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ACUTE UPPER RESPIRATORY TRACT INFECTIONS: DIAGNOSTIC CHALLENGES AND THERAPEUTIC APPROACH

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ABSTRACT

Background. Upper respiratory tract infections (URTIs) remain one of the most prevalent diagnoses in primary care. In medical practice most of them are self-limiting, therefore symptomatic management is the primary approach. Appropriate treatment is beneficial for the patient and for entire healthcare system.
Purpose. Aim of this study is to assess advantages and potential risks, when approaching treatment of acute upper respiratory tract infections based on particular etiology, while also highlighting the diagnostic challenges associated with identifying the causative pathogen.
Material and Methods. A narrative review was conducted using PubMed and Google Scholar databases. Main focus was put on recent clinical guidelines and research papers.
Results. The great diversity of etiological factors causing URTI and very similar clinical presentation means that more specific tests like PCR are required to properly distinguish pathogens. Furthermore, most URTI are of viral etiology, therefore causal treatment is rarely possible. Combining those facts with over-the-counter availability of NSAIDs means that COX-inhibitors became a staple in quick symptomatic relief.
Conclusion. Timely intervention in URTI leads to better outcomes and well-being of patients. In cases where etiology-based treatment is available, early intervention may contribute to reducing the infectious period and lowering the risk of hospitalization in high-risk patients. However, the potential increase in antimicrobial resistance should always be considered when making a treatment-related decision involving antibiotics. Objective medical tools, such as the Centor score may aid and quicken the decision process, while ensuring that antibiotics are administered when genuinely indicated.

KEYWORDS

Upper Respiratory Tract, Croup, Epiglottitis, Inflammation, Rhinovirus

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1. Introduction

Acute upper respiratory tract infections (URTIs) are one of the most common illnesses. In clinical practice their symptoms may include: mild to moderate fever, nasal congestion, rhinorrhea, pharyngitis, cough, malaise, headache. Due to the fact, that they are mostly caused by viruses and tissue damage accompanied by inflammation is considered to be main source of symptoms, NSAIDs remain preferred treatment for those affected by disease. (Azh et al., 2022; Eccles, 2023)

Acute URTIs are, in the vast majority of cases, self-limited. Despite that fact due to their high occurrence rate and impact on quality of life they remain one of the most prevalent diagnoses in primary care. Furthermore, they also predispose to more serious complications such as paranasal sinusitis. Prolonged disease duration also contributes to unnecessary prescriptions of antibiotics. (Eccles, 2023; Heikkinen & Ruuskanen, 2006)

2. Research materials and methods

A literature search was conducted using PubMed and Google Scholar databases`. The search was conducted using the following keywords and their combinations: “URTI”, “common cold”, “treatment”, “COX inhibitors”, “pharyngitis”, “rhinosinusitis” and “COVID-19”. Time restrictions were not applied; however, emphasis was put on more recent publications in order to reflect current clinical guidelines and emerging evidence.

3. Results

3.1. Pathophysiology of URTI

Most common symptoms of URTI are strictly connected to body response via inflammation. After tissue gets damaged by any pathogen, recruitment of immune cells gets started. Innate cells activate signaling network, which leads to migration of macrophages, mast cells and dendritic cells. As a result, more pro-inflammatory cytokines are produced and the inflammation progresses. In cases of influenza virus, cytopathic effect on the epithelium may also be observed. This is not the case when it comes to the most common virus causing URTI – rhinovirus. For this exact reason, cytokines are believed to be the direct cause of most symptoms of URTI, especially the systemic ones like fever. It is also worth noting that the vast majority of viruses, capable of causing URTI, manifest with flu-like symptoms and are indistinguishable from one another based solely on symptoms and physical examination. (Eccles, 2005; Heikkinen & Ruuskanen, 2006)

One of the major enzymes that takes part in pro-inflammatory cytokines production is cyclooxygenase (COX). Its isoforms COX-1 and COX-2, although very similar in function, have some very distinctive characteristics. Both isoforms catalyze conversion of arachidonic acid into prostaglandin. Furthermore, they are considered to inhibit neutrophil function and inducible nitric oxide synthase. (Qureshi et Dua, 2024)

COX-1 is a constitutively expressed isoform, synthesized by most tissues. It regulates platelet aggregation and plays a pivotal role in sustaining homeostasis of kidneys, uterus, endothelium and gastrointestinal mucosa.

COX-2 is defined as an inducible enzyme, whose expression increases during inflammation. Its role, although not as clear as that of COX-1, is considered to involve increasing vascular permeability, pain mediation, vasodilation and chemotaxis. (Qureshi et Dua 2024; Bassetti et al., 2024)

3.2. Manifestations

Considering the fact that upper respiratory tract consists of more than one organ, URTI may manifest in different ways. Disease presentation is also modulated by age, physiological state and immunological experience of the host. Furthermore, immunological response is partially influenced by nature of the infecting pathogens. The two most common clinical conditions are acute pharyngitis and rhinosinusitis. Both of these diagnoses are well recognized by the general population and are often treated without any prior contact with healthcare professionals. (Eccles, 2005, 2023)

The most common clinical features of rhinosinusitis include nasal congestion, hoarseness, scratchy throat, coughing due to postnasal drip, headache, fever, malaise

and hyposmia. Typically, rhinosinusitis lasting up to 10 days is considered to be of viral etiology. If symptoms persist beyond this point or worsen after a brief period of improvement, bacterial superinfection should be suspected. During physical examination pressure tenderness of affected sinuses may be observed. (Romano et al, 2025, Wolford et al, 2023)

Manifestations of acute pharyngitis vary depending on etiology. Viral infection often causes sore throat, headache, muscle pain, mild increase in body temperature, conjunctivitis, nasal congestion, diarrhea and rarely lymphadenopathy. It may also predispose to bacterial complications such as acute otitis media. Bacterial pharyngitis is most commonly caused by Group A β-hemolytic *Streptococcus.* It shares many common symptoms with viral etiology, but there are a few key differences, especially considering prevalence of certain manifestations, including sudden onset, severe pain when swallowing, fever, tonsillar exudates, large anterior cervical lymph nodes and strawberry tongue. (Sahu & Sahoo, 2021; Ashurst et al., 2025)

Another noteworthy URTI presentation is pharyngitis caused by Epstein-Barr virus (EBV), which is also known as infectious mononucleosis. The most characteristic symptom of this disease is anterior and posterior cervical lymphadenopathy. It is also worth noting that posterior lymphadenopathy is more specific to EBV infection. Moreover, it also manifests with headache, tonsillar hypertrophy, fatigue, lymphocytosis and fever. Changes outside upper respiratory tract may include hepatomegaly and splenomegaly. The clinical presentation of EBV-associated pharyngitis may sometimes be misleading and imitate bacterial pharyngitis. If in this situation amoxicillin is used for treatment, a morbilliform rash may develop. In laboratory tests most characteristic change is the presence of atypical leukocytes, which constitute more than 10% of the total lymphocyte count. The monospot test is specifically designed to detect the serum heterophile antibodies of infectious mononucleosis. (Wolford et al., 2023; Leung et al., 2024)

Inflammatory processes can also affect lower structures of upper respiratory tract. One of such locations is epiglottis. Epiglottitis occurs more frequently in children, due to infections with *Haemophilus influenzae* type B. This potentially life-threatening condition can present with varying symptoms. Patients most

commonly complain of sore throat, fever and dysphagia. Visualization of the airways must be performed cautiously, especially in pediatric population. Progressing inflammatory process eventually leads to obstruction of the airways. To aid the diagnostic process radiographs may be obtained to reveal enlarged epiglottis and loss of the vallecular air space. (McDermott et al., 2024)

Croup is an inflammatory disease that causes changes in larynx and sometimes lower parts of the respiratory system such as trachea and bronchi. The age group with the highest incidence is children between 6 months and 3 years old. Viruses, especially parainfluenza viruses, are the most common cause of croup. Bacterial etiology is rarer, but may lead to several conditions, including laryngotracheobronchopneumonitis and diphtheria. Tost characteristic symptom is barking cough accompanied by difficulty breathing that worsens at night, runny nose and low-grade fever. During physical examination stridor may be heard. The illness typically lasts 3 to 7 days. Most severe symptoms occur usually on days 3 or 4. Westley Croup Score is the ideal tool of objectivization of croup severity. (Kadam et al., 2025)

Table 1. Comparison between viral and bacterial pharyngitis

Etiology / Feature	viral	bacterial
fever	absent or mild	often high
sore throat	mild	severe pain, while swallowing
tonsillar exudates	usually, absent	common, especially in pharyngitis caused by Streptococcus pyogenes
onset	gradual	acute
cough	common	less common
nasal congestion	common	less common
strawberry tongue	absent	characteristic in pharyngitis caused by Streptococcus pyogenes
cervical lymph nodes	lymphadenopathy not characteristic (anterior and posterior cervical lymphadenopathy in infectious mononucleosis)	anterior cervical lymphadenopathy

3.3. Treatment

Symptoms, duration, etiology and condition of the patient should all be taken into consideration, when attempting URTI therapy. Treatment should concentrate, as far as possible, on elimination of the cause of infection, for this reason in most cases etiology pays pivotal role in the therapeutic approach.

3.3.1. Treatment of Streptococcal pharyngitis.

In cases of bacterial pharyngitis, especially those caused by Streptococcus pyogenes, patients benefit significantly from early treatment. First line therapy includes penicillin or amoxicillin. For patients with a nonanaphylactic reaction to β-lactams, first generation cephalosporins are recommended. Macrolides or clindamycin should be utilized in patients with a known anaphylactic reaction to β-lactam antibiotics. (Romano et al., 2025, Ashurst et al., 2025)

Early administration of antibiotics leads to a significant reduction in the infectious period. Approximately 80% of patients with streptococcal pharyngitis become non-infectious within 24 hours of initiating appropriate antibiotic therapy. Without any intervention transmission remains possible for around 2-5 days. Furthermore, antibiotics reduce the duration of illness by approximately one day. Improvement in symptoms may depend on the speed with which antibiotics are administered. Several studies note that treatment initiated within 48 h of the onset of symptoms provides the greatest symptomatic relief. (Ashurst et al., 2025; Van Brusselen et al., 2014; Mustafa & Ghaffari, 2020)

Aside from treatment of pharyngitis caused by Streptococcus pyogenes where antibiotics are a staple, there are also other clinical states that strongly suggest bacterial infection and are indication towards antibiotics. Indications are as follows: acute otitis media, sinusitis lasting more than 10 days or when sinus symptoms worsen after a period of initial improvement. (Romano et al., 2025, Tobin et al., 2025)

Antibiotics also reduce the incidence rate of complications, of which the most notable are rheumatic fever and peritonsillar abscess. However, their preventive effect is limited, when the patient presents after a

complication has already begun to develop. Inappropriate use of antibiotics may cause resistance to occur. Therefore, decision of antibiotic administration should always be made, based on more objective measures, such as Centor score, while also taking all patient-related factors into account. (Van Brusselen et al., 2014; Ibrahim et al., 2025)

3.3.2. Treatment of viral URTI

Targeting any of COX isoforms leads to decrease in tissue damage caused by cytokines. Most of the viruses causing URTIs lack specific anti-viral therapy, thus their treatment is largely symptomatic. For this reason, NSAIDs became the primary way of symptom control. By inhibition of COX enzymes, they not only reduce the inflammatory symptoms, but also have the potential to stop disease progression before serious complications develop. This leads to decrease in probability of hospitalization. Some concerns were raised regarding the fact, that NSAIDs may cause prolonged illness time, however few studies suggest that there is no significant difference in UTRI duration, but the quality of evidence is limited. (Bassetti et al, 2024; Nicolas et al, 2023; Kim et al, 2015)

The efficacy of NSAIDs on symptoms of URTI differ depending on the exact substance used. Ibuprofen and naproxen have been shown to moderately reduce fever. When it comes to sore throat both NSAIDs present little to no difference compared to placebo, although substantial evidence is still lacking. Several studies point to ibuprofen decreasing time period, in which individuals experience cough. However, one study suggests paradoxical increase in its severity. Diclofenac, although very similar to two aforementioned NSAIDs, presents one major difference in context of symptom control. Similarly to ibuprofen and naproxen, diclofenac is capable of reducing fever. When compared to aspirin, it exerted up to 2 h longer antipyretic effect. Difference comes in the fact, that diclofenac usage results in large reduction in sore throat. Aspirin is capable of significant fever reduction. Most studies do not suggest any reduction of pain in patients with sore throat. Data regarding its effectiveness on cough is still insufficient. (Azh et al., 2022)

There are also non-pharmacological interventions that can prove most helpful especially for patients experiencing sore throat or cough. Honey and other demulcents exert soothing effect on pharyngeal mucosa, which is mediated by adhesion of polysaccharides to membranes. If the dry cough is caused by reflex response of irritated receptors in the oropharynx, demulcents may reduce its severity and frequency. Other home method includes usage of saline. It may be most helpful in nasal or respiratory hygiene and reduction of viral load. Saline also promotes ciliary activity and contributes to mucus gelation, making it easier to cough up mucus. Furthermore, these kinds of interventions are well tolerated and most patients consider them helpful in symptom control. (Sebo et al., 2023; Smith et al., 2025)

Specific antiviral treatment may be considered, in case of influenza. Possible choices, when it comes to therapy, include neuraminidase inhibitors, M2 ion channel inhibitors and endonuclease inhibitors. Additionally, these drugs may be used in prophylaxis of influenza, which reduces the risk of symptomatic influenza regardless of whether they were given before or after the exposure. Unfortunately, antiviral resistance develops further every year. To counteract this process, combination therapy of 2 or potentially even more compounds may be considered. Early administration of antiviral drugs proves beneficial mainly for reduction of disease duration by up to 2.5 days, while also decreasing the risk of influenza complications. It can also reduce transmission of infection. Furthermore, patients receiving antiviral treatment are able to return to their normal activities significantly faster. Influenza infection is, in most cases of individuals who do not possess any comorbidities, self-limited. For this reason, patients suffering from mild influenza infections, who are otherwise healthy, do not require administration of antiviral drugs. (Duwe et al., 2021; Benjamin et al., 2025)

Similarly to influenza Coronavirus disease 2019 (COVID-19) can also be treated with specific antivirals, such as nirmatrelvir-ritonavir or remdesivir. Before any of the aforementioned drugs can be administered, coronavirus etiology must be confirmed. It is impossible to distinguish URTI caused by COVID-19 from other viral etiologies without additional testing, such as PCR. Early administration of specific antiviral treatment in COVID-19 may potentially lead to reduced risk of hospitalization, but due to the nature of the disease, unless the infection spreads to other internal organs beyond the respiratory system or the patient belongs to a high-risk group, COVID-19 is unlikely to be suspected. (Tobin et., al, 2025; Chung et al., 2024)

3.3.3. Treatment of acute epiglottitis

Management of acute epiglottitis tends to be more conservative in adults compered to children. The most important objective is airway management. It ranges from observation and antibiotic administration to intubation of the patient. Stridor in adult patients is suggestive of impending airway obstruction. Frequent monitoring is advised to notice any life-threatening changes. (McDermott et al., 2024)

Antibiotics are crucial part of treatment, because in most cases infection is of bacterial etiology. Recommended first line therapy includes administration of third-generation cephalosporin along with an antistaphylococcal agent. For patient with epiglottitis complicated by sepsis, concomitant meningitidis or those from areas with an increased prevalence of clindamycin-resistant methicillin-resistant *S aureus*, vancomycin is recommended. For patients allergic to penicillin combination therapy of vancomycin and fluoroquinolone antibiotic agent is the treatment of choice. (Dowdy & Cornelius, 2020; Ward, 2002)

Adjuvant therapies may help be utilized to aid management of patients. Humidified oxygen along with IV hydration can limit the risk of sudden airway obstruction. Corticosteroids usage remains controversial due to the paucity of data regarding its efficacy. There is no correlation between the usage of corticosteroids and shorter duration of intubation. Hospital stay also does not appear to shorten. (Dowdy & Cornelius, 2020)

3.3.4. Treatment of croup

Although in most cases croup is self-limiting it may potentially lead to serious clinical states that require intervention. Treatment of croup is strictly dependent on severity of symptoms. First line of therapy should always be glucocorticoids. They not only decrease symptoms of croup but also shorten hospital stays. Dexamethasone is the drug of choice because of its availability and effectiveness. Lower doses of 0.15 mg/kg may be equally as effective as higher doses such as 0.3 mg/kg and standard dose of 0.6 mg/kg. Other forms of interventions include nebulization of epinephrine and in extreme cases intubation. (Aregbesola et al., 2023)

4. Conclusions

URTIs are a heterogeneous group of diseases, therefore treatment varies depending on the etiological factor and the location of infection. For this exact reason objective medical tools combined with additional tests provide the highest probability of selecting appropriate therapy. However, NSAIDs remain effective regardless of etiology, making them a reliable option for every patient with URTI. There seems to be no correlation between NSAIDs treatment and prolonged disease duration, but the available materials are not sufficient to draw definitive conclusions. There are also many non-pharmacological interventions, such as honey administration in cases of irritated pharyngeal mucosa and saline solutions for nasal hygiene. While most patients report improvement with these measures, the data available in literature remains insufficient to draw definitive conclusions on their exact influence.

In cases of bacterial pharyngitis, the most common pathogen is Stretococcus pyogenes. Its characteristic clinical presentation makes the Centor score an ideal tool for guiding antibiotic administration. It is worth noting that in case of Streptococcus pyogenes early therapy not only decreases the infectious period, but also reduces illness duration and reduces the risk of complications. For the appropriate treatment, the antibiotic of choice is penicillin or amoxicillin. Macrolides should be reserved for patients with anaphylactic reaction to β-lactams.

Specific antiviral treatment, although theoretically possible, has several limitations. Firstly, only a few viruses, such as influenza virus and coronavirus, have causal treatment available. Secondly, in URTI clinical presentation is not pathogen specific, so additional testing would be required to confirm specific etiology. Lastly, antiviral treatment is not recommended for immunocompetent patients without any comorbidities. Epstein-Barr virus is an interesting case, because aside from causing pharyngitis it also presents with additional characteristic symptoms such as anterior and posterior lymphadenopathy, hepatomegaly and splenomegaly.

Rare, but life-threatening manifestation of URTIs is epiglottitis. It manifests as sore throat, fever and dysphagia. Patients with this condition should be actively observed, due to potential risk of airway obstruction. Epiglottitis is caused mainly by bacteria; therefore, proper treatment consists of combination of two antibiotics mainly III-generation cephalosporin and an antistaphylococcal agent. Available data does not support usage of corticosteroids.

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