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Review

Pharyngitis and sore throat: A review

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Pharyngitis is a sore throat caused by inflammation of the back of the throat. It is one of the most common reasons for visits to family physicians. Throat may be scratchy and swallowing can be painful. Usually, a sore throat is the sign of another illness, such as a cold or the flu. In this review article, epidemiology, national perspective, regional perspective, pathogenesis, clinical diagnosis, clinical presentation and causes of pharyngitis was described.

Key words: Pharyngitis, sore throat, inflammation.

INTRODUCTION

Among the many infections that confront clinicians every day, there is probably no more common and yet controversial one than acute pharyngitis caused by group A β-hemolytic streptococcus (*Streptococcus pyogenes*) and viruses (Susan et al., 2001).

This illness concerns clinicians because not only is it an acute illness for an individual patient, but the potential spread of the organism and the resulting public health implications cannot be ignored either. At the outset of the 21st century, the acute pharyngitis and sore throat was unique and to date, the clinical management of these upper respiratory tract infections remains controversial. The clinical diagnosis is not specific. Laboratory data can be misleading and frequently misinterpreted. Epidemiological evidence suggests that the complexities and the controversies of these infections remain uncontrolled in all populations (Mcfarlane et al., 1998).

A sore throat affects a person in many ways and the symptoms vary from one individual to another. Accordingly, some describe the peculiar symptoms of the disorder as a burning sensation, while others feel a tickling or scratchy sensation in the throat. By and large, a sore throat affects the person as a general sore feeling that starts at the back of the oral cavity, gradually spreading out into the region of the middle throat; these symptoms are generally felt along with varying degrees of pain in individual cases. A sore throat can usually be seen more as a symptom of another illness and arises as a result of inflammation in the sensitive tissues of the throat. The body responds by increasing the rate of circulation of blood in the throat as soon as the initial inflammation or irritation has begun. Therefore, the swelling and the pain felt in the throat and the subsequent reddening of the tissues is an actual reaction of the immune system, as the increase in the circulating blood transports and increased load of white blood cells and other substances to counter the initial infection, therefore, the actual symptoms present are merely signs that the body is fighting back the infection (Wiesner et al., 1973).

Some of the usual causative agents of soreness in the throat-or the real triggers of the condition-are primary physiological reactions such as allergies, environmental factors such as dust and smoke and low humidity also play important roles. Additionally, soreness in the throat can be experienced as a result of viral infections and infection by other pathogens such as bacteria; the body may react to all of these factors and thus trigger the soreness in the throat. External events such as the draining of excessive mucus from the nose and from the sinuses down the back of the throat and even things like a postnatal drip are often followed by soreness in the throat and in such cases, the sore throat usually arises because of infection from viral sources or from an allergic reaction of the body to these physical intrusion.

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Moreover, the sensitive tissues in the throat are primary targets for the viruses that bring about colds and other throat infections. It normally takes several days at a stretch and a persistent infection for the development of a virally caused soreness in the throat. There are also differences in the way different sore throat causing pathogens elicit symptoms from the affected individual, for example viral infections commonly persist for longer periods but are comparatively mild to moderate in the symptoms that they bring about viz a viz bacterial infection (Andersson et al., 1987). Bacterial infections often strike suddenly and can bring out acute symptoms and give a lot of discomfort to the individual, a good example is strep throat, and this type of bacterial infection can quickly establish itself over some hours. Bacteria infect abruptly generate symptoms such as severe pain in the throat and other uncomfortable physical symptoms such as difficulty in swallowing; the presence of fever is also typical of bacterial infections (Glezen et al., 1957).

EPIDEMIOLOGY

Pharyngitis is prevalent all over the world, more commonly in temperate climates especially during the winter and early spring months. In the United States, acute respiratory tract infections in 1998 resulted in an estimated 84 million visits to physicians; of which 25 million were due to upper respiratory tract infection. According to the National Ambulatory Medical Care Survey, upper respiratory tract infections, including acute pharyngitis, are responsible for 200 visits to a physician per 1000 population annually in the United States (Peltola, 1982; Gonzales, 2001).

CLIMATOLOGICAL SETTINGS

From the tropics to the arctic, climate and weather have powerful direct and indirect impacts on human life. People adapt to the conditions in which they live, and human physiology can handle substantial variation in weather. Changes in climate are likely to lengthen the transmission seasons of important vector borne diseases.

The epidemiology of pharyngitis derives largely from studies conducted mostly in the Northern or the temperate climate countries where pharyngitis is a common complain. In the tropical countries (mostly, though not in all), there are few prospective studies that provide data on pharyngitis, its epidemiology and clinical presentation. As a result, it is problematic to determine the magnitude of true differences between geographic settings, and to assess if apparent differences are related to geographic/climatological or other factors (Hendrix et al., 1999). Long term studies in North America show the proportion of pharyngitis, that is, streptococcal has not varied for over 50 years, although the incidence of rheumatic fever and rheumatic carditis have declined remarkably.

SOCIOECONOMIC SETTING

There is a vast difference between the lifestyles of individuals from the high income and those from the low income population at large which reflects in the health of those individuals. The individuals from the high income bracket are in a position to exercise multiple options in addressing their health issues, like attending tertiary care centers or clinics from the private sector and can gain access to costly diagnostic tools as opposed to those individuals from the lower income population (Gonzales et al., 2001).

The crowded living style of the low income population accentuates further their risk of contacting disease by their excessive exposure to infectious diseases that are spread by droplet. Usually, in the low income living areas, there are limited diagnostic facilities which are of course inadequate for the number of individuals living there, which further hampers the possibility of early diagnosis of disease and in turn does not allow that sector of the population to obtain early treatment or resolution of their disease by treatment where the needed diagnostic and treatment facilities themselves are grossly inadequate (Kaplan et al., 1972).

HIGH INCOME COUNTRIES

In high-income countries, pharyngitis is common in children ages 3 to 15 years. On average in the USA, each child has approximately one GABHS pharyngitis infection by age 5, with a mean of 3 episodes (range 108) by 13 years of age. After the availability of penicillin, the incidence of acute rheumatic fever (ARF) declined by 50%. From 1935 to 1960, the incidence of acute rheumatic fever in the USA ranged between 40 and 65/100,000 in all age groups. From the late 1960s, there was a marked decline in acute rheumatic fever, and since 1970, incidence of rheumatic fever has ranged from 0.023 to 1.88 per 1000,000 populations (Dajani et al., 1995).

LOW-INCOME COUNTRIES

Few studies have been conducted to ascertain the incidence and prevalence of GABHS in developing countries. The studies were non-standardized with regards to the laboratory investigation methods for throat culture diagnosis (Schwartz et al., 1985).

Few precise estimates of the incidence of GABHS pharyngitis in low income countries are available. The reported incidence of culture-proven GABHS pharyngitis in prospective studies in a few sites appears to be much higher than that reported from the United States in the1950s: up to 900 versus approximately 200 per 1,000 child-years of observation (US Census, 2004).

NATIONAL PERSPECTIVE

Pakistan is a developing country and has poor health indicators. It ranks 136th of the 177 countries on the Human Development Index of the United Nations of 2007-2008 (US Census, 2004). In Pakistan, over a third of the people are living in poverty and have a fragile health structure; many patients cannot afford the costly treatment (US Census, 2004). The NHDR/PIDE 2001 Survey and the National Health Survey of Pakistan data show that from the low income persons of 45 years and above, as many as 45% suffer from poor health and 80% suffer from poor-to-fair health.

Usually, the low income individuals are more susceptible to disease due to inadequate nutrition which of course lowered the individual's immunity. Moreover, the lack of access to safe drinking water as well as unhygienic conditions of consumption, storage and production of food would be expected to result in a relatively high frequency of infection disease amongst the poor (Poses et al., 1985).

The respiratory tract infections are common in children as well as in adults. The estimated incidence of respiretory infections in children and adults are 1192 visits to the physicians per 2000 population per annum. According to the National Health Survey, upper respiratory tract infection including pharyngitis and sore throat are responsible for 800 visits to a physician per 2000 population annually in Pakistan (US Census, 2004; WHO, 2008).

REGIONAL PERSPECTIVE

Karachi is the largest city and the economic hub of Pakistan with an estimated population of 10 million people of diverse ethnic and socioeconomic groups. The metropolitan area along with its suburbs comprises the world's second most populated city, which spread over 3,530 km^2 (US Census, 2004). The city credits its growth to the mixed populations of economic and political migrants and refugees from different national, provincial, linguistic and religious origins that have largely come to settle here permanently.

In Karachi, like other regions of Pakistan, acute pharyngitis and sore throat is very common and frequent, and peak seasons for sore throat and acute pharyngitis are winter and early spring (November to April). Air pollution due to peripheral industrial area and a great number of automobiles in the Karachi city increases the risk of viral and/or bacterial sore throat and pharyngitis as well.

PATHOGENESIS OF INFECTIOUS DISEASES

Unani perspective: Pathogenesis

In the Unani system of medicine, the concept of temperament is a main procedure of diagnosis (Galen, 1997; Ahmed et al., 1980). Temperament is regarded as a measure of equilibrium or homeostasis which exists at different levels of complexity in the body, starting at the simple cell, and passing through tissue and organs and complex organ systems, to the whole person, and how the individual interacts with the external environment. Temperament along with the humours (Akhlat) also protects the body from diverse types of offences as it maintains the optimal level of immunity and helps maintain the defense mechanism of the body (Breese et al., 1954).

The taking of personal history as part of the temperamental evaluation is very important because at the end of this in-depth assessment, a person's dominant and subdominant temperament is determined. This provides guidelines for both the subsequent treatment of the clinical disorder, and the prevention of the disorder's recurrence.

In Unani medicine, the concept of cause relates to the etiology from which originates the existence or outcome of a certain state of the human body, is a state of health or disease. Ibn Sina describes three conditions for a cause to produce an effect. These conditions are:

A. The cause must have sufficient active power to produce an effect.
B. There must be a sufficient receptive component for the cause to have an effect.
C. There has to be an appropriate period of contact between the active power and the receptive component.

He further elaborated on four kinds of causes:

A. Those associated with the humours/body fluids
B. Those associated with the temperament
C. Those associated with the governing/lifestyle factors
D. Those associated with the functions of the body.

These principles of cause and effect provide valuable insights to the understanding of all the pathological processes that take place within the body (Young et al., 1978).

The concept of a single cause of a disease, whether it is a microbe, toxin or any other factor is not reasonable. Common sense and logic stress that every morbid condition is the result of many factors, occurring in combination, either sequentially or simultaneously. The existence of pathogenic organisms is expected, because this is the original imbalance in temperament which provides an altered biotic environment in the living tissue in which bacteria, viruses and other microbes can thrive. This growth of microbes in the internal environment provokes a reaction from physis on the affected tissues; this reaction often manifests as symptoms of infection if the disease state becomes established. It is acknowledged that the microbes or germs do have a role in the

onset of disease, but the patient's temperament has a major role to play in the patient succumbing to the disease. Although, infections may affect the person having phlegmatic temperament, they are comparatively more susceptible to infections, most probably because such people posses rather low level of immunity. Not everyone gets colds and flu, or skin disorders (Chishti et al., 1988).

The presence of bacteria can be reduced markedly by antibiotics, thus providing a temporary cure, but if the temperamental imbalance is not properly addressed, the infection will reoccur, because the body's immune system is not able to deal with the remaining infectious agents. For example, the common cold and bronchitis is notoriously prone to regular recurrence, as is vaginal thrush. The cause of the initial imbalance in temperament can usually be found in the governing factors- the patterns of existence and behavior that influence us all. These include breathing activities, the food and drink consume, rest and activity spectra, life stresses and emotional situation, and kidney and bowel functions.

Pathogenesis

The pathogenesis of infectious diseases in modern or allopathic system of medicine is dependent on the relationship among the human host, the infectious agent and the external environment. The infectious agent can be either exogenous (not normally found on or in the body) or endogenous (one which may be routinely cultured from a particular anatomic site but that does not normally cause disease in the host). Infection results when an exogenous agent is introduced into a host from the environment or when an endogenous agent overcomes innate host immunity to cause disease. Clearly, host susceptibility plays an important role in either of these settings (Breese, 1954). Infectious diseases cause significant morbidity and mortality. The human body has the ability to control infection through a number of different mechanisms (Breese et al., 1954).

Physical barriers impede the entry of bacteria from the external environment and from normally colonized sites in the body into sterile anatomic areas. When these physical defenses are breached, the immune system is activated.

Constitutive or innate immunity

This is provided by performed proteins (complement) and immune cells (phagocytes) that are activated by non-specific foreign proteins allow an immediate response to foreign material.

Induced or adaptive immunity

This includes early and late adaptive responses activated by specific antigenic proteins (production of antibodies active against the specific strains of *Streptococcus pneumoniae* contained in the pneumococcal vaccine in a previously vaccinated individual). Induction of these specific immune receptor cells, which may take several days in the immunologically naive host, occurs much more rapidly during re-infection, when the immune system has been primed by prior exposure. Protective immunity, which occurs after initial exposure (infection or vaccination) through generation of memory lymphocytes and pathogen-specific antibody, allows a much more rapid response to re-infection (Breese et al., 1954).

CLINICAL DIAGNOSIS

Sore throat most often is caused by direct infection of the pharynx (pharyngitis), primarily by viruses or bacteria (Kljakovic et al., 1993). There is no evidence that bacterial sore throats are more severe than viral ones or that the duration of the illness is significantly different in either case.

CLINICAL PRESENTATION

An upper respiratory tract infection commonly begins with malaise, headache, fever and then coryza and sore throat. Precise clinical diagnosis is difficult in practice (Breese et al., 1954). There are many agents which cause pharyngitis. There is great importance in differentiating GAS pharyngitis from all other causes because GAS is the only major organism which has the associated infections regarded as complications. These complications include acute rheumatic fever, toxic shock syndrome and acute glomerulonephritis. Viruses play a significant role in the pathogenesis of pharyngitis. Viral infections account for approximately 70% of all pharyngitis, with bacteria causing 20 to 30% of pharyngitis (Stillerman et al., 1961) (Table 1).

In infectious pharyngitis, bacteria or viruses may invade the pharyngeal mucosa directly, causing a local inflamematory response. Other viruses, such as rhinovirus causes irritation of pharyngeal mucosa, secondary to nasal secretions. Bacterial pharyngitis has important suppurative and non-suppurative sequelae.

VIRAL PHARYNGITIS

Viral Infections account for approximately 70% of all pharyngitis. Rhinovirus is the most common cause of viral infection. The other common causes of viral infection in descending order are coronavirus, adenovirus, parainfluenza, and influenza virus. Viral infections are more common during the winter months with the exception of adenoviruses which occur year round.

Viral pharyngitis is spread through similar mechanism

Table 1. Causes of pharyngitis.

Bacteria	
Corynebacterium other spp.	*Arcanobacterium haemolyticum* *Corynebacterium diptheriae* *Haemophilus influenzae* *Legionella pneumophilia* *Neisseria gonorrhoeae* *Neisseria meningitides* *Streptococcus pyogenes* (group A beta-hemolytic) *Streptococcus* spp. (groups B, C and G) *Treponema palidium* *Yersinia enterolitica*
Fungal/rickettsial/intracellular organisms	Candida spp. *Mycoplasma pneumoniae* *Coxiella burnettii* *Chlamydia pneumoniae*
Viruses	
Parainfluenza	Rhinovirus Adenovirus Coronavirus Coxsackie A virus Cytomegalovirus Epstein-Barr virus Herpes simplex virus Human immunodeficiency virus-1 Influenza A and B Measles Reovirus Respiratory syncytial virus

as other viral infections. Hand to mouth contact, contact with oral secretions and sharing common utensils all contribute to viral spread. Prevention of the spread of disease is based on frequent hand washing and

Clinical symptoms of different viruses are more prevalent during certain seasons. Coryza, conjunctivitis, malaise or fatigue, hoarseness, and low-grade fever suggest the presence of viral pharyngitis. Patients with viral pharyngitis can also have atypical symptoms such as mouth breathing, nausea, vomiting, abdominal pain and diarrhea.

BACTERIAL PHARYNGITIS

Patients with bacterial pharyngitis generally do not have rhinorrhea, cough or conjunctivitis. The incidence of bacterial pharyngitis is increased in temperate climates during winter and early spring. The most common agents involved in bacterial pharyngitis are group A hemolytic Streptococcus. Its importance lies not only in its frequency of occurrence, but due to its two serious sequelae, that is, acute rheumatic fever and post-streptococcal glomerulonephritis. β-Hemolytic Streptococci other than group A (group C and G) produce symptoms similar to, but milder than those of group A strains. They are not associated with rheumatic fever as a non-infectious sequel (Middleton, 1991). Other uncommon bacteria include *Anaerobes*, *Arcanobacterium Haemolyticus*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae, Neisseria gonorrhea,* and *Corynebacterium diphtheria.*

The clinical presentations of streptococcal pharyngitis is seen by observing an inflamed and edematous pharyngeal mucosa in a patient who reports sore throat, difficulty in swallowing, fever higher than 38.5°C (101.3°F), headache and tender anterior cervical lymph nodes. Purulent exudates over the posterior pharynx and

Table 2. Streptococcal score card.

Symptom	Point
Fever (subjective or measured in office)	1
Absence of cough	1
Tender anterior cervical adenopathy	1
Tonsillar swelling or exudates	1
Age	
Younger than 15 years	+1
15 to 45 years	0
Older than 45 years	-1

Scoring: 0 or –1 points: Streptococcal infection ruled out (2%); 1 to 3 points: Throat culture test and treatment accordingly; 4 to 5 points: Probable streptococcal infection (52%).

tonsillar area may also be observed.

Group A streptococcal is transmitted through inhalation or contact with secretions. Symptoms develop after a short incubation period of 24 to 72 h. Untreated GABHS infection lasts for 7 to 10 days (Stillerman et al., 1961; McIsaac et al., 1997).

DIAGNOSTIC GUIDELINES

Essentials of diagnosis

1. Pharyngeal discomfort or pain and pain on swallowing (odynophagia).
2. Associated symptoms such as myalgia, fever, rhinorrhea and lymphadenopathy depend on the etiologic agent.
3. Pharyngeal erythema with or without exudate or lymphadenopathy.
4. Leukocytosis and bacterial culture or other serologies may provide the definitive microbiologic diagnosis.

Clinical sign and symptoms

The severity of the pharyngitis may vary from mild to life threatening depending on the etiologic agent. Symptoms of mild pharyngitis are irritation and sore throat. With increasing severity, there may be severe pain that increases on swallowing plus cervical lymphadenopathy with or without fever.

General approach

When a patient presents with sore throat, there is a wide range of illnesses which has to be considered. Infectious causes range from generally benign viruses to GABHS. Inflammatory presentations may be the result of allergy, reflux disease or rarely, neoplasm or Kawasaki disease (Caplan, 1979).

In determining the underlying cause and thereby deciding if, when, and how to treat the patient with pharyngitis, the information from the history and physical examination must be integrated.

There are some important historical elements with GABHS (group A β-hemolytic streptococcus) infection which include the onset, duration, progression, and severity of the associated symptoms (fever, cough, respiratory difficulty and swollen lymph nodes).

The presence of tonsillar or pharyngeal exudate and a history of exposure to streptococcus in the previous two weeks were the most useful clinical features in predicting current GABHS infection. The absence of tender anterior cervical adenopathy, tonsillar enlargement and tonsillar or pharyngeal exudate was most useful in ruling out GABHS. However, no single element in the history or physical examination is sensitive or specific enough to exclude or diagnose strep throat. This difficulty has inspired investigators to develop scoring systems to facilitate the diagnostic process (Bisno et al., 1997).

In evidence-based guideline from the Centers for Disease Control study investigators identified four findings from the history and physical examination that independently predicted a positive throat culture for GABHS in a population of adults and children. The findings were tonsillar exudates, anterior cervical lymphadenopathy, absence of cough, and history of fever higher than 100.4°F (38°C). When combined with the patient's age, these findings allow the physician to place patients in a low-, moderate-, or high-risk group (Seppala H et al, 1993) (Table 2).

Low-risk patients require no further diagnostic testing, high-risk patients should be considered for empiric therapy, and moderate-risk patients should undergo further evaluation with a throat culture to make the

diagnosis (Meland et al., 1993; McIsaac et al., 1997).

DIAGNOSTIC CRITERIA FOR PHARYNGITIS

Associated with streptococcal pharyngitis

1. Absence of cough
2. Discrete patchy exudate
3. Exposure to GABHS in the previous two weeks
4. Fever
5. Palatine petechiae
6. Scarlatiniform rash
7. Strawberry tongue
8. Tender anterior cervical nodes
9. Tonsillar Swelling

Associated with viral pharyngitis

1. Anterior stomatitis
2. Conjunctivitis
3. Coryza
4. Cough
5. Diarrhea
6. Discrete ulcerative lesions
7. Hoarseness

LABORATORY EVALUATION

Consider the clinical, historical and epidemiologic evidence before deciding to perform microbiological tests to evaluate patients with symptoms of acute pharyngitis. Those who have signs and symptoms that are not suggestive of streptococcal infection do not require diagnostic tests. Diagnostic confirmation of strep throat is helpful in those patients whose presentation suggests it, however, it is because symptoms of bacterial and viral infections often overlap and bacteriologic confirmation is necessary to resolve any uncertainty as to the etiology.

THROAT CULTURE

Culture of a throat swab remains the standard for the documentation of the presence of group A streptococci in the upper respiratory tract and for the confirmation of the clinical diagnosis of acute streptococcal pharyngitis. If done correctly, culture of a single throat swab has a sensitivity of 90 to 95% for the detection of the presence of group A β-hemolytic streptococci in the pharynx. Several variables affect the accuracy of throat culture results. For example, the way in which the swab is secured has an important impact on the yield of streptococci from the culture. Throat swab specimens should be obtained from the surface of both tonsils or tonsillar fossae and the posterior pharyngeal wall. Other areas of the oral pharynx and mouth are not acceptable sites, and these sites should not be touched with the swab before or after the appropriate areas have been sampled. In addition, false-negative results may be obtained if the patient has received antibiotics shortly before or at the time the throat swab is obtained. It has also been reported that the use of anaerobic incubation and selective culture media may increase the proportion of positive culture results. However, data are conflicting with regard to the impact of the atmosphere of incubation and the culture media, and, in the absence of a definite benefit, the increased cost and effort associated with use of anaerobic incubation and selective culture media are difficult to justify, particularly for physicians who process throat cultures in their own offices (Gerber et al., 1989, Brien et al., 1985).

The clinical significance of the number of group A β-hemolytic streptococcal colonies present on the throat culture plate is problematic. Although, patients with true acute group A streptococcal pharyngitis are likely to have more-strongly positive cultures than patients who are Streptococcus carriers. There is so much overlap in the degree of positivity of throat culture results that the differentiation cannot be made accurately on this basis alone.

RAPID ANTIGEN DETECTION TESTING

This is more expensive than obtaining a throat culture; however, results are available within a few minutes as compared to one or two days. This rapid result allows patients to receive treatment sooner, helping to prevent the spread of the infection and allowing the patient to return to work or school more quickly. Many of the rapid antigen detection tests (RADTs) have excellent specificities of 95% or higher; a high specificity means that the test is reliable if it is positive.

A confirmed diagnosis of streptococcal pharyngitis can be based on positive findings on throat culture results. Children and adolescents have a higher prevalence of infection with GABHS and subsequent RF confirm a child's negative RADT result by culturing throat swabs (Lauer et al., 1983).

ANTI-STREPTOCOCCAL ANTIBODY TITERS

These reflect past and not present immunologic events and are of no value in the diagnosis of acute pharyngitis. They are valuable for confirmation of previous streptococcal infections in patients suspected of have acute rheumatic fever or post-streptococcal acute glomerulonephritis. They are also helpful in prospective epidemiological studies, for distinguishing patients with acute infection from patients who are carriers.

The main reason for treating pharyngitis and sore throats with antibiotics is to prevent rheumatic fever, not

to relieve the symptoms. This practice has dissipated in recent situations. Since the rheumatic fever occurrence in the general population is very low, and has declined dramatically over the past 30 years, the number of prescriptions written for antibiotic drugs can safely be reduced. The patients visiting a physician with complaints of sore throat do not develop rheumatic fever at a high rate (Cooper et al., 2001).

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