Considerations in the Management of **PEDIATRIC ACUTE STREPTOCOCCAL PHARYNGITIS**

Instruction

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Sixty-Second Summary

- The primary goal of antibiotic therapy is eradication of group A beta-hemolytic streptococcal (GABHS) from the pharynx.
- There have been frequent reports of increased bacteriologic and clinical failure rates associated with traditional penicillin therapy for streptococcal pharyngitis.
- Pooled, multi-center studies and a meta-analysis of 35 qualified studies revealed superior bacteriologic and clinical cure rates of streptococcal pharyngitis with a cephalosporin compared with penicillin.
- The cost of treatment failure includes increased morbidity and risk of complications, loss of productivity or absence from school or work, return office visits, and spread to close contacts.

Learning Objectives:

After completing this activity, the participant should be able to:

- Summarize the various etiologies to consider and develop a differential diagnosis when approaching a child with acute pharyngitis
- Identify the features and predictors that guide the diagnostic testing of acute pharyngitis
- Describe the role of antibiotics for children with pharyngitis
- Recognize the rationale for the increased bacteriologic and clinical failure rates associated with traditional penicillin therapy for streptococcal pharyngitis
- Identify the most recent clinical data describing effective strategies for the treatment of acute pharyngitis in children

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Target Audience

This CME program is intended for primary care clinicians including Family Physicians, Internal Medicine, Physician Assistants, Nurse Practitioners and other clinicians with an interest in Considerations in the Management of Pediatric Acute Streptococcal Pharyngitis.

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Dr. Fromer reports that he has no real or apparent conflicts to report.

Dr. Pichichero reports that he has received grant or research support from and is a consultant for Abbott, Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Medimmune, sanofi-aventis, and Sanofi-Pasteur.

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Commercial Support Statement

This program is made possible by an educational grant from Abbott Laboratories.

■ CASE STUDY ■

WH is a 6 yo Hispanic male who has been brought in by his mother because he had a temperature of 38.7°C during the night. His temperature decreased to 37.3°C after his mother gave him acetaminophen. He had felt well during the recent winter school vacation, but began complaining of a sore throat yesterday. WH's mother reports that he has no cough, and that he has not had a runny nose or chest tightness.

On physical examination, you note that his anterior cervical nodes are tender and that his pharynx is slightly red, but is not swollen and is without an exudate. The physical examination is otherwise normal. His current oral temperature is 37.5°C. He has been in otherwise good health; he takes a multivitamin daily.

This clinical scenario is common in primary care practice. Acute pharyngitis was the cause of 2.9% of all office visits involving children 1 to 12 years of age in 2004, accounting for 400,000 office visits. In children 13 to 21 years of age, 3.3% of all office visits were due to acute pharyngitis.[1] The incidence of group A beta-hemolytic streptococcal (GABHS) infection (the main cause of bacterial pharyngitis) has increased.[2]

Question 1

What percentage of children with sore throat are diagnosed with GABHS pharyngitis?

a. 4%

▶ Incorrect. Please choose again. ■

b. 7%

▶ Incorrect. Please choose again. ■

c. 17%

▶ Correct. ■

d. 37%

▶ Incorrect. Please choose again. ■

Estimates of the incidence of GABHS pharyngitis range from 15% to 30%.[3-6] A recent investigation of children with sore throat in the outpatient setting found that 34% had acute pharyngitis, 17% had streptococcal pharyngitis, and 17% had upper respiratory tract infection.[6]

While acute pharyngitis is common in children, its management is fraught with many important decisions. These include:

- What are the management goals for acute pharyngitis?
- What is the best management approach for acute pharyngitis in children?
- Is the cause of the sore throat a virus, GABHS, non-GABHS bacteria, or other medical condition?
- Which patients should be tested using the rapid antigen detection test and which using a throat culture?
- Which antibiotic is recommended as first-line empiric therapy?
- Is it important to eradicate GABHS?
- What other microbial factors should be considered in the selection of antibiotic therapy?
- What other antibiotic-related factors should be considered in the selection of antibiotic therapy?

The principal management goal for acute pharyngitis is to use antibiotics only in persons infected with GABHS since only patients with GABHS pharyngitis are at risk of serious suppurative and non-suppurative complications. These complications include acute rheumatic fever (ARF), post-streptococcal glomerulonephritis, post-streptococcal reactive arthritis, Syndenham's chorea, post-streptococcal autoimmune dystonia, and pediatric autoimmune neuropsychiatric disorders (PANDAS).[7-12] Consequently, once it is concluded that GABHS is the definite or likely cause, the single most important goal of therapy is to eradicate GABHS from the pharynx[13,14] because all the benefits of antibiotics rely on eradication of the bacteria from the throat.

Other than GABHS pharyngitis and pharyngitis that is rarely caused by *C. diphtheriae* and *N. gonorrhea*, there is no current justification for using antibiotic therapy in patients with pharyngitis caused by other bacteria, including other beta-hemolytic species, such as groups C and G streptococci[3,13], which may simply be innocent bystanders during viral infection. Groups C and G streptococci do not increase the risk of post-infectious complications as does GABHS and have been identified mostly in college epidemics.[15] One preliminary report, however, has shown that *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are frequently isolated in children with acute tonsillopharyngitis and that these children have a high risk of lower respiratory illness.[16]

Additional desired management outcomes identified by the Infectious Diseases Society of America (IDSA) include reducing contagion, providing for rapid resumption of usual activities, and overall improvement in clinical signs and symptoms.[13]

Question 2

What would be your next step in managing WH?

a. Begin penicillin empirically

▶ Incorrect. Please choose again. ■

b. Observation with symptomatic treatment.

▶ Incorrect. Please choose again. ■

c. Continue the diagnostic workup

▶ Correct. ■

Since the information currently available is insufficient to determine if WH suffers from acute pharyngitis with GABHS as the cause, further diagnostic workup is needed. Empiric antibiotic treatment at this point has several disadvantages, not the least of which may be the unnecessary and inappropriate use of antibiotics since the vast majority of children with acute pharyngitis have a cause other than GABHS.[3,6,13] (Table 1) Observation is not a good option because the symptoms of GABHS pharyngitis will subside over 4 to 5 days with or without treatment. Yet in the absence of detection and appropriate treatment, eradication will not be achieved and the patient will be put at risk for sequelae. However, antibiotic therapy can still be beneficial even if started late because if eradication can be achieved within 9 days after the onset of symptoms, prevention of acute rheumatic fever is still possible.[13]

Table 1. Possible management approaches for acute pharyngitis in children.[17]

Approach	Advantages	Disadvantages
■ Treat without testing	■ No case of GABHS is untreated	■ 70-90% are treated unnecessarily ■ Exposure to antibiotic side effects ■ May promote bacterial resistance
■ Test before deciding who to treat	■ Avoids risks associated with antibiotics	■ Cost of the test ■ Patients want treatment

Question 3

What further diagnostic workup should be done?

a. Complete blood count.

▶ Incorrect. Please choose again. ■

b. Administer a rapid antigen detection test.

▶ Possibly correct. Please choose again. ■

c. Take a throat specimen for culture.

▶ Possibly correct. Please choose again. ■

d. Triage based on signs and symptoms

▶ Correct. ■

There are several options for the diagnostic workup of acute pharyngitis in children, each with its advantages and disadvantages.[17] (Table 2)

Table 2. Possible laboratory workup for acute pharyngitis in children.[17]

Approach	Advantages	Disadvantages	Recommended by
■ Test all patients with pharyngitis using rapid antigen detection test → treat if positive	■ Identifies nearly all patients with GABHS pharyngitis ■ Avoids antibiotic exposure by those without GABHS pharyngitis	■ Parents want treatment and may be disappointed if no antibiotic is prescribed	■ American Academy of Pediatrics[18] ■ Infectious Diseases Society of America[13]
■ Test all patients with pharyngitis using throat culture → treat if positive	■ Identifies nearly all patients with GABHS pharyngitis	■ 2-day delay in initiating antibiotics if culture is positive ■ Prolonged morbidity due to symptoms of GABHS pharyngitis ■ Lost parental wages	■ American Academy of Pediatrics[18] ■ Infectious Diseases Society of America[13] ■ Institute for Clinical Systems Improvement[19]
■ Test all patients with pharyngitis using rapid antigen detection test → treat if positive; throat culture if negative	■ Therapy initiated immediately in most patients with GABHS pharyngitis ■ Identifies nearly all patients with GABHS pharyngitis	■ Adds expense of a throat culture for the 70-90% with non-GABHS pharyngitis	■ American Academy of Pediatrics[18] ■ Infectious Diseases Society of America[13]
■ Triage using McIsaac score[20,21] (Table 2)	■ Identifies most patients with GABHS pharyngitis ■ Avoids antibiotic exposure by those without GABHS pharyngitis ■ Therapy initiated immediately in most patients with GABHS pharyngitis	■ Misses some patients with GABHS pharyngitis → risk of peritonsillar abscess, acute rheumatic fever, rheumatic heart disease, death	■ American Academy of Family Physicians[22]

Unless the patient presents with acute onset of symptoms, significant fever, red and exudative tonsillitis, tender swollen anterior cervical glands and absence of cough or runny nose, it is extremely difficult to determine if the cause of acute pharyngitis is likely to be GABHS. However, when the signs and symptoms are evaluated using a validated scoring system such as the one developed by McIsaac et al[20,21] (Table 3), patients can be triaged simply and effectively. This has the added advantage of avoiding the use of the rapid antigen detection test and a throat culture in patients when there is an extremely low risk of GABHS pharyngitis.

Table 3. McIsaac scoring system.[20,23]
[Adapted from: "A clinical score to reduce unnecessary antibiotic use in patients with sore throat"—Reprinted from, *CMAJ* 13-Jan-98; 158(1), Page(s) 75-83 by permission of the publisher. © 1998 Canadian Medical Association]

Criteria	Points	WH case
■ Temperature > 38°C	1	1
■ No cough	1	1
■ Tender anterior cervical adenopathy	1	1
■ Tonsillar swelling or exudate	1	
■ Age 3-14 y	1	1
■ Age 15-44 y	0	
■ Age ≥45 y	-1	
Total score:		**4**

Total score	Chance of GABHS* (%)	Suggested management[23]
-1	—	GABHS pharyngitis ruled out; consider other causes
0	2-3	GABHS pharyngitis ruled out; consider other causes
1	4-6	Administer rapid antigen detection test
2	10-12	Administer rapid antigen detection test
3	27-28	Administer rapid antigen detection test
4	38-63	Probable GABHS pharyngitis; consider empiric antibiotics

*In community with usual levels of infection

■ CASE STUDY ■

The McIsaac score for WH is 4, which indicates that he has a high probability of GABHS pharyngitis. Consequently, empiric antibiotic therapy is planned. Since WH has no known allergy to penicillin or other beta-lactam antibiotics, amoxicillin suspension 15 mg/kg three times daily for 10 days is started.

While many antibiotics are effective in treating GABHS pharyngitis, penicillin has been the drug of choice for decades because of its proven efficacy and safety, narrow spectrum of activity, and low acquisition cost.[3,13] Amoxicillin is often used alternatively, especially in children because the oral formulation is more palatable than penicillin.[13] Nonetheless, bacteriologic failure with penicillins does occur with reports[24-27] of bacterial eradication of GABHS less than the 85% required by the US Food and Drug Administration for first-line therapy for pharyngitis.[28]

■ CASE STUDY ■

Two-and-a-half weeks following the initial visit, the mother returns to the office with her son. She relates that her son's symptoms improved 2 or 3 days after starting the amoxicillin and that he felt better at the end of 10 days. Late this morning the school nurse called and asked her to pick up her son since he complained of a sore throat during morning snack. He was found to have a temperature of 38.1°C.

The mother stated that she had administered 3 doses of amoxicillin every day, missing only 1 dose during the 10 days.

Physical examination revealed tender anterior cervical nodes and a red, swollen pharynx with an exudate. The physical examination was otherwise normal.

A rapid antigen detection test indicates the presence of GABHS. A throat culture also is ordered to confirm GABHS and determine if other pathogens are present.

A preliminary diagnosis of persistent GABHS pharyngitis is made.

Question 4

What is the most likely cause of his persistent symptoms?

a. 15mg/kg tid dose of amoxicillin is too low.

▶ Incorrect. Please choose again. ■

b. Poor medication adherence.

▶ Incorrect. Please choose again. ■

c. New infection.

▶ Incorrect. Please choose again. ■

d. Bacteriologic failure

▶ Correct. ■

The dose of amoxicillin used to treat WH is the dose recommended for mild/moderate acute pharyngitis in children.[29] While poor medication adherence seems to not be an issue in this case, it must be acknowledged that three times daily administration of a suspension presents logistical challenges. A new infection is a possibility although the timing of the recurrence of symptoms suggests that his infection was not bacteriologically eradicated.

Bacteriologic failure is the most likely cause of WH's symptoms and clinical course. Bacteriologic failure, which occurs when GABHS persists on throat culture[30], has generally been observed in 10% to 37% of cases treated with penicillin; about 25-50% are carriers and 50-75% are true treatment failures.[11,14,15,31-34] Potential causes for treatment failure include bacterial co-aggregation or co-pathogenicity with penicillin-destroying beta-lactamase-producing bacteria (BLPB), as well as bacterial interference.

Co-pathogenicity

Co-pathogenicity is the situation in which bacteria resistant to a class of drugs protect other, co-localized bacteria that are normally susceptible to the same class of drugs.[35] Since the pharynx normally can be colonized by BLPB, such as *S aureus*, *H influenzae*, *H parainfluenzae*, *M catarrhalis*, or anaerobes[36], it is theorized that these BLPB inactivate penicillin in some patients with GABHS pharyngitis. Prior recent or repeated penicillin use is thought to select for BLPB.[37] There is a clear association between penicillin treatment failure and the pre-existence of BLPB co-pathogens in patients with recurrent GABHS

pharyngotonsillitis.[34,38,39] Some drugs that resist beta-lactamase degradation (e.g., amoxicillin-clavulanate and some cephalosporins) are more effective at eradicating GABHS than penicillin.[32,40]

Co-aggregation

Co-aggregation involves the ability of one bacterium to enhance the attachment of a different bacterium to local tissue. This has been described recently wherein beta-lactamase-producing *M. catarrhalis* enhanced the attachment of GABHS to pharyngeal epithelial cells resulting in a 10-fold higher colony count of GABHS than when *M. catarrhalis* was not present.[41] The association between GABHS and *M. catarrhalis* and *H influenzae* has been observed clinically in children with pharyngitis.[42]

Bacterial interference

In most healthy individuals, there is a balance between normal oropharyngeal flora and potential pathogens, including GABHS and others. The normal flora, such as alpha- and non-hemolytic streptococci and other bacteria, interfere with colonization and subsequent infection by competing with pathogens for nutritional substances. In addition, the normal flora produce bacteriocins, which are antibiotic-like substances that kill other bacteria.[15,33,34] The importance of bacterial interference has been shown in several studies. In one study, children with GABHS pharyngitis who subsequently did not respond to penicillin were less likely to have alpha-hemolytic streptococci as part of their normal flora than children who were effectively treated with penicillin.[37] In another study, children suffering from tonsillitis had their nasopharynx therapeutically colonized with alpha-hemolytic streptococci or placebo. Recurrence occurred in 2% and 23%, respectively.[43] A third study involved children with multiple episodes of recurrent tonsillitis.[44] Prior to tonsillectomy, children received 10 days of penicillin (17 mg/kg or 250 mg every 8 hours) or cefdinir (14 mg/kg or 600 mg once daily), which is a beta-lactamase stable cephalosporin. Cultures of tonsillar tissue revealed GABHS in 11 (55%) of the penicillin group and 3 (15%) of the cefdinir group. Thirty-three BLPB were isolated from 17 children in the penicillin group and 4 BLPB in 3 children in the cefdinir group. Alpha-hemolytic *Streptococcus* was isolated in 6 children in the penicillin group and 15 in the cefdinir group. This study found that cefdinir was more effective in eradicating GABHS, reducing the number of BLPB, and preserving alpha-hemolytic streptococci than penicillin.

As these studies show, different antibiotics vary in their ability to alter the balance between normal flora and GABHS. While penicillin, cephalosporins, and macrolides are similarly effective in eradicating GABHS, penicillin (and amoxicillin) is much more effective than cephalosporins and macrolides in eradicating potentially protective alpha-hemolytic streptococci. Cephalosporins and macrolides are more likely to preserve alpha-hemolytic streptococci as an interfering bacterium. Within the cephalosporin class, the third-generation drugs are the least active against alpha-hemolytic streptococci.

GABHS carrier state

Although not a reason for treatment failure, the GABHS carrier state is important since it may represent a false positive treatment failure. Persons who are carriers of GABHS have a throat culture positive for GABHS, but do not show signs or symptoms of pharyngitis or a rise in streptococcal antibodies. Increases in antibody titers are, however, attenuated after early antibiotic therapy.[40] Carriers with an acute viral pharyngitis cannot be differentiated from true positives using microbiology tests.

Question 5

To what antibiotic/class should WH be switched?

a. Amoxicillin/clavulanate

▶ Correct and other choices are possible. ■

b. Cephalosporin

▶ Correct and other choices are possible. ■

c. Clindamycin

▶ Correct and other choices are possible. ■

d. Macrolide

▶ Correct and other choices are possible. ■

Amoxicillin/clavulanate

The amoxicillin component disrupts bacterial interference as previously discussed, while the addition of clavulanate to amoxicillin is effective in killing BLPB (co-pathogens) that also may colonize the pharynx of children with GABHS infection. This has been demonstrated by most[45-47], but not all[48], studies showing improved eradication of GABHS with amoxicillin/clavulanate compared with oral penicillin.

Cephalosporins

Significantly lower failure rates have been observed with cephalosporins compared with penicillin. A meta-analysis applying the Cochrane Collaborative methodology often used to generate evidence-based medicine conclusions

was published in 2004 comparing cephalosporins to penicillin in the treatment of children with GABHS pharyngitis. The analysis included 35 carefully selected studies involving 7125 children published from 1966 through 2000.[31] The odds ratio (OR) for bacterial (OR=3.02) and clinical (OR=2.34) cure rates were significantly in favor of first-, second-, and third-generation cephalosporins as groups compared with penicillin ($p<0.001$) and were consistent over each of the three decades of data analyzed. The specific individual agents that were found to have higher clinical and bacteriologic cure rates were cefadroxil, cefdinir, cefixime, cefpodoxime, cefprozil, ceftibuten, cefuroxime, and cephalexin.

An attribute of many cephalosporins that may explain their higher success rates than penicillin could be their resistance to degradation by BLPB or that cephalosporins are less likely to eradicate the protective interfering alpha-hemolytic streptococci and throat anaerobes.[34,38]

Clindamycin

Clindamycin is an alternative to penicillin and has shown bacteriologic and clinical cure rates comparable to amoxicillin/clavulanate in older children and adults.[50] Clindamycin is generally reserved for patients who do not tolerate beta-lactam antibiotics[13], in part because of gastrointestinal side effects and concerns of pseudomembranous colitis.

Macrolides

Erythromycin for 10 days may be used as an alternative for patients with streptococcal pharyngitis and penicillin allergy since it has a low serious side effect profile (although gastrointestinal side effects are common), relatively narrow spectrum of activity, and relatively low cost.[13,15] While GABHS resistance to erythromycin has generally remained less than 8% in the US[3,51-54], considerable geographic variability exists. An outbreak of erythromycin resistant group A streptococcus (48%) was observed in Pittsburgh from 2001-2002.[55] This prompted a national, multicenter surveillance study that found macrolide resistance rates varied by site from 3.0% to 8.7%, as well as by month (<2% to >10%).[56]

■ CASE STUDY ■

You conclude that based on considerations related to bacteriologic activity, switching to a cephalosporin would be the best choice, with amoxicillin/clavulanate and a macrolide as alternatives. Before selecting an agent, you weigh other factors that should be considered. These include: allergic potential, medication adherence, frequency and duration of treatment, palatability, safety, and cost.[3,11,13,51]

Fortunately, WH appears to have no history of drug allergies based upon his medical record and discussion with his mother. If this investigation had revealed that WH had a previous IgE-mediated allergic reaction or had a positive penicillin skin test, cross-reactivity with other antibiotics, including penicillin congeners and cephalosporins would need to be considered. Although a cross-reactivity rate of 10% or more has often been cited, this may be an overestimate.[57,58] Recently, Pichichero estimated that the incidence of an allergic reaction (mostly unspecified rash) due to cross-reactivity was more likely about 3%, and of a bona fide allergy about 0.5%.[59] This estimation was based on an incidence of cephalosporin allergy in penicillin-allergic patients (confirmed by skin test) of 10.9% and accounted for a 3-fold increased coincidental risk of adverse reactions to unrelated drugs among penicillin-allergic patients and a review of the literature demonstrating an absence of evidence for higher cross allergy rates. This analysis also found that first-generation cephalosporins with a 7-position side chain similar to benzylpenicillin are more likely to cross-react with penicillin, which is consistent with other investigations.[60] Consequently, it seems prudent to avoid the first- and second-generation cephalosporins with the 7-position side chain (cefadroxil and cephalexin) similar to penicillin or amoxicillin in a patient who is penicillin allergic.[59]

Question 6

Which would be the least desirable based on dosing frequency and duration?

a. Amoxicillin/clavulanate

▶ Correct. Amoxicillin/clavulanate is given twice daily for 10 days.[61] ■

b. Azithromycin

▶ Incorrect. Azithromycin is given once daily for 5 days.[62] ■

c. Cefdinir

▶ Incorrect. Cefdinir can be given twice daily for 5 days.[63] ■

d. Cephalexin

▶ Correct. Cephalexin can be given twice daily for at least 10 days.[64] ■

e. Cefuroxime axetil

▶ Correct. Cefuroxime axetil is given twice daily for 10 days.[65] ■

Dosing frequency and duration are important determinants of medication adherence, with adherence improved with drugs given less frequently and for a shorter duration.[66,67] Azithromycin and cefdinir are approved by the US Food and Drug Administration for 5-day treatment of pharyngitis; cefpodoxime is as well. Treatment for acute pharyngitis with amoxicillin/clavulanate, cefuroxime axetil, and cephalexin requires 10 days.

Question 7

Which oral liquid formulation would be the best choice based on palatability?

a. Amoxicillin/clavulanate

▶ Incorrect. The oral liquid formulation of amoxicillin/clavulanate was found to be poorly tolerated (9th out of 11) in a controlled study.[68] ■

b. Azithromycin

▶ Incorrect. The oral liquid formulation of azithromycin was found to be generally well tolerated (4th out of 11) in a controlled study[68], but not the best among the choices offered in this question. ■

c. Cefdinir

▶ Correct. The oral liquid formulation of cefdinir was found to be well tolerated (2nd out of 11) in a controlled study.[68] ■

d. Cefpodoxime proxetil

▶ Incorrect. The oral liquid formulation of cefpodoxime proxetil was found to be poorly tolerated (tied for last out of 11) in a controlled study.[68] ■

e. Cefuroxime axetil

▶ Incorrect. The oral liquid formulation of cefuroxime axetil was found to be poorly tolerated (tied for last out of 11) in a controlled study.[68] ■

Palatability is an important consideration in children, especially young children since the suspension formulation is normally utilized. A controlled study involving 86 adult evaluators concluded that loracarbef, cefdinir, and cefixime were the most palatable.[68]

While most drugs commonly recommended for acute pharyngitis have a long history of being safe in children, gastrointestinal complications are the most common.

Question 8

Which is the most likely to cause gastrointestinal side effects?

a. Amoxicillin/clavulanate

▶ Correct. Dose-dependent diarrhea occurs with amoxicillin/clavulanate, affecting 14% of children when given twice daily and 34% when given three times daily.[61] ■

b. Azithromycin

▶ Incorrect. Vomiting occurs in 5%, and is the most common side effect in children.[62] ■

c. Cefdinir

▶ Incorrect. Diarrhea occurs in 8% of those older than 2 years.[63] ■

d. Cephalexin

▶ Incorrect. Diarrhea is uncommon.[64] ■

e. Cefuroxime axetil

▶ Incorrect. Diarrhea occurs in 9% of children.[65] ■

Question 9

Which is the largest contributor to the cost of care for GABHS pharyngitis?

a. Cost of the office visit.

▶ Incorrect. ■

b. Cost of the rapid strep test or throat culture.

▶ Incorrect. ■

c. Cost of the antibiotic.

▶ Incorrect. ■

d. Cost of parent time for the office visit and alternative child care.

▶ Correct. ■

The cost of care is influenced not only by the medication acquisition cost but also by direct costs, such as office-based doctor visits, and indirect costs, such as child school absence and caregiver/parent missed work days. The risk of complications also is increased with treatment failure. In cases of treatment failure, the indirect costs of care can far exceed the costs associated with successful therapy. One study of children with tonsillitis found that 75% of the total cost of care was attributed to lost parental productivity, while the cost of the antibiotic accounted for 3%.[69] A recent cost-effectiveness study observed that cephalosporins decreased overall costs and morbidity rates for children.[17]
The acquisition costs of antibiotics vary considerably from region to region and to health care plans; Table 4 lists many of the drugs of interest and their relative costs.

Table 4. Antibiotic therapy for GABHS pharyngitis in children.[70]

Drug	Regimen	Cost per regimen*†
Penicillin V	250 mg tid x 10d	+
Amoxicillin/clavulanate	20 mg/kg bid x 10d	++
Cefdinir	7 mg/kg bid x 5d	+++
Cefpodoxime proxetil	5 mg/kg bid x 5d	+++
Cefprozil	7.5 mg/kg bid x 10d	+++
Cefuroxime axetil	10 mg/kg bid x 10d	+++
Cephalexin	25 mg/kg bid x 10d	+++
Erythromycin	10 mg/kg bid x 10d	+
Azithromycin	12 mg/kg qd x 5d	++
Clarithromycin	7.5 mg/kg bid x 10d	+++
Clindamycin	4 mg/kg tid x 10d	++

*20 kg child
†Source: DrugStore.com as of 1/10/2007
+ = $1-24; ++ = $25-49; +++ = ≥$50

Summary

Testing is recommended in most children with acute pharyngitis to identify GABHS as the cause since this group is at highest risk of complications. Rapid antigen detection tests increasingly play an important diagnostic role since the sensitivity and specificity of newer tests approach those of a throat culture. While penicillin has been the first-line treatment for non-allergic patients for more than 50 years, data from recent clinical trials and meta-analyses, as well as clinical experience, suggest this role should be reconsidered. Much of the new evidence points to a first-line role for oral cephalosporins. Factors such as co-aggregation, co-pathogenicity, bacterial interference, and poor medication adherence may contribute to better success rates with this drug class. Additional factors supporting a reassessment of the role of cephalosporins in the treatment of GABHS pharyngitis include a shorter duration of therapy and improved tolerability and palatability.

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