CONTENTS

CHAPTER 1

INFECTIOUS DISEASES

1.1. VIRAL RESPIRATORY TRACT INFECTIONS

Formulating a diagnosis

Components of the diagnosis:
- clinical form;
- severity;
- complications

Viral respiratory tract infections (*VRTI*) *are a heterogeneous group of diseases, the etiologic agents of which are various respiratory viruses that mainly affect the upper respiratory tract epithelium.*

Upper respiratory tract infections are the commonest infections seen in both pediatric and adult populations, with the majority caused by viruses, such as adenovirus, Epstein–Barr virus, parainfluenza, influenza A, Coxsackie A, respiratory syncytial virus, and herpes simplex, among others.

Nearly all of these viral infections are of short duration and require only symptomatic management.

Clinical form

VRTI clinical presentation can vary significantly depending on the etiology, patient's age, immune system state, and presence of concomitant diseases. *The symptoms of VRTI usually include nasal obstruction*, *headache*, *sore throat*, *sneezing*, *cough*, *malaise*, *nasal discharge*, *low- or high grade fever*, *mild myalgias*, *and fatigue.*

The types of VRTI, and clinical manifestations depending on the pathogens are presented at table 1.1.

Table 1.1. Viral respiratory tract infections types and their clinical manifestations

Disease	Etiologic agent*	Clinical manifestations
Influenza**	RNA-viruses *of the Orthomyxoviridae family*	Symptoms vary from a mild respiratory disease confined to the upper respiratory tract and characterized by fever, sore throat, runny nose, cough, headache, muscle pain and fatigue to severe and in some cases lethal pneumonia owing to influenza virus or to secondary bacterial infection of the lower respiratory tract***

Table 1.1 (Cointinued)

Disease	Etiologic agent*	Clinical manifestations
Parainfluenza	RNA-containing paramyxovirus	Systemic signs and symptoms are mild or moderate, *catarrhal respiratory syndrome* (laryngitis, moderate rhinitis, pharyngitis)
Adenovirus infection	DNA-containing viruses from the *Adenoviridae* family, *Mastadenovirus* genus	• Systemic signs and symptoms are expressed mildly. • *Catarrhal respiratory syndrome* — rhinitis, pharyngitis, conjunctivitis. • *Lymphadenopathy* — acute tonsillitis, hepatosplenomegaly; *dyspeptic syndrome*
Respiratory syncytial infection	Respiratory syncytial virus from the paramyxovirus family	• Systemic signs and symptoms are expressed mildly. • *Catarrhal respiratory syndrome* (rhinitis, pharyngitis, bronchiolitis)
Rhinovirus infection****	RNA-containing *Human rhinovirus, Enterovirus* genus, *Picornaviridae* family	• Systemic signs and symptoms are expressed mildly. • *Catarrhal respiratory syndrome* (rhinitis, pharyngitis)
Rotavirus infection	RNA-containing virus of the *Reoviridae* family	• Systemic signs and symptoms are expressed poorly. • *Catarrhal respiratory syndrome* (pharyngitis). • *Pain syndrome* (cramping pains in the epigastrium). • *Dyspeptic syndrome*
Coronavirus infection[1]	RNA-containing virus of the *Coronaviridae* family	Systemic signs and symptoms are expressed mildly or significantly (depending on the strain of the virus), *catarrhal respiratory syndrome* (rhinitis, pharyngitis), loss of smell, pneumonia

[1] Considering the lack of reliable data on diagnosis, clinical course and treatment of new coronavirus infection COVID-19 (agent of SARS-CoV-2 — severe acute respiratory syndrome coronavirus 2), presence of only «Temporary methodological guidelines for prevention, diagnosis and treatment of new coronavirus infection» (reference is given in the bibliography) at the time of writing this Chapter, the information about this disease is not included in the chapter of the textbook.

End of table 1.1

Disease	Etiologic agent*	Clinical manifestations
Metapneumo-virus infection	*Human metapneumovirus*	• Systemic signs and symptoms are expressed mildly. • *Catarrhal respiratory syndrome* (rhinitis, pharyngitis, bronchiolitis)

* There are at least 200 viral types and other infectious agents that can cause the VRTI. The rhinoviruses are the most common and are responsible for 40% of cases: corona viruses causing 10%; respiratory syncytial virus, parainfluenza and influenza virus approximately 10 to 15%; and others 5 to 20%.

** Influenza is an acute respiratory illness caused by influenza A or B viruses that occurs in outbreaks and epidemics worldwide, mainly during the winter season.

*** Initially, nonspecific symptoms predominate, including fever, chills or frank shaking, headaches, myalgia (muscle pain), malaise (discomfort) and anorexia. The onset of these symptoms is sudden, and respiratory symptoms, particularly a dry cough, sore or dry throat (possibly with hoarseness) and nasal obstruction and discharge, are usually also present. Cough can be accompanied by substernal discomfort or burning. Influenza virus infection can also lead to a wide range of non-respiratory complications in some cases — affecting the heart, central nervous system and other organ systems.

**** Rhinoviruses are the most common type of virus and are found in slightly more than half of all patients.

The fig. 1.1 below illustrates the peak incidences of various viruses by season.

Severity

The severity of the patient's condition is determined by the severity of systemic signs and symptoms and the presence of complications.

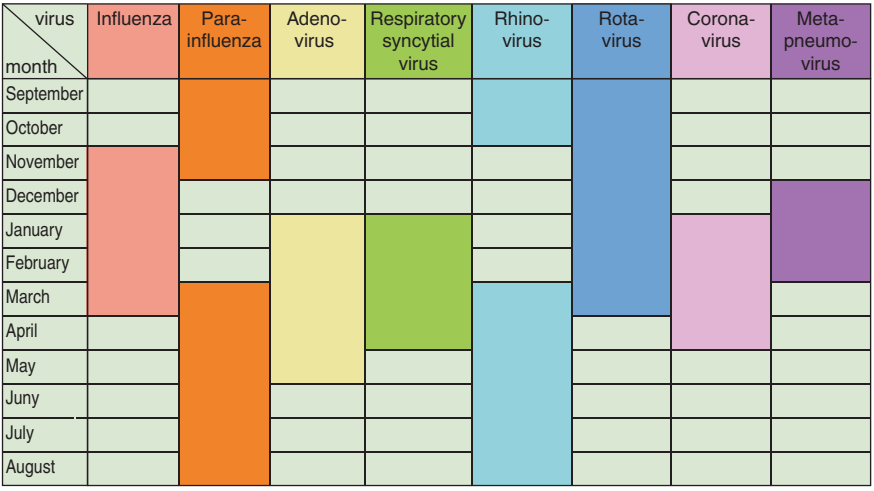

Fig. 1.1. Seasonal variation of selected upper respiratory tract infection viruses

Mild degree — an increase in body temperature of no more than 38,0 °C; moderate headache; heart rate <90 beats/min; systolic blood pressure (SBP) ⩾110 mm Hg; respiratory rate (RR) less than 24 per minute; oxygen saturation (SpO_2) >95%, no dyspnea, no clinical and auscultation pattern of pneumonia.

Moderate degree — body temperature within 38,1–40 °C; severe headache; hyperesthesia; heart rate 90–120 beats/min; SBP <110 mm Hg; RR 24–28 per minute.

Severe degree — acute onset, body temperature more than 40 °C, *severe headache*, *body aches*, *insomnia*, *delirium*, *anorexia*, *nausea*, *vomiting*, *meningeal symptoms*; heart rate over 120 beats/min, pulse of poor volume, possible arrhythmias; SBP <90 mm Hg; muffled heart sounds; respiratory rate >28 per 1 minute.

Complications

Severity of infection in humans is associated with replication of the virus in the lower respiratory tract, which is accompanied by severe inflammation owing to immune cell infiltration. Depending on the route of transmission, the virus targets epithelial cells of the respiratory or intestinal tract for infection and productive replication.

Quick tips

In selected instances, especially in patients with an underlying immune deficiency, chronic diseases, or elderly, these types of infections can progress clinically to become fulminant infections associated with severe complication and even death.

VRTI complications

1. Bacterial superinfections (pneumonia, bronchitis, otitis, rhinosinusitis, pyelonephritis, etc.).
2. Myocarditis.
3. Damage to the nervous system (meningitis, encephalitis, arachnoiditis).
4. Decompensation of concomitant chronic diseases (bronchial asthma, COPD, diabetes mellitus, chronic heart failure, liver and kidney diseases).

Examples of diagnoses

DS: Influenza, severe degree, viral lower lobe right-sided pneumonia.

DS: acute respiratory viral infections, rhinitis, mild degree, reconvalescence period.

DS: Coronavirus infection (COVID-19), severe degree, type 2 respiratory failure.

Diagnosis verification

VRTI diagnosis is made mostly on the basis of clinical presentation and epidemiological likelihood of infection.

Patient complaints

The VRTI clinical pattern is composed of the following symptoms that represent *patient's complaints*:

1) **systemic signs and symptoms:**
   - fever;
   - chills;
   - headache;
   - muscle pain;
   - weakness;
   - decreased appetite;
   - sweating.
2) **catarrhal symptoms:**
   - may include sore throat, rhinitis (nasal congestion, discharge of mucous, impaired nasal breathing), and dry cough.
3) **less common symptoms:**
   - other systemic bleeding problem, dyspeptic symptoms (belch, nausea, bloating, diarrhea, lack of appetite) and lymphadenopathy.

Patient history

Taking patient history includes answers to these questions.

- Onset of the disease (acute, gradual), development of symptoms?
- Was there any contact with people with similar clinical symptoms?
- Was there an episode of hypothermia the day before the disease occurrence?
- Did the patient take any medication on his own. If «yes», then what medication and dosage. Did he/she noticed the effect from the treatment?
- Had the patient visited a doctor before? What was the diagnosis, treatment prescribed and its effectiveness?

Quick tips

Colds that do not resolve in two weeks or get better and then worsen should suspect bacterial superinfection.

Physical examination

Physical signs of damage to the upper and lower respiratory tract are revealed during the examination.

Detection of pharyngoconjunctival, bronchoobstructive, abdominal or hemorrhagic syndrome, skin rash, lymphadenopathy, etc., has a significant diagnostic value.

Laboratory and instrumental examinations

- Pulse oximetry (performed at all medical care stages for early diagnosis of respiratory disorders in complicated course of the disease).
- Clinical blood analysis for suspected bacterial complications.
- Clinical urine analysis in case of suspected bacterial complications (pyelonephritis).
- Chest X-ray (at suspicion of pneumonia).
- Radiography of paranasal sinuses (at suspicion of sinusitis).
- ECG (in presence of cardiac symptoms, concomitant cardiovascular and bronchopulmonary pathology).
- Polymerase chain reaction in an atypical course of the disease — based on the detection of RNA or DNA of viruses (*as influenza-like illness can be caused by many viruses*, *the gold standard laboratory tests used for influenza are viral culture and reverse transcription PCR* (*RT-PCR*). If the patient has undergone a virological examination, the etiological variant is indicated in the diagnosis. If the etiology is not established, then the diagnosis is formulated as «VRTI».

Differential diagnosis

Differential diagnosis is carried out with diseases, the clinical presentation of which includes the above-listed syndromes.

Indications for hospitalization

Examination and treatment of patients with VRTI in an outpatient setting is possible only after excluding indications for emergency hospitalization:

- severe degree of the disease;
- signs of acute respiratory failure;
- lack of clinical effect from the outpatient treatment;
- exacerbation/decompensation of concomitant diseases;
- development of complications;
- age over 65 years (with moderate and severe influenza);
- pregnancy and postpartum period (with influenza);
- epidemiological indications: inability to isolate the patient (*for example*, *accommodation in a hotel*, *hostel*, *facility for disabled*, *etc.*);
- infections that are covered by international health standards (*the need to comply with all necessary measures to limit the infection spread from the moment it is detected*, *for example*, *human infection with SARS-CoV-2*).

During the epidemic rise in morbidity, emergency hospitalization in an infectious hospital is indicated until day 4–5 of the disease, in a specialized hospital (depending on the type and severity of the complication) — after the 5th day of the disease.

Treatment

The goal of VRTI treatment is rapid and complete clinical recovery of the patient.

The main objectives of VRTI treatment:

- suppression of virus replication at the early stages of the disease;
- reversal of clinical symptoms;
- prevention and treatment of complications.

Treatment of mild and moderate forms of VRTI is carried out in the outpatient setting and should begin from the moment the first symptoms of the disease.

Principles of treatment

Most patients with mild symptoms do not require any symptomatic therapies. Such patients should be advised to return for review if their condition worsens or exceeds the expected time for recovery.

Patients with moderate to severe symptoms may use a variety of therapies to relieve symptoms.

Management of acute influenza has traditionally relied on supportive measures such as control of fever, symptomatic treatment, rehydration and treatment of complications, such as bacterial pneumonia, if they occur.

Nonpharmacological treatment

In everyday clinical practice, the emphasis in treatment of VRTI is on ***general measures:***

- *compliance with home regimen*;
- *increased fluid intake* (*20–40 ml/kg of body weight per day as drinking water, fruit drinks, juices, etc.*);
- *airing the rooms*;
- *control of fever*, *symptomatic treatment*, *and treatment of complications*, *such as bacterial pneumonia*, *if they occur.*

Pharmacological treatment

1. ***Antiviral drugs.***

- Three classes of antiviral drugs are available for the treatment of influenza:
- The neuraminidase inhibitors, *zanamivir*, and *oseltamivir*, which are active against both influenza A and B.

- The selective inhibitor of influenza cap-dependent endonuclease, *baloxavir*, which is active against influenza A and B.
- The adamantane, amantadine and rimantadine, which are only active against influenza A.
- *Oseltamivir* is recommended for oral administration, during the first 36 hours from the onset of symptoms, 75 mg twice a day (daily dose is 150 mg, in severe cases — 300 mg) for 5–10 days.
- *Zanamivir* is recommended for inhalation through a diskhaler, 2 inhalations 2 times a day for 5 days at a daily dose of 20 mg (with vigilance in patients with bronchospasm).
- It is possible to use the above-mentioned drugs for influenza treatment in pregnant and lactating women.
- *Baloxavir marboxil* is recommended for use *once* per os, 40 mg at a body weight of <80 kg, 80 mg — at a body weight of ⩾80 kg *for influenza treatment* in patients at the age of 12 and more with symptoms lasting for no more than 48 hours.
- Baloxavir marboxil is a polymerase acidic endonuclease inhibitor indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours and who are:
  - otherwise healthy, or
  - at high risk of developing influenza-related complications.
- The use *of adamantane* is limited, due to a marked increase in resistant isolates except in selected circumstances.

2. ***Therapies that may be effective:***
   - analgesics;
   - decongestant combinations;
   - intranasal ipratropium bromide.
3. ***Therapies with minimal benefits:***
   - decongestants;
   - saline nasal spray;
   - expectorants;
   - herbal products.

The main antiviral agents in VRTI treatment are presented below in table 1.2.

Patients with moderate to severe symptoms may use a variety of therapies to relieve symptoms.

Analgesics, decongestant combinations, intranasal ipratropium bromide, saline nasal spray, expectorants may provide symptomatic relief to patients with VRTI (table 1.3).

Table 1.2. The antiviral drugs

Drug name	Mechanism of action	Recommended dosage and administration
Oseltamivir	Viral neuraminidase inhibitor	75 mg; 1 capsule 2 times a day for 5 days
Zanamivir	Viral neuraminidase inhibitor	1 inhalation — 5 mg; 2 inhalations 2 times a day for 5 days
Baloxavir marboxil	The selective inhibitor of influenza cap-dependent endonuclease	1. Two 20 mg tablets taken at the same time for a total single dose of 40 mg — *patient's body weight 40 to less than 80 kg.* 2. Two 40 mg tablets taken at the same time for a total single dose of 80 mg — *patient's body weight at least 80 kg*

Table 1.3. Therapies that may be effective, or with minimal benefits

Drug name	Recommended dosage and administration
NSAIDs	
Acetaminophen (also called paracetamol)	500 mg; 1 tab. when the body temperature rises above 38.5 °C or with poor tolerance of systemic signs and symptoms
Ibuprofen	200–400 mg; 1 tab. when the body temperature rises above 38.5 °C or with poor tolerance of systemic signs and symptoms
Mucoactive drugs	
Guaifenesin	200–400 mg; 10–20 ml; 3 times a day for 7 days
Acetylcysteine	200mg 3 times a day; 600 mg 1 time a day for 5–10 days
Bromhexine	8 mg; 3–4 times a day for 4–6 days
Ambroxol	30 mg; 3 times a day for 4–5 days
Erdosteine	300 mg; 2 times a day for 10 days
Antitussive drugs	
Butamirate	20–50 mg; 2–3 times a day for 5 days

Agents containing NSAIDs/antihistamines/vitamin C (table 1.4) help to avoid polypragmasy and increase treatment adherence.

Some of the fixed-dose combinations contain phenylephrine, a sympathomimetic with a vasoconstrictive effect, which should be taken into account when prescribing patients with cardiovascular diseases.

Prevention

Prevention for the VRTI is reviewed here:

- restricting contacts;
- face covering (face masks) in public places during the epidemic;
- covering nose and mouth when sneezing or coughing with a tissue;
- hands hygiene;
- vaccination.

Vaccines types:

- whole-virion — live attenuated or inactivated vaccines;
- split vaccines — contain surface and internal proteins, are purified from lipopolysaccharides;
- subunit vaccines — contain only surface antigens.

Self-assessment quiz

1. Antiviral drugs for patient with influenza.
2. Differential diagnosis of VRTI.
3. Complications of VRTI, and indications for hospitalization.

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1.2. ACUTE TONSILLOPHARYNGITIS

Formulating a diagnosis

Components of the diagnosis:
- etiological variant;
- clinical form;
- severity;
- complications

Acute tonsillopharyngitis (*ATP*) *is an acute infectious inflammation of the oropharynx lymphatic structures* (*palatine tonsils*, *lymphoid follicles of the posterior pharyngeal wall*) *and the posterior pharyngeal wall.*

Etiological variant

ATP is mainly caused by viruses, such as double-stranded DNA viruses (human adenoviruses, Epstein–Barr Virus), single-stranded DNA viruses (Human Boca Virus), single-stranded RNA viruses [influenza and para-influenza viruses; rhino-viruses; enteroviruses including Coxsackie viruses; corona viruses; respiratory syncytial virus (RSV); human metapneumovirus], retro-viruses [human immunodeficiency viruses (HIV)].

The most important pathogens that cause bacterial ATP, are group A β-hemolytic streptococci (GABHS) or *Streptococcus pyogenes*. The disease transmission generally occurs via droplet infection transmitted by other patients with acute GABHS tonsillitis, very rarely by asymptomatic carriers.

ATP is mainly found in children and young people (up to 35 years old).

ATP classification depending on the etiological factor.
- Primary.
- Secondary:
  - in infectious diseases;
  - in hematologic diseases.

ATP classification by pathogen type:
1. Acute streptococcal tonsillopharyngitis.
2. Acute tonsillopharyngitis caused by other specified pathogen (non-streptococcal).
3. Acute tonsillopharyngitis, not otherwise specified.

Clinical form

There are typical and atypical forms.

ATP classification based on clinical and morphological characteristics.

- *Typical forms:*
  1. Catarrhal.
  2. Follicular.
  3. Lacunar.
- *Atypical forms:*
  1. Ulceromembranous.
  2. Ulceronecrotic.

ATP clinical pattern

The incubation period is on average 1–4 days. The disease is characterized by an acute onset and is followed by systemic signs and symptoms, regional lymphadenopathy, and sore throat syndrome. The severity of fever, systemic signs and symptoms and pharyngoscopic signs depend on the disease form.

Catarrhal tonsillopharyngitis

It is usually a viral disease manifestation, often combined with other VRTI manifestations (cough, rhinitis). The clinical symptoms are determined by pathogen characteristics.

Follicular and lacunar tonsillopharyngitis

In most cases, GABHS is the causative agent. These tonsillitis forms occur with more overt symptoms. Systemic signs and symptoms are expressed (an increase in body temperature to 39–40 °C, general weakness, headache, joint and muscle pain).

Severity

There are three degrees of severity depending on the severity of systemic signs and symptoms.

1. Mild degree.
2. Moderate degree.
3. Severe degree.

Complications (typical for streptococcal tonsillitis)

- Peritonsillitis.
- Peritonsillar abscess.
- Purulent lymphadenitis of regional lymph nodes.
- Sinusitis.
- Otitis.

- Tonsillogenic mediastinitis.
- Metatonsillary diseases (rheumatism, infectious and allergic myocarditis and polyarthritis, glomerulonephritis).

Examples of diagnoses

DS: Acute lacunar tonsillopharyngitis, streptococcal etiology, severe degree, paratonsillar abscess on the right.

DS: Acute follicular tonsillopharyngitis, unspecified etiology, moderate degree.

DS: Acute catarrhal tonsillopharyngitis, viral etiology, mild degree.

Diagnosis verification

ATP diagnosis is stated on the basis of patient complaints, medical history, physical examination, including body temperature, skin, and lymph nodes assessment, mesopharyngoscopy, and exclusion of other diseases.

The clinical diagnosis in symptomatic patients can be confirmed either by means of bacterial culture or rapid antigen detection, otherwise it remains only a clinical suspicion.

Patient complaints

The following syndromes forming *patient complaints* are distinguished: sore throat, lymphadenopathy, catarrhal respiratory syndrome.

Systemic signs and symptoms may include:

- *fever;*
- *chills;*
- *headache;*
- *muscle pain;*
- *weakness;*
- *decreased appetite;*
- *sweating.*

A typical ***sore throat syndrome*** is discomfort or pain in a throat, which increases when swallowing. With an overt inflammatory process or complications, pain radiates into the ear.

Lymphadenopathy syndrome *is* an enlargement of the lymph nodes with their structural and functional impairment.

Catarrhal-respiratory (***respiratory***) ***syndrome*** — inflammation of the respiratory tract mucous membrane with mucous hyperproduction and activation of local defensive reactions, includes:

- *rhinitis* (nasal congestion, discharge of mucous, impaired nasal breathing, cough with mucus excretion along posterior pharyngeal wall, sneezing);
- *pharyngitis* (throat irritation and dryness, painful swallowing);

- *tonsillitis* (hyperemia and swelling of tonsils, mucous membrane of palatopharyngeal arches, uvula and posterior pharyngeal wall);
- *laryngitis* (dry «barking» cough, hoarseness);
- *tracheitis* (soreness behind the sternum, dry cough).

Patient history

Taking patient history includes answers to these questions.

- Onset of the disease (acute, gradual), development of symptoms?
- Was there any contact with people with similar clinical symptoms?
- Was there an episode of hypothermia the day before the disease occurrence?
- Did the patient take any medication on his own. If «yes», then what medication and dosage. Did he/she noticed the effect from the treatment?
- Had the patient visited a doctor before? What was the diagnosis, treatment prescribed and its effectiveness?

Physical examination

Physical signs of damage to the upper respiratory tract are revealed during the examination.

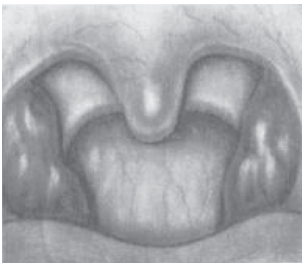
Mesopharyngoscopy using a spatula is recommended for all patients. Depending on the ATP type, *catarrhal tonsillopharyngitis is distinguished*: hyperemia of the soft palate, palatine arches, tonsils, no plaque, tonsils are enlarged mainly due to infiltration and swelling. *Follicular tonsillopharyngitis* — tonsils are hypertrophied, sharply edematous, suppurated follicles as whitish-yellowish formations as large as a pinhead are visible through the epithelial lining. Suppurated follicles rupture, forming a purulent plaque that does not spread beyond the tonsils. *Lacunar tonsillopharyngitis* — overt hyperemia, edema and infiltration of tonsils, lacunae expansion. The yellowish-white fibro-purulent lacunae contents form a loose plaque on the tonsil surface that looks like small foci or membrane. The plaque stays within the tonsils, it is easily removed without leaving a bleeding defect (fig. 1.2).

Laboratory and instrumental examinations

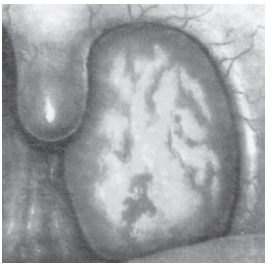
Microbiological diagnosis — sampling of material (mucus or matter) from palatine tonsils:

a) throat culture (to determine the pathogen, as well as sensitivity and resistance to antibiotics);
b) rapid antigen tests (used to detect GABHS).

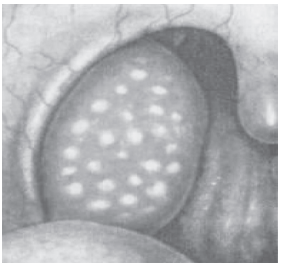
The McIsaac criteria are a validated scoring system used to determine the likelihood of an acute sore throat being caused by GABHS to stratify patients who need strep testing (table 1.5).



Catarrhal tonsillopharyngitis



Lacunar tonsillopharyngitis



Follicular tonsillopharyngitis

Fig. 1.2. Types of acute tonsillopharyngitis (V.T. Palchun. Guide to practical otorhinolaryngology // V.T. Palchun, L.A. Luchikhin, M.M. Magomedov. Medical Information Agency. 2010. P. 344)

Table 1.5. The McIsaac (modified Centor) scoring system

Symptom		Score
Body temperature (in the history) >38 °C		1
No cough		1
Cervical lymph node swelling		1
Tonsillar swelling, or exudation		1
Age (years)	3–14	1
	15–44	0
	≥45	–1
Scores	**Risk of infection with GABHS (%)**	**American College of Physicians/Centers for Disease Control and Prevention guidelines**
0	1–2	Do not test, Do not treat
1	5–10	
2	11–17	Treat if rapid test positive
3	18–35	Treat if rapid test positive, or Treat empirically
≥4	36–53	Treat empirically

Note. To calculate the score, patients receive one point for each of the following: fever, absence of cough, presence of tonsillar exudates, and swollen, tender anterior cervical nodes. Based on these signs and symptoms, the score is calculated (0–4).