COMMITTEE REPORT

Prevention of Rheumatic Fever
A Statement Prepared by the Rheumatic Fever Committee of the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association

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SUMMARY
Rheumatic fever is a recurrent disease which frequently can be prevented. Infection with group A streptococci precipitates both initial and recurrent attacks; therefore, prevention of rheumatic fever and rheumatic heart disease depends upon the control of streptococcal infections. This may be accomplished by (1) prevention of streptococcal infections in rheumatic subjects, and (2) early and adequate treatment of streptococcal infections in all individuals.

Bacterial endocarditis may result from dental and other surgical procedures in patients with rheumatic or congenital heart disease. When such procedures are undertaken, these patients should be protected by administration of antibiotics in therapeutic doses.

Prevention of Recurrences in Rheumatic Individuals
Necessity for Continuous Prophylaxis

Many streptococcal infections occur without producing clinical manifestations. For this reason, prevention of recurrent rheumatic fever must depend on continuous prophylaxis rather than solely on recognition and treatment of acute attacks of streptococcal disease.

General Considerations
Who Should Be Given Prophylaxis?
In general, all patients who have a well-documented history of rheumatic fever or chorea, or who show definite evidence of rheumatic heart disease, should be given continuous prophylaxis.

How Long Should Prophylaxis Be Continued?
The risk of acquiring a streptococcal infection and the possibility of recurrent attacks of rheumatic fever continue throughout life. It is, therefore, suggested that the safest general procedure is to continue prophylaxis indefinitely, particularly if rheumatic heart disease is present.

Should Exceptions Be Made?
Although recurrent attacks of rheumatic fever occur at any age, the risk of recurrences decreases with the passage of years. Some physicians may wish to make exceptions to
instituting or maintaining prophylaxis in certain of their adult patients. Before exceptions are made, however, the physicians should carefully weigh the risks of acquiring streptococcal infection as well as the recurrence rate per infection, and the consequences of recurrence. Individuals with a high risk of exposure to streptococcal infections include young men in military service, mothers of young children, school teachers, physicians, nurses, and allied medical personnel. Individuals with high recurrence rates per infection are those with rheumatic heart disease, those with a recent previous attack of rheumatic fever, or those with multiple attacks. Low socioeconomic groups are also at a high risk and special efforts should therefore be made to insure that regular prophylaxis is maintained in these groups. Regardless of socioeconomic status, adolescents are particularly likely to be delinquent in their prophylaxis so that careful follow-up of patient compliance is essential in this age group.

When Should Prophylactic Treatment Be Initiated?

Prophylaxis should be initiated as soon as the diagnosis of active or inactive rheumatic fever is made.

Patients with rheumatic fever or rheumatic heart disease are often exposed to increased hazards in hospital wards as the result of contact with streptococcal carriers or patients with active streptococcal infections. Care should be taken to avoid interruption or delay in initiating prophylaxis in hospitalized patients.

Should Prophylaxis Be Continued During the Summer?

Yes, continuously. Streptococcal infections can occur at any season, although they are more prevalent in the winter and spring months.

Initial Eradication of Residual Streptococci

Before initiating continuous prophylaxis in patients with active or inactive rheumatic fever, a full therapeutic course of penicillin (as outlined under Recommended Treatment Schedules) should be given to eradicate streptococci which may or may not be detectable by the usual culture techniques.

Choice of Prophylactic Program

Benzathine Penicillin G—Intramuscular*

This is the method of choice because it is considerably more effective than the oral methods. In a controlled study, patients on benzathine penicillin had a ten-fold reduction of streptococcal infections as compared to those on oral penicillin (0.4 as compared to 5.5 per 100 patient years). This greater effectiveness is of special value in patients with a high risk of rheumatic recurrence, as specified above, and particularly in patients with rheumatic heart disease, in whom recurrences are more dangerous. This advantage must be weighed in each patient against the discomfort and pain of the injection, which may cause some patients to discontinue the prophylaxis program.

Dosage—1,300,000 units a month.

Reactions—Some discomfort at the injection site is usual.

Urticaria and angioneurotic edema may occur in a few patients.

Reactions similar to serum sickness include fever and joint pains and may be mistaken for rheumatic fever.

A careful history of allergic reactions to penicillin should be obtained. Although many individuals who have had reactions to penicillin may subsequently be able to tolerate the drug, it is safer not to use penicillin if the reaction has been severe and particularly if angioneurotic edema has occurred.

Alternate Methods

Successful oral prophylaxis depends on the compliance of the patient, which may be poor even in those who appear to be cooperative. Most failures occur in patients who fail to

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*Mixtures containing procaine penicillin in addition to benzathine penicillin have been used to reduce the pain of injection. If such a mixture is employed, it must contain benzathine penicillin in the doses recommended.

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ingest the drug regularly. Patients should receive careful and repeated instructions on this point from the physician.

If the doses recommended below, sulfadiazine and oral penicillin are about equally effective. Streptococci resistant to sulfonamides have not been a problem in the prophylaxis of recurrences, and streptococci resistant to penicillin have not been encountered. Patients on oral penicillin prophylaxis are more likely to harbor in their mouth penicillin-resistant microorganisms which are of no importance for rheumatic fever, but may be involved in subacute bacterial endocarditis. Sensitization to penicillin may be more of a problem than sensitization to sulfonamides. For these reasons, oral sulfadiazine may be preferable to oral penicillin.

**Sulfadiazine—Oral**

Dosage—1 g once a day for patients over 60 pounds; 0.5 g for patients under 60 pounds.

Reactions are infrequent and usually minor. A blood count may be advisable after two weeks of prophylaxis and also whenever a rash develops in association with sore throat or fever, because leukopenia has been reported in such cases. The drug should be discontinued if the white count falls below 4,000 and polymuclear neutrophils fall below 35%.

Use of sulfisoxazole—Data comparing sulfadiazine and sulfisoxazole are not available but experience with sulfisoxazole suggests that it is also an effective prophylactic agent.

Long-acting sulfonamides should be avoided because of a high incidence of side effects.

**Penicillin—Oral**

Dosage—200,000 or 250,000 units twice a day.

Although other kinds of penicillin may be used, buffered penicillin G is satisfactory. Better blood levels may be obtained if the penicillin is ingested half an hour before or at least one hour after a meal, but the necessity of administering penicillin in this manner in order to obtain adequate protection against streptococcal infection has not been established.

Reactions are similar to those with intramuscular penicillin, but occur less frequently and tend to be less severe. A careful history concerning penicillin allergy should, however, be obtained.

**Other Drugs**

For the exceptional patient who may be sensitive to both penicillin and sulfonamides, erythromycin can be used. Appropriate doses have not been established but 250 mg twice a day has been suggested.

**Treatment of Streptococcal Infections in Rheumatic Individuals**

When streptococcal infections occur despite a prophylactic regimen, or occur in a rheumatic subject who is not receiving continuous prophylaxis, they should be treated promptly and vigorously. Minimal therapy for these patients should consist of injectable benzathine penicillin G as recommended for streptococcal infections in the general population. Some physicians may prefer to use additional penicillin for part or all of the treatment period, but care should be taken not to reduce the amounts of benzathine penicillin G used.

Despite optimal therapy, it is sometimes not possible to prevent rheumatic recurrences once streptococcal infections occur in the rheumatic subject.

**Streptococcal Infection in the General Population**

During epidemics it has been found that about 3% of untreated streptococcal infections are followed by rheumatic fever. Attack rates following sporadic infections are less firmly established. In endemic situations, attack rates may be lower, although it may be more difficult under these circumstances to differentiate infection from the carrier state. Adequate and early penicillin treatment will eliminate streptococci from the throat and prevent most attacks of rheumatic fever.

**Diagnosis of Streptococcal Infections**

The accurate recognition of individual streptococcal infections, their adequate treatment, and the control of epidemics in the community presently offer the first practical
means of preventing initial attacks of rheumatic fever. The following section on diagnosis has been included in order to assist physicians in making a correct diagnosis and assuring adequate treatment.

**Symptoms**

Sore throat—sudden onset, pain on swallowing

Headache—common

Fever—variable, but generally from 101° to 104°F.

Abdominal pain—more common in children than in adults

Nausea and vomiting—common, especially in children

**Signs**

Red throat

Exudate—usually present, may not appear until after the first day

Lymphadenopathy—swollen, tender lymph nodes at angle of jaw

Rash—scarlatiniform, when present, usually diagnostic of a streptococcal infection

Acute otitis media } may be due to

Acute sinusitis } the streptococcus

In the absence of the above symptoms and signs, occurrence of any of the following symptoms is usually not associated with a streptococcal infection: simple coryza, hoarseness, cough, conjunctivitis.

**Throat Culture**

Although a streptococcal infection may be suspected from the above symptoms and signs, a throat culture is the only method by which the diagnosis can be confirmed. In untreated patients, a negative culture almost always excludes a streptococcal infection.

To obtain an adequate culture,* the tongue should be depressed, the throat adequately exposed, and a sterile cotton or Dacron swab rubbed vigorously over each tonsillar area and

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*PREVENTION OF RHEUMATIC FEVER*

The posterior pharynx. Mail-in techniques for processing throat cultures in municipal laboratories are available in many communities. However, many physicians have found it desirable to process their own cultures in small office incubators, using sheep blood agar plates available commercially.

A culture taken during an active infection will usually show a large number of colonies. The presence of a few colonies may indicate the carrier state or that there has been an error in obtaining, processing, or interpreting the culture. In such cases, if symptoms persist a second culture is indicated.

**Treatment of Streptococcal Infections**

Treatment should be started as soon as possible, but the short delay entailed in making a diagnosis by awaiting the results of a throat culture does not appreciably reduce the efficacy of antibiotic treatment in preventing the occurrence of rheumatic fever. Even when therapy is delayed as long as a week, a significant reduction in the attack rate occurs.

Penicillin is the drug of choice. Continued therapy for a period of 10 days is necessary to prevent rheumatic fever, which depends upon eradication of streptococci from the throat. Despite prolonged treatment, streptococci may sometimes fail to be eradicated, especially when oral therapy is used. If possible in patients treated orally, a follow-up culture several days after discontinuing treatment is desirable to ascertain the absence of hemolytic streptococci.

Penicillin may be administered by either the intramuscular or oral route. Administration of the very long-acting repository benzathine penicillin G is recommended as a method of choice since it insures continued treatment for a sufficient length of time. Oral therapy, by contrast, is dependent upon the cooperation of the patient.

**Recommended Treatment Schedules**

**Intramuscular Penicillin**

*Benzathine Penicillin G.* Mixtures containing shorter acting penicillins in addition to benzathine penicillin have not been shown to be superior to benzathine penicillin alone. If

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*A statement entitled "A Method for Culturing Beta Hemolytic Streptococci" may be obtained from your local Heart Association or the American Heart Association.*
such a mixture is employed it must contain benzathine penicillin in the doses recommended below.

Children—one intramuscular injection of 600,000 to 900,000 units. The larger dose is probably preferable for children over 10 years of age.

Adults—one intramuscular injection of 900,000 to 1,200,000 units.

Oral Penicillin

Children and adults—200,000 or 250,000 units* three or four times a day for a full 10 days. Therapy must be continued for the entire 10 days even though the temperature returns to normal and the patient is asymptomatic.

Combined Therapy

Various combinations of oral and intramuscular penicillin should be effective provided adequate coverage is continued for 10 days. For example, one or more injections of procaine penicillin G (600,000 units every 12 to 24 hours) might be followed by oral penicillin for 10 days or an injection of benzathine penicillin G in recommended doses.

Other Antibiotics

Penicillin G is definitely the drug of choice, but in patients sensitive to penicillin, erythromycin is second best. Lincomycin is similarly effective, but diarrhea may be bothersome. Both drugs should be given for 10 days. It should be noted that a few strains of streptococci resistant to erythromycin and lincomycin have already appeared.

Not Recommended

Tetracyclines should not be used because of the very high prevalence of strains resistant to this antibiotic.

The sulfonamide drugs should not be used for the treatment of streptococcal infections. In an established infection, they will not eradicate the streptococcus and therefore will not prevent rheumatic fever. However, the sulfonamides are effective in preventing reinfection and recurrences when administered as continuous prophylaxis to rheumatic subjects. (See specific prophylactic methods.)

Antibiotic troches and lozenges are also inadequate for the treatment of streptococcal infections because they do not eliminate the streptococcus.

Streptococcal Infections in Contacts

Approximately 25% of household contacts of index cases will contract streptococcal infections, which may vary in degree or severity from asymptomatic disease to frank clinical illness. Therefore, when a well-documented streptococcal infection is found, efforts should be made for detection of infections in other members of the family by a careful history, inspection of the throat, and a routine throat culture, when available. Contacts who have manifestations of a respiratory tract infection or large numbers of beta hemolytic streptococci on culture should be treated. Because even delayed therapy will significantly reduce attack rates of rheumatic fever, contacts who have had clinical evidence of a recent streptococcal infection likewise should receive treatment.

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