Prevention of Rheumatic Fever and Bacterial Endocarditis Through Control of Streptococcal Infections*

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, one by prevention of streptococcal infections in rheumatic subjects, and, two 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

A. 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 Recommendations

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.

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.

How long should prophylaxis be continued?

The risk of acquiring a streptococcal infection and the possibility of rheumatic fever recurrences continue throughout life. It is, therefore, suggested that the safest general procedure is to continue prophylaxis indefinitely, particularly if rheumatic heart disease is present.

When should prophylactic treatment be initiated?

Active rheumatic fever: Prophylaxis should be initiated as soon as the diagnosis of rheumatic fever is made, or any time thereafter when the patient is first seen. The streptococcus should be eradicated with penicillin (see Treatment Schedules p. 153), and following this the prophylactic regimen should be instituted.

Inactive rheumatic fever: In inactive rheumatic fever, prophylaxis should be instituted when the patient is first seen.

Should prophylaxis be continued during the summer?

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

Specific Prophylactic Methods

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

Oral vs. intramuscular route—Oral medication 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 have proved unreliable in taking oral medication should receive long-acting depot penicillin, given intramuscularly once a month.

Penicillin vs. sulfonamides—Sulfadiazine has the advantage of being easy to administer, inexpensive, and effective. Although resistant streptococci have appeared during mass prophylaxis in the armed forces, this is rare in civilian populations.

Penicillin rarely produces serious toxic reactions. It has the further advantage of being bactericidal for group A streptococci, and strains of group A streptococci resistant to penicillin have not been encountered.

1. BENZATHINE PENICILLIN G—INTRAMUSCULAR

Dosage—1,200,000 units once a month.

Toxic reactions

Urticaria and angioneurotic edema

*This statement was prepared by the Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis appointed by the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association. The committee is cognizant of the fact that no recommendations of any group can be final at this time. The present approach may not be the eventual solution of the problem of preventing rheumatic fever. Revisions and changes will be made as new knowledge may indicate.
Reactions similar to serum sickness include fever and joint pains and may be mistaken for rheumatic fever.

Some discomfort due to local irritation at the injection site is usual.

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.

2. SULFADIAZINE—ORAL

Dosage—from 0.5 to 1.0 Gm., once a day. The smaller dose is to be used in children under 60 pounds.

Toxic reactions are infrequent and usually minor. In any patient being given sulfonamides, consider all rashes and sore throats as possible toxic reactions, especially if they occur in the first eight weeks. In patients on this prophylactic regimen, it is hazardous to treat toxic reactions or intercurrent infections with sulfonamides.

The Chief Toxic 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 count falls below 4,000 and polymuclear neutrophils fall below 35% because of possible agranulocytosis which is often associated with sore throat and a rash. Because of these reactions, weekly white blood 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.

3. PENICILLIN—ORAL

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

Toxic reactions—except for local irritation, 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.

B. 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. At least the maximal dose regimen recommended for treatment of streptococcal infections in the general population (Section II, p. 153) should be employed. Despite optimal therapy, it is sometimes not possible to prevent rheumatic recurrences once streptococcal infections occur in the rheumatic subject.

C. Protection of Rheumatic Fever Patients in Hospital Wards

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.

Patients with inapparent rheumatic fever or rheumatic heart disease should be placed on continuous streptococcal prophylaxis on admission to the hospital or as soon thereafter as the diagnosis is established. (See Section IA, "Continuous Prophylaxis.") If oral penicillin is used, a dosage of 200,000 to 250,000 units twice a day is preferable.

Patients with acute rheumatic fever should be treated first with therapeutic doses of penicillin to eradicate streptococci. (See "General Recommendations—When should prophylactic treatment be initiated?" Section I, and "Recommended Treatment Schedules," Section II.)

II. Treatment of Streptococcal Infections in the General Population

During epidemics, and in certain population groups, it has been found that about 3% of untreated streptococcal infections are followed by rheumatic fever. Adequate and early penicillin treatment, however, will eliminate streptococci from the throat and prevent most attacks of rheumatic fever.

A. 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.

About half of the streptococcal infections which 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 scarlatiniform rash, it is impossible to differentiate streptococcal infections with certainty on clinical grounds alone. Therefore, bacteriological 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.

1. SYMPTOMS

Sore throat—sudden onset, pain on swallowing

Headache—common
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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

2. SIGNS
Red throat
Exudate—usually present
Lymphadenopathy—swollen, tender lymph nodes at angle of jaw
Rash—scarlatiniform, when present, usually diagnostic of a streptococcal infection
Acute otitis media
Acute sinusitis

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.

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

White blood count—generally over 12,000.

B. Treatment of Streptococcal Infections
Treatment should be started as soon as possible, but the 18 to 24 hour delay entailed in making a diagnosis by awaiting the results of a throat culture does not reduce the efficacy of antibiotic treatment in preventing the occurrence of rheumatic fever.

Penicillin is the drug of choice. Effective blood levels should be maintained for a period of 10 days to prevent rheumatic fever by eradicating the streptococci from the throat. Even with this prolonged treatment, streptococci may sometimes fail to be eradicated, especially when oral therapy is used. If possible, a follow-up culture two days after discontinuing treatment is desirable to ascertain the absence of hemolytic streptococci.

Penicillin may be administered by either intramuscular or oral route. Intramuscular administration is recommended as the method of choice since it ensures adequate blood levels for a sufficient length of time. Oral therapy, by contrast, is dependent upon the cooperation of the patient.

Recommended Treatment Schedules
1. 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.

or
Procaine penicillin with aluminum monostearate in oil:
Children—one intramuscular injection of 300,000 units, every third day for 3 doses.
Adults—one intramuscular injection of 600,000, every third day for 3 doses.

2. ORAL PENICILLIN
Children and adults—200,000 to 250,000 units, three 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.

3. OTHER ANTIBIOTICS
Broad-spectrum antibiotics, such as erythromycin and the tetracyclines are useful in patients who are sensitive to penicillin. If given for 10 days, these antibiotics are possibly as effective as oral penicillin in the treatment of streptococcal infections, but are subject to the same uncertainties of administration by the oral route.

CAUTION!
The sulfonamide drugs should not be used for the treatment of streptococcal infections. In an established infection, they will not eradicate the streptococci 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 streptococci.

III. Prophylaxis against Bacterial Endocarditis
In individuals with rheumatic or congenital heart disease, bacteria may lodge on the heart valves or other parts of the endocardium, producing bacterial endocarditis.

Although transient bacteremia is a rather common phenomenon and may occur after the mere chewing of hard candy or brushing of teeth, it is likely that the number of organisms entering the blood stream is usually relatively low under such
Transient bacteremia is especially apt to occur after dental extraction or other procedures in which the gums are manipulated, after removal of the tonsils and adenoids, and as a consequence of genitourinary operative procedures such as catheterization or cystoscopy. It is also probable that delivery is associated with transient bacteremia.

Since patients with rheumatic or congenital heart disease are especially vulnerable to bacterial endocarditis, it is advisable to protect such patients with antimicrobial agents when they are to be subjected to any of the above procedures. Some cardiologists are of the opinion that these patients should also receive prophylaxis against bacterial endocarditis when subjected to any surgery involving general anesthesia, or to diagnostic procedures such as cardiac catheterization.

**General Recommendations for Dental Manipulations and Oral Surgery**

Penicillin is the drug of choice for administration to patients with rheumatic or congenital heart disease undergoing dental manipulations or surgical procedures in the oral cavity.

Although the exact dosage and duration of therapy are empirical, there is some evidence that for effective prophylaxis, reasonably high concentrations of penicillin must be present at the time of these procedures. The dosage regimens employed for long-term prophylaxis against Group A streptococci in rheumatic susceptibles are inadequate for preventing bacterial endocarditis. To prevent organisms from lodging in the heart valves or to eradicate them promptly before the formation of a vegetation, high levels of penicillin in the blood over a period of several days after the given procedure are recommended.

Extraction of teeth from badly infected gums is apt to result in more intense bacteremia than when infection is minimal or absent. If prophylaxis is instituted 24 to 48 hours prior to the operative procedure, it may decrease the intensity of bacteremia. Since occult infection may be present, some workers recommend that treatment always be started several days prior to the operative procedure. On the other hand, some workers have been concerned that pretreatment might lead to the emergence of antibiotic-resistant microorganisms. These would constitute a very difficult therapeutic problem if they implanted in the valves. It has, therefore, been argued that prophylaxis should not be instituted until immediately before the operative procedure.

In view of the lack of definitive evidence to support categorically either method, the physician must evaluate the likelihood of infection and decide whether a period of preliminary treatment prior to the operative procedure is indicated. It is emphasized that there is no disagreement regarding the advisability of using antimicrobial agents immediately before and subsequent to the operative procedure.

**Suggested Treatment Schedules**

Two regimens are presented. In one, the intramuscular route is used throughout. In the other, oral therapy is combined with a single injection of penicillin one hour prior to the surgical procedure. Because of practical considerations some physicians and dentists rely on oral penicillin alone when the full cooperation of the patient is assured. It should be emphasized that these regimens are only empirical guides.

**Intramuscular Regimen:**

Step I.° Prophylaxis extended to two day period before surgery:

600,000 units of procaine penicillin I.M. on each day.

Step II. Day of surgery:

600,000 units procaine penicillin I.M. supplemented by 600,000 units of crystalline penicillin I.M., one hour before surgical procedure.

Step III. For two days after surgery:

600,000 units procaine penicillin I.M. each day.

**Intramuscular Plus Oral Regimen:**

Step I.° Prophylaxis extended to two day period before surgery:

500,000 units of buffered penicillin G or phenoxymethyl penicillin (penicillin V), by mouth four times a day.

Step II. Day of surgery:

500,000 units of buffered penicillin G or phenoxymethyl penicillin (penicillin V), by mouth four times a day, supplemented by 600,000 units of crystalline penicillin I.M. one hour before surgical procedure.

Step III. For two days after surgery:

500,000 units of buffered penicillin G or phenoxymethyl penicillin (penicillin V), by mouth four times a day.

**Contraindications to above regimens:**

Sensitivity to penicillin. All patients should be carefully questioned for previous history of penicillin sensitivity. In patients with such a history, even if equivocal, penicillin should not be given. Under such circumstances, erythromycin should be employed in a dose of 250 mg., by mouth four times daily for adults and older children. For small children, a dose of 20 mg. per pound per day, divided into three or four evenly spaced doses, may be used. No dosage should exceed a total of 1 Gm. per day.

°Step I may be omitted if desired.
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For Childbirth and Surgical Procedures of the Genito-Urinary and Lower Intestinal Tract

For childbirth and procedures such as catheterization of the bladder, surgery of the genito-urinary tract, or surgery of the lower intestinal tract, the following regimen should be employed:

In addition to either of the penicillin regimens outlined above, streptomycin should be administered in full dosage for five days, with treatment beginning, when possible, two days prior to the surgical procedure. In patients who are sensitive to penicillin chloramphenicol may be substituted.

Selected References


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