

Infectious Diseases

-Lecture -

ACUTE RESPIRATORY INFECTIONS (ARI)



General part

- ARI are the most common infectious diseases in humans (2/3 of all infections),
- An adult suffers from ARI 2-5 times a year, and children 8-12 times a year,
- ARI are mainly droplet infections that occur primarily in the cold months,
- The most common causative agents of ARI are primarily respiratory viruses (PRVs): influenza viruses, parainfluenza viruses, adenoviruses, rhinoviruses, respiratory syncytial virus and coronaviruses,
- PRVs can cause various clinical syndromes: the common cold, pharyngitis, laryngitis, respiratory febrile catarrh, pharyngoconjunctival fever, tracheobronchitis, pneumonia, croup and bronchiolitis,
- ARI leave short-term, type-specific immunity.

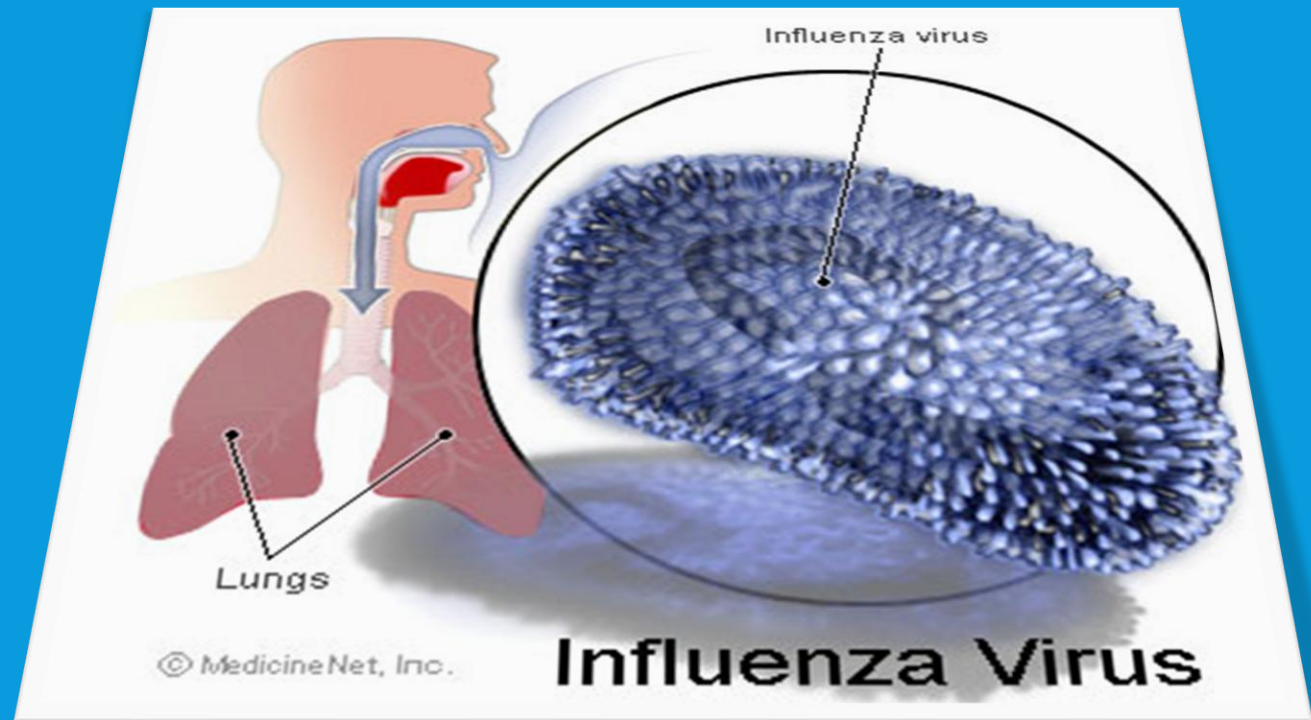
THE MOST COMMON CAUSATIVE AGENTS OF ARI ARE PRIMARILY RESPIRATORY VIRUSES



Influenza viruses
Parainfluenza
viruses
Adenoviruses
Rhinoviruses
Respiratory syncytial
virus
Coronaviruses

Common cold,
Pharyngitis
Laryngitis
Pharyngoconjunctival
fever
Tracheobronchitis,
Pneumonia
Croup
Bronchiolitis

INFLUENZA (FLU)

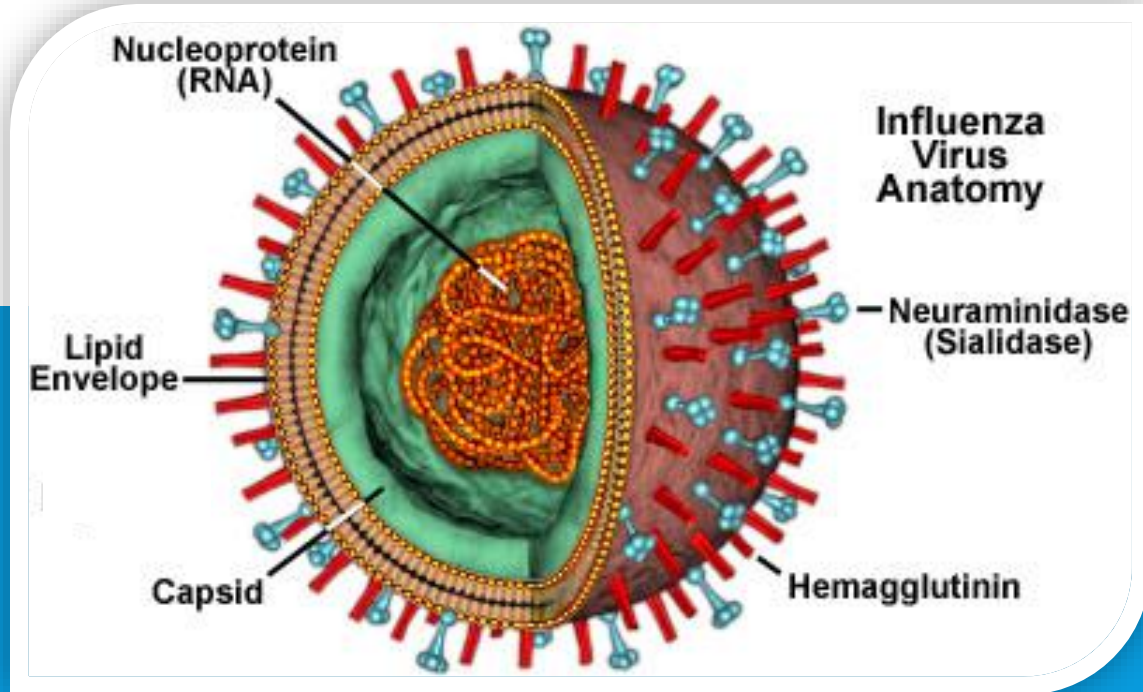


Definition

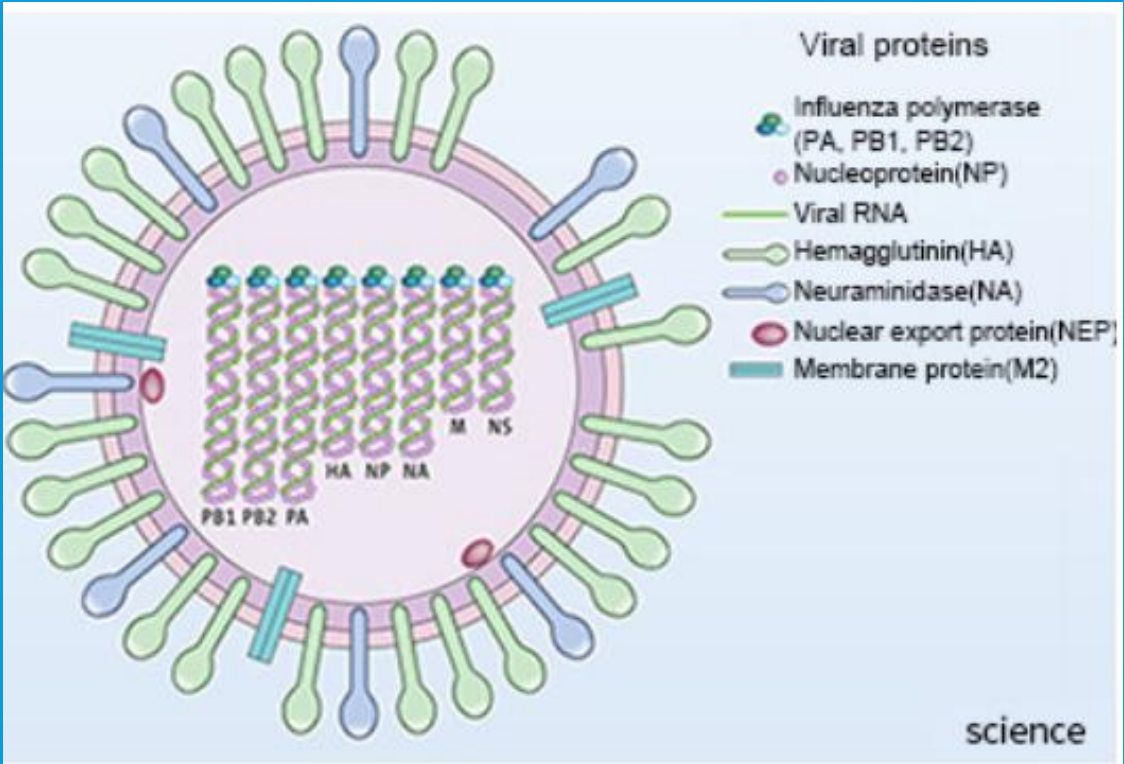
Influenza is an acute, highly contagious infectious disease caused by **influenza viruses type A, B and C**. Although the respiratory tract is the primary and main site of infection, the clinical picture of influenza is not dominated by respiratory symptoms, but rather by general infectious symptoms resulting from severe toxemia.

Thus, influenza is a local-respiratory disease accompanied by general intoxication of the body.

Etiology

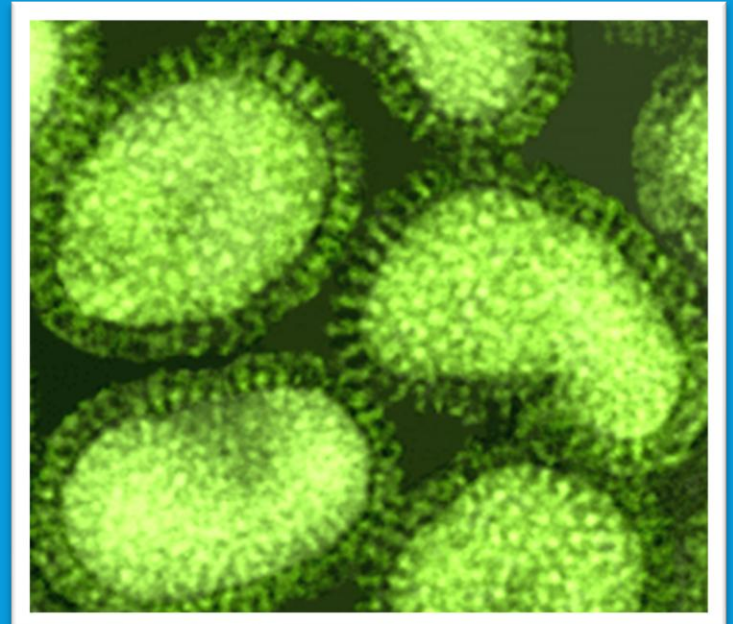
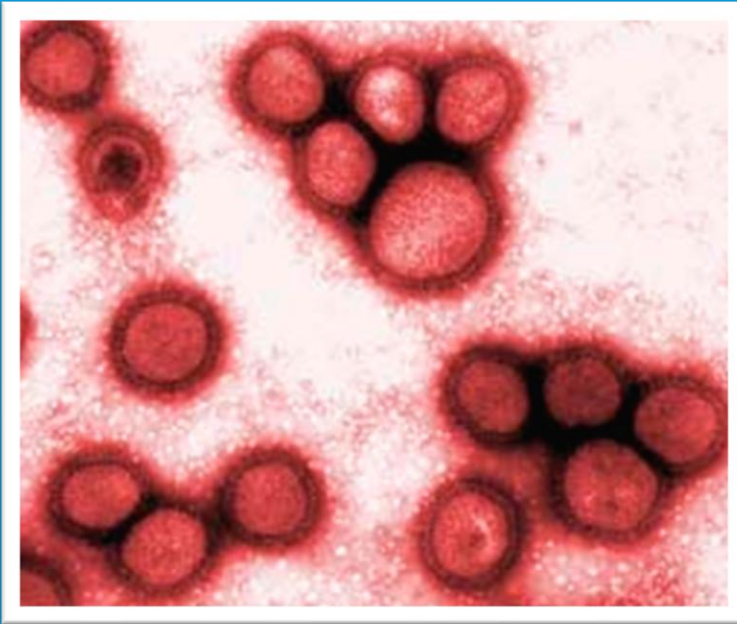


- Influenza viruses are enveloped, single-stranded ribonucleic acid (RNA) viruses of the family Orthomyxoviridae. The viruses are classified as type A, B, or C and subtyped based on differences in the surface hemagglutinin (H) and neuraminidase (N) glycoproteins.
- External viral antigens (hemagglutinin and neuraminidase) are highly susceptible to structural (antigenic) changes, which explains the emergence of a large number of subtypes (variants) of influenza viruses. There is no cross-immunity between individual types and subtypes of influenza viruses.

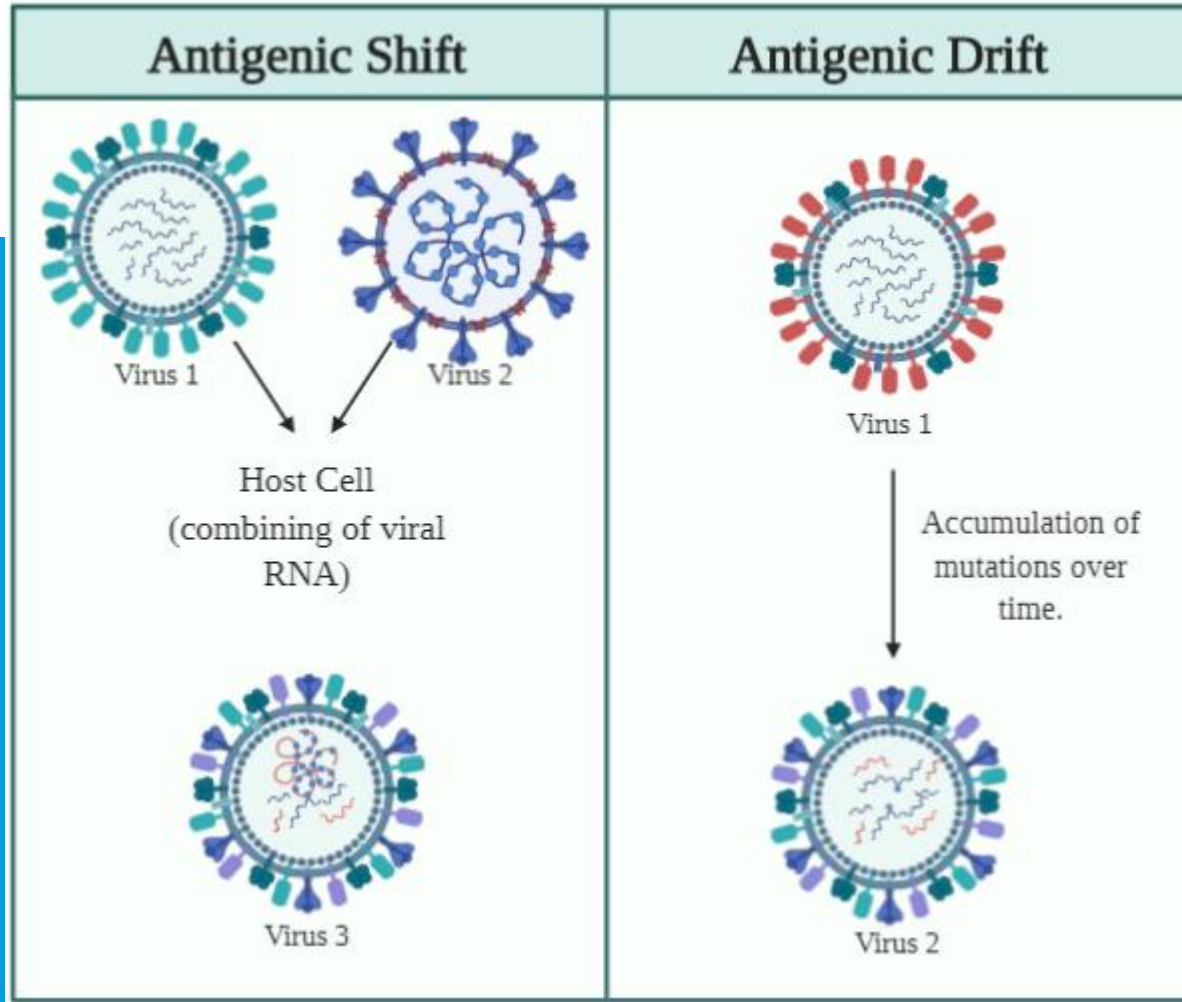


- The viruses that circulate among human populations are influenza A (H1N1 and H3N2) and B viruses
- Occasional infection and global spread in human populations occurs with avian and swine influenza viruses, including the highly pathogenic avian influenza A (H5N1 and H7N9) and the swine influenza A (H1N1, H1N2, and H3N2)

*The appearance of the influenza virus under an
electron microscope*



Influenza virus variation



The influenza virus must develop ways to evade a person's immune system

Antigenic drift involves continual small changes or mutations to a virus's surface antigens

Antigenic shift is a major, abrupt change in one or both surface antigens

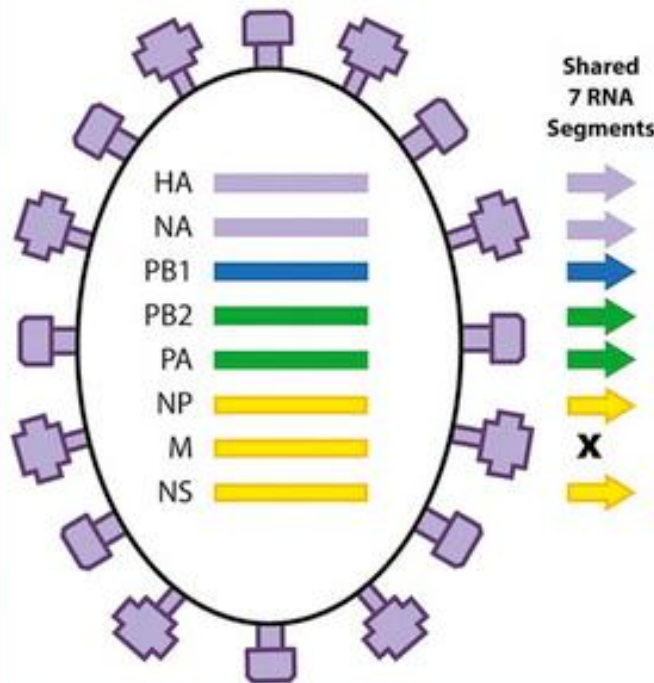
Viruses do this through evolutionary processes called antigenic drift and antigenic shift. Influenza type A viruses undergo both kinds of changes, while influenza type B and C viruses change only by the gradual process of antigenic drift.

The human cases of swine-origin H3N2 influenza in Indiana and Pennsylvania resulted from existing influenza viruses exchanging genetic material through a process called "reassortment"

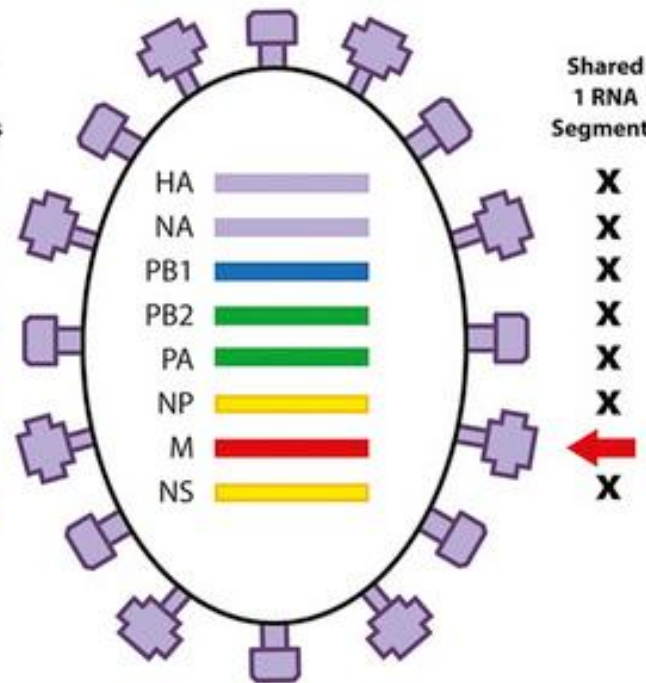
(Influenza A viruses have 8 RNA segments: HA, NA, PB1, PB2, PA, NP, M, NS)

1998-2011

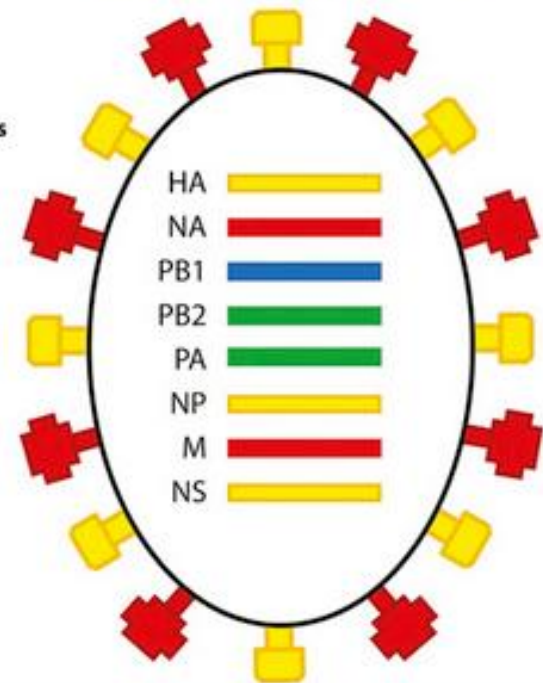
Swine H3N2 triple reassortant viruses



2011 human cases of
swine-origin H3N2 influenza in
Indiana and Pennsylvania



Pandemic 2009 H1N1 viruses



Hemagglutinin (HA) protein*



Neuraminidase (NA) protein*



RNA segments shared between viruses



RNA segments not shared between viruses



Human origin HA and NA (antigenically and genetically different from those of current human H3N2 viruses)



Human PB1



Avian - North American



Classical swine - North American



Swine - Eurasian

The human cases of swine-origin H3N2 influenza in Indiana and Pennsylvania contain the "M" RNA segment from the 2009 H1N1 virus and 7 RNA segments from swine H3N2 triple-reassortant viruses.

* The RNA segments for HA and NA determine the structure of the HA and NA proteins on the surface of influenza viruses.

Epidemiology

- Cosmopolitan disease,
- Source of infection is human (contagious in the first 2-3 days of illness),
- Routes of infection spread: droplet (most common), contact (less common),
- Occurs in epidemics (every 2-3 years) or pandemics (every 10–40 years),
- Immunity is short-lived and type-specific (primarily based on secretory antibodies of the IgA class located on the surface of the mucosa).

H1, H3, H4, H5,
H7, H10, and H13



- Receptor binding specificity
- Acid Stability
- Mammalian adaptive mutations



H1-H13, N1-N9

H1-H13, N1-N9



- Receptor binding specificity
- Acid Stability

H3-H7, H9

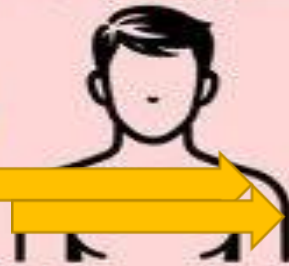
H1N1, H1N2, H3N2



- Receptor binding specificity
- Mammalian adaptive mutations

H1 and H3

H1N1, H3N2, (H2N2)



H5N1



- Mammalian adaptive mutations

H1, H3, H5,
H9, and H10

H3, H5, H8,
H7, H9, and H11

H3N2



- Receptor binding specificity
- Acid stability
- Mammalian adaptive mutations

H5N1



- Mammalian adaptive mutations

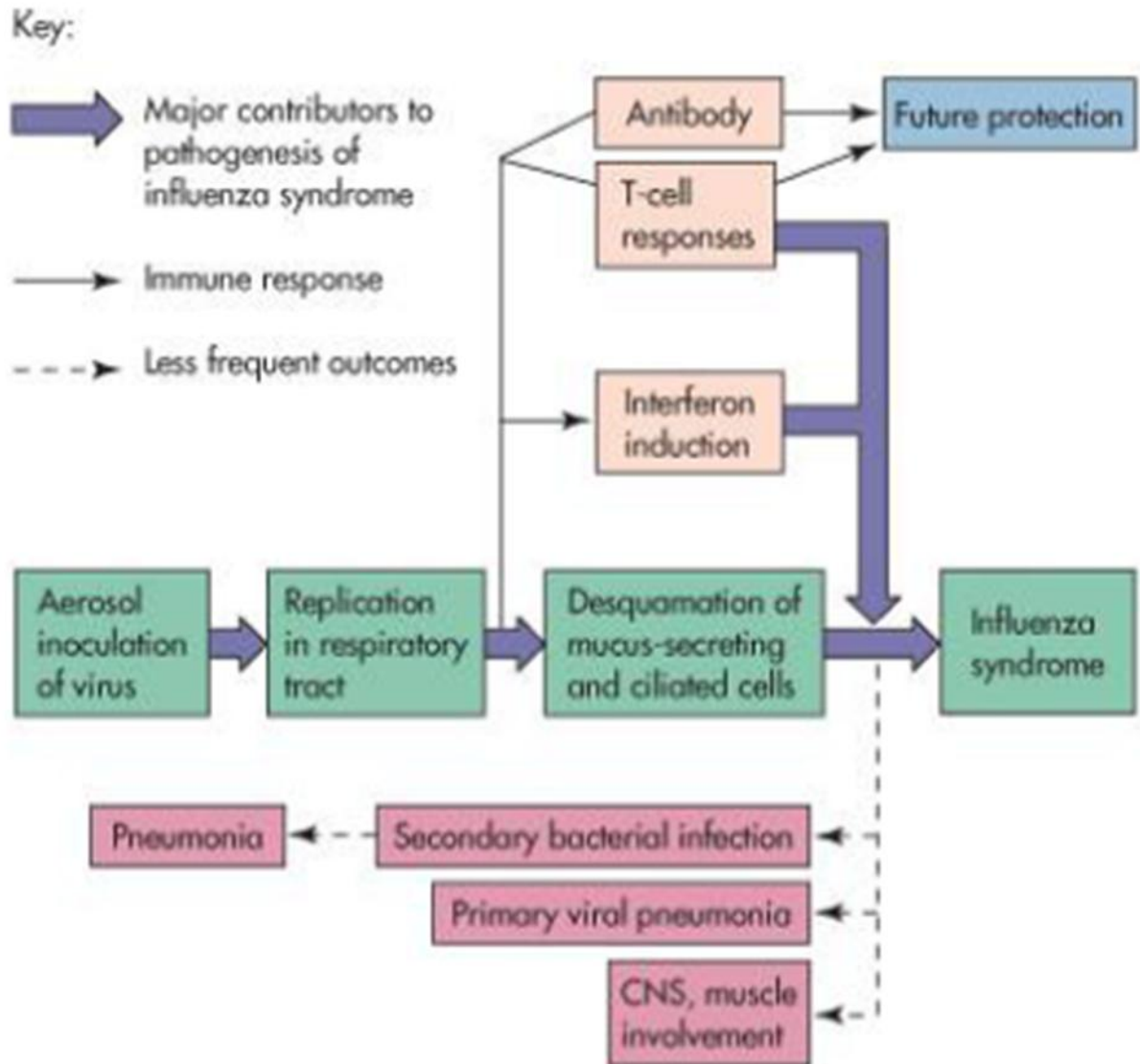


- Receptor binding specificity
- Mammalian adaptive mutations

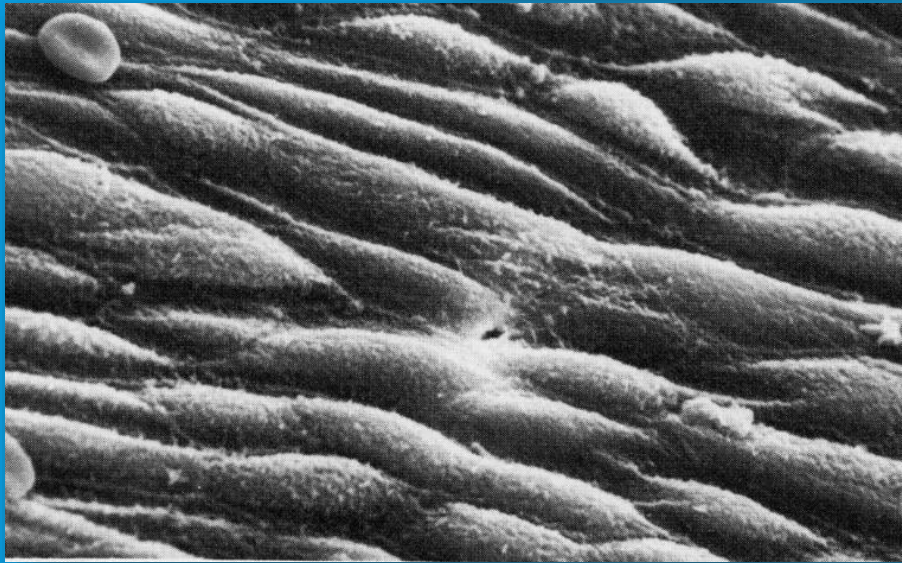
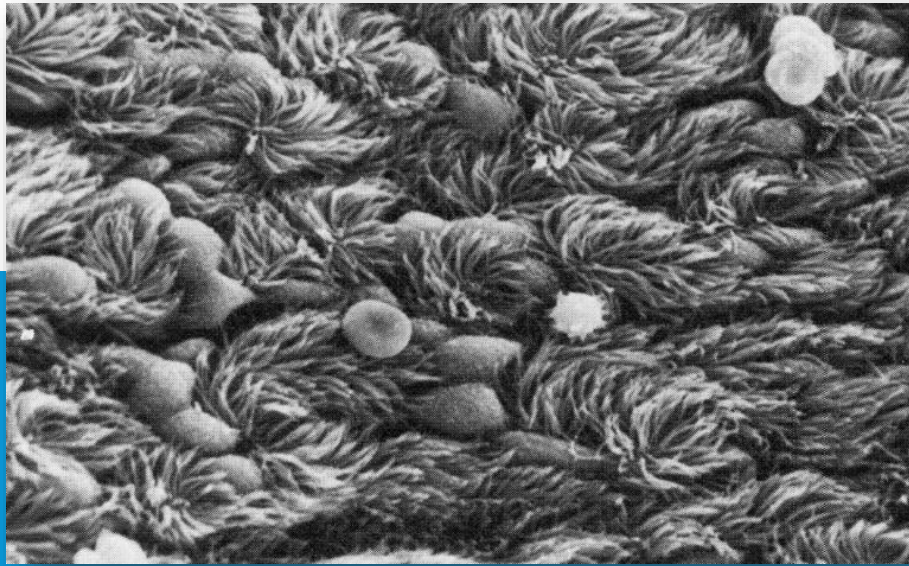
Pathogenesis

The entry point of infection is the mucous membrane of the respiratory tract (upper and middle segments of the respiratory tract)

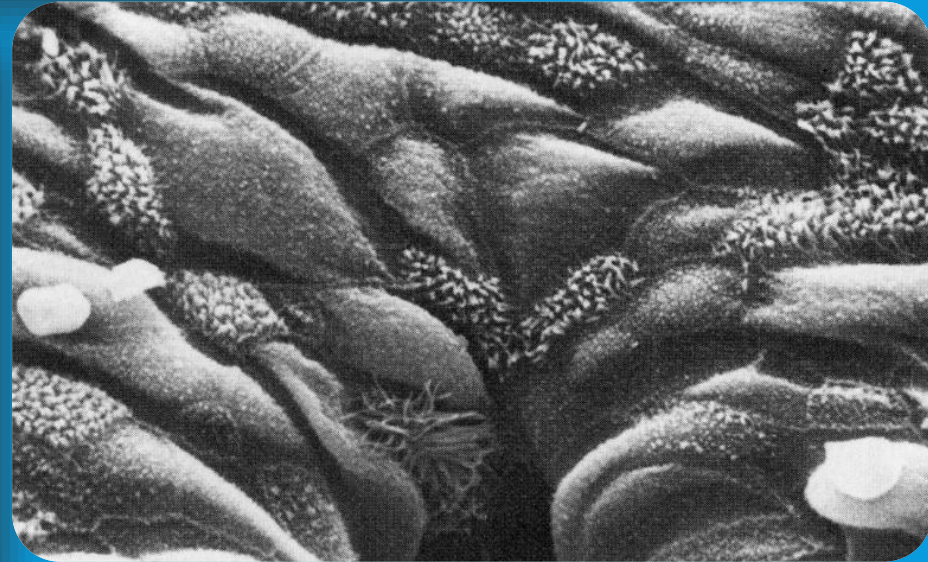
Influenza pathogenesis



NORMAL TRACHEAL MUCOSA



3 DAYS POST-INFECTION



7 DAYS POST-INFECTION

Pathogenesis

- The infection remains localized to the respiratory tract mucosa (no viremia!),
- Systemic manifestations of the disease (t°, headache, myalgia, ...) **are a consequence of the secretion of some cytokines (TNF- α , IL-6)**
- Influenza viruses depress the phagocytic function of polynuclear cells and macrophages,
- Due to necrosis and desquamation of the ciliary epithelium and depression (reduced) function of polynuclear cells and macrophages, the defense function of the respiratory tract is significantly impaired, i.e. favorable conditions are created for the development of secondary bacterial infection of the respiratory tract,
- Accordingly, in the pathogenesis of influenza we distinguish two phases: the initial (viral) and the later (bacterial) which follows it

Clinical picture

- Incubation - 1-3 days,
- The disease begins abruptly with general infectious symptoms: high fever up to 40 °C, headache, myalgia, arthralgia, anorexia,
- Somewhat later, respiratory symptoms appear: stuffy nose, watery eyes, mild sore throat, hoarseness and dry cough,
- Physical findings: fever, pale skin, weakness to prostration. The mucous membrane of the pharynx is hyperemic and edematous. Bronchitic findings in the lungs,
- The flu usually lasts 5-7 days.

Complication

Pulmonary complications (pneumonia)

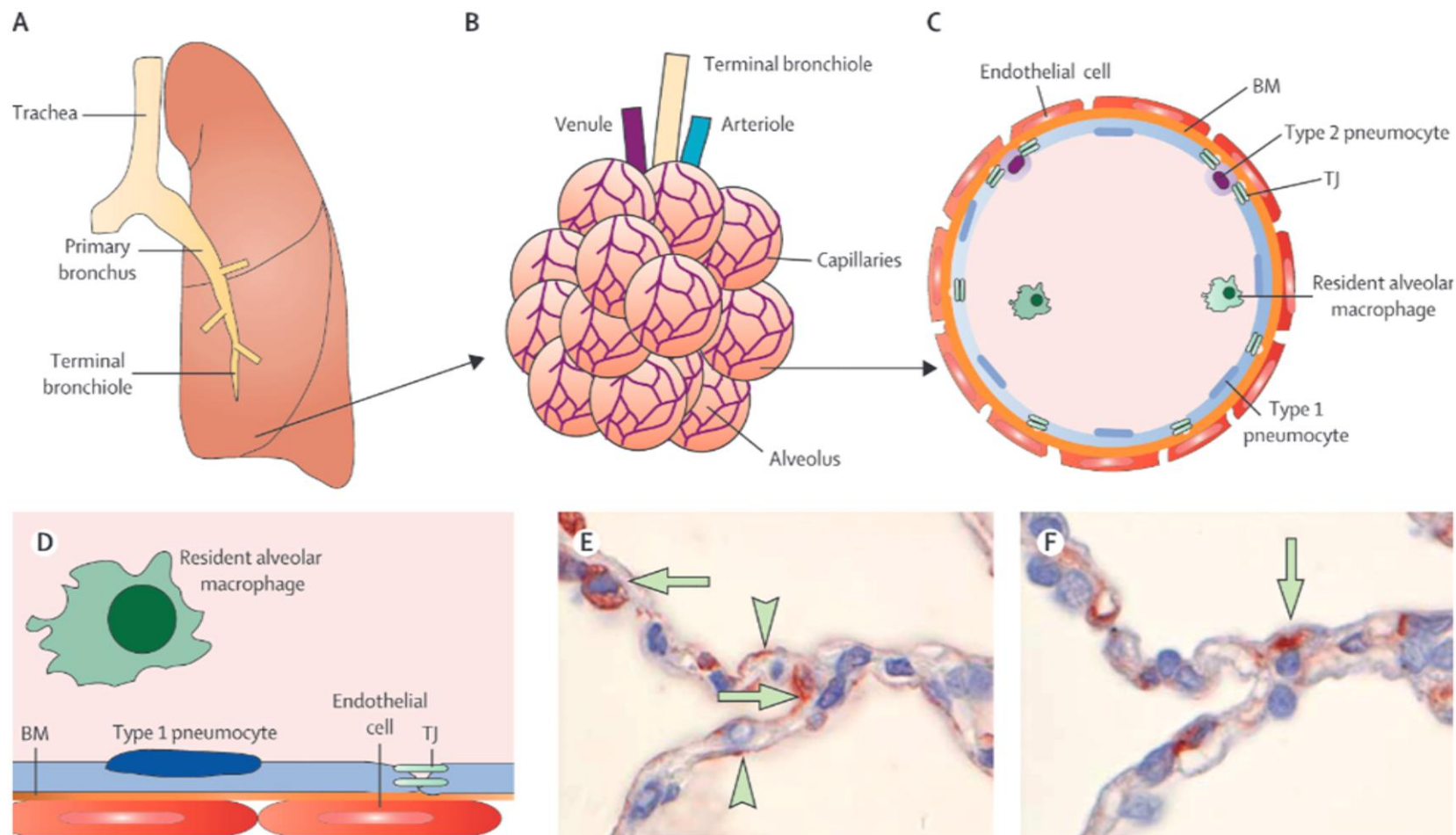
- Primary influenza pneumonia
- Secondary bacterial pneumonia (“post-influenza”)
- Combined viral-bacterial pneumonia

Primary influenza pneumonias

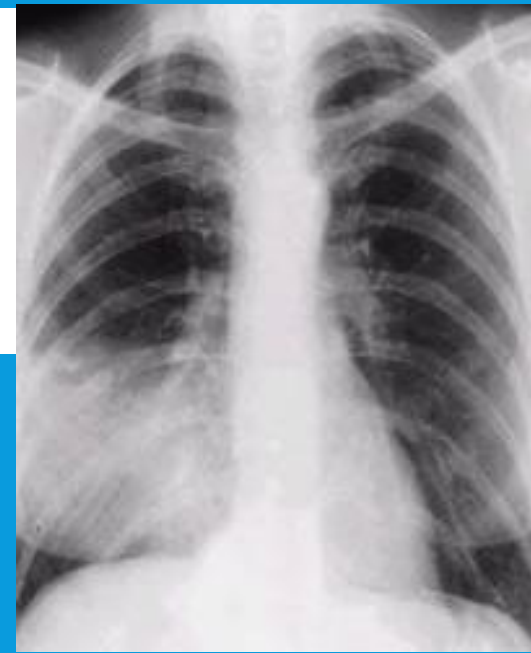


- Causative agent: influenza virus
- Most commonly occurs in people with rheumatic heart disease, pregnant women and immunodeficient people
- Occurs early (1 or 2 days of illness): with worsening of general symptoms, cough, dyspnea and cyanosis occur
- ARDS with a lethal outcome is also possible
- **Physical findings on the lungs:** mass of high-pitched or low-pitched wheezes without signs of pulmonary condensation
- **Radiological:** extensive, bilateral interstitial infiltrates

Among the first cells that influenza virus encounters after entering the alveolus are epithelial cells, either type 1 or type 2 pneumocytes

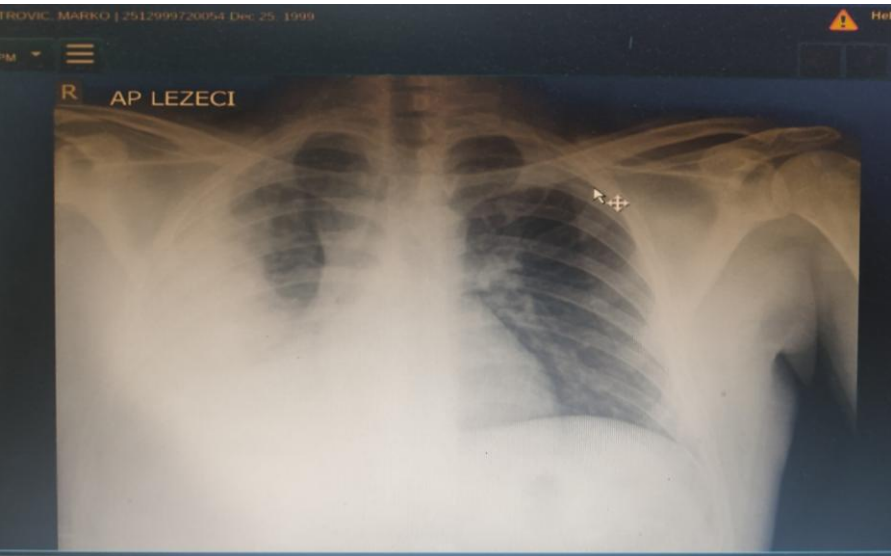


“Post-influenza” pneumonia

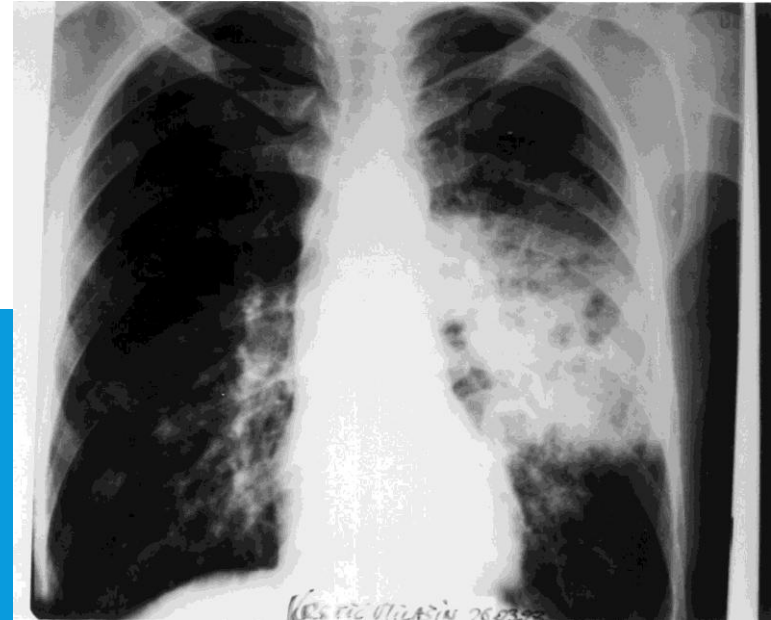


- They are caused by bacteria (secondary bacterial infection),
- They occur later, in the convalescent stage of influenza,
- They present clinically and radiologically as lobar (croupous) pneumonia,
- They most often occur in the elderly, heart patients, patients with metabolic diseases, patients with COPD and immunodeficient individuals.

"POST-INFLUENZA" PNEUMONIA



Combined viral-bacterial pneumonias



- They are caused by the combined action of the influenza virus and bacteria
- They occur early, in the acute phase of the disease: general symptoms are more severe, and respiratory symptoms and signs are pronounced from the beginning of the disease
- They are often complicated by abscess, gangrene and empyema of the lung

Extrapulmonary complications

- Otitis media
- Sinusitis
- Myocarditis
- Encephalitis
- Reye's syndrome
- Guillian-Barre syndrome

Diagnosis

- Clinical picture,
- Epidemiological data,
- Blood count nonspecific.

Etiological diagnosis

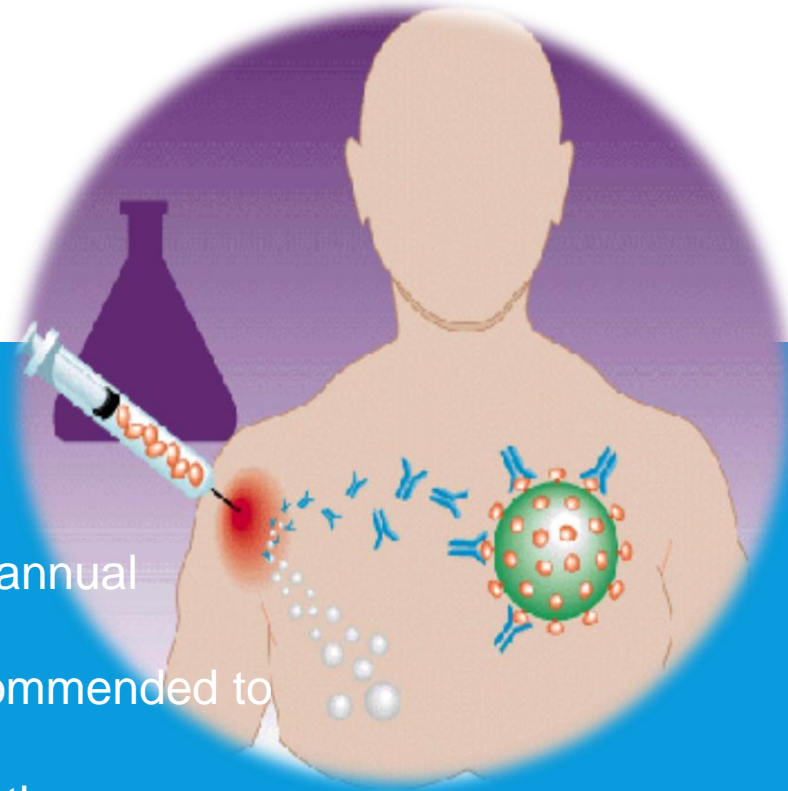
- Virus isolation from nasopharyngeal secretions or sputum (cultivation)
- Serological reactions (RVK, RIH, ELISA, RIA)
- Molecular diagnostics (PCR)

Diagnostic Tests for Viral Infections

Respiratory syncytial virus infection	Tracheal aspirate or bronchial alveolar lavage for viral culture, antigen testing by ELISA and fluorescein conjugate monoclonal or polyclonal antibody, RT-PCR
Parainfluenza	Nasal and bronchial secretions for viral culture and immunofluorescent assays, RT-PCR Serum for complement fixation and hemagglutination
Influenza	Respiratory secretions for viral cultures and immunofluorescent and ELISA assays, RT-PCR
Adenovirus infection	Respiratory secretions for viral culture, complement fixation, hemagglutination inhibition, and neutralization, PCR
Rhinovirus/Enterovirus	Respiratory secretions for viral culture, PCR
Coronavirus	Respiratory secretions for viral culture, PCR

ELISA, Enzyme-linked immunosorbent assay; *RT-PCR*, reverse transcription–polymerase chain reaction.

Prophylaxis



- The most effective means of prevention is with annual influenza vaccination
- All persons older than 6 months of age are recommended to have annual seasonal influenza vaccination
- Several vaccine formulations are available with the considerations being quadrivalent versus trivalent (most are quadrivalent now), intranasal live attenuated versus intramuscular recombinant or inactivated, high dose versus standard dose
- These vaccines contain the three or four virus strains that are projected to be responsible for the annual epidemic.
- Vaccination is usually effective from about 2 weeks to 4 to 6 months postvaccination.

Therapy

- Rest in the acute phase of the disease,
- symptomatic therapy,
- Antiviral therapy (amantadine, rimantadine, zanamivir, oseltamivir),
- Antibiotherapy.



PARAINFLUENZA

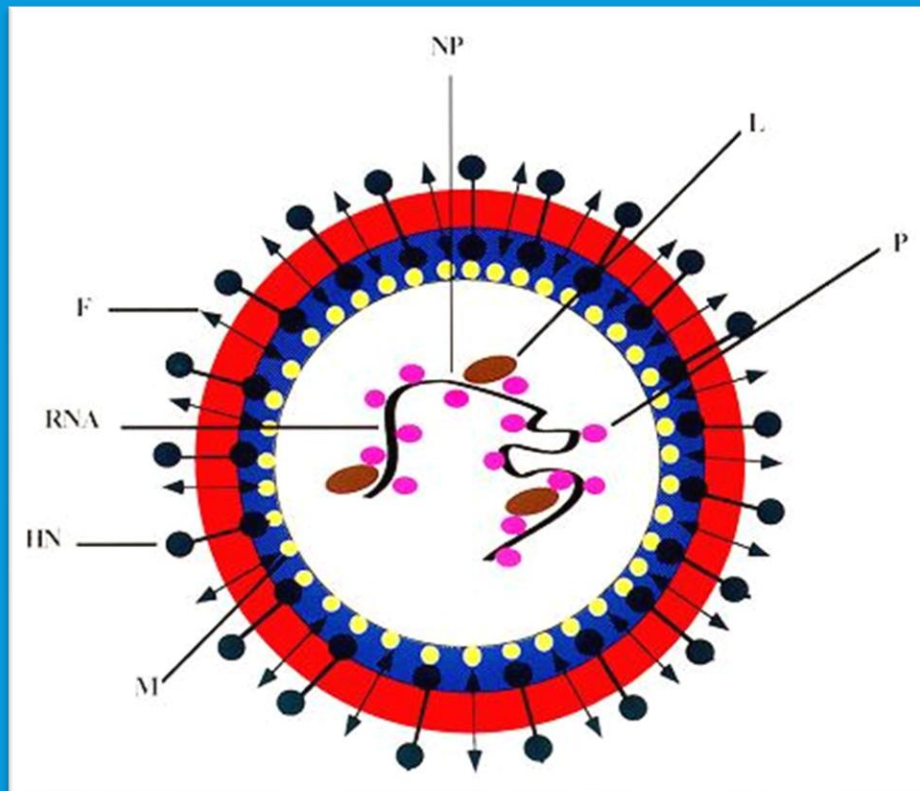
It is one of the major causes of morbidity and mortality in infants worldwide

These respiratory viruses were first observed in the late 1950s when they were isolated from children with croup and were known as croup-associated viruses



Etiology

➤ The human parainfluenza virus (HPIV) is an enveloped, negative-sense, single-stranded RNA virus that belongs to the family of Paramyxoviridae



Epidemiology

- The source of infection is human.
- droplet infections,
- They occur epidemically, most often in the winter months.

Pathogenesis

- Local respiratory disease (no viremia),
- Specific IgE immunoglobulins play an important role in the pathogenesis of croup.

Clinical picture

Type of virus	Age	Clinical manifestations of primary infection
Parainfluenza 1 i 2	8-30 months	the common cold croup bronchitis
Parainfluenza 3	4-24 months	croup pneumonia bronchiolitis
Parainfluenza 4	under 6 years old	a cold bronchitis

Diagnosis

- Virus isolation from nasopharyngeal secretions or sputum (cultivation)
- Serological reactions
- Molecular diagnostics (PCR)

Therapy

- Symptomatic,
- Causal (ribavirin)

Prevention

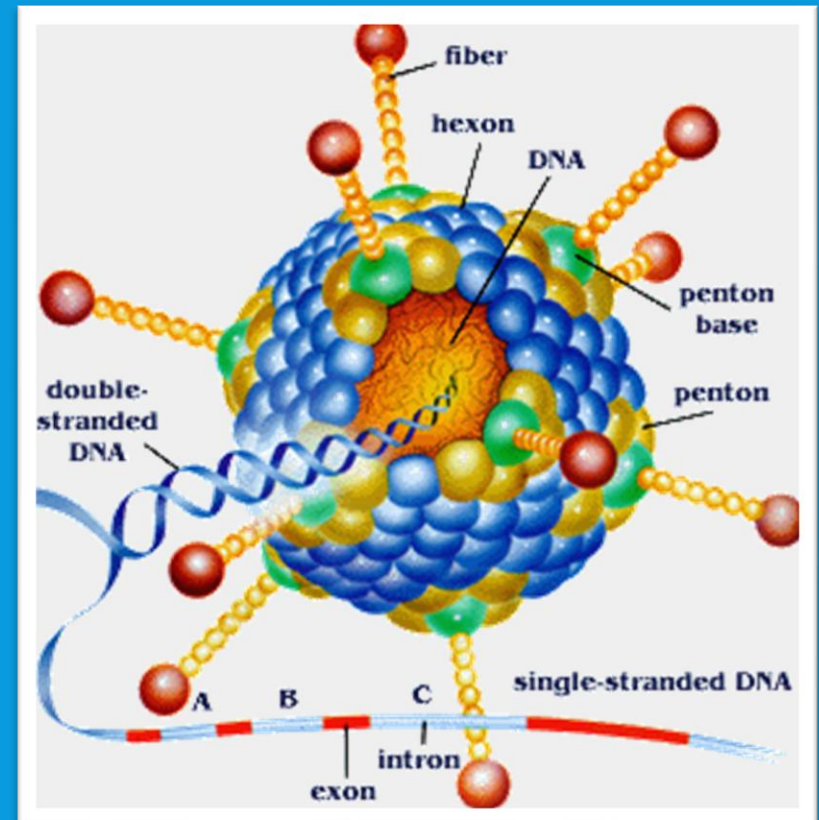
- Live (attenuated) vaccine against parainfluenza 3 virus.

ADENOVIRUS INFECTIONS

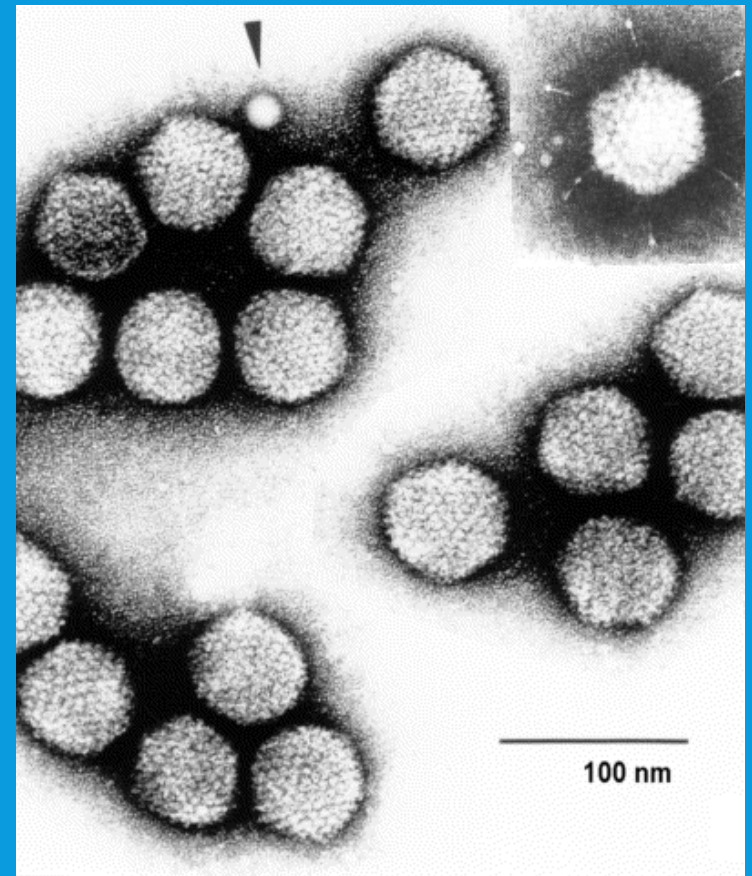
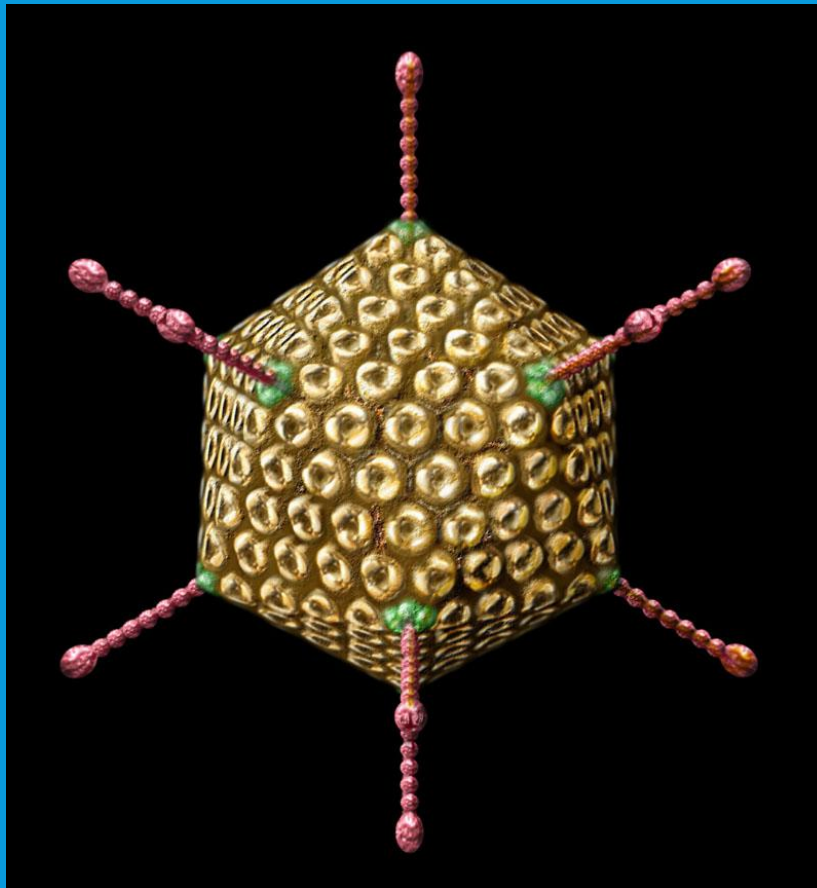


Etiology

- Adenoviruses (DNA viruses) - 49 serotypes,
- Affinity to adenoid tissue (lymphatic tissue),
- They have oncogenic properties



Adenovirus appearance and structure



Epidemiology

- The source of infection is a sick person (contagiousness lasts up to 25 days),
- **Transmission path:**
 - ✓ droplet (entry site respiratory mucosa),
 - ✓ through pool water (conjunctiva) and
 - ✓ fecal-oral (mucous membrane of the gastrointestinal tract).

Pathogenesis

- Adenoviruses multiply in epithelial cells of the mucosa, accompanying lymph follicles and regional lymph glands,
- After the primary infection, they can persist for a long time in the adenoid tissue in a latent state,
- Later, latent infection may reactivate (during pertussis or rash),
- Generalized adeno-infections are common in immunodeficient persons.

Clinical manifestations of adenovirus infections

Age	Syndromes	Adenovirus serological type
Small children	Nasopharyngitis	1, 2, 5
Children	Febrile respirat. Qatar Pharyngoconjunctival fever Hemorrhagic cystitis Diarrhea Meningoencephalitis Intussusception	1, 2, 4 - 6 3, 7 11, 21 2, 3, 5, 40, 41 2, 6, 7, 12 1, 2, 4, 5
Adults	Epidemic keratoconjunctivitis	8, 19, 37
Immunodeficient sick people	Hepatitis Pneumonia CNS infections	34, 35, 39 7, 12, 32

Epidemic keratoconjunctivitis



Diagnosis

- Isolation of the causative agent from biological material (by cultivation),
- Detection of viral antigens in biological material (IF, RIA, ELISA),
- Serological reactions (RVK, RIH, ELISA)
- Molecular diagnostics (PCR)

Therapy

- symptomatic,
- Ribavirin and cidofovir (in immunodeficient persons).

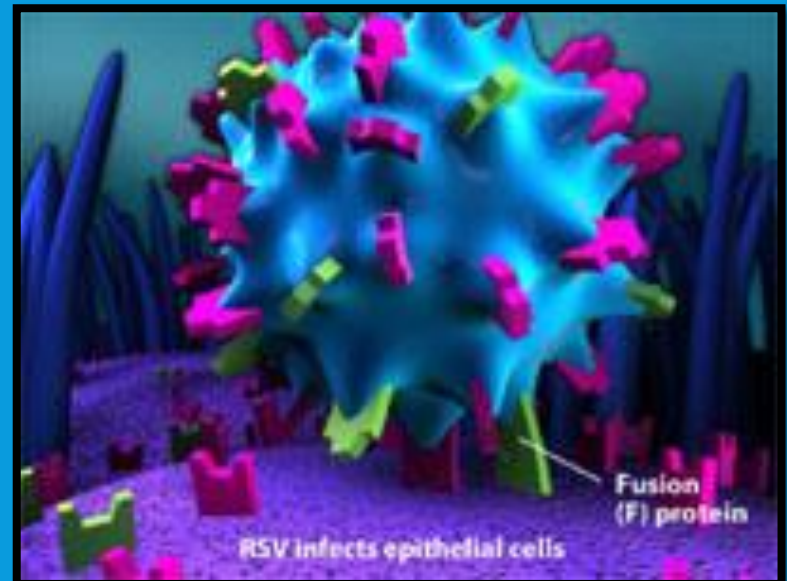
RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTIONS

RSV is an enveloped, single-stranded RNA virus of the Pneumoviridae family
RSV is the most common cause of lower respiratory tract infections in infants and children, although infection in adults is possible



Etiology and epidemiology

- RSV (RNA, A i B),
- Premature infants and children with bronchopulmonary dysplasia, congenital heart disease, and immunodeficiency are at greatest risk
- There is no geographic predilection for infection
- With the presence of pneumonia, the death rate is reported to range from 11% to 78%



Respiratory diseases in children caused by RSV

Syndromes	Frequency %
Bronchiolitis	43-90
Pneumonia	5-40
Tracheobronchitis	10-30
Croup	3-10

Diagnosis

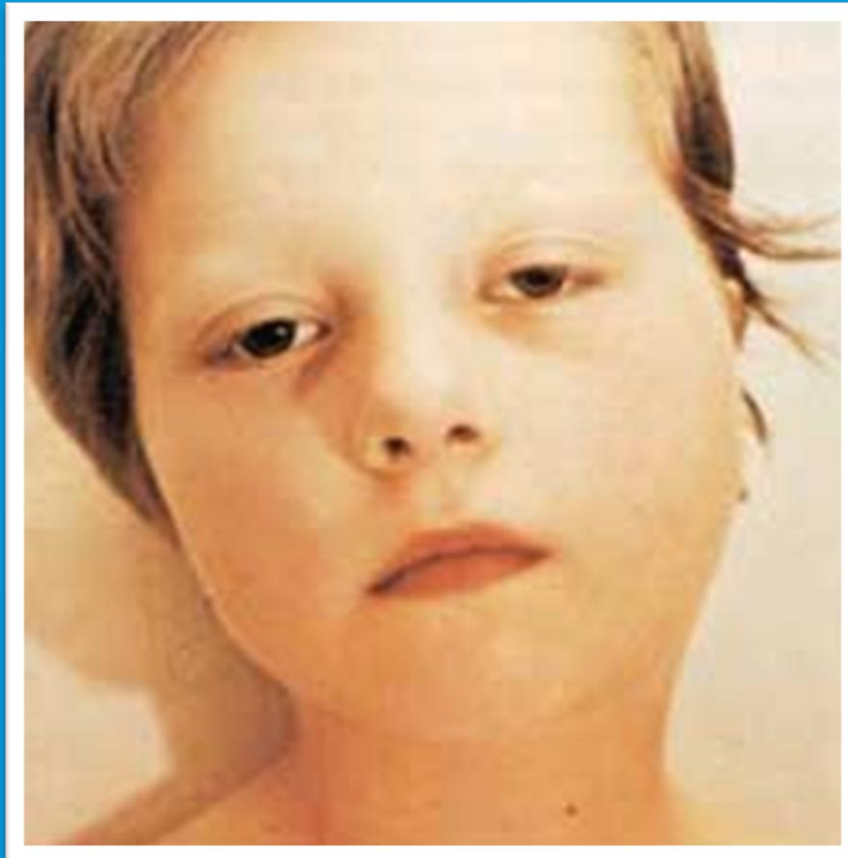
- Identification of viruses in respiratory secretions (electron microscopy)
- Detection of viral antigens in respiratory secretions (RIA and ELISA),
- Serological reactions (RVK, TN)
- Molecular diagnostics (PCR)

Therapy

- symptomatic,
- Aerosolized ribavirin and palivizumab



MUMPS (PAROTITIS EPIDEMICA, MUMPS)

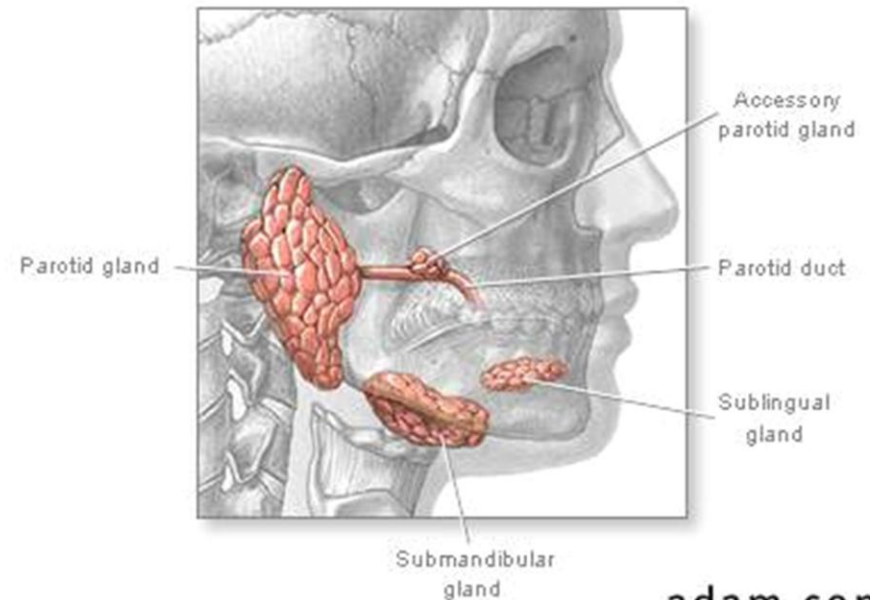
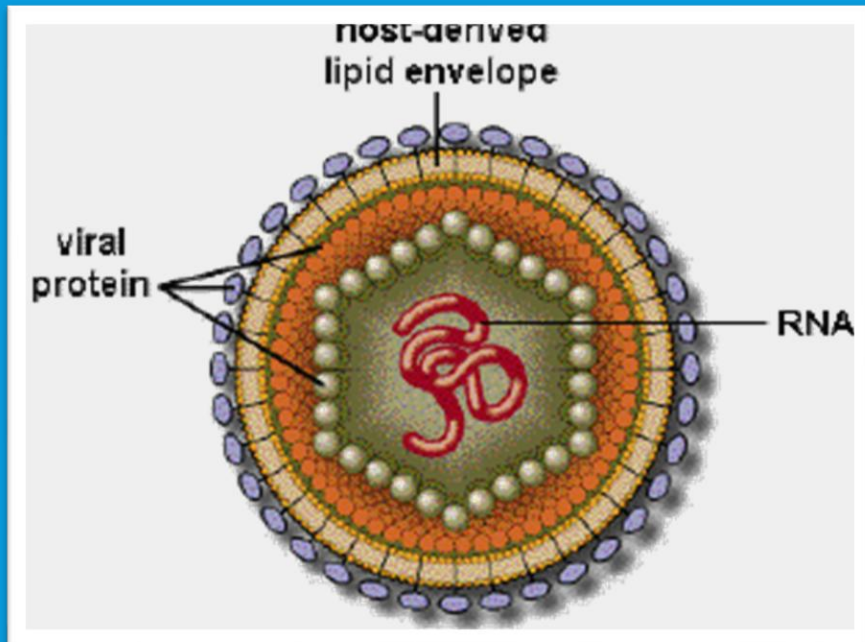


Definition

Mumps is an acute infectious disease of viral etiology that is clinically characterized by inflammation of the salivary glands and sometimes other organs.

Etiology

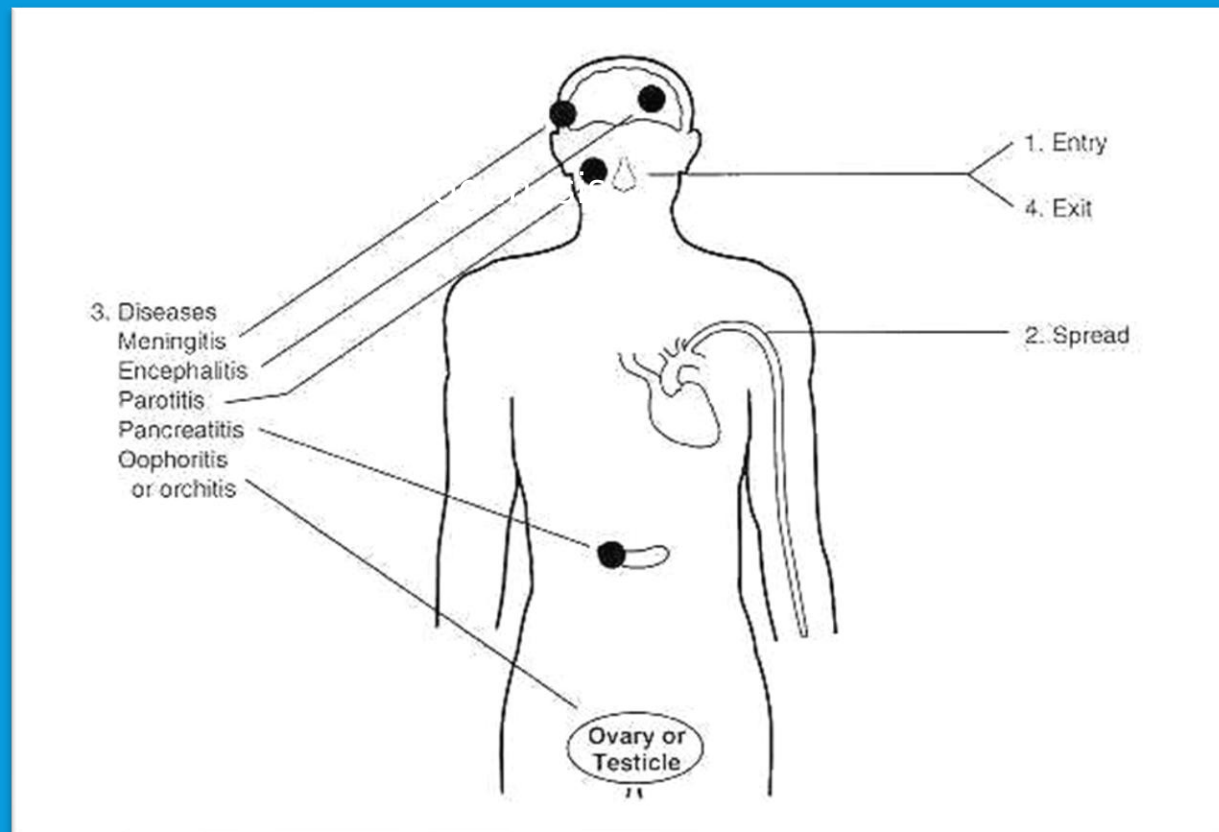
- Mumps virus (Paramyxoviridae),
- Affinity: salivary glands, brain, meninges, testes, ovaries, pancreas.



adam.com

Pathogenesis

- Nasopharynx or salivary glands → blood → target organs.



Epidemiology

- Source of infection: the patient (infected from the end of incubation until there is parotid swelling),
- Route of spread: droplet,
- The disease occurs sporadically or in epidemics (spring and winter),
- Children aged 5-15 are most often affected.
- The contagion index is 30-50%.

Clinical picture

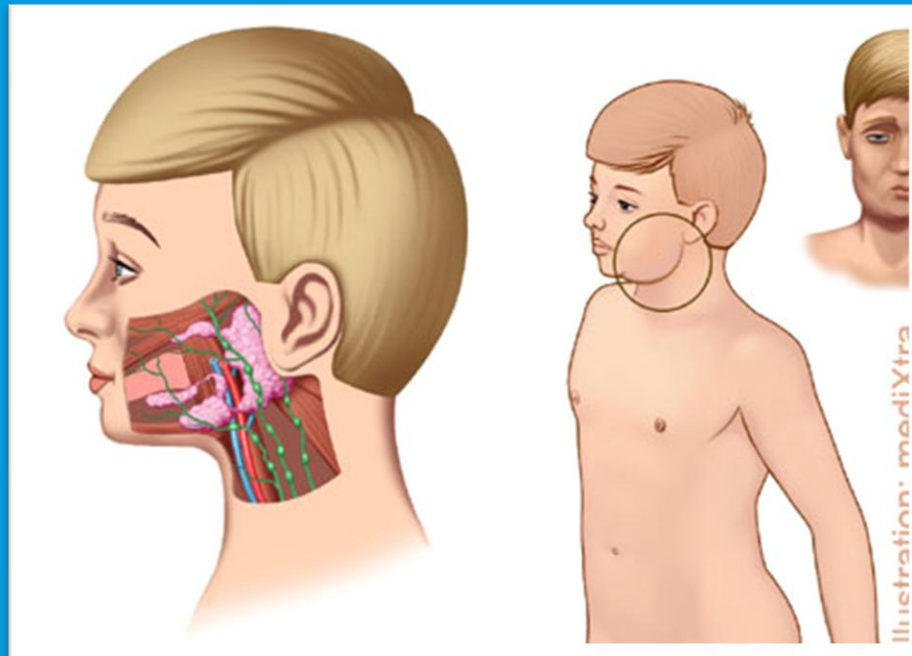
- In 1/3 of infected mumps, the infection proceeds inapparently,
- In 2/3 of those infected, it is clinically manifest.

Frequency of clinical manifestations of mumps infections

Clinical manifestations	Frequency %
Parotitis	60 – 70%
Infection of the submandibular and/or sublingual salivary glands	10%
Epididymorrhitis	25% (након пубертета)
Oophoritis	5% (након пубертета)
Meningitis	1 – 10%
Encephalitis	0,02%
Transient hearing loss	4%
Pancreatitis	7%

Epidemic parotitis

- Incubation: 14-21 days
- The disease begins gradually with optimal symptoms of infection, after 1-2 days swelling of one and soon the other parotid gland appears (the swelling is pale, vaguely limited, elastic, easily sensitive).



Swelling in the area of the parotid lobes

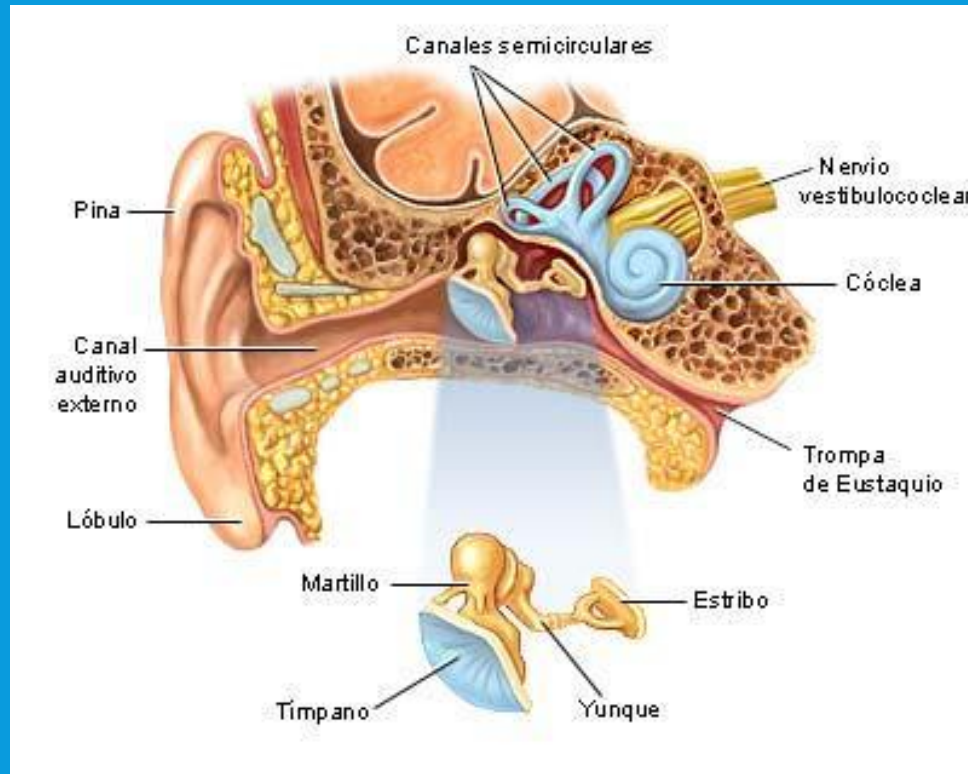


Mumps: Note the bilateral parotid and submandibular gland enlargement.



Complication

- Deafness (damage to the acoustic nerve or organ of Corti).



Diagnosis

- clinical picture
- Epidemiological data
- Laboratory analyses:
leukopenia,
increased amylase activity in serum and urine,
isolation of the causative agent from cerebrospinal fluid, saliva
or urine (not a routine diagnosis)
- serological reactions (ELISA)
- molecular diagnostics (PCR)

Therapy

➤ Symptomatic



- Prevention

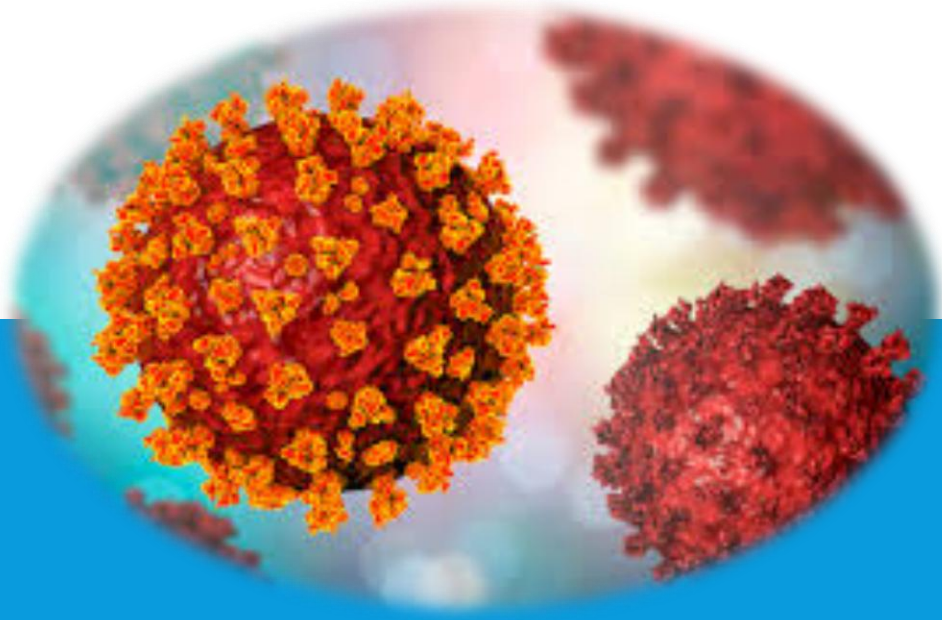
- Live (attenuated) vaccine,
- Hyperimmune mumps immunoglobulin.

COVID-19

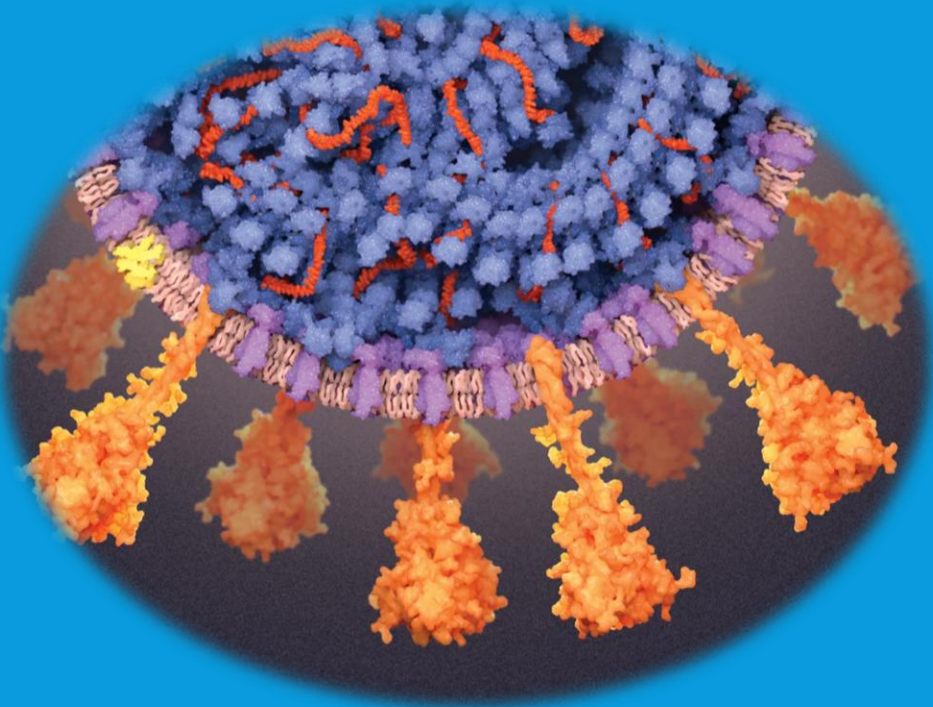


- Coronavirus disease 2019 (COVID-19) is defined as a disease caused by a novel coronavirus called acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- SARS-CoV-2 is the cause of the respiratory disease called COVID-19
- First identified amid an outbreak of respiratory disease cases in Wuhan City, Hubei Province, China



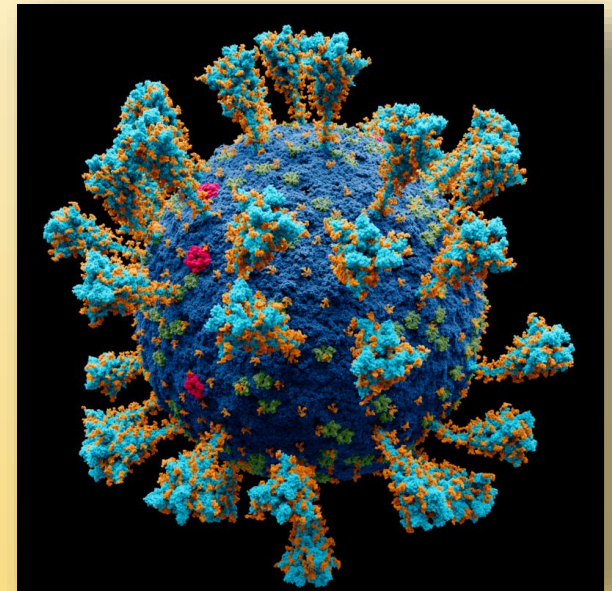


- SARS-CoV-2 has rapidly spread throughout the world on a scale not seen since the 1918 influenza pandemic



ETIOLOGY OF SARS-COV-2

- SARS-CoV-2 is a strain of the Betacoronavirus species (SARSr-CoV), like SARS-CoV-1, the virus that caused the 2002–2004 SARS epidemic
- There are animal-borne coronavirus strains more closely related to SARS-CoV-2, the most famous relative being the Banal-52 coronavirus
- SARS-CoV-2 is of zoonotic origin
- Research is ongoing on whether SARS-CoV-2 came directly from bats



EPIDEMIOLOGY OF SARS-COV-2

The virus is airborne and spreads through aerosols with people in close contact with respiratory droplets

By August 11, 2024, over 775 million people worldwide have been confirmed to have COVID-19

The World Health Organization estimates that the total number of deaths directly or indirectly related to the pandemic is around 15 million

The World Health Organization - declared SARS-CoV-2 a public health emergency on January 30, 2020, and a pandemic was declared on March 11, 2020

EPIDEMIOLOGY SARS-COV-2



Transmission most likely occurs person to person via respiratory droplets passing among close contacts

One concerning feature that has contributed to community spread of SARS-CoV-2 is that transmission can occur from both asymptomatic and presymptomatic individuals. Typically those exposed develop symptoms 4 to 5 days postexposure, but the incubation period can be as long as 14 days.

Transmission of viral infection outdoors is much rarer

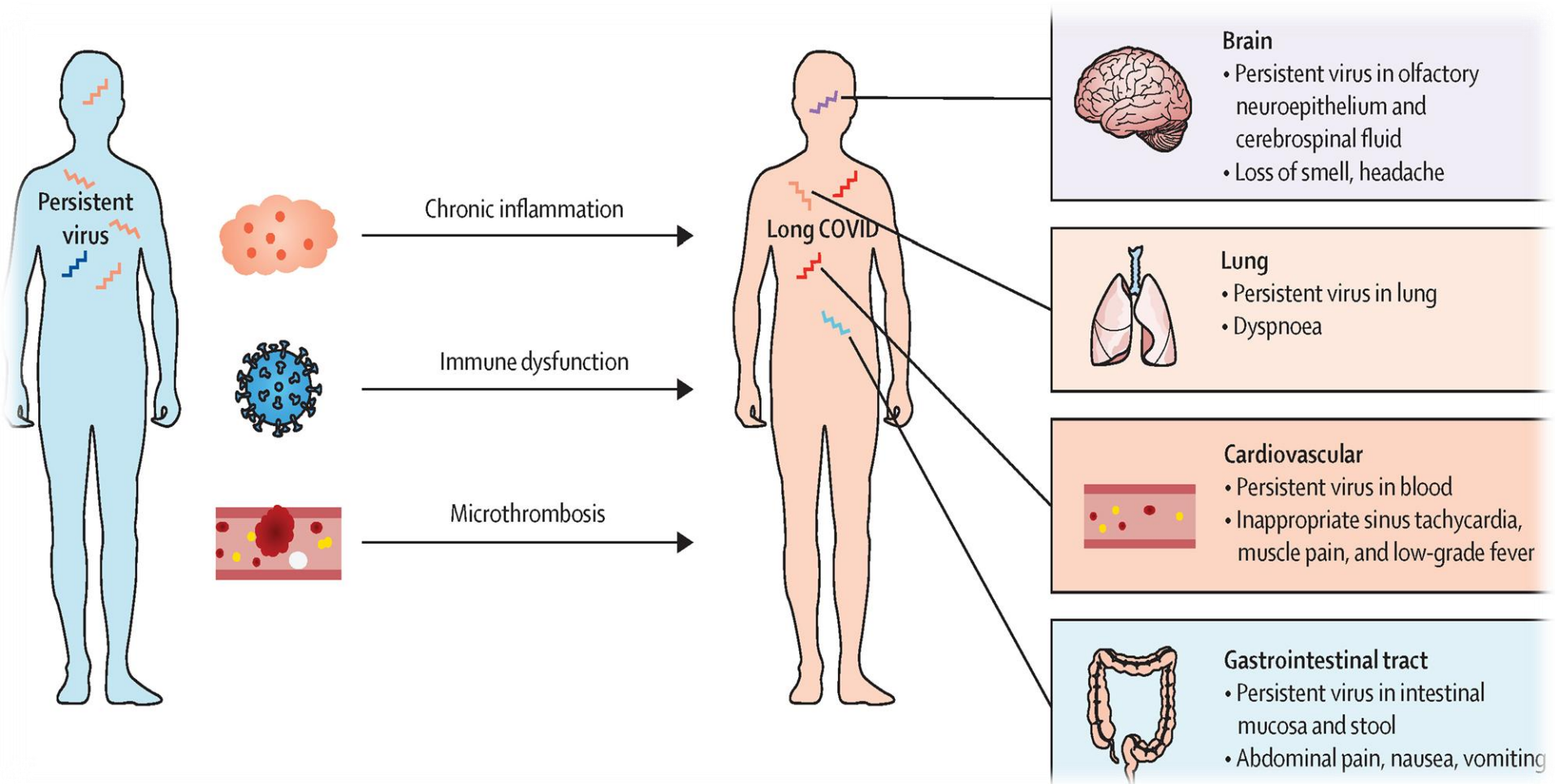
Transmission of the virus via contaminated surfaces is possible, but is not the dominant mode of transmission

PATHOGENESIS OF COVID-19

SARS-CoV-2 binds to ACE2 receptors on nasal mucosa cells, allowing the virus to enter a human cell

The virus then undergoes intracellular replication, causing the host to produce interferon and other cytokines to limit viral replication

- COVID-19 is able to evade these defenses, leading to a persistent inflammatory response that can spread the infection to other organs
- ORF 3a (open reading frame) is a viral protein of COVID-19 that plays a role in viral replication, inflammation and the immune response, contributing to the cytokine storm and cell death seen in severe cases
- Interaction between respiratory/nasal tract epithelium and endothelium may also contribute to thromboembolic events associated with COVID-19



CLINICAL MANIFESTATIONS

➤ **Pulmonology**

➤ **Cardiovascular**

➤ **Neurological**

➤ **Gastrointestinal**

➤ **Renal manifestations**

➤ **Psychiatric manifestations**



RISK FACTORS FOR SEVERE COVID-19

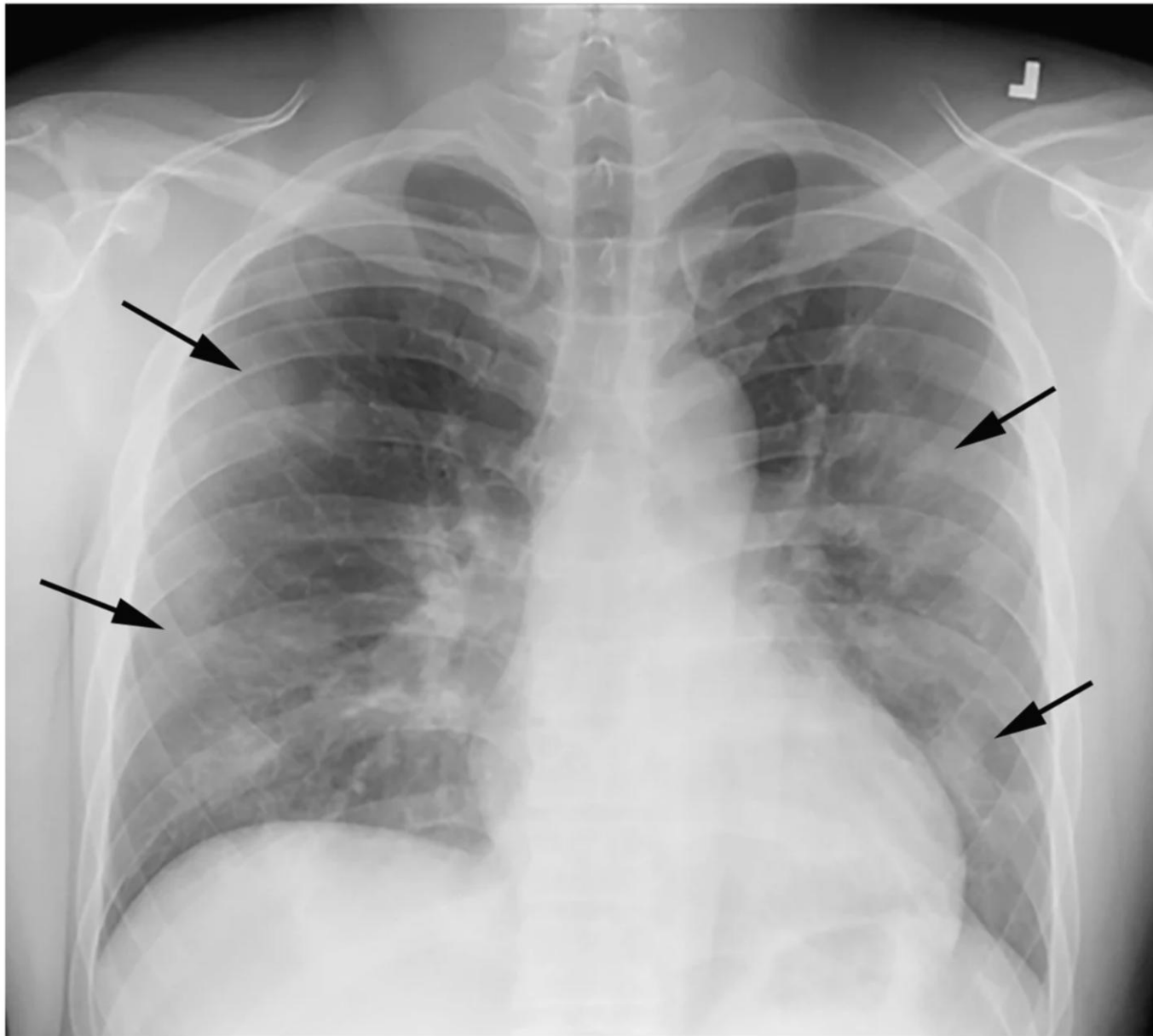
- Over 95% of deaths from COVID-19 occur in people over the age of 45, and >80% of deaths occur in people over the age of 65
- Male gender is associated with a higher risk of severe disease
- Most people who die have pre-existing comorbidities
- The risk of severe COVID-19 increases significantly with an elevated body mass index (BMI)
- Overweight (BMI >25 kg/m² but <30 kg/m²), obesity (BMI ≥30 kg/m² but <40 kg/m²)

Diagnosis

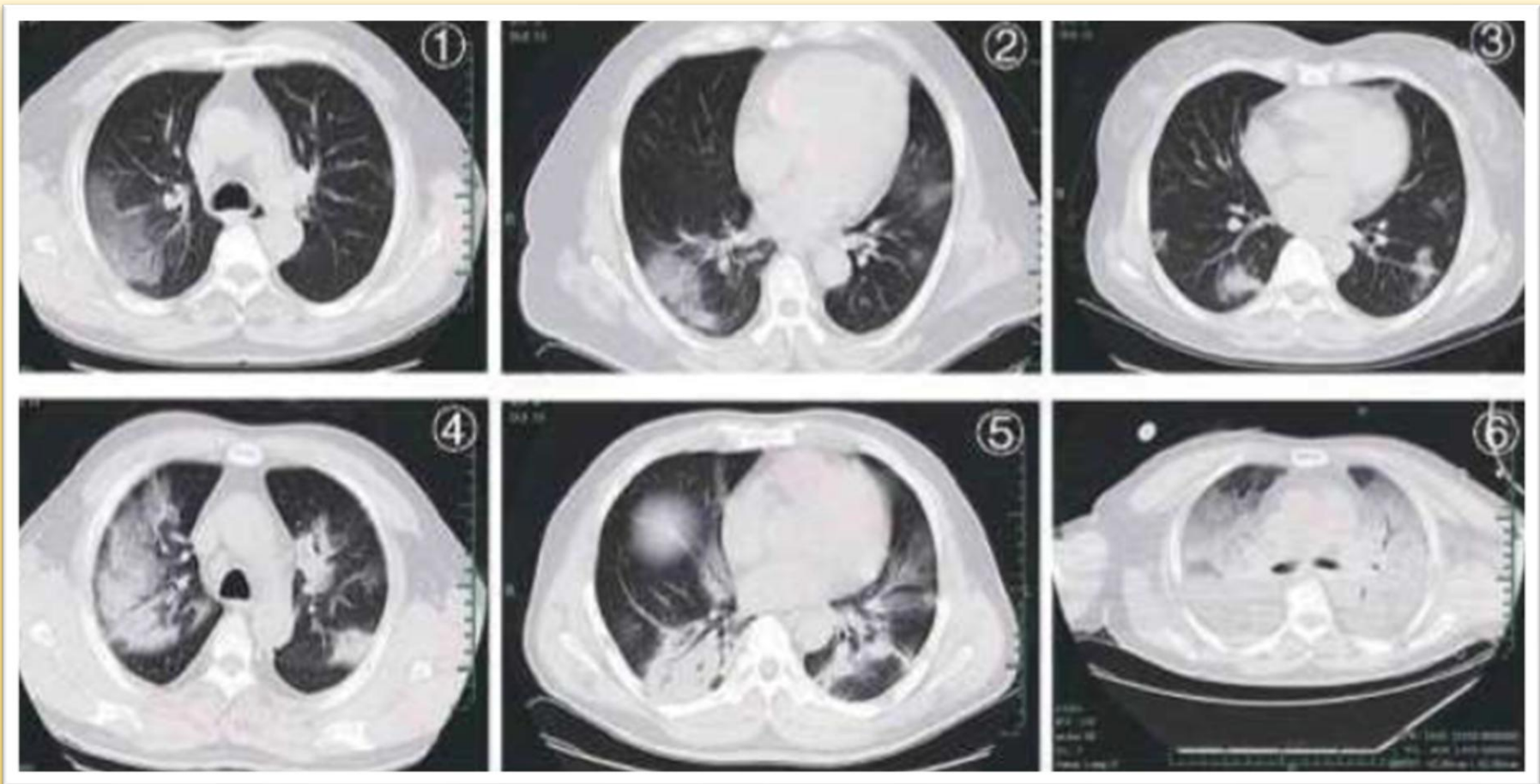
- clinical picture,
- Epidemiological data,
- Laboratory findings:
 - Leukopenia, lymphopenia, thrombocytopenia,
 - Increased activity of LDH, AST, ALT, Ferritin, D-dimer, CRP, PV

Etiological diagnosis

- Virus isolation from blood, stool, respiratory secretions (by cultivation)
- Detection of SARS-CoV-2 (PCR)
- Demonstration of specific antibodies using the IFA or ELISA method



Multiple peripheral GGO in patient - COVID-19



Typical CT findings for COVID-19:

Image 1/2: patchy ground glass opacities

Figure 3: nodules and patchy exudate

Figure 4/5: multifocal consolidated lesions

Figure 6: diffuse consolidation, "white lung"

COVID 19 THERAPY - THERAPEUTIC PROTOCOLS HAVE CHANGED IN ACCORDANCE WITH CURRENT SCIENTIFIC RESEARCH AND VIRUS STRAINS THAT HAVE CHANGED SINCE 2020 (CURRENT VERSION OF THE PROTOCOL FOR THE TREATMENT OF COVID-19 - NUMBER 13.)

- Antibiotic therapy - only in proven or probable bacterial superinfection
- Corticosteroid therapy - after the 5th day of illness
- Immunomodulatory therapy - Tocilizumab, Anakinra
- Monoclonal antibodies
- Antiviral drugs: nirmatrelvir plus ritonavir (Paxlovid), molnupiravir (Lagevrio) remdesivir (Veklury), Favipiravir
- Anticoagulant therapy
- Vitamin therapy - Vitamin C and alfacalcidol
- Immunoglobulins
- Plasma recovaesceneta

Prevention

- Patient isolation (mandatory),
- Protection of persons in contact with patients (masks, gloves),
- Vaccination

Forecast

- The case fatality rate for confirmed cases is estimated at 1%-5%

Thank you for your
attention