THE NATURAL HISTORY OF ACUTE RHEUMATISM

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This paper presents an analysis of 1,033 cases of acute rheumatism and chorea followed until death or for 5 to 40 years after the onset. 56 of the patients died within 5 years of the onset, but of the remaining 977 the average follow-up was nearly 12 years; 451 were traced for more than 10 and 108 for more than 20 years. The majority of the first attacks (644/1033) occurred between the ages of 6 and 10. In 163 cases the age at onset was 5 or under and in 215 it was 11 to 15 years. These features are in accordance with previous observations.

Clinical Features of the First Attack

Accurate information was available in 1,006 cases (406 boys and 600 girls). This male to female ratio of 1:1.5 is higher than in some other recorded series. For instance, Roth, Lingg, and Whittemore (1937) in the U.S.A. reported almost equal numbers, and Wilson (1940) and Ash (1948) both reported 1:1.2. In fact the sex incidence in the present series is much closer to that found in Cairo by Abdin and Eissa (1965), which was 1:1.7. Part but not all of this difference was due to the higher incidence of chorea amongst the girls. Only 63 (15 per cent.) of the 400 boys as opposed to 184 (30 per cent.) of the 606 girls had chorea either alone or in combination with some other manifestation, *i.e.* arthritis and/or carditis, in the first attack. The incidence of chorea in girls was thus twice that in boys. This is a much greater difference than recorded by Roth and others (1937), who found chorea one and a half times as common in girls as in boys, and by Wilson (1940), who found chorea in 25 per cent. of the boys and 30 per cent. of the girls. But even if all cases with chorea in the first attack are excluded, we are left with 337 boys and 422 girls, still a considerable preponderance of girls.

In all, 1,766 attacks or recurrences were studied in the 1,033 patients. The clinical features of the first attack were arthritis alone in 15 per cent., chorea alone in 12 per cent., and carditis with no other recognized manifestation in 14 per cent. Recognizable carditis occurred in 72 per cent. In all, 628 exhibited arthritis and in 478 of these there was an associated carditis. Chorea was seen in 257, of whom 107 had carditis. Arthritis and chorea occurred in the same episode in 31 (3 per cent.), but in each case the chorea followed the onset of arthritis by some weeks and in none did the two coincide. Thirteen (just over 1 per cent.) of the patients exhibited an episode of cardiac failure in the first attack.

Turning to less common manifestations, subcutaneous nodules were observed in 89 first attacks (just over 8 per cent.) and erythema marginatum in only 26 (just under 3 per cent.). These percentages are set out in Table I.

TABLE I
CLINICAL FEATURES OF FIRST ATTACK OF ACUTE RHEUMATISM (per cent.)

Features		Boys	Girls	Total
No carditis	Arthritis	18	13	15
	Chorea	6	15	12
	Arthritis and chorea	1	1	1
	Total with no carditis	25	29	28
Carditis	Carditis	15	13	14
	Arthritis and carditis	50	42	45
	Chorea and carditis	8	13	11
	Arthritis, chorea, and carditis	1	3	2
	Total with carditis	74	71	72
Other	Nodules	11	6	8
	Erythema marginatum	2	3	2

Mortality

Of the total, 99 (nearly 10 per cent.) were dead at the time of follow-up; eight of these died within 1 year of the onset (0.8 per cent.), another 35 within 5 years (4.3 per cent.), and another twenty within 10 years, making a total of 15 per cent., of those followed for so long. Wilson (1940) recorded a death rate of 1.8 per cent. in the first year, 10 per cent. in 5 years, and 29 per cent. in 10 years. Ash (1948) found 7 per cent. dead in the first year, 16 per cent. in 5 years, and 24.4 per cent. in 10 years. Schlesinger (1938) recorded 12 per cent. dead in a varying period up to 10 years, and Bland and Jones (1951) reported 12 per cent. dead in 5 years and 20 per cent. in 10 years. It is thus clear that the greatest mortality, as found by Findlay (1931), still occurs in the first few years after the onset, 8 per cent. of the total deaths occurred in the first year, 43 per cent. within 5 years, and 63 per cent. within 10 years. This may be compared with two sets of figures from the U.S.A., where Bland and Jones (1951) found 62 per cent. and Ash (1948) 74.1 per cent. of their deaths occurred in the first 5 years. Wilson and Lubschez (1948) also found the highest mortality within a year of the onset; the death rate for every 1,000 cases at risk per year was high in the first 5 years, and then tended to fall but rose again 20 to 40 years after the onset. This gives some support to Findlay's statement that there are two peaks of mortality, one at the age of 10 to 15 and the other at the age of 35 to 45. In 68 (about two-thirds) death occurred from active carditis, in eleven from subacute bacterial endocarditis, in nineteen from heart failure, and in two from peripheral emboli; in eleven the precise cause of death was unknown. The main causes of death, as might be expected, changed with the passage of time. In the first 10 years the vast majority died of active carditis, from 6 to 15 years after the onset subacute bacterial endocarditis was present as a cause of death, and after 10 years congestive cardiac failure began to appear. These findings are set out in Table II.

TABLE II
PRINCIPAL CAUSES OF DEATH IN CASES OF ACUTE RHEUMATISM

Time from Onset (yrs)	Total	Acute Attack	Subacute Bacterial Endocarditis	Congestive Cardiac Failure
Less than 1	8	8	—	—
1-5	35	26	1	1
6-10	20	9	6	2
11-15	19	6	4	7
16-20	5	1	—	3
21-25	4	—	—	4
26-30	3	—	—	2

Effects on the Heart

When last seen 439 (43 per cent.) had a clinically normal heart (Table III). Thus, a number with carditis in the acute phase finally made a complete clinical recovery. 41 (4 per cent.) had a cardiac murmur of doubtful significance, 513 had mitral murmurs (51 per cent.), and 141 (14 per cent.) aortic murmurs. It is interesting to note that there was a higher incidence of aortic involvement in boys than in girls; 19 per cent. of the boys were left with an aortic murmur and only 10 per cent. of the girls. When apparently isolated aortic lesions are considered, there were thirteen boys and only three girls.

TABLE III
HEART CONDITION WHEN LAST SEEN (per cent.)

Heart Condition	Boys	Girls	Total
Normal heart	47	42	43
Doubtful murmur	3.5	4.5	4
Mitral valve lesion	50	53	51
Aortic valve lesion	19	10	14

This curious sex distribution of aortic valve involvement has been pointed out before (Perry, 1938). Mitral stenosis is usually found to be commoner in females than in males. When last seen few of the patients had a pure presystolic murmur (5 per cent.) but this was rather more than twice as frequent in the females than in the males (6 and 3 per cent. respectively).

Only 35 of the patients had developed atrial fibrillation at an average time of about 20 years after the first attack (17 per cent. of those followed for 20 years). 28 developed subacute bacterial endocarditis (5 per cent. of those followed for 15 years), one boy having three attacks. The average time at which this complication occurred was 15 years after the initial attack. The risk of this complication remained fairly constant at 0.1 to 0.2 per cent. of those at risk per year. This may be compared with the calculation of Cosh (1957) that the incidence of bacterial endocarditis in patients with patent ductus arteriosus was about 0.4 per cent. per year. Ten (1 per cent.) had been submitted to surgery.

Cases Analysed according to Time of First Attack

In view of the well-recognized decrease in incidence and apparent severity of the disease during the 20th century the cases were divided into four groups. Those whose first attack occurred before 1939, those whose illness started between 1939 and 1945 during the war, those starting in the 10 years following 1945, and those starting after 1955 when an intensive

campaign for prophylaxis of recurrences was initiated (Table IV). This analysis confirms the change in the character of the disease during this period. Of the 528 cases in the period up to 1938, carditis was recognized in the first attack in 80 per cent. There were 187 cases during the second period, when the incidence of carditis was 66 per cent. In the next period there were 223 cases with carditis in 59 per cent., and in the final period 68 cases with carditis in 55 per cent. There was a reciprocal rise in the incidence of uncomplicated arthritis from 8 to 36 per cent. The other striking feature is the marked fall in the incidence of chorea from 28 per cent. before 1939 to 13 per cent. after 1955. The prognosis correspondingly improved. Of those whose illness started before 1939 12 per cent. died and 67 per cent. had established heart disease, whereas the relative figures for those starting after 1955 was 0 and 9 per cent. (Table V). It is thus clear that parallel with the decrease in incidence there has been a striking fall in severity. This decline in severity probably accounts for the lower mortality rate in the series as a whole as compared with the other reports which have been quoted.

TABLE IV
CLINICAL FEATURES OF FIRST ATTACK OF ACUTE RHEUMATISM AT FOUR DIFFERENT PERIODS OF TIME (per cent.)

Time of Onset		Before 1939	1939-46	1947-54	1955-62
No carditis	Arthritis	8	14	26	36
	Chorea	10	17	11	5
	Arthritis and chorea	2	2	2	3
	Total with no carditis	20	33	39	44
Carditis	Carditis	18	14	6	5
	Arthritis and carditis	46	43	46	45
	Chorea and carditis	15	8	5	3
	Arthritis, chorea, and carditis	1	1	2	2
	Total with carditis	80	66	59	55
Total with chorea		28	28	20	13

TABLE V
HEART CONDITIONS WHEN LAST SEEN, BY PERIOD OF ONSET (per cent.)

Period of Onset	Before 1939	1939-46	1947-55	After 1955
Normal heart	29	40	60	82
Doubtful murmur	2	4	7	7
Established heart disease	67	49	38	9
Dead	12	7	5	0

Prognosis related to Clinical Features of Initial Attack

Age at Onset

163 had their first attack at the age of 5 or less (15 per cent.), 644 between the ages of 6 and 10 (63 per cent.), and 215 (21 per cent.) between the ages of 11 and 15. The age at onset surprisingly did not influence the death rate significantly, the figures for the three groups being 8, 9, and 11 per cent. respectively. However, the outlook as regards recovery with a normal heart was marginally better for those with a late onset (42 per cent. as against 36 per cent.). This conforms with the view of Cohn and Lingg (1943) that the later the age at onset the fewer the cases of carditis.

Clinical Manifestations

ARTHRITIS AND/OR CHOREA.—Those whose first attack was characterized by arthritis and/or chorea with no evidence of cardiac involvement fared better than those with clear evidence of carditis in the initial illness. Thus 211 of the 274 (77 per cent.) with no clinical carditis had normal hearts when last seen, but 18 per cent. (50) had developed established heart disease.

CARDITIS.—Many of the patients with clear-cut carditis in the acute attack, 217 out of 701 (30 per cent.), had lost all signs of heart disease when last seen. Many of these, of course, lost their abnormal cardiac physical signs on recovery from the acute attack. But even those who after recovery from the acute attack had signs of mitral or even aortic valve disease might finally lose all clinical signs of heart disease—129/613 (21 per cent.). This disappearance of physical signs of heart disease was perhaps first noted by Coombs (1924), who found that of 44 cases of definite carditis the signs of disease disappeared in fifteen (34 per cent.) over a period of 10 years. Similarly, Bland and Jones (1951) found that, of 653 patients who after recovery from the initial attack had unequivocal signs of heart disease, 108 (16 per cent.) had clinically normal hearts after 20 years. Conversely, those with clinically normal hearts after the first attack might finish with heart lesions 67/387 (17 per cent.) or even be dead 10/387 (nearly 3 per cent.).

SUBCUTANEOUS NODULES.—These occur late in the attack and as long as 4 to 8 weeks or more after the initial manifestations; they were observed in 172 of the total 1,766 attacks (just under 10 per cent.). They occurred more frequently in boys (13 per cent.) than in girls (8 per cent.). The fell significance

usually attributed to the appearance of nodules probably dates from Cheadle's statement in his lectures to the Harveian Society in 1889 to the effect that he regarded "the eruption of large nodules as almost equivalent to a sentence of death". In the present series nodules were never recognized in uncomplicated chorea. In first attacks they were seen in 5 per cent. of the cases of arthritis, 8 per cent. of those with carditis, 12 per cent. of those with arthritis and carditis, 18 per cent. of those with arthritis, chorea, and carditis, but in only 2 per cent. of those with chorea and carditis. The picture was similar in recurrences, except that nodules became more common with each recurrence. So that although commoner in those with carditis nodules may occur when there is no clinical evidence of carditis. Massell, Fyler, and Roy (1958) found that 5 per cent. of the cases with nodules had no clinical evidence of carditis. The similar figure in this series was about the same, *i.e.* nearly 6 per cent. The serious significance of nodules, however, is shown by the fact that, of the 42 exhibiting congestive cardiac failure during an attack, 35 per cent. (15) had nodules. On the other hand, once the attack was over, the significance of nodules was not so serious. Nevertheless, of those with nodules in the first attack, 15 per cent. had died (compared with nearly 10 per cent. for the whole group), and only 38 per cent. had clinically normal hearts compared with 43 per cent. of the whole group.

ERYTHEMA MARGINATUM.—This appeared to have little effect on prognosis. It was seen in 58 of the 1,766 attacks observed (3 per cent.). It has been suggested that this rash occurs very frequently in association with nodules. Massell and others (1958) found that 29 per cent. of patients with nodules also had erythema marginatum. This is borne out in this series. Of the 58 patients seen with erythema marginatum, fifteen (25 per cent.) had nodules, the incidence for the whole group being 10 per cent. Conversely, of the 172 patients with nodules, fifteen (8 per cent.) had erythema compared with an incidence of erythema of 3 per cent. for the whole group.

PERICARDITIS.—As might be expected, the recognition of pericarditis was of serious import. In the 1,006 first attacks, pericarditis was recognized in 38 and of these fifteen died, a mortality of nearly 40 per cent. compared with just under 10 per cent. for all those seen in the first attack. In the total 1,766 attacks observed, pericarditis was recognized 85 times and of these forty were dead (46 per cent.).

Recurrences

It has long been recognized that one of the striking features of the natural history of acute rheumatism is the frequency with which recurrences occur. They may vary in severity from attacks of "miniature rheumatic fever" as described by Schlesinger (1938) to full-blown serious and even fatal attacks. It is this, of course, which explains the fact that so many of the patients recovering from their first attack with a clinically normal heart finally develop unequivocal evidence of established heart disease. In this series as a whole, only 552 (53 per cent.) escaped a recurrence and 81 per cent. of the second attacks occurred in the first 4 years after the onset. As might be expected, recurrences were commoner in earlier periods; thus in the group starting before 1939 only 44 per cent. had no recurrence, 32 per cent. had one recurrence, 14 per cent. two, 6 per cent. three, and 4 per cent. four or more. The comparable figures of the other periods are shown in Table VI, where the effects of the institution of an intensive campaign for prophylaxis in 1955 are especially noteworthy. In fact only one relapse has been seen among patients believed to be taking prophylaxis conscientiously. This incidence of recurrences is not as high in some reported series. For instance Wilson (1940) found that 85 per cent. of her patients had a recurrence within 8 years of the onset and Ash (1948) found 63 per cent. relapsing within 10 years (and 40 per cent. in the first 2 years). The main clinical features of the recurrences were the same as those of the first attack except for a rather higher incidence of carditis. Roth and others (1937) stressed the great importance of recurrences on the final outcome and Schlesinger (1938) drew attention to this problem in the Milroy lectures. Biörck (1955) also showed the rising incidence of valvular heart disease with each recurrence. This effect on the end-result is shown clearly by the fact that, of the 551 with no recognized recurrence, 303 (55 per cent.) recovered with no obvious heart lesion and only 4 per cent. were dead. Of the 282 with one recurrence only 34 per cent. had normal hearts and 12 per cent.

TABLE VI
INCIDENCE OF RECURRENCES RELATED TO DIFFERENT PERIODS OF ONSET OF ACUTE RHEUMATISM (per cent.)

Period of Onset		Before 1939	1939-46	1947-55	After 1955
No. of Recurrences	None	44	52	68	91
	One	32	28	20	6
	Two	14	12	8	3
	Three	6	5	3	—
	Four or more	4	3	1	—

were dead. After two recurrences the incidence of normal hearts fell to 27 per cent. and the death rate rose to 16 per cent. With three recurrences there were 9 per cent. normal hearts and 32 per cent. dead. The numbers for four or more relapses were small, but only 4 per cent. of these had normal hearts when last seen (Table VII).

TABLE VII
EFFECT OF RECURRENCES ON END-RESULT
(per cent.)

No. of Recurrences	Percentage of Whole Group	Dead	Established Heart Disease	Doubtful Murmur	Normal Heart
None	53	4	35	6	55
One	27	12	39	2	34
Two	12	16	64	2	27
Three	6	32	71	3	9
Four or more	2	34	88	—	4
			96		

The importance of recurrences in the causation of serious heart disease is shown also by the incidence of congestive cardiac failure during an acute episode. In first attacks congestive cardiac failure were recognized in 1 per cent., but in the fifth attack this figure had risen to 20 per cent.

Nature of Recurrences

Fairly recently Feinstein and Spagnuolo (1960, 1962) have drawn attention to the fact that recurrences of rheumatic fever tend to be mimetic and to repeat the features of the first attack. They claimed that if the first attack did not involve the heart subsequent recurrences were unlikely to do so. They further indicated that if their findings were confirmed it might be possible to recommend that long-term prophylaxis might be confined to those likely to develop heart disease. This is clearly of great importance. While the broad tendency for relapses to follow the pattern of the first attack may be conceded, most observers have not found it to be at all constant. Cheadle (1889) stated . . . "the combinations of the different phases of the rheumatic series may follow any order of sequence".

Jones and Bland (1935), studying 482 cases with chorea in the first attack, found that 72 per cent. exhibited other features of acute rheumatism within 8 years. Roth and others (1937) followed 149 children with polyarthritis who had no carditis in the first attack and found that 51 (34 per cent.) had a definite carditis in the second attack. It therefore

seemed desirable to study these mimetic features in more detail.

Of 55 children with uncomplicated arthritis in the initial attack who had a second attack, only 21 (38 per cent.) had a similar illness in the recurrence, whereas ten developed chorea (three with carditis) and a total of twenty-seven (50 per cent.) had carditis. The incidence of carditis in subsequent attacks rose, so that all five of the original 55 with a "benign" onset who had a third recurrence had carditis at this stage. A similar state of affairs holds for those presenting initially with simple chorea, although not so strikingly. Thus 67 of the 117 children with an initial onset of uncomplicated chorea had a recurrence. In 41 this was similar to the initial illness, but 26 developed carditis. In the case of those with recognized carditis in the initial illness, it is clearly often difficult to decide that no carditis occurs in a relapse unless, as may happen, all signs of heart disease have disappeared after the first attack. However, of the 298 patients whose initial illness involved the heart and who had a recurrence, eight were thought to have arthritis and eight chorea, each with no further carditis. So while there is a tendency for recurrences to follow the same pattern as the initial attack this is by no means constant. This is in accord with the findings of Kuttner and Mayer (1963), who stated that at least 25 per cent. of cases did not follow a repetitive pattern in recurrences. This can hardly justify withholding regular prophylaxis from any patient in whom a firm diagnosis of acute rheumatism is made.

Conclusions

The main conclusions to be drawn from this study is that one attack of acute rheumatism has a fairly good prognosis. Many patients who have unequivocal signs of cardiac involvement ultimately present no abnormal cardiac physical signs. The picture is, however, quite different when there are recurrences, and I therefore emphasize once again, if emphasis is necessary, the supreme importance of long-term prophylaxis for all patients who have had an attack of acute rheumatism, however mild it may seem to be.

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