RATIONALE FOR AVOIDING INDISCRIMINATE ANTIBIOTIC THERAPY IN TREATING PHARYNGITIS

By

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An analysis of current published literature with recommendations for practice changes, submitted in partial fulfillment of the requirements for the degree of MASTER OF NURSING

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December 1998
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ACKNOWLEDGMENTS

I cannot fail to appreciate the support from family, friends, and instructors during my pursuit of the Master of Nursing degree in the Washington State University and Whitworth College Intercollegiate Center of Nursing Education. I would like to express my gratitude and thanks to the following special people:

To Rory and Wally, my sons, for the love, financial support, and housekeeping hours you put in so unfailingly, my love and thanks;

To my church family who helped support me spiritually and financially in this goal, my thanks;

To the Intercollegiate Center for Nursing Education graduate faculty and staff, especially Dr. Lorna Schumann and Margaret Ruby, for the education and guidance you have so ably given, and for invaluable advice which helped me reach my goals so quickly, my deepest appreciation;

To Dr. Henry Arguinchona, for reading my manuscript and providing invaluable, expert advice, my sincere thanks;

To God goes the most credit: first, for calling me to this great profession of nursing, second, for giving me understanding in each patient (or exam!) I faced, and last, but most important and precious, for sending His beloved Son to die for me, and thus take away my reproach.
Pharyngitis is among the top three complaints of patients visiting their health care providers (HCP). Antibiotics are prescribed in as many as 80% of these sore throat visits. Studies have shown viruses to be the cause of up to 90% of pharyngitis. Research has shown no benefits of antibiotic therapy in treating viruses. It is easy to conclude that pharyngitis is over treated.

The issues of treatment of pharyngitis are complex. Clinicians fear missing the diagnosis of Group A beta-hemolytic streptococcus (GABHS) and causing the patient an ensuing rheumatic condition. They also believe they can diagnose GABHS accurately by clinical signs and symptoms alone. Add to this the fears of causing other complications, and perhaps offending the patient by refusing the “expected” antibiotic prescription, and one can see why approximately half of all outpatient antibiotics used are for sore throat (pharyngitis).

The most current literature demonstrates that acute rheumatic fever, caused by GABHS, is the only complication that can be prevented with surety by antibiotics, and that most patients with GABHS never seek the care of a HCP. More people in the United States die each year of
drug reactions than complications of pharyngitis.

Providers should be aware that studies have shown clinical signs and symptoms to be poorly sensitive in diagnosing GABHS. With bacterial resistance a constant threat, and ballooning costs of treating this largely self-limiting disease, antibiotic therapy should be restricted to treating only documented cases of GABHS. Rapid tests for GABHS are becoming more sensitive and specific, and traditional cultures provide answers in plenty of time to ward off complications.

Patients should be taught not to expect antibiotics for sore throat, and to treat their sore throat symptomatically and rest for a day or two before running to the HCP. The time spent waiting may be well-spent, usually preventing unnecessary antimicrobial therapy, and when GABHS does turn up in the diagnosis, the wait gives the patient’s immune system time to mount an attack, decreasing the likelihood of relapse.
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Rationale for Avoiding Indiscriminate Antibiotic Therapy in Treating Pharyngitis

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Introduction

Sore throat may be written in the diagnosis as pharyngitis, which indicates infection, inflammation or irritation of any part of the pharynx, including the tonsils and nasopharynx. It is among the top three complaints leading patients to visit their health care providers (HCPs), and is the chief complaint of 40 million adults and 10% of all children seen in various health care settings yearly (Dobbs, 1996; Muhrer, 1991; Rupert, 1996; Simon & Wilkes, 1998; Smith, 1996). The National Center for Health Statistics’ data indicates, nearly 75% of all outpatient pediatric prescriptions are written for upper respiratory tract infections (Dowell, Schwartz, & Phillips, 1998). Jackler and Kaplan (1997) estimate that 50% of all outpatient antibiotics used are specifically for treatment of sore throat.

Traditionally, pharyngitis has been treated with antibiotics for many reasons. Asked when and why sore throat should be treated, clinicians will cite studies that show the danger of ensuing rheumatic fever or glomerulonephritis (non-suppurative complications) or, more legitimately perhaps, suppurative complications such as peritonsillar cellulitis or peritonsillar abscess (quinsy), or otitis media (Little, Gould et al., 1997). Clinicians may also name studies claiming earlier symptom relief with antimicrobial therapy (Dagnelie, Van Der Graaf, & De Melker, 1996; Howe et al., 1997).

HCPs may also believe that certain signs and symptoms are more likely indicative of bacterial or viral infection and treat the sore throat empirically according to the interpretation of these. Almost as often, one will hear the assertion that antibiotic therapy is fairly benign. Since patients have come to expect a prescription when they visit their HCP, why not provide one, thereby possibly preventing a bad outcome, or at least maintaining good patient relations. HCPs
are confounded by a wide disparity in the approach to treatment of sore throat. Practitioners need to consider the emerging concerns of resistant strains of bacteria, that drug reactions and interactions are a leading cause of death in the U.S., and the awareness that costs need to be contained (Lazarou, Pomeranz, & Corey, 1998; Slawson, Baer, & Richardson, 1991).

It is the aim of this paper, through a review of recent literature, to provide the rationale for treatment strategies for HCPs practicing in family or urgent care settings. Additionally, tools to educate the patient seeking treatment for sore throat are provided.

**Etiology and Incidence**

Pharyngitis is most often an inflammatory condition of the pharynx caused by the immune system’s response to infection. It may also be an irritation of the pharyngeal mucosa caused by trauma or contact with irritating smoke, chemicals, allergens or post-nasal drip (which may or may not be infective). Table 1 presents possible etiologies of pharyngitis.

**Viral etiology and incidence.**

Sore throat is caused by viral infection 50% to 90% of the time (Berman & Chan, 1997; Middleton, 1996). This wide range in reported incidence is due to variations per locality, and the fact that many viruses are not easily identified. The most common viral etiologies are rhinoviruses, coronaviruses, the adenoviruses, coxsackie viruses (Herpangina and Hand, Foot, and Mouth Disease), Epstein Barr Virus (infectious mononucleosis), and influenza and parainfluenza viruses (Goldstein 1992; Middleton, 1996; Muhrer, 1991; Vukmir, 1991). Herpes simplex virus has also been increasing in incidence, especially among college-age patients (McMillan, Weiner, Higgins, & Lamparella, 1993; Simon, 1995).
Bacterial etiology and incidence.

Kazzi and Wills (1998), McIsaac, White, Tannenbaum, and Low (1998), and Pichichero (1995) theorize that 5-30% of cases of sore throat are of bacterial origin. This percentage varies due to population characteristics (children evidencing the higher rates) and differences in incidence from location to location nationwide (Dobbs, 1996; McIsaac et al., 1998; Poses et al., 1993). The most common bacterium causing pharyngitis, Group A beta-hemolytic streptococcus (GABHS), also known as Strep pyogenes or strep A, accounts for an average of 10% to 15% of sore throat cases in the United States (Berman & Chan, 1997; Kazzi & Wills, 1998; Middleton, 1996; Schwartz, Marcy, Phillips, Gerber, & Dowell, 1998). The pediatric population has the higher incidence (30%), and adult incidence reportedly is as high as 15% in some urban areas. However, in most areas, adult incidence is closer to 5%. Even though somewhat expensive and time consuming to determine, it is helpful for the practitioner to know the incidence of GABHS in his or her practice setting, as it may help direct testing and treatment decisions.

The incidence of GABHS is often noted to be higher in pediatric cases, peaking between the ages of five and ten, continuing somewhat less frequently in the ten to fifteen year old age group, and dropping off significantly in frequency after that age group (Dobbs, 1996; McIsaac et al., 1998; Simon & Wilkes, 1998). Incidence of GABHS in adults declines rapidly after age 40, and is a rare etiology of sore throat after age 50. Occurrence of GABHS in children under age three is also rare and manifests with low-grade fever, rhinorrhea, pallor and/or otitis media, but not pharyngitis (Ogle, 1997).

THE CARRIER STATE.

The carrier state develops after an acute infection with GABHS. These patients throat
cultures are positive for GABHS. It is not known how many of the patients are simply carriers of avirulent strains of GABHS, with superimposed viral or other bacterial infection causing the symptoms of sore throat (Pichichero, 1995; Simon & Wilkes, 1998). Little and Williamson (1996) and Middleton (1996) indicate the most reliable studies on asymptomatic subjects place the average carrier rate between 10% and 15%. The carrier state usually lasts two to six months, rendering reculturing and retreating the asymptomatic child pointless because the pathogen is not obliterated by penicillin anyway (Gerber, 1997; Smith, 1996). In the carrier state, GABHS is not known to produce non-suppurative or supplicative sequelae (Dagnelie et al., 1996; Gerber, 1997).

**Non-suppurative complications.**

GABHS is transmitted via contact with oral or nasal secretions and droplet spread. Preventing its feared complication of acute rheumatic fever (ARF) is the rationale most often given for treating sore throat with antibiotics. Acute rheumatic fever is known to occur only as a complication of GABHS pharyngitis. The most widely held theory in its pathogenesis purports that a patient who is genetically predisposed develops an autoimmune response to epitopes of the pathogen which are cross-reactive with epitopes in the patient’s heart, joints, skin or brain cells (Simon, 1998; Wolfe, Boucek, Schaffer & Wiggins, 1997). The incidence of ARF in recent years averages 1/100,000 cases of GABHS, and the incidence is highest in urban areas (Del Mar, 1992; Dippel, Touw-Otten, & Habbema, 1992; Mc Isaac, Goel, et al., 1997). The decreasing incidence is hypothesized to be largely due to changes in immunopathogenicity and socioeconomic factors, and not as much to antibiotics since the incidence was declining rapidly during the early part of the 20th century, well before the advent of penicillin therapy in the 1940's.
There have been relatively small pockets of ARF outbreaks in the U.S. during this century, usually occurring in settings such as army barracks, boarding schools, and other closely quartered populations. Reports of patients with ARF indicate that most don’t seek health care prior to the ARF onset, that less than half have sore throat symptoms, and up to one-fifth had received antibiotics, but developed ARF anyway (Mc Isaac, Goel, et al., 1997; Simon & Wilkes, 1998; Wallace, Garst, Papadimos, & Oldfield, 1989). A study of the 43 patients in the 1990 Pennsylvania outbreak of ARF showed that only 32 (74%) had upper respiratory infection symptoms, 20 (46%) had sore throats, 11 (25%) saw a HCP, and 8 of the 11 had throat cultures. Of the eight cultures, six were positive for GABHS (Middleton, 1996). Compliance rate with antibiotic regimens was unknown in the Pennsylvania study.

Similar percentages were demonstrated in the winter of 1986 Naval Training Center outbreak, although there were only ten patients in that epidemic. Of the three naval recruits who sought medical attention for their sore throats, one tested positive for strep, all three were treated with antibiotics, and none were compliant (Wallace et al., 1989).

Glomerulonephritis (GN) is another feared complication of GABHS. GN appears to be caused by an antibody-antigen complex being deposited in the glomeruli (Kazzi & Wills, 1998). It is not known why it develops in only 15 or so of the 80-plus types of GABHS (Simon, 1998). Generally, these nephritogenic strains are seen more frequently as pyoderma rather than pharyngitis (Chambers, 1997; Coggins, Rennke, & Rose, 1995). According to the American Academy of Pediatrics Committee on Infectious Diseases and other sources, GN as post-streptococcal sequela is not prevented by antimicrobial treatment (Coggins et al., 1995; Del Mar,
SEPTICEMIA AND STREPTOCOCCAL TOXIC-SHOCK SYNDROME

Septicemia rarely develops, and occurs from strep strains that typically present with soft tissue foci or as empyema and osteomyelitis (Little & Williamson, 1996; Simon, 1998). A toxic shock-like syndrome from GABHS, which can be fatal, usually presents as skin or soft tissue infection. It is theorized that an exotoxin stimulates the release of large amounts of inflammatory cytokines which leads to the systemic renal, cardiac and respiratory problems. Toxic shock results more commonly from staphylococcus infection (Chambers, 1997). Patients with toxic shock-like syndrome that develops from GABHS infection become ill very quickly so this differential diagnosis should be kept in mind since fatality may occur in as many as 15-30% of cases (Chambers, 1997; Simon, 1998). Sore throat is usually not the main complaint, but may accompany signs and symptoms of headache, fever, vomiting, watery diarrhea, and myalgias.

Suppurative sequelae

The suppurative complications of GABHS result slightly more commonly, and antibiotics can prevent some of these from occurring. However, some subjects in clinical trials have developed quinsy, sinusitis, and otitis media (OM) even while receiving penicillin therapy (Howe et al., 1997; Little & Williamson, 1996). There is conflicting judgement regarding these treatment failures. They may be due to virulent bacteria or viruses, poor patient compliance to treatment regimens, or possibly to resistant strains of pathogens (Kearsley et al., 1997; Little & Williamson, 1996; Pichichero & Cohen, 1997).

Uncommon causes of sore throat

Other less common bacterial causes of sore throat are Mycoplasma pneumoniae,
Arcanobacterium hemolyticus (previously known as Corynebacterium hemolyticus), Group C and G beta-hemolytic streptococcus, Chlamydia pneumoniae, and Neisseria gonorrhoea, all of which may cause fever and pharyngeal exudate. However, none of these have demonstrated serious sequelae if left untreated (Huovinen, 1990; Middleton, 1996; Schwartz et al. 1998). The patient should be monitored for complications of pneumonia, peritonsillar abscess (quinsy) or cellulitis, otitis media, and mastoiditis, all of which may occur in many of the viral or bacterial etiologies of pharyngitis.

A rare cause of sore throat is Corynebacterium diphtheria. There is a grayish membrane which may cover the tonsils. Diagnosis is made on clinical grounds (not waiting for culture results), because admission to the hospital for treatment is emergent.

Other causes of pharyngitis are irritants such as allergens and inhaled smoke (first or second-hand, or wood-smoke from stoves or fireplaces) or chemicals in work and home environments. Gastroesophageal reflux disease (GERD) occasionally presents with the complaint of sore throat, though cough is a more frequent sign. Mouth breathing while sleeping may cause transient sore throat. Also in the differential diagnosis are foreign body lodged in the pharynx or esophagus, burns, radiation therapy and neoplasms. Leukemia and AIDS and other systemic diseases such as Kawasaki Syndrome may first present with pharyngitis, but are usually accompanied by other signs or symptoms.

**Signs and symptoms and scoring systems**

Sore throat as the chief complaint may be the only symptom in an illness, or it may be accompanied by many other signs and symptoms. The history of the patient’s illness is equally important. Sometimes these clinical features can lead a provider to suspect a certain diagnosis.
Viral and bacterial entities may manifest with similar symptoms. Viruses may more often appear as sore throat with cough, rhinitis, conjunctivitis, and oral or pharyngeal ulceration (Smith, 1996). Bacterial etiologies more often produce exudate in the throat, higher fever (usually >101 degrees), and tender cervical lymphadenopathy. However, it is generally agreed that clinicians cannot, on the basis of any of these signs or combination of them, differentiate viral from bacterial etiology (Jackler & Kaplan, 1997; Mc Isaac, Goel, et al., 1997; Putto, 1987; Schwartz et al., 1998; Simon, 1995).

**Scoring systems**

GABHS may be suspected when fever, exudative pharyngitis, and tender, swollen cervical lymph nodes are all present, and there is no cough (not valid in patients who smoke). Scoring systems which give each of these signs one point, would assign the patient with all of these signs a score of +4 (give 1 point for absence of cough). A score of 0 or +1 represents a probability of 7% or less of GABHS, while a score of +2 represents approximately a 4-18% chance of strep. A score of +3 equals a 19-36% chance of strep and +4 gives a probability of 26-62% chance of GABHS (Mc Isaac et al., 1997; Ruoff, 1996). The ranges given account for variations in population prevalences, varying from 5% to 20%. For example, in a person complaining of sore throat with fever greater than 101 degrees, no cough, and no tender lymph nodes or exudate, a score of +2 would be assigned. In an urban area with strep A prevalence of 20%, the probability of a positive culture would be 18%. In an area with the usual prevalence of 5%, the probability is closer to 4%.

The subjects in the above study reported by Mc Isaac, Goel et al., (1997) with scores of 0 and +1 accounted for nearly half of all the subjects, and the subjects with scores of +4 accounted
for 10-15% of all subjects. These values are in keeping with normal population prevalences of GABHS. If a provider is practicing in a rural area where throat cultures or rapid antigen methods of testing are prohibitive, a case could be made for treating these patients with scores of +4 empirically. However, over treatment is a surety, with as many as three out of four patients not infected with strep receiving unnecessary antibiotics. The dangers of developing resistant bacteria and adverse drug reactions should also be considered in the decision equation. The above study did not include children under 15 years old, and the scoring system was used in adult patients only.

**Pharyngeal exudate.**

Most viruses do not present with pharyngeal exudate, with the distinct exceptions of adenovirus and Epstein Barr virus (EBV). EBV is the infecting agent in infectious mononucleosis and is often not diagnosed until patients are unresponsive to empiric penicillin therapy (Berman & Chan). The exudate is more diffuse and shaggy in appearance compared to the more distinct patches of white in the GABHS patient, but early mononucleosis may look like GABHS. An exam of the abdomen may reveal a palpable spleen and/or enlarged liver. Odynophagia, next to sore throat, is the most prominent symptom in mononucleosis and occurs in 80% of cases (Vukmir, 1991). Anterior cervical nodes are less prominent and posterior cervical lymphadenopathy is pronounced. Of course, the monospot will be positive in mononucleosis, and leukocytosis is present (lymphocytes predominate), but it should be kept in mind that approximately one-third of these patients will also test positive for strep. One-third of these are carriers only (Jackler & Kaplan, 1997; Levin & Romero, 1997). Palatal petechiae, headache, anorexia, and myalgias may also be present. These patients should not be treated with
ampicillin, as a pruritic rash may develop in 90-100% of cases. Children treated with penicillin for concurrent GABHS infection may also develop a rash (Levin & Romero, 1997).

Other viruses that may initially appear as exudative are herpes simplex and some coxsackie viruses. A thorough exam of the buccal mucosa usually locates herpetic ulcers in the anterior mouth. Coxsackie viruses cause herpangina and Hand, Foot and Mouth Disease (HFMD) which usually present with lesions on the tonsils and/or uvula and soft palate and, in HFMD, further forward in the mouth or on the tongue. Lymphonodular pharyngitis, also caused by coxsackie virus, has small, non-ulcerating, yellowish-white papules in the same distribution pattern as herpangina.

A patient with primary HIV or leukemia and/or receiving cancer treatment may present with pharyngeal exudate caused by candidal infection or other opportunistic pathogens. The HCP should examine the mouth for white exudate on the buccal mucosa or tongue. Group C and G streptococcal infections, C. diphtheria and many other bacteria may mimic GABHS. Corynebacterium diphtheria’s exudate has a grayish and membranous appearance, and these patients, while appearing ill, usually have low-grade fever, which belies how truly ill they are. A history of no, or out-of-date, immunization or indigence and/or alcoholism may help distinguish this entity, since it occurs most often in these populations (though still rare).

An exudative pharyngitis is often seen in adenovirus infection, and fever is low-grade. The adenoviruses also demonstrate conjunctivitis in one-third to one-half of the cases. If conjunctivitis accompanies sore throat, the cause can be presumed viral. Cervical lymphadenitis may also be present. This pathogen is sometimes passed in poorly-maintained swimming pools or ponds, and gastrointestinal symptoms are common.
Rashes. —

Scarlet fever appears with diffuse erythema and a sandpaper-like rash that develops with certain strains of GABHS that produce an erythrogenic toxin. Scarlet fever begins with mild to severe sore throat, and progresses to a fine rash over the upper body that spreads to neck, face and extremities, blanching when pressed with the finger. Skin folds (antecubital fossae, neck, etc.) are dark red (Pastia’s lines), and the rash gives the appearance on the face of circumoral pallor (Wiener, 1993). Desquamation may follow the rash.

Arcanobacterium hemolyticum is known to produce a scarlatiniform rash in almost 70% of cases, and even the seasoned practitioner may be fooled by a viral exanthem into diagnosing a strep infection where none exists (Wiener, 1993). Measles (rubeola) may present with sore throat and morbilliform rash that in its early stages may mimic a mild or early scarlatiniform rash, but the history will describe the rash beginning on the face or forehead. Many viruses produce exanthema, and enanthems (mucosal lesions) of varying appearances sometimes accompany them (Fitzpatrick, Johnson, Wolff, Polano, & Suurmond, 1997). Hand, foot, and mouth disease begins with sore throat and lesions on tonsils and/or soft palate and uvula, and progresses to small maculopapular lesions on the palms of the hands and soles of the feet and, and on rare occasions, to buttocks or back.

*Palatal petechiae*

Another common mistake is to assume that palatal petechiae are produced only by strep A. In actuality, EBV, rubella, and several viruses produce this sign occasionally (Fitzpatrick et al., 1997), although overall, it appears in less than 5% of pharyngitis cases (Poses et al., 1993). Other viruses may produce vesicular or papular lesions that have the appearance of petechiae.
initially. A good dermatology picture atlas may help the unseasoned practitioner differentiate these rashes and mouth lesions.

**Emergencies**

Patients with severe dysphagia, drooling or wiping the mouth and spitting should be suspect for epiglottitis. Foreign body obstruction may also present in this manner. These cases should be referred to the local emergency department without instrumentation of the throat, since this may stimulate laryngospasm in the patient with epiglottitis or lead to complete airway obstruction in the patient with foreign body.

**Testing and Treatment Decisions**

Generally, practitioners agree that the most dreaded complication of sore throat is acute rheumatic fever (ARF) caused by GABHS. The rare suppurative complications such as otitis media or quinsy (peritonsillar abscess) which follow sore throat may as frequently be caused by viral and non-GABHS bacteria (Little & Williamson, 1996; Schwartz et al., 1998). Much overtreatment of viral and non-GABHS etiologies results because of the fear of missing complications (Little & Williamson, 1996; Mc Isaac, Goel et al., 1997; Schwartz, 1998).

Since the advent of managed care, costs have become a concern for all practitioners. The old practices of either culturing all sore throats or treating most patients with antibiotics are no longer viable decisions since both carry high costs, especially when providers’ management time of drug reactions is considered.

**History**

It is important to collect a careful history to help determine the patient’s approximate risk of complications resulting from the current pharyngeal infection. It is important to ask if there
are known cases of strep in the patient’s environment or if there is a history of rheumatic fever, if immunizations including diphtheria are up-to-date, what medications the patient is taking (including oral contraceptives and inhaled medications), concurrent history of diabetes mellitus. The patient’s living situation may also be of significance, if living in a closely quartered barracks or dormitory situation where an outbreak of strep is occurring, or in a homeless situation. If gonococcal or chlamydial pharyngeal infection is suspected, it may help to know whether the patient has engaged in orogenital sex, because different culture media are used to diagnose these pathogens.

In patients with history of ARF, there is a higher risk of rheumatic fever developing if subsequent strep A attacks are inadequately treated. Since no tests are 100% sensitive for GABHS, all patients with history of ARF are treated for strep when sore throat presents. Preferred treatment is benzathine penicillin G intramuscularly since full eradication is imperative. If patient compliance can be assured, oral penicillin is an acceptable substitute.

When there is documented GABHS in the close environment of the patient presenting with sore throat, throat culture should be performed. Health care providers may elect to treat these patients with antibiotics without testing if the patient presents with a score of +3 or +4, since probability of strep is much higher and since tests may miss some of the truly infected patients.

Efficacy of oral contraceptives is decreased with some antibiotics, and steroidal inhalers increase likelihood of bacterial infection. Diabetics are more often bothered by candidal infections which can mimic strep exudate. The homeless may have problems with follow-up and compliance both.
When to test

GABHS infection is the only pathogen for which antibiotic therapy has a clear benefit in uncomplicated pharyngitis (Huovinen, 1990; Schwartz et al., 1998). Early antimicrobial therapy may lead to recurrent disease due to the suppression of the immune system (Little & Williamson, 1996). Therefore, culturing patients with moderate probabilities of positive cultures (scores of +2 or +3 [in populations with low prevalence of GABHS]), and waiting for results before treating, and using rapid antigen tests (with follow-up culture in negative results) in patients with high probability of GABHS (+3 [in populations with higher prevalence of GABHS] or +4), may be the most beneficial to patients and least expensive plan overall (Mc Isaac, Goel, et al., 1997). Thus, far fewer patients would receive unnecessary drugs. This plan also has the best risk/benefit ratio, since starting antibiotics for GABHS infections as late as nine days after symptoms begin has been shown to prevent ARF complications (Dowell et al., 1998; Schwartz et al., 1998; Simon, 1998). Using the rapid strep test in patients with only the highest probability of a positive result will give the greatest yield, and allow for immediate prescription and least amount of time spent following up on positive cultures. For patients with scores of 0 or +1, a watch and wait policy may be adopted unless the patient appears very ill.

Culture usually costs less to perform than a rapid antigen strep test, since, in the case of a negative result, the rapid test requires a backup culture test. If performed correctly (vigorously swabbing the tonsils and posterior pharynx, avoiding contact with the tongue, soft palate, and uvula), cultures reveal approximately 90% of GABHS infections (sensitivity). However, the average sensitivity is reported to be as low as 70% (30% of GABHS infections are missed) (Chambers, 1997; Facklam, n.d.; Nicoll, McPhee, Chou, & Detmer, 1997). Rapid antigen tests
are usually compared to the “gold standard” of throat culture in clinical trials, and have produced as high as 96% sensitivity, though most often the sensitivity is closer to 80% to 85% (Hoffmann, 1990). The newer enzyme-linked immunoassay rapid tests may miss only 10% of infections (Jackler & Kaplan, 1997; Nicoll et al., 1997). Both rapid tests and cultures have high specificity (98-99%). This means there are rare false positives. The rapid tests have higher specificity than some culture methods, as Group C and G beta-hemolytic streptococci will be read as positive for GABHS 7-8% of the time when bacitracin disks are used in culture methods (Facklam, n.d.). Some manufacturers claim rapid tests also will not show positive results for the carrier state as often as culture media.

The value of rapid strep tests is that the results are available in 5-15 minutes, and if positive, follow-up time is minimized as a prescription can be given during the same visit. Another benefit is derived when the mildly ill-appearing individual seems unsure about leaving the clinic without a prescription for antibiotics; a negative result may persuade acceptance of symptomatic management. With careful collection procedure, using a tongue blade to avoid contamination (and dilution) by normal mouth flora, latex agglutination rapid tests can give a practitioner a fairly high confidence level of detection. This may obviate the need for follow-up cultures in negative rapid test results, especially since pharyngitis, even if caused by GABHS, is largely a self-limiting disease; what few complications result are very rarely serious. Avoiding the many problems associated with antibiotic prescription seems a good trade-off.

The Strep A optical immunoassay (OIA) is gaining more recognition over the last year as sensitivity seems to be proving to be higher than throat culture, though specificity is slightly lower. This or nucleic acid amplification techniques may replace cultures eventually as the
standard diagnostic test for GABHS (Garcia-deLomas & Navarro, 1997; Harbeck et al., 1993).

OTHER TESTS IN A WORKUP.

In the very ill-appearing patients, a CBC should be drawn if rapid tests are negative, and a double swab technique should be used to collect the throat specimen so that if rapid tests are negative, a follow-up culture can be done without having to recollect the specimen. A low white count on the CBC may lead one to suspect a viral cause, and a high WBC may indicate bacterial infection. Early GABHS often demonstrates leukocytosis with polymorphonuclear neutrophils. Also, in approximately 70% of ARF patients, the CBC may indicate anemia. It may also help the clinician clarify the differential diagnosis, ruling out leukemia and other possible blood dyscrasias. Hospitalization may be necessary in some cases. Signs and symptoms of diphtheria, epiglottitis (H. influenza), acute leukemia, AIDS, and blood dyscrasias such as agranulocytosis should be kept in mind so these are not missed.

An ESR level may be slightly elevated in GABHS, but will be more increased in the ARF patient, and should be performed on all patients with symptoms of polyarthritis, since 92% of ARF patients have this complaint (Wallace et al., 1989). In the event of negative strep tests and high white count in the very ill patient, and no other obvious source of infection, empiric antibiotic therapy may be started, after considering hospitalization and the collection of other studies. It would be wise to perform urinalysis and consider drawing blood cultures in the patient with fever greater than 101 degrees. A serum heterophil agglutination test will help to elucidate mononucleosis.

The patient with orogenital contact and a pharynx coated with an asymmetric gray membranous exudate should have a culture done. The clinician should specify that chocolate
agar or modified Thayer-Martin media be used, or at least be sure lab technicians know the suspected infecting organism is gonococcus. Other tests may be dictated by accompanying signs or symptoms, but should not be performed unless results will change the plan of care or are necessary to confirm a diagnosis.

Deciding not to culture or treat with antibiotics in patients with accompanying signs or symptoms of conjunctivitis, rhinorrhea, diarrhea, hoarseness, and cough is widely acceptable protocol, as these are all good indicators of viral infection. However, it is wise to consider that some patients will present with concurrent viral and bacterial infection, especially if symptoms of sore throat have been present for 7 days or more, and rapid strep testing would be advisable in any patient with such established symptoms.

Choice of antibiotic

Penicillin is the drug of choice in treating GABHS. If we are to keep the excellent efficacy of this drug, it is essential that treatment only be instituted in patients with documented GABHS infection, or with a history of ARF and current sore throat. Penicillin has a good safety profile, has a narrow spectrum which limits development of resistance, costs little, and prevents ARF. Some studies have shown its efficacy to be somewhat questionable (up to 25% treatment failures), but poor compliance, and evidence of the carrier state are the probable factors involved in those studies (Pichichero, 1995; Little & Williamson, 1996). Markowitz, Gerber and Kaplan (1993) compared penicillin failure rates in studies on GABHS infection from 1953 to 1979 and 1980 to 1993 and found no significant difference in failure rates.

In the case of allergy to penicillin, erythromycin is recommended, and the broader spectrum macrolides, azolides and cephalosporins are discouraged by the CDC since their
broader range exerts selective pressure for the development of resistant strains of bacteria (Schwartz et al., 1998).

In the patient for whom compliance is an issue, Benzathine penicillin G injection should be chosen. While clinicians usually consider the homeless among these possibly non-compliant patients, busy business people or older teens are prone to forget medications once their symptoms are resolved. It should be remembered that penicillin given intramuscularly has a higher likelihood of severe reaction in the patient allergic to it.

**Patient education**

It is important to teach patients who are given antibiotics that they may develop resistant pathogens when medicine is stopped too soon or when the patient does not finish the prescription. Emphasizing the need to finish all the medicine may help prevent bad outcomes.

Whether strep tests are positive or negative, all patients will benefit from symptomatic treatment. Ibuprofen or Tylenol will provide relief of most patient’s sore throat, and overall perceptions of health will be improved. The discomfort of fever can also be minimized. A French study showed ibuprofen to provide the best relief of symptoms in children, and its advantageous less frequent dosing makes it easier to use (Bertin et al., 1991).

For adults and older children, throat lozenges and anesthetic sprays like Chloraseptic may provide temporary relief of sore throat. Gargling warm salt water ( ½ to 1 teaspoon in ½ cup water) can help as well.

It is important to educate patients on the signs and symptoms of developing sepsis. Give patients an easy to read, brief handout, reviewing it verbally in the office. This will give patients something to help them determine when a return to the HCP is needed. Handouts (see example
in appendix) may also help the patient with decisions regarding future sore throats.

Encourage the patient to drink plenty of fluids and eat a soft diet for a day or two, including soups and warm beverages. These routines have proved helpful in alleviating symptoms. Some patients prefer herbal remedies such as echinacea or garlic. Patients should be taught that echinacea is not a vitamin, and should not be taken on a regular basis. If the patient is on many medications, efforts should be made to determine drug interactions as well. Other home remedies such as lemon juice or apple cider vinegar in sweetened hot water may prove beneficial, and chicken soup seems to be a favorite remedy for viruses.

Of all the things a provider may suggest to a patient to improve the situation, rest should be the first and foremost recommendation. The immune system actively produces cells which fight infection during deep sleep. Patients should be taught that sleep is the best remedy for their illness.

**Risk to benefit ratio**

Surveys report that only 9% to 15% of all patients with sore throat seek care from their HCP (Huovinen, 1990; Mc Isaac, Goel, et al., 1997). Few develop ARF, and, at most, only 15% of ARF patients develop chronic problems (arthritis, carditis, chorea, etc.) in the U.S. today (Dippel et al., 1992; Marcovitch, 1990). Considering these figures, what is the likelihood of preventing ARF, and how many patients would we have to treat with antibiotics to prevent one case from occurring?

An average of more than 106,000 hospitalized patients die yearly in the United States from drug reactions and interactions alone, and the risk of anaphylaxis from penicillin therapy is 2.5/10,000 with 1 in 50,000 resulting in death (Del Mar, 1992; Lazarou et al., 1998; Marcovitch,
The risk to benefit ratio is in favor of treating only verified cases of GABHS.

Medicalization and prescriptive practices

While few patients with sore throat seek treatment, this number is rising, probably due to the impression that antibiotics are necessary for sore throats to heal (Little, Gould et al., 1997; Little, Williamson, et al., 1997). This has been labeled “medicalization”. One study reports that 60% of patients who receive antibiotics for pharyngitis return within a year with complaints of sore throat, and that 40% return if they were given only treatment for symptoms at their prior visit (Little & Williamson, 1996). That number will reduce still further over time with consistent patient education, if antibiotics are withheld appropriately (Herz, 1988; Little & Williamson, 1996).

Prescriptive practices vary greatly and studies have shown that physicians largely believe they can differentiate by clinical signs between viral and strep pharyngitis (Mc Isaac & Goel, 1996). Pichichero (1995) claims experienced physicians will overestimate Group A strep 80-95% of the time. Many studies have demonstrated that clinical signs are not sensitive or specific enough to warrant basing treatment decisions upon them (Mc Isaac, Goel et al., 1997; Putto, 1987; Schwartz et al, 1998). Some declare that the most significant variable in whether a patient receives antibiotics for a sore throat is not any particular sign or symptom, but the particular physician he or she sees (Slawson, Baer & Richardson, 1991). Such empiric treatment leads to much overtreatment.

Resistance

Overtreatment with antibiotics leads to the development of resistant bacterial strains (Mc Isaac, Goel et al., 1997; Pichichero, 1995; Schwartz, 1998). In Japan, there is a 50-60%
resistance of GABHS to erythromycin due to overtreatment with macrolides (Kazzi & Wills, 1998). Seppala and her colleagues (1997) reported in the New England Journal of Medicine that the 16.5% resistance to erythromycin which had developed in Finland, had declined to 8.6% after a nationwide reduction in prescription of the drug. Kearsley et al. (1997) reported treatment failures with both clarithromycin and amoxicillin. Other studies on cephalosporins show evidence of drug resistance and the more these are prescribed for strep, the more resistance will be seen (Schwartz et al, 1998). So far, there is no known GABHS resistance to the beta-lactam antibiotics, and in the United States at least, penicillin is still effective against GABHS, but there is the danger that with time and overuse, resistance will develop (Dowell et al., 1998; Schwartz et al., 1998; Vukmir, 1991). As we have seen resistance grow in many organisms over the last decade, it behooves us to be very wary of providing antibiotics to persons whose immune systems may well fight and win its own wars.

**Conclusions**

If previously reported numbers are to be believed, more than half of the strep infections are never seen and only one-third are ever treated with antibiotics. Yet our acute rheumatic fever rate remains low. This is because most throat infections, including streptococcus, are self-limiting, leading rarely to any complications (Schwartz et al., 1998). It is only particular strains of GABHS that lead to ARF, and only 15% of the population appear to have the necessary genetic predisposition to develop it (Wolfe et al., 1997). Other bacterial infections, while responsive to certain antibiotics in vitro, do not appear to respond in vivo, and suppurative complications may ensue whether treated with antibiotics or not (Huovinen, 1990; Schwartz et al., 1998).
Signs and symptoms of viral and bacterial causes of sore throat may be indistinguishable, and treatment should be reserved for proven GABHS. Scoring systems may help the HCP to decide whom to test for GABHS. Scores of +2 in communities with high incidence of GABHS, or higher scores (+3 or more) in other communities should probably all be tested, and if the patient with +3 or +4 appears ill, antibiotic treatment may be implemented and stopped if cultures are negative. At the clinicians discretion, if there is a known epidemic in the community or close exposure to a documented case of GABHS, testing individuals with fewer signs is justifiable.

Costs for treatment of pharyngitis include not only the cost of the antibiotics prescribed, visits to the HCP, and tests for diagnosis, but as resistance develops, more costly drugs are required, and returns to the practitioner for further management are necessary. This adds up to more time and money spent chasing the elusive cure. Drug side effects lead to lost productivity as well, and require provider time to follow these. Treating simple pharyngitis adds up to a substantial slice of the dollars spent in health care (Slawson et al., 1991).

The patient who receives an antibiotic for sore throat leaves the practitioner’s office with the perception that cure could not be effected without a visit to the HCP and medicine. This leads the patient to visit again in the event of future sore throats. Educating the patient on the benefits of waiting a day or two before starting treatment of strep throat (50% fewer relapses), on the low likelihood of GABHS being the cause of the sore throat, on the lack of efficacy of antibiotics for viral etiologies, on the dangerous pathogens developing because of overuse of antibiotics, and on the countless adverse events following antibiotic therapy can help the patient institute symptomatic treatment for his or her sore throat. This strategy may decrease the number
of visits to the HCP for sore throat, which would bring benefits to all.
References


British Journal of General Practice, 46, 461-464.


A randomized controlled trial of antibiotics on symptom resolution in patients presenting to their general practitioner with a sore throat. British Journal of General Practice, 47, 280-284.


Appendix

SORE THROAT
Common questions and answers

What causes sore throats?
Many things can cause a sore throat. The causes include infections with viruses or bacteria. Allergies or sinus drainage, breathing air with very little moisture in it (low humidity), and breathing with the mouth open while sleeping can also cause sore throat. Smoking tobacco or breathing someone else’s tobacco smoke or smoke from a wood stove can also irritate the throat.

What is the difference between viruses and bacteria?
Viruses cause colds, most coughs and sore throats and cannot be killed by antibiotics. The body fights these infections effectively when the immune system is healthy. Infections caused by bacteria can be treated with antibiotics to kill the infection.

How can I help my immune system fight a virus?
The body replenishes your immune system while you sleep, so getting plenty of rest and avoiding vigorous work or activities for few days can help the most. This will also help prevent the spreading of the infection to others.

When should I visit my health care provider (HCP)?
If you have a sore throat with a fever but only feel mildly ill, you may stay home for a day or two until you are better. If you have a sore throat and a high fever, feel faint, or have problems breathing or swallowing and feel more than just mildly ill, you should call your HCP and make an appointment.

How will my HCP know if I need antibiotics?
Antibiotics are usually prescribed only for ‘strep throat’, a bacterial infection caused by Group A streptococcus (a type of germ). After your HCP listens to the history of your illness and examines you, he or she may decide a test is necessary to determine if your sore throat is caused by ‘strep’ (or rarely, some other bacteria). If the test is positive, your HCP will give you antibiotics to kill the germ. If you have had rheumatic fever, your HCP will give you antibiotics for any sore throat you develop since you have a much greater chance of getting rheumatic fever again.

Why don’t HCPs just give antibiotics to everyone with a sore throat?
Antibiotics may cause mild to serious side effects. Examples of side effects are stomach upset (nausea), diarrhea, and/or stomach pains (abdominal cramping). Antibiotics may also cause allergic reactions, which can be life threatening in rare instances. Examples of these are rashes, and swelling in the throat or face which can cause difficulty breathing. Another serious problem with giving antibiotics too frequently is that bacteria can become ‘resistant’ to the antibiotics, and then the antibiotic will not cure the illness anymore. HCPs prevent resistance from developing by giving patients antibiotics only when they are needed. Remember, antibiotics only kill bacteria and not viruses.

What other things can I try to relieve my symptoms?
Gargling with warm salt water (1 tsp. in 1/2 cup water) will help and may stimulate your immune system to fight the infection whether it’s viral or bacterial. Cough drops or anesthetic throat sprays may also help your sore throat. Ibuprofen or tylenol can relieve pain of sore throat and fever, and congestion or other symptoms such as sinus drainage may be treated with over-the-counter medicines. Just ask your pharmacist to help you decide what you need.

You can help your body keep fighting the infection and feel the best by drinking plenty of fluids as well. Eating soft foods like soup, popsicles, and Jell-O are easier to swallow, too.
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