Treatment of streptococcal pharyngitis

I. Clinical evaluation

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Summary: A study was undertaken to evaluate the therapy of streptococcal pharyngitis. The compliance of 118 patients with beta-hemolytic streptococcal pharyngitis to follow-up was 72%. Of 74 patients checked by means of urine tests 66 took their oral medication. No differences were detected in the clinical and bacteriological results (>98% streptococcal eradication) after the 7th or 10th day of therapy after taking either cephalexin or penicillin.

It was concluded that: (a) for effective surveillance and follow-up special attention should be given to the uncooperative segment of the patient population; (b) a seven-day course of penicillin may be satisfactory in the eradication of BHS from the throat; and (c) cephalexin appears to be an effective alternative to penicillin for the treatment of streptococcal pharyngitis.

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Current concepts of diagnosis and therapy of beta-hemolytic streptococcal (BHS) pharyngitis include an adequate screening program[1] and penicillin treatment of the infected patients.[2] Both a 10-day course of oral penicillin and an intramuscular injection of benzathine penicillin are effective in eradicating streptococci from the throat,[3] and penicillin treatment of BHS pharyngitis results in a decreased incidence of rheumatic fever.[4] The present study was designed to evaluate the streptococcal screening program at the Montreal Children's Hospital (MCH) by measuring the following: (a) compliance of the patients with surveillance and follow-up; (b) compliance of the cooperative patients with a course of oral antibiotherapy; and (c) efficacy of therapy in reducing the population of streptococci in the throat. The investigations were also designed to assess therapeutic efficacy after the 7th and 10th days of therapy, and to evaluate a new antibiotic, cephalexin, as an alternative to penicillin, by comparing the clinical and bacteriological effects of these forms of treatment in BHS pharyngitis.

Materials and methods

One hundred and eighteen patients with BHS pharyngitis detected by the MCH streptococcal screening program were studied. The population studied was derived from the outpatient clinic at the Montreal Children's Hospital. The majority of these patients were from lower socio-economic groups where large families, crowded home situations and low incomes were common. In this program every patient suspected of having BHS pharyngitis had a swab of the throat cultured and was given a prescription for a 10-day supply of oral penicillin, to be filled only after notification by the hospital that the throat swab results were positive. Cultures were made from cotton swabs streaked on 5% sheep blood (in trypticase soy agar) plates. The cultures were incubated at 37°C. for 18 to 24 hours and examined for characteristic beta-hemolytic colonies. When a positive identification was made, one colony was subcultured and a bacitracin "A" disc (BBL) applied for identification of probable group A strains. When growth was inhibited by bacitracin the patient was notified and instructed to have the prescription filled. For the purposes of this study the usual streptococcal screening procedure was changed so that prescriptions were not issued but patients were asked to come to the hospital for their medications whenever bacitracin-sensitive BHS was identified.

Each patient was given a 10-day supply of either penicillin G or V (250,000 to 400,000 units q6h) or cephalexin (125 mg. q6h) in ran-

dom fashion and verbal treatment instructions about when and how to take the drug. In addition, literature* prepared in English, French and Italian was handed out explaining to the parents the importance of adhering to the 10-day schedule of treatment. Each patient was asked to return after seven days of therapy to submit a specimen of urine and have a throat swab taken. A *Sarcina lutea* inhibition test[5] was performed on each urine specimen to detect the presence of penicillin or cephalexin and a throat swab was cultured for BHS. Upon completion of the 10-day course of therapy each patient was to return to have a throat swab taken to be cultured for BHS. Records were kept of side effects of the drugs and of the patients' clinical course.

Results

During July and August, October and November 1971, 118 patients had BHS pharyngitis detected by the MCH streptococcal screening program and were included in this study. A lack of parental cooperation and refusal to return for follow-up care was encountered in 33 patients (28%). Urine could not be obtained from 11 patients. Of the 74 patients tested, 66 (89%) had penicillin or cephalexin in the urine specimen taken after seven days of treatment (Table I).

The number of patients with positive throat cultures after seven days of treatment and after 10 days was almost identical. As seen in Table II, this was true for both the group receiving penicillin and the group receiving cephalexin. In two instances positive throat cultures were found after seven days of therapy; one became negative upon completion of the 10-day course. In that particular patient no urine bioassay for the antibiotic was available. When only those patients who took their drugs were considered, the bacteriological success rates after 7 and 10 days approached 100% with either drug.

Penicillin and cephalexin therapy resulted in equally high bacteriological success rates as seen in Table III; there were no clinical failures in either group. No side effects were observed in either the penicillin or cephalexin treatment groups.

*Available from authors

Table I
Compliance of cooperative patients

Medication	Positive for drug in urine
Any drug	66/74 = 89%
Penicillin	29/36 = 81%
Cephalexin	36/38 = 95%

Discussion

By testing random weekly urine specimens Gordis, Markowitz and Lilienfeld[6] demonstrated that 36% of the patients attending rheumatic fever prevention clinics took their penicillin 25% of the time or less. Widely divergent results in different study populations have been reported by investigators who have attempted to quantitate completeness of therapy for streptococcal pharyngitis in children. Of the 74 patients in this study tested for drug in their urine during the course of therapy 66 (89%) were positive. This high compliance rate may be attributable to the explicit oral and written treatment instructions delivered to each patient, stressing the importance of therapy and follow-up. It is possible that this group of patients did not comply as well with the prescribed treatment. Parents were not informed that follow-up included a check on drug compliance. However, the random nature of the urine bioassay cannot assure complete compliance throughout the course of therapy.

Breese, Disney and Talpey[7] compared a 10-day course of oral penicillin to an intramuscular injection of benzathine penicillin for the treatment of BHS pharyngitis. Based on a two-month follow-up period, they reported an 85% bacteriological cure rate for patients on oral antibiotherapy and one of 95% for parenteral medication. Mohler *et al*[8] found that 17.3% of their patients on seven-day courses of oral penicillin had positive throat cultures three days after discontinuance of therapy. However, almost one third of their patients admitted to not taking the prescribed

Table II
Presence of BHS in throat after 7th and 10th days of therapy

a. Patients who may have taken drug (excludes those without drug in urine)			
		Positive for BHS	
Days of therapy completed	Either drug	Penicillin	Cephalexin
7	(2/75) 2.7%	(2/36) 5.6%	(0/39) 0%
10	(3/88) 3.4%	(3/49) 6.1%	(0/39) 0%
b. Patients who took drug			
		Positive for BHS	
Days of therapy completed	Either drug	Penicillin	Cephalexin
7	(1/61) 1.6%	(1/26) 3.8%	(0/35) 0%
10	(1/60) 1.7%	(1/26) 3.8%	(0/34) 0%

Table III
Comparison of efficacy of penicillin and cephalexin

a. Patients who may have taken drug (excludes those without drug in urine)		
	Penicillin	Cephalexin
No. of evaluable cases	54	43
No. of bacteriological successes	51	43
No. of bacteriological failures	3	0
% of bacteriological successes	94.4%	100%
b. Patients who took drug		
No. of evaluable cases	29	36
No. of bacteriological successes	28	36
No. of bacteriological failures	1	0
% of bacteriological successes	96.6%	100%

amount of oral antibiotic. Edmond *et al*[9] found that 69% of their patients on seven-day courses of oral penicillin for BHS pharyngitis redeveloped positive throat cultures during a 10-week period after the cessation of therapy. There is no indication, however, of how well their patients followed the treatment schedule. It is also impossible to estimate the percentage who had actually developed new BHS infections during the follow-up period. Based on the follow-up throat cultures taken one day post-therapy, the bacteriological cure rate achieved in our study is about 98%. It is possible that more bacteriological failures would have been detected had the patients been followed up for a longer period after therapy. The study design employed does not allow differentiation of bacterial "suppression" from eradication. It was employed because of the data available for penicillin, the similar mechanisms of action of the two drugs and the impossible task of differentiating endogenous relapse from exogenous reinfection in longer follow-up designs. The results indicate that a seven-day course of oral penicillin may be satisfactory in the eradication of BHS from the throat. Investigations with longer follow-up are necessary to confirm this.

Cephalexin is a new cephalosporin derivative which has less *in vitro* activity against BHS than penicillin but achieves higher serum concentrations after oral administration.[10] Stillerman and Isenberg[11] treated 142 private patients for streptococcal pharyngitis with 10-day oral courses of cephalexin, penicillin or cyclacillin. Based on an 18-day post-therapy follow-up period, they found a 13% (6 of 46) bacteriological failure rate for cephalexin-treated patients, and a 20% (10 of 50) failure rate for penicillin-treated patients. Gau *et al*[12] allocated 75 private patients equally to three treatment schedules: (1) penicillin for 10 days, (2) cephalexin for 10 days, or (3) cephalexin for 5 days. The bacteriological cure rates achieved, based on a two-week follow-up period, were 92, 96 and 88% respectively. The above results, in combination with those presented in this paper, indicate that cephalexin is an effective alternative to penicillin in the treatment of BHS pharyngitis. More recently, Azimi *et al*[13] treated 25 children for streptococcal pharyngitis with a 10-day oral course of cephalexin and reported a 92% bacteriological success rate, based on a three-week follow-up period. Although their study does not include a comparative penicillin treatment group or an analysis of patients' treatment compliance, the results confirm the efficacy of cephalexin in the treatment of this infection.

A significant proportion of parents (28%) did not comply with the requirements of this study. In any streptococcal screening program, for surveillance and follow-up to be effective special measures would have to be taken for this uncooperative segment of the patient population. These might include spot checks by a public-health nurse for drug in patients' urine[14] and the use of parenteral medication. A seven-day course of penicillin may be satisfactory in the eradication of BHS from the throat, and cephalexin appears to be an effective alternative to penicillin for this purpose. The cost of the medications, their spectra of activity and proof of efficacy in the prevention of rheumatic fever, are factors that support the continued use of penicillin in the treatment of BHS pharyngitis.

The cooperation of Dr. Elizabeth Hillman and the nursing and medical staff of the outpatient department are gratefully acknowledged.

Résumé

Le traitement de la pharyngite streptococcique

I. *Evaluation clinique*

La présente étude avait pour objet d'évaluer le traitement de la pharyngite streptococcique. Une pourcentage de 72% des 118 malades souffrant de pharyngite à streptocoques bêta-hémolytiques s'est plié aux visites de contrôle. Sur 74 malades dont on avait vérifié par une analyse d'urine qu'ils prenaient leur médicament orale, 66 avaient effectivement pris leur médicament. Après un traitement à la céphalexine ou à la pénicilline, on n'a

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Examinations

The examinations of the Royal College are held in September of each year. Candidates wishing to sit for the examinations should note the following:

1. Every candidate for admission to the examinations must submit an application for assessment of training.

2. Candidates in training in Canada should apply for preliminary assessment of training at least one year before the date on which they expect to sit for the examinations, that is to say not later than September 1st of the preceding year. Candidates who have had all or a major portion of their training outside of Canada should submit their initial application for assessment at least eighteen months before they expect to sit for the examinations, that is by March 1st of the preceding year. Only candidates whose assessment of credentials is complete will be accepted to sit for the examinations.

3. Candidates who desire to sit for an examination, having complied with the above requirement of preliminary assessment of training, must notify the College in writing of their intent before February 1st of the year of the examination. Upon receipt of this notice of intent, the evaluation of the candidate's performance during training will be added to the previously completed assessment of credentials. Each candidate will then receive notification as to eligibility together with an application form for admission to the examination which he will complete and return.

4. The following documents may be obtained from the College office:

(a) Application forms for assessment of training.

(b) General Information booklet of regulations relating to the examinations.

(c) Specific requirements for training and regulations relating to the examinations of each specialty. Requests should indicate the specialty or specialties of interest to the applicant.

(d) Listing of specialty training programmes in Canada approved by the College.

5. Address all enquiries to:

Secretary,
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constaté aucune différence dans les résultats cliniques et bactériologiques (plus de 98% de cas d'élimination des streptocoques) au 7ème ou au 10ème jour après le traitement.

De cette étude, il a été possible d'arriver aux conclusions suivantes: a) pour arriver à une surveillance et à un contrôle efficaces, il faut améliorer le pourcentage de malades qui ne coopèrent pas; b) une cure de sept jours de pénicilline peut suffire à éliminer le streptocoque bêta-hémolytique de la gorge et c) la céphalexine est un substitut efficace de la pénicilline pour traiter la pharyngite streptococcique.

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II. In vitro studies of antibacterial activity

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Summary: One hundred and forty isolates of beta-hemolytic streptococcus cultured from patients with clinical pharyngitis were studied by disc diffusion for antibiotic sensitivity to lincomycin, erythromycin, cephalexin and penicillin and by agar dilution to cephalexin and penicillin. All isolates were sensitive to ≤ 0.1 μg./ml. penicillin and ≤ 1.56 μg./ml. cephalexin. The disc-diffusion test was reliable in predicting the sensitivities *in vitro*. One strain of group A beta-hemolytic streptococcus was resistant to erythromycin by disc diffusion. When compared to Lancefield grouping 18% of strains were incorrectly identified as group A by the bacitracin-disc test. Cephalexin was uniformly effective *in vitro* in inhibiting beta-hemolytic streptococci and the 30 μg. cephalexin disc was reliable in predicting these sensitivities.

Cephalexin is a new oral derivative of cephalosporin with an antibacterial spectrum similar to that of cephalothin and cephaloridine.[1-3] Low toxicity,[4] good oral absorption[1] and bactericidal activity against gram-positive bacteria[5] warrant consideration of this antibiotic as an alternative to penicillin in the treatment of streptococcal pharyngitis. Our previous study[6] has confirmed the *in vivo* efficacy of this antibiotic in the treatment of beta-hemolytic streptococcal pharyngitis. The present investigation was undertaken to provide *in vitro* data comparing the sensitivities of beta-hemolytic streptococcus to lincomycin, erythromycin, cephalexin and penicillin by disc diffusion studies, and the sensitivities of the same strains to cephalexin and penicillin by agar-dilution methods.

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Materials and methods

One hundred and forty isolates of beta-hemolytic streptococcus cultured from the throats of patients from the clinical study previously reported[6] were isolated in pure culture on 5% sheep blood (in trypticase soy) agar, subcultured weekly and maintained at 4°C. The cultures were incubated at 37°C. for 18 to 24 hours and examined for characteristic beta-hemolytic colonies. When a positive identification was made, one colony was subcultured and a bacitracin "A" disc (BBL) applied for identification of probable group A strains. Any zone of inhibition by bacitracin was read as positive. The antibiotic sensitivities of these isolates were determined by a standardized disc-diffusion technique, employing the following