PREVENTION OF RHEUMATIC FEVER: APPROACHES AND PROBLEMS

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Since William Charles Wells described the cardiac complications of rheumatic fever over 160 years ago[1] and, 40 years after him, Beitz suggested "an essential relation between the cause of acute rheumatism and that of Scarlatina"[2], considerable advances have been made in understanding the epidemiology of rheumatic fever. It is sobering to reflect, however, that while we know much about its immunopathology, the precise mechanism of pathogenesis is still not clear[3]: while we have powerful tools for the treatment of streptococcal infections, medical science can claim no credit for the decrease in rheumatic fever incidence that has occurred in many countries.

The main advances in knowledge, relevant to prevention, have been made during the past 30 years since careful studies in the American armed forces showed an attack rate of rheumatic fever (RF) of about 3% in untreated patients infected in epidemics of streptococcal pharyngitis[4]. These outbreaks were preceded by new intakes of recruits, crowding in barracks and the introduction and spread of new types of A streptococci, rich in M protein and of high virulence. Many subsequent studies [5, 6] have shown that the same factors may operate in normal populations although not to the same extent. The age distribution is, of course, different, the rheumatic fever is not always clinically as severe, the attack rate may be as low as 0.5-3.0 per 1,000 sore throats and several streptococcal strains are usually involved. But crowding, in association with other attributes of poverty, is still a factor and Stamler's comment[7] is true for many countries. "……rheumatic fever—rheumatic heart disease is a social ailment increased in incidence by poverty, substandard and overcrowded housing, and decreased in incidence by improvement in living standards". As for tuberculosis, where the mycobacterium is only one of the factors involved, so in rheumatic fever, the streptococcus alone plays almost a minor role.

In this lecture we shall take a pragmatic look at the options available for rheumatic fever prevention with emphasis on those approaches having the widest applicability. For purposes of discussion, the options have been grouped under three headings, the ideal, the theoretically practical and the realistic, or feasible.

1. THE IDEAL APPROACH

Despite our antibiotic and therapeutic armamentarium, the only method of preventing RF and rheumatic heart disease (RHD) that has proved successful on a population basis, is a general rise in the standard of living. Thus, in Malmö, Sweden, there was a reduction of 90% in the incidence of rheumatic fever over the 25 years 1935-60: 50% before 1949 and the widespread use of antibiotics and steroids[8]. School children in the poor areas of New York showed a 60% drop in RF incidence and 68% in RHD prevalence between 1949 and 1963[9]. In the United States, childhood mortality from acute rheumatic fever fell 50% between 1920 and 1950 and 90% by 1960[7]. Even in Jerusalem, the prevalence of RHD in school children, estimated at 3-5% in the 1950's has fallen by nearly 90%.

Another change, reported from New York, Sweden, Jerusalem and elsewhere, is that the proportion of cases of RF with cardiac involvement has decreased and that the disease is milder [8, 10]. These mild forms, atypical with respect to classical RF give rise to many diagnostic difficulties and Jones' criteria may no longer be an adequate yardstick.

To wait for the millenium however, is a solution unacceptable to both profession and public and there are more immediate, practical, approaches within the realm of medical practice. These are based on the control of streptococcal infections and we shall begin with the theoretically possible.

2. POSSIBLE APPROACHES TO PREVENTION

2.1 The most desirable method would be to prevent streptococcal infections and considerable work has been done on purification of the M substance for preparation of a vaccine[12]. While early results have been promising in respect of production of immune response, the side effects, both observed and theoretical, are not encouraging[13,14]. A further problem, as in the case of influenza vaccination, is the multiplicity of strains and the constantly changing frequency of the predominant strains (Fig. 1) which would necessitate the use of a polyvalent vaccine in open populations varying in composition from place to place[14]. One still hopes, however, for progress in this approach.

2.2 Primary prevention of rheumatic fever based on the early detection and prompt treatment of streptococcal sore throats, particularly in school children, is an approach which has received the imprimatur of the American medical profession[15]. There can be no question of the responsibility of the physician to treat, preferably with penicillin, every patient with a streptococcal sore throat: doubts arise as to whether this approach, even in a well doctored society with adequate laboratory facilities could have much effect in reducing the total incidence of acute rheumatic fever in the community. Dutch workers have found that only a quarter of patients with sore throats see their doctors[16] and in our own prospective study, only one third of first attacks of RF in school children were preceded by a clinically detected sore throat. (Fig. 2). Moreover, when the attack rate is low, it may be necessary to treat 600-2,000 cases of streptococcal sore throat, or 4-5 times that number in the absence of laboratory facilities, to prevent one case of rheumatic fever[16, 17]. To prevent each case of RHD, these numbers would have to be tripled (Fig. 3).

This, somewhat simplistic approach, is complicated by the problems of diagnosis of streptococcal sore throat. Clinical judgement is wholly inadequate[18] and bacteriological diagnosis based on a single swab may give false negative results in one case out of 8 [19]. Even when the patient seeks medical aid, the doctor may, in his ignorance, prescribe therapeutic regimens that are far from ideal (Fig. 4)[18].

Thus in areas where the incidence of rheumatic fever is low, primary prevention is not a realistic approach for community prevention.

2.3 In special situations however, where the proportion of streptoccal sore throats is higher and the RF attack rate very high, the considerations could be quite different.

In army barracks, settlements and schools, under epidemic or endemic conditions, mass chemoprophylaxis has many times proved its worth in stopping an outbreak of pharyngitis and preventing cases of RF[20,21].

2.4 Secondary prophylaxis is the mainstay of the medical approach and is universally practiced to some extent. There is still discussion as to how long chemoprophylaxis should be continued and whether patients without cardiac involvement need the same intensive surveillance as those with [22,23]. Penicillin is still the

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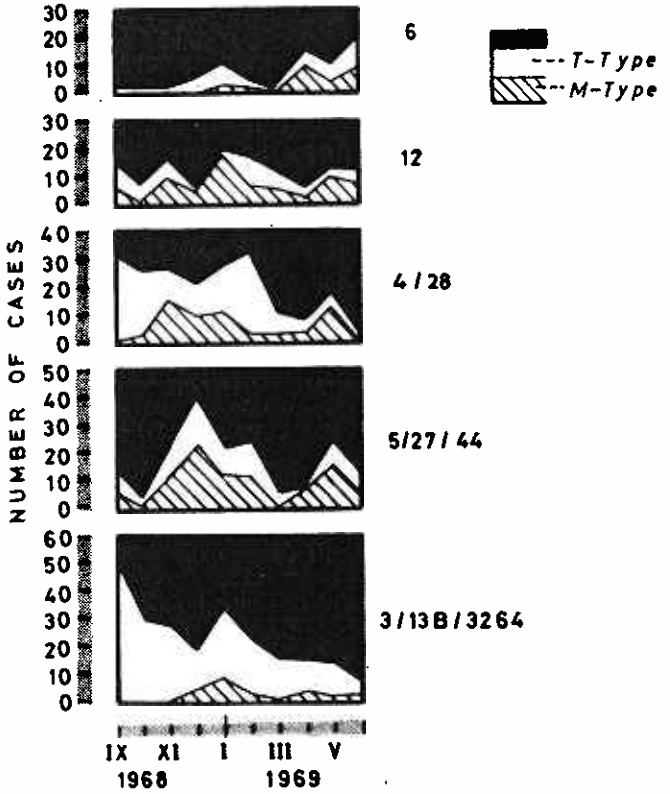

Fig. 1. Variations in prevalence of selected streptococcal types isolated from school children with sore throats during one school year.

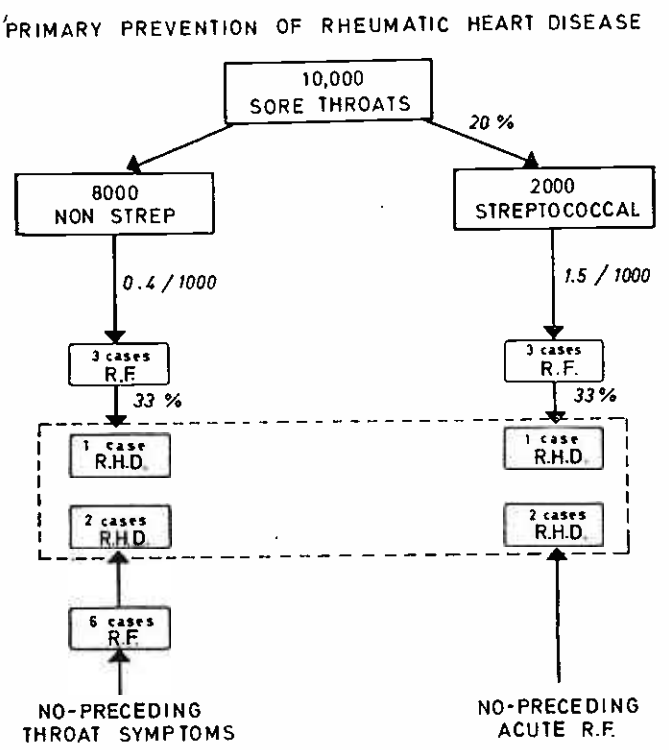

Fig. 3. Statistical considerations in a program for the primary prevention of rheumatic fever and rheumatic heart disease in school age children.

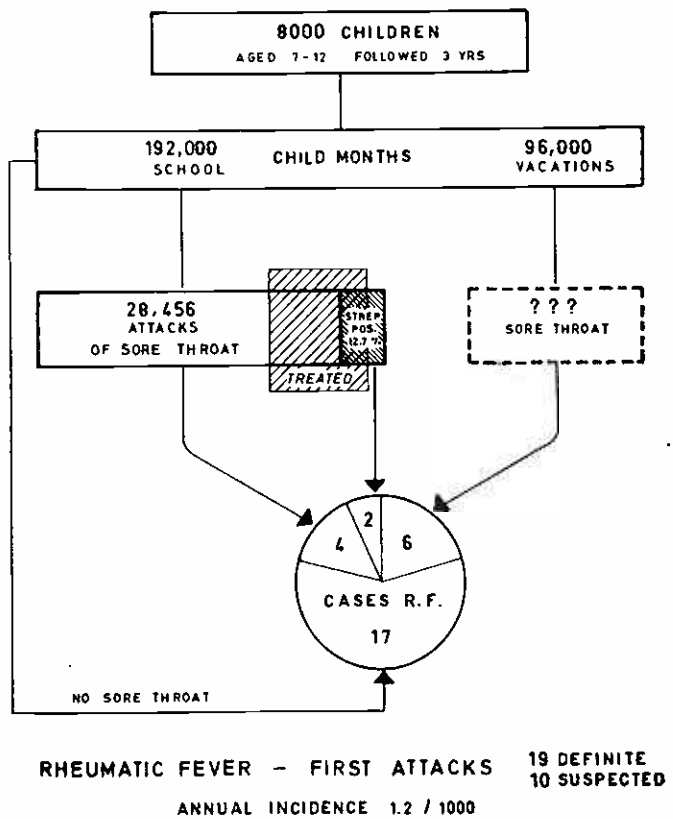

Fig. 2. Sore throats, streptococcal recovery and rheumatic fever among 8,000 Jerusalem school children, 1967-1969.

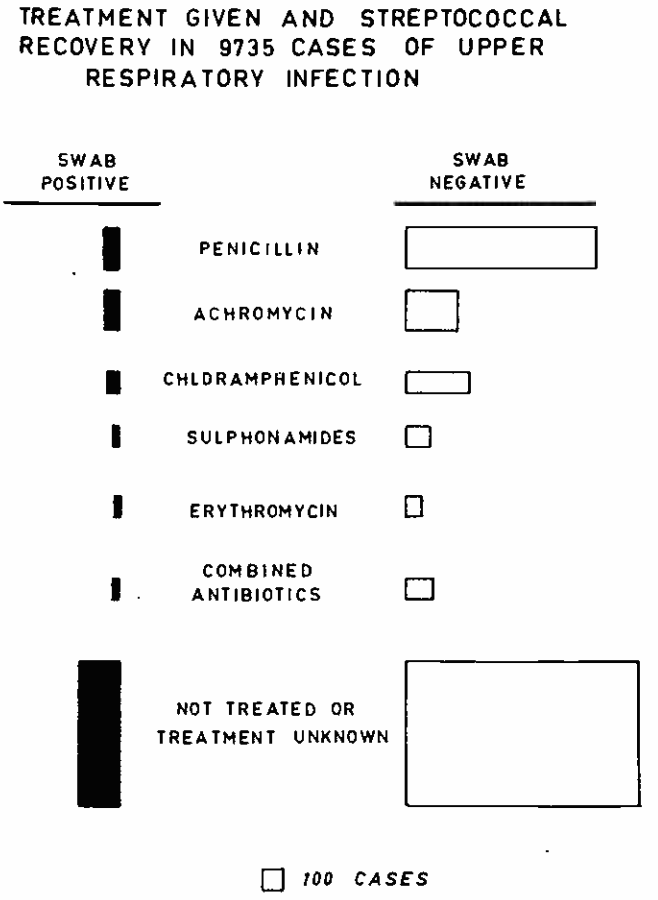

Fig. 4. Treatment of sore throat by family doctor.

drug of choice[15, 24] but the literature is replete with reports of failures of penicillin and other antibiotics taken orally to prevent RF recurrences. Many authors, however, have failed to take into account the fact that the patient may not be taking the drug. Only half of Jerusalem school children on chemoprophylaxis with oral penicillin were found to be excreting the antibiotic in their urine. Serial studies showed that 30% never took their tablets and only 10% took them for more than 3 weeks each month. Similar results were obtained in surveys in Baltimore[25]. Needless to say, without a well organized health delivery system, a positive approach by patients and unrestricted access to facilities, a program for secondary prophylaxis will be confined to selected patients.

2.5 Prevention of disability and death must be mentioned for completeness. The measures, which include adequate treatment of patients during acute attacks, correction of heart failure, valvotomy and valve replacement, are our traditional medical tasks. It must be pointed out however, that such facilities are available to only a minority of patients in most countries and represent a very expensive approach which attempts to compensate, in part, for our failure to prevent the disease in the first place.

3. REALISTIC APPROACH

If the palliatives of modern medicine are inadequate to solve the problem of RF for the richest countries, what can be done by the poor? Where financial and medical resources are limited, strategy in RF prevention must be confined to the feasible and governed by considerations of cost and benefit.

However limited the resources, a start can be made by registering known patients who are over the acute phase and instituting a system of surveillance which will ensure continuing chemoprophylaxis. If, due to shortage of drugs or other resources, only selected patients can be enrolled in such a program, it is well to remember that those with existing RHD are more susceptible to recurrences (Fig. 5).

The next phase, also requiring little additional effort, is to update the register with all newly discovered cases, preferably recording part of the clinical information in a standard way. As coverage increases and information accrues on all patients in a defined area where the size of the population can also be estimated, we have a measure of incidence.

Aside from private medicine for those who can afford it, for those who cannot, the resources of public medicine must be geared to the size and importance of the problem and this is especially true in organizing schemes for prevention. If the incidence of RF and the disability from RHD are low, then prevention programs are unlikely to be of high priority in over all health planning. It is thus essential to obtain some measurement of the size of the problem and as there may be considerable geographical variation, the estimate must be made for different localities. Information from hospitals can tell us if there are many cases but not how many. It cannot tell us if there are few because we may not be seeing them. In many places, women attend doctors much less frequently then men, a hospital with a religious affiliation may attract some and deter others while considerations of distance and provision of facilities have a marked effect on who seeks medical care. It has been repeatedly shown that the ages, sex and clinical severity of patients in the community may be sufficiently different to change concepts of the natural history of the disease which derived from studies of hospitalized cases only[26].

Measurement of the size of the rheumatic fever problem will thus require the addition of information from population surveys to that already recorded. On the whole, cases previously undetected are milder than those receiving medical care, with all the attendant difficulties of diagnosis. Fig. 6 shows the considerable observer variation between three eminent cardio-

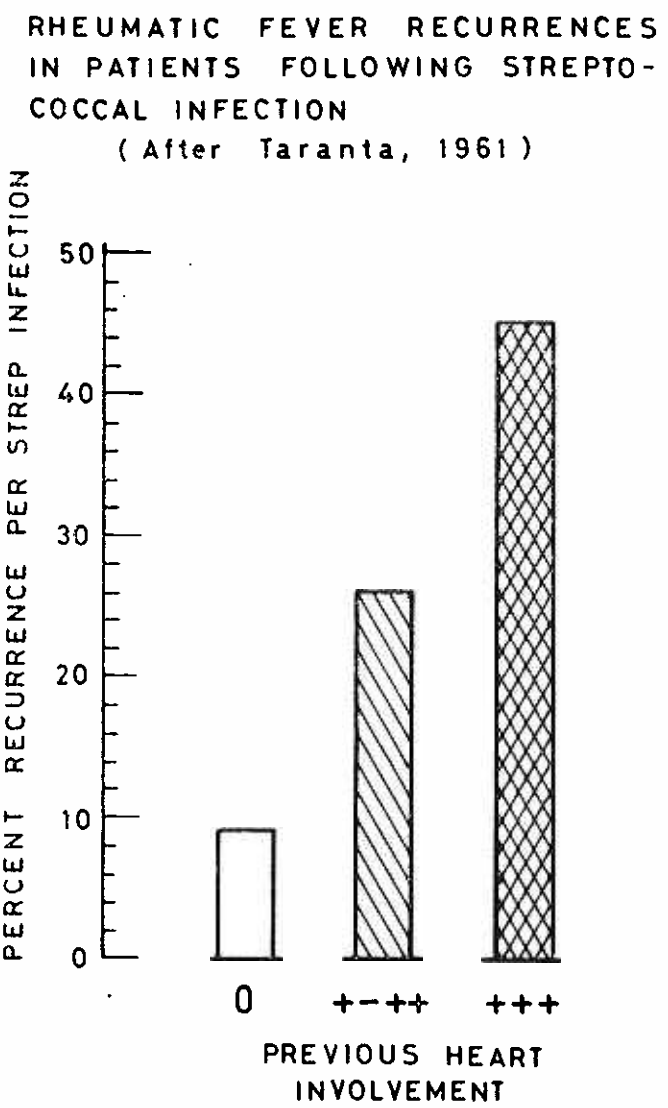

Fig. 5. Increased susceptibility of children with previous carditis to RF recurrences.

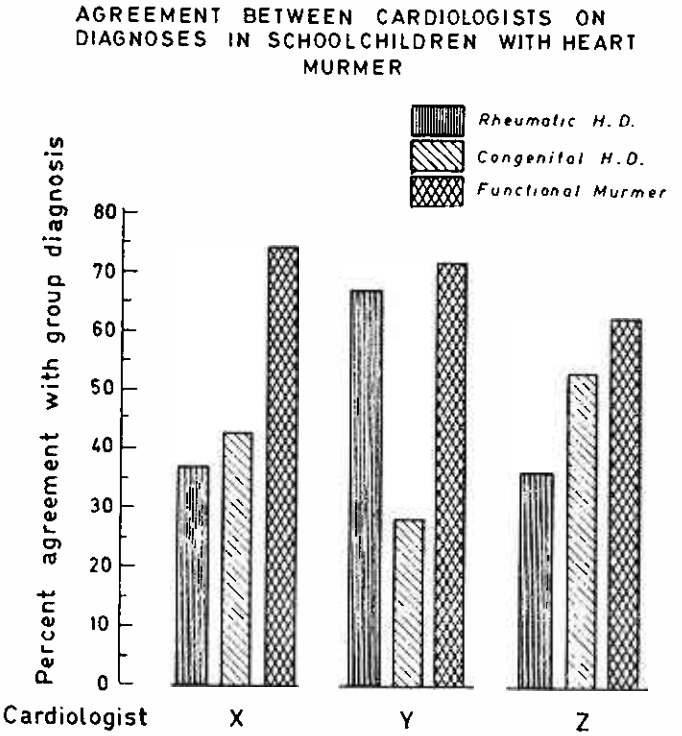

Fig. 6. Degree of inter-observer variation between cardiologists in a survey among school children in Jerusalem.

logists who examined over 1,000 Jerusalem children selected from the school population on the basis of a history of RF and Phono-CardioScan screening[27]. The main disagreements, as expected, were in difficult and doubtful cases.

There are said to be great differences in the natural history of RF in different parts of the world[28] and it is important to document these both to permit some measure of the burden of the disease on the community and to determine whether the findings reported from other countries can be extrapolated to the local situation. Frequently, reported differences are due to use of different diagnostic criteria (Fig. 7) and it has been said that the only cases of RF fulfilling the Jones' criteria in Delhi, for instance, are second and subsequent attacks. One authority has suggested that in the West, only cases with carditis or chorea should be considered as true RF[29] and the time has surely come to modify or extend the Jones' criteria[24].

DIFFERENCES IN THE NATURAL HISTORY OF RHEUMATIC FEVER MAY BE DUE TO:

Different Diagnostic Criteria
Selection of Patients Studied
True Biological Differences
— Unusual Patient Response
— Unusual Streptococci
Environmental Differences
— Crowding
— Malnutrition
— Cultural Patterns
— Medical Care

Fig. 7. Some reasons for reported differences in RF and RHD frequency and severity.

There may be true biological differences in the expression of rheumatic fever or particularly virulent rheumatogenic streptococci endemic in some localities but this remains to be proved. The effect of poverty and crowding is well documented: we have found, in addition, that the cultural background of our different population groups is an important determinant of the symptomatology of response to disease[30]. Moreover the attitudes and education of our patients are prime factors in determining compliance, or otherwise, with therapeutic regimes.

To measure the burden of rheumatic fever and establish priorities in health services, we need some estimate of costs. These estimates include those of case finding, treatment chemoprophylaxis and surveillance as well as the cost to the patient and community of neglected disease and death. Such information will permit the design of programs to reduce the morbidity and mortality due to RF, to set goals, while the register will provide a check on their success.

Lest it be thought that these are pipe dreams, the World Health Organization has recently proposed a basic program with several options, adaptable to local conditions[31]. Pilot studies along these lines have started in Cairo and Teheran[32] while the first year's operation in Barbados has had considerable success, with 97% of patients maintaining chemoprophylaxis[33].

Time does not permit consideration of other options such as the possibility of concentrating on groups at special risk. School children for instance, in areas of high streptococcal endemicity, could be protected by chemoprophylaxis especially at the beginning of the school year when infection is highest. Siblings of patients with RF, residents of neighbourhoods with a high attack rate and troops in crowded barracks are all deserving of special attention and offer the chance of prevention at minimal cost.

In conclusion, the theme of this paper is that the prevention of RF and RHD is difficult, but possible at least in part; that a start can be made with a minimum of resources but that a logical, all-out attack on the diseases requires study and understanding of local conditions and thought and improvisation on the part of each and every member of the medical team.

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