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David J. Clark

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Based on a Dissertation read before the Royal Medical Society on Friday. 27th February 1959.
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SOME ASPECTS OF RHEUMATIC FEVER

By DAVID J. CLARK

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In relating the acute rheumatic illness to the cardiac damage, a general tendency for a severe acute indisposition to be followed by serious cardiac deformity may be distinguished, and children who go into cardiac failure have a particularly poor life expectancy. Nevertheless it is unwise to make prophesies for the individual patient. A mild attack of rheumatic fever may be followed by crippling endocardial disorganisation, while a healthy middle-aged individual will cheerfully announce that during childhood he was extremely ill with acute rheumatism. The rheumatic patient may therefore first present with tonsillitis, with rheumatic fever itself, in cardiac failure later on in life, or with the sequelae of cardiac disease (notably bronchitis, pneumonia and subacute bacterial endocarditis).

This absence of quantitative relationship between infection, fever, and chronic heart disease has made the statistical study of rheumatic fever very difficult. The following statistics may perhaps interest the reader, but their accuracy is impossible to guarantee.

The annual disability in terms of days per thousand of population was in 1955 equal to that for tuberculosis.

Ten years ago there were two new cases per thousand school children per year. Today the figures are probably only a tenth of that number.

Approximately 20,000 people die each year in Great Britain from rheumatic heart disease.

Findlay (1937) reported that of 700 rheumatic patients, one third died before middle age, one third reached it with clinically detectable rheumatic heart disease and one third appeared to be unscathed. Hill agrees with these figures.

Rheumatic fever is commonest in February and March and least common in July. The affliction is rarer in hot dry climates than in cold damp ones, and it prefers to attack the poor and the overcrowded. These tendencies can all be assigned to the epidemiology of streptococcal infections. The

strong familial tendency that is sometimes found, and the slight preponderance of female children, are more difficult to explain, and though the familial tendency may, to some extent, reflect a liability to infection, it is likely that both of these factors reflect a property of the rheumatic process *per se*.

But what is the rheumatic process *per se*? It has been shown that the streptococcus is not itself present in the lesions. It has been proved that no particular one of Griffith's types is involved, and some workers have suggested on the basis of animal experiments that a series of Griffith's types may be needed like the ingredients in a cocktail. This suggestion has received little support. For the moment the "allergic" explanation seems to be preferred, but what this adds to our knowledge of the fundamental processes is very hard to say. It was found by autopsy at the Post Graduate Medical School in London that of those who died between the ages of 40 and 60, 6% showed gross evidence of rheumatic heart disease, and 90% showed microscopic evidence. One wonders whether streptococcal infection is always followed by some degree of cardiac damage which reaches serious proportions in those who are called "allergic."

The importance of rheumatic fever stems largely from its tendency to damage the cardiac valves and the first aim of treatment is to minimise this effect. The available methods are to some extent symptomatic but they do tend to reduce the damage

Hilton's classic work "Rest and Pain" was followed by the introduction of bed rest in rheumatic fever therapy. The obvious importance of this measure has prevented any modern scientifically inclined physician from running a clinical trial with a non-resting control series. In 1941, however, a resting "obedient" group of patients were compared with a "disobedient" group and Taussig and Goldberg were convinced that improved results were obtained by virtue of bed-rest. Moreover, it has been claimed since that time that there is a relationship between cardiac output and cardiac damage. When one crosses the gulf between theory and practice, however, a different problem arises. It is difficult for a child to remain as inactive as science demands. One has seen children, in the earliest stages of convalescence having pillow fights, playing football, wrestling, sprinting up and down the ward and jumping in and out of bed, doing, one assumes, grave damage to their hearts. Several such episodes were followed in a few hours by relapse. There seemed little sense in feeding these children from drinking cups and giving them bed baths in the morning (sister being on duty), when, unsupervised, they were creating riots in the evening. The ideal is that little boys and girls should lie as still as possible for many weeks, and Bywaters is investigating the use of sedatives to help make this ideal attainable.

In 1874 MacLagan introduced salicylates for acute rheumatism, and though some workers regard them as exclusively symptomatic, others believe that they reduce the cardiac involvement as well. Their antipyretic action must lessen the demands on the cardiac output, and they certainly reduce the ESR, which is the best index of the patient's progress during the acute phase. Reduction of the salicylate dosage is sometimes followed by relapse, which is again controlled by increasing the amount. This should be enough to control the ESR and joint pains and yet not enough to produce severe toxic symptoms. When these aims cannot be achieved steroids may be of dramatic assistance. There are at least six main theories for the method of action of the salicylates, but these need not be thrust upon the reader.

The supporters of the focal infection theory were proved wrong when penicillin failed to prevent cardiac damage in the established case of rheumatic fever, and one wonders whether the reputation of penicillin is still

suffering from this blow. Penicillin should be used in large dosage as soon as the diagnosis is made, not in the hope of reducing the cardiac damage but rather to eradicate any residual streptococcal infection. Before the discovery of penicillin it was not uncommon for an unhappy surgeon to be forced to perform an emergency tonsillectomy on a critically ill child.

The high recurrence rate of rheumatic fever can be completely abolished by faithful dosage with penicillin or sulphonamides. The prognosis is worse after two attacks than it is after one, and since two patients out of three do sufler from more than one attack if untreated, this prophylactic measure is of the greatest importance. Its value goes yet deeper than this. Comparison of a treated group with a non-treated group who had not suffered a second clinical attack indicated a better cardiac state among the treated than the untreated patients. From this it would seem that periodic subclinical infection may have caused additional though unsuspected damage, and in this discovery may lie part of the answer to the question "Why is a mild attack sometimes followed by severe cardiac disability in middle age?" Prophylactic antibacterial therapy should prevent any such infection. Once again, however, there is a great difference between theory and practice. "It is surprising that routine protection of rheumatic children in this country should lag behind that in the United States, where, during the last twenty years, it has been universally accepted. In this country it has been practised in only a few centres. There are only a few consultants and practitioners who at this moment employ what is now a proven method of prevention," says Bywaters in an illuminating article in the *Practitioner*. Rheumatic fever is the result of an abnormal relationship between the body and certain streptococci. By using drugs to maintain a constant antibacterial level in the blood we can prevent the presence of those streptococci and so make it impossible for the abnormal relationship to occur. Either the doctor is not giving the patient his drugs or the patient is not taking them regularly. Both of these faults occur fairly commonly in this country.

Work on tuberculosis has shown that the public are often very careless when they are entrusted with their own care, and it is extremely difficult to ensure that children will swallow their sulphonamides or penicillin in the proper amounts and at the proper times. As in diabetes, the more intelligent patients might derive great benefit from education in this matter. In others the long-acting penicillins could be injected regularly by a district nurse. It is obviously difficult for a busy doctor to give such patients adequate care. There can be no doubt that much better and more effective treatment could be given to the vast majority of rheumatic children.

The common objections to the prophylactic therapy are that the treatment is expensive, that allergic reactions might be evolved, and the presence of resistant stages of bacteria encouraged, according to Professor Bywaters. None of these arguments is valid. The cost of prophylactic antibacterial drugs is about 2d. per patient per day. By saving recurrences and by limiting cardiac damage, the country will be spared heavy expense. In the course of five years treatment of 500 patients at Taplow there was one serious case of allergy to the prophylactic penicillin, and one case of agranulocytosis, recovering after treatment among the sulphonamide-takers. Of the third argument Bywaters says: "Streptococcal resistance to penicillin does not occur, and only under epidemic conditions has sulphonamide resistance appeared. Staphylococcal resistance to penicillin may be a nuisance but is unlikely to cause trouble in home conditions. We have no trouble on this score." No doubt every regime has its disadvantages, but in this case these are so heavily outweighed by the advantages of prophylaxis that they can

be dismissed. Prophylactic treatment has been advised for the following groups:—

(*a*) For patients who have had one attack—treatment is advised until they are 25 years old.

(*b*) For children of susceptible families.

(*c*) For National Service recruits.

Another field of preventive treatment arises in tonsillitis. Until the fifth day of a streptococcal throat infection vigorous penicillin treatment can save the patient from rheumatic fever. Every rheumatic fever patient should be told to report to his doctor whenever he gets a sore throat. If prophylactic therapy is not being given, or if the patient becomes careless, this can very easily occur.

In 1953 cortisone appeared, and it was hoped that rheumatic carditis could be suppressed if the anti-inflammatory action prevented vascularisation and fibrosis of the valves. A clinical trial was held in twelve centres in Britain, America and Canada, and after a year the results for cortisone and corticotrophin were no better than those obtained with the humble aspirin. The pendulum of opinion seemed now to swing away from cortisone, and it seemed that no progress had been made by introducing the drug. Illingworth *et al*, however, tried the effect of combining cortisone and aspirin, and they claimed better results for the combination than for either drug separately. Later, it was decided to hold a second international clinical trial, this one to last for three years and to use a wider range of cortisone dosage. This trial is still in progress.

In the meantime Hill comforts us with the news that, in some cases, steroids are remarkably effective. Unfortunately, there seems no way of telling which cases these are except by trial and error. Some of the drug houses think that steroids should be used in preference to the nasty-tasting salicyclates, but no independent body has yet lent support to this view.

In this short article no mention has been made of surgical treatment, since it belongs not in the preventive category but rather to that of undoing damage which has already occurred.