

- Caused by measles virus. Extremely contagious (one of the highest R0 of any virus). Characterized by: High fever, respiratory symptoms, maculopapular rash
- Complications are common, especially in children and immunocompromised patients
- Transmission: Respiratory secretions such as airborne and droplet spread. Initial replication in the respiratory tract followed by viremia and dissemination to the skin causing rash and to the eyes causing conjunctivitis. Also spread to the CNS and cause transient immune suppression, predisposing to secondary infections.

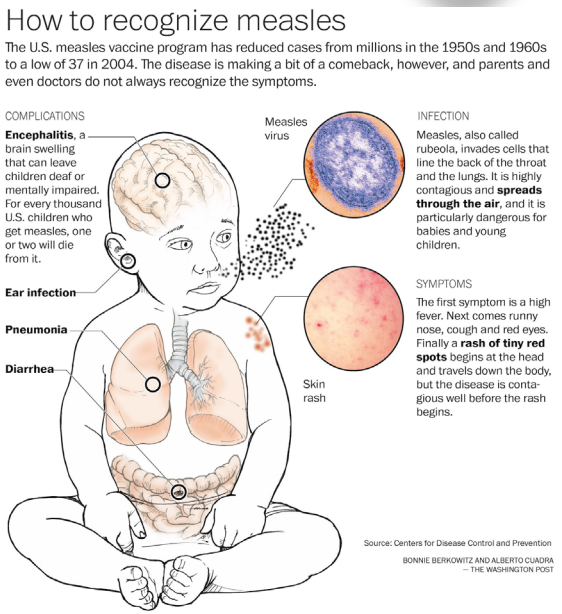
Disease	Route of transmission	R_0	Herd immunity threshold
Diphtheria	Saliva	6–7	83–85%
Measles	Air borne	12–18	92–94%
Mumps	Droplet spread	4–7	75–86%
Pertussis	Droplet spread	12–17	80–94%
Poliomyelitis	Fecal-oral transmission	5–7	50–95%
Rubella	Droplet spread	5–7	83–85%
Smallpox	Contact transmission	6–7	80–85%

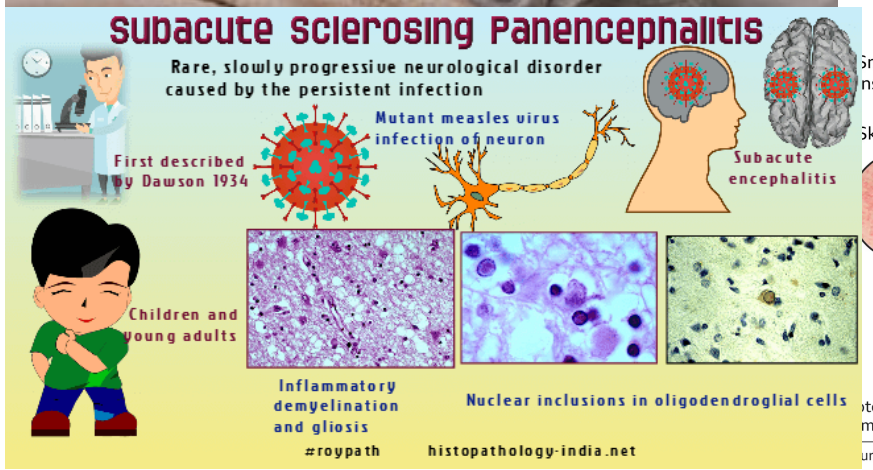


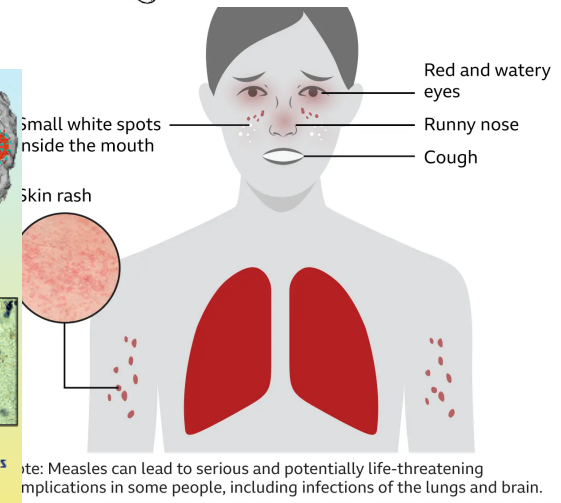
Measles

- Clinical features: Fever and 3C (Cough, Coryza, Conjunctivitis). Maculopapular rash begins on the face and spreads downward.

- Complications: Otitis media is the most common. Severe pneumonia often due to secondary bacterial infection which is the most common cause of measles-related death. CNS involvement: Acute encephalitis, post-infectious encephalomyelitis, subacute sclerosing panencephalitis (SSPE) which is rare, fatal, delayed (years after infection).

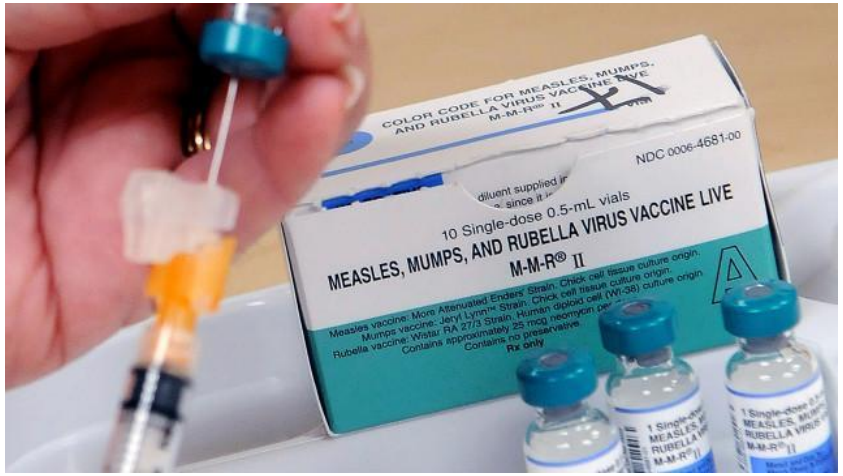






Measles

- Koplik spots are blue-white raised lesions on a red base located on buccal mucosa opposite the first molar which appear 1–2 days before the rash and is pathognomonic for measles.
- Measles infection causes transient but profound immune suppression. Measles increases risk of secondary bacterial infections.
- Only one antigenic type of measles virus which means that natural infection results in lifelong immunity.
- For diagnosis, serology is used for the detection of measles-specific IgM antibodies
- Treatment is supportive. Treat secondary bacterial infections and vitamin A supplementation reduces mortality and morbidity.
- Live-attenuated vaccine MMR vaccine is highly effective



Mumps

- Caused by mumps virus which is highly infectious and characterized by painful enlargement of one or both salivary glands (classically parotitis). The disease is usually mild in children while complications are more common and severe in adults. About 30% of infections are subclinical

- Transmitted by respiratory secretions. Initial respiratory infection is followed by viremia and then dissemination to salivary glands, CNS, gonads, and pancreas.

Mumps

- Complications: aseptic meningitis (common), encephalitis (rare), orchitis (post-pubertal males) which is extremely painful and may cause testicular atrophy and sterility. Oophoritis (females). Pancreatitis.
- Only one antigenic type of mumps virus and infection results in long-lasting immunity.
- Diagnosis is based on serology through the detection of mumps-specific IgM antibodies
- Treatment is supportive
- Prevention is via the live-attenuated MMR vaccine

Thank You…
Wishing you all the best!