



## ACUTE TONSILLOPHARYNGITIS EARLY DIF DIAGNOSIS AND TREATMENT METHODS IN CHILDREN (REVIEW)

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### Summary

Acute tonsillopharyngitis is a common infectious disease in which sore throat has been observed as the main symptom of acute tonsillopharyngitis, is the most common reason for seeking outpatient medical care. Spicy tonsillopharyngitis is a polyetiological disease and during treatment it requires mandatory clarification of the etiological factor. Viral tonsillitis is most common in pediatric practice among pediatricians. Group A beta-hemolytic streptococcus (GABHS Streptococcus pyogenes) and from 5 to 15% of cases of acute tonsillopharyngitis are associated with this pathogen, of which in the adult population and 20–30% in children [5,7,9]. Today, there are no reliable criteria for the differential diagnosis of viral and bacterial acute tonsillopharyngitis. As a result, the choice of treatment tactics for acute tonsillopharyngitis is a responsible task, in which this pathology is most often associated with excessive and unreasonable prescription of systemic antibiotic therapy and refusal of antibiotics can contribute to the development of serious complications. Given the high frequency of viral acute tonsillopharyngitis, an important direction in pediatric practice is the use of local antiseptic, anti-inflammatory drugs, therefore, topical drugs can be used both as monotherapy and, if necessary, in combination therapy for acute tonsillopharyngitis. Timely etiological diagnosis and rational therapy of acute tonsillopharyngitis are an important link in the effectiveness of the treatment of acute tonsillopharyngitis in children and the prevention of antibiotic resistance of microorganisms.

**Keywords:** Acute tonsillopharyngitis, pharyngitis, Epstein-Barr virus, angina Simanovsky about-Plauta-Vincent, adhesion.

In the structure of acute respiratory infections, acute tonsillopharyngitis is at least 15% [1, 2,23,24,31], and sore throat, as the main symptom of this disease, is the most common reason for seeking outpatient medical care [3,13,21,29]. The incidence of acute tonsillopharyngitis is 82 per 1000 children and is most diagnosed at the age of 1 to 3 years and in children 7–18 years old is only 32 per 1000 [4,20,28]. Taking into account the high frequency of acute tonsillopharyngitis in childhood, in the last





decade, more and more attention of medical communities has been paid to the creation of national guidelines that define algorithms for managing patients with acute tonsillopharyngitis in practical healthcare [4,20,28] . According to the recommendations, acute tonsillitis (from lat. tonsillae - tonsils, a synonym - angina (from lat. Ango - "squeeze, squeeze, soul") is an acute inflammation of the lymphoid tissue of the pharyngeal ring. National guidelines for acute tonsillitis [3,17,18] it is proposed to use the term " acute tonsillopharyngitis ", Since isolated inflammation of the tonsils without inflammation of the mucous membrane of the posterior pharyngeal wall (pharyngitis) is rare and the term " acute tonsillopharyngitis " more correctly reflects the pathological process of the pharyngeal organs. Some experts suggest abandoning this term "tonsillitis", based on the pharyngoscopic picture, does not correlate with the etiology and therapeutic tactics [5]. Depending on the choice of criteria, there is a different classification of acute tonsillopharyngitis a . Some of them distinguish primary acute tonsillopharyngitis a and secondary (with infectious (diphtheria, tularemia) diseases, as well as blood diseases). The classification of B.S. Preobrazhensky, which is based on pharyngoscope signs [6,15,22], and of course, according to this classification, the following forms of angina are distinguished: 1 - catarrhal, 2 - follicular, 3 - lacunar, 4 - fibrinous, 5 - herpetic, 6 - phlegmonous , 7 – ulcerative necrotic (gangrenous) tonsillitis of Simanovskog about– Plauta - Vincent , 8 - mixed forms. To this main diagnosis, after obtaining the appropriate data, the name of the microbe that caused the acute tonsillopharyngitis a (streptococcal, staphylococcal), however, in outpatient practice, it is more logical for a pediatrician to use the international classification of diseases of the 10th revision. It is the etiology of acute tonsillopharyngitis that determines the tactics of therapy and the advisability of prescribing systemic antibacterial drugs, due to the fact that it is a polyetiological disease. The causative agent of acute tonsillopharyngitis and can be a bacterial, viral, intracellular and fungal infection. According to numerous studies, the most common causative agents of acute tonsillopharyngitis are respiratory viruses, in which the leading position among viral pathogens is occupied by adenovirus, Epstein- Barr virus and enterovirus . However, other respiratory viruses can also lead to inflammation of the lymphoid pharyngeal ring [3–5,33,34,35]. Among bacterial pathogens, group A beta-hemolytic streptococcus is of paramount importance . From 5 to 15% of cases of acute tonsillopharyngitis in the adult population, including 20–30% of cases in children , are associated with this pathogen [5,9]. The pathogenicity of group A beta-hemolytic streptococcus is determined by the presence of a capsule for attachment to mucous membranes (adhesion), its resistance to phagocytosis, the release of numerous exotoxins, including those that cause a strong immune response, and the





presence of antigens (M-protein) that cross-react with the heart muscle . There are more than 80 serotypes of group A beta-hemolytic streptococcus for the M-protein, while antibacterial immunity is narrowly type-specific, which makes possible reinfection as a result of infection with new serotypes. Although not the most common, group A beta-hemolytic streptococcus tonsillitis is of paramount social and medical importance, due to the rapid spread of group A hemolytic streptococcus and its high contagiousness , as well as the ability to cause serious complications. In streptococcal acute tonsillopharyngitis a , “early” and “late” complications are distinguished, in which among the early complications, paratonsillar , lateral pharyngeal and retropharyngeal abscesses are most common , purulent lymphadenitis in which ultimately requiring emergency surgical intervention. Late (weeks 2–3 of the disease) complications include systemic immunopathological diseases, in which acute rheumatic fever, glomerulonephritis , bacterial endocarditis, and streptococcal toxic shock syndrome are the most dangerous. A number of authors point to a certain role of such bacterial pathogens as streptococci of groups C and G, *Streptococcus pneumoniae* , *Arcanobacterium haemolyticum* , anaerobes, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in the etiology of acute tonsillopharyngitis a [7,8,10,11,12]. Even rarer bacterial pathogens of acute tonsillitis are spirochetes (Simanovsky's angina - Plaut - Vincent) and anaerobes. It must be remembered that acute tonsillitis is still one of the main symptoms of diseases such as diphtheria (*Corynebacterium diphtheriae*), gonorrhea ( *Neisseria gonorrhoeae* ), which must be taken into account when diagnosing acute tonsillopharyngitis a , but in general statistical studies they occupy no more than 1% [9]. Mycotic lesions of the pharynx are also not frequent. According to the literature, *Candida albicans* is the main causative agent in 93% of patients with mycotic acute tonsillopharyngitis a [10,11,12,26,27], of course, it must be taken into account that *Candida albicans* is a normal inhabitant of the oropharynx and causes pathological processes mainly in conditions of systemic or local immunodeficiency [4,5] . The clinical picture of acute tonsillopharyngitis a , regardless of the etiological factor, is represented by the main symptoms - fever, sore throat, regional lymphadenitis, the most common symptom in acute tonsillopharyngitis a in children is a symptom of intoxication, which is manifested by fever. temperature in acute tonsillopharyngitis a does not correlate with the etiological factor and is present in both viral and bacterial infections. So, with adenovirus infection, fever can persist for 5–10 days and does not respond to systemic antibiotic therapy. At the same time, for acute tonsillopharyngitis a due to group A beta-hemolytic streptococcus, a significant drop in temperature 12–24 hours after antibiotic use is significant. The division of angina into catarrhal, lacunar, follicular





and ulcerative-membranous led to the identification of the first form with a viral infection, the last 3 with a bacterial one, and nevertheless raids on the palatine tonsils can be equally a symptom of both streptococcal acute tonsillopharyngitis and many SARS (adenovirus, rhinovirus, etc.), infectious mononucleosis, oropharyngeal candidiasis. On the contrary, the picture of catarrhal angina does not contradict GABHS-etiology of inflammation [11,30,32], and only petechial enanthema on the soft palate and uvula can be the only significant symptom that in the early stages can most likely indicate streptococcal etiology of acute tonsillopharyngitis [5,7]. In the light of modern knowledge, it is necessary to dwell on the term "herpetic sore throat". This term reflects a pharyngoscopic picture, reminiscent of lesions in herpes simplex virus types 1 and 2, as a result, unreasonable prescription of antiherpetic drugs for "herpetic sore throat" is often found. However, this lesion of the oral mucosa and less often the tonsils is most often a manifestation of an enterovirus infection (most often Coxsackie B). This helps in the diagnosis of enteroviral vesicular pharyngostomatitis, a characteristic double sharp increase in temperature and a peculiar rash in the mouth, hands and feet. In the treatment of enteroviral acute tonsillopharyngitis, it is not advisable to prescribe drugs of the acyclovir group. Sore throat with changes in the pharyngeal mucosa, tonsils is often accompanied by phenomena of regional lymphadenitis (enlargement, induration, soreness of the submandibular, anterior and posterior lymph nodes), which is especially pronounced regional lymphadenitis in infectious mononucleosis. Epstein tropism of Barr virus to blood lymphocytes contributes to the persistence of the virus in the organs of the lymphatic system. So, along with the defeat of the tonsils, there is a clinic for the defeat of adenoid vegetations (adenoiditis), lymphadenopathy, hepatosplenomegaly. Despite the fact that atypical lymphocytes in the blood of infectious mononucleosis help to make a diagnosis, they are detected only in 6% of patients [8,14]. Thus, such clinical signs as fever and raids on the palatine tonsils are equally common in both viral and bacterial forms of tonsillitis, which significantly complicates the etiological diagnosis and early treatment of this disease. However, there are some clinical features that make it more likely to diagnose viral acute tonsillopharyngitis, since adenoviral infection is characterized by hyperemia and loose white plaques on the tonsils, viral conjunctivitis and severe nasopharyngitis with an abundance of mucus on the back of the pharynx and the last two signs are the most significant differences between viral tonsillitis and bacterial ("adenoviral pharyngo-conjunctival fever"). Streptococcal acute tonsillopharyngitis differs from the viral one in the absence of cough, severe catarrhal symptoms, conjunctivitis, and sometimes tenderness of the lymph nodes is determined by palpation [10,12,19], in the diagnosis of viral acute tonsillopharyngitis





a, it is necessary to take into account the seasonality of the disease and epidemiological data. Viral acute tonsillopharyngitis, as well as any acute respiratory viral infection, is characterized by high contagiousness and rapid spread in the team. The presence of catarrhal phenomena (hyperemia of the conjunctiva, difficult nasal breathing, rhinorrhea) is also highly likely to indicate in favor of the viral etiology of the disease, but, however, it must be remembered that mixed infections (viral-viral, viral-bacterial) play an important role as an etiological factor and therefore, the clinical picture of the disease often does not reflect the significance of the pathogen, and the presence of symptoms of an acute respiratory viral infection can mask bacterial acute tonsillopharyngitis [12]. The absence of clear clinical symptoms and the need for etiological differentiation of tonsillitis led to the creation of clinical rating scales. So, according to the update in January 2018 by the National Institutes of Health of Great Britain (National Institute for Health and Care Excellence -NICE) NICE guidelines for the management of patients with acute sore throat, it is recommended to use the FeverPAIN or Centor criteria to decide whether antibiotic therapy is appropriate [13,25,32]. Deciphering the FeverPAIN criteria indicator includes an assessment of the following symptoms: "Fever" - fever (within 24 hours), "P - Purulence" - the presence of pus on the tonsils, "A - Attend rapidly" - rapid treatment (within 3 days after the onset of symptoms), "I - Severely Inflamed tonsils" - severe inflammation of the tonsils; "N - No cough or coryza" - no cough or runny nose (inflammation of the mucous membranes of the nose) and each positive FeverPAIN criterion is 1 point (maximum score 5). Higher scores suggest more severe symptoms and possible bacterial (streptococcal) infection, which is considered a score of 0 or 1 associated with a 13 to 18% chance of strep isolation. A score of 2 or 3 is associated with a 34 to 40% chance of isolating streptococcus. A score of 4 or 5 is associated with a 62 to 65% chance of streptococcal isolation [11,13]. The Centor criteria also include a score for symptoms such as the presence of tonsillar exudate, cervical lymphadenopathy or lymphadenitis, the severity and duration of fever, absence of cough, and each of the Centor criteria is scored 1 point (the maximum score is 4). It is believed that a score of 0, 1 or 2 is associated with a probability of streptococcal isolation from 3 to 17%, and also, a score of 3 or 4 is associated with a probability of streptococcus isolation from 32 to 56% [13,30]. However, the use of these scales in pediatrics has its limitations. Thus, the scales do not take into account cases of tonsillitis in children under 3 years of age, and in addition, if there is a maximum score, according to the scales, GABHS infection can only be suspected with a probability of no more than 53–65%. An American retrospective study covering a 3-year period, which included more than 200 thousand children aged 3 years and older





with acute tonsillitis, showed that among children with already proven streptococcal tonsillitis, half of the clinical signs fit into 0-3 points on the Centor scales and McIsaac [14], and the age of the child can serve as an additional differential diagnostic criterion for viral and bacterial acute tonsillopharyngitis. It has been established that children of the first year of life have antitoxic and antimicrobial streptococcal immunity acquired from the mother, and therefore GABHS is rarely an etiological factor in acute tonsillopharyngitis in this group of patients [15], including studies that have shown that in children under 3 years of age in 70–90% of cases of acute tonsillopharyngitis is a manifestation of a viral respiratory infection, while the likelihood of GABHS tonsillitis at the age of 2 years is minimal (3%), but in children after 5 years the role of the bacterial factor increases to 30–50% [5,12]. The highest prevalence of acute streptococcal tonsillopharyngitis occurs in childhood (>3 years) and adolescence [5,40,42]. In people older than 45 years, the probability of streptococcal etiology again becomes minimal [15,42]. The complexity of the differential diagnosis of viral and bacterial acute tonsillopharyngitis also lies in the ambiguity of laboratory markers of the infectious process in children. It has been established that many viral infections, especially those associated with DNA viruses (adenoviruses, herpesviruses), cause changes in laboratory parameters of a clinical blood test, which is more characteristic of a bacterial infection. So, in a clinical blood test, an increase in the number of leukocytes often exceeds  $10 \times 10^9 / l$  and even  $15 \times 10^9 / l$ , which greatly complicates the etiological diagnosis, and that is why, at present, leukocyte numbers above  $15 \times 10^9 / l$  are considered to be a characteristic sign of a bacterial infection. The absolute (rather than relative) number of neutrophils is above  $10 \times 10^9 / l$  and stab neutrophils is above  $1.5 \times 10^9 / l$  [12,16,38,39]. Markers such as C-reactive protein (CRP) and procalcitonin test (PCT) are also not definitive in the diagnosis of bacterial acute tonsillopharyngitis. Often, the level of CRP in patients with a viral infection is in the range of 15-30 mg / l. Therefore, an increase in CRP above 30 mg/l should be considered significant for the diagnosis of a bacterial infection. Another marker of bacterial infection - PCT is a predictor of bacterial infection when its level rises above 0.5 ng / ml, but, however, this limit should now be raised to 2 ng / mL, as values of 0.5–2 ng / mL occur in 20% of children with acute viral infections. These levels cannot be considered an absolute criterion for a viral or bacterial infection, and they often increase with a viral infection and are not achieved with a bacterial one [16,40,41]. Taking into account the absence of significant clinical and laboratory criteria for the etiological diagnosis of acute tonsillopharyngitis, the "gold standard" for diagnosing GABHS tonsillitis are methods for identifying an infectious agent. The use of express methods is especially justified. Thus, the use of test systems for the detection of group





A streptococcal antigens makes it possible to obtain a positive result in 15–20 minutes with high specificity (about 90%) and sensitivity (up to 95%). The use of these techniques is limited by their low availability in practical healthcare. On the other hand, ideally, in all cases of acute tonsillopharyngitis a , a throat swab should be cultured for hemolytic streptococcus, the sensitivity of this method reaches 90% [10,12,36,37]. However, the difficulty of collecting and preserving the material, as well as the early use of antibiotics in acute tonsillopharyngitis a , sharply reduce the likelihood of streptococcus inoculation and limit the use of this method in medicine. Thus, at present, despite the achievements of modern medicine, significant difficulties remain in determining the etiology of acute tonsillopharyngitis in practical public health. There are no reliable clinical and laboratory criteria that allow for a highly reliable differential diagnosis of viral and bacterial acute tonsillopharyngitis a , and as a result, the choice of etiotropic therapy for acute tonsillopharyngitis a is a responsible task for outpatient doctors. On the one hand, excessive and unreasonable prescription of systemic antibiotic therapy is most often associated with this pathology, on the other hand, refusal of antibiotics can contribute to the development of serious complications. Given the high frequency of viral acute tonsillopharyngitis a , an important direction in pediatric practice is the use of local antiseptic and anti-inflammatory drugs, in which topical drugs can be used both as monotherapy and, if necessary, in combination therapy for acute tonsillopharyngitis a . Timely etiological diagnosis and rational OTP therapy using combined preparations is an important link in the effectiveness of the treatment of acute tonsillopharyngitis a in children and the prevention of secondary antibiotic resistance of microorganisms.

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