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Management of streptococcal pharyngitis reconsidered

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Much has been written about the management of Group A beta-hemolytic streptococcal (GABHS) pharyngitis. Some might say "too much," and by exaggerating the importance of this entity we have created a national "streptococcal neurosis." ~~However, pharyngitis is still a common problem as evidenced by estimates that 11% of all school-age children visit a physician with this complaint annually.¹~~ In addition even though the clinical disease appears to be milder and the risk of complications considerably less than in the past, GABHS pharyngitis is still considered a potentially serious disease.

Despite the voluminous literature on the subject, a discussion of GABHS pharyngitis is guaranteed to generate much debate and numerous questions such as the following. Considering the current rarity of rheumatic fever, is our zealous approach to GABHS pharyngitis still justified? Are there other valid reasons for treating GABHS pharyngitis apart from prevention of rheumatic fever? Are throat cultures being used appropriately and what is the status of nonculture, rapid diagnostic techniques? Is penicillin still the drug of choice in view of the apparent increase in treatment failures? Is a full 10-day course of antibiotic therapy still required? What is the cause of treatment failures, are they important and how should they be managed?

The purpose of this report is to attempt to respond to these and related questions.

Considering the Current Rarity of Rheumatic Fever in This Country, Is Our Zealous Approach to GABHS Pharyngitis Still Justified?

The history of the modern approach to managing pharyngitis in children dates back to 1950 to 1951 when it was shown that the initial attack of rheumatic fever could be prevented by treating the preceding

episode of GABHS pharyngitis with a course of penicillin.^{2,3} Thus rheumatic heart disease became one of the very few preventable chronic diseases of childhood. This placed a premium on accurate diagnosis and ultimately led to the widespread use of throat cultures. It also required careful attention to compliance for an adequate course of therapy. While the ability to prevent rheumatic heart disease was heralded as an important advance, it nevertheless took 10 to 15 years before the recommendations aimed at preventing rheumatic fever became a widely accepted standard for the management of pharyngitis in this country.

We have now reached the point when rheumatic fever has become a comparatively rare disease in the United States, ~~with a reported incidence as low as 0.64 case per 100,000 in the general population.⁴~~ Is the dramatic decline in rheumatic fever due to changes in the organism, changes in the host, greater efforts to diagnose and treat GABHS pharyngitis according to established standards or a combination of these factors? We believe that to a large extent it is due to the expanded availability of health care through Medicaid for the high risk child population and to the widespread use of penicillin for GABHS pharyngitis.⁵ Non-believers point out that the incidence of rheumatic fever began to fall long before the availability of antibiotics. Indeed this is true, yet between 1952 and 1961, 258 children with rheumatic fever were admitted to the Johns Hopkins Hospital. Even as late as 1965, incidences ranging from 20 to 60 cases per 100,000 population were still being reported in this country.^{6,7} It could hardly be said at that time that rheumatic fever was nearly eradicated.⁸

It has been only during the past 15 years that rheumatic fever has fallen almost to the vanishing point in this country.^{9,10} There were only 33 admissions for rheumatic fever to Johns Hopkins between 1972 and 1981 compared to 258 two decades earlier (Fig. 1). This striking decline could not have been due to changes in host resistance in so short a period of time. Changes in the virulence of streptococci render-

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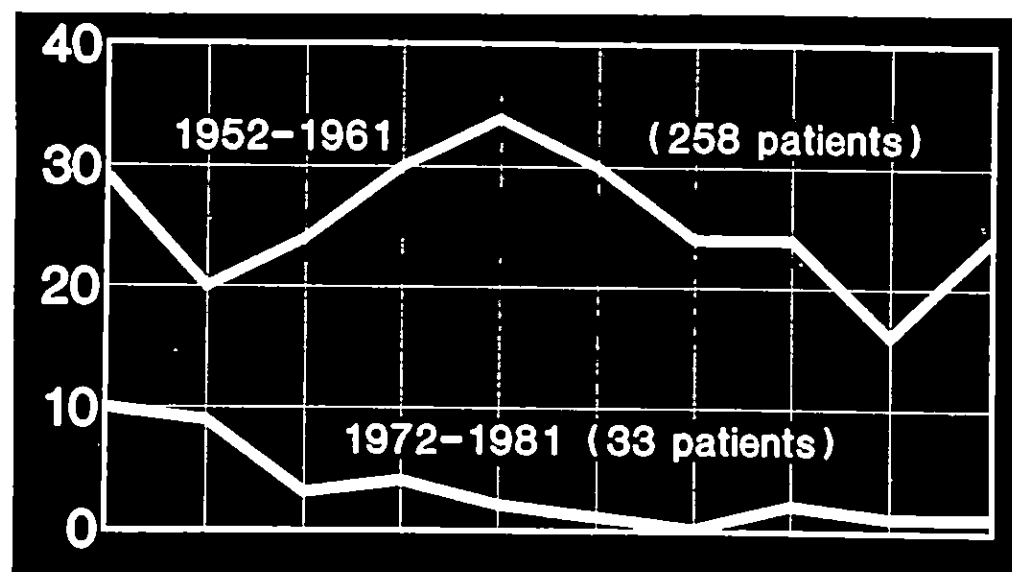


FIG. 1. Comparison of number of admissions to the children's service, Johns Hopkins Hospital, 1952 to 1961 and 1972 to 1981.⁵

ing the organisms less "rheumatogenic" may have occurred but proof is lacking.⁵ The authors participated in a recent national conference on the "Management of Pharyngitis in an Era of Declining Rheumatic Fever," at which it was concluded that the diagnosis and treatment of GABHS pharyngitis is an important factor in the decline of rheumatic fever.¹¹ We agree with this conclusion but at the same time believe that several aspects of this approach need to be reexamined and modifications considered.

Are There Other Valid Reasons for Treating GABHS Pharyngitis Apart from Prevention of Rheumatic Fever?

Glomerulonephritis. Prevention of the other non-supportive complication of GABHS pharyngitis, acute glomerulonephritis, is more difficult. While one study showed a 50% reduction, most authorities believe that glomerulonephritis cannot be prevented by treatment of the preceding episode of GABHS pharyngitis.^{12,13} However, eradication of GABHS by adequate therapy in a patient with nephritis will prevent the spread of the nephritogenic strain of GABHS to others and the appearance of multiple cases of nephritis in the family.

Suppurative complications. There is no disagreement about the value of antibiotic treatment for preventing suppurative complications of GABHS pharyngitis such as peritonsillar abscess and cervical adenitis. These and other complications accounted for as much as 13% of hospital admissions before 1940.¹⁴ When penicillin became available but was still scarce, it was given for only 3 days to patients with scarlet fever. Thirty-nine percent of the patients developed suppurative complications. However, when the duration of treatment was increased to 6 days this figure dropped to 5%.¹⁵ Currently, suppurative complications are rarely seen in antibiotic-treated patients.

Spread of infections. Another important and often overlooked reason for treating GABHS pharyngitis is to minimize the spread of infection. The risk of an untreated patient with *bona fide* GABHS pharyngitis transmitting the organism to other children is

very high. In one study 35% of the household contacts acquired GABHS within a few days after the index case had been identified.¹⁶ Untreated patients often become asymptomatic in 3 to 4 days and upon return to normal activities become an occult source for spread to others. Approximately 97% of patients with GABHS pharyngitis become culture-negative within 24 hours of initiating antibiotic therapy.¹⁷ However, if treatment is stopped after 3 days, the cultures will again become positive in more than half the patients and if stopped after 6 days the cultures will again become positive in 34%.¹⁸ Studies on the duration of treatment with oral penicillin to control outbreaks of streptococcal infections in the armed forces showed that a 10-day course of penicillin prevented the resurgence of GABHS following cessation of treatment, whereas a 5-day course did not.^{19,20}

Effect on clinical course. Some have questioned the impact of antibiotic therapy on the clinical course of streptococcal pharyngitis citing investigations carried out at Warren Air Force Base in the early 1950s to support their position.^{21,22} In these studies the rate of improvement in young adults with GABHS pharyngitis treated with antibiotics was only marginally greater than in comparable patients who did not receive antibiotic therapy. However, many practicing pediatricians have had the impression that antibiotic therapy has a dramatic impact on the clinical course of streptococcal pharyngitis.²³

We conducted a randomized, placebo-controlled investigation in 194 children with proven GABHS pharyngitis.¹⁷ After a throat culture had been obtained each child was evaluated for the presence of signs and symptoms and was then randomized in a double-blind manner to receive penicillin V, cefadroxil or placebo. Approximately 18 to 24 hours later each patient returned for a reevaluation of their clinical status. Significantly fewer of the children who had received either penicillin or cefadroxil had persistence of objective signs (Fig. 2) and subjective symptoms (Fig. 3) than did the children who had received placebo. In addition the evaluating physician, parents and patients all had the general impression that significantly fewer of the antibiotic-treated patients failed to demonstrate an overall clinical improvement at the follow-up evaluation than did the placebo-treated patients.

When throat cultures are used to diagnose GABHS pharyngitis, a decision has to be made as to whether to initiate antibiotic therapy immediately or wait for the results of the throat culture. Although we are not advocating routine, immediate antibiotic therapy for every child with suspected GABHS pharyngitis, we believe that the dramatic impact that early antibiotic therapy can have should be taken into consideration when attempting to make this decision. By shortening the duration of the clinical illness and by reducing the period of infectivity, early antibiotic therapy of

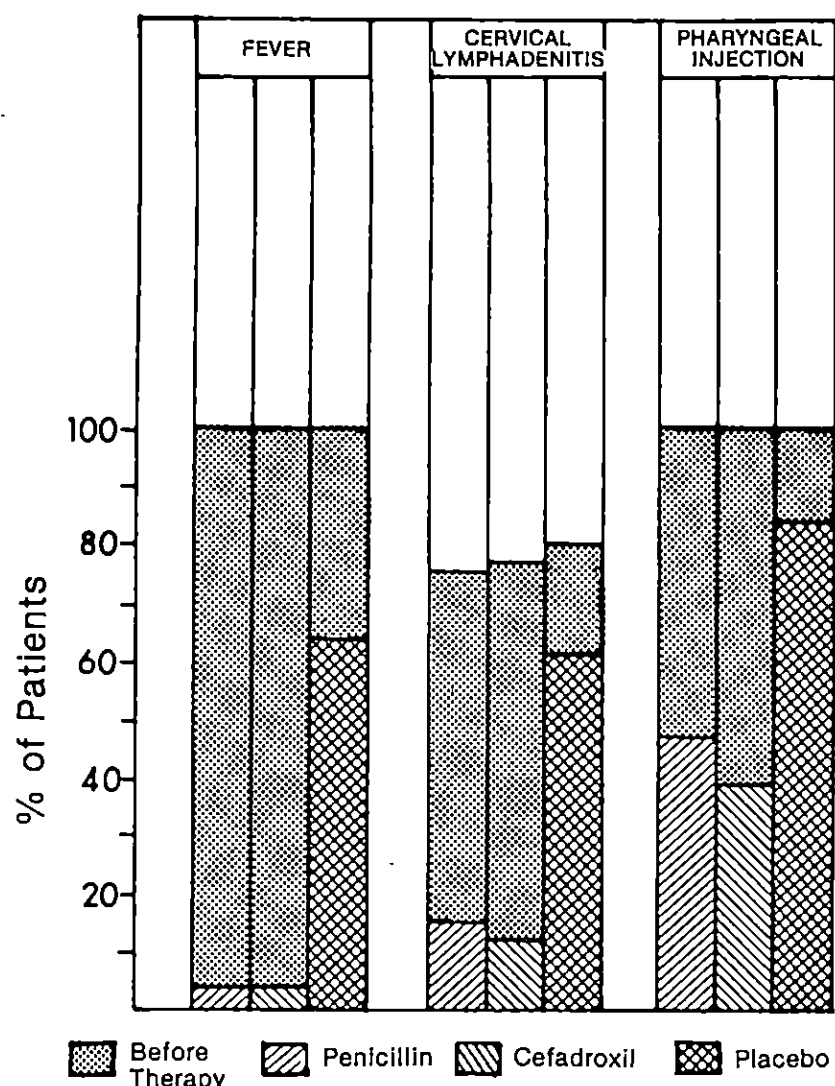


FIG. 2. Patients with the presence of specific clinical signs before and after 24 hours of therapy.¹⁷

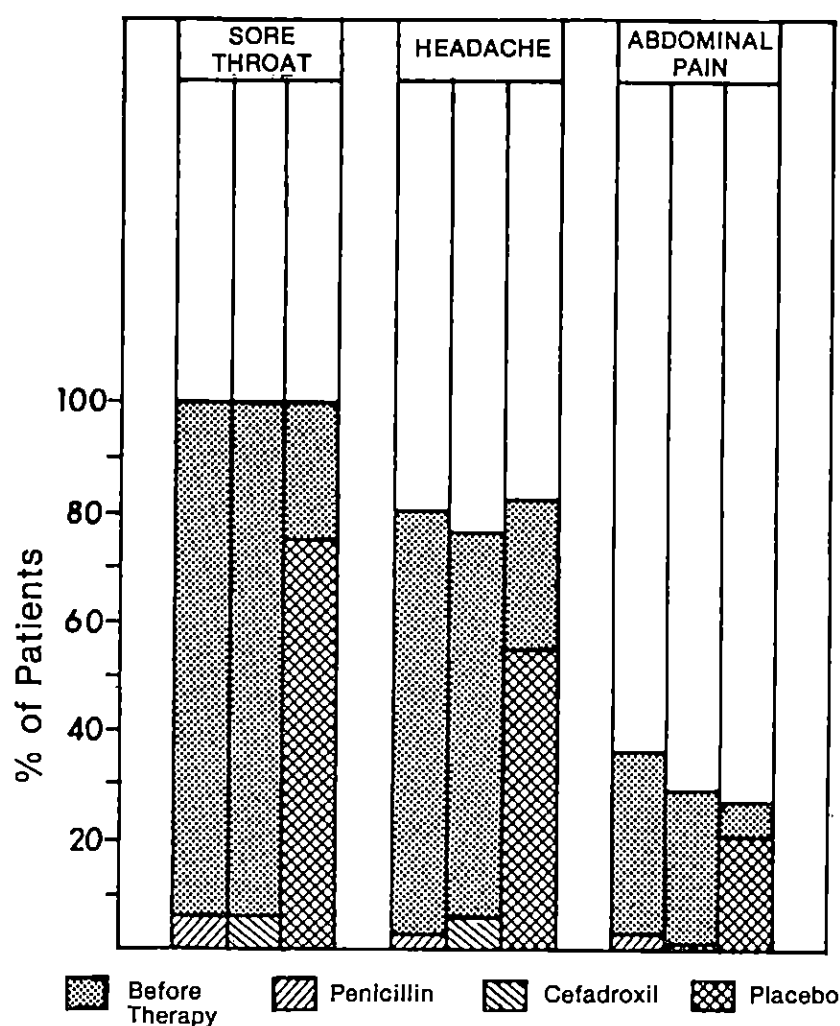


FIG. 3. Patients with the presence of specific clinical symptoms before and after 24 hours of therapy.¹⁷

GABHS pharyngitis may not only allow the patient to return to school or day care sooner than if therapy had been withheld until the results of the throat culture were known, but may also allow a parent to return to work 24 to 48 hours sooner. The new rapid diagnostic test for GABHS pharyngitis may eliminate the need to make a decision as to whether to initiate antibiotic therapy immediately or wait.

What Is the Status of Nonculture Rapid Diagnostic Tests for GABHS?

The nonspecific nature of many of the signs and symptoms of GABHS pharyngitis makes the clinical diagnosis of this disease, even for the most experienced physician, difficult.²⁴ An accurate diagnosis therefore depends upon bacteriologic confirmation. In 1954 Breese and Disney²⁴ first described the use of throat cultures on blood agar plates in a pediatric office. Over the past two decades many pediatricians have incorporated this diagnostic test into their office routine. However, culturing throat swabs on blood agar plates has not been without problems; primary among them has been the 24 to 48 hours required to obtain the culture results. This inherent delay has led some physicians to initiate antibiotic therapy before knowing the results of the throat culture. Since the majority of children with acute pharyngitis do not have GABHS disease and will not benefit from antibiotic therapy,¹⁷ this approach causes a large number of children to receive unnecessary antibiotics. Of additional concern is that once antibiotic therapy has been initiated, some physicians are reluctant to discontinue it, even when the throat culture is later reported to be negative.^{25,26} On the other hand those physicians who wait the 24 to 48 hours for the results of the throat culture before initiating antibiotic therapy may be prolonging the clinical course and the period of infectivity and may be faced with the problem of poor compliance in a patient who is already improving. A rapid diagnostic test that could provide an alternative to the blood agar culture would therefore be tremendously helpful to the practicing physician.

One of the most exciting developments in recent years in the area of GABHS pharyngitis has been the appearance of commercial antigen detection tests for the rapid identification of GABHS directly from throat swabs. Although these rapid diagnostic tests may be more expensive than the blood agar culture (about \$2.00 and about \$0.50, respectively), the advantage they offer over the traditional procedure is the speed with which they can provide results. Identification of GABHS with a rapid diagnostic test allows the prompt initiation of specific antibiotic therapy, while rapid exclusion of GABHS pharyngitis should eliminate the temptation to initiate unnecessary and costly antibiotic therapy in these patients.

The rapid diagnostic tests for GABHS that have received the most extensive evaluations are the Directigen Group A Strep Test Kit® (Hynson, Westcott, and Dunning, Baltimore, MD) and the Culturette Brand Ten Minute Group A Strep ID Kit® (Marion Scientific, Kansas City, MO). Several investigations of the accuracy of these tests when compared to blood agar cultures have been performed primarily in large diagnostic microbiology laboratories or in university hospitals (Table 1).²⁷⁻³¹ These studies have demon-

TABLE 1

Comparison of two latex agglutination tests for the detection of GABHS directly from throat swabs with blood agar cultures

Study	% of Results							
	Directigen®				Culturette®			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
Slifkin and Gil ²⁷					95 (100) ^a	100	100	99
Chang and Mohla ²⁸					90	99	96	98
Gerber et al. ²⁹	84 (95)	99	99	93	83 (95)	99	97	93
McCusker et al. ³⁰	91 (97)	99	98	96				
Miller et al. ³¹	91 (100)	98	88	98				

PPV, positive predictive value; NPV, negative predictive value.

^a Sensitivity if cultures with less than 10 colonies of GABHS per plate are not considered positive.

strated that these tests have a sensitivity of 82 to 95%, a specificity of 84 to 100%, a positive predictive value of 96 to 100% and a negative predictive value of 93 to 99% when compared with results from blood agar cultures.

The Directigen® and Culturette Brand® tests are comparably priced; however, the Directigen® test is moderately complex, requires special equipment and supplies and takes approximately 75 minutes to perform. While easily adapted to a diagnostic microbiology laboratory, it is unlikely that a practicing physician would be able to use the Directigen® test routinely in their office. The time requirement alone would preclude the performance of this test while the patient waited for the results. In contrast the Culturette Brand® test is simple to perform, requires no additional materials or special equipment, takes between 12 and 15 minutes to complete and can be performed in a physician's office while the patient waits for the results.

Of the false-negative Directigen® and Culturette Brand® test results, a large number occurred in patients who had less than 10 colonies of GABHS on their blood agar culture (1+ cultures). When these 1+ cultures were not considered positive, the sensitivity of both the Directigen® and Culturette Brand® tests was 92 to 100%. There has been a great deal of debate in recent years about the significance of throat cultures with less than 10 colonies of GABHS per plate. Some have suggested that these patients are merely carriers of GABHS (positive throat culture but no antibody response to GABHS) and are not truly infected (positive throat culture and an antibody response to GABHS).^{32,33} Others believe that the differentiation of patients with streptococcal infections from those who are carriers cannot be made on the basis of degree of positivity of the throat culture alone.³⁴ If the majority of patients with negative antigen detection test results and 1+ positive throat culture were carriers, then the sensitivity of these

antigen detection tests, in terms of identifying *bona fide* streptococcal infections, would be much higher.

Further investigations of the accuracy and practicality of these rapid, antigen detection tests must be performed before they can be fully accepted as a replacement for the blood agar culture. In the meantime, given the infrequency of false-positive rapid test results, a physician could treat a patient with a positive antigen detection test and dispense with performing a blood agar culture. However, until more is known about the true clinical significance of a false-negative rapid test result, negative antigen detection test results should be confirmed with a blood agar culture. A physician could swab a patient's throat with two swabs simultaneously, run the antigen detection test on one and put the other aside. If the antigen detection test were positive then the second swab could be discarded, while if the antigen detection test were negative then the second swab could be used for the blood agar culture.

Are Diagnostic Tests for GABHS Being Used Appropriately?

In order for throat cultures (and antigen detection tests) to remain useful and cost-effective diagnostic procedures, it is important that they be used selectively. When attempting to decide whether to perform a throat culture (antigen detection test) on a particular patient, a consideration of the epidemiologic and clinical findings will help to achieve this aim.³⁵ For example GABHS pharyngitis is a disease of the winter and early spring in temperate climates and primarily affects children between 3 and 18 years old. Therefore physicians should be performing few throat cultures (antigen detection tests) in the summertime and in children younger than 3 years or older than 18 years of age. An awareness of a large amount of GABHS in the community or the presence of a viral agent causing pharyngitis would also be helpful in deciding whether to perform a throat culture (antigen detection test),

as would a history of close contact with a well-documented case of GABHS pharyngitis. In addition there are certain clinical findings associated with pharyngitis which suggest GABHS as the etiology, while there are other clinical findings which suggest a nonstreptococcal cause (Table 2).

Selective use of these diagnostic tests would increase the positivity rate and the percentage of identified patients who are truly infected while reducing the percentage of identified patients who are merely streptococcal carriers. Consequently there would be an increase in the percentage of patients who would benefit from antibiotic therapy and a decrease in the percentage of patients, who as carriers, would be receiving an unnecessary course of antibiotics. It has been estimated that over 30 million throat cultures are performed annually in this country.^{25,26} Unfortunately many throat cultures are being performed by physicians who routinely culture every patient with an upper respiratory tract infection. This indiscriminate use of the throat culture not only contributes to the excessive cost of health care but in addition is not in the best interest of the patient.

Is Penicillin Still the Drug of Choice for the Treatment of GABHS Pharyngitis?

Shortly after penicillin was introduced for the treatment of GABHS pharyngitis, it was shown to be more effective than the sulfonamides¹⁵ and has since been considered the drug of choice for this disease for almost 40 years. There have been extensive clinical trials comparing treatment failure rates with new antibiotics or with new formulations of old antibiotics to those with oral or benzathine penicillin G. In the case of tetracyclines it is well known that a large percentage of GABHS strains have become resistant to this class of antibiotics. Trimethoprim-sulfamethoxazole is also ineffective.³⁶ Claims have been made that some antibiotics, most recently the cephalosporins, yield fewer bacteriologic treatment failures than does penicillin. However, the differences are small and the

results inconsistent as can be seen in Tables 3 and 4.^{37,38} It is therefore difficult to reach any conclusions about the superiority of one antibiotic over another based on bacteriologic failure rates. Differences in methodologies probably account for much of the variation in results. What is needed are more fundamental studies to gain a better understanding of why treatment failures occur and not more clinical trials comparing various antibiotics.

For the present and until there is more convincing evidence, penicillin remains the drug of choice. Other antibiotics should not be used, not only because they are generally more expensive and their toxicity less well-known but also because their usefulness for other infections may be impaired. For patients in this country allergic to penicillin, erythromycin remains the drug of choice, in contrast to Japan where erythromycin can no longer be used because of the emergence of resistant GABHS strains.³⁹

A single injection of benzathine penicillin G remains the "gold standard" for the treatment of GABHS pharyngitis and it was once widely used to avoid problems with noncompliance. Pain in the region of the injection has been a drawback to the use of benzathine penicillin G. This can be partially overcome by using a combination of benzathine and procaine penicillin.^{40,41} Nevertheless many physicians prefer to prescribe penicillin orally, because of the pain and the increased risk of an allergic reaction associated with the use of benzathine penicillin G. However, these allergic reactions are infrequent and generally mild.⁴²

TABLE 2

Clinical features of streptococcal pharyngitis^a

Sudden onset
Sore throat (pain on swallowing)
Fever
Headache
Nausea, vomiting, abdominal pain (especially in children)
Marked inflammation of throat and tonsils
Patchy discrete exudate
Tender, enlarged anterior cervical nodes
Scarlatiniform rash
Suggestive of other etiologies
Conjunctivitis, cough, diarrhea
Nasal discharge (except in young children)
Viral exanthem

^a Modified from work of Wannamaker.³⁵

TABLE 3

Comparison of bacteriologic failure rates for oral cephalosporin and penicillin^a

Investigator	% of Bacteriologic Failure		
	Cephalosporin	Orally administered penicillin	Benzathine penicillin G, intramuscular
Disney, Breese, 1971	19	24	
Stillerman, 1970	9	14	
Gau, 1972	4	8	
Rabinovitch, 1973	0	6	
Matsen, 1974	3	3	4
Derrick, Dillon, 1974	4	8	5

^a From Dillon.³⁷

TABLE 4

Range of bacteriologic failure rates for various antibiotics^a

Antibiotic	% of Bacteriologic Failures
Benzathine penicillin G	6-25
Penicillin G	10-20
Penicillin V	10-20
Ampicillin/amoxicillin	10-25
Erythromycin	5-15
Clindamycin	5-20

^a From Eickhoff.³⁸

TABLE 5

Summary of previous studies that examined the effectiveness of oral penicillin given twice a day in the treatment of GABHS pharyngitis

Reference	No. of Patients	Treatment Regimens	Treatment Failure Rate (%)	Serotyping of GABHS	GABHS Serology	Monitoring Compliance
Breese et al. ⁴³	221	400,000 units penG b.i.d.	15	No	No	History
	228	800,000 units penG b.i.d.	16			
	368	200,000 units penG q.i.d.	14			
	216	400,000 units penG q.i.d.	15			
Rosenstein et al. ⁴⁴	170	400,000 units penV b.i.d.	10.0	Yes	No	Antibiotic activity in urine
	161	400,000 units nafcillin b.i.d.	13.7			
Vann and Harris ^{45 a}	414	800,000 units penG b.i.d.	11	No	No	Unused medicine
Stillerman et al. ⁴⁶	22	250 mg penV b.i.d.	14	Yes	No	Antibiotic activity in urine
	29	125 mg penV t.i.d.	21	No	No	Unused medicine
Spitzer and Harris ⁴⁷	173	500 mg penV b.i.d.	17			
	154	250 mg penV t.i.d.	16			

^a Uncontrolled.

penG, oral penicillin G; penV, oral penicillin V; b.i.d., twice a day; t.i.d., three times a day; q.i.d., four times a day.

When there is real doubt about a family's ability to complete a prescribed course of oral medication, especially with indigent children who have a greater risk of developing rheumatic fever, benzathine penicillin G should be used.

How Many Times a Day Must Oral Penicillin Be Given to Be Effective for Treatment of GABHS Pharyngitis?

Although most authorities recommend that oral penicillin be given either three or four times daily for the treatment of GABHS pharyngitis, there have been several reports which suggest that oral penicillin given twice daily is effective in the treatment of this disease (Table 5).⁴⁵⁻⁴⁸

We performed a prospective, randomized, controlled investigation to compare the effectiveness of oral penicillin V given twice daily with that of oral penicillin V given three times daily in the treatment of GABHS pharyngitis in children. All isolates of GABHS were serotyped to distinguish between relapses and reinfections, streptococcal antibody titers were obtained to distinguish between streptococcal carriers and *bona fide* infections, and compliance was monitored using a modification of the method of Markowitz and Gordis.⁴⁸ The patients in the twice daily and three times daily treatment groups were comparable with respect to age, sex, duration of illness prior to treatment, formulation of medication, compliance, clinical findings and antibody titers to streptococcal antigens. ~~We found no significant difference in the bacteriologic failure rates for the twice-daily and three-times-daily treatment groups~~ (MA Gerber, LJ Spadaccini, LL Wright, et al: unpublished data). These results as well as those of earlier investigations suggest that penicillin V given twice daily is as effective as penicillin V given three times daily in the treatment of GABHS pharyngitis.

One of the obvious advantages of a twice daily regimen of oral penicillin therapy for GABHS pharyngitis is that it is more convenient to administer than a three or four times daily regimen especially for a child who is attending school. In addition there have been several reports which suggest that reducing the frequency of dosing results in improved patient compliance.^{49,50} Physicians who are not already doing so should consider using twice daily oral penicillin to treat their patients with GABHS pharyngitis.

Does Oral Penicillin Have to Be Given for 10 Days to Be Effective in the Treatment of GABHS Pharyngitis?

~~In 1953 the American Heart Association Council on Rheumatic Fever and Congenital Heart Disease recommended that oral penicillin therapy for GABHS pharyngitis be given for a full 10 days.~~⁵¹ and this recommendation remains unchanged more than three decades later.⁵² This recommendation was initially based on several investigations which demonstrated that a 10-day course of penicillin was more effective than a 5-day course in eradicating GABHS from asymptomatic carriers^{19,20} and in preventing clinical and bacteriologic recurrences in patients with GABHS pharyngitis.¹⁸ A recent investigation supported these earlier findings. In this study Schwartz et al.⁵³ found that children who had received oral penicillin V three times daily for 10 days had a significantly lower clinical and bacteriologic recurrence rates than did children who had received the same regimen for 7 days.

The implication of this recommendation is that a course of penicillin of less than 10 days is associated with an increased risk of rheumatic fever. Are there data available to support this concept? In the original and only controlled, prospective investigations of the relationship between penicillin therapy for GABHS pharyngitis and the subsequent risk of rheumatic fe-

~~ver, it was shown that the attack rate of rheumatic fever was significantly reduced by 5 to 7 days of penicillin therapy.^{2,3} Subsequently, Catanzaro et al.,⁵⁴ in a retrospective study, demonstrated that persistence of GABHS in the upper respiratory tract after a course of penicillin therapy was a significant risk factor for the subsequent development of rheumatic fever. These findings have been~~ interpreted as indicating that eradication of GABHS from the upper respiratory tract is the *sine qua non* for the prevention of rheumatic fever. Therefore a treatment regimen of less than 10 days that results in an increased incidence of bacteriologic recurrences would also presumably result in an increased incidence of rheumatic fever. However, the incidence of rheumatic fever in this country continues to decline despite the observation that many children with GABHS pharyngitis do not receive a full 10 days of oral penicillin therapy.⁵⁵ Perhaps in the 1980s eradication of GABHS from the upper respiratory tract is not necessarily a prerequisite for the prevention of rheumatic fever.

Is the Incidence of Penicillin Treatment Failures Increasing and What Is the Significance?

The earliest reports of the effectiveness of penicillin in the treatment of GABHS pharyngitis described treatment failure rates of approximately 5 to 10% with benzathine penicillin G and 10 to 15% with orally administered penicillin.^{43,44,56-58} However, several recent reports have described treatment failure rates of 19 to 25% with benzathine penicillin G and 23 to 30% with oral penicillin.^{59,60} A number of explanations have been proposed for penicillin treatment failures: increasing resistance to penicillin among GABHS; bacterial interference from normal oral flora; presence of beta-lactamase-producing staphylococci or *Bacteroides* sp. in the upper respiratory tract; penicillin tolerance among GABHS; bacteriocin production by GABHS; lack of patient compliance in taking oral medication and reinfection from household contacts.⁶¹ There is no evidence that GABHS have become resistant to penicillin⁶² and there are few data to support any of the other theories. There are data which suggest that as many as 50% of children with pharyngitis and a positive throat culture for GABHS may be merely streptococcal carriers and not truly infected.⁶³ There is also evidence which suggests that GABHS are more difficult to eradicate from the upper respiratory tract of a streptococcal carrier than from someone with a *bona fide* streptococcal infection.⁶¹ Therefore it has been suggested that many of the observed penicillin treatment failures are occurring in children who are merely streptococcal carriers^{59,60} and that the apparent increase in treatment failures probably is due to the more widespread (and indiscriminate) use of throat cultures.

Additional studies must be performed to determine

the true incidence of these penicillin treatment failures as well as their etiology and clinical significance.

What Is the Appropriate Management of Treatment Failures?

Routine follow-up throat cultures of asymptomatic patients who have completed a full course of antibiotic therapy for GABHS pharyngitis is not recommended for, as previously noted, the majority of asymptomatic patients who continue to harbor GABHS in their upper respiratory tracts are thought to be streptococcal carriers.⁶¹ Streptococcal carriers are not at risk of developing either suppurative or nonsuppurative sequelae or of transmitting the GABHS to others; therefore the carrier state poses no threat to the patient or to their contacts.⁶¹

The situation is more complicated in patients who become symptomatic after completing a course of antibiotic therapy and who on reculturing have GABHS in their pharynx. In such cases it is impossible to distinguish a streptococcal carrier who has an intercurrent, nonstreptococcal pharyngitis from a patient with a *bona fide* streptococcal infection. A second course of therapy, preferably with benzathine penicillin G, is therefore justified. However, if thereafter the throat culture is still positive for GABHS, no further treatment is indicated. All too often in such patients, physician or parental anxiety results in multiple courses of antibiotics in an attempt to eradicate the GABHS. Not only is this practice costly, ineffective and potentially dangerous but it may also serve to intensify the state of anxiety surrounding the case.

Although most streptococcal carriers require no medical intervention, there are specific situations in which follow-up throat cultures should be performed and in which eradication of the streptococcal carrier state would be desirable. These would include families in which there is an inordinate amount of anxiety about GABHS, families with a history of rheumatic fever, families in which "ping-pong" spread of GABHS has been occurring, outbreaks of GABHS pharyngitis in closed or semiclosed communities or when tonsillectomy is being considered only because of chronic carriage of GABHS. Two recent reports have described a new approach to the eradication of the GABHS carrier state, a short course of rifampin.^{64,65} In one study rifampin (20-mg/kg dose every 24 hours for 4 doses) was given for the last 4 days of a 10-day course of oral penicillin V.⁶⁴ In the other rifampin (10-mg/kg dose every 12 hours for 8 doses) was used in conjunction with benzathine penicillin G.⁶⁵ Both regimens were highly effective in eradicating GABHS from the upper respiratory tract of the streptococcal carriers. While the routine use of rifampin to treat patients with GABHS pharyngitis or all streptococcal carriers is not recommended, for those situations described above a brief course of rifampin could be

justified. Further investigations are required to determine the optimal regimen for using rifampin in these situations.

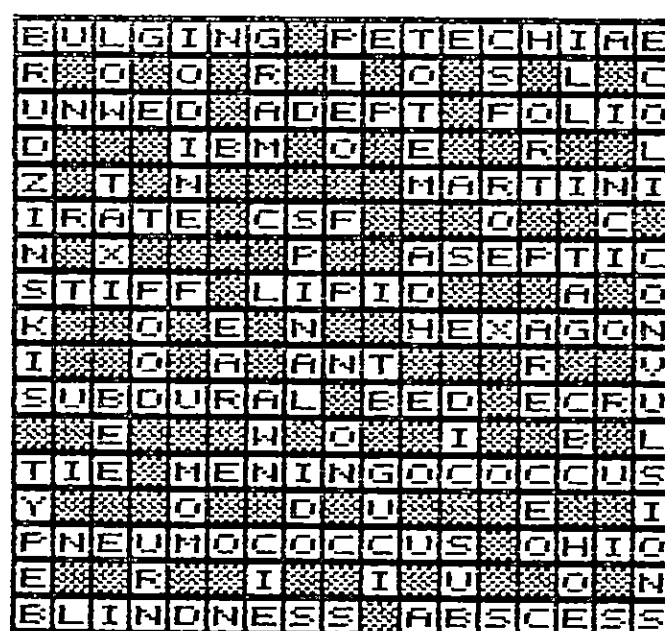
Summary

Adequate treatment of GABHS pharyngitis with penicillin shortens the course of illness, reduces the spread of streptococci and prevents suppurative complications. It has also been a major factor in the markedly accelerated decline in the incidence of acute rheumatic fever in this country. Difficulties in the clinical diagnosis of GABHS pharyngitis make bacteriologic confirmation highly desirable. Currently a properly performed throat culture is the best way to obtain this bacteriologic confirmation. However, it is possible that rapid antigen detection tests will replace the throat culture in the future. These diagnostic tools should be used more selectively and only in conjunction with clinical and epidemiologic data. Greater selectivity will help control costs and will increase the chances of identifying patients who are truly infected and are not merely streptococcal carriers. Penicillin is still the drug of choice and an oral preparation given twice daily is as effective as more frequent doses. Patients at risk for noncompliance should be treated with a single injection of benzathine penicillin combined with procaine penicillin to lessen the local discomfort. Routine follow-up cultures of asymptomatic patients should be abandoned. Persistence of GABHS following a course of treatment may no longer be an important risk factor for the development of rheumatic fever. However, there are exceptional cases, as noted in the text, in which eradication of GABHS carriage with a short course of rifampin may be desirable.

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Answers to Crossword