REVIEW ARTICLE

Suggestive Implementation of McIsaac Score as Pediatrics Department's KPI in Revision of the Use of Antibiotics for Acute Pharyngitis

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ABSTRACT

Prescribing antibiotics for acute pharyngitis usually depend on physician's clinical judgment, which could be affected by many factors such as parents' preference of treatment. This subjective clinical approach to this common problem need to be solved; and we thought that the best way to do so, is by making clinical guideline for the management of acute pharyngitis, and then to monitor the compliance to this guideline through a key performance indicator (KPI). This includes rational the prescription of antibiotics in query pharyngeal infection. Presumptive pharmaceutical treatment, such as administering antibiotics without laboratory evidence, requires fulfillment of characteristic signs and symptoms by McIsaac Score in pharyngitis for this group of patients. The authors after a revision of the literature, describe how the physician can use suggested algorithms to minimize the irrational antibiotics prescription in acute pharyngitis, and preserve the risk of drug resistance, in which suggested as pediatrics department's KPI, by recording the modified Centor criteria (or McIsaac score) in each dispensed prescription for acute pharyngitis within the department, through suggested stamp design, applied in each revised antibiotics prescription. On conclusion, the authors reached ten points, which most of them would not be familiar to the regular health practitioners, including but not limited to the following: The most common cause of pharyngitis is viruses. On the absence of viral infection symptoms and signs; no antibiotics prescription is justified without a confirmatory laboratory test. The treatment is specified on easing the child condition only without antibiotics as far as bacterial Group A streptococci infection is not the underlying etiology. The financial impact of antibiotics misuse is genuinely harmful to the health sector. Following the McIsaac Score in pharyngitis would positively impact the long-term consequences of drug-resistance organisms.

Categories: Infectious Disease, Pediatrics, Quality Improvement
Key words: Antibiotics therapy, Anti-infectives, Drug stability

BACKGROUND

Key performance indicator (KPI)

A measurable expression for the achievement of a desired level of results in an area relevant to the evaluated entity's activity (The KPI Institute).

Causes of acute pharyngitis

Acute pharyngitis in kids and minors is often resulted from viral infection or Group A *Streptococcus* (GAS) Possible duration of illness – Throat pain caused by infections usually lasts for few days and will improve in a regular pattern without worsening.[1]

What is the indication of antibiotics use in acute pharyngitis?

Antibiotics are only indicated for patients suffering pharyngitis caused by bacteria. Empirical antibiotic therapy may be considered in patients with a Centor score of 4 or higher who are at high risk (>50%) of streptococcal pharyngitis.[2]

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Certain bacteria are the only indication for antibiotics in treating patients suffering pharyngitis. Patients with a Centor score of 4 or higher who are at high risk (>53%) of streptococcal pharyngitis, can be considered for empirical antibiotic therapy.[2] However, the use of antimicrobial therapy has no proven benefit in treating organisms other than GAS, as will be explained at the end of the article.

What does centor criteria stand for?

Centor criteria is formulated in; 1-high grade of fever (>38.5°C), (2-exudatoustonsils, 3-swollen and tender anterior cervical lymph nodes, and 4-the absence of cough). Used as an algorithm to assess the origin of sore throat, and the probability of Group A β hemolytic *Streptococcus* (GABHS) as the underling pathogen.[3]

What does modified Centor criteria or MCISAAC score stand for?

The Centor score is modified to McIsaac score by considering the differences in incidence of GAS infection in children (which occurs between 3 and 14 years of age) versus older adults. The Centor score is used, but if the patient is younger than the age of 15, one point is added, while another point is subtracted if the patient is aged 45 years or older.[4]

INTRODUCTION

Antibiotics misusing and overusing creates a great risk for all of us, the usage of antibiotics when it is not indicated quicken emergence of antibiotic resistance, one of the major threats to global health. Overuse of antibiotics lead to resistant bacteria, that is, current therapeutic lines will no longer be effective.[5]

To improve the rationality of antibiotic, The World Health Organization (WHO) founded the International Network for Rational Use of Drugs (INRUD) through the design, evaluation, and promotion of effective strategies in 1989.[6]

Moreover, considerable numbers of countries have adopted a policy of rational antibiotic usage to standardize prescribing attitude, and augmenting the integrity of medical units. However, the dilemma of irrational antibiotic usage stays unsettled in the health-care industry worldwide, especially in developing countries.[7]

Pharyngitis is known as an infection or irritation of the pharynx and, or tonsils. The etiology is usually infectious, with viral origin in most cases, and most bacterial presentation attributable to GAS. Other causes include toxins, allergy, trauma, and neoplasia.[8]

However, viral infections are the most common cause of pharyngitis.[9]

Here, in which we are focusing on the two common causes of pharyngitis "viral and bacterial" and trying to describe the importance of distinguishing between them in acute clinical settings, to minimize the irrational prescription of antibiotics in pharyngitis. In addition, studies have proven that antibiotics resistance is one of the urging complications of irrational use of antimicrobial agents. Furthermore, the harmful financial impact to the health sector from irrational prescription of antibiotics is one of the main reasons behind the conducted studies of the performance indicators optimization. Weighing both the patients and health industry benefits, the authors have reached into a conclusion of a suggested mechanism to minimize the risk of irrational antibiotics use in acute pharyngitis.

REVIEW

Causes of acute pharyngitis

Bacterial pharyngitis

GAS, also known as *Streptococcus pyogenes*, is the most common cause of bacterial pharyngitis in children and adolescents.[10]

It is the main bacterial cause worldwide of pharyngo-tonsillitis in children and adults. GAS is one of the few causes for which antibiotic treatment is permissible.[11]

GAS; *S. pyogenes* is an aerobic Gram-positive coccus that causes a broad range of infections. GAS is commonly associated with pharyngitis or skin and soft tissue infection; these are not typically associated with invasive infection.[12]

Less commonly, GAS causes invasive disease; refers to infection in the setting of culture isolation of GAS from a normally sterile site, for example, blood.[12]

Forms of invasive GAS infection include meningitis, osteomyelitis, bacteremia, deep soft-tissue infection, and bacteremic pneumonia.[12]

Types of GAS infections

GAS can cause symptomatic infection or can colonize the oropharynx.

Active infection

Refers to symptomatic infection caused by GAS.

Persistent infection

Refers to symptomatic infection caused by GAS that does not resolve after appropriate antibiotic treatment. This is synonymous with treatment failure.[10]

Types of viral pharyngitis by medscape

It can be caused by different numbers of viruses. Acute pharyngitis is an inflammatory syndrome of the pharynx

and/or tonsils caused by several different groups of microorganisms. Pharyngitis can be part of a generalized upper respiratory tract infection or a specific infection localized in the pharynx.

Rhinovirus

More than 100 different serotypes of rhinovirus cause approximately 20% of cases of pharyngitis and 30–50% of common colds, causing obstructive symptoms. The virus does not invade the pharyngeal mucosa. Transmission occurs by large particle aerosols or fomites.

Adenovirus

In children, adenovirus causes uncomplicated pharyngitis or pharyngoconjunctival fever, which is characterized by fever, sore throat, and conjunctivitis. Unlike rhinovirus infections, adenovirus directly invades the pharyngeal mucosa.

Epstein-Barr virus (EBV)

It is the agent of infectious mononucleosis. EBV usually spreads from adults to infants, through saliva and rarely through blood transfusion. In addition to edema and hyperemia of the tonsils and pharyngeal mucosa, an inflammatory exudate and nasopharyngeal lymphoid hyperplasia also develop. Pharyngitis or tonsillitis is present in about 82% of patients with infectious mononucleosis.

Herpes simplex virus (HSV)

HSV types 1 and 2 cause gingivitis, stomatitis, and pharyngitis. Acute herpetic pharyngitis is the most common manifestation of the first episode of HSV-1 infection. After HSV enters the mucosa, it either infects sensory or autonomic nerve endings. The virus then spreads to other mucosal surfaces through centrifugal migration of infectious virions through nerves. This mode of spread explains the high frequency of new lesions distant from the initial crop of vesicles.

Influenza virus

Half of the patients with "influenza A", develop severe pharyngitis and sore throat, and in a smaller percentage of patients with influenza B. The influenza virus invades the respiratory epithelium, causing necrosis, which predisposes the patient to secondary bacterial infection. Transmission of influenza occurs by aerosolized droplets.

Parainfluenza virus

Usually the common cold syndrome becomes the manifestation of pharyngitis caused by parainfluenza virus types 1–4. Mainly in late fall or winter Parainfluenza virus type 1 infection occurs in epidemics, while sporadically type 2 infection occurs. Parainfluenza virus type 3 infection occurs either way.

Coronavirus

Common cold usually is the manifestation of pharyngitis caused by coronavirus. However, as in rhinovirus colds, mucosal invasion of the respiratory tract does not take place.

Enterovirus

Coxsackievirus and echovirus are the major groups of enteroviruses that can cause pharyngitis. Enteroviruses are transmitted by the oro-fecal route primarily, although the airborne transmission remains important for certain serotypes.

Respiratory syncytial virus (RSV)

Fomites or large-particle aerosols produced by coughing or sneezing is the main transmission pathway of RSV. The pathogenesis remains unclear, although a number of theories exist. Immunologic mechanisms may contribute to the pathogenesis of the severe disease in infants and elderly patients.

Cytomegalovirus (CMV)

Sexual contact, breast milk, through respiratory droplets among nursery or day care attendants, and by blood transfusion; these are the source of transmission in acute acquired CMV infection. Infection in the immunocompetent host is very seldom to results in clinically ill presentation of the disease. Infrequently, immunocompetent hosts exhibit a mononucleosis-like syndrome with mild pharyngitis.

Human immunodeficiency virus (HIV)

Pharyngitis can develop in HIV patients as part of the acute retroviral syndrome, mononucleosis like syndrome that is the initial presentation of HIV infection in 50–75% of newly diagnosed individuals.[13]

Detection of bacterial pharyngitis and spectrum of the diseases by Medscape

A wide-ranging organism, *S pyogenes* is the most common bacterial cause of acute pharyngitis, accounting for around 30% of cases in children and near 10% of cases in adults. Infection with *S. pyogenes* GAS, a beta-hemolytic bacterium that belongs to Lancefield serogroup A, lead to a wide variety of diseases in humans. During the winter, up to 20% of asymptomatic schooler children may be GAS carriers.[14]

GAS is one of the most common pathogens responsible for cellulitis, along with *Staphylococcus aureus*, infection with this pathogen is also causally associated with two serious non-suppurative complications. Moreover, infection with *S pyogenes* has emerged again as an important cause of toxic shock syndrome (TSS) and of life-threatening skin infections, especially necrotizing fasciitis.[14]

Identification of GAS

Group A organisms can be identified more cost effectively by numerous latex agglutination, coagglutination, or enzyme immunoassay procedures.[14]

The only strains of bacteria that can be distinguished from other groups by their sensitivity to bacitracin, are Group A strains. A disk that contains 0.04U of bacitracin inhibits the growth of more than 95% of Group A strains, whereas 80–90% of non–group A strains are resistant to this antibiotic. The bacitracin test is easy to perform and interpret in an office-based laboratory and is sufficiently accurate for presumptive identification of GAS. Theoretical identification of GAS can also be made on the basis of production of the enzyme L-pyrrolidonyl-beta-naphthylamide (PYRase). Among the isolated beta-hemolytic streptococci from throat culture, only Group A isolates produce PYRase, which can be identified on the basis of the characteristic color change (red) after inoculation of a disk on an agar plate followed by overnight incubation. Another important clue to the classification of *S pyogenesis* when cultured on blood agar plates, the production of a characteristic zone of complete hemolysis (beta-hemolysis).[14]

Spectrum of diseases caused by GAS infections

In the era of pre-antibiotic, streptococci frequently caused significant morbidity and were associated with significant mortality rates. However, in the post-antibiotic period, diseases due to streptococcal infections are well-controlled and uncommonly cause death. GAS can cause a diverse variety of suppurative diseases and non-suppurative post-infectious sequelae.

The suppurative spectrum of GAS diseases

- Pharyngitis – With or without tonsillo-pharyngeal cellulitis or abscess
- Impetigo – Purulent, honey-colored, crusted skin lesions
- Pneumonia
- Necrotizing fasciitis
- Cellulitis
- Streptococcal bacteremia
- Osteomyelitis
- Otitis media
- Sinusitis
- Meningitis or brain abscess (a rare complication resulting from direct extension of an ear or sinus infection or from hematogenous spread).

The non-suppurative sequelae of GAS infections

- ARF – Defined by Jones criteria (two majors or one major and two minors + labs)
- Rheumatic heart disease – Chronic valvular damage, predominantly the mitral valve
- Acute glomerulonephritis

A superantigen-mediated immune response may result in the development of scarlet fever or streptococcal TSS. Scarlet fever is characterized by an upper-body rash, generally following pharyngitis.[14]

Some conflicting studies

Centor criteria ineffectiveness in predicting GABHS

In a retrospective cohort study, conducted in Belgium in 2013, about evaluating the correlation between Centor criteria and presence of GABHS in children with sore throat admitted to pediatric emergency department, it concluded the ineffectiveness of Centor criteria as a predicting factor for finding GABHS in a throat swab culture in children.[3]

Effectiveness of incorporating Centor scoring into antibiotic prescription

In a comprehensive (retrospective and prospective) study in primary care in London, UK; establish the effect of incorporating Centor scoring into antibiotic prescribing after the introduction of an educational package and prescribing software tool; it found with a low probability of bacterial infection, children with exudate or anterior lymphadenopathy almost always received antibiotics. This is interesting, since studies have previously found that the presence of tonsillar exudate had no significant association with culture-confirmed streptococcal tonsillitis.[15]

Various causes of pharyngitis and the available therapeutic options

In a reviewing article published in 2014 by a US physician in some of the various causes of pharyngitis and the available therapeutic options; has found: Diagnosis of GAS pharyngitis is based on the presence of clinical findings, with laboratory confirmation. Rapid antigen detection tests (RADTs) have a documented specificity of higher than 95% but a variation in sensitivity from 70 to 85%. However, when compared to the gold standard "throat swab specimen culture," which remains the standard for confirming the clinical diagnosis of acute GAS pharyngitis, with sensitivity of 90–95%. For the previous half-century, the antimicrobial agent of choice for the treatment of GABHS pharyngitis was penicillin; except in penicillin allergy cases, and remains the drug of choice today. However, studies have shown that penicillin may be less effective at eradicating GABHS from the upper respiratory tract if we compared it with another antimicrobial agent. A 10-day course of oral penicillin V or a single injection of benzathine penicillin is effective in treating GAS pharyngitis. Moreover, the macrolide class of antibiotics (erythromycin, clarithromycin, and azithromycin) is an acceptable alternative for the treatment for patients allergic to penicillin.[16]

Johns Hopkins approach to treat children with pharyngitis

If a child has a bacterial infection, then he or she will be treated with antibiotics. If bacteria are not the cause of the

infection, then the treatment will focus on making the child comfortable. Treatment may include taking acetaminophen or ibuprofen, increasing oral hydration, eating smooth, cool foods, and gargling with salt water (for older kids).[9]

The role of McIsaac score in bacterial pharyngitis workup

A score of 2 or more should prompt the clinician to perform a pharyngeal swab for rapid testing or bacterial culture to evaluate for beta-hemolytic streptococci. If the score is 3 or more, it would be reasonable for the clinician to treat as GAS pharyngitis. Routine blood tests for acute pharyngio-tonsillitis are unnecessary. Anti-streptolysin O (ASO) testing and other antistreptococcal antibody testing provides no additional help in acute tonsillo-pharyngitis, and so should not be performed.[4]

Some Uncommon Causes of Pharyngitis by Health line.

- Measles and Chickenpox Viruses
- Gonorrhea, Chlamydia, and *Corynebacterium*. However, if caused by a bacterial infection, and antibiotics prescription, will be done by the doctor. According to the Centers for Disease Control and Prevention (CDC), amoxicillin and penicillin are the most commonly prescribed treatments for strep throat. It is important to take an entire course of these antibiotics-which usually-lasts 7–10 days, to prevent the infection from returning or worsening.[17]

Approaching Viral Pharyngitis by CDC.

Symptoms may include:

- Cough
- Rhinorrhea
- Hoarseness
- Oral ulcers
- Conjunctivitis.

Patients with clear viral symptoms do not need testing for Group A strep. Clinicians need to use either a RADT or throat culture to confirm Group A strep pharyngitis. RADTs have high specificity for Group A strep but varying sensitivities when compared to throat culture. Throat culture is the gold standard diagnostic test.[18]

Financial impact of irrational antibiotics prescription

Antibiotic overdose or misuse lead to excessive wastage of scarce healthcare resources and also may cause medical accidents and thus lead to an increase in mortality rates.[19] In 2006, two common HAIs (sepsis and pneumonia) were found to be responsible for the deaths of nearly 50,000 Americans and cost the U.S. health-care system more than $8 billion.[20] Antibiotic-resistant infections add considerable costs to the nation's already overburdened health-care system. When first-line and then second-line antibiotic treatment options are limited or unavailable, health-care professionals may be forced to use antibiotics that are more toxic to the patient and frequently more expensive.[20]

Instructions for acute pharyngitis by Nelson textbook of pediatrics

On a revision of the textbook by the authors, the use of antimicrobial therapy is no proven benefit as treatment for acute pharyngitis due to organisms other than GAS.

Antibiotic treatment should not be delayed for children with symptomatic pharyngitis and a positive test for GAS. Presumptive antibiotic treatment can be started when there is a clinical diagnosis of scarlet fever, a symptomatic child has a household contact with documented streptococcal pharyngitis, or there is a history of acute rheumatic fever (ARF) in the patient or a family member, but a diagnostic test should be performed to confirm the presence of GAS and antibiotics should be discontinued if GAS are not identified.[21]

Untreated GAS pharyngitis

Antibiotic therapy of bacterial pharyngitis depends on the organism identified. Based on the *in vitro* susceptibility data, oral penicillin is often suggested for patients with Group C streptococcal isolates, and oral erythromycin is recommended for patients with A. hemolyticum, but the clinical benefit of such treatment is uncertain. Most untreated episodes of GAS pharyngitis resolve uneventfully within a few days, but early antibiotic therapy hastens clinical recovery by 12–24 h and also reduces suppurative complications of GAS pharyngitis such as peritonsillar abscess and cervical adenitis. The primary benefit and intent of antibiotic treatment is the prevention of ARF; it is highly effective when started within 9 days of onset of illness. Antibiotic therapy does not prevent acute poststreptococcal glomerulonephritis.[21]

Prolonged pharyngitis

Pharyngitis for more than 1 week occur in infectious mononucleosis and Lemierre syndrome, but it also suggests the possibility of another disorder such as neutropenia, a recurrent fever syndrome, or an autoimmune disease such as SLE or IBD.[21]

Suggestion of KPI implementation

Based on the reviewed scientific literature, an importance to rational the prescription of antibiotics for acute pharyngitis in children has been addressed. Hence, approaching algorithms were suggested to decrease the irrational use of antibiotics, and assigned as Pediatrics Department KPI, through stamp design, recording the McIsaac score in each dispensed antibiotic prescription for acute pharyngitis [Figures 1-4].

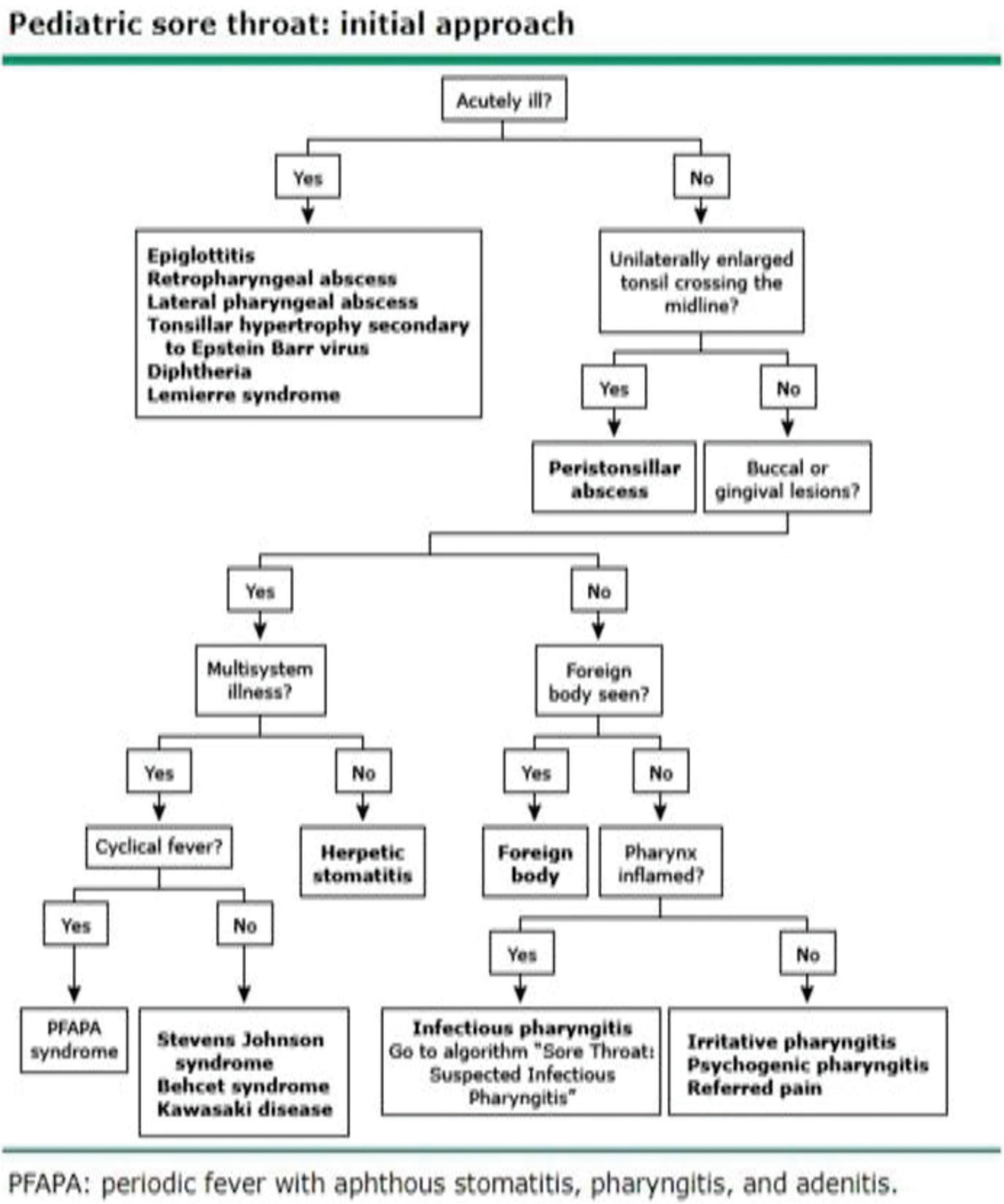

Figure 1: Algorithm of initial approach of the "sore throat" patient (UpToDate)

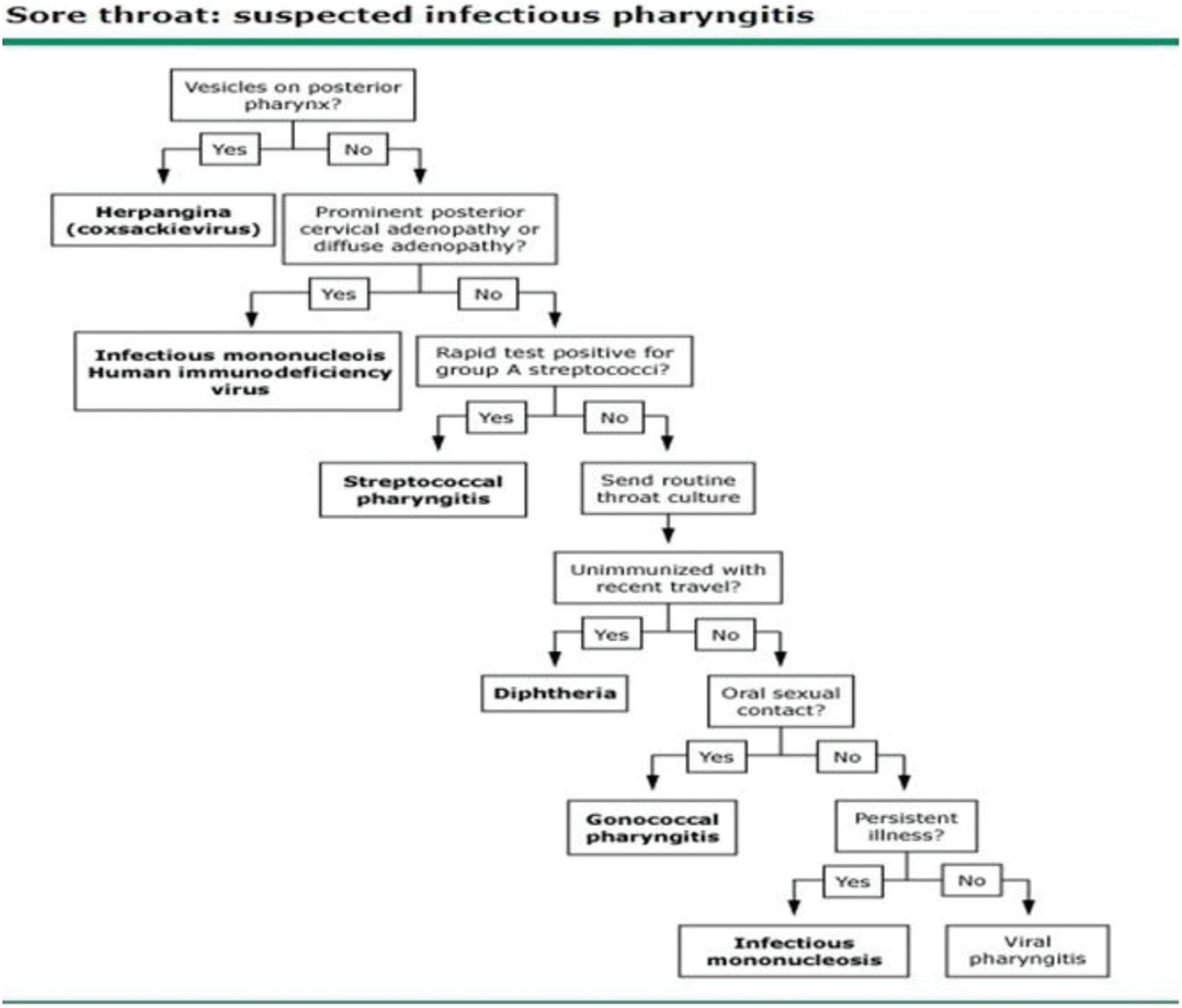

Figure 2: Algorithm of suspected infectious pharyngitis patient (UpToDate)

Modified Centor Criteria (or McIsaac Score) correlate directly with risk of positive throat culture for GAS.

Bacterial	Viral
Rare before 3 years (common 3-7 years) up to 14 years	
Exudate or swollen tonsils	
Tender, Swollen anterior cervical LN	
Fever > 38	
Absent cough	
Each = 1 point: 0–1 points: streptococcal infection ruled out (2%); 2-3 points: order rapid test and treat accordingly (Single Abx dose can change results); 4-5 points: probable streptococcal infection (52%), consider empiric antibiotics.	
+ Sudden onset, more headache, vomiting, Severe throat pain with dysphagia	With cough and rhinorrhea
With rash = Scarlet fever	Throat vesicles or skin rash

Figure 3: McIsaac scoring system for suspected GAS pharyngitis (UpToDate)

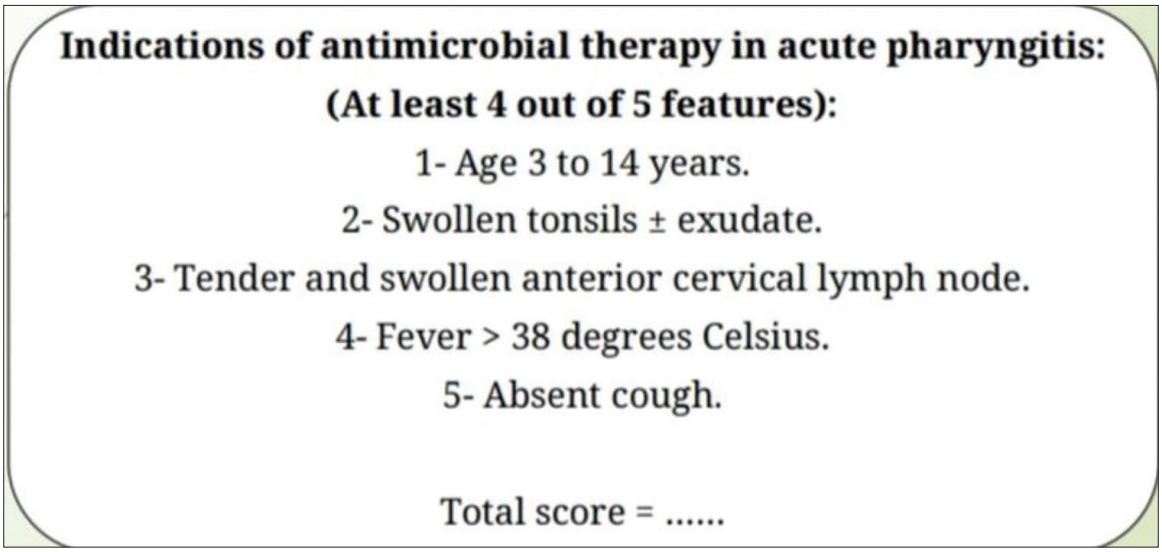

Figure 4: Suggested stamp design for pediatrics department's KPI

The KPI will be: % Rational Antibiotics Prescription in Pediatrics Department for Acute Pharyngitis in 2020–2021.

CONCLUSION

1. The inflammation of the throat is known as Pharyngitis, and usually referred to as "sore throat," while the one of the tonsils is known as Tonsillitis
2. The most common cause of Pharyngitis is viruses, and no antibiotic is required for their treatment, most of the cases resolved without treatment within a week
3. The treatment is specified on easing the child condition only without antibiotics, as far as bacterial GAS infection is not the underlying etiology of the Pharyngitis
4. It is difficult for doctors to distinguish viral pharyngitis from bacterial, on the absence of viral infection symptoms and signs; in which no antibiotics prescription is justified without a confirmatory laboratory test
5. Controlling the prescription of unnecessary antibiotics by following the McIsaac Score in Pharyngitis, would positively impact the long-term consequences of drug-resistance organisms
6. More accurate diagnosis of GAS pharyngitis, and antibiotic treatment regimen simplification to prevent the development of suppurative and non-suppurative complications, shall be the emphasized to focus on
7. Preventive vaccines for the invasive and local GABHS disease are in development, and clinical trials are yet in progress[16]
8. The financial impact of antibiotics misuse is genuinely harmful to the health sector
9. Following McIsaac scoring system to achieve the targeted KPI
10. Report the outcome of the project in the end of the targeted year.

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DISCLOSURE

Human subjects: Written consent was obtained from all participants in this study.

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships: All authors have declared that they have no financial relationships at present or within the previous years with any organization that might have an interest in the submitted work.

Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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