MEDICAL PRACTICE

Contemporary Themes

Cardiovascular Disease in the Tropics*—I, Rheumatic Heart

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Throughout the "Suggestions for Consideration by the Council of the Royal College of Physicians of London," written by Dr. Gavin Milroy almost 100 years ago, runs a considerable concern with public health in the tropical countries then under British administration. "I would express my strong desire that more diligent and continued attention may be paid than has yet been attempted in this country to the study of the accurate geography of disease . . . which is often essential to the complete determination of their true natural history." He respectfully left it to the council of the college to determine "whether it would be advisable to invite from time to time the co-operation of medical men from foreign lands . . . able and willing to deliver their lectures in the English language," . . . and I am grateful to the council for having so determined.

In these lectures I will present material on rheumatic heart disease and endomyocardial fibrosis, on blood pressure and hypertension, and on coronary heart disease. I make no apology for not discussing Chagas's disease of the heart, idiopathic arteritis, ventricular aneurysms, electrocardiographic abnormalities, or any of the other fascinating problems peculiar to the tropics. I am concerned to show that the differences in natural history made evident from tropical experience give a perspective on disease in our own community that we cannot possibly obtain from studies limited to our own environment. This is the message of these lectures, which are concerned with public health and the prevention of cardiovascular disease both in the tropics and in the temperate regions.

The word "tropical" calls to mind sleeping sickness, schistosomiasis, and other diseases directly related to the environment. It also suggests exotic flora and fauna and unusual communities.

* The Milroy lectures delivered at the Royal College of Physicians of London on 9 March 1972.

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What we are really concerned with is the standard of living and not the vegetation or the temperature. The tropical countries are in general all engaged in the crises implicit in passing from a peasant rural society to an industrialized and urban one. It is poverty, malnutrition, widespread and poorly controlled infectious and parasitic diseases, inadequate medical services, and inadequate means of communication that are inherent in the term "tropical." Children form a relatively high proportion of the population, and the registration of births and deaths and the notification of many important diseases is incomplete or absent. Urbanization has already led to slum conditions, and the rapid increase in schools is producing community aggregation in a pattern not previously encountered. These are comments and not criticisms; they describe situations as they really exist outside the capital cities and often within their boundaries as well.

Rheumatic Heart Disease

I will say very little in detail about rheumatic fever and rheumatic heart disease in the tropics but more about some fundamental aspects of streptococcal infection and rheumatic fever. There is little point in emphasizing minor clinical differences which may or may not exist. There is no single standard natural history of rheumatic fever; there are a number of natural histories possible. The problem in the tropics today is essentially the same as existed in many of the developed countries at the turn of the century, and it concerns the ecology of the streptococcus.

Rheumatic fever is an active inflammatory process initiated by group A streptococcal infection, and it affects the heart valves, myocardium, and pericardium in a variable combination. The evidence supporting the aetiological relation of group A streptococci to rheumatic fever is overwhelming, but it is, nevertheless, *indirect*. Clinical and epidemiological studies show a close association of group A streptococci and rheumatic fever. Antecedent streptococcal infection can always be shown immunologically in the acute stages of rheumatic fever, and rheumatic

fever does not recur in the absence of intercurrent streptococcal infection. Finally, primary and secondary attacks can be prevented by the prevention or the prompt and adequate treatment of streptococcal infections.[1]

Much work strongly supports the concept of rheumatic fever as an autoimmune disorder, but even the most ardent protagonists of this hypothesis accept that the gaps in present knowledge are numerous and relate practically to the total pathogenesis of rheumatic fever.[2]

I make these introductory remarks about aetiology and pathogenesis to emphasize how little we know of the essential nature of rheumatic fever in the countries of the world where it has been actively studied for many decades. It is therefore not surprising that we know even less about its problems in tropical environments, where the situation is complicated by genetic and nutritional differences and by the immunological responses invoked by a multiplicity of microorganisms and parasites.

There has been a recorded decline in the incidence of acute rheumatic fever over the past 70 years, and whether one looks at the figures for England or the United States or Denmark they all look very much the same.[3] The decline has been progressive and has well preceded the advent of antibiotics. The presumption is that there has been a diminution in the severity of both rheumatic fever and carditis associated with improved social conditions and an altered virulence of the streptococcus, more recently assisted by the earlier treatment of streptococcal infections and prophylaxis in known rheumatic cases.[4]

Since the early 1950s there has been a steady flow of publications from Mexico, tropical and subtropical Africa, Central America, the Phillipines, the Indian subcontinent, Indonesia, and the Middle East on the subject of rheumatic fever and rheumatic heart disease. There is overwhelming evidence from hospital inpatient and necropsy studies, highly selective though they may be, that rheumatic heart disease is today the commonest form of heart disease in children and young adults in most tropical or developing countries and one of the most common cardiovascular diseases in adults. Not only is it common but there is clinical and necropsy evidence from several countries that the frequency of the disease is increasing.

In examining these reports we rapidly become aware that there is no uniform "tropical pattern" of rheumatic fever or rheumatic heart disease. From one part of India to another, from one community in Israel to another, and from one racial group in South Africa to another there are apparent differences in the presentation and course of the rheumatic disorder.

The general impression gained from these reports on rheumatic fever is that the process is in some way different in the tropics. It is said, and I summarize the general statements, that acute rheumatic fever is rare despite the frequency of chronic rheumatic heart disease, that migratory polyarthritis is rarely seen, that chronic valvular lesions present at an unusually early age, that the streptococcus is rarely found in the throat, that skin lesions are more important as a source of streptococci than throat lesions, and that the pathology is more florid than that which is seen in Europe or America. How much truth is there in all these statements based on material selected in a wide variety of ways? And if there are differences in the rheumatic fever/rheumatic heart disease situation in the tropics, of what relevance are these differences to the prevention and treatment of the disease?

Acute Rheumatic Fever

In almost all tropical studies on acute rheumatic fever the proportion of very young children affected is regarded as higher than in temperate countries. In Johannesburg, when African children admitted under 10 years of age were compared with American and British children, the African group showed twice the percentage of children under 5 years of age.[5,6] A similar picture is presented from Jamaica, Jerusalem, and India, and in many children with acute rheumatic fever under 10 years of age chronic valvular lesions are already well established. Rheumatic fever is universally a disease affecting predominantly the young, and for age differences of this kind to have significance one would require that the conclusions be based on comparable data with incidence figures being provided for each age and sex. This information cannot possibly be obtained in tropical countries by virtue of their defined characteristics, and so we remain with the clinical impression of a greater proportion of very young children being affected than has been recorded in temperate countries over the past two or three decades. This situation may merely reflect the much larger proportion of young children in the population at risk in these tropical countries.

Extracardiac Manifestations

There is widespread agreement that erythema marginatum and subcutaneous nodules are rarely seen and that chorea is less frequent than in Europe and America. Most reports claim that acute migratory polyarthritis is unusual and that arthralgia is more commonly encountered. It is virtually impossible to assess the significance of these reports, not because they may not be true for the situations in which they occur but because from time to time in the same place and from place to place at the same time there is considerable variation in the frequency of these signs.

I would suggest that the frequency of these extracardiac signs of rheumatic fever is of little real importance to our problems, if not completely irrelevant. Subcutaneous nodules and erythema marginatum almost always occur in association with arthritis, chorea, or carditis. And even the frequency of chorea or arthritis are of little real moment. Rheumatic fever is important because of what it does to the heart, and what really matters are the questions concerning carditis[7] (see Fig. 1).

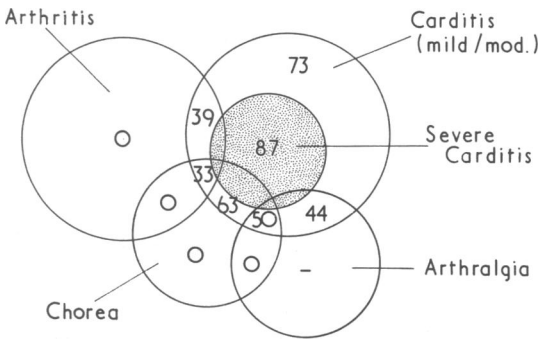

FIG. 1—Prognosis of acute rheumatic fever (from Feinstein[7]). Figures indicate the percentage of those presenting in an initial attack of acute rheumatic fever who developed or died from rheumatic heart disease eight years after the initial episode of acute rheumatic fever.

Acute Carditis

In the absence of carditis rheumatic heart disease seldom if ever develops in patients with only arthritis or chorea, even during recurrences of rheumatic fever in such patients. The worst results are in those with severe carditis. The damage is permanent, the patients are particularly susceptible to recurrences of rheumatic fever, and it is in this group that death is most likely to occur at a young age. In mild carditis the evidence of cardiac damage disappears in about half of the patients, particularly if they also have arthritis or arthralgia rather than having no joint symptoms at all.

We have no data on which to accept the suggestion that carditis is more frequent in rheumatic fever in the tropics or that it is followed more frequently by rheumatic heart disease than it is elsewhere. There is some suggestion that mortality may be higher during the acute attack. In Johannesburg 4% of the African children died at this stage due to severe carditis with valvular damage and irreversible heart failure, while in Ameri-

can and British children the first-year mortality was only 1%.[5 6] In a Jamaican study 11% of the children admitted with acute rheumatic fever died within a few weeks of progressive pancarditis, and a further 11% were dead within one to three years, mainly from cardiac failure.[8] We are left with the strong impression that tropical rheumatic fever affects a younger age group and that the severity, as measured by early mortality, may be greater than at present in the temperate countries.

Rheumatic Heart Disease

In established rheumatic heart disease it is again the *age* difference which is the striking clinical feature in the tropics. Undoubtedly chronic valvular lesions are present at a much earlier age than seen in Europe or America, and the term "juvenile" mitral stenosis is widely used in India and elsewhere. A comparison has been made of the proportion of young subjects among those with mitral stenosis selected for valvotomy in different countries.[5] In the U.K. and U.S.A. between 1953 and 1959 some 1-3% of subjects were less than 16-20 years of age. In Israel 8% were less than 16 years old and in Johannesburg (African) 21% were less than 20 years old. In one Indian series 34% of the subjects for mitral valvotomy were less than 20 years old. Further confirmation of this tropical predilection for the younger age groups is seen in a necropsy study of rheumatic heart disease in Uganda covering a 16-year period[9] (Fig. 2). Altogether 21% of male subjects and 35% of female subjects

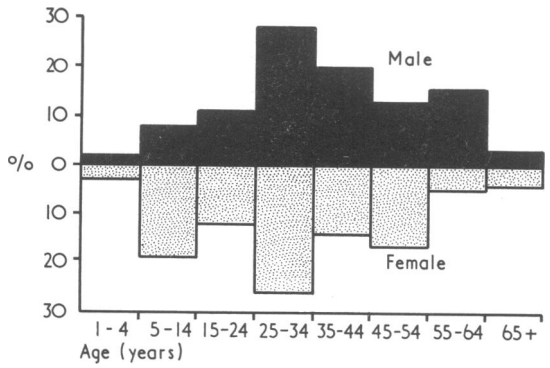

FIG. 2—Age distribution of subjects with rheumatic heart disease at necropsy; Mulago Hospital, Kampala, Uganda, 1950-65 (from Shaper *et al.*[9]).

were under 25 years of age. The female predominance was even more pronounced in the group under 15 years of age, which included 10% of the male and 22% of the female subjects. The pattern of gross pathology is very much the same as that seen in many European or American series, and there is nothing to suggest that rheumatic heart disease in the tropics is grossly different from that in other parts of the world.

Rheumatic fever has long been known to be a disease of poor socioeconomic conditions, and it is tempting to assume that the conditions prevailing in the tropical countries would provide very suitable host situations for rheumatic fever. In the 1930 Milroy lectures on rheumatic diseases Glover[10] said "No disease has a clearer cut 'social incidence' than acute rheumatism, which falls perhaps 30 times as frequently upon the poorer children of the industrial town as against the children of the well-to-do. I agree with those who hold that the incidence increases directly with poverty, malnutrition, overcrowding and bad housing." Malnutrition has frequently been discussed as a possible factor in conditioning the incidence and course of rheumatic fever, but studies designed to assess nutritional status as a factor determining individual susceptibility or determining prognosis have been remarkably successful.

The question of the host has largely been left in abeyance and attention has focused with intensity on the streptococcus. It is at present widely accepted that variations in the geographical distribution, incidence, and severity of rheumatic fever have little to do with environmental or host factors but are in general a reflection of the frequency and severity of the preceding streptococcal infection.[1] Thus latitude, altitude, crowding, dampness, economic factors, and age all affect the incidence of the disease because they are related to the incidence of streptococcal infection in general. Host variables may also be important, but to what extent such host variables are genetic or acquired has not been settled.

However, two important variables of streptococcal infection influence the attack rate of rheumatic fever and are relevant to the tropics. Firstly, the duration of throat carriage of group A streptococci during convalescence from throat infection. Failure of treatment to eradicate streptococci during three to five weeks of convalescence gives a high attack rate. The importance of this variable to the "tropical" situations is devastatingly apparent. Where diagnosis is delayed and uncertain and where treatment is inadequate or absent the duration of throat carriage of group A streptococci must inevitably be prolonged and the attack rate must inevitably be high. Secondly, the attack rate is influenced by the degree of immune response to the antecedent streptococcal infection. A strong immune response corresponds with an attack rate as high as 10%, which is at least three to five times the attack rate in most temperate communities.

In Uganda antistreptolysin O titres have been estimated in rural and periurban children aged 1 month to 6 years and in cord blood.[11] From 1 to 3 months of age through to 6 years some 40% of all age groups had antistreptolysin O titres above 200 units. At levels of over 400 units the frequency rose from 8% in the 1 to 3 months age group to 29% at 4 to 11 months and 33% at 1 to 2 years of age. From 3 to 6 years only 13% had antistreptolysin O titres over 400 units. Titres of over 600 units first appeared in the second 6 months of life and were more frequent from 7 months to 2 years (18%) than at 3 to 6 years (5%) (Fig. 3).

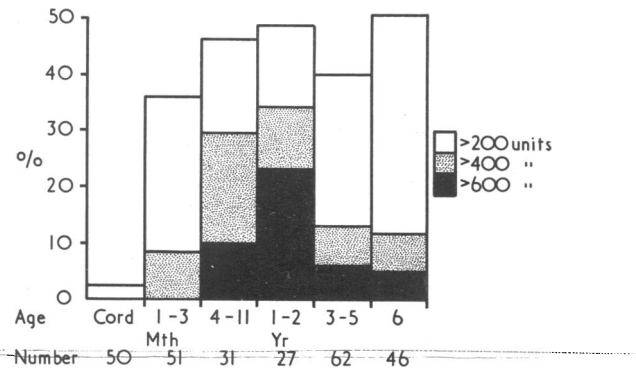

FIG. 3—Antistreptolysin O titres in cord blood and in children aged 1 month to 6 years in Uganda (Stanfield and Bracken[11]).

A high frequency of raised antistreptolysin O titres has also been reported from Ceylon[12] and Khartoum[13] and in a W.H.O. survey of Thailand, Pakistan, and Eastern Nigeria.[14] The Ugandan study, however, stresses the early age at which streptococcal immune responses are present, and these findings are consistent with the early age at which rheumatic heart disease is seen in Uganda and in other tropical countries.

I would add only a brief comment on the suggested role of streptococcal skin infection in rheumatic fever in the tropics. There is at present no evidence for this, and considerable evidence from studies of streptococcal pyoderma, acute glomerulonephritis, and acute rheumatic fever indicates that skin lesions play little or no part in the incidence of rheumatic fever in the tropics.[15 16 17]

I want to end this comment on rheumatic fever in the tropics on a rather pessimistic note. I have already referred to the recorded decline in the incidence of the disease over the past 70 years. We are clearly dealing with a socioeconomic phenomenon and not with the effects of modern therapeutics. Given the present social and economic situation of the tropical world,

which seems unlikely to change radically for many years, it seems hard to believe that any major decline in the incidence or severity of acute rheumatic fever and its consequences is imminent. If anything increasing urbanization, school attendance, and group organization may aggravate the situation further.

If rheumatic fever is different in the tropics it is in terms of incidence and severity, and this may be entirely a function of the streptococcus or it may, in addition, relate to host susceptibility. It is these two facets, the streptococcus and host susceptibility, which deserve a major investment in research time and public health money. The rewards may be of universal benefit and not limited to the tropics.

Part II of these lectures will appear in next week's issue. A list of references will be given with Part IV.

Hospital Topics

Dialysis and Transplantation: The National Picture over the Next Five Years

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Now that haemodialysis and transplantation have become an accepted form of treatment for patients with "end-stage" renal failure we need to define the commitments in this field of medicine (in terms of numbers of patients and costs within the different treatment programmes currently in use) for the next few years. In this paper we present some of the changes which we expect to occur, given that no immediate dramatic changes in dialysis and transplantation survival will take place. Our results have come from an analysis of data collected by the Joint Colleges Committee*[1] and from an examination of the returns made from units to the Department of Health and Social Security.[2] The Joint Colleges Committee data referred to patients accepted for treatment between 1 January 1967 and 1 May 1970. Replies were received from 29 centres in time for this analysis; a total of 1,120 patients were considered, and of these 365 received transplants and 246 died during the period of the survey.

Study of these data has enabled us to predict the number of patients undergoing treatment in five years' time. An estimate has also been made of the possible transplantation rates. We have also assessed the efficiency of the different treatment programmes currently in use in Britain in terms of patient survival, cost, and yearly intake of new patients.

Analysis

A comparison of dialysis and transplantation survival times taken from the Joint Colleges Committee data is shown in Fig. 1. Percentage survival is shown and the figures are given at monthly intervals. The top line represents survival on dialysis and includes both unit and home dialysis. Patients receiving transplants were excluded from subsequent analysis. Two-year dialysis survival was 75%. The middle line represents survival of patients from the time of the first transplant. It does not refer to pretransplant or post-transplant dialysis survival, nor does it include second or third transplant survival. The two-year survival was 55%. The bottom line represents survival of the graft, and includes grafts in patients who died, whether or not deaths were due to graft failure. It would, however, be possible simply to omit these grafts from subsequent analysis when the patient died of other causes. This would involve very precise data on the exact state of the graft at the time of death, and this information is not at present available. The two-year graft survival was 41%.

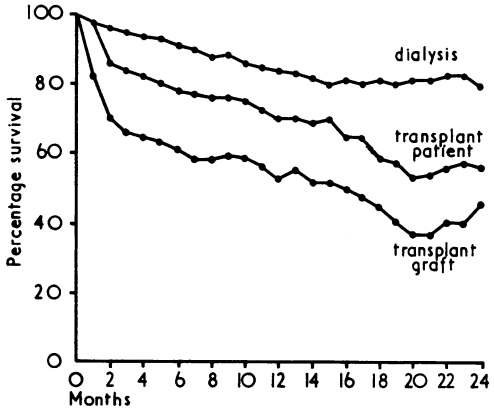

FIG. 1—Joint Colleges Committee data on monthly survival of patients and grafts. Method of analysis involved calculating each month the proportion of patients who survived out of those who could have survived. (Not the actuarial method.) The two year survival figures of 75%, 55%, and 41% refer respectively to dialysis patients, transplant patients, and grafts and been obtained from computer-fitted curves derived from this data.

Data were analysed to ascertain the end result in patients with graft failure. The numbers of patients who were successfully returned to dialysis in terms of the length of time their transplants had been functioning are shown in Table I. Successful

TABLE I—*Length of Time Graft had functioned before Patients returned successfully to Dialysis (Joint Committee Data on First-graft Failure)*

	Transplant Function (Months)				Total
	1	2	3	4 and over	
No. of patients	48	28	12	26	114
No. (%) returning to dialysis	35 (73)	14 (50)	4 (33)	8 (31)	61

*The Joint Committee comprised representatives from the Royal College of Physicians of London, the Royal College of Surgeons of England, the Royal College of Obstetricians and Gynaecologists, the Royal College of Pathologists, the Royal College of Physicians of Edinburgh, the Royal College of Physicians and Surgeons of Glasgow, the British Paediatric Association, and the Renal Association. It was established in May 1970 under Lord Rosenheim's chairmanship.

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