COMMITTEE REPORTS

Prevention of Rheumatic Fever

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 (1) by prevention of streptococcal infections in rheumatic subjects and (2) by 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.

I. 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, particularly those without heart disease who have had no rheumatic attacks for many years. Before exceptions are made, the physician should carefully weigh the risks of acquiring streptococcal infection as well as 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, and hospital nurses. Adolescents are particularly likely to be delinquent in regard to prophylaxis and should be urged to continue with this protection.

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.

*A statement entitled "Prevention of Bacterial Endocarditis" may be obtained from your local Heart Association or the American Heart Association.
Choice of Prophylactic Program

Several effective methods of continuous prophylaxis are available, and the physician must decide which is most suitable for an individual patient.

**Intramuscular vs. Oral Route**

The most consistently reliable results have been obtained with intramuscular benzathine penicillin G. Although many physicians and most patients prefer oral medication, successful oral prophylaxis depends on patient cooperation. Most failures occur in patients who fail to ingest the drug regularly. Patients should receive careful and repeated instructions on this point from the physician. Patients who may be considered unreliable in taking oral medication should receive benzathine penicillin G intramuscularly.

**Oral Penicillin vs. Oral Sulfonamides**

In the doses recommended sulfadiazine and oral penicillin are equally effective in preventing streptococcal infection and recurrence of rheumatic fever. Although streptococci resistant to sulfonamides have appeared during mass prophylaxis in the armed forces, this is rare in civilian populations. Strains of group A streptococci resistant to penicillin have not been encountered. Patients on penicillin prophylaxis are more likely to harbor staphylococci which are resistant to penicillin, but only rarely does this appear to be of clinical significance.

**Benzathine Penicillin G—Intramuscular**

*Dosage*—1,200,000 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.

**Sulfadiazine—Oral**

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

*Reactions* are infrequent and usually minor. In any patient being given sulfonamides, all rashes and sore throats should be investigated as possible reactions, especially if they occur in the first eight weeks. The chief reactions are: *Skin eruptions*. Morbilliform—continue drug with caution. Urticaria or scarlatiniform rash associated with sore throat or fever—discontinue drug.

**Leukopenia.** Discontinue drug if white blood-cell count falls below 4,000 and polymorphonuclear neutrophils fall below 35 per cent because of possible agranulocytosis which is often associated with sore throat and a rash. Because of the possibility of leukopenia developing, weekly white blood-cell counts are advisable for the first two months of prophylaxis. The occurrence of agranulocytosis after eight weeks of continuous prophylaxis with sulfonamides is extremely rare.

**Penicillin—Oral**

*Dosage*—200,000 or 250,000 units once or twice a day. Twice daily is probably more effective.

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.

**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 (see Section II). Some physicians may prefer to use injections of 600,000 units of procaine penicillin once or twice daily for 10 days under these circumstances.

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

**II. Streptococcal Infections in the General Population**

During epidemics it has been found that about 3 per cent 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 most practical means of preventing initial attacks of rheumatic fever.

About half the streptococcal infections that occur are likely to escape detection because they are asymptomatic or atypical. The other half can often be suspected by their clinical manifestations. However, in the absence of a scarlatinial rash, it is impossible to differentiate streptococcal infections with certainty on clinical grounds alone. Therefore, *bacteriologic support (by throat culture) of the clinical impression is highly desirable.* 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* 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.

**Laboratory findings**

Throat culture—hemolytic streptococci are almost invariably recovered on culture during acute streptococcal infections. A single well-done culture with a quantitative report is usually sufficient, although hemolytic streptococci which are occasionally missed on initial culture may be detected in subsequent cultures.

White blood-cell count—generally over 12,000.

**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:

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.

†Mixtures containing shorter acting penicillin should not be substituted for the recommended doses of benzathine penicillin G.

‡Of the various oral forms available, buffered penicillin G is satisfactory and less expensive. Although higher blood levels may be achieved with alphaphnoxyethyl penicillin (penicillin V) or alphaphnoxyethyl penicillin (penicillin G), especially when taken near meals, their superiority in the prevention of rheumatic fever has not been documented.

*A statement entitled “A Method for Culturing Beta-Hemolytic Streptococci” may be obtained from your local Heart Association or the American Heart Association.
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

Erythromycin is the most effective antibiotic in patients who are sensitive to penicillin. If given for 10 days, this antibiotic is probably as effective as oral penicillin in the treatment of streptococcal infections. Although tetracycline may be effective, a high prevalence of strains resistant to this antibiotic makes it unreliable.

Not Recommended

The sulfonamide drugs should not be used for the treatment of streptococcal infections. In an established infection, they will 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, Section I.) 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 per cent of household contacts of index cases will contract streptococcal infections, which may vary in degree of 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.

This statement was prepared by the Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis of the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association:

LEWIS W. WANNAKAVER, M.D., Chairman
FLOYD W. DENNY, M.D.

ANTONI DIEHL, M.D.
ERNEST JAEKHETZ, M.D.
WILLIAM M. M. KIRBY, M.D.
MILTON MARKOWITZ, M.D.
MACLYN MCCARTY, M.D.
EDWARD A. MORTIMER, M.D.
PHILIP Y. PATTERSON, M.D.
WILLIAM MERRY, M.D.
CHARLES H. RAMMELKAMP, JR., M.D.
GENE H. STOLLERMAN, M.D.

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