

THE RELATION OF RHEUMATIC FEVER TO POSTSCARLATINAL ARTHRITIS AND POSTSCARLATINAL HEART DISEASE—A FAMILIAL STUDY¹

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INTRODUCTION

The relationship which postscarlatinal arthritis and postscarlatinal heart disease may bear to rheumatic fever has for many years been an unsettled question. Furthermore, since there is no exact information as to the nature of these sequelae of scarlet fever, nor of the nature of rheumatic fever, it is obviously difficult to compare them. It should be possible, however, to say whether or not fundamental similarities, or differences exist between the familial conditions under which these two syndromes arise, and it is with such a comparison that this paper will be concerned.

Postscarlatinal rheumatism and heart disease—A brief clinical review. The syndrome of postscarlatinal nonsuppurative arthritis or rheumatism with which carditis may or may not be associated, represents an entity so well-known that it hardly merits a review of its clinical features. However, some statements concerning the type, and incidence of these scarlet fever complications seem necessary. Various types of lesions may of course involve either the joints or the heart during or following scarlet fever; the lesions of the joints may be either suppurative or nonsuppurative, and the cardiac lesions may be classified, according to Swift (1), into three groups: viz., (i) toxic lesions which generally occur early in the disease; (ii) septicopyemic lesions which may appear early or late; and (iii) so-called allergic lesions which usually appear late in the disease. Our use of the terms postscarlatinal arthritis and postscarlatinal carditis refers solely to the nonsuppurative arthritis and to the so-called allergic carditis, respectively, both of which arise ordinarily during the secondary phase of scarlet fever. When present, this secondary phase, the frequency and importance of which was first emphasized by Schick (2), appears after an interval of from 7 to 30 days following the primary, exanthematous or toxic phase of scarlet fever. If the picture is not confused by the presence of suppurative complications, or of serum disease, the secondary phase (which frequently may be quite mild and of but a few days' duration) generally becomes manifest by recurrence of fever, moderate soreness of the throat and enlargement of some of the lymph nodes. It is usually at this time that in addition to the symptoms just mentioned, arthritis, carditis or acute hemorrhagic nephritis may also appear.

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Postscarlatinal nonsuppurative arthritis has been roughly divided into two groups on the basis of severity, the severer grades having been termed "rheumatism," and the more common, milder forms "serous synovitis." Both forms may simulate the arthritis seen in rheumatic fever, the serous type recalling in particular the mild forms of arthritis or periartthritis characteristic of juvenile rheumatic fever. Arthritis of both types is said to occur in about 6 to 10 per cent of all cases of scarlet fever (3, 4). The incidence seems to be greater in some epidemics of scarlet fever than in others and to increase with the age of the patient. Thus, according to Weaver's statistics (3), only 2.2 per cent of patients develop postscarlatinal arthritis in the first decade of life, whereas the incidence is 4.5 per cent in the second decade, and 13.3 per cent in the third.

Estimates with regard to the usual per cent of patients who develop residual heart disease following scarlet fever are much more difficult to obtain. Convincing data of this kind are scanty because they should be derived from large series of scarlet fever cases which have been followed for at least one or two years. The importance of prolonged observation is based upon the fact that the so-called allergic type of postscarlatinal carditis may become manifest rapidly or not until many months have elapsed, which is again similar to the manner in which indisputable rheumatic carditis develops following an upper respiratory infection.

Nevertheless, many estimates on the incidence of various cardiac lesions during or following scarlet fever have been reported and warrant mentioning. Transient cardiac murmurs appear frequently during the acute or early convalescent stage of scarlet fever, and are said to occur in from 18 to almost 50 per cent of the cases (5). The significance of such murmurs is unknown, although when accompanied by abnormalities of the pulse most of them have been considered as manifestations of actual, although temporary, myocardial damage of the so-called toxic type. Evidences of myocarditis of this and other forms have been described in about 5 per cent of cases of scarlet fever (6). As for the incidence of endocarditis it has generally been placed at less than 0.5 per cent (6, 7, 8). If this is correct postscarlatinal heart disease differs from rheumatic heart disease in at least one respect, namely, that in clinical rheumatic heart disease endocarditis is present in the great majority of cases.

As for the association between carditis of any kind and arthritis following scarlet fever, the great difference between the total incidence of the two, has led to the belief that such an association is infrequent. This conception is held in spite of the fact that the converse of the above situation is altogether different, in that it has been stated that about half the patients with postscarlatinal endocarditis or pericarditis have suffered also from postscarlatinal arthritis (9). It is in evaluating such data that we would again point out that owing to the lack of adequate follow-up studies upon patients who have sustained postscarlatinal arthritis there is little information as to the number who eventually develop carditis.

Some have considered postscarlatinal rheumatism and so-called allergic carditis to be more or less specific manifestations or complications of scarlet fever, though perhaps distinct from the toxic lesions of the disease. Their views find expression in the majority of text-book articles on scarlet fever which we have consulted. They agree, however, that if a patient, who has previously had rheumatic fever, sustains an attack of scarlet fever, the chances of his developing postscarlatinal arthritis are greatly enhanced, and under these circumstances the clinical picture more nearly corresponds

to that of rheumatic fever. Others do not recognize this distinction and believe that the majority of cases of postscarlatinal rheumatism and carditis, with or without a previous history of rheumatic fever, may be better regarded as rheumatic fever "activated" perhaps by scarlet fever in the same manner in which other streptococcus infections are prone to do this in a patient who either has "latent" rheumatic fever, or (for want of a better term) a rheumatic diathesis (10, 11, 12, 13).

The major purpose of this study is to test the adequacy of the two views above quoted, by approaching the problem from the standpoint of familial epidemiology. Experience has shown rheumatic fever to be a disease in which the familial incidence is high (14, 15, 16). Consequently it has seemed important to determine whether or not this high incidence of rheumatic fever exists in the families of those who sustain postscarlatinal arthritis or carditis. Such an investigation should also shed some light on the circumstances under which these sequelae of scarlet fever develop. Our aim therefore is to answer the question as to whether the acquisition of arthritis or carditis following scarlet fever is ubiquitous, or whether it represents the manner in which a patient with familial "rheumatic tendencies" may react to scarlet fever.

METHODS

The family approach. The idea of considering the family as a unit through which disease may spread is a concept which has proved of increasing value in the study of human disease. Its value is based on the fact that in the family, common hereditary and environmental conditions exist in a group of individuals living in intimate contact with one another, who are generally quite conscious of their group life. In studies on the spread of tuberculosis within families, this approach has been emphasized by Opie and his collaborators (17), and it is to the latter work we are particularly indebted for our methods. In a previous study by two of us (18) on the spread of rheumatic fever through families a more detailed outline of the methods which are used in the present paper has been presented.

Source of families and methods of study employed. The patients whose families were enrolled in this study were drawn from the Pediatric and Medical wards, and from the Dispensary Clinics of the New Haven Hospital. All of them lived in the City of New Haven or its environs. It was our object to restrict the group to some extent to those families which had utilized the Dispensary as their "family doctor," and whose members had visited it from time to time for trivial illnesses as well as those of a more serious nature. The records of some of them covered a period of twenty years. Occasionally it was necessary to draw upon the records of other hospitals or of private physicians to fill certain gaps.² Most of the families described in this paper, including the control groups, were selected at some time between 1928 and 1932. Subsequent to their selection they were visited at least once a year and, at the time of the visit,

² We are indebted to the Superintendents of Grace and St. Raphael Hospitals for the privilege of examining some of their medical records and also for the information generously supplied by many New Haven physicians, whose number is too great to warrant mentioning them individually.

histories were taken and all available members were examined. If any member of the family happened to be under the care of a practicing physician, the physician was either seen personally or called on the telephone in order to explain our reason for questioning or examining his patient.

We believe that this type of family study is necessary if one is to determine even with rough accuracy the familial incidence of rheumatic fever. It is not enough to ask a parent or child whether other members of the family have had "rheumatism," "St. Vitus dance" or "heart disease," or even scarlet fever, for the information thus obtained is apt to be very different from that obtained by a personal talk with each member, a physical examination with particular attention to the heart, and a careful perusal of his or her previous medical records when available. We also believe that the value of such determinations of familial incidence is greatly enhanced by the inclusion of a reasonable number of control "non-rheumatic" families.

In the course of the work the assistance of social workers and members of the New Haven Visiting Nurse Association have been utilized for making appointments and for gathering non-medical data, but all visits for ascertaining data on the health of the family were made by one of us.

Nomenclature and diagnostic criteria. The term *rheumatic fever* hardly requires definition, but has been employed by us to designate any of the manifestations which, we believe, have represented a period of activity of the disease in question. Thus acute or subacute arthritis, active endocarditis, myocarditis, and pericarditis, Sydenham's chorea, otherwise unexplained fever and malnutrition, frequent nose-bleeds, etc., have all under certain circumstances been considered as manifestations of active rheumatic fever in this report.

The term *postscarlatinal arthritis* or *rheumatism*, as previously stated, has been employed to designate those examples of nonsuppurative arthritis in which joint pains of moderate severity, with or without demonstrable swelling of the joints, occurred over a period of several or more days, and began within one to four weeks following the onset of scarlet fever. Similarly in the diagnosis of *postscarlatinal carditis* we have included those cases in which active valvular, myocardial or pericardial lesions of the heart (exclusive of acute bacterial endocarditis or suppurative pericarditis) were manifest within a similar period from the onset of scarlet fever. Cases in which the only evidence of possible myocarditis consisted in the presence of transient murmurs, which may or may not have been accompanied by a brief period of tachycardia, were not included; nor were those cases included which did not develop clear-cut cardiac lesions until months after their attack of scarlet fever.

Charting results. A chart was designed for each family similar to the type which has been used routinely during the past five years for recording data on patients admitted to the Medical Rheumatic Fever Clinic and the Pediatric Cardiac Clinic of the New Haven Dispensary. The type of chart employed, together with a brief explanatory note is shown in Figure 1. It is constructed to represent the life history of the family, and the time relationships within the family between incidents with which we have been concerned.

Selection of families. Four groups of families were selected.

Group A. *Control* families chosen because one of the members, who did not present any signs of having had rheumatic fever or postscarlatinal rheumatism or carditis, and did not give a history of having had any of the manifestations of these conditions, was attending either the General, or one of the special Pediatric Clinics. This group totalled 16 families; 9 were chosen from the

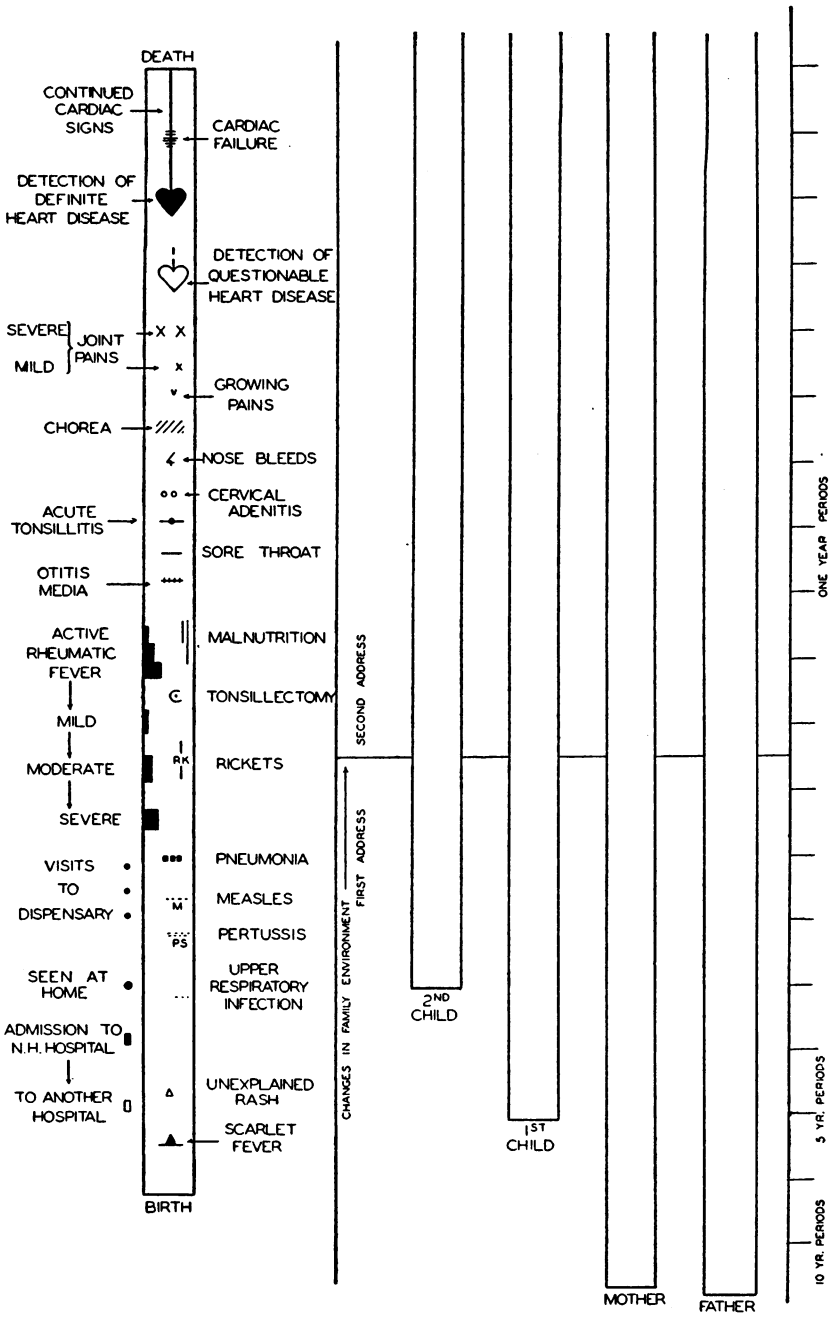


FIG. 1. CHART FOR RECORDING FAMILY DATA

On the right of the figure the age of the group starting with the birth of the parents has been marked in periods of years. The life span of each individual is designated by vertical columns enclosing a space for the chronological tabulation of illnesses and other pertinent events. On the left of the figure are shown the legends for designating these illnesses and events.

General Clinic, 4 from a Clinic for mentally defective or backward children, and 3 from the Syphilis Clinic.³

Group B. *Control scarlet fever* families chosen because one of the members, attending the General Pediatric Clinic, had not had rheumatic fever but was known to have had scarlet fever without a subsequent attack of rheumatism or carditis. A special effort was also made in the selection of this group to include families in which several cases of scarlet fever had occurred besides the one which represented the basis on which the family was chosen.

Group C. *Rheumatic* families, chosen because one of the members either had, or was known to have had, one of the manifestations of rheumatic fever, the onset of which did not follow an attack of scarlet fever.

Group D. *Postscarlatinal rheumatism or carditis* families, chosen because in one of the members the onset of rheumatism or carditis had followed immediately upon an attack of scarlet fever.

The families were also chosen so that the ages of individual members in each of the four groups would be about the same. Thus in all groups about 70 per cent represented individuals under 20 years of age, and 40 per cent under 10 years.

From the family charts (similar to those shown in Figures 2 and 3) the incidence of various manifestations of rheumatic fever was determined in the case of members other than the one who represented the basis on which the family had been selected. Of course in assembling these incidence determinations no examples of frank postscarlatinal rheumatism or carditis were listed as examples of rheumatic fever.

RESULTS

The rheumatic background of individuals who develop postscarlatinal rheumatism or carditis. Our aim, as already stated, has been to obtain a more adequate past and family history from patients who have sustained postscarlatinal rheumatism or carditis, by going to the patient's family and by determining whether or not a high incidence of the manifestations of rheumatic fever could be detected in the other members. An interpretation of this incidence determination can be made only when it is compared with similar incidence determinations from the control groups. These appear in Table I. In the control group A the total incidence of individuals who at any time in their life had shown manifestations of rheumatic fever, was 4.3 per cent. This is a little higher than the incidence (2.9 per cent) found by Faulkner and White (15) in a group of normal families in which an intensive search for the manifestations of rheumatic fever was also made. A considerably higher familial incidence of rheumatic fever manifestations (12 per cent) was found in our control scarlet fever families (Group B). One possible explanation of the high figure in this group is

³ Originally included in this group were a number of families selected from the Tuberculosis Clinic. Somewhat to our surprise we found a high incidence of rheumatic fever in these so-called tuberculous families, quite out of proportion to the incidence in the other control families. We believe this fact deserves further study and for that reason the attempt will not be made to include them in this paper.

TABLE I
The rheumatic background of individuals who develop postscarlatinal rheumatism or carditis

Type of family	Num-ber of fam-ilies	Num-ber of indi-viduals*	Per cent of those examined showing:				Any manifes-tation of rheu-matic fever. Total of I, II and III
			I. History of one or more attacks of rheumatic fever without heart disease	II. History of one or more attacks of rheumatic fever with suspicious rheumatic heart disease†	III. Definite rheu-matic heart dis-ease with or with-out a history of rheumatic fever	Any manifes-tation of rheu-matic fever.	
A. Control families from general and special pediatric clinics...	16	92	0	0	4.3	4.3	
B. Control scarlet fever families.....	19	100	6.0	3.0	3.0	12.0	
C. Rheumatic fever families.....	47	297	7.2	4.6	9.0	20.8	
D. Postscarlatinal rheumatism and carditis families.....	12	58	8.6	6.9	20.3	35.8	

* This includes all members of the family who were interviewed and on whom a physical examination was performed, exclusive of that member who represented the basis on which the family was chosen.

† This represents the occurrence of one or more attacks of rheumatic fever in a patient who showed a systolic murmur, which might under other circumstances be interpreted as a functional murmur.

suggested below. The incidence of rheumatic heart disease in the control groups (A and B) was found to be between 3.0 and 4.3 per cent, which is about the same, or a little above, that found by Cohn (16) in his assembled figures obtained by different observers from control families in the North-eastern part of the United States. In the rheumatic families (Group C) the incidence of heart disease also closely approaches that given by Cohn, namely: 8 to 10 per cent, and recalls the observation of St. Lawrence (14), that the familial incidence of rheumatic fever simulates the familial incidence of clinical tuberculosis. In our postscarlatinal rheumatism families (Group D), the highest familial incidence of rheumatic heart disease, and of the total rheumatic manifestations was recorded, the latter being 35.8 per cent.⁴

Although our D Group is a small one on which to draw final conclusions our interpretation of these results is that many examples of postscarlatinal rheumatism or carditis either represent a lighting up of a previously unsuspected, latent or sub-clinical form of rheumatic fever, or represent the manner in which an individual possessed of a "rheumatic diathesis" may react to scarlet fever. Furthermore, if this implication is correct, namely

⁴ A theoretical correction might be applied to this figure (35.8 per cent) representing as it does the per cent of individuals in Group D who at any time had shown evidence of rheumatic fever. Some of these individuals sustained attacks of arthritis or carditis following *Scarlatina sine exanthemate*, in which the scarlatinal nature of the infection was not detected because of the absence of the rash. Such attacks owe their identification to the fact that they occurred coincidentally with one or more cases of scarlet fever in other members of the family. Five attacks of this type occurred among members of Group D, two of which occurred in individuals who had suffered from rheumatic fever prior to their attack of *Scarlatina sine exanthemate*. Theoretically all these attacks might be considered as examples of "specific scarlet fever rheumatism or carditis," and consequently should not be listed as examples of rheumatic fever. Their elimination would reduce the incidence figure of the total manifestations of rheumatic fever in Group D from 35.8 to 26.2 per cent—a figure which is still well above that found in the Group C rheumatic fever families.

FIG. 2

A family in which three members had sustained definite attacks of rheumatic fever prior to the occurrence of three cases of scarlet fever in January 1932. All of these cases of scarlet fever were followed by rheumatism. The youngest boy Arthur, who unfortunately had not been examined before, but who gave no previous history of rheumatic fever, developed postscarlatinal rheumatism, associated with suspicious evidences of carditis. When seen 20 months later he had definite mitral insufficiency. The girl Hazel had previously developed aortic and mitral disease in association with an attack of chorea and joint pains at the age of 6. Following her attack of scarlet fever she sustained a severe "re-activation" of her carditis from which she subsequently died in the New Haven Hospital. The mother developed postscarlatinal rheumatism but has not shown evidences of a cardiac lesion. It is interesting to note that the father had also suffered from a severe attack of postscarlatinal rheumatism during adolescence.

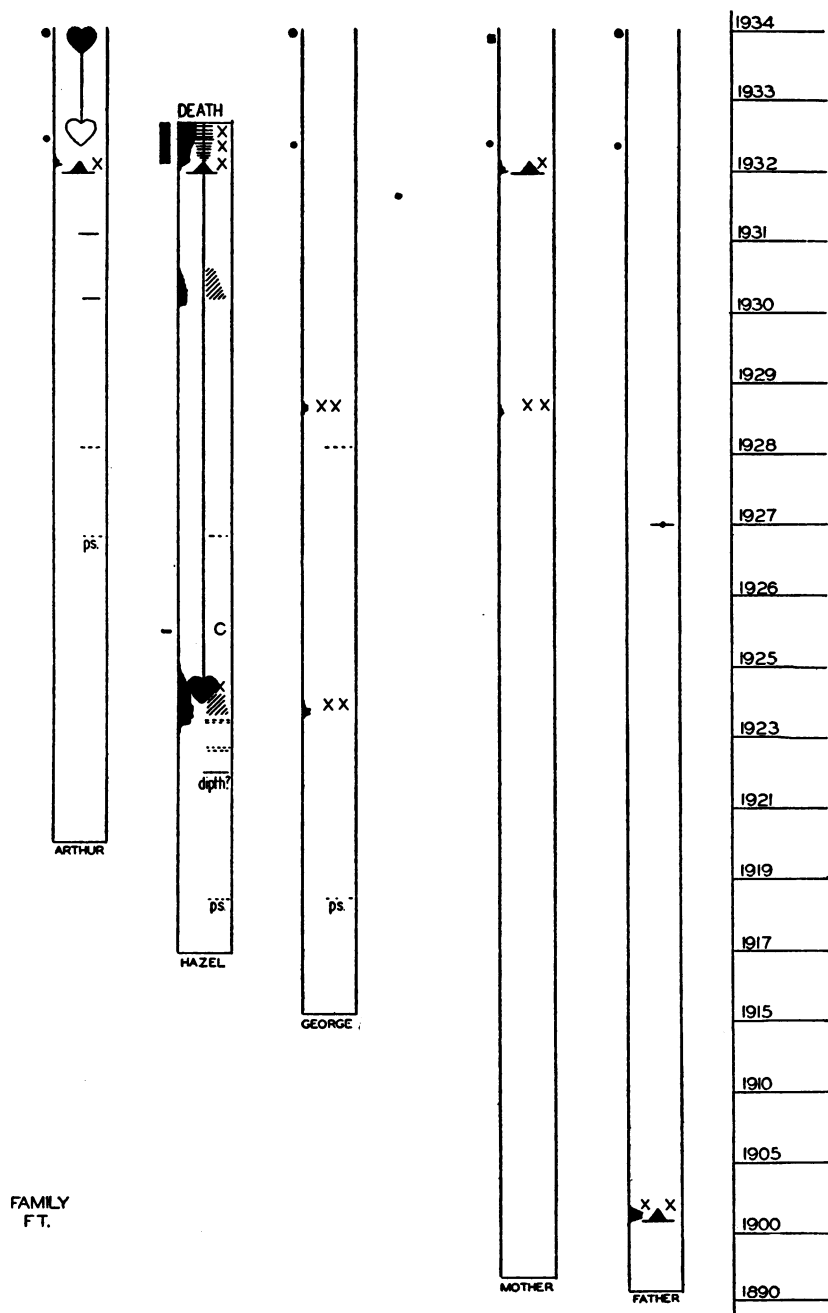


FIG. 2

that the patient who develops postscarlatinal rheumatism comes from a "rheumatic background," it is not surprising that the highest incidence of the manifestations of rheumatic fever should occur in our Group D, for in this group we would have a combination of two factors thought to be of significance in producing the disease rheumatic fever, namely—(i) a rather severe and contagious type of streptococcus infection; and (ii) a "rheumatic background." The presence of the first factor in Group B might also explain why the incidence of rheumatic fever is higher in this group than in the control group A in which both factors are hypothetically absent. The term "rheumatic background" demands some explanation. It has been used to express the idea that the patient comes from a family in which rheumatic fever is known to be present. It may or may not be analogous to the term "rheumatic diathesis," or to Swift's "hyperergic state," (19) or to Coburn's "rheumatic state" (20); all of which represent terms expressive of the major underlying obscure feature of the disease known as rheumatic fever. As the nature of this state is not known, and as it is impossible to measure the relative extent which hereditary or environmental factors play in producing it, the use of a broad or even vague term such as "rheumatic background" to express this idea seems to us at present to be the one of choice for the purpose of the present discussion.

As another means of testing this theory, namely, that if patients who develop these scarlatinal sequelae do so as an expression of this "rheumatic background," it should follow that when multiple cases of scarlet fever occur within families possessing this background, one might expect them to be followed by multiple cases of rheumatism and carditis. That such situations occur is shown by two families taken from Group D, which appear in Figures 2 and 3. Both of these families sustained epidemics of scarlet fever to be followed by multiple cases of rheumatism and carditis, but it will be noted that in both families rheumatic manifestations had been recognized in at least one member prior to the appearance of the epidemic of scarlet fever. It is possible that almost all of the members had previ-

FIG. 3

This family had recently moved to New Haven and, although first hand records of past illnesses were not available, they had previously been under the care of several physicians, and were quite cognizant of the types of illness which members of the family had sustained. Both the father and mother now have rheumatic heart disease and several of their respective siblings had also had rheumatic fever. No evidences of rheumatic fever were thought to exist in the children prior to the appearance of scarlet fever in this family in February 1931. The three cases of scarlet fever which occurred at this time were followed by rheumatism and carditis in the child Rita; by rheumatism in the child Lawrence, who now presents a systolic murmur at the cardiac apex which may be a "functional" murmur; and by a "reactivation" of rheumatism in the mother. It is possible that the mother may have had heart disease prior to 1931 although she believed that it developed after her attack of scarlet fever.

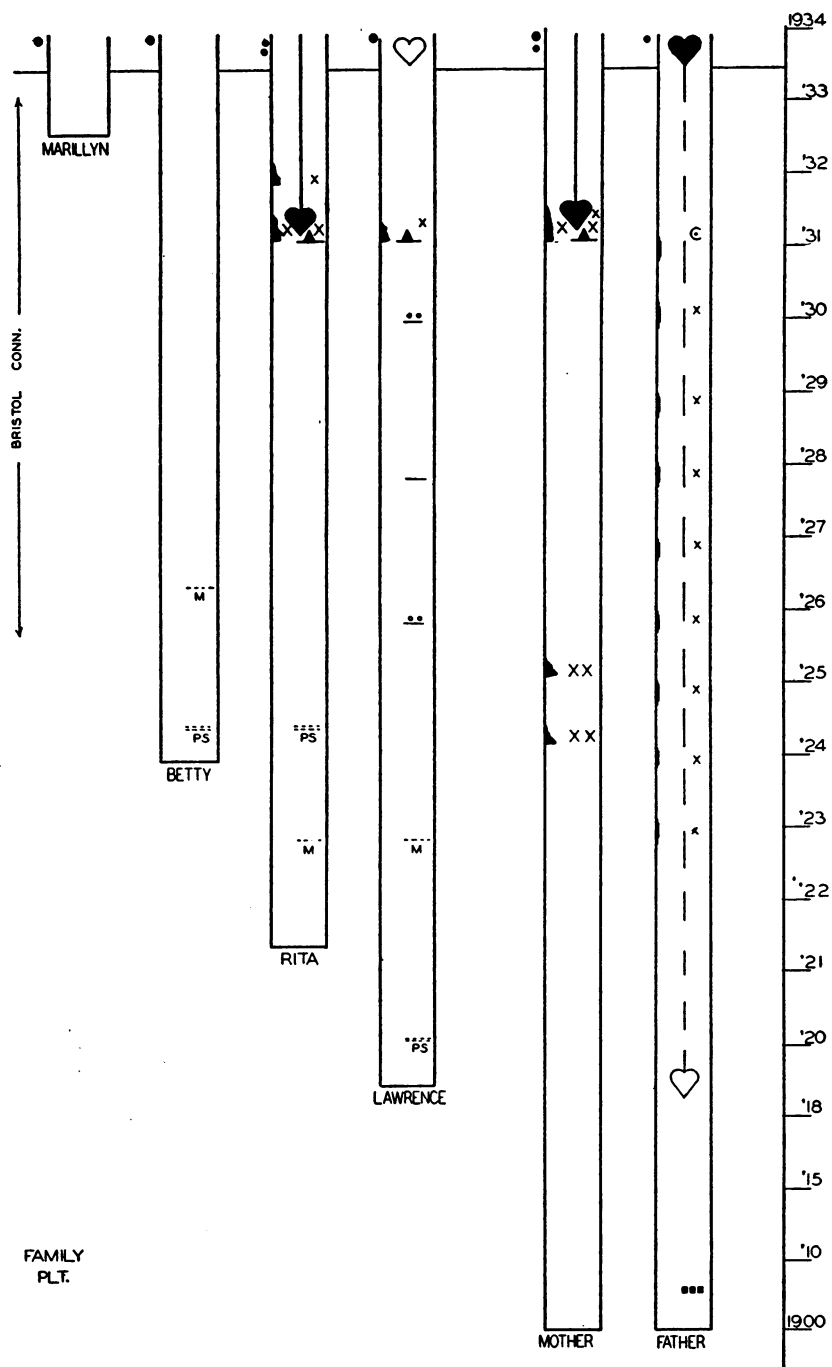


FIG. 3

ously had mild and unrecognized rheumatic fever. This, as we have already intimated, would seem to be quite likely because, although "primary" cases of postscarlatinal rheumatism are common enough, yet we have observed no instances of this occurring in several members of the same family; or, in our own limited experience, we have never seen a familial epidemic of three or four cases of scarlet fever all complicated by "primary" rheumatism. To illustrate this point further let us take the child Arthur in Figure 2. When viewed individually, his case appears as an example of "primary" postscarlatinal rheumatism followed by postscarlatinal carditis. When viewed in relation to his family, his case might be better classified as rheumatic fever. The same feature holds true for the children Rita and Lawrence in Figure 3.

The frequency with which the situations shown in Figures 2 and 3 occurred, has been roughly determined in Group D, and has been compared with similar information derived from the control scarlet fever families (Group B). This comparison revealed the fact that those members of the Group D families, who sustained an attack of scarlet fever, developed rheumatism or carditis as a complication at a rate which was higher by almost three times than that which occurred after scarlet fever in the families of the Group B controls. It was evident, however, that the high rate of postscarlatinal complications in Group D was due, or at least associated with, the fact that many of the members of these families had sustained frank attacks of rheumatic fever prior to their acquisition of scarlet fever.

DISCUSSION

There are, obviously, obscurities which cloud the results of the comparative study presented in this paper, and not the least of these is the fact that we have compared two poorly-defined clinical entities. For, as the clinical limits of rheumatic fever are ill-defined, so also are the clinical limits of scarlet fever, and there is small wonder that an attempt to define their mutual relationships leads to difficulties. Nevertheless, added to the evidence which exists in medical literature that, in spite of minor differences, the clinical course of postscarlatinal rheumatism and carditis is essentially similar to that of rheumatic fever (11, 12, 13), and that some of the myocardial lesions of postscarlatinal myocarditis are similar to those of rheumatic fever (10, 21, 22, 23), there appears to be still another similarity in so far as the family histories of patients suffering with these conditions are concerned, namely, the familial incidence of rheumatic fever is high in both groups. This last finding has distinct bearing on the crux of the supposed differences between the two conditions, because, as has been already mentioned, if a patient, who has previously had rheumatic fever, sustains an attack of scarlet fever which is followed by rheumatism or carditis or both, these complications are generally regarded as recurrences of rheumatic fever; whereas, if a patient sustains these postscarlatinal com-

plications in the absence of a previous history of rheumatic fever, the conditions under these circumstances have been regarded by some as another form of rheumatism or carditis perhaps specifically allied to scarlet fever. The difficulty in accepting this latter interpretation lies in the fact that it owes its validity to a negative history for rheumatic fever. It disregards the fact that a negative history may be of questionable value, at least as far as the so-called subclinical forms of rheumatic fever are concerned; for the frequency with which one encounters cases of rheumatic heart disease in individuals who fail to give a history of rheumatic fever, bears witness to the frequency with which the manifestations of this disease lie below the clinical horizon. It has been shown in this paper that knowledge of the background of individuals who have sustained an attack of postscarlatinal rheumatism may be supplemented by data obtained from the patient's family, and the high familial incidence of rheumatic fever existing in these families suggests that after all, many cases of so-called postscarlatinal "primary" rheumatism or carditis may not be as "primary" as was once supposed. When viewed from this aspect the actual differences between many cases of postscarlatinal rheumatism and rheumatic fever approach the vanishing point.

It is to be emphasized, of course, that we do not maintain that every case of nonsuppurative arthritis or carditis following scarlet fever is necessarily a manifestation of rheumatic fever. In fact this would be quite unlikely. However, it would seem that a greater percentage, at least, of these postscarlatinal complications should fall into the rheumatic fever group than has hitherto been placed in this category. Nor does our interpretation carry with it the idea that scarlet fever and rheumatic fever are one and the same disease, but rather it again emphasizes the dual nature of factors which are responsible for the obscure condition known as active rheumatic fever, consisting as it does of an underlying rheumatic "diathesis" or "state," which is apparently activated or brought to the surface by an acute infection.

CONCLUSIONS

The families of patients who have sustained an attack of postscarlatinal nonsuppurative arthritis or carditis have been carefully investigated and a high incidence of the manifestations of rheumatic fever has been found. This would support the view already held by some other observers, that it is not necessary to postulate that most of these scarlatinal sequelae are "specific" complications of scarlet fever. Under the broad view which is taken today of rheumatic fever, they may be more easily explained as manifestations of rheumatic fever "activated" by a *Streptococcus hemolyticus* infection, and whatever the actual pathogenesis of rheumatic fever may be, the mere presence of scarlatinal toxin in the blood and a rash during the initial infection does not seem to alter the process fundamentally.

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