Acute respiratory viral infections

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• ARVI is the group of infectious diseases which includes known for a long time viruses (influenza virus) and recently discovered ones (bocavirus, metapneumovirus) that are transmitted predominantly by airway route and that damage respiratory tract mucosa.
• The highest morbidity of ARVI is seen in 6-month—3-year-old children.
• Influenza virus A is prone to mutations by mechanisms of antigenic shift and drift.
• Viremia is possible, but it plays a role in pathogenesis of only ade-noviral infection.
• The majority of diseases in immunocompetent people have spontaneous recovery.
• Effective etiologic drugs are rimantadine, oseltamivir (for influenza), ribavirin (for RS infection)
• The only indication for antibiotic prescription in ARVI is development of bacterial complications
• Vaccination prevents development of influenza
• ARVI is a group of infectious diseases caused by viruses with airborne way of transmission which are characterized by symptoms of infectious toxicosis and predominant involvement of respiratory tract mucosa.
# Etiological Structure of ARVI in Children

<table>
<thead>
<tr>
<th>Causative Agent</th>
<th>Children under 2 Years</th>
<th>Children Older than 2 Years</th>
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</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>10%—15%</td>
<td>40%—50%</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td>20%—30%</td>
<td>7%—10%</td>
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<tr>
<td>Rhinovirus</td>
<td>20%</td>
<td>50%</td>
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<tr>
<td>RS-virus</td>
<td>25%—30%</td>
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<tr>
<td>Metapneumovirus</td>
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<tr>
<td>Adenovirus</td>
<td>10 %-15 %</td>
<td>12 %—15 %</td>
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<tr>
<td>Other viruses</td>
<td>flo 5 %</td>
<td>Up to 10 %</td>
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Influenza

- *Influenza* (flu) is an acute infectious disease caused by different sero-types of influenza virus and characterized by damage of respiratory tract and intoxication.
Influenza

• **Etiology:** Virus of influenza belongs to family *Orthomyxoviruses*, contains RNA. Virion has spherical form, is of 80—120 nm in diameter. According to differences of inner antigens (nucleoprotein and matrix protein), influenza virus is divided into three types: A, B, C.

• Types A and B belong to one genus, type C to another. Particularity of influenza A virus is instability of antigenic properties of superficial proteins: hemagglutinin (H) and neuraminidase (N). Pointed mutations of hemagglutinin and neuraminidase, which lead to changes in immunological properties of the virus, are called antigenic drift. Mutations which simultaneously cause changes of two antigens and appearance of new combination of H and N, are called shift. Drift occurs every 2—3 years whereas shift is observed once every 20—30 years. Drift provides evolvement of epidemics of influenza whereas shift is responsible for pandemics.
Influenza

- **Etiology:** For influenza A virus currently 16 subtypes of hemagglutinin (HI—HI6) are described and 9 subtypes of neuraminidase (N1—N9).
- The 3 subtypes of hemagglutinin (HI, H2, H3) and 2 subtypes of neuraminidase (N1 and N2) cause disease in humans. Other subtypes of influenza A viral antigens cause diseases in animals and birds.
- However, in the world, cases of human infections with subtypes of avian influenza A virus (H5N1, H7N2, H9N2, H7N3, H7N7) are described. Influenza B virus is prone to lesser change-ability and influenza C virus has constant antigenic structure.
• **Diagnosis:** Diagnosis of influenza can be made based on the presence of typical disease presentations, especially during epidemic outbreaks:

• acute onset;

• fever to 38.0—40 °C, sometimes it can be subfebrile or absent;

• prominent symptoms of general condition disturbance which develop during the first days of the disease (headache, pain in muscles, joints, eyeballs, hyperesthesia, malaise, adynamia, vomiting);

• hemorrhagic syndrome is possible: nasal and other bleedings, petechial rash on the face, neck and upper part of the trunk;

• moderate signs of rhinopharyngitis (nasal congestion, moderate serous nasal discharge, discomfort and pain in the throat, hyperemia of posterior pharyngeal wall, soft palate with vessel injection and petechial hemorrhages on the mucosa);

• sclera vessel injections;

• signs of tracheitis (dry, painful cough with retrosternal pain);

• sometimes diarrhea and vomiting can be present.

• In the period between epidemics, as well as for diagnosis of atypical forms of the disease, laboratory methods of investigation are used.
Symptoms of Influenza

- **Central**
  - Headache

- **Systemic**
  - Fever (usually high)

- **Muscular**
  - (Extreme) tiredness

- **Joints**
  - Aches

- **Nasopharynx**
  - Runny or stuffy nose
  - Sore throat
  - Aches

- **Respiratory**
  - Coughing

- **Gastric**
  - Vomiting
SYMPTOMS OF INFLUENZA A (H1N1-2009)

Systemic
- Fever

Psychological
- Lethargy
- Lack of appetite

Nasopharynx
- Runny nose
- Sore throat

Respiratory
- Coughing

Intestinal
- Diarrhea

Gastric
- Nausea
- Vomiting
Paraclinical investigations in influenza:

• Detection of viral antigen in nasopharyngeal washing with the reaction of immune fluorescence and immune chromatography analysis;

• Detection of viral antibodies with the reaction of complement fixation and reaction of hemagglutination delay. The method of paired serum is used: 4-fold antibody titer increase during 10—14 days is diagnostic.
Complications of influenza:

Respiratory complications:

- acute bronchitis;
- secondary bacterial pneumonia;
- primary viral pneumonia;
- exacerbation of bronchial asthma;
- exacerbation of chronic diseases of respiratory tract;
- pulmonary abscess;
- lung empyema;
- sinusitis.
Complications of influenza:

*Non-respiratory complications:*

- febrile seizures;
- otitis media;
- sepsis;
- myositis;
- myocarditis;
- Rey syndrome;
- encephalitis;
- myelitis;
- Guillain—Barre syndrome.
Parainfluenza

- **Parainfluenza** is an acute respiratory viral disease caused by different serotypes of parainfluenza virus, characterized by involvement of upper and medium parts of respiratory tract, predominantly larynx and trachea, with presentation of moderate intoxication and catarrhal syndrome.
Parainfluenza

• **Etiology:** Parainfluenza virus belongs to the family *Paramyxoviridae*, genus *Paramyxovirus*, which includes 5 types of human parainfluenza vi-rus, Sendai virus (Murine parainflueza virus) and Newcastle disease virus (avian adenovirus).

• The main serotypes of parainfluenza virus are:
  • parainfluenza virus type 1 (Pll) which includes hemadsorption vi-rus (HA1) and Sendai virus with antigenic similarity;
  • parainfluenza virus type 2 (Pl2);
  • parainfluenza virus type 3 (Pl3);
  • parainfluenza virus type 4 (Pl4).
Clinical manifestations: *Incubation period* is 1—7 days (on average, 3—4 days).

**Diagnosis:**

- *clinical signs:*
- typical epidemiological history (contact);
- age more often 1—5 years;
- acute onset;
- moderate intoxication;
- prominent catarrhal syndrome;
- typical clinical signs — laryngitis syndrome which develops at the beginning of the disease: barking cough, coarse voice, loud breathing with impeded inspiration.
Diagnosis:

*laboratory signs:*

- virusological investigation (virus extraction on cell culture);
- express methods: immunoenzyme, immunofluorescent;
- serological methods (reaction of indirect hemagglutination, reaction of complement fixation, reaction of neutralization, immunoenzyme analysis, immuno-chromatographic analysis). Investigation is performed in paired serum taken with interval of 10—14 days. Confirmatory is 4-fold titer and higher increase (retrospective method);
- non-specific methods: complete blood count in acute period of the disease shows leukopenia and lymphocytosis.
- etiological diagnosis is confirmed by laboratory investigation. In its absence the diagnosis of ARVI is made and its leading clinical syndrome is pointed out.
Adenoviral Infection

- Adenoviral infection is an acute infectious disease caused by different serotypes of adenovirus with airborne way of transmission which is characterized by predominant involvement of nasopharynx, conjunctiva, lymphoid tissue, with signs of intoxication, catarrhal syndrome with prominent exudative component.
Adenoviral Infection

- **Etiology:** The causative agent of adenoviral infection is DNA-containing virus from the family of *Adenoviridae*, genus *Mastadenovirus*. Adenoviruses include 49 serotypes with different antigenic, biophysical and hemagglutination properties, but common soluble antigen; they are divided into 7 subgroups (A, B, C, D, T, F, G).

- The disease is mainly caused by representatives of B-, C-, E-subgroups, and serotypes 1, 2, 3, 4, 5, 7, 14 and 21. Clinically prominent infections are caused by viral serotypes 3, 4, 7, 14, 21. Adenoviruses of 1st, 2nd, 5th and 6th types are latent; they cause subclinical disease forms in children. However, in an unfavorable host conditions they can activate and cause typical ARVI. Serotypes 8, 19, 29 cause conjunctiva inflammation; serotypes 12, 18, 31, 40, 41 initiate development of enteritis. Adenoviruses are resistant to low temperatures, are epithelium tropic and cytopathogenic.
• **Epidemiology:** Adenoviral infection is a widespread disease affecting all age groups. The sources of infection are sick people, people during recovery and healthy carriers. The patient is contagious since first days of the disease and up to 2—3 weeks from disease onset. In acute period the virus is excreted with mucus from nose, pharynx and conjunctiva; later with stool. Patients excrete the virus in the mean up to 7—12 days, some of them up to 50 days and longer.

• The main way of transmission is airborne; alimentary way is not ex-cluded. Index of contagiosiy is up to 50%.

• Outbreaks of adenoviral infection can be noticed all year round; they can be seen in pediatric medical institutions. Their typical particularity is a long course (up to 1—1.5 months).
• Incubation period continues from 4 to 14 days, in the mean 5—7 days.

• Clinical forms of adenoviral infection:
  • upper respiratory tract catarrh;
  • rhinopharyngitis;
  • tracheobronchitis;
  • pharyngoconjunctival fever;
  • conjunctivitis, keratoconjunctivitis;
  • tonsillopharyngitis;
  • adenoviral pneumonia;
  • gastroenteritis;
  • hemorrhagic cystitis;
  • mesenteric lymphadenitis
Respiratory syncytial (RS) infection is an acute infectious disease caused by respiratory syncytial virus with airborne way of transmission and predominant damage of lower respiratory tract with development of fever, mild intoxication and catarrhal syndrome.

*Incubation period* continues from 2 to 7 days.
Diagnosis:

1) clinical criteria:

- typical epidemiological history;
- the disease is more often seen in first year children;
- gradual disease onset;
- mild intoxication signs;
- body temperature is subfebrile as a rule;
- mild catarrhal syndrome;
- typical involvement of lower parts of respiratory tract (bronchiol-itis, obstructive bronchitis) on the 2\textsuperscript{nd}—3\textsuperscript{rd} day after disease onset;
- prominent respiratory insufficiency with rapid reverse dynamics;
- discordance between severity of lower tract involvement (a lot of dry and wet fine crackles over the whole lung surface, thorax emphysema) and degree of fever and intoxication;
2) laboratory criteria:

• virusological method (virus growth on cell culture);

• express methods: immunoenzyme, immunofluorescent;

• serological methods (reaction of indirect hemagglutination, reaction of complement fixation, reaction of neutralization): investigation is performed with paired serum taken with an interval of 10—14 days in between. Diagnostic is titer increase 4 times and higher.
Rhinoviral Infection

- **Rhinoviral** infection or prolonged common cold is an acute infectious disease caused by different serotypes of rhinoviruses with airborne way of transmission and with predominant involvement of nasal mucosa and absent or mild intoxication.
Rhinoviral Infection

- **Etiology:** The causative agent belongs to the family *Picornaviridae*, genus *Rhinovirus*. Currently there are about 114 serotypes of human rhino-viruses described, which provide different clinical presentation of rhinitis. They do not have any common group antigen, every serotype has specific virus neutralizing and complement fixating antigens.

- Viral genome is presented by non-fragmented single-stranded viral RNA. There are no lipids and carbohydrates in virion structure, which leads to ether resistance of the virus. Viral replication occurs in cytoplasm. Rhinoviruses have tropism to respiratory epithelium, predominantly of nasal mucosa.

- *Incubation period* is 1—6 days.
Diagnosis:

- **clinical criteria:**
  - typical epidemiological history;
  - prominent rhinorrhea;
  - mild intoxication;
  - normal or subfebrile body temperature;

- **laboratory criteria:**
  - express methods: immunoenzyme, immunofluorescent;
  - serological methods (reaction of indirect hemagglutination, reaction of complement fixation, reaction of neutralization): investigation is performed with paired serum taken with an interval of 10—14 days in between.
Metapneumoviral Infection

• Metapneumoviral infection is an acute infectious disease caused by metapneumovirus with predominantly airborne way of transmission which is characterized by involvement of upper respiratory tract and gastrointestinal tract with catarrhal signs and frequent diarrhea syndrome.
**Coronavirus Infection**

- **Coronaviruses** are species in that belong to one of two subfamilies *Coronavirinae* and *Torovirinae* in the family *Coronaviridae*, in the order Nidovirales.

- Coronaviruses are enveloped viruses with a positive-sense RNA genome and with a nucleocapsid of helical symmetry. The genomic size of coronaviruses ranges from approximately 26 to 32 kilobases, extraordinarily large for an RNA virus.

- The name "coronavirus" is derived from the Latin *corona*, meaning crown or halo, and refers to the characteristic appearance of virions under electron microscopy (E.M.) with a fringe of large, bulbous surface projections creating an image reminiscent of a royal crown or of the solar corona. This morphology is created by the viral spike (S) peplomers, which are proteins that populate the surface of the virus and determine host tropism.

- Proteins that contribute to the overall structure of all coronaviruses are the spike (S), envelope (E), membrane (M) and nucleocapsid (N). In the specific case of the SARS coronavirus, a defined receptor-binding domain on S mediates the attachment of the virus to its cellular receptor, angiotensin-converting enzyme 2 (ACE2). Some coronaviruses (specifically the members of Betacoronavirus subgroup A) also have a shorter spike-like protein called hemagglutinin esterase (HE).
Severe Acute Respiratory Syndrome

Severe acute respiratory syndrome (SARS) is a serious, potentially life-threatening viral infection caused by a previously unrecognized virus from the Coronaviridae family, the SARS-associated coronavirus (SARS-CoV). Since the 2002-2003 outbreak of SARS, which apparently began in southern China but eventually involved more than 8000 persons worldwide (see the image below), global efforts have virtually eradicated SARS as a threat.
Signs and symptoms

• The clinical course of SARS generally follows a typical pattern. Stage 1 is a flulike prodrome that begins 2-7 days after incubation, lasts 3-7 days, and is characterized by the following:
  • Fever (>100.4°F [38°C])
  • Fatigue
  • Headaches
  • Chills
  • Myalgias
  • Malaise
  • Anorexia
• Less common features include the following\textsuperscript{[1, 2, 3]}:
  • Sputum production
  • Sore throat
  • Coryza
  • Nausea and vomiting
  • Dizziness
  • Diarrhea
Stage 2 is the lower respiratory tract phase and is characterized by the following:

- Dry cough
- Dyspnea
- Progressive hypoxemia in many cases
- Respiratory failure that requires mechanical ventilation in some cases
- Chest radiography findings may initially be normal, and 7 days or longer may elapse before findings become abnormal. Radiographs may show focal interstitial infiltrates that may progress to a patchier, generalized distribution. Respiratory failure that requires mechanical ventilation may occur.
- This phase is thought to be secondary to immunopathologic injury and is characterized by a decreasing viral load.
Diagnosis:

- Initial tests in patients suspected of having SARS include the following:
  - Pulse oximetry
  - Blood cultures
  - Sputum Gram stain and culture
  - Viral respiratory pathogen tests, notably influenza A and B viruses and respiratory syncytial virus
  - *Legionella* and pneumococcal urinary antigen testing should also be considered
  - Modest lymphopenia, leukopenia, and thrombocytopenia: Series have shown white blood cell (WBC) counts of less than $3.5 \times 10^9/L$ and lymphopenia of less than approximately $1 \times 10^9/L$
  - Mild hyponatremia and hypokalemia
  - Elevated levels of lactate dehydrogenase, alanine aminotransferase, and hepatic transaminase
  - Elevated creatine kinase level
Diagnosis:

- Coronavirus antibody testing methods include indirect fluorescent antibody or enzyme-linked immunosorbent assays, which are used to test for specific antibodies after infection. Although these antibodies are found in some patients during the acute phase (ie, within 14 d of onset), a negative test finding using a sample that has been obtained less than 28 days after symptom onset does not exclude the diagnosis of SARS.[54, 55]

- Reverse-transcriptase PCR (RT-PCR) assay results can be positive in some patients within the first 10 days of fever. RT-PCR assay can be used to detect SARS-CoV in serum, stool, and nasal secretions. SARS-CoV can also be isolated in viral cultures.

- A negative SARS-CoV antibody test finding less than 28 days after symptom onset, a negative PCR assay finding, and a negative viral culture finding do not exclude the diagnosis of SARS. Obtaining convalescent serum for a final antibody determination 28 days or more after symptom onset is critical to the disease’s diagnosis.
HRCT scanning of the chest

• The role of HRCT scanning in the evaluation of SARS is still controversial. Patients with abnormal chest radiographic findings do not need HRCT scanning. However, when SARS is a strong clinical possibility despite a normal chest radiographic finding, the clinician should consider HRCT scanning.

• Findings consistent with SARS include ground-glass opacification, with or without thickening of the intralobular or interlobular interstitium, or frank consolidation. Indeed, a combination of ground-glass opacification (with or without thickening of the interstitium) and frank consolidation may be noted.
DDX diagnosis:

- Foreign body aspiration
- Influenza
- *Mycobacterium avium-intracellulare* and other atypical mycobacterial diseases
- Mycoplasma infections
- Parainfluenza virus
- Pleural effusion
- Pneumococcal infections

- Pneumocystis (carinii) jiroveci pneumonia
- Aspiration pneumonia
- Bacterial pneumonia
- Fungal pneumonia
- Viral pneumonia
- Psittacosis
- Q fever
- Rhinoviruses
- Rickettsialpox
- Bacterial sepsis
- Upper respiratory infection
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- Bacterial sepsis
- Upper respiratory infection
DDX diagnosis:
- Adenoviruses
- Arenaviruses
- Atelectasis
- Bronchiectasis
- Bronchiolitis
- Bronchitis
- Chronic Obstructive Pulmonary Disease (COPD)
- Coxsackieviruses
- Cytomegalovirus
- Echoviruses
- Emphysema
Treatment

Currently, no definitive medication protocol specific to SARS has been developed, although various treatment regimens have been tried without proven success. The CDC recommends that patients suspected of or confirmed as having SARS receive the same treatment that would be administered if they had any serious, community-acquired pneumonia.
Medications

• Corticosteroids
• **Antiviral agents** (The most widely used of these to date is ribavirin (usually in conjunction with steroids).
• **Protease inhibitors** (Lopinavir/ritonavir was shown to have in vitro effects against the SARS-CoV.)
• **Interferon** (Type 1 IFNs inhibit a wide range of RNA and DNA viruses, including SARS-CoV)
• **Monoclonal antibodies**
• **Intravenous immunoglobulin**
• **Glycyrrhizin**
MERS is a respiratory illness caused by a coronavirus, usually referred to as the Middle East Respiratory Syndrome Coronavirus, or MERS-CoV.

MERS-CoV was first reported in Saudi Arabia in September 2012. In a press release issued May 2, 2014, the Centers for Disease Control and Prevention (CDC) identified 401 confirmed cases of MERS-CoV infection in 12 countries, with all reported cases originating in the Arabian Peninsula. Most patients developed severe acute respiratory illness, with fever, cough, and shortness of breath, and 93 patients have died. The case fatality rate in symptomatic patients is 30%.
Most people confirmed to have MERS-CoV infection have had severe acute respiratory illness with symptoms of:

- fever
- cough
- shortness of breath

Some people also had gastrointestinal symptoms including diarrhea and nausea/vomiting. For many people with MERS, more severe complications followed, such as pneumonia and kidney failure. About 3-4 out of every 10 people reported with MERS have died. Most of the people who died had an underlying medical condition. Some infected people had mild symptoms (such as cold-like symptoms) or no symptoms at all; they recovered.
Symptoms

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  - shortness of breath
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Laboratory Findings

• Laboratory findings at admission may include leukopenia, lymphopenia, thrombocytopenia, and elevated lactate dehydrogenase levels. Co-infection with other respiratory viruses and a few cases of co-infection with community-acquired bacteria at admission has been reported; nosocomial bacterial and fungal infections have been reported in mechanically-ventilated patients.

• MERS-CoV virus can be detected with higher viral load and longer duration in the lower respiratory tract compared to the upper respiratory tract, and has been detected in feces, serum, and urine. However, very limited data are available on the duration of respiratory and extrapulmonary MERS-CoV shedding.
Please download: Clinical management of severe acute respiratory infections
Human metapneumovirus (hMPV) is a single negative-stranded RNA-enveloped virus classified in the Pneumovirinae subfamily of the Paramyxoviridae family. This virus is second only to respiratory syncytial virus (RSV) as the most commonly identified cause of pediatric lower respiratory illness. However, hMPV can also cause upper respiratory tract infections across all age groups.
Diagnosis:

**clinical criteria:**

- typical epidemiological history;
- intoxication syndrome, shortness of breath;
- combination of nasopharyngitis, bronchitis or bronchiolitis and enteritis;
- hepatomegaly and not rarely splenomegaly;
- possible diarrhea syndrome;

**laboratory criteria:**

- for detection of RNA hMPV real time polymerase chain reaction is used with hybridization and detection of fluorescence (RT-PCR).
Human Bocaviral Infection

- Bocaviral infection is an acute infectious disease caused by bocavi- ruses with predominantly airborne way of transmission characterized by upper respiratory tract and gastrointestinal tract involvement, which presents with catarrhal signs and frequent diarrhea syndrome.

- Etiology: Human bocavirus (HBoV) belongs to the family *Parvoviridae*. It was identified in 2005. The virus is still understudied.
Thank you for your Attention!