A STUDY OF RHEUMATIC FEVER

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I N D E X

A STUDY OF RHEUMATIC FEVER

OBJECTIVES OF THE THESIS

It was decided to investigate the incidence of rheumatic fever in patients (up to, and including, the age of 21 years) admitted to the Western District Hospital, Glasgow, from the years 1950-1959 inclusive. As these cases alone would give a limited picture of the incidence of this disease, those available cases of rheumatic fever admitted from the Glasgow area to the Sick Children's Hospital, Yorkhill, Glasgow, were also studied over the same period. "Rheumatic Fever" is taken here to include cases of rheumatic arthritis and rheumatic chorea. The two will be sub-divided as necessary.

It has become an established fact that the incidence of rheumatic fever has been greatly affected by the advent of chemotherapeutic agents. However, it was felt that many other factors were also involved including the improvement in housing conditions, change in locality of the population (away from damp water-ways, etc.), the effect of rainfall, fog and frost. These factors will be discussed later.

The year 1952-1953 was a peak period for the occurrence of rheumatic fever, and it was decided to undertake a scheme of prophylaxis. An endeavour was made at the Western District Hospital, Glasgow, to prevent this disease recurring, by the use of /

of long-acting penicillin.

All patients, on recovering from an acute attack of rheumatic fever were allocated, by means of random selection, into one of two groups, A and B.

Group A received fortnightly injections of Benzethacil N.N'-Dibenzylethylenediamine Dipenicillin G. /"Penidural" Penicillin (Wyath)/ during the months of October to June each year.

Group B did not receive injections, but were instructed to attend at regular intervals, and they acted as controls.

The advantages, disadvantages and incidental factors which came to light during the investigation period will be described. In addition, a method of prophylaxis has been proposed, which appears to be effective when dealing with the modern "teen-age" patient.

The clinic had ultimately to be discontinued because firstly, the number of admissions of rheumatic fever (excepting those over the age of 21 years) to the Western District Hospital dropped to three in 1957 and one in 1959 - there were no admissions of such cases during 1958. Secondly, it was found impossible to retain the patients' interest in attending for injections.

The findings, and the conclusions reached, will be discussed in full.

CHAPTER I.

Introduction

A fleeting arthritis, accompanied by fever, has been a known clinical entity for many centuries. In what may perhaps be the earliest published account of rheumatic fever, Guillaume Baillou(1762) states that "..... when this disease attacks, a spontaneous lassitude precedes it and the blood is diseased, and indeed this is found to be the case, as was noted by Hippocrates. They are obviously sick as soon as they are attacked."

Attention was first drawn by David Pitcairn(1788) to the frequent association of heart disease and rheumatism, and a classic account is given by Charles Wells(1812) of several cases of rheumatic heart disease. The history of rheumatic heart disease will be discussed more fully in a later chapter in this work.

Ludwig-Aschoff(1904) gave the first clear description of the more or less specific rheumatic myocardial lesion which has since been called by his name (Aschoff body).

The role of the beta-haemolytic streptococcal infection of the naso-pharynx, and its relation to rheumatic fever was first clearly demonstrated by Coburn.(1931)

Further evidence relating the streptococcus to rheumatic fever developed when a great reduction in the incidence of the disease occurred /

occurred after treatment with antibiotic drugs came into general use. Since the introduction of these drugs, rheumatic fever in all countries has been steadily declining in incidence. Proof of this can be seen in the results of work done in this field by Massell(1957), Stollerman(1954), and Diehl et al(1958).

The introduction of penicillin prophylaxis will be discussed in a later chapter of this work.

CHAPTER II

Criteria of Diagnosis

The Jones' Criteria (Modified) for the diagnosis of rheumatic fever, which was accepted by the Committee of the Executive Council of the American Heart Association on The Standards and Criteria for the Programs of Care of Rheumatic Fever and Congenital Heart Disease in their Report(1955), are as follows:-

Major Criteria - Carditis; polyarthritis; chorea; subcutaneous nodules; erythema marginatum.

Minor Criteria - Fever; arthralgia; prolonged P-R interval in electrocardiograph recordings; increased E.S.R., white blood count, or presence of C-reactive protein; evidence of preceding haemolytic streptococcal infection; previous history of rheumatic fever and inactive rheumatic heart disease.

The diagnosis of rheumatic fever, in this series was considered absolute in each case, if the patient had presented with two major criteria and one minor criteria; or one major and two minor criteria.

Numerous tests have been evolved in aiding the diagnosis of rheumatic fever. Unfortunately, however, there were no laboratory facilities available at the Western District Hospital or its sister establishments to carry out any of these tests on the patients upon whom /

whom this series was evolved at the time the work was done.

Taken in conjunction with other criteria, seriological tests are now most valuable diagnostic aids, the two most frequently used being the anti-streptolysin-O and C-reactive protein tests as described by S.S. Milton(1955). Further procedures have been proposed for estimating rheumatic activity, namely -

The Weltman serum coagulation reaction.

The determination of serum muco-protein.

The bacterial activity of blood against Bacillus Subtilis.

The serum precipitative reaction with a quartenary ammonium salt.

Again, none of these is entirely satisfactory, and they have not been described as they were not employed in this thesis.

CHAPTER III

Personal Investigations Regarding The Incidence of Rheumatic Fever.

(a) The Total Number of Cases, Sex and Age with the Incidence of Rheumatic Fever

Altogether, 437 cases of rheumatic fever were studied. Of these, 317 presented with arthritis, 115 with chorea and 5 cases were suffering from both arthritis and chorea simultaneously. The following diagrams reveal the distribution of attacks according to the age at onset, together with the number of the attack, as found to apply to the cases studied in this work.

From the figures in Diagram 1, it is shown that a first attack of rheumatic fever presenting with arthritis was commonest between the ages of seven years and sixteen years. Three cases occurred at the early age of three years.

Second attacks appeared most commonly around the age of twelve years.

The ratio of females to males is 1 : 1.1.

Rheumatic Fever. (Arthritis ± Carditis).

No. of Cases and Age Incidence in Attacks.

Age in Years	No. of Cases. 1	2	3	4	5	6th attack.
3	3					
4	7					
5	3					
6	11					
7	22	1				
8	37	4				
9	34	2	3			
10	32	4	1			
11	22	3	2			
12	24	8	3			
13	16	4	2			
14	7	3	1	1		2
15	9	3	2			
16	7	1	1			
17	3	1	1	2		
18	4	2				
19	5	1	2	1		
20	2	4	1			
21	·	2	1			

1st Attack.
118 Females : 130 Males.

2nd Attack.
24 Females : 19 Males.

3rd Attack.
9 Females : 11 Males.

4th Attack.
1 Female : 3 Males.

5th Attack.
No Cases.

6th Attack.
2 Females only.

Total No. of Cases = 317. (154 Females : 163 Males.)

DIAGRAM 1.

Rheumatic Fever. (Chorea ± Carditis)

No. of Cases and Age Incidence in Attacks.

Age in Years	No. of Cases. 1	2	3	4	5 th attack.
3					
4					
5	2				
6	9				
7	11				
8	15				
9	8	3			
10	14	6		1	
11	14	4			
12	8	3			
13	5	1			
14	3	-			
15	2	1			1
16		1			
17		-			
18		1			
19					
20			1		
21			1		

1st Attack.
70 Females 21 Males.

2nd Attack.
15 Females : 5 Males.

3rd Attack.
2 Females only.

4th Attack.
1 Female only.

5th Attack.
1 Female only.

Total No. of Cases = 115 (89 Females : 26 Males.)

DIAGRAM 2.

From the figures in Diagram 2, it is shown that the first attack of rheumatic fever presenting with chorea was commonest at the ages of 8, 10 and 11 years of age.

The commonest age of onset of a second attack was 10 years. The ratio of females to males attacked was found to be 3.4 : 1.

In agreement with the findings of R.A.N. Hitchins(1958) the incidence of recurrence of rheumatic fever was found to be relatively low up to the age of 7 years but remained at a high level from the age of 7 years to 15 years. It is therefore suggested that ages 7-15 are the most imperative years for preventing recurrences of rheumatic fever.

Arthritis & Chorea (±Carditis) occuring at once.

1.	Female	6yrs old.
1.	"	8 - "
1.	"	12 - "
1.	"	15 - "
1.	Male	11 - "

DIAGRAM 3.

As shown in Diagram 3, five cases occurred in which the patient suffered from arthritis and chorea at one and the same time. This is a comparatively rare occurrence, and in this series it was not confined to any particular age group. The ratio of females to males affected was 4 : 1.

There were no recurrences in these five cases which presented with arthritis and chorea, and none of them gave a history of previous rheumatic fever.

Sex and Age Incidence.

As stated previously, in this series of 437 cases, arthritis was more frequent in males than in females by the ratio of 1.1 : 1.

Chorea was more frequent in females than in males by a ratio of 3.4 : 1.

Leonard Findlay(1931), on studying a series of cases, found that arthritis was more common in females than in males by a ratio of 1.1 : 1. In the present series, arthritis was found to be slightly more common in males. However, he found that chorea was more common in females than in males by a ratio of 2.8 : 1. The findings in this present series shows a higher incidence amongst females.

(b) The Yearly Incidence of Cases of Rheumatic Fever.

On studying the incidence of cases of rheumatic fever over the ten year period from 1950-1959, it became obvious that the greatest number occurred during the year 1952-1953, with a steady decline in numbers from that date.

This is illustrated in Diagram 4 below.

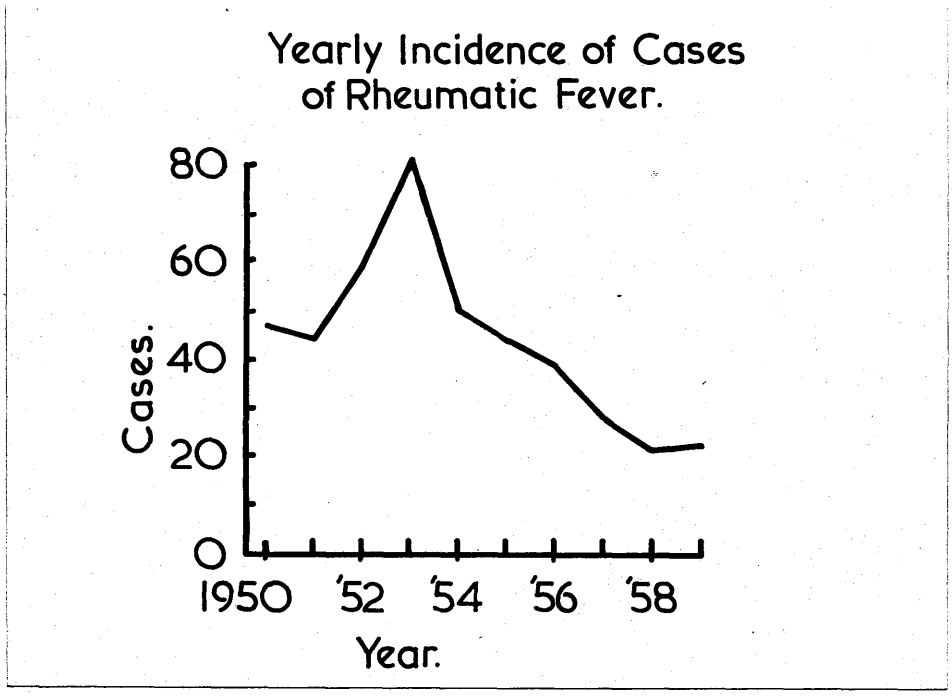


DIAGRAM 4.

The steady decline in incidence over the years dating from 1954 suggests that there are many factors at work which are altering the course of the disease as a whole, and this led to a series of investigations.

The actual number of cases of rheumatic fever occurring each month and year are shown in Table I in Appendix A.

(c) Factors suspected of Affecting the Disease.

(1) The Seasonal Incidence.

A study was undertaken to discover in which seasons of the year rheumatic fever was most prevalent in the Glasgow area. The results, as indicated in the following diagram, revealed that the greater number of cases occurred during the months of December, January and March, with an increase in cases occurring during the month of July.

Each case was carefully studied, as to the actual date of onset of the symptoms, and this date was used in the investigation, not the date of admission to hospital.

As can be appreciated, in young children for example, the onset may date from attacks of abdominal pain, at first undiagnosed, and subsequently discovered to be due to rheumatic fever affecting one or both hip joints. With few exceptions, it was discovered that all the cases gave a history of a sore throat, or an attack of coryza some weeks prior to the onset of symptoms.

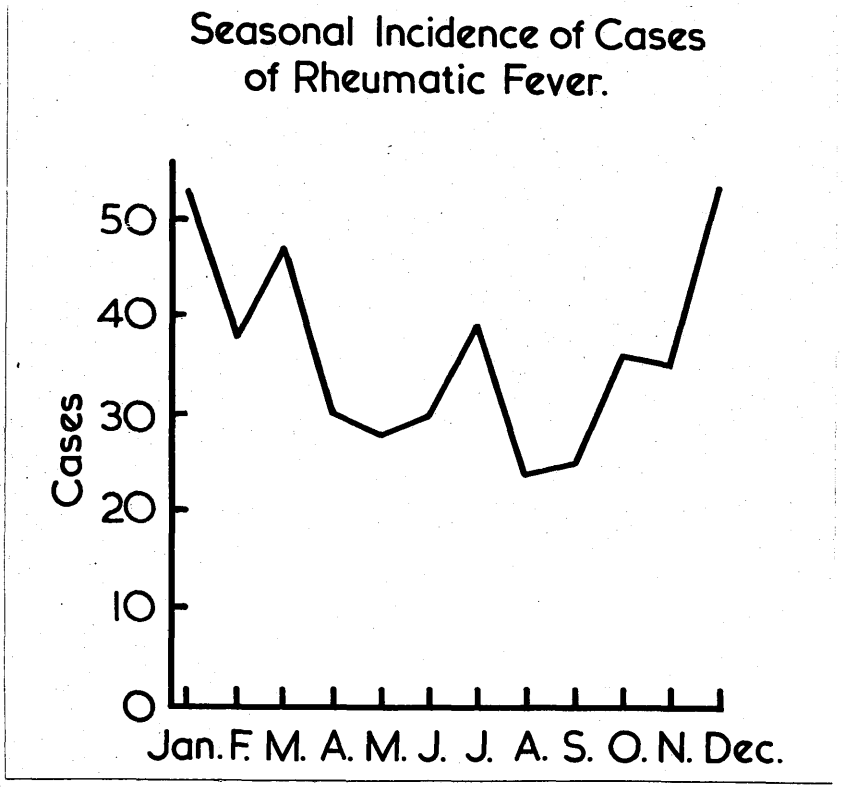


DIAGRAM 5.

Statistically, in this present series 12.2 per cent of cases occurred in the months of December; 12.2 per cent in the months of January; and 10.8 per cent in the months of March. A rise in the number of cases occurred in the months of July (8.9 per cent altogether).

The lowest recorded number of cases occurred in the months of August (5.5 per cent) and September (5.7 per cent).

G. F. Still(1921) found that the months of November (12 per cent) and January (11 per cent) had the greatest incidence of cases whilst June and July (5 per cent in each case) showed the lowest number of cases of rheumatic fever.

The seasonal incidence in the present series shows a tendency to increase during the month of July, which is at variance with the findings of authors Leonard Findlay and G. F. Still, both of whom found that there was a continued drop in the number of cases during the summer months. However, R.A.N. Hitchens(1958), in the paper written on conclusion of a twenty year study of rheumatic fever in Wales, also noticed that there was a marked seasonal trend in frequency, but that the number of attacks in the summer months was <u>not</u> negligible. This led to the thought that weather conditions might have some bearing as a factor in the causation of the disease, and in retrospect, the prescribing of prophylactic treatment in this present series should have been continued during the summer months.

Table I in Appendix A, shows the number of admissions of rheumatic /

rheumatic fever in each month from 1950-1959.

(2) Correlation of Monthly Incidence of Cases to Monthly Rainfall during the Years 1950-1959 Inclusive.

The average was taken of rainfall in mm. (as recorded at Paisley and Springburn Observation Centres), each month during the years 1950-1959 inclusive. Full details as regard to data are shown in Table I in Appendix A. The rainfall per month was then correlated with the number of cases of rheumatic fever occurring in the corresponding month.

The correlation coefficient was 0.003. This indicates that there is no connection between rainfall and the occurrence of rheumatic fever.

As it is well known that rheumatic fever is almost always preceded by a sore throat or coryza some weeks previously, the rainfall figures for the previous month were then correlated with each monthly incidence of cases.

The correlation coefficient in this instance was found to be 0.014, also revealing a negative relationship.

(3) Correlation of the Monthly Incidence of Cases to the Days of Ground Frost Occurring each Month

In a manner similar to the above, the average was taken of the number of days of Ground Frost occurring each month, as recorded at the Paisley and Springburn Observatories. When correlated to the monthly incidence of cases, the coefficient was found to be 0.21, /

0.21, both for the month in question and for the preceding month. This is significant at the 5% level, showing that frost is a definite factor in the occurrence of rheumatic fever.

This is one of the reasons for the higher incidence rate of the disease during the late winter months when frost is prevalent.

(4) Correlation of the Monthly Incidence of Cases to the Monthly Incidence of Fog

In the same manner, the average was taken of the number of days of fog, as recorded at the Observatories at Paisley and Springburn.

When correlated to the monthly incidence of cases, the coefficient was found to be 0.093, which reveals a negative relationship. A similar negative relationship was found on investigating the effect of the number of days of fog in the preceding month.

Table I in Appendix A shows the month by month rainfall, frost and fog as an average of the recordings taken at Springburn and Paisley Observatories during the years 1950-1959. It also shows the number of cases of rheumatic fever occurring each month.

(5) Changing Population

It was decided to investigate the incidence of occurrence of rheumatic fever in relation to the changing density of population, in order to ascertain whether this had any effect on the diminishing number of cases, which has been very obvious over the last five years.

The admissions from the Glasgow area to the Western District Hospital and Sick Children's Hospital, Glasgow, were plotted on maps. The general outlay of the maps is shown in Diagram 6. Those cases admitted /

admitted during the years 1950-1954 are portrayed in Diagram 7; those admitted during the years 1955-1959 are portrayed in Diagram 8.

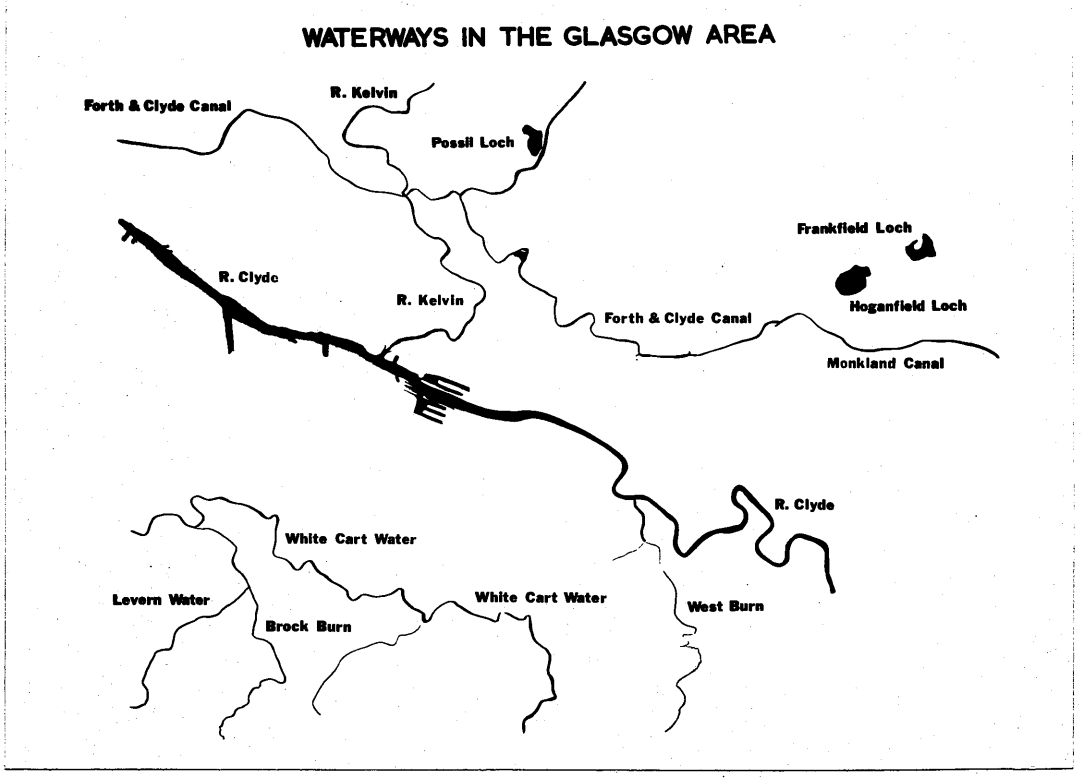


DIAGRAM 6.

As the greatest exodus of the population to new housing estates occurred in the years 1954-1955, the period 1950-1954 and the period 1955-1959 were taken as best representing the incidence of cases occurring amongst the density estimations which accrued from the 1951 and 1958 Census respectively. This latter information was kindly supplied by the City Architect of Glasgow.

Please see Appendix A, Table II for further data.

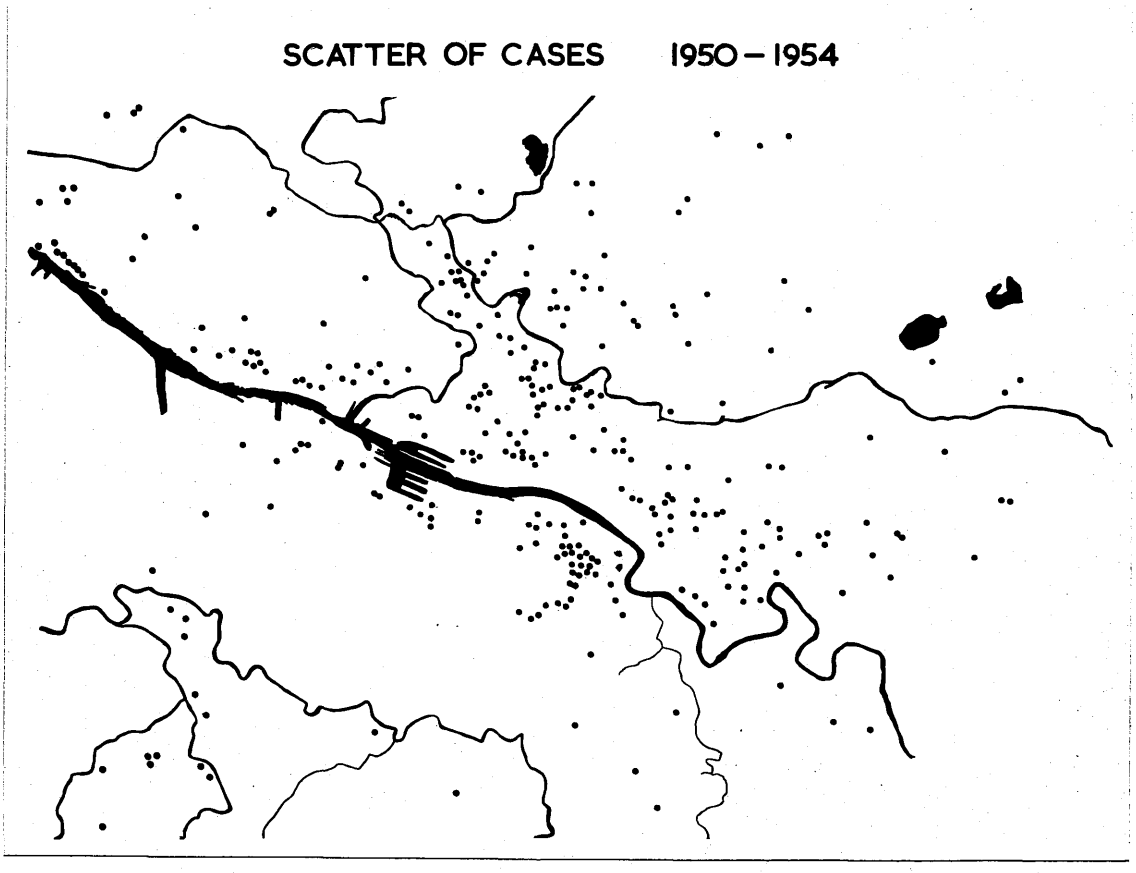


DIAGRAM 7.

As can be seen from this diagram, the distribution of cases is clustered mostly around the main waterways which (as will be shown later) are the most heavily populated areas.

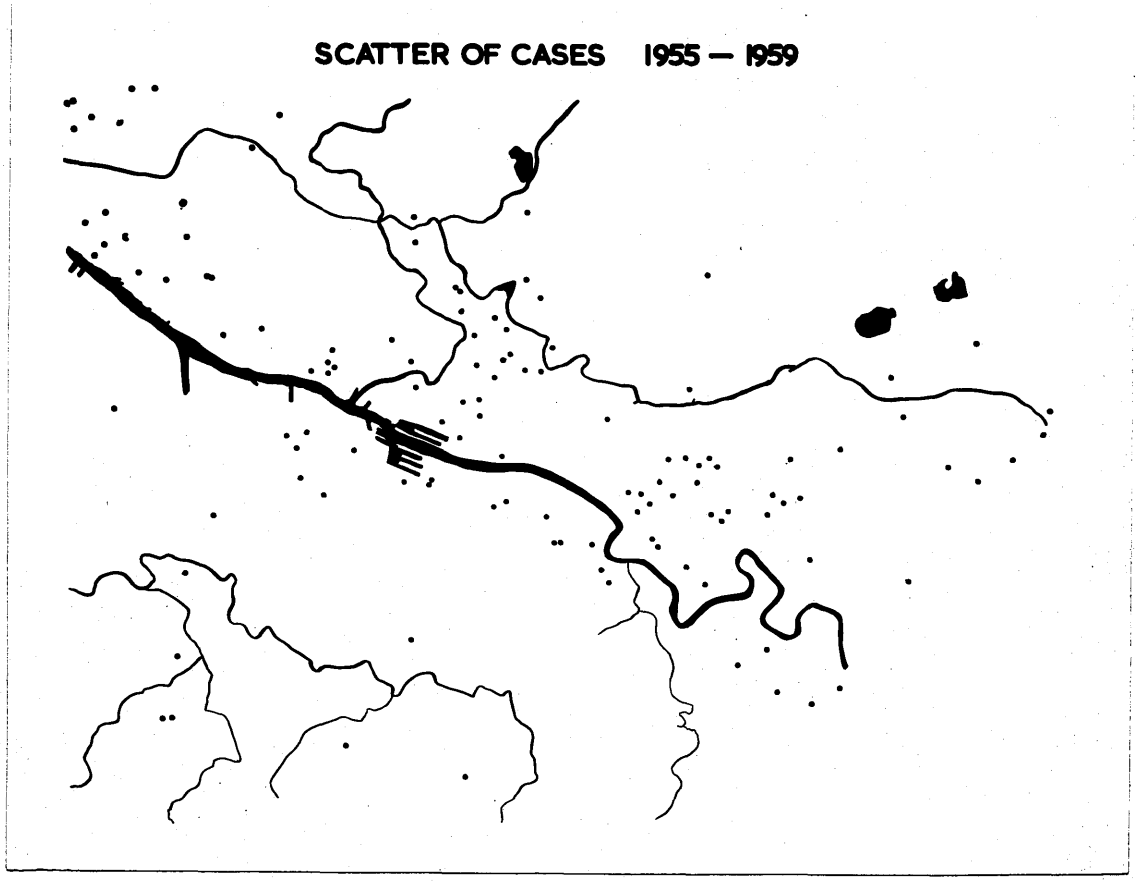


DIAGRAM 8.

The distribution of cases in this diagram shows a great reduction in number from the previous one. Once again, however, the cases occurred mostly around the waterways.

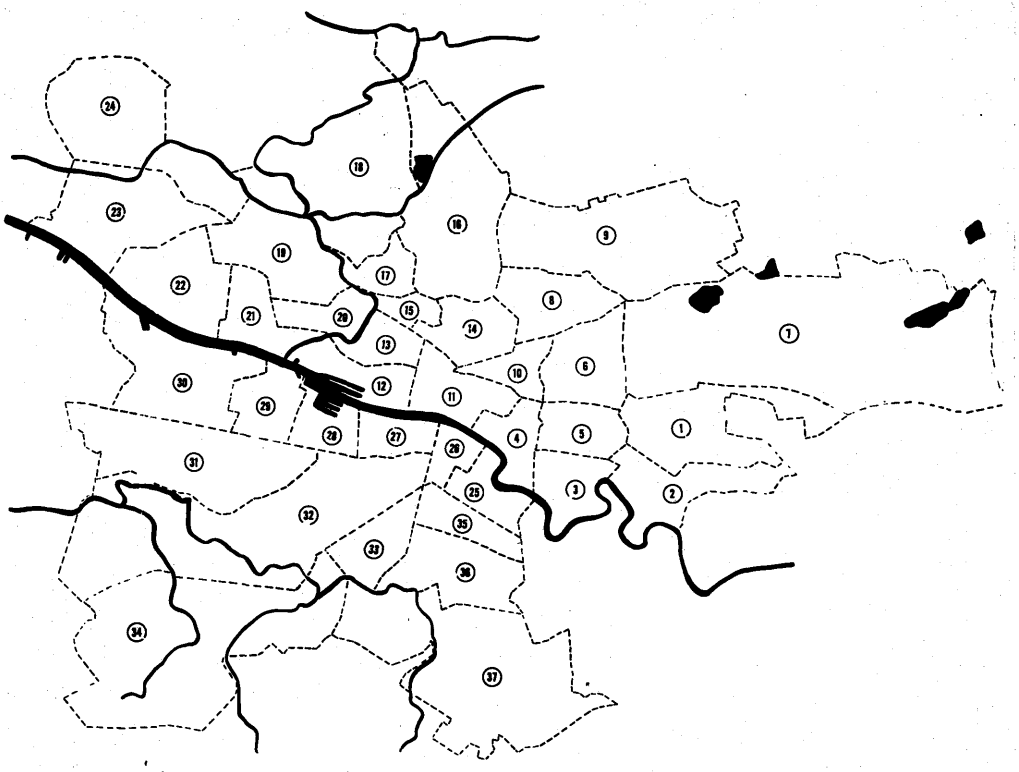
It must be realised, however, that the number of cases shown here do not indicate the true incidence of rheumatic fever in the districts served by these hospitals as, in some instances, the patients were treated in their own homes.

From data as to acreage and population per electoral ward kindly supplied by the Architect of the City of Glasgow (see Appendix /

Appendix A, Table II) maps were drawn up showing the relative densities of the 37 electoral wards as analysed from the Census compiled in 1951, and again in 1958. (Please see Appendix A, Table III, for further data).

Diagram 9 gives the key to the various wards together with the population per acre, as estimated from the Census of 1951 and of 1958.

ELECTORAL WARDS OF GLASGOW



NO.	WARD	POPn./ACRE 1951	POPn./ACRE 1958
1.	SHETTLESTON & TOLLCROSS	94	87
2.	PARKHEAD	85	75
3.	DALMARNOCK	301	258
4.	CALTON	320	270
5.	MILE-END	302	261
6.	DENNISTON	149	133
7.	PROVAN	73	60
8.	COWLAIRS	231	198
9.	SPRINGBURN	191	81
10.	TOWNHEAD	278	234
11.	EXCHANGE	291	235
12.	ANDERSON	310	246
13.	PARK	143	113
14.	COWCADDENS	336	272
15.	WOODSIDE	355	287
16.	RUCHILL	139	97
17.	N. KELVIN	213	191
18.	MARYHILL	128	110
19.	KELVINSIDE	52	47
20.	PARTICK EAST	121	103
21.	PARTICK WEST	138	120
22.	WHITEINCH	73	67
23.	YOKER	50	46
24.	KNIGHTSWOOD	47	63
25.	HUTCHESON TOWN	348	319
26.	GORBALS	324	239
27.	KINGSTON	332	274
28.	KINNING PARK	207	183
29.	GOVAN	206	180
30.	FAIRFIELD	150	133
31.	CRAIGTON	45	42
32.	POLLOCKSHIELDS	47	49
33.	CAMPHILL	87	78
34.	POLLOCKSHAWS	70	76
35.	GOVANHILL	170	156
36.	LANGSIDE	69	59
37.	CATHCART	39	43

AVERAGE POPn. FOR 1951 - 112/ACRE
AVERAGE POPn. FOR 1958 - 92/ACRE

DIAGRAM 9.

The following map (Diagram 10) reveals the densely populated areas in 1951 as being Dalmarnock, Calton, Mile-end, Anderson, Cowcaddens, Hutchesontown, Gorbals and Kingston, each with over 300 persons per acre.

Cowlairs, Townhead, Exchange, North Kelvin, Kinning Park and Govan each had over 200 persons per acre.

In the scatter of cases shown in Diagram 7, the greatest concentration appeared in those areas.

Table III in Appendix A shows the total population per acre in each electoral ward in Glasgow as estimated at the 1951 Census.

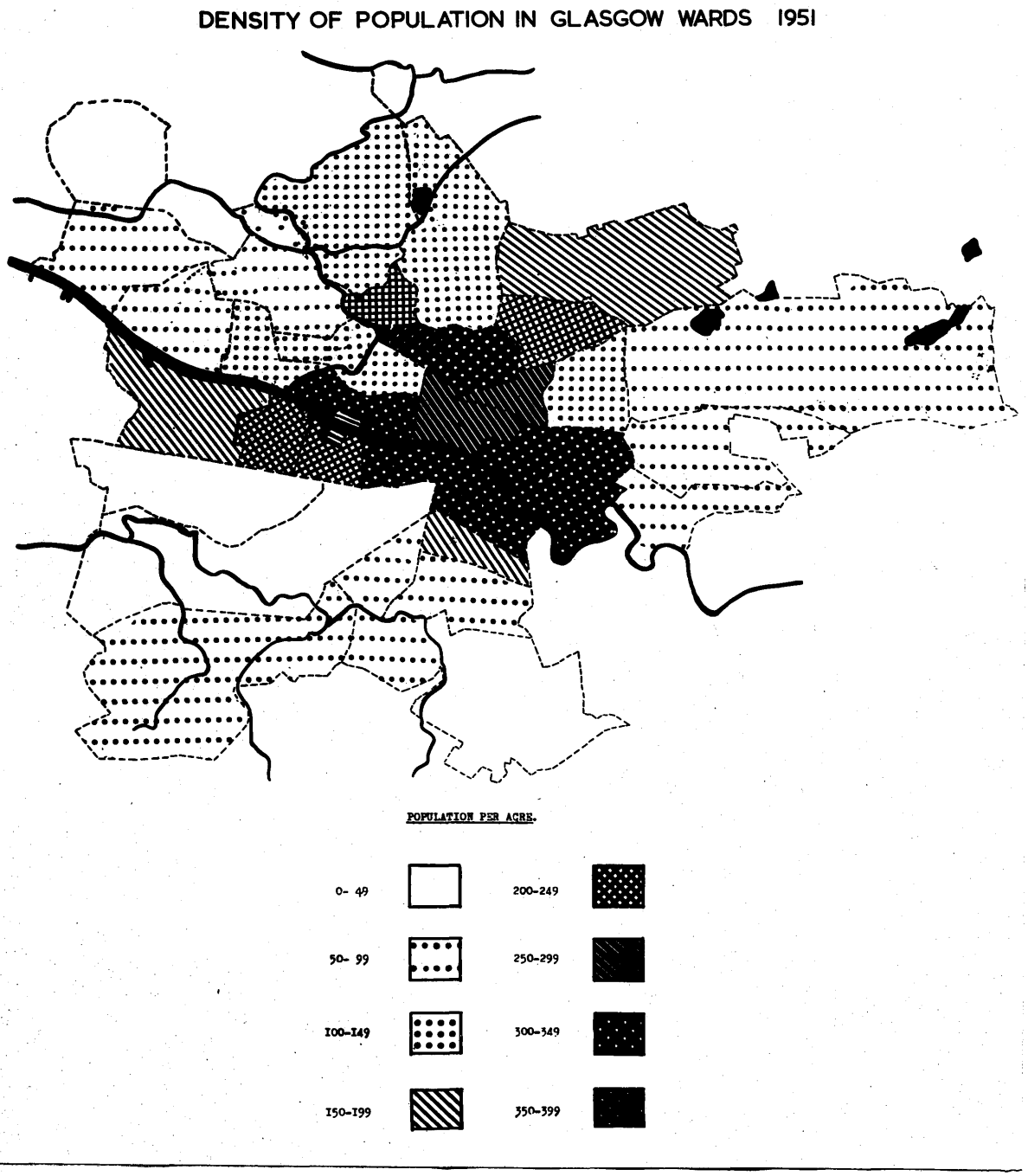

DENSITY OF POPULATION IN GLASGOW WARDS 1951
POPULATION PER ACRE.
0- 49
50- 99
100-149
150-199
200-249
250-299
300-349
350-399

DIAGRAM 10.

The corresponding analysis from the 1958 Census (see Diagram 11) revealed that the density of the population had decreased markedly in practically all the wards which had previously been heavily populated.

In this Census, the most densely populated areas were found to be Hutchesontown, with 239 persons per acre (previously 348 persons per acre); Dalmarnock, Calton, Mile-end, Exchange, Anderson, Cowcaddens, Woodside, Gorbals and Kingston, each with a population of over 200 persons per acre. In the scatter of cases shown in Diagram 8, the greater concentration appeared in these areas.

Table III in Appendix A shows the total population per acre in each electoral ward in Glasgow, as estimated at the 1958 Census.

DENSITY OF POPULATION IN GLASGOW WARDS 1958

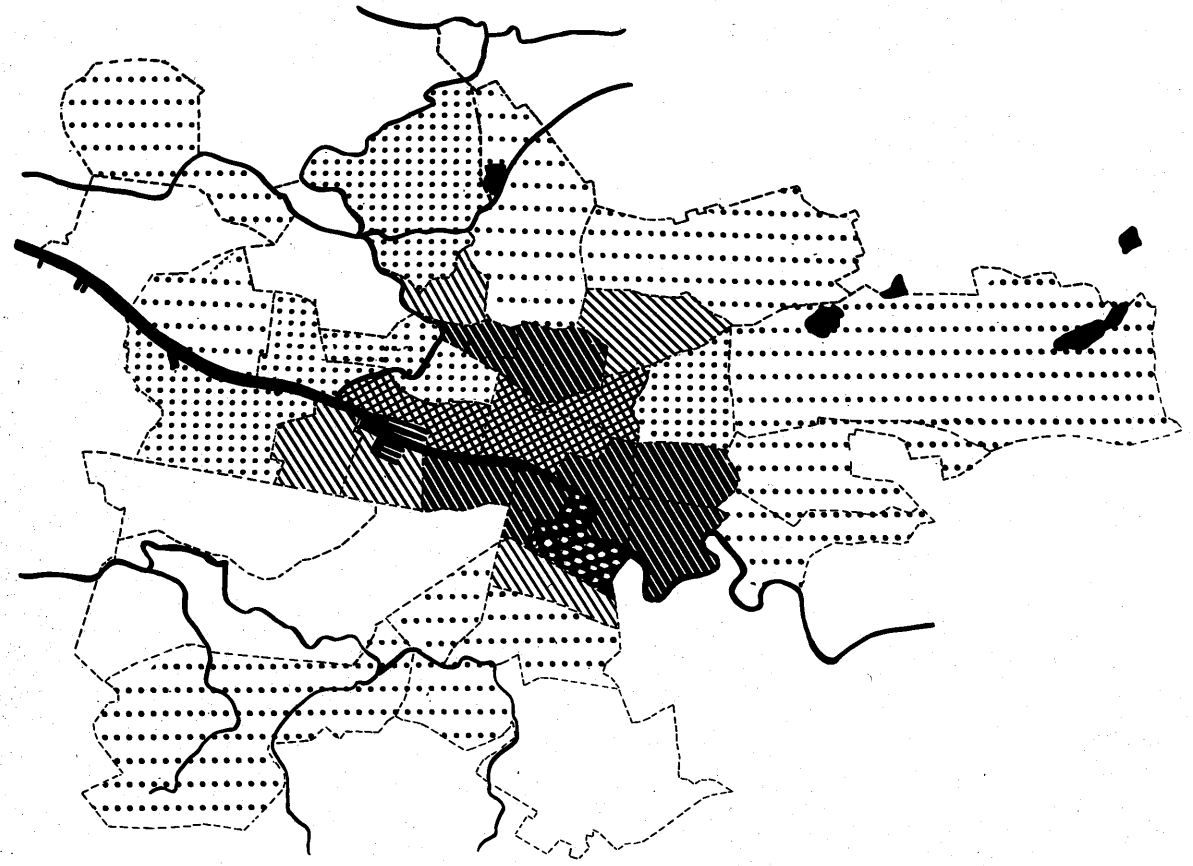


DIAGRAM 11.

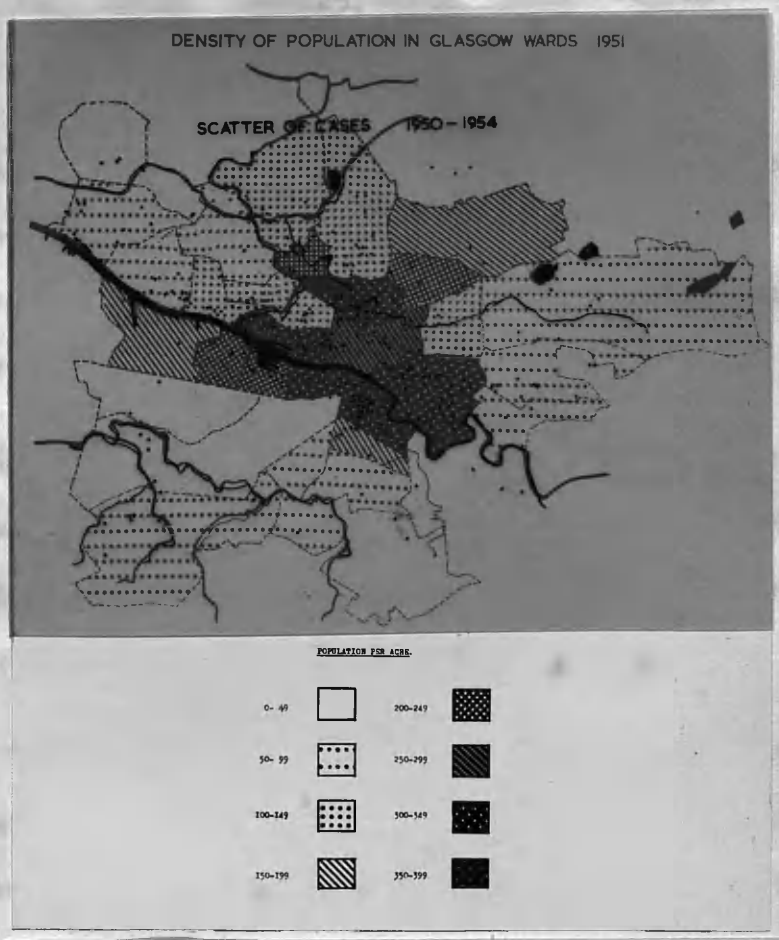


DIAGRAM 12.

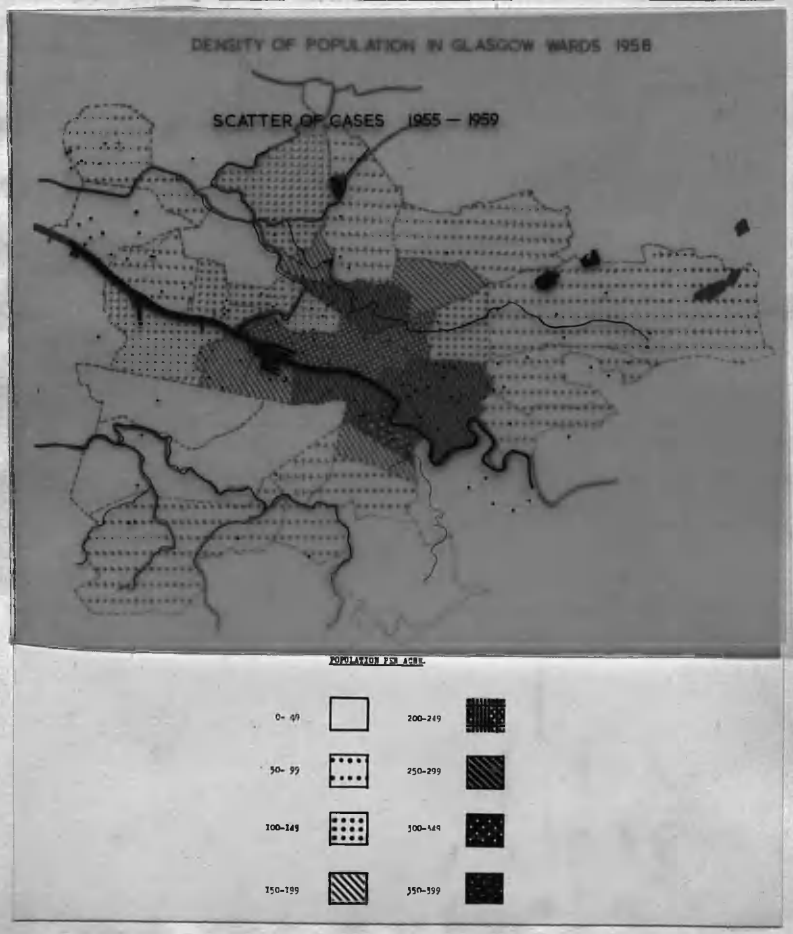


DIAGRAM 13.

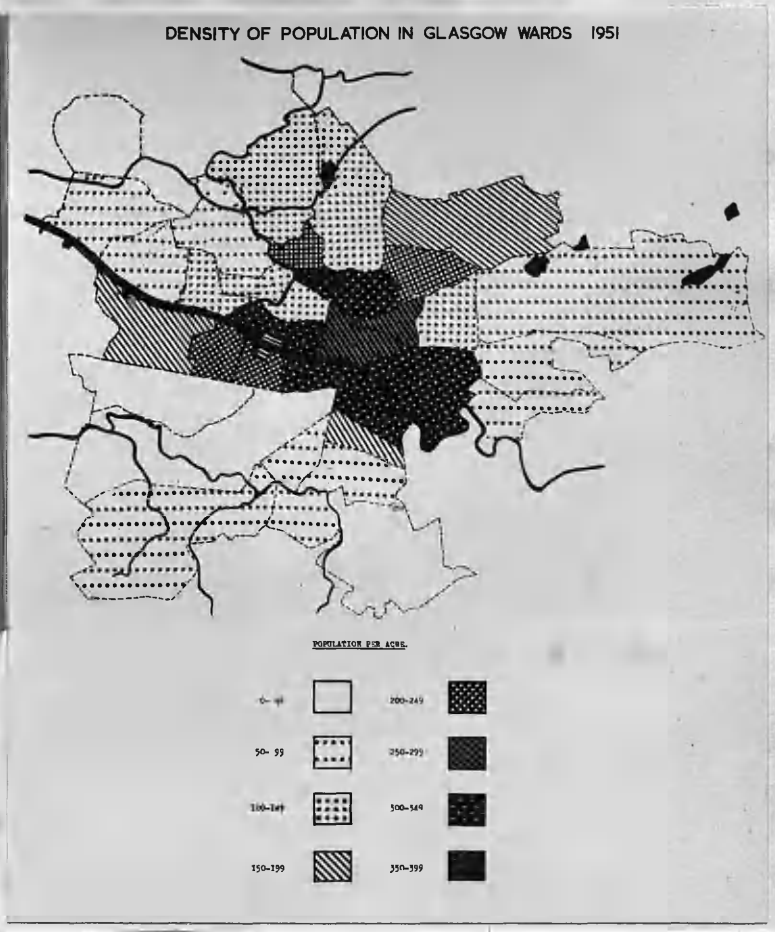


DIAGRAM 12.

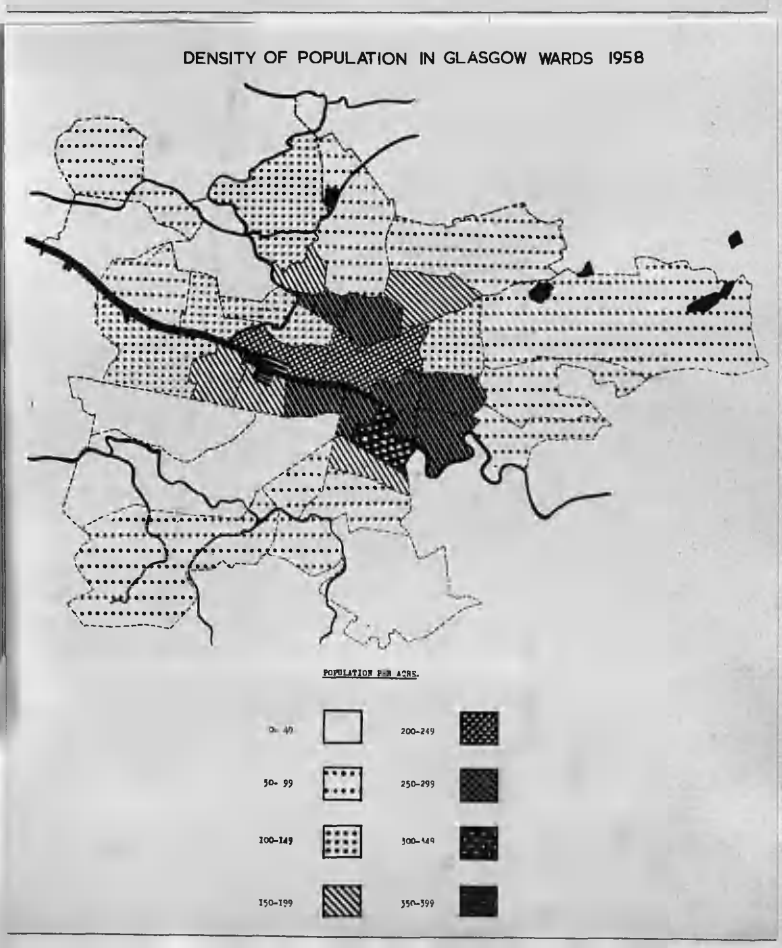


DIAGRAM 13.

Consideration of Diagrams 7, 8, 10 and 11 (shown superimposed in their respective relationships in Diagrams 12 and 13), suggests a relationship between the decrease in density of the population and the lowered incidence of cases of rheumatic fever.

Knowing the number of persons per acre, and the number of cases per ward for each of the periods 1950-1954 and 1955-1959, it was a simple matter to estimate the number of cases per thousand of the population.

Table III in Appendix A shows the number of cases, together with the rate per thousand of the population of cases of rheumatic fever occurring in each electoral ward of Glasgow during the years 1950-1954 and 1955-1959.

The correlation coefficient between the cases per thousand of the population, and the total population per ward was found to be 0.76. This is significant at the 0.1% level, indicating that there is a definite correlation between the density of the population and the incidence of cases of rheumatic fever.

Diagrams 14 and 15 represent the facts as shown by means of scattergrams.

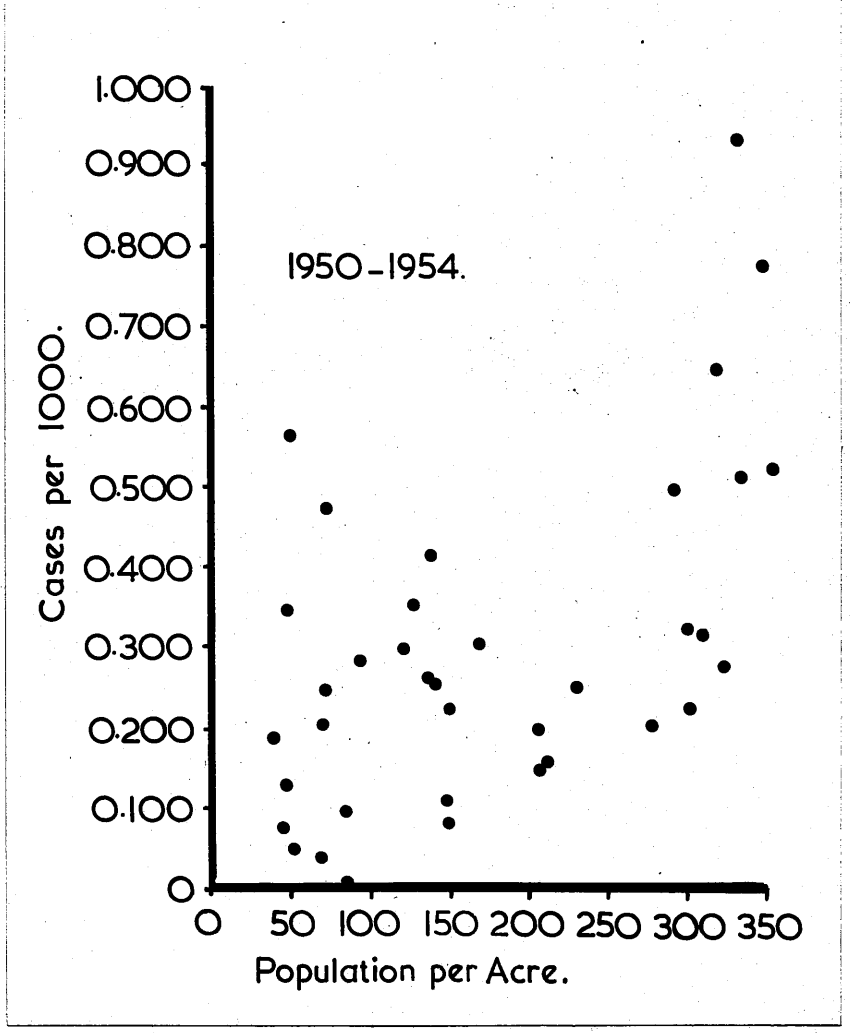

1.000
0.900
0.800
0.700
0.600
0.500
0.400
0.300
0.200
0.100
0
Cases per 1000.
1950-1954.
0 50 100 150 200 250 300 350
Population per Acre.

DIAGRAM 14.

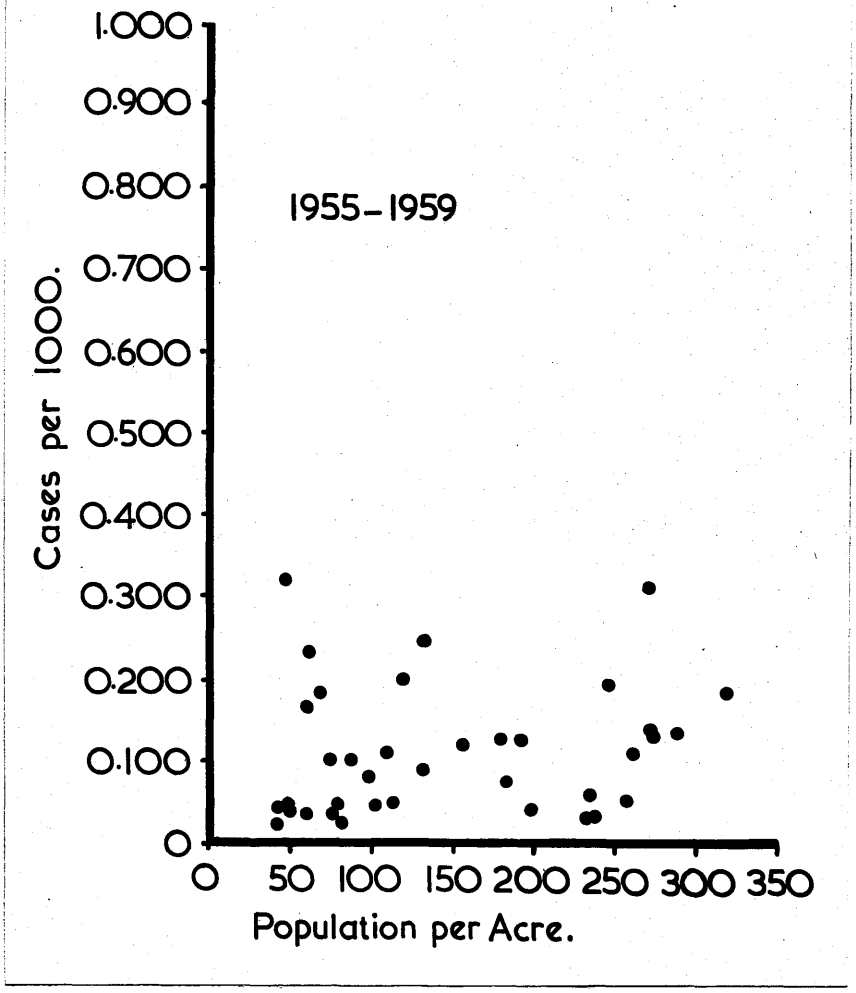


DIAGRAM 15.

The correlation coefficient for the period 1955-1959 was found to be 0.34. This is significant at the 5% level. This also indicates that there is a correlation between the density of population and the incidence of cases during this period, but the significance is not so marked as in the previous period 1950-1954.

These facts lead one to seek further evidence statistically and, as a control, the correlation coefficient was also calculated between the decrease in population per acre between the two periods, and the rise or fall in incidence of cases in each ward per thousand of the population. This is illustrated graphically in Diagram 16.

Table III in Appendix A shows the total decrease or increase per acre of the population in each electoral ward as between 1950-1954 compared to 1955-1959. The figures for the decrease in incidence of rheumatic fever cases per thousand of population are also shown.

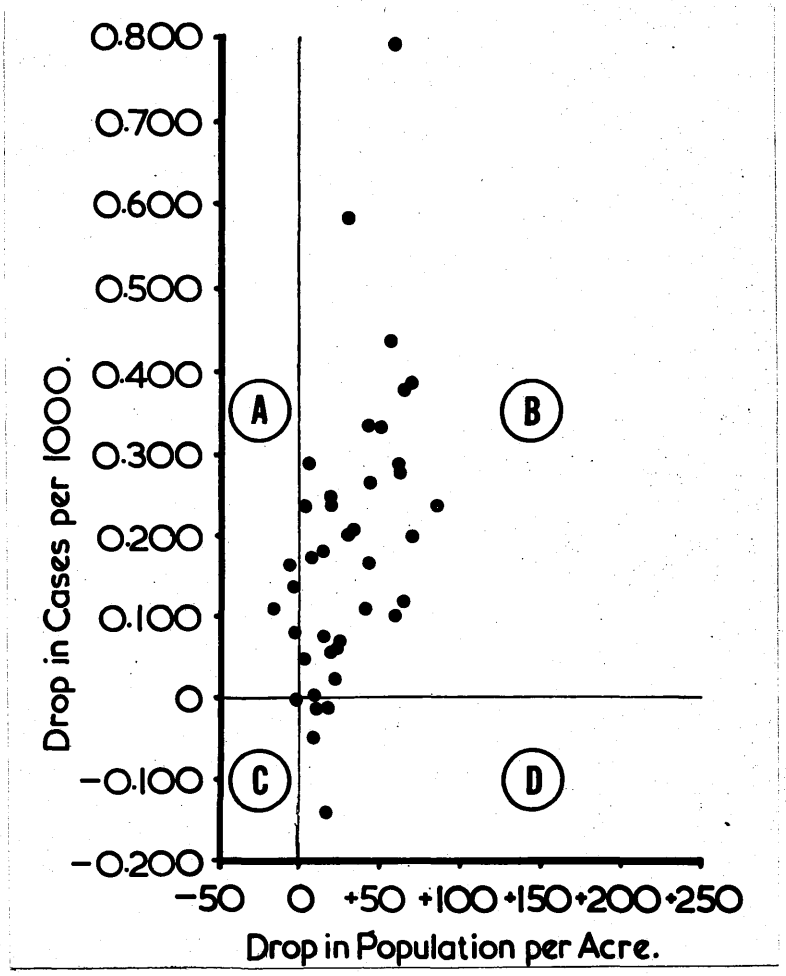


DIAGRAM 16.

The correlation coefficient, calculated from the figures shown in Appendix A, Table III, was found to be 0.5. This is significant in the 1% level. Therefore, a major factor in the reduction of cases of rheumatic fever in the Glasgow area is the great improvement in rehousing persons from the damp, heavily populated areas to dry, pleasant, uncrowded housing schemes.

The explanation of Diagram 16 is as follows:-

The area marked "B" shows the positive drop in the number of cases related to the drop of population per acre. The area marked "A" shows the drop in the number of cases where there has been an increase in the population. The area marked "D" shows the few incidences of an increase in the number of cases where there has been a drop in the population per acre. The area marked "C" has no significance.

(6) Housing Conditions

It was possible to assess the living conditions of only 354 of the 437 cases of rheumatic fever studied. The remaining 83 patients did not supply the information required.

In the majority of cases, the conditions were over-crowded and damp. The standard of "overcrowding" used in the Report by the Royal Commission on Housing in Scotland(1917) was "more than three persons living in one room".

The Scottish Housing Advisory Committee's Recommendation (1944) to the Secretary of State for Scotland was that the following standards of occupancy should be applied to all houses covered by the Housing Acts (i.e., all Local Authority houses) -

Number of Rooms.	Number of Persons	
1	0	
2	2	
3	4	
5	8	with an additional 2 persons in respect of each room over 5.

All children were to count fully as an individual. Sex separation for sleeping of children over age of ten years was obligatory. Each house had to possess a living room which was not to be used for sleeping persons.

The following diagram illustrates the state of overcrowding (using the criteria stated in the Act of 1944), which existed in the homes of the majority of the patients.

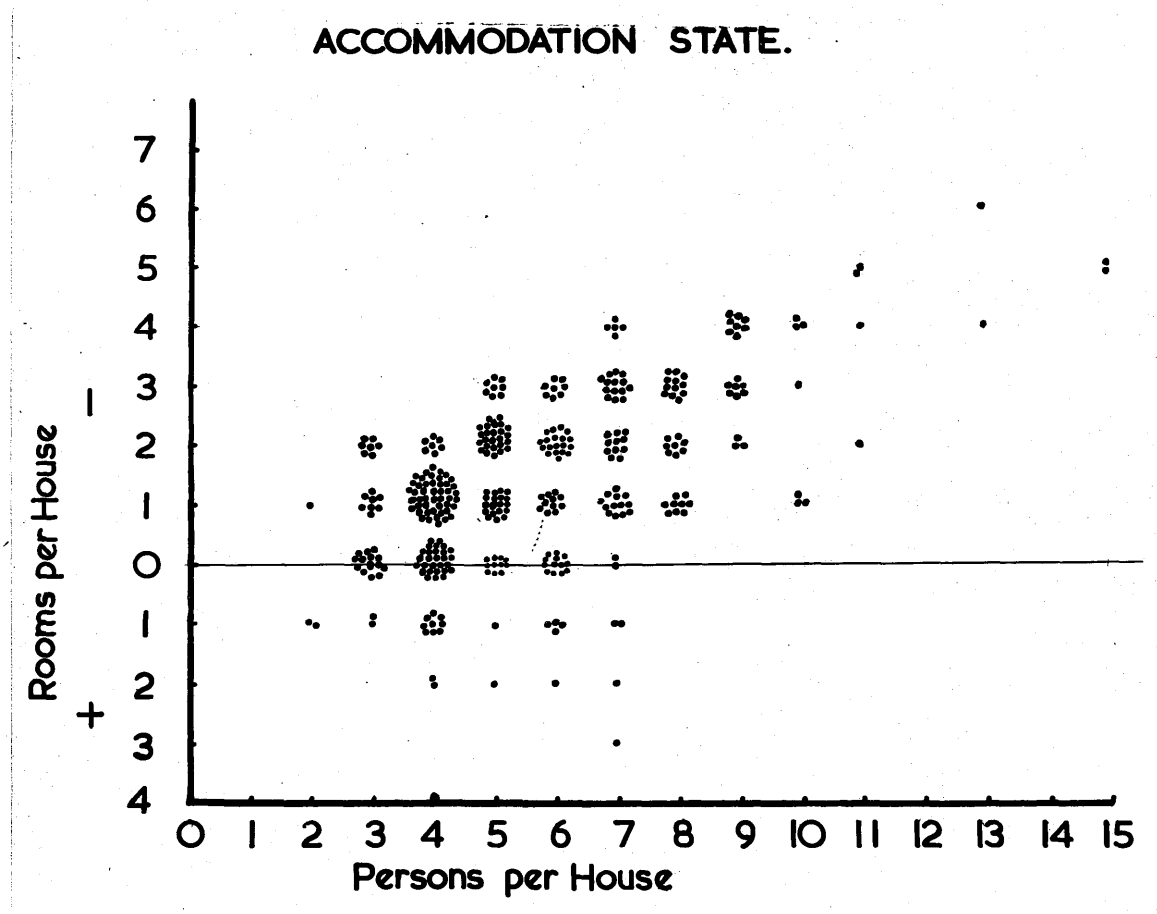


DIAGRAM 17.

The houses to which many of the patients were transferred have excellent accommodation, and every effort must be spared to prevent these homes becoming over-crowded by sub-letting and the "taking-in" of lodgers.

Diagram 17 reveals the overcrowding which was present until housing conditions began to show marked improvement (around 1954).

The horizontal base-line shows the accommodation state as recommended in agreement with the aforementioned Housing Act of 1944. The "scatter" above shows the over-crowding with regard to the number of rooms of which each family were short, according to this Act. The "scatter" of cases below the horizontal base-line indicates the housing conditions of the cases who had accommodation in excess of the recommendation.

(7) Occupation and Consequent Earnings.

The occupations and consequent earnings of the heads of the households from which the cases originated were investigated in respect of 354 of the 437 patients in the series. Information regarding the remaining 83 patients was not available.

Pro formas (see Appendix B) were sent to the heads of households of those patients who had been admitted to the Western District Hospital with rheumatic fever. Response was very gratifying, but some people refused to answer the questionnaire, and other letters were returned by the Post Office as they were unable to trace the persons concerned.

Information regarding the patients at the Sick Children's Hospital was obtained from the case sheets.

Using the classification as taken by the Registrar General (see Report of the Census, Scotland(1951)) of the population of Scotland into five Social Groups depending upon the occupation of head of the household, the incidence of cases in each Social Class was as follows:-

Class I	:	4 families	:	1.1%
Class II	:	No families	:	0.0%
Class III	:	151 families	:	42.7%
Class IV	:	94 families	:	26.6%
Class V	:	105 families	:	29.6%

From this it appears that the greatest incidence arises in Social Classes III, IV and V, but especially in Class III.

Of recent years, much has been done to alleviate suffering due to insufficient money being earned in individual households. Wages

of /

of all classes of workers have increased in accordance with the rise in the cost of living. Those unable to work are aided by National Assistance.

Young children are well looked after, both from medical and dental aspects whilst at school and are no longer, as in days gone by, allowed to run about ill-fed, ill-clad and uncared for. All these factors have a marked effect on the health of present-day children and adults, and this in turn is yet another factor in the rapidly declining incidence of rheumatic fever.

Earnings.

Altogether, of the 120 pro formas (see Appendix B) sent to parents of the patients who had been admitted to the Western District Hospital, Glasgow, between the years 1950-1959 inclusive, only 62 declared the total income of their households. The average total income was £9. 9s. per week. These families practically all had other siblings at work (one household, however, was dependant on the retirement pension of a Grandfather). This total income of £9. 9s. is low, compared to the fact that, according to the report on the Third Statistical Account of Glasgow(1958), two-thirds of the population of Lanarkshire (all of whom live in Lanarkshire) had an average income, each of £338.10s. per year between the years 1949-1956. This is approximately £6 per week.

Although no control was carried out regarding other diseases in the lower income groups, these figures suggest that there was a definite /

definite relationship between the poorer classes and the incidence of rheumatic fever.

Over the past five years, nearly all trades and professions have received increases in their wages, thus leading to improved living conditions as regards food and clothing, yet another probable factor in the gradual reduction in the incidence of rheumatic fever.

CHAPTER IV.

RHEUMATIC HEART DISEASE

Historical Survey

In 1788 David Pitcairn, in his lectures to the students of St. Bartholomew's Hospital, first drew attention to the frequent occurrence of heart disease in patients who had been affected with rheumatism. Unfortunately, he did not publish these original observations, but William Wells(1812), in his classical article "Rheumatism of the Heart", pays tribute to this important and original observation by Pitcairn. This article by Wells was the first ever to be printed on the subject, and it gives the full story and a number of very pertinent cases illustrating this first association of heart and joint disease. Tribute must also be paid to Edward Jenner, who independently in 1789, at a meeting of the Gloucestershire Medical Society at the Fleece Inn, Redborough, described "an affection of the heart following acute rheumatism." This also failed to reach print, but was reported by Keil(1936). However, it was left to Jean Bouilland(1836) to describe this association in his famous law of coincidence "in the great majority of cases of acute generalised febrile articular rheumatism, there exists a variable degree of rheumatism of the fibrous tissue of the heart. This coincidence is the rule, and the non-coincidence is the exception."

Clinical Aspects /

Clinical Aspects

In childhood the heart often bears the brunt of an attack, and on occasion the joints may escape entirely.

Once the heart has been involved, carditis or valvulitis should be assumed in all subsequent attacks.

In all cases, the patient should be treated on the assumption that he is suffering from an active carditis.

Rheumatic carditis, which refers to active inflammation of the heart, is more likely to be associated with polyarthritis (61 per cent) than with chorea (20 per cent). These figures are stated by Paul Wood(1956a), who estimates that subacute rheumatism accounts for 38 per cent of cases.

Evidence of Carditis

To establish the diagnosis of an active carditis occurring in a proven case of rheumatic fever, at least one of its five chief manifestations must be present. According to Paul Wood(1956b) these manifestations are as follows:-

(1) Mitral Valvulitis - as indicated by a pan-systolic murmur embracing both heart sounds at the mitral area; or the development of a soft, short mid-diastolic murmur, also known as a Cary Coombs(1924) Murmur.

(2) Aortic Valvulitis - as indicated by an aortic diastolic murmur.

(3) /

(3) Partial Heart Block - as indicated by prolongation of the P-R interval in the electrocardiograph.

(4) Pericarditis - may be transient with little or no pain, but usually indicated by considerable praecordial pain, high fever, tachycardia, and obvious distress. E.C.G. may show characteristic early elevation of the S-T segment, followed by flattening, or slight inversion, of the T waves in most leads.

(5) Heart Failure - as indicated by elevation of venous pressure, distension of the liver, and a fall in cardiac output, with or without oedema or ascites.

Other manifestations which occur in carditis, but are not conclusive proof of rheumatic carditis, even in the presence of a proven rheumatic state are -

(a) Tachycardia - may be due only to anxiety.

(b) Gallop Rhythm - may be difficult to distinguish from a third heart sound in a child.

(c) Enlargement of the heart - may be due to collapse of the left lower lobe of lung.

The cardiac murmurs indicating carditis are described by the Rheumatic Fever Committee of the Royal College of Physicians, London, in their Further Report(1957), and by the American Heart Association in the Statement issued by their Committee on Standards and Criteria for Programs of Care of the Council on Rheumatic Fever and Congenital Heart Disease(1955).

Rheumatic /

Rheumatic carditis, as stated previously, refers to active inflammation of the heart. The after-effects may be valvular sclerosis, patchy myocardial fibrosis, or adherent pericardium.

Parkinson and Hartly(1946), state that 5% of healthy young adults give a previous history of rheumatic fever in childhood. Therefore, it appears that all those patients who have rheumatic fever do not necessarily develop clinical rheumatic heart disease. Parkinson(1945) published an article which stated that during examination of recruits for military service between 1939-1945, about 240,000 cases of rheumatic heart disease of both sexes were found in Great Britain at that time. This number represented 2.6 per cent of the population in that age group.

Rheumatic heart disease accounts for approximately 20 per cent of all cases of heart disease in temperate climates, and causes about 10,000 deaths annually in Great Britain. Practically all cases of inactive rheumatic heart disease have one or more valvular lesions.

R. C. Cabot(1926) in his book "Facts on the Heart" reported the incidence of the relative valvular lesions in cases of rheumatic heart disease as follows:-

Mitral Valve	is	involved	in	85%
Aortic Valve	"	"	"	44%
Tricuspid Valve	"	"	"	10-16%
Pulmonary Valve	"	"	"	1 - 2%

De Graff and Lingg(1935) analysed 644 fatal cases of rheumatic heart disease, and they found that once a patient reached the level of /

of total incapacity, the average expectation of life was three years.

The Joint Five-Year Study by U.K. and U.S.A.(1960) of 497 cases of rheumatic fever paid special attention to the cardiac status of patients who had previously suffered from one or more attacks of rheumatic fever.

The workers stressed the fact that the major factor in determining the incidence of rheumatic heart disease at the end of five years is the status of the heart at the time treatment was begun.

For cases without carditis initially, the progress was excellent, since in 96 per cent there was no residual heart disease. In cases with carditis initially, but without pre-existing heart disease, the proportion without residual heart disease decreased progressively from 82 per cent for those with only a grade I apical systolic murmur, to 30 per cent for those with failure and/or pericarditis.

In cases with pre-existing heart disease, the prognosis was poor. Only 30 per cent of those without pericarditis or failure, and none of those with pericarditis and/or failure, were without heart disease five years later.

These results indicate the trend of rheumatic heart disease.

Fenstein and Spagnuolo(1960), after observing a large number of children and young adolescents who had had at least two attacks, found that recurrences of rheumatic fever run very true to the form of the first attack, especially as regards cardiac features. Altogether, 161 cases were studied. With very few exceptions, patients who /

who had no organic murmur during one attack emerged equally unscathed from the next. If an organic murmur had been audible during the earlier illness, the cardiac damage persisted, recurred or increased, during subsequent episodes. The majority of their patients were between six and eleven years of age and they found that within these limits, cardiac damage was not confined to any particular age-group. However, they pointed out that their observation in this restricted age group does not invalidate the accepted fact that older patients with a first attack of rheumatic fever are less liable to cardiac complications.

In patients who escape damage to their hearts, the pattern of non-cardiac manifestations - arthropy, chorea, erythema marginatum, abdominal pain - in one attack, tended to repeat itself in later attacks. They found, however, that this tendency was less marked when cardiac lesions were present.

Mortality of Rheumatic Fever.

Bland and Jones(1938) published their results after a study of 1,500 cases of rheumatic fever in children and adolescents under the age of 21 years, who had been admitted to their hospital since 1921.

Among these patients, there were 306 deaths. Rheumatic fever was the outstanding cause of death in 250 (82 per cent) proven instances.

The early years after the onset of an attack of rheumatic fever /

fever proved to be a critical period.

In approximately half (47 per cent) of the fatal cases, death had occurred during the first three years, and in two-thirds (62 per cent), during the initial five years. Thereafter the extent of residual cardiac enlargement and, to a lesser degree, the rapidity with which it developed, aerved as the most reliable criteria of the severity of the preceding infection, as well as an index of the future susceptibility of the individual patient to subsequent fatal rheumatic fever. The age of the patient at the time of onset of rheumatic fever during the first 15 years of life was of no significance so far as duration of life was concerned.

G.E.M. Scott(1943), after a seven-year study on rheumatic fever, found that there were 42 deaths (6.5 per cent) among 645 patients suffering from rheumatic fever.

Pathogenesis of Rheumatic Endocarditis.

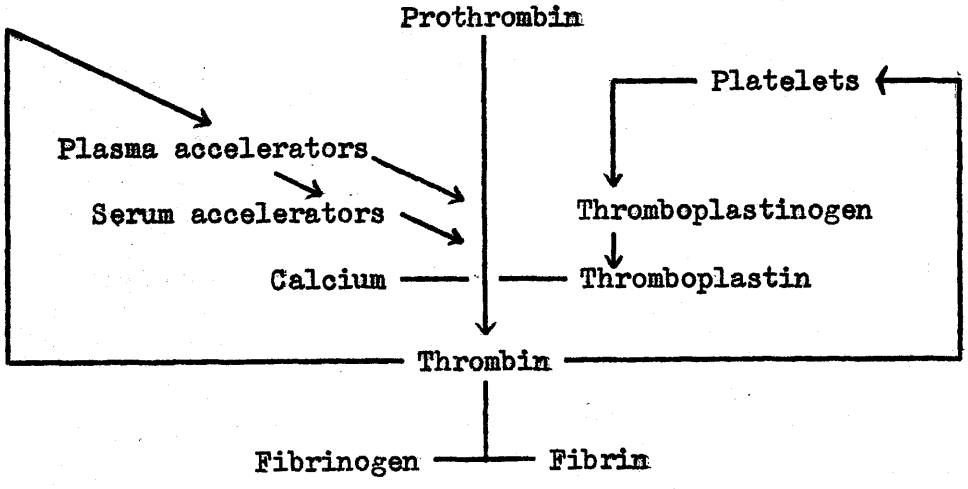
Vegetations of acute rheumatism are caused by the deposition of blood platelets and fibrin on the valves. Hitherto, it has been an accepted fact that the chronic thickening and stenosis occurring in heart valves which have been affected by acute rheumatism, are produced by inflammation.

Two workers in recent years have thrown light on a most interesting subject. F.R. Magarey(1951), on the lines of the thrombus hypothesis, has shown how vascular thickenings can be produced by the organisation of fibrin deposits.

These /

These findings were corroberated by P.S. Tweedy(1956). Magarey showed that when fibrin is deposited on a heart valve, it undergoes organisation, and is converted into fibrous tissue which becomes incorporated into the valve substance, and so adds to its thickness. He also showed how deposits at the junctions of the cusps form adhesions between them, and thus narrow the orifices. Both Magarey and Tweedy identify this deposit as incompletely organised fibrin.

This biochemical relationship between fibrin and plasmofibrinogen may be represented diagramatically as follows:-



This diagram is illustrated in "Textbook of Medicine", (9th Edition) by Cecil and Loeb, Saunders and Co., London 1955, p.1197.

The significance of this relationship will be considered in Chapter V of this work.

CHAPTER V.

A Resumé of the Treatment of Rheumatic Fever

Rest

The first rational approach to the treatment of rheumatic fever was made by Sibson(1877), by introducing rest. Few people have seriously questioned the principle that if the work of the heart could be reduced during the illness, the amount of inflammation, and consequently the amount of residual scarring, might be reduced.

Nowadays, absolute rest in bed is insisted upon during the acute stage and for those with cardiac failure.

Bywaters et al(1956) recommend that the length of rest in bed be limited by improvement in the clinical condition and laboratory evidence of quiescence of the disease

Pointers to clinical activity include tachycardia; fever; joint involvement; failure to gain in weight (in children); chorea, (unless it has become a tic); nodules; and erythema marginatum.

Laboratory evidence of quiescence is provided by disappearance of C-Reactive protein from the serum and by return to normal of the erythrocyte sedimentation rate for a minimum of two weeks. (The normal, per Westergren Method, is up to 15 mm. in the first hour).

Diet

Diet during the course of rheumatic fever should be light and easily /

easily digested. Ann Purdy(1957) stresses that the diet should have a high-protein, high carbohydrate content. Milk, fish, citrus foods, whole-grain cereals and breads are all examples of food stuffs which should be given.

Drug Therapy

Milton S. Saslow(1955) advised that the medicinal treatment of rheumatic fever should be broken down into four stages viz. -

(1) that of the acute streptococcal infection if any.

(2) that of the active stage of the disease.

(3) that of the patient during convalescence.

(4) that of the patient in later stages, if cardiac involvement occurs.

Each of these stages will now be dealt with in turn.

(1) Treatment of the Acute Streptococcal Infection

An extract from the American Heart Association's Statement(1960) on the diagnosis of streptococcal infections, and their treatment during the course of rheumatic fever, and in the after-care of the rheumatic individual, is to be found in Appendix D of this work.

Penicillin is the drug of choice in the treatment of streptococcal infections as it is bactericidal in action. Sulphonamides, having only a bacteriostatic action, should not be used therapeutically.

I have made a practice of administering a course of Crystalline Penicillin, in a dosage of one million units daily, followed by 500,000 units twice daily for six days, to all patients found to be /

be harbouring haemolytic streptococci in their throats. If, at the end of this treatment, the organisms are again isolated on a throat swab culture, the course of penicillin is repeated.

Milton S. Saslow(1955) recommends either of two courses -

(a) Oral Course

200,000 units four times daily for children
300,000 units four times daily for adults
} for 5 days

followed by three doses daily for an additional 5 days.

(b) Injection Dose

300,000 units of Procaine Penicillin with aluminium monostearate in oil, intramuscularly every day for three doses in children and 600,000 units for each of three daily injections for adults.

Mortimer et al(1958) conducted a clinical trial in which a series of patients were given penicillin for six weeks during their illness. At the end of one year, on comparing this group with their control series, they found that those who had received penicillin during their illness, had a difference of highly probable statistical significance in the incidence of organic murmurs in patients without advanced valvular heart disease on admission. However, there was no significant difference between the two groups in symptomatology, laboratory phenomena or cardiac manifestations, during the first six weeks.

(2) Treatment of the Active Stage

It has been common knowledge for many years, that Salicylates are /

are of unequivocal value in the treatment of rheumatic fever. Ann Purdy(1957) advises salicylates to be given in the dosage as estimated by one grain per pound of bodyweight, in divided doses every five hours day and night.

The Rheumatic Fever Committee of the Royal College of Physicians in London, in their Report(1947) suggested as a general rule, a dose of 1½ grains for every year of a child's age, an equal amount of sodium bicarbonate being given with each dose. The dose should never be given on an empty stomach. This dosage is normally regulated by estimating the serum salicylate levels, and adjusted so that this level remains between 30-40 mgms. per 100 ml.

Recently there has been much controversy regarding the use of Cortisone, either alone or in conjunction with salicylate treatment.

K.S. Holt et al(1954) made an attempt to prove whether cortisone had a beneficial effect in the treatment of acute rheumatic fever. From their results it appeared that salicylate given alone was not the better drug of choice in the treatment of rheumatic fever, although they admitted that further study was required to determine whether the addition of salicylate to cortisone treatment was of value or not.

The United Kingdom and United States co-operative clinical trial was set up in 1951-1952 to compare the relative merits of A.C.T.H., Cortisone and Aspirin, in the treatment of rheumatic fever and prevention of rheumatic heart disease. Their conclusion, as stated in their Joint Report(1955) was that there was no evidence that treatment with either A.C.T.H., Cortisone or Aspirin resulted in uniform termination /

termination of the disease. Treatment with either A.C.T.H. or Cortisone had resulted in more prompt control of certain acute manifestations, but this more rapid improvement was balanced by a greater tendency for the acute manifestations to re-appear for a limited period upon cessation of treatment. Treatment with the hormones was followed by a more rapid disappearance of nodules and soft apical systolic murmurs. At the end of one year, however, no significant difference among the three groups, occurred in the status of the heart.

The Five-Year Joint U.K. - U.S.A. Report(1960), recorded the state of the patients after a follow-up of five years. The conclusion was reached that prognosis is not influenced more by one treatment than by another.

In a Leading Article in the British Medical Journal(1960), it is suggested that perhaps larger doses of hormone, adjusted to the age and weight of the patient, and possibly combined with higher dosage of salicylates than those used in the trial, might prove to be helpful. However, both these treatments have dangers attached.

Work of outstanding importance in support of salicylate treatment in rheumatic fever has been carried out by several workers.

Magarey(1951) and Tweedy(1956), as mentioned earlier have shown that when fibrin is deposited on a heart valve, it undergoes organisation and is converted into fibrous tissue which becomes incorporated in the valve substance, so adding to its thickness with consequent valvular damage.

A /

A published account of plasma fibrinogen in rheumatic fever was written by C. A. Ernstene(1930). On studying twenty-two patients with rheumatic fever, he found that the mean plasma fibrinogen concentration level did not reach the normal value of 0.3G. per 100 ml. until about 12 weeks of intermittent salicylate therapy, and that there was pronounced individual variation in the rate of fall of plasma fibrinogen so that the distribution of fibrinogen concentrations apparently becomes increasingly dispersed with the passage of time.

Again, Reid and Sproul(1957) studied 33 consecutive cases of acute rheumatic fever during the first 21 days of full salicylate therapy, controlled by serum salicylate levels; maintaining these at between 30 and 45 mg. per 100 ml. They found an abnormally high plasma fibrinogen concentration in each of the cases on admission to hospital. This fell rapidly and uniformly during a continuous intensive course of salicylate treatment.

This result was sharply in contrast to Ernstene's results, but he used short intermittent courses of salicylates.

Reid and Sproul reported relapses in six patients, when salicylate therapy was discontinued, each relapse being accompanied by elevation of plasma fibrinogen, which returned to normal after a second course of salicylate.

Their results provide definite evidence that salicylate does more than just relieve symptoms, having a direct effect in eradicating excess /

excess of plasma fibrinogen in the circulating blood of rheumatic fever patients, and preventing at least some degree of cardiac damage, though this is not the complete answer to preventing subsequent cardiac damage. As seven of their patients showed fibrinogen levels still slightly above normal after 21 days of treatment, this confirms, as is generally regarded to be the case, that there is no set optimum dosage level of the drug.

In each case, the dose and duration of treatment should be controlled not only by frequent estimations of serum salicylate levels, but also with reference to the fibrinogen concentration, in conjunction with other better known tests of activity, e.g., erythrocyte sedimentation rate and C-reactive protein.

On considering the above results of Reid and Sproul, Holt et al, and those of the Combined U.K. and U.S. Clinical Trial, it appears that to date, the only really adequate treatment of rheumatic fever at present is with salicylate therapy in adequate dosage and for a sufficient period of time.

Digitalis and Diuretics may be required if the patient develops cardiac failure during the course of the illness, but salicylate therapy must also be continued at that time.

Intercurrent Infections

The patient must be isolated from all infected persons, especially if the infection is suspected as being due to haemolytic streptococci. Any infection occurring in the patient must be immediately treated with a course of penicillin.

(3) Care of the Patient During Convalescence

As soon as active symptoms and signs of rheumatic fever have abated, the rheumatic child should have occupational therapy, continued general education, and physiotherapy. A continual watch must be kept for recurrence of active rheumatic disease.

(4) After Care of the Rheumatic Patient

To remove possible foci of infection, septic teeth, tonsils and adenoids should be removed under cover of penicillin therapy.

Immediately after an attack of rheumatic fever, the patient should commence a prophylactic regime to prevent a recurrence of the disease. Prophylaxis is discussed in Chapter VII of this work.

A patient whose heart has been affected, must be taught how to live with his disability, and with these patients, great help is often obtained from the advice of a Social Welfare Worker. However, it must be stressed that it is imperative to avoid a patient being converted into a cardiac neurotic. Those patients with valvular disease must be observed in case they require valvulotomy.

Paul Wood(1956c) states that "in general, any patient suffering from the effects of mitral stenosis requires valvotomy, any who is able to continue his normal occupation without distress, does not".

CHAPTER VI

Findings on 437 Cases of Rheumatic Fever Studied Within the Glasgow Area.

437 cases of rheumatic fever were studied in this work. Of these, 37 cases were re-admissions, leaving a total of 400 patients studied. Data for the patients in the Sick Children's Hospital, Yorkhill, Glasgow, was obtained from Case Histories, as was that pertaining to those patients admitted to the Western District Hospital, Glasgow, between the years 1950-1952 inclusive.

Several very interesting findings arose, viz. -

Three patients presenting with arthritis and carditis, also had congenital heart disease, one of whom died.

One patient who presented with chorea also had rheumatoid arthritis.

Three patients had choreiform movements of one side of the body only; one was left, and two were right-sided.

Only seven patients were noted as having rheumatic nodules. Two of these patients presented with both arthritis and chorea occurring simultaneously.

Two patients presenting with arthritis also developed acute nephritis which subsided spontaneously.

Two patients presented with arthritis and erythema nodosum.

One case with chorea had erythema marginatum on admission.

Six cases which presented with arthritis were recorded as having palpable /

palpable rheumatic nodules. Four of these presented with arthritis, and two presented with arthritis and chorea occurring simultaneously.

Four cases presenting with arthritis relapsed, to present with chorea within intervals of six weeks, three, sixteen and seventeen months, respectively.

One case of chorea was re-admitted twenty-one months later with rheumatic fever.

One patient presenting with arthritis relapsed within 33 months and again 19 months later.

One patient with chorea relapsed within five months, again 15 months later, and again five months later.

The earliest recurrence of patients presenting with arthritis occurred four months after discharge from hospital. The longest period of time which occurred before a first recurrence was 81 months.

The earliest recurrence of chorea was six weeks and the longest period prior to a first recurrence was 26 months.

From these results it is noticeable that there is still a risk of a first recurrence of rheumatic fever for as long as 81 months (approximately seven years) after the initial attack.

It should be noted, that this does not represent the natural recurrence rate of rheumatic fever in this series as many latterly were on prophylactic regimes.

Mortality Rate

Of the 400 patients studied, there were 7 deaths (1.75 per cent) attributable /

attributable to acute rheumatic fever. The ratio of females to males was 5 : 2.

Three of these patients had developed mitral stenosis, aortic incompetence, pericarditis, and ultimately congestive cardiac failure prior to death.

Two died after developing congestive cardiac failure superimposed upon mitral stenosis and aortic incompetence.

Two died with acute bacterial endocarditis superimposed on mitral stenosis and aortic incompetence.

Their ages were 5, 7, 10, 13 and 15 years in females and 14 years and 15 years of age in males.

A further patient, (a female aged 17 years) who had developed mitral stenosis subsequent to an attack of chorea, was readmitted (31 months after her discharge from hospital), suffering from a right hemiplegia due, it was decided, to a cerebral embolism in the left lenticulo-striate branch of the middle cerebral artery. She greatly recovered from this, only to collapse and die suddenly, two days after returning home. Autopsy was not performed.

The total mortality rate was therefore 8 (2 per cent), the ratio of females to males being 3 : 1.

Results of Electrocardiograph Recordings (E.C.G.s)

There were 130 records of electrocardiograph tracings available for study.

88 of these were taken during the course of an attack of rheumatic /

rheumatic fever, and include those records available at Yorkhill Hospital, as well as at the Western District Hospital. The findings were as follows:-

30 E.C.G.s showed normal tracings.

31 were "within normal limits".

3 showed "splintering of the Q.R.S complex" (of no significance).

2 showed "sinus bradycardia with left axis deviation". (of no real significance).

4 showed "early right axis deviation" (of no real significance).

4 showed "prominent Q waves" (of doubtful significance).

2 showed "abnormal P waves" - indicating previous rheumatic infection.

5 showed evidence of "early mitral stenosis".

Only 7 E.C.G.s (7.9 per cent) showed "prolongation of the P-R interval" - which is indicative of an active myocarditis.

42 E.C.G. tracings were recorded on discharge from the ward prior to entering the Rheumatic Fever Prophylactic Clinic and these will be described in Chapter VII.

Table Showing Incidence of
Carditis in the Present Work

Age Incidence	0-4 yrs.	5-9 yrs.	10-15 yrs.	16-21 yrs.	Total
Total Cases with Arthritis	10	117	149	41	317
with Carditis	3	47	76	26	152
w'out Carditis	7	70	73	15	165
Total Cases with Chorea	-	48	63	4	115
with Carditis	-	8	19	3	30
w'out Carditis	-	40	44	1	85
Total Cases with Arthritis and Chorea	-	2	3	-	5
with Carditis	-	1	2	-	3
w'out Carditis	-	1	1	-	2

From this table the following facts emerge:-

Of the 317 cases presenting with arthritis, 152 (47.9%) had carditis and 165 (52.1%) were free from carditis.

Of the 115 cases presenting with chorea, 30 (26.1%) had carditis and 85 (73.9%) were free from carditis.

Of the 5 cases presenting with arthritis and chorea together, 3 had carditis, and two were free from carditis.

Carditis occurring during rheumatic fever was most common in 10-15 age group.

Valvular Damage

In the 37 recurrent cases, only the final valvular damage was taken into account, no murmur was therefore counted twice in the one patient.

The following table illustrates the incidence of valvular disease.

	Mitral Valve Lesions	Aortic Valve Lesions	Combined M.and A. Lesions.
Arthritis patients	67	9	29
Chorea patients	14	-	8
Arthritis + Chorea	1	-	1
TOTALS:	82	9	38
% of 400 cases :	20.5	2.25	9.5

As can be seen from the above table, the mitral valve was the most affected, damage being present in 20.5 per cent of the total 400 cases of rheumatic fever.

The following table reveals the sex and age incidence of valvulitis occurring amongst the 400 patients.

Valvular Damage During Illness

Age Incid.		0 - 4		5 - 9		10 - 15		16 - 21	
Sex		M.	F.	M.	F.	M.	F.	M.	F.
No. of attack of Rheumatic Fever (Carditis)	1	-	3	14	11	14	16	5	4
	2	-	-	3	2	6	6	2	3
	3	-	-	1	1	5	3	2	3
	4	-	-	-	-	-	-	-	1
	5	-	-	-	-	-	-	-	-
	6	-	-	-	-	-	1	-	-
		- : 3		18 : 14		25 : 26		9 : 11	
No. of attack of Rheumatic Fever (Chorea)	1	-	-	-	3	1	7	-	1
	2	-	-	1	-	1	3	-	1
	3	-	-	-	-	-	-	-	1
	4	-	-	-	-	-	1	-	-
	5	-	-	-	-	-	-	-	1
		-	-	1 : 3		2 : 11		- : 4	
Carditis and Chorea		-	-	-	1	-	1	-	-
TOTALS:		- : 3		19 : 18		27 : 38		9 : 15	

74 females : 55 males (ratio 1.3 : 1).

Thus valvulitis was found to be more common in females and the greatest incidence of valvulitis occurs between the ages of 10 - 15 years.

It was not possible for me to assess the amount of residual valvular damage in the Yorkhill Hospital patients, so this will not be discussed here.

It was interesting to note that one female patient aged 14 years had /

had had six attacks of rheumatic fever(presenting with arthritis) and had no resultant cardiac damage.

A nineteen year old male had had four attacks of arthritis and had no resulting cardiac lesion.

Arthritis, Chorea, Arthritis and Chorea Considered Together (437 Cases)

	0-4 yrs.	5-9 yrs.	10-15 yrs.	16-21 yrs.
Age Incidence	10	167	215	45
No. with Carditis	3	56	95	28
No. without Carditis	7	111	20	17
No. with Valvular Damage	3	37	65	24

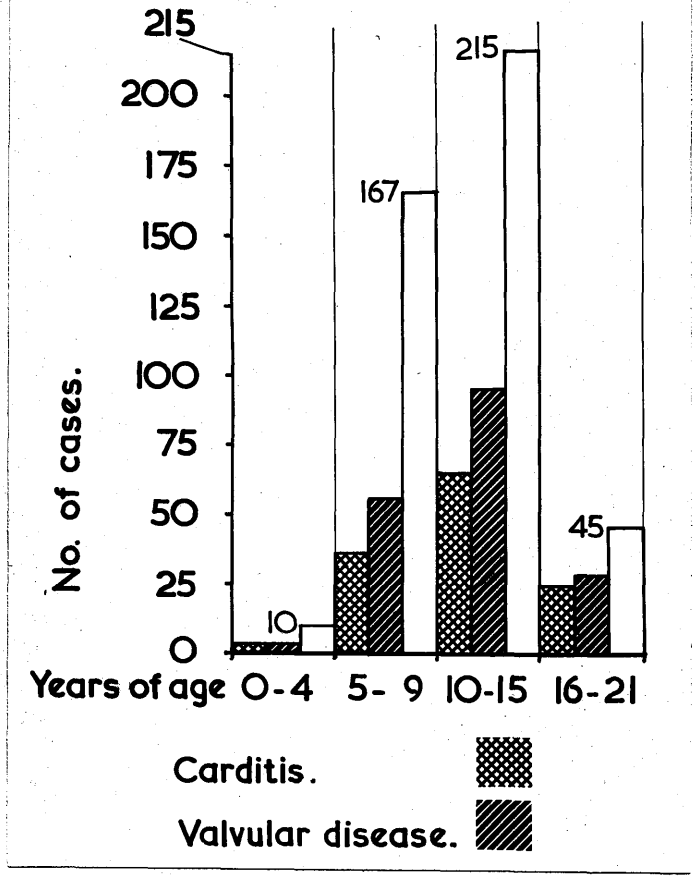


DIAGRAM 18.

The above diagram illustrates the incidence of carditis and valvular damage in the various age groups of the 400 patients studied. The numbers at the top of each column indicate the total number of patients in that particular age group.

Incidence of Pericarditis

Of the 400 patients studied, 11 of those presenting with arthritis developed pericarditis, and 4 of those patients presenting with chorea also developed pericarditis. The total number was therefore 15 cases (3.75%).

Recurrences of Rheumatic Fever with Resultant Cardiac Status.

Of the 37 recurrent attacks in 29 patients, 18 patients had no organic murmur present, either during the earlier attack or subsequently; 4 patients had organic murmurs during the earlier attack, and the murmurs persisted unchanged; in the remaining 7 patients, 2 had no organic murmurs in the earlier attack but developed gross organic murmurs after subsequent episodes, and 5 had organic murmurs during the earlier attack, and these increased after subsequent attacks.

Thus with two exceptions, patients who had no organic murmur during one attack, emerged equally unscathed from subsequent attacks. In 5 cases when the organic murmur was audible during the earlier illness, the damage increased subsequently, but in 4 cases the original murmur remained unchanged in subsequent attacks. These results are similar to those found by Feinstein and Spagnuolo(1960).

Incidence of Family History

24 patients presenting with arthritis gave a family history of either chorea or rheumatic fever.

The corresponding number in those presenting with chorea was 13.

In only one case was there a history of a further sibling being affected by rheumatic fever at the same time.

CHAPTER VII

Prophylaxis of Rheumatic Fever

The Need for Prophylaxis

It is well known that rheumatic fever is a common source of heart disease.

The Rheumatic Fever Committee of the Royal College of Physicians, London, issued an Interim Report(1947), which resulted in the compulsory notification of acute rheumatism (including chorea) in certain English Local Health Authority areas. As a result of this the Rheumatic Fever Committee were able to state in their Further Report(1957) that in 1956 in England and Wales, there were 8,208 deaths attributed to chronic rheumatic heart disease, many of them in persons under 35 years of age, and 208 deaths directly attributable to rheumatic fever. This number of deaths due directly to rheumatic fever, showed a marked decrease over the previous ten years. Even so, the results indicated that rheumatic fever is still of outstanding importance as a cause of death and disablement in the younger population.

Leff(1956) showed that in notifying areas 0.027% of school children are attacked by rheumatic fever each year.

Rheumatic fever is a disease that can usually be prevented by early detection and adequate treatment of streptococcal infections. Recurrences /

Recurrences have been reported in as many as 50% of these cases who develop attacks of streptococcal disease. This has been ably shown by Massel et al.(1951), in their work on prevention of rheumatic fever by prompt penicillin therapy of haemolytic streptococcal respiratory disease.

According to work done by Rantz et al.(1948), it is reported that rheumatic fever follows on approximately 3 per cent of all group 'A' beta-haemolytic streptococcal infections.

R.A.N. Hitchins(1958) described the experiences of recurrent attacks of rheumatic fever in a group of Cardiff school children with rheumatic heart disease, who attended the School Rheumatic Clinic from 1931-1950. He observed that recurrent episodes occurred in about one third of the whole group.

The classic study which reveals the risk of recurrent attacks of rheumatic fever, and the natural history of the disease, was that done by Dr. E. F. Bland, and the late Dr. T. Duckett Jones(1951). After studying 1,000 patients since childhood, over a period of 20 years, they noted that the recurrence rate of rheumatic fever remained roughly stable for the five years after the initial attack and then slowly began to decline.

R. Ash(1948) published his findings after studying 588 children for the first ten years following their initial attack of rheumatic infection. During this time, <u>forty per cent</u> of the group had developed recurrences of rheumatic infection within the first <u>two</u> years; <u>fifty-eight per cent</u> within <u>five</u> years; and <u>sixty-three per</u> /

per cent within ten years.

He considered that two-thirds of the recurrences might have been prevented by adequate antibiotic therapy for a period of two years after the attack.

In order to prevent such recurrences, it was recommended by the American Heart Association (through their Committees Appointed by the Council on Rheumatic Fever and Congenital Heart Disease(1953)), that after an attack of rheumatic fever a patient should be placed on a prophylactic regime against streptococcal infection, which regime should continue indefinitely.

The pioneer work in the prophylaxis of rheumatic fever was carried out by Thomas and France(1939) and Coburn and Moore(1939). They introduced the prophylactic use of small daily doses of Sulphonilamide over long periods, and found that this was of good effect in preventing recurrences of acute rheumatism.

P.J. Burke(1947) published the first results with penicillin prophylaxis, finding that rheumatic manifestations were five times more frequent, and throat infections six times more frequent in the control group than in the treated group.

Elias et al.(1951) first reported on N.N'dibenzylethylenediamine penicillin (known also as intramuscular Benzathine Penicillin G). In the following year, the preparation first appeared on the market, and Stollerman and Rusoff(1952) made the important discovery that of 16 patients, mostly children, given 1.25 million units of Benzathine Penicillin G, /

Penicillin G, all had assayable levels after 21 days, and that even 28 days after the injection had been given, 75% of the patients still had assayable penicillin blood levels.

It was not technically possible to have Penicillin blood levels assayed at the Western District Hospital during the years the Prophylactic Follow-up Clinic was in progress (commenced in 1953). However, using the figures of Stollerman and Rusoff, stating that the administration of 1.25 million units of intramuscular Benzathine Penicillin resulted in assayable blood levels after 21 days, it was decided to commence prophylaxis in a number of patients (chosen by random selection) with 600,000 units (2 cc.) every two weeks of Benzethacil N.N'-dibenzylethylenediame Dipenicillin G aqueous suspension. This dosage was recommended by the manufacturers, Messrs. Wyath Ltd., who kindly supplied us with this material, known under the trade-name of "Penidural" L.A. Each cc. of "Penidural" L.A. contains 300,000 units (approximately 300 mg.) of N.N'-dibenzylethylenediamine Dipenicillin G with 0.014% propylparahydroxybenzoate and 0.12% of methylparahydroxybenzoate as preservatives.

Before discussing clinical work and results, it is necessary to consider whether the dosage of penicillin given could be regarded as adequate.

(1954)

It was gratifying to learn from work done by Putnam and Roberts that in their series of 64 injections of Benzathine Penicillin G to 7 patients (each of whom were susceptible to streptococcal infections), by the intramuscular route, in doses of 1.2 million units at monthly intervals /

intervals, blood concentrations of penicillin taken from 5 to 39 days after injection, varied from 0.02 unit per ml. to 0.210 unit per ml. Not one of these patients failed to show penicillin in the serum up to 39 days after administration of the injection.

Later, Stollerman(1954a) stated that an intramuscular injection of 600,000 units of Benzathine Penicillin resulted in a penicillin blood level of 0.1 - 0.4 unit per ml., continuing up to 0.4 unit per ml. for ten days, then falling to 0.3 unit per ml., until the twelvth day after the injection - the level then dropping steadily thereafter. He concluded that "The injection of 600,000 units of N.N'-dibenzylethylenediamine Dipenicillin G provides low serum levels of penicillin for 12-14 days".

In a study of the prophylaxis of the recurrence of rheumatic fever by Kohn et al(1953), it was repeatedly found that the group 'A' strains of the haemolytic streptococcus were sensitive within the range of 0.001 to 0.008 Oxford unit of penicillin per ml. Of these, 80% were sensitive within the range of .001 to .02 unit.

This is proof indeed that penicillin, if adequately given, is lethal to the haemolytic streptococcus.

However, since carrying out my work for this Thesis, I am now of the opinion that in some instances, with the use of long-acting intramuscular penicillin, the patient harbours haemolytic streptococci in some inaccessible region, which allows them to escape the effects of the penicillin with the possibility of recurrence of rheumatic fever. The reason for this statement is the fact that

five /

five of my patients who were on a prophylactic regime with intramuscular penicillin, were found to have haemolytic streptococci on routine throat swab culture. These organisms had not become insensitive to penicillin, and after a course of oral benzathine penicillin given for five days (the intramuscular penicillin also having been given) there were no haemolytic streptococci found on a repeat throat swab culture taken on the sixth day.

These cases will be described later.

At the time of my work, as stated before, it was not technically possible to have penicillin blood levels performed. Cope et al(1960), have proved that by using penicillin G. orally, in a dose of 200,000 units b.d., the blood penicillin level reaches the required 0.08 unit per ml. within 30-60 minutes, and is maintained for longer than three hours.

The dosage administered (for eradicating haemolytic streptococci found on routine throat swab cultures) in my series was Permapen Penicillin (Benzathine Penicillin) 400,000 units thrice daily for five days. This dose, in comparison with the findings of Cope et al, was more than sufficient for eradicating haemolytic streptococci.

In their work, the above authors, whilst administering oral penicillin as a prophylactic measure found that many children developed a high anti-streptolysin 'O' titre in the absence of evidence of rheumatic disease and they remarked that they were unable to isolate group 'A' streptococci from the throats of their patients before or during a period of rising titre of ASO, despite constant /

constant effort. This finding, together with the suggestion of Massel et al(1951) " ..... that the Group 'C' or Group 'G' streptococci were responsible for the ASO rise in their patients" led Cope et al(1960) to state "that it seems open to question whether the ASO rise in these (their own) cases were due to a streptococcal other than group 'A' or whether the group 'A' streptococcus was harboured by the patient in some inaccessible region, and thus despite penicillin prophylaxis." This is in agreement with my findings.

Experience of Rheumatic Fever Prophylactic Clinic at the Western District Hospital, Glasgow

As stated earlier in this work, it was decided in 1953 to commence a prophylactic regime for the cases of rheumatic fever (up to the age of 21 years) which were admitted to the Western District Hospital, Glasgow.

This work was greatly hindered by the fact that many laboratory facilities were unobtainable at that time, viz. - typing of haemolytic streptococci; estimation of anti-streptolysin 'O' titre, C-reactive protein.

It was not possible to have the blood penicillin levels of the patients estimated.

This work is presented with a view to suggesting a method of prophylaxis which has not been tried before. It also proposes an alternative method of dealing with the rather difficult teen-age group of patients.

As the number of patients was necessarily small, (because of the /

the falling incidence of rheumatic fever generally) it is not possible to generalise in the manner possible when several hundred patients are considered. Altogether 42 patients were studied.

The prophylactic drug of choice was finally considered to be intramuscular Benzathine Penicillin G. (Benzethacil N.N'-Dibenzyl-ethelenediamine Dipenicillin G. - also known as "Penidural" Penicillin).

The broad-spectrum antibiotics (chloromycetin, erythromycin, aureomycin, tetracycline) were considered, but in view of the fact that there is a high occurrence rate of digestive upsets and fungus infections associated with these drugs it was decided that their place in continuous prophylaxis was limited. The broad-spectrum antibiotics are also costly, and are less effective against haemolytic streptococci.

The Sulphonamide drugs were also considered, but though they have the advantage of being of low cost, they have the disadvantages that they are liable to cause skin eruptions, blood disorders, particularly agranulocytosis; also, the sulphonamides are known to cause the development of resistant micro-organisms in the throat. Penicillin is relatively inexpensive, more effective against haemolytic streptococci, and toxic manifestations such as allergic reactions, urticaria, oedema and joint inflammation are less severe than with any of the aforementioned drugs.

The intramuscular penicillin was chosen, as against the oral variety, so as to ensure if possible, continuous supervision of the patients, and thus, continuous prophylaxis.

The /

The final reason towards making the choice of Penicillin as the prophylactic drug to be used, was the fact that, to that date, there had been no reports of any strain of resistant haemolytic streptococci resulting from continuous prophylaxis.

(a) The Rheumatic Fever Prophylactic and Follow-up Clinic at the Western District Hospital, Glasgow

Method

The Rheumatic fever Prophylactic and Follow-up Clinic was commenced in 1953 at the Western District Hospital, in view of the increase in the number of cases of rheumatic fever which were being admitted that year. The prophylactic regime, which is described below, was an original attempt at estimating the benefit using Penicillin as a prophylactic agent.

The series was limited to children and young persons up to 21 years of age.

All patients entering the trial had been admitted to hospital suffering from rheumatic fever, as diagnosed according to the Jones' Criteria (Modified), which was accepted by the Committee of the Executive Council of the American Heart Association on the Standards and Criteria for the Programs of Care of Rheumatic Fever and Congenital Heart Disease, in the Report(1955).

In all, 42 patients entered the trial. Two (both females) presented with chorea, and 40 presented with arthritis. This number is necessarily small, as the incidence of cases admitted to the hospital began to fall during the following years until by the end of 1959, /

1959, there were none.

Ratio of females to males was 1 : 1.2. Average age of the patient was 13.8 years.

The cases were divided by random selection, into two groups, viz.:-

Group (A) - Those receiving fortnightly injections of 2 cc. (600,000 units) of Benzethacil N.N'-dibenzylethylenediamine Dipenicillin G. (as recommended by Messrs. Wyath Ltd., the manufacturers), during the months of October to June each year. This limited duration of time was necessary as, almost without exception, the patients were against the idea of regular injections for an indefinite period of time. It would have been preferable to have continued the prophylaxis regularly every month. There were 23 patients in this group.

Group (B) - Those who were to act as a control series. There were 19 patients in this group. They were instructed to attend the clinic at intervals of six weeks, but were very erratic in attending.

The ages of the patients ranged from seven years to twenty-one years of age. With the exception of one patient (J.S. who failed to attend for her injections until after she had had a recurrence), all were included in the trial immediately after their discharge from hospital.

At each visit to the Clinic the patient was examined, a throat swab culture was taken, and the erythrocyte sedimentation rate was estimated, /

estimated, using the Westergren Method.

Haemoglobin estimation (using the Sahli method) and Chest X-rays were performed when indicated.

In all, 485 injections of "Penidural" Penicillin were given.

Difficulties Encountered

As stated previously, it was not technically possible, at that time, to have blood penicillin levels estimated, nor was it possible to have antistreptolysin titres carried out, nor typing of any haemolytic streptococci which were present on culturing throat swabs.

Seven of the patients (A.G., J.McH., C.J., K.G., H.G., J.B., and R.S.) latterly attended well. However, the remaining sixteen had poor attendance records -

There were seven defaulters after fourteen to twenty-one injections and the remaining nine patients defaulted after injections varying in number from two to eight. This reveals that it proved to be most difficult and, in some cases, impossible, to persuade the patients to continue to attend the clinic.

Those with good attendance records were either accompanied each time by a parent, or were constantly enforced by their parents to attend. The defaulters gave varied reasons for discontinuing their treatment. It was very much in evidence that the majority were going through the difficult teen-age era, and that their respective parents or guardians had very little interest in their health. /

health. The "five-year" routine follow-up clinics had to be held on Sunday afternoons, and without the help of nursing staff, due to lack of accommodation of examination rooms during weekdays, and general shortage of nursing staff at weekends.

The help of a Welfare or Social Worker was greatly missed to help "bring it home" to all the parents just how important it was to have their children attend for treatment. Repeated requests were sent to parents and guardians by letter - without avail. Several of the defaulters' homes were then visited personally but, in two cases, visited on several occasions, there was no reply, and in others, luke-warm promises were made to see that the children would attend, but these came to nothing.

One patient (J.M.) repeatedly ignored all communications after her second injection, and finally no trace of her could be found even through the local Executive Council. A.G., an inmate of a Reform School prior to admission to hospital, attended the clinic for so long as he was under the jurisdiction of the Headmaster, and thus attended for only six injections. He was very aggressive and refused any further treatment. For three years no trace of him could be found until finally, (knowing his character) he was traced through the After-Care Council of H.M. Prisons, but again he ignored appeals to attend the Clinic, or even for examination.

T.D. defaulted after sixteen injections, giving no reason, and ignored requests to return to the Clinic.

G.A. /

G.A. was very averse to injections, and though he was persuaded (by judicious bullying on his Mother's part!) to attend for 18 injections, she finally wrote to say that she greatly appreciated all that was being done for her son, but that he was now "too big" for her to "man-handle" to the Clinic! It was only after he received written proof that no further injections would be given, that he finally attended for a routine examination five years later.

After receiving 19 injections, I.K. changed her employment, and at her new work, money was deducted from her wages after each attendance at the Clinic. She was given the opportunity to attend on Saturdays or Sundays, or even after working hours, but she refused, saying that this would interfere with her social life, as would attending her own General Practitioner for the injections. Her employer was then contacted to see if he could be persuaded to be more lenient, but no reply was received.

Similar arguments were put forward by J.McK. (who received seven injections); E.M. (who received three injections); J.J. (seven injections); S.W. (fourteen injections); D. McC. (seven injections); S.McC. (fourteen injections); and by H.McQ. (eight injections. P.C. attended for only six injections as he stated that they "were of no use".

M.F., who attended for four injections, wrote to say that her employer did not believe that it was necessary for her to attend the Clinic and that if she did she would require to find fresh employment. A letter was sent explaining matters to her employer, and /

and requesting his permission to allow her to attend, but this met with no result. She too, refused to attend for her injections after working hours. All further trace of this patient was lost, and it is now understood that she had emigrated soon afterwards.

Two patients, J.McG. (who attended for eighteen injections) and J.S. (who attended for twenty-one injections), did not wish any further treatment, as "they felt so well".

Real financial hardship was experienced by several of the patients in travelling to and from the Western District Hospital, more especially those who had been rehoused in outlying schemes.

It became very obvious, that these adolescents were very much against having long-term prophylaxis, several because it made them feel like invalids, and "different from other people", and several because they frankly "could not be bothered". In the latter group it was obvious that any attempt at oral prophylaxis to be taken regularly at home, was out of the question. There was difficulty found also in persuading some of the control patients (Group B) to attend for routine visits, even at fairly long intervals. In most cases, they defaulted after an average of two years. However, they were all willing to return whenever they felt unwell, or had a sore throat. With some patients, it was becoming evident that they were becoming markedly neurotic, as too much attention was being focused on prophylaxis.

By the end of 1956, because of the almost minimal occurrence of cases of rheumatic fever, and because the number of patients attending the /

the clinic had fallen to four and they were all wishing to discontinue regular treatment as they "felt so well", it was decided to discontinue the routine follow-up clinic. The patients of both groups were then instructed to contact their own doctors whenever they suffered from a sore throat, or were in direct contact with a person so suffering. The respective doctors were each asked to then prescribe Permapen Penicillin (Benzathine Penicillin) 400,000 units thrice daily for five days.

This arrangement met with whole-hearted approval from the patients. This, to them, was a much more rational and pleasant method of prophylaxis.

Without exception, they had admitted that they probably would not remember to take daily oral prophylaxis, or even for a few days each month, for an indefinite number of years, as suggested by Kohn et al(1953).

It must be mentioned here, that letters had been sent, where possible, to all defaulters, instructing them to attend their own doctors for the above treatment with Permapen Penicillin on developing, or coming into direct contact with, a throat infection. The family doctors had been contacted previously, and were agreeable to co-operate.

Results of the Trial:-

(a) Recurrences of Acute Rheumatism

The recurrence rate in group A (those allocated to receive fortnightly /

fortnightly injections of Penidural), markedly reflects the attitude of the modern younger generation who only worry when ill-health attacks them. There were two patients readmitted to hospital with a frank recurrence of rheumatism; one other, with cardiomegally and tachycardia. Yet another patient returned to the clinic (after a long absence) with a letter from his own doctor to say that he had had a recurrence of his symptoms for two weeks.

The details of these patients are as follows:-

(1) A.G. - Patient attended for only one injection after his discharge from hospital. There was no reply to letters sent asking him to return for further treatment. Three months from the date of his discharge, he returned to the Clinic looking very toxic, and was readmitted suffering from an acute recrudescence of rheumatic fever. On his subsequent discharge after having "learned his lesson", he was one of the most faithful attenders at the clinic. Alas, the damage to his heart had been done. In all, he received 59 injections of "Penidural".

(2) J.S. - After her discharge from hospital, this patient neglected to attend the clinic despite many requests to do so. Fifteen months later, she was readmitted with an acute recrudescence. She then attended for 21 injections - only to default thereafter.

(3) J.McG.- After his discharge from hospital he attended for /

for only one injection of Penicillin, and thereafter defaulted, until he returned to the Clinic (five weeks after discharge) complaining of extreme dyspnoea. He was found to have a cardiomegally and a sinus tachycardia. This condition improved with rest alone. As his erythrocyte sedimentation rate was normal, no salicylates were given, but prophylactic penicillin was given fortnightly whilst in hospital. On subsequent discharge he attended for a further 13 injections, thereafter defaulting.

(4) J.McK.- This patient also neglected to return to the clinic after his discharge from hospital. Seven months later, he returned with a letter from his own doctor stating that he had been treated at home for the two previous weeks, with a recrudescence of rheumatic fever. However, he appeared well and his erythrocyte sedimentation rate was normal. Thus there is no definite proof that he actually had had a recurrence. Thereafter, he attended for 7 injections of penicillin, only to default once again.

(5) E.M. - Defaulted after 3 injections. On routine review five years later, she stated that she had had a "recurrence" treated at home by own doctor. This is doubtful.

Thereafter, none of these patients suffered a recurrence of rheumatic fever.

Thus /

Thus it can be seen that no recurrence actually occurred during regular prophylactic penicillin therapy.

In group B, there were four recurrences of rheumatic fever. The details of the patients were as follows:-

(1) M.McA. - was readmitted with a recrudescence 27 months after discharge.

(2) R.B. - was readmitted with a mild recrudescence 2 months after discharge. He did not require salicylate medication.

(3) W.McK. - This boy was readmitted 7 months later, and died within a few weeks. The post-mortem report stated that - "Examination of the heart valves revealed acute rheumatic lesions superimposed upon old hyaline rheumatic lesions." There was also an incidental subacute phthisis, with slight miliary spread. It was concluded that the condition was an acute exacerbation of chronic rheumatic endocarditis (mitral, aortic and tricuspid valves) with terminal rheumatic pericarditis and heart failure.

(4) E.M. - This girl was admitted to a fever hospital by her own doctor 32 months later. He had suspected an acute meningitis. The child died, and at post-mortem examination the findings were "An acute bacterial endocarditis, plus an area of cerebral haemorrhage in /

in the left occipital lobe, which was considered to be probably embolic in origin. As well as the bacterial thrombi present on the mitral valve, firm thrombi were present along the lines of contact of the valve cusps. These had the appearance of an acute rheumatic infection. A blood culture performed at the time of admission produced a growth of coagulase positive staphylococci.

(b) Throat Culture

In all, 485 routine throat swab cultures were taken in group A. (Those attending for penicillin prophylaxis). Six (1.2 per cent) of these revealed the presence of haemolytic streptococci. (as mentioned before, it was technically impossible to have the different strains of streptococci typed). These organisms were discovered after varying numbers of regular injections of Penicillin had been given. They were discovered only on one occasion in each of six patients. Five of these patients were treated with oral Benzathene Penicillin ("Permapen" - Pfizer) 400,000 units thrice daily before meals, for five days. A repeat throat swab, in each case, taken at the end of this treatment did not produce haemolytic streptococci on culture. The remaining patient, (P.C.) whose throat was very badly inflamed on a routine visit, was given a five-day course of Sulphatriad (2 gm. initially and 1 gm. four-hourly) pending the result of a throat swab, in case he had developed an infection with a penicillin-resistant organism. This in fact had not occurred, the culture of the throat swab revealing no colonies of haemolytic streptococci /

streptococci but a heavy growth of organisms, predominanty neisseria. A repeat swab, taken at the end of the course of Sulphatriad, revealed only a light growth of normal throat commensals.

The varying number of regular penicillin injections given prior to the occurrence of haemolytic streptococci in a routine throat swab culture were as follows:-

(1)	G.A.	- developed haemolytic streptococci in throat after	9 injections
(2)	J.S.	" " " "	11 injections
(3)	C.J.	" " " "	25 injections
(4)	J.B.	" " " "	27 injections
(5)	M.F.	" " " "	3 injections
(6)	P.C.	" " " "	6 injections

There were no recurrences amongst these patients.

In group B, the patients were requested to attend less frequently than those in group A, and thus the number of routine throat swabs (from those who actually attended) numbered only 180. Amongst these, six (3.3 per cent) revealed the presence of haemolytic streptococci on culture. They were also treated with "Permapen" oral penicillin, in the same dosage as above, with resulting eradication of the organisms from the throat, as shown by a repeat throat culture at the end of the treatment. None of these patients had recurrences of rheumatic fever. In addition, two "control" patients (M.McA. and R.B.), on readmission with recurrent attacks of rheumatic fever, were found to have haemolytic streptococci on culture of a throat swab. R.B. was given a course of Crystalline Penicillin (1 million units initially, followed by 500,000 units twice daily, intramuscularly, for six days) and /

and became free from the presence of the offending organisms. M.McA. however had haemolytic streptococci in her throat on three other occasions during her second stay in hospital. On each occasion, the organisms were sensitive to penicillin, and she responded to courses of Crystalline Penicillin given intramuscularly, in the same dosage as used in the case of R.B. Incidentally, both these patients defaulted from the Follow-up Clinic.

(c) Reactions in Patients Receiving Prophylactic Penicillin.

All patients who received the intramuscular injections of "Penidural" Penicillin, mentioned a pricking and burning sensation at the site of the injection. This occurred a few seconds after each injection and lasted for two to three minutes. Some patients stated that they had experienced local muscle stiffness at the site of the injection.

One particular batch of "Penidural" caused general malaise of varying degree, together with extreme pain at the site of injection, in all patients receiving an injection that day. Only one patient (J.McH.), developed a marked local reaction, with erythema and swelling at the injection site but it was thought that there was some secondary infection present. He also felt very nauseated and complained of headache. His symptoms subsided on treatment with bed rest and calamine lotion locally. Further injections caused no further reactions in any of the patients. This batch of "Penidural" was returned to the manufacturers for analysing. The report /

report was as follows:-

" ..... the representative samples of the unopened vials and the contents of the two partly used vials of "Penidural" L.A. Injection have been found to be sterile, and satisfactory in every respect.

We are at a loss to explain why, after having used the preparation successfully for several months, you should have suddenly experienced a series of adverse reactions ....."

There were no reactions amongst those patients who received "Permapen" oral penicillin.

There were no hypersensitivity reactions to either the oral or the intramuscular penicillin used.

(d) Alteration in Cardiac Murmurs

(1) Group A.

Of the 23 patients instructed to attend for prophylaxis with "Penidural", only seven can be seriously considered as to the alteration in cardiac murmurs as a result of penicillin prophylaxis.

These seven attended regularly for many injections.

Three of them had clinical evidence of rheumatic valvular disease on entering the trial. One (A.G.) still had systolic and diastolic murmurs at the mitral area five years later.

C.J., on entering the trial had an audible mitral diastolic murmur; 32 months later, she was admitted with signs suggestive of

a /

a cerebral embolism, but no diastolic murmur was audible at the mitral area.

J.B., on entering the trial, had systolic and diastolic murmurs at the mitral area. The heart sounds were pure five years later.

The other four patients were free from evidence of valvular damage prior to entering the trial and remained so. Of these, J.McH. had been almost one year in hospital with rheumatic fever.

Seven other patients attended for shorter intervals, ranging from 14 to 21 injections only. Of these, one (J.McG.) had systolic and diastolic murmurs at the apex before entering the trial, and these were still audible when he was examined five years later.

The remaining six had no evidence of valvular disease either before the trial or several years later.

Nine patients defaulted from the clinic after a number of injections varying between two to eight.

The resultant cardiac conditions in this group were as follows:-

Two, E.M. and D. McC., who showed evidence of valvular damage on entering the trial, had no change in their murmurs several years later.

E.M. had presystolic and systolic murmurs at the mitral area, and D.McC. had systolic and diastolic murmurs at the aortic and the mitral area.

The remaining seven defaulters in this group all remained free from evidence of valvular damage several years later as far as could be ascertained.

(2) Group B.

Three patients had evidence of valvular damage on admission to the series. Their respective cardiac lesions were as follows:-

(1) E.M. Ventricular systolic and diastolic murmur at the apex. This patient was initially admitted with chorea. She died 32 months later during an acute attack of rheumatic fever and bacterial endocarditis.

(2) W.McK. Systolic and diastolic murmurs were present at the mitral and aortic areas. He died 8 months later during a recurrence of rheumatic fever and congestive cardiac failure.

(3) A.H. A mid-diastolic murmur was present at the mitral area on entering the trial, and remained unchanged.

The remaining 16 patients were free from evidence of valvular damage on admission to the trial, and had remained so when reviewed several years later, despite the fact that two of them (M.McA. and R.B.) had had a recurrence of rheumatic fever.

Electrocardiographic Changes (E.C.G.)

Of the 42 patients entering the trial, only 2 (4.8 per cent) showed E.C.G. evidence of cardiac involvement.

The E.C.G. of patient (C.J.), in group A, showed broadening of the /

the P wave in all leads, which persisted in later tracings.

The E.C.G. of W.McK., in group B, showed slow conduction through the A-V bundle. This had subsided five months later. The remaining 40 E.C.G.s revealed no significant abnormality.

(e) Intercurrent Infections During the Trial

In group A, three patients, each regularly receiving penicillin prophylaxis, developed intercurrent infections.

(1) K.G., was subject to frequent attacks of coryza, and a subacute sinusitis. The offending organisms were not isolated.

(2) J.B., was subject to frequent attacks of coryza and bronchial asthma, but stated that his asthma had improved greatly since commencing his penicillin prophylaxis. The offending organisms were not isolated.

(3) C.J., developed an acute coryza on one occasion. There were several colonies of staphylococci present on the throat swab culture but no haemolytic streptococci. She had no evidence of recurrence of chorea.

In group B, three patients had recurrent attacks of coryza, one of whom also developed a sinusitis, and later, an acute appendicitis (J.S.).

One patient developed Sonne Dysentry; one an atypical virus pneumonia; one had a urinary infection with Bacillus Coli, and one (E.M.) developed a septic finger on one occasion, and a hordeolum of /

of her right upper eyelid some weeks later - both of which were treated at the Casualty Department of another hospital.

As the number of patients receiving regular penicillin therapy in this series was so small, a comparison between the relative rates of intercurrent infection would be meaningless.

(f) Mortality Rate

In group A, there was one death (4.35 per cent), amongst the 23 patients. (As mentioned previously, this girl, C.J., died as the result of a cerebral embolism, 33 months after discharge from hospital after her initial attack).

In group B, there were two deaths (10.5 per cent), amongst the 19 patients. (As mentioned previously, W.McK. died as a result of acute rheumatic endocarditis, pericarditis, and heart failure, and E.M. died as a result of acute bacterial endocarditis and cerebral embolism.)

As the numbers in each group were necessarily small, the mortality rates cannot be compared.

(b) Discussion

It is stated in a Leading Article in the British Medical Journal(1956) that the incidence of rheumatic fever has fallen in Great Britain over the last 50 years.

As has been discussed elsewhere in this work, the beta haemolytic streptococci have long been associated with the occurrence of rheumatic fever. Stollerman(1954b) showed the range of penicillin sensitivity in vitro of group A streptococci to be 0.01-0.04 units/ml.

Therefore, because of this high sensitivity, the low but sustained concentration of penicillin resulting from an injection of Benzathine penicillin (as previously discussed), is adequate.

Diehl et al(1954), in a trial of long-acting repository penicillin with 96 children over a period as long as 14 months, reported that only one child suffered a mild recurrence. Out of 10,000 injections, only two reactions occurred, but almost all patients complained of a burning or stinging sensation whilst the injection was being given.

Of 1,045 throat cultures taken, 40, or 3.8% showed the presence of beta-haemolytic streptococci, only 4 of which proved to be Lancefield Group A.

In the trial carried out at the Western District Hospital, Glasgow, (where the series, of necessity, was much smaller) no reactions peculiar to any one patient occurred out of 485 injections, although one batch of Penidural penicillin (suspected of being faulty) caused /

caused minor upsets in all the patients to whom it was given. The complaints were of nausea, generalised malaise, an elevation of temperature (according to several patients), and varying degrees of local reactions at the site of injection, only one patient showing a fairly severe reaction which (at the time) was thought to be due to local infection.

There were no recurrences of rheumatic fever amongst those patients who attended regularly for penicillin prophylaxis. Out of the 485 throat swabs taken routinely, 6 or 1.2% revealed the presence of haemolytic streptococci on culture.

Literature is replete with reports on the efficacy of Benzathine Penicillin as a prophylactic agent against the recurrence of rheumatic fever. In accordance with Diehl et al(1954), Stollerman et al(1955), and again Diehl et al(1956), found no recurrences on using this substance over varying periods of time.

Oral penicillin has also been widely used in the prevention of streptococcal infection. J.R. Seal(1955) has reported the results of studies carried out in several different groups of U.S. Navy recruits in order to find out (a) the minimal effective dosage necessary to suppress outbreaks of acute upper respiratory infections, and (b) the minimal effective dosage necessary to eliminate streptococci from carriers.

He concluded that epidemics of streptococcal infection can be prevented by the continuous administration of oral penicillin G in

a /

a dose as small as 50,000 units daily; that epidemics can be abruptly stopped by the use of 250,000 units twice daily for 10 days; and that a succession of 10-day courses of penicillin in the higher dosage can be relied upon to keep streptococcal infection under control, and to prevent rheumatic fever. Further evidence in support of oral penicillin as an efficient prophylactic agent, is found in the report by M.D. Markowitz(1957). However, he stated that a dose of at least 400,000 units daily should be given. Cope et al(1960) published their report on the use of Penicillin V 60 mg. b.d. and Penicillin G 200,000 units b.d. for one year. Neither regime proved completely effective, as of those receiving Penicillin V, 7 relapsed out of the 40 patients in the series; 2 developed chorea, and one congestive cardiac failure.

Of the 39 patients receiving Penicillin G, 3 relapsed; one developed chorea, and one congestive cardiac failure. There were 6 cases with intercurrent infection in the Penicillin V group, and 3 in the Penicillin G group.

They concluded that larger doses would be more effective, and are working on this at present.

In the prophylactic trial at the Western District Hospital, oral Benzathine penicillin (Permapen) was prescribed for those patients who were found to have haemolytic streptococci present when routine throat swab cultures were taken, and excellent results were obtained in each case (i.e., eradication of the offending organisms from the throat, and no subsequent recurrence of rheumatic fever).

Lim /

Lim and Wilson(1960) have published a report on a 6-year study on the recurrence rate of rheumatic carditis in patients receiving penicillin by mouth prophylactically, or on indication. They found that there was no significant difference in the recurrence rate of actual carditis among the patients receiving continual oral prophylaxis, and those on adequate penicillin therapy given during a respiratory illness, when the interval since the last attack was considered.

Therefore, they concluded that with children under close medical supervision, continuous oral penicillin prophylaxis has no advantage over adequate penicillin therapy given as and when required.

On reading their report, however, it appears that these workers did not ascertain the number of subclinical streptococcal infections in either group by estimating the anti-streptolysin titre, or taking routine throat cultures. It must be noted here, that J.M. Miller(1959) reported that rheumatic fever can recur after subclinical streptococcal infections, and that they could not be effectively prevented by the use of penicillin for only overt respiratory tract infections.

Markowitz et al(1957) compared the use of oral and intramuscular Benzathine penicillin G for the prevention of streptococcal infections and recurrences of rheumatic fever. They concluded from their results that a single daily oral dose of 200,000 units of Benzathine penicillin G taken regularly, proved as effective as monthly injections of 1,200,000 units of intramuscular Benzathine penicillin G.

Mou /

Mou et al(1960) reported their results of a 3-year period during which 139 patients, with either rheumatic heart disease, or an acceptable history of previous rheumatic fever, were provided with streptococcal prophylaxis either with Benzathine penicillin G, 200,000 units daily by mouth, or 900,000 units intramuscularly each month. Both regimen appeared to be effective in preventing clinical group A streptococcal infections and recurrent acute rheumatic fever. A modest increase in acute streptolysin O titres were noted with equal frequency in both the treatment groups, and were related to clinical illnesses. These were noticed particularly in the spring months.

Lunther and Franklin(1959), to quote yet further experience in the field of prophylaxis, described the effects of 636 individuals who had had previous attacks of rheumatic fever, and who were supplied with prophylactic Benzathine penicillin, for varying periods of time. The patients had the choice of having either the tablet form (200,000 units daily), or the intramuscular form (1,200,000 units each month). It was found that this had resulted in a 13-fold decrease in the recurrences of rheumatic fever since the plan was initiated. Undesirable side reactions occurred in 0.9 per cent of all patients, with very little difference noted between the different routes of administration. No severe reactions to penicillin were seen.

Kaplan(1958) using oral Phenoxymethyl penicillin (125 mg. daily, increasing to 625 mg. daily for 10 days, on finding beta-haemolytic streptococci on routine throat swabbing of asymptomatic patients), found a very low incidence of intercurrent infection due to group A beta-haemolytic /

beta-haemolytic streptococci. He concluded that this form of prophylaxis was practicable and successful.

Amongst 266 patients in the second year of his study, only two patients receiving 125 mg. of Phenoxymethyl penicillin had streptococci present on a routine throat swab, and there was only one recurrence of rheumatic fever. It was interesting to note from Kaplan's discussion that he had tried monthly injections of long-acting Benzathine penicillin in a small group of patients, but had had to discontinue this method of prophylaxis, because regular attendance had dropped when patients and parents refused a monthly, painful injection, whilst the patient was well. The prophylactic follow-up rheumatic fever clinic at the Western District Hospital, Glasgow, was disbanded for this, as well as other reasons.

Apart from being unpopular with children and adults, there is a higher incidence of allergic reactions occurring with intramuscular penicillin, than with the oral type. As high as 5.2 per cent of reactions was found by Chancey et al(1955) amongst patients receiving intramuscular Benzathine penicillin, as compared with 1.1 per cent amongst those receiving oral Benzathine penicillin.

Inherent in every attack of rheumatic fever is the threat of yet another. It is reported in a Leading Article in the British Medical Journal(1959) that, while the relapse rate of rheumatic fever with continuous penicillin prophylaxis is about 4 per cent, the rate without such treatment is likely to be anything from 40 - 70 per cent.

The /

The American Heart Association (Committees Appointed by the Council on Rheumatic Fever and Congenital Heart Disease : "Prevention of Rheumatic Fever)(1953), and also Rantz et al(1948) stated that in the general population, about 3 per cent of untreated cases of streptococcal infections are followed by rheumatic fever. This was again confirmed by the American Heart Association in the Statement of the Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis(1960).

Therefore it is of importance to treat all streptococcal infections in all patients with adequate therapy. In all cases of known streptococcal infection under my care, I have been accustomed to prescribing Crystalline Penicillin, in a dosage of 1 million units initially, followed by 500,000 units twice daily, for 6-10 days, depending on the severity of the infection. Excellent results have always been obtained.

The conclusion reached at the Symposium of Streptococcal Infections, held at the New York Academy of Medicine(1954) was that penicillin was the drug of choice in the prophylaxis of rheumatic fever. The Statment of the American Heart Association's Committee on the Prevention of Rheumatic Fever and Bacterial Endocarditis(1960) gives their recommendations (using penicillin or sulphadiazine), for preventing the recurrences of rheumatic fever, together with the relative merits of the different methods; the duration of prophylaxis; the indications for prophylaxis; and prevention of subacute bacterial endocarditis. (Extracts from this Statement are printed in /

in Appendix E of this work).

According to the American Heart Association, the safest general procedure is to continue prophylaxis indefinitely, particularly if rheumatic heart disease is present. Knowing the difficulty experienced at the Prophylactic Clinic at the Western District Hospital, it does not appear feasible to prescribe such long-continued treatment. Young children can be supervised by their parents, but once the typical modern "teenagers" have outgrown parental control, they cannot be relied upon to attend the clinic, or to take oral medication regularly, if at all. They do appreciate, however, (as became evident during the Prophylactic Clinic sessions), that as soon as they develop a sore throat, they must take measures to have this treated.

In their "Further Report", the Rheumatic Fever Committee of the Royal College of Physicians, London(1957), state their recommendations with regard to dosages of their drugs of choice for the prophylaxis of rheumatic fever - viz. oral or intramuscular penicillin, together with the indications for this, and the prevention of subacute bacterial endocarditis.

This Committee advocates that prophylaxis against rheumatic fever should be continued for 5 years, or until the child has left school, whichever is the longer.

Bywaters and Thomas(1958), agree with this advice. Also in support of the 5-year prophylactic regimen, is the finding by Bland and /

and Jones[1951] after a long-term study of the natural history of the disease, that the recurrence rate remained roughly stable for the first five years after the initial attack, and then slowly began to decline. In this present work, it was found that there was a risk of a first recurrence up to seven years after the initial attack.

R.A.N. Hitchins[1958] in his article, noted a similar finding. This suggests that supervision of the rheumatic patient should be extended up to seven years after the initial attack.

There are several drawbacks to long-term treatment with penicillin. For example, the withdrawal effects, if any, after its use over a prolonged period of years is not yet known, and at the end of this time a susceptible patient might be even more likely to suffer a recurrence of rheumatic fever, having maybe no natural immunity to the haemolytic streptococcus.

Though the literature, as discussed above, is replete with proof that penicillin-resistant strains of streptococci do not develop, before long other organisms resistant to penicillin will grow in the throats of those patients receiving continuous prophylactic penicillin, leaving them liable to many severe infections, to which otherwise, they would most probably have had a natural resistance. This state of affairs must be avoided. It would appear that it would be of great value to have throat swab cultures taken at, say, 3-monthly intervals to ascertain whether any penicillin-resistant organism has developed. In this event, penicillin therapy should be discontinued /

discontinued for several weeks, and if it is considered essential to continue prophylaxis, this could be done by using, for example, Sulphadiazine 0.5 to 1.0 gm. daily during this time - the smaller dose being used in children under 60 pounds in weight, as recommended by the American Heart Association in their Statement issued in 1960. (Please see Appendix E).

CHAPTER VIII

SUMMARY

437 cases of rheumatic fever occuring within the Glasgow area were studied during 1950-1959. Of these, 37 were recurrences, leaving a total of 400 individuals studied.

The total number of cases presenting with arthritis was 317, the ratio of females : males being 1 : 1.1. Initial attacks were most common between the ages of 7 - 16 years. Recurrent attacks occurred most commonly at the age of 12 years.

The total number of cases presenting with chorea was 115, the ratio of females : males being 3.4 : 1. Initial attacks were commonest between the ages of 8 - 11 years. The commonest age of a recurrent attack was 10 years, subsequent attacks being rare.

There were 5 cases of arthritis and chorea occurring together, the ratio of females : males being 4 : 1. There were no recurrences in this group.

On studying the yearly incidence of cases of rheumatic fever since 1950, an increase in incidence of cases was noticed in the year 1952-1953, with a steady decline thereafter. The greatest number of cases occurred during the months of December, January and March, with a rise in incidence in the month of July. There was no connection between the onset of rheumatic fever, and the amount of rainfall, or the amount of fog in the Glasgow area, during the years 1950 /

1950 - 1959. However, there was found to be a correlation between the amounts of ground frost occurring, and the incidence of rheumatic fever. There is a definite correlation between the density of the population and the number of cases - as the population decreased, so also did the incidence of rheumatic fever, with a few exceptions, in the areas studied.

Practically all the patients had come from over-crowded homes, but it was interesting to note that only 37 patients (or 9.3 per cent) were described with a family history of the disease, and in only one case, was there a history of a further sibling having rheumatic fever at the same time. It was evident that the majority of patients came from homes which were situated near waterways.

The majority of cases of rheumatic fever occurred in Social Classes III, IV, and V of the population, but more especially in Class III. The average total household income of the families of 62 patients was £9.9.0d. which is below the average for population of Lanarkshire as a whole.

In the 400 patients studied, the mortality rate was 2 per cent, the ratio of females to males being 3 : 1.

Out of 88 records of electrocardiograph tracings studied during the acute phase of rheumatic fever, only 7 (7.9 per cent) showed definite evidence of active myocarditis. Out of 42 E.C.G.s studied after discharge from hospital, only 2 (4.8 per cent) showed evidence of cardiac damage (one showed no significant abnormality, when repeated five months later).

Of the 317 cases presenting with arthritis, 47.9 per cent showed evidence of carditis.

Of the 115 cases presenting with chorea, 26.1 per cent had evidence of carditis.

Of the 5 cases presenting with arthritis and chorea occurring simultaneously, 3 (60 per cent) had evidence of carditis.

Valve lesions occurred with the following frequency - mitral in 20.5 per cent of cases; aortic in 2.25 per cent; combined aortic and mitral valvular damage in 9.5 per cent.

Valvulitis was found to be more common in females, the ratio of females to males being 1.3 : 1 and in the 10 - 15 years age group.

Pericarditis was present in 3.75 per cent of the 400 patients studied.

With two exceptions, patients who had had no organic murmur during the earlier illness emerged equally unscathed from subsequent attacks.

In 1953 a Rheumatic Fever Prophylactic Clinic was commenced at the Western District Hospital, Glasgow. 42 patients entered the trial, whereby, by means of random selection, they were divided into (a) those receiving long-acting penicillin every two weeks, and (b) those acting as controls. There were 23 in the first group and 19 in the second. The average age of the patients was 13.8 years. There were 19 females and 23 males in the series (1 : 1.2).

There were no recurrences in those of Group A who were receiving regular /

regular intramuscular Benzathine Penicillin. In the control group, there were four recurrences of rheumatic fever.

485 routine throat swabs were taken in Group A (those receiving prophylactic intramuscular Benzathine penicillin) and six (1.2 per cent) were found to have grown haemolytic streptococci on culture.

Of the 180 routine throat swabs in the control group B, six (3.3 per cent) were found to have grown haemolytic streptococci on culture.

Comparison of throat swab cultures between the two groups is not possible, as the control group were seen much less frequently than the group on prophylactic treatment.

All patients found to have haemolytic streptococci in their throats on routine culturing, were given a 5-day course of Permapen (oral Benzathine Penicillin) and on repeating the throat swab culture at the end of this treatment, it was found that without exception, the culture did <u>not</u> contain haemolytic streptococci.

Apart from one batch of Penidural penicillin, which caused minor upsets in all those receiving it, and a severe local reaction (which at the time was thought to be due to secondary infection) in one patient, there were no reactions observed in any patient, either with the oral or intramuscular group. There was no recurrence of a local reaction in the aforementioned patient, on receiving further injections of benzathine penicillin. Only 3 patients suffered intercurrent infections whilst receiving continuous intramuscular Benzathine penicillin, whilst amongst the control group there were

10 such incidences.

Three patients, each receiving regular "Penidural" penicillin injections, had evidence of rheumatic valvular disease on entering the trial; one showed no alteration in cardiac murmurs five years later; one had no evidence of valvular damage five years later; one died 32 months after the initial attack, as a result of a cerebral embolism.

Other four patients who had attended regularly for many months, were all free from evidence of valvular damage prior to entering the trial, and had remained so when reviewed five years later.

Seven other patients, attended for shorter intervals ranging from 14 - 21 injections - of these, only one patient had evidence of valvular damage on entering the trial, and this had remained unchanged when he was examined five years later.

The remaining six of this group had no evidence of valvular damage at any time.

Of the remaining nine patients who defaulted after a number of injections varying from 2 - 8, seven had no evidence of valvular damage on entering the trial, and remained thus five years later, as far as could be ascertained.

The remaining two had valvular damage on entering the trial, and the murmurs had remained unchanged five years later.

Apart from one exception, it was evident in both groups that if the patient excaped valvular damage during the initial attack, he emerged equally unscathed from subsequent attacks.

It proved most difficult to maintain the patient's interest in a prophylactic regime whilst they felt in good health.

CHAPTER IX.

CONCLUSION

It has now become an established fact that prophylaxis against streptococcal infection is essential in the after-care of the rheumatic fever patient, and as can be seen from the literature studied in this thesis, penicillin has become the drug of choice.

Long-term prophylaxis of rheumatic fever, using fortnightly injections of 600,000 units of long-acting penicillin (Benzethacil N.N'-dibenzylethylenediamine Dipenicillin G, known also as "Penidural" was used in the present work, being supplemented by a 5-day course of oral Benzathine penicillin (400,000 units thrice daily before meals) whenever haemolytic streptococci were isolated from a routine throat swab culture. This combined oral and intramuscular long-term method was found to give most satisfactory results, and so far has not been suggested by any other worker.

In retrospect, if 1,200,000 units of "Penidural" had been administered monthly (instead of 600,000 units fortnightly) attendance at the Follow-up Clinic might have risen, as the injection method of prophylaxis, though very efficient, has the great drawback that patients dislike having "the needle". Whilst the younger age group of patients still under parental control have good attendance records, once they become "teenagers", they default, with a few exceptions, from the prophylactic regime. These teenagers, so long as they feel fit /

fit and well, spurn all attempts at medication - all the more so, when it is given by injection. It is in those patients who fear injections but are willing to have prophylactic treatment, that oral Benzathine penicillin, as recommended by the Rheumatic Fever Committee of the Royal College of Physicians, London(1957) is of great value. An extract of the American Heart Association's most recent recommendations on the use of oral penicillin prophylaxis is printed in Appendix E. of this work.

It was very evident amongst the wayward defaulters, that as soon as they felt ill, they were most anxious to accept treatment. This type of patient should be instructed to report to their physician at any sign of infection, such as a "cold" or a sore throat, or if they are in close contact with a person so suffering, when they should thereupon receive a 5 to 10-day course of Permapen penicillin (400,000 units thrice daily before meals): the duration of the treatment depending on the severity of the signs and symptoms. This latter course proved very effective in the control series (Group B) in this present work.

It was found that a risk of a first recurrence of rheumatic fever lasts up to 7 years, therefore, it is suggested that close observation of the patients be continued for this period, even though they cannot be persuaded to take continuous prophylaxis throughout that length of time.

Post-rheumatic fever patients should be taught to avoid overcrowded living conditions, and to choose if possible, localities

away /

away from the close proximity to waterways. Those who decline to attend for regular prophylaxis should also be instructed to contact their physicians during frosty weather, in order that they may be provided with a course of oral penicillin, such as 400,000 units thrice daily for 10 days, or for as long as conditions persist (ground frost having been found to have a direct correlation to the onset of rheumatic fever).

It is deemed advisable in those patients on continuous penicillin prophylaxis, to take routine throat swab cultures at, say, 3-monthly intervals, to ascertain whether any organisms resistant to penicillin have arisen. This condition could be corrected by discontinuing the penicillin for several weeks, and another drug, such as Sulphadiazine (0.5 to 1.0 Gm. daily, depending on the age of the patient), substituted during this time.

SUMMARIES OF CASES COMPRISING THE RHEUMATIC FEVER PROPHYLACTIC CLINIC AT THE WESTERN DISTRICT HOSPITAL, GLASGOW.

SUMMARIES OF CASES COMPRISING THE RHEUMATIC FEVER PROPHYLACTIC CLINIC AT THE WESTERN DISTRICT HOSPITAL, GLASGOW.

This description is divided into two parts, viz:-

Part A - Those cases chosen by random selection, to attend for fortnightly injections of Penidural long-acting Penicillin /Benzethacil N.N'-Dibenzylethylenediamine Dipenicillin G Aqueous Suspension (Wyeth)/, after their discharge from hospital.

Part B - Those cases, also chosen by random selection, to act as controls in the series. These cases did not receive Penidural Penicillin. They were seen at two-monthly intervals, or more frequently if the occasion arose.

As stated previously, at each patient's visit to the hospital a throat swab culture was made, and the Erythrocyte Sedimentation Rate was estimated. A chest X-ray was taken routinely at six-monthly intervals, and more frequently if indicated, to assess the cardiac size.

To avoid repetition, the following points can be made here:-

(a) Salicylates when administered, were prescribed in the dosages stated, and in each case were continued until the erythrocyte sedimentation rate had remained normal for two weeks, when the dose was gradually decreased before finally being discontinued.

(b) An alkaline mixture of Potassium Citrate and Sodium Bicarbonate (containing 30 grains of each), was administered when required (as indicated), and continued until symptoms of salicylism had subsided. This averaged seven days.

(c) Whenever oral iron was prescribed, the duration of treatment was for 21 days, unless otherwise stated.

(d) When a course of Crystalline Penicillin was given, the dose, in every case, was 1,000,000 units initially, followed by 500,000 units morning and night, for five days.

(e) /

(e) Permapen Penicillin /Benzathine Penicillin (Pfizer - 200,000 units per tablet)/ when mentioned, was given in each case in the following dosage:- 2 tablets (i.e. 400,000 units) thrice daily before meals for five days.

The following abbreviations are used throughout the summary:-

E.S.R. Erythrocyte sedimentation rate, as estimated by the Westergren Method, and read in millimetres at the end of one hour.

Hb. Haemoglobin, estimated as a percentage, using the sahli method, 100% ≡ 14.8 gms. Hb. per 100 ml.

W.B.C. White blood count - the number of Leucocytes per cubic millimetre of blood.

R.B.C. Red blood count - the number of red corpuscles per cubic millimetre of blood.

E.C.G. Electrocardiogram.

H.S. Haemolytic streptococci.

T. Temperature, in degrees Farenheit.

P.R. Pulse rate per minute.

R. Respirations per minute.

B.P. Blood pressure as estimated in mms. of mercury.

A.B. Apex Beat of the heart, as estimated in inches from the mid-sternal line (M.S.L.), in appropriate left (L.) intercostal space.

M.C.L. Mid-clavicular line.

G. Gramme.

gr. Grains.

Agglutination Tests. Include those for Typhoid, paratyphoid and Paul Bunnell Test.

All throat cultures were made on Blood Agar plates.

PART A.

1. A.G.

Aged 9 years. Male. Second attack of rheumatic fever.

Admitted 2.6.54. Discharged 29.11.54. No. of days in hospital: 121

Complaint: Flitting joint pains of four weeks' duration.

History: First attack three years previously.
Sore throat three weeks prior to admission
No family history of rheumatic fever.

Clinical Examination: T. 101°F. P.R. 100/min. Regular. R. 26/min.
Hb. 86%. W.B.C. 4,200/c.mm. E.S.R. 39 mm.
Tonsils enlarged and septic.
Knees and wrists swollen.

Heart: B.P. 100/70.
A.B. ½" outside the M.C.L. in 5th L. space.
Systolic murmur audible at apex, and down left border of the sternum.

Lung Fields: Normal.

Examination of urine: No abnormality detected.

X-ray Chest: Heart of "mitral" shape, although not enlarged.
Lung fields clear.

Barium Swallow: "Slight enlargement of left auricle, right ventricle, and pulmonary trunk, consistent with mitral stenosis".

E.C.G. "Early right axis deviation".

Laboratory Findings: Throat swab - numerous H.S. grown on culture.
Blood cultures, Agglutination Tests } Consistently negative.

Treatment: Aspirin gr. 15, four times daily.
A course of Crystalline Penicillin was given on account of tonsillitis.

Progress: Normal and uneventful. E.S.R. slowly returned to normal.

Condition on Discharge: A loud systolic murmur audible at the apex.
Hb. 98%. E.S.R. 3 mm. E.C.G. "Early right axis deviation".

Follow-up: After discharge, he only attended for one injection of penicillin, and neglected to return despite many requests to do so. When next seen, he arrived at the Clinic, looking very toxic and complaining of a sore throat and painful, stiff knees. He was re-admitted to hospital.

Re-admission: /

Re-admission: 12.2.55. Discharged: 21.7.55. No. of days in hospital : 155.

Clinical Examination: T. 99°. P.R. 98/min. R. 26/min.
Hb. 86% W.B.C. 7,000/c.mm. E.S.R. 30 mm.
Acute tonsillitis. Swollen knees.

Heart: B.P. 100/75.
A.B. ½" outside M.C.L. in fifth L. space. Systolic and diastolic murmurs audible at apex. Occasional extrasystoles present.

Lung Fields: Normal.

Examination of urine: No abnormality detected.

X-ray Chest: Cardiac shadow enlarged, and of mitral configuration. Lung fields clear.

E.C.G.: Again showed early right axis deviation.

Laboratory Findings: Throat swab - No H.S. grown on culture but many colonies of strep. viridans were obtained.
Blood cultures, Agglutination Tests } Consistently negative.

Treatment: Aspirin gr. 15, five times daily.
Sulphatriad, 1 gm. initially and ½ gm. four hourly thereafter for six days was given on account of his tonsillitis.
(The patient stated that his own doctor had given him "injections" at home. ?"Penicillin".)

Progress: Four days after admission, a diastolic murmur became audible at aortic area. Two months later, no diastolic murmurs were audible. Patient gradually became symptom-free and E.S.R. slowly subsided to normal. He was then transferred for removal of tonsils and adenoids, commencing his fortnightly Penidural injections.

Condition on Discharge: Hb. 100%. W.B.C. 4,200/c.mm. E.S.R. 5 mm.
Heart - A.B. ½" outside M.C.L. in fifth left space. Loud rough systolic murmurs at apex, base and pulmonary areas.

X-ray Chest: Cardiac outline not quite so large.

Follow-up: Remained well and symptom-free.
In all he received a total of 59 injections of Penidural penicillin. The patient and his parents then decided that he had had sufficient treatment, and, as he was now perfectly well, did not require further injections.
16.5.56 - Mitral stenosis, and aortic incompetence present. No signs of congestive cardiac failure.

Routine Review: /

1. A.G. (Continued).

Routine Review: 5.4.59. (aged 14 years) - Well and enjoying splendid health. No history of recurrence of rheumatism.

Heart: A.B. $\frac{1}{2}$" outside M.C.L. in 5th left space. Systolic and diastolic murmurs at apex only.

2. G. A.

Aged 12 years. Male. First attack of rheumatic fever.

Admitted 9.9.53. Discharged 21.1.54. No. of days in hospital: 135.

Complaint: Flitting joint pains of five weeks' duration.
Feeling easily tired.

History: Sore throat ten weeks previously.
Nervous "tic" of head of many years' duration.

Clinical Examination: T. 99°. P.R. 90/min. Regular. R. 20/min. Hb. 105%
W.B.C. 12,500/c.mm. R.B.C. 4.9M/c.mm. E.S.R. 40 mm.
Left ankle and left knee swollen.
Mild erythematous rash on shoulders.

Heart: B.P. 100/75.
A.B. 3½" from M.S.L. in 5th L. space.
Short soft systolic murmur at base at pulmonary area.
Splitting of second sound at pulmonary area.

Examination of urine: No abnormality was detected.

X-ray Chest: Normal.

E.C.G.: Sinus tachycardia.

Laboratory Findings: Throat swab - No H.S. present.
Blood cultures) Negative.
Agglutination Tests)

Treatment: Aspirin gr. 15 four times per day.

Progress: Patient's condition steadily improved and convalescence was uneventful.

Condition on Discharge: Hb. 80%. W.B.C. 6,200/c.mm. E.S.R. 1 mm.
E.C.G. Normal.

Heart: A.B. 3" from M.S.L. in 5th L. space. Soft systolic murmur was audible at the apex.

Follow-up: Child remained very well. A routine throat swab revealed H.S. on culture after 9 regularly administered injections of Penidural penicillin. A course of Permapen penicillin was given and on repeating the throat swab culture thereafter, no H.S. were grown.
This child received only 18 injections of Penidural. Though of a quiet, pleasant nature, he had a violent dislike for injections, and ultimately refused to attend any longer. A very humerous letter from his mother stated that he was no "unfortunately too big and strong for her to manhandle to the clinic".
This patient emigrated to Canada, where he continued to remain well. When traced (after some difficulty) on his return to this country, he could only be persuaded to attend for a routine follo-up examination after receiving written confirmation that no further injections would /

2. G.A. (Continued).

would be given him.

Routine Review: 5.4.59. (aged 18 years) - remained well. No recurrences of rheumatic fever. Had had three attacks of sore throat in the previous year which responded to oral Penicillin.

Heart: A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space. Systolic murmurs at mitral and aortic areas.

X-ray Chest: Normal.

3. I.K.

Aged 18 years. Female. First attack of rheumatic fever.

Admitted 19.12.55. Discharged 4.2.56. No. of days in hospital: 47.

Complaint:	Pains in knees, ankles and feet of four days' duration. No family history of rheumatic fever.
Clinical Examination:	T. 99.6°. P.R. 108/min. Regular. Both knees and left ankle swollen and painful.
Heart:	B.P. 115/75. A.B. 3½" from M.S.L. in 5th L. space. Soft systolic murmur at apex.
Lung Fields:	Normal.
Examination of urine:	No abnormality detected.
X-ray chest:	Normal.
E.C.G. :	No abnormality.
Laboratory Findings:	Throat swab - No H.S. found on culture. Blood cultures, Agglutination Tests } Negative.
Treatment:	Aspirin gr. 20 five times daily.
Progress:	Patient made a normal uneventful recovery.
Condition on Discharge:	Hb. 90%. W.B.C. 6,200/c.mm. E.S.R. 3 mm.
Heart:	A.B. 3½" from M.S.L. in fifth L. space. Soft systolic murmur at apex.
E.C.G. :	Normal.
Follow-up:	Remained well and symptom free. It is important, and interesting to note, that in this case, the patient was very willing to come for her injections, but for two reasons, she decided to discontinue the treatment, viz: (1) it cost 1/4d. in bus fares each time she attended. (2) the more important to her, was the fact that her employer deducted money from her wages during the time she was away from her work. Similar reasons held when she changed to another type of employment. She had no wish to attend hospital, or even her own doctor, in evenings or at weekends. In all, she attended for 19 injections of Penidural Penicillin.
Routine Follow-up:	1959 (aged 22 years). Patient did not attend as requested but according to her own doctor she remains well, and examination of her heart reveals only a soft systolic murmur at the mitral area.

4. P.C.

Aged19 years. Male. Third attack of rheumatic fever.

Admitted 18.5.54. Discharged 30.7.54. No. of days in hospital: 73.

Complaints: Flitting joint pains, especially in knees and elbows for one week.

History: Sore throat three weeks previously.
No family history of acute rheumatism.

Clinical Examination: T. 100.2°. P.R. 120/min. Regular. R. 22/min.
Hb. 98%. W.B.C. 9,200/c.mm. E.S.R. 46 mm.
Both elbows stiff and painful.
Left knee swollen and painful. Movement limited to about 10° flexion.

Throat: Fauces slightly inflamed.

Heart: B.P. 115/65.
A.B. 3½" from M.S.L. in 5th L. space.
Soft ventricular systolic murmur at apex.

Examination of urine: No abnormality detected.

X-ray Chest: Normal.

E.C.G.: Normal.

Laboratory Findings: Throat swab - no H.S. obtained on culture.
Blood cultures, Agglutination Tests) Negative.

Treatment: Aspirin gr. 20 five times daily.

Progress: Patient made a good recovery, with an uneventful convalescence.

Condition On Discharge: Hb. 100%. W.B.C. 6,200/c.mm. E.S.R. 4 mm.

E.C.G.: Normal.

Heart: B.P. 115/65.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur at apex.

Follow-up: At his first visit to the Follow-up Clinic, he was found to have a markedly inflamed throat. His own doctor was asked to give him a course of Penicillin at home, as he did not wish to come back into hospital again. The throat swab culture at that time revealed a heavy growth of organisms, including a moderate growth of H.S.
On return to the Clinic one week later, his throat was still grossly inflamed, and it was discovered that he had only received Penicillin once daily and not twice daily as requested. In view of the fact that the offending /

4. P.C. (Continued).

offending organisms might have become resistant to Penicillin, it was decided to give him a course of Sulphatriad (2 gm. initially and 1 gm. four hourly for six days).
A throat swab taken at that visit, however, revealed on culture, a heavy growth of organisms predominantly neisseria. No H.S. were present on culture.
By his next visit, his throat infection had subsided. Penidural prophylaxis was then commenced, but he was a very erratic attender, and in all, received only 6 injections. He claimed that the injections "were of no use".
When last seen he was well, and had no evidence of cardiac damage.

Routine Review: May, 1959 (aged 24 years). Patient could not be traced, as he had removed from Glasgow. His own doctor stated that when he last examined him, one year previously, he was very well and had had no recurrence of acute rheumatism. His heart sounds were pure at that time.

5. S. McC.

Aged 14 years. Male. First attack of rheumatic fever.

Admitted 3.1.55. Discharged 8.3.55. No. of days in hospital: 64.

Complaint: Fleeting pains, affecting all his joints of twelve days' duration.

History: Sore throat three days prior to onset of joint pains. No family history of acute rheumatism.

Clinical Examination: T. 100°. P.R. 98/min. Regular. R. 20/min. Hb. 80%. W.B.C. 8,200/c.mm. E.S.R. 30 mm. Fauces inflamed. Ankles and wrists swollen and painful.

Heart: B.P. 100/60.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at all areas.

Examination of urine: No abnormality detected.

X-ray Chest: Normal.

E.C.G. "Suggests mitral stenosis."

Laboratory Findings: Throat swab - Heavy growth of H.S. grown on culture.
Blood cultures, Agglutination Tests } Negative.

Treatment: Aspirin gr. 20 four times daily.
Course of Crystalline Penicillin.

Progress: Patient made a steady uneventful recovery.

Condition on Discharge: Hb. 98%. W.B.C. 6,200/c.mm. E.S.R. 3 mm.

Heart: B.P. 100/60.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur present at apex.

Follow-up: Patient remained very well, but attended for only 14 injections. His reason for discontinuing treatment was that his salary was deducted by three hours pay each fortnight during the time he was absent whilst attending the hospital. He declined to attend his own doctor for the injections and also to attend in evenings or week-ends.

Routine Review: May, 1959 (aged 18 years). Very well. Patient had had no recurrences of acute rheumatism.

Heart: B.P. 125/75.
Soft systolic murmur was audible at all areas.

6. J.S.

Aged 11 years. Female. First attack of rheumatic fever.

Admitted 26.2.53. Discharged 16.6.53. No. of days in hospital: 110.

Complaint: Flitting joint pains of three days' duration, mainly affecting knees and ankles.

History: Sore throat two weeks previously.
No family history of rheumatic fever.

Clinical Examination: T. 101°. P.R. 104/min. Regular. R. 22/min.
Hb. 75%. W.B.C. 11,600/c.mm. E.S.R. 60 mm.
Tonsils unhealthy in appearance.
Both knees swollen and painful.

Heart: B.P. 110/70.
A.B. 4½" from M.S.L. in 5th L. space.
Systolic murmur at apex.

Examination of urine: A few red cells were present, but no casts or albumen.

X-ray Chest: Slight cardiac enlargement.

E.C.G. Within normal limits.

Laboratory Findings: Throat swab - No H.S. grown on culture.
Blood cultures } Consistently negative.
Agglutination Tests }

Differential W.B.C. (Total 11,600/c.mm.)

Lymphocytes 45%	Eosinophils 1%
Neutrophils 55%	Basophils 1%
Monocytes 3%	

Treatment: Aspirin gr. 15 five times daily.
Course of Crystalline Penicillin.

Progress: Three weeks after admission, a routine throat swab revealed a heavy growth of H.S. on culture. This responded to the course of Penicillin. Recovery thereafter was steady and uneventful.

Condition on Discharge: Hb. 90%. W.B.C. 6,500/c.mm. E.S.R. 5 mm.

Heart: B.P. 110/70. A.B. 3½" from M.S.L. in 5th L. space.
Ventricular systolic and presystolic murmurs at mitral, aortic and pulmonary areas.

X-ray Chest: Cardiac size normal. Lung fields clear.

E.C.G. No abnormality detected.

Tonsillectomy was arranged and performed.

Follow-up: Patient failed to attend for her Penidural inections, and despite repeated requests, she was not seen again until she was readmitted with a recurrence of her acute rheumatism fifteen months later.

Readmission /

6. J.S. (Continued).

Readmission:

Aged 12 years. 2nd attack of rheumatic fever.

Admitted 27.9.55. Discharged 9.1.56. No. of days in hospital: 104.

Complaint: Flitting joint pains of three days' duration.

History: No history of recent sore throat.

Clinical Examination: T. 99.2°. P.R. 122/mm. Regular. R. 28/min.
Hb. 104%. W.B.C. 14,000/c.mm. E.S.R. 45 mm.
Both knees swollen and painful.

Heart: B.P. 120/70.
A.B. 4" from M.S.L. in 5th L. space. A loud presystolic murmur was heard at the mitral area, followed by a blowing systolic murmur, which was propagated into the axilla. The second sound at the pulmonic area was accentuated and split.

Examination of urine: No abnormality detected.

X-ray Chest: Cardiac outline, and lung fields normal.

E.C.G.: Within normal limits.

Laboratory Findings: Throat swab - No H.S. grown on culture.

Treatment: Aspirin gr. 20 five times daily.

Progress: Three weeks after admission, the patient developed symptoms of Salicylism (tinnitus, nausea and vomiting), and because of this, was given a mixture containing Potassium Citrate gr. 30 and sodium bicarbonate gr. 30. three times daily for 10 days, when these symptoms subsided. The only other occurrence of note during convalescence was a series of minor epistaxes; and the development of a mid-diastolic murmur at the mitral area four weeks after admission.

Condition on Discharge: Hb. 100%. W.B.C. 6,200/c.mm. E.S.R. 10 mm.

Heart: B.P. 120/70.
A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space.
Crescendo presystolic murmur present at mitral area.

X-ray Chest: "Heart is of mitral shape".

E.C.G.: "Within normal limits".

Follow-up: Patient remained well. She attended for 21 injections of Penidural, and thereafter defaulted mainly for financial reasons (money deducted from her wages when attending hospital), but also because she "felt like an invalid" whilst still under care of a hospital or doctor.

By /

6. J.S. (Continued).

By February, 1956, she had developed a definite diastolic murmur at the mitral area, propagated into the axilla.

X-ray Chest: then showed - "Cardiac enlargement with mitral configuration".

E.S.R.: At that time was 2 mm.

After she had received 11 injections regularly of Penidural a routine throat swab culture was made, and several colonies of H.S. were grown. She was given a course of Permapen penicillin which eradicated the infection.

X-ray Chest: October, 1957. "Lung fields clear. Cardio-thoracic ratio now within normal limits".

Routine Review: April, 1959. (Aged 17 years). Patient still subject to flitting pains in her joints, especially in damp weather. Becomes breathless on exertion. Had had two attacks of sore throat in the previous 18 months, which subsided on treatment with oral penicillin, supplied by own doctor, on our recommendation, after she failed to attend for her Penidural injections. She had no evidence of congestive cardiac failure.
B.P. 120/65. P.R. 80/min. Regular.
A.B. 4" from M.S.L. in 5th L. space.
Systolic and diastolic murmurs audible at mitral and aortic areas. E.S.R. 4 mm. This was repeated two days later, and was 3 mm.
Patient did not attend as requested for an X-ray of chest.

7. J.McK.

Aged 15 years. Male. First attack of rheumatic fever.

Admitted 28.5.54. Discharged 14.9.54. No. of days in hospital: 109.

Complaint: Flitting joint pains of two weeks' duration.

History: No history of recent sore throat.
Two months prior to admission, he noticed that his feet and ankles were swollen "for about 10 days".
No family history of rheumatic fever.

Clinical Examination: T. 100°. P.R. 100/min. Regular. R. 20/min.
Hb. 88%. W.B.C. 9,400/c.mm. E.S.R. 35 mm.

Throat: No abnormality present.

Both wrists swollen and painful. Left knee painful and stiff, but not swollen.

Heart: B.P. 120/60.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic and diastolic murmurs at mitral area.
No other murmurs present.

Examination of urine: Normal.

X-ray Chest: Lung fields clear. Cardiac outline normal.

E.C.G.: Normal.

Laboratory Findings: Throat swab - no H.S. grown on culture.
Blood cultures } Negative.
Agglutination Tests }

Treatment: Aspirin gr. 20 five times daily.

Progress: Patient made an uneventful recovery.

Condition on Discharge: X-ray chest and E.C.G. were normal.
Hb. 94%. W.B.C. 4,600/c.mm.

Heart: A.B. 3½" from M.S.L. in 5th L. space.
Loud systolic murmur at apex.

Follow-up: The patient failed to return to the Follow-up Clinic, despite many communications, until seven months later, when he attended with a letter from his own doctor, which stated that he had had a recurrence of fever and polyarthritis, which was treated at home with "large doses of salicylates for several weeks".
On examination he was symptomfree.
B.P. 130/85. P.R. 76/min. Regular.
A.B. 3½" from M.S.L. in 5th L. space.
There was a loud systolic murmur present at all areas, and a definite mid-diastolic "whiff" at the mitral area.
E.S.R. 4 mm. W.B.C. 5,200/c.mm.

X-ray Chest: /

7. J. McK. (Continued).

X-ray Chest: No active lung disease.
No cardiomegally.

Thereafter he attended for 7 Penidural Penicillin injections. He stated that if he attended hospital regularly it would mean that his wages would be cut accordingly. He was unwilling to attend his own doctor for the injections, as he would be kept too long at the surgery.

Routine Review: April, 1959 (aged 20 years). Patient unemployed at that time. Had remained well.
B.P. 140/90.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur at apex.
No diastolic murmur present even after exercise.

8. J. McH.

Aged 9 years. Male. Third attack of rheumatic fever.

Admitted 6.3.53. Discharged 24.2.54. No. of days in hospital: 355.

Complaint: Pains in elbows, knees and ankles of eight days' duration.

History: Patient had a "cold" four weeks prior to onset of symptoms. Mother had several attacks of rheumatic fever and has mitral stenosis.

Clinical Examination: T. 101°.
P.R. 120/min. - Occasional extrasystoles present.
Hb. 60%. R.B.C. 3.78 M./c.mm. W.B.C. 14,000/c.mm.
E.S.R. 112 mm.
Pale child very much smaller than average for his age.
Knees and ankles swollen.
B.P. 100/60.
A.B. 4½" from M.S.L. in 4th L. space. Diffuse and heaving in character. Pericardial friction rub present, best heard at the apex. No murmurs detected.

Examination of urine: Normal.

X-ray Chest: Moderate cardiac enlargement. Small effusion at right base.

E.C.G. Upper limit of abnormality.

Laboratory Findings: Differential W.B.C.

Lymphocytes	30%
Neutrophils	65%
Monocytes	3%
Basophils	1%
Eosinophils	1%

Pleural Effusion: Clear, straw-coloured fluid. No growth obtained on culture.

Throat swab - No H.S. grown on culture.

Blood cultures
Agglutination Tests } Persistently negative.

Treatment:
1. Aspirin gr. 25 four times daily. One week later treatment was changed to Disprin gr. 25 five times daily, because of gastric irritation.
2. Ferri-et-ammon. cit. gr. 30 thrice daily for 28 days.

Progress: This was very slow indeed. E.S.R. remained elevated and the joint pains continued for many months. Any attempt at reducing salicylates during an apparent remission was immediately met with a recurrence of symptoms. By 9.3.53 the pericardial friction rub had subsided, but an apical diastolic murmur became audible. X-ray chest revealed that cardiomegally was present, but that /

8. J. McH. (Continued).

that the right basal effusion had been absorbed.
Hb. was now 90%.
In November, 1953, he was allowed to sit in a chair, but developed a mild recondescence which necessitated his returning to complete bed rest for six weeks. He was allowed up again in January, 1954, and on this occasion, he remained symptom-free and E.S.R. remained at 24 mm.
February, 1954 - X-ray Chest - cardiac shadow slightly enlarged, but on screening there was no evidence of mitral stenosis.

Condition on Discharge: Hb. 90%. W.B.C. 10,500/c.mm. E.S.R. 20 mm.

Heart: B.P. 100/60.
A.B. 3" from M.S.L. in 5th L. space.
Prolonged blowing ventricular systolic murmur at mitral area.

Throat Swab: No evidence of H.S. on throat swab.

X-ray Chest: Normal.

E.C.G. No abnormality detected.

Follow-up: Patient was the most faithful attender at the Clinic, due to his mother personally bringing him, though the child did not like having injections. In all, he received 54 injections. This was really a magnificent attendance, as it cost 2/6d. in bus fares each visit for the child and his mother. By February, 1955, a pre-systolic and a diastolic murmur was audible at the mitral area. E.S.R. 4 mm. at that time.
By October, 1956, no diastolic murmurs were detected even after exercise. The child remained wonderfully well.
This child made wonderful progress, rapidly gaining in weight and stature.

Routine Review: March, 1959, (aged 15 years). Patient extremely well. Had not a day's illness since discharge from hospital. Gained $2\frac{1}{2}$ stones in weight over previous three years.

Heart: B.P. 120/70.
A.B. $3\frac{3}{4}$" from M.S.L. in 5th space.
No murmurs present.

9. E.M.

Aged 15 years. Female. First attack of rheumatic fever.

Admitted 14.4.54. Discharged 18.6.54. No. of days in hospital: 64.

Complaint: Pains in both knees for several days.

History: Tonsillitis five weeks previously.
No family history of rheumatic fever.

Clinical Examination: T. 100°. P.R. 120/min. Occasional extrasystoles present.
Hb. 86%. W.B.C. 10,000/c.mm. E.S.R. 29 mm.
A well-nourished child. Left knee swollen and extremely painful with marked limitation of movement. Right knee painful but only slightly swollen.

Heart: B.P. 115/70.
A.B. 3½" from M.S.L. in 5th L. space. Soft systolic and short mid-diastolic murmurs at mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

Screening Of Chest: Normal.

Ba. Swallow: Negative.

E.C.G.: Normal.

Laboratory Findings: Throat swab - Scanty growth of H.S. grown on culture, but many colonies of strep. viridans present.
Blood cultures, Agglutination Tests) Negative.

Treatment:
1. Aspirin gr. 20 six times daily.
2. Course of Crystalline Penicillin, which eliminated H.S. from throat.

Progress: Patient's condition steadily improved. Convalescence was uneventful.

Condition on Discharge: Hb. 95%. W.B.C. 6,000/c.mm. E.S.R. 4 mm.

X-ray Chest:
E.C.G. } Normal.

Heart: B.P. 115/70.
A.B. 3½" from M.S.L. in 5th L. space. Soft ventricular systolic murmur was present at the apex. No diastolic murmur was audible even after exercise.

Follow-up: Patient remained very well, but after her third injection of Penidural, she did not return to the Clinic. Her mother was contacted and she then attended for a further two weeks. She then decided against having any further treatment. However, when her mother was again contacted /

9. E.M. (Continued).

contacted she admitted that the main reason for which her daughter had ceased attending the Clinic was the fact that money was deducted from her wages during the time she spent away from work when going up to the hospital. The patient refused to attend at any other times offered to her.

Routine Review: April, 1959 (aged 20 years). Patient had married one year previously and had had a child. The pregnancy was normal; delivery and puerperium were uneventful. However, she gave a history of having been treated at home (for 18 weeks in 1959) for a recurrence of rheumatic fever. This information was confirmed by her own doctor.

Heart: B.P. 120/80.
A.B. 4" from M.S.L. in 5th L. space. Systolic and presystolic murmurs were present at the mitral area. There was no evidence of congestive cardiac failure.

X-ray Chest: Normal.

10. H.McQ.

Aged 14 years. Male. First attack of rheumatic fever.

Admitted 4.3.55. Discharged 4.5.55. No. of days in hospital: 61.

Complaint: Pains in "all" joints of two days' duration.

History: Coryza four weeks previously.
No family history of rheumatic fever.

Clinical Examination: T. 101°. P.R. 104/min. Regular. R. 26/min.
Right knee and left ankle swollen and painful.
Hb. 85%. W.B.C. 14,000/c.mm. E.S.R. 72 mm.

Heart: B.P. 110/75.
A.B. 5" from M.S.L. in 5th L. space.
Soft systolic murmur at apex.

Examination of urine: Normal.

X-ray Chest: Slight cardiac rotation and displacement to the left.
? secondary to dorsal scoliosis.
Lung fields clear.

E.C.G. Normal.

Laboratory Findings: Throat swab - Scanty growth of H.S. on culture.

Treatment: Aspirin gr. 20 five times daily.

Progress: Patient made an uneventful recovery.

Condition on Discharge: Heart - A.B. 4½" from M.S.L. in 5th L. space.
A soft systolic murmur was heard at all areas.
The second sound at aortic area was accentuated.

X-ray Chest - Normal.

E.C.G. - Normal.

Hb. 102%. W.B.C. 6,700/c.mm.

Throat Swab - Two small colonies of H.S. grew on culture.

Follow-up: Patient remained well but attended for only 8 Penidural injections. He maintained that his work prevented his attending the hospital, or his own doctor.

Routine Follow-up: May, 1959 (aged 18 years). Despite many requests the patient did not attend for examination, but his own doctor states that he remained well and symptom-free, and no cardiac murmurs were present.

11. K.G.

Aged 15 years. Female. First attack of rheumatic fever.

Admitted 6.3.54. Discharged 15.10.54. No. of days in hospital: 202.

Complaint: Fleeting joint pains of five days' duration.

History: Sore throat three days previously.
No family history of rheumatic fever.

Clinical Examination: T. 102°. P.R. 120/min. Regular. R. 22/min.
Both elbows and left knee swollen and painful.
Hb. 55%. W.B.C. 11,000/c.mm. E.S.R. 128 mm.

Heart: B.P. 105/30.
A.B. 4½" from M.S.L. in 5th L. space.
Harsh systolic murmur at apex.

Examination of urine: An ordinary specimen contained many pus cells but microscopical examination of a catheter specimen was normal.

X-ray Chest: Slight cardiomegally present.

X-ray Sinuses: Negative.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. present on culture.
Blood cultures, Agglutination Tests } Negative.
Intravenous pyelogram - Negative.
Urine - No growth on culture or guinea pig inoculation.

Treatment:
1. Aspirin gr. 15 five times daily.
2. Ferrous Gluconate gr. 10 thrice daily for five weeks.
3. Course of Crystalline Penicillin (before and after extraction of a carious tooth).

Progress: On 19.6.54 a mid-diastolic murmur was present at the mitral area. This was audible for several days and subsequently no diastolic murmur was audible even after exercise. Progress was slow and E.S.R. remained elevated for several months, but ultimately her symptoms subsided and E.S.R. returned to normal (7 mm.).

Condition on Discharge: Hb. 100%. W.B.C. 6,200/c.mm. E.S.R. 7 mm.

E.C.G. Normal.

X-ray Chest: Moderate cardiac enlargement to the left.
Lung fields clear.

Heart: B.P. 105/30.
A.B. 3¾" from M.S.L. in 5th L. space. A soft systolic murmur was audible at the base.

Follow-up: /

11. K.G. (Continued).

Follow-up: The patient continued very well. E.S.R. remained normal. She attended faithfully for 30 injections of Penidural Penicillin but then ceased to attend, as she found that this interfered with her work. She declined to attend at any other times offered to her, or to attend her own doctor for the same.
15.5.58 - X-ray Chest - normal cardiac outline.
lung fields clear.

Routine Review: April, 1959 (aged 20 years). Patient was extremely fit. She had had no recurrence of her symptoms, and no sore throats.

Heart: B.P. 105/65.
A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space. A soft systolic murmur was audible at the apex.

12. C.J.

Aged 14 years. Female. First attack of rheumatic fever (chorea).

Admitted 4.6.54. Discharged 20.8.54. No. of days in hospital: 67.

Complaint: Twitching of hands and legs of three weeks' duration.
Sore throat of five days' duration.

History: No history of recent sore throat prior to onset of symptoms.
No family history of rheumatic fever.

Clinical Examination: T. 100°. P.R. 104. Regular. R. 24/min.
Hb. 70%. W.B.C. 4,200/c.mm. E.S.R. 45 mm.
Thin girl. Flushed. Marked choreiform movements of face, hands and legs. Tonsils enlarged and unhealthy.

Heart: B.P. 105/80.
A.B. 3½" from M.S.L. in 5th L. space. A rough systolic murmur, and an early diastolic murmur, were present at the apex.

Examination of urine: Normal.

X-ray Chest: Slight cardiac enlargement. Cardiac contour is "mitral" in shape. Calcified glands present at left lung root.

E.C.G. "Broad P.2 in lead A.V.F. fits with clinical diagnosis of mitral stenosis".

Laboratory Findings: Throat swab - H.S. grown on culture.

Treatment: Aspirin gr. 20 three times daily.
Ferrous gluconate gr. 5 three times daily.
Phenobarbitone gr. 1 twice daily.
Course of Crystalline Penicillin.

Progress: Movements gradually subsided, and E.S.R. slowly returned to normal. By 22.7.54 a definite diastolic murmur was audible at the mitral area, and propagated to the axilla. X-ray chest at time was reported as follows - No change. Mitral configuration of heart.

Condition on Discharge: Hb. 98%. W.B.C. 4,000/c.mm. E.S.R. 5 mm.

X-ray Chest: Lung fields clear.
Cardiac outline of mitral configuration.

E.C.G. Compatible with mitral stenosis.

Heart: B.P. 105/80.
A.B. 3½" from M.S.L. in 5th L. space. Systolic and diastolic murmurs present at apex.

Follow-up: Patient remained well. Tonsils and adenoids were removed /

12. C.J. (Continued).

removed five months after her discharge from the medical ward. She was the most faithful attender at the Clinic and in all she received 54 injections of Penidural Penicillin. Despite the fact that she received Penidural regularly, a routine throat swab was cultured after she had had 25 injections and a heavy growth of H.S. appeared. She was then treated with a course of Permapen penicillin which eliminated the H.S. from her throat.
On 23.2.55 a diastolic murmur was audible at the aortic area, as well as at the mitral area.
By 13.4.55 a presystolic murmur rumbling in character was now audible at the mitral area.

1.10.55: On this visit no diastolic murmur was audible at the aortic area. A crescendo presystolic, and a diastolic murmur were present at the mitral area. Patient remained well. No recurrences of choreiform movements.

16.5.56: Patient was readmitted to hospital for 16 days, as on attendance at the clinic she was found to have had a T. 101.6°. P.R. 112/min., Regular. She complained of "aches and pains all over" and had a severe head cold. E.S.R. was 22 mm. Hb. 84%. W.B.C. 12,900/c.mm.
X-ray Chest: Moderate cardiac enlargement as before.
She had no evidence of a recurrence of chorea.
Her signs and symptoms subsided in a few days.

Condition on Discharge: W.B.C. 4,000/c.mm. E.S.R. 7 mm.

Heart: B.P. 110/75.
A.B. 3½" from M.S.L. in 5th L. space. Forceful and heaving in character. A presystolic, and a diastolic murmur were present at the mitral area.
A diagnosis of acute coryza was made.
No H.S. were isolated.

16.3.57: Patient was again readmitted, having collapsed at her work (as a Grocer's Assistant).
On admission, she was semi-comatose, restless, and with a flaccid right arm and right leg.

Clinical Findings: T. 97°. P.R. 96/min. Regular in rate and rhythm. R. 22/min. Hb. 90%. W.B.C. 6,000/c.mm. E.S.R. 3 mm.

Heart: B.P. 116/75.
A.B. 4½" from M.S.L. in 5th L. space. An opening snap, together with a systolic murmur were audible at the mitral area. No diastolic murmurs were present.

The spleen was not enlarged. Liver and kidneys were impalpable.

Central Nervous System: Patient was aphasic. Pupils were equal and central, both reacted to light and accommodation. The 3rd, 4th and /

12. C.J. (Continued).

and 6th cranial nerves were intact. There was paralysis of the 7th and 12th right cranial nerves. Patient was able to obey simple commands, such as moving left arm and left leg. Right arm and right leg were flaccid, but occasionally both "twitched". She had control over bowel and bladder sphincters.

Examination of urine: Normal.

Laboratory Findings: Blood cultures - repeatedly negative.
Throat swab - No H.S. were grown on culture.
Cerebrospinal fluid - Clear. Pressure 100 mm.
No blood staining was present.
Wassermann reaction - negative.
Pandy's Test - negative.
Colloidal gold test - 000,000,000 (normal).

X-ray Chest: This was delayed until patient's general condition had improved.

Screening Report: Enlargement of left auricle and left ventricle and also of pulmonary conus. No abnormal pulsation noted.

E.C.G.: Right ventricular hypertrophy and strain. Marked clockwise rotation present.
A diagnosis of cerebral embolism was made.

Treatment: General nursing care.

Progress: By 22.3.57, the patient was able to speak, but in a very slurred manner. Her general condition improved slowly, but she was left with a residual paresis of her right arm and right leg.

Condition on Discharge: By 2.5.57, she was able to walk but had only limited movement present in her right arm and her speech remained very slurred.
She was then allowed home.

Follow-up: The patient died very suddenly, three days after returning home.

Post-mortem examination was not performed.

13. J. McG.

Aged 16 years. Male. Third attack of rheumatic fever.

Admitted 12.12.52. Discharged 18.12.53. No. of days in hospital: 361.

Complaint: Severe pain in all joints during previous 24 hours.

History: Sore throat four weeks previously.
This patient lived in very overcrowded conditions - 7 adults and 9 children in a room-and-kitchen apartment. One brother and 2 sisters had had rheumatic fever at different times, several years before.

Clinical Examination: T. 100.4°. P.R. 98/min. Regular. Hb. 80%.
W.B.C. 9,200/c.mm. R.B.C. 4.03M/c.mm. E.S.R. 50 mm.
Both ankles and right elbow were swollen, stiff and very painful.

Heart: B.P. 130/70.
A.B. 5½" from M.S.L. in 6th L. space. Systolic and diastolic murmurs were audible at the mitral area and propagated into the axilla. A systolic murmur was present at the aortic area, with reduplication of the second sound.

Examination of urine: Normal.

X-ray Chest: Lung fields clear.
Generalised cardiomegally present.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture.
Blood cultures - B. coli (? a contaminant) were grown on culture of one specimen - but other specimens were consistently negative.
Agglutination Tests - Negative.

Treatment: Aspirin gr. 20 four times daily.

Progress: Patient's condition improved slowly. Six months after admission he was allowed up but his E.S.R. which had returned to normal, again rose (to 32 mm.) and his temperature became elevated to 100°F. With further bed rest and salicylates, the condition again subsided. By November, 1953, a diastolic murmur was present at the aortic area, and was propagated down left border of sternum.

Condition on Discharge: Hb. 88%. W.B.C. 8,000/c.mm. E.S.R. 3 mm.
Throat swab - No H.S. on culture.

X-ray Chest: Slight generalised cardiomegally.
Lung fields clear.

E.C.G.: Normal.

Heart: /

13. J. McG. (Continued).

Heart: B.P. 130/70.
A.B. 4¾" from M.S.L. in 5th L. space. Presystolic and systolic murmurs at mitral area. Systolic murmur only at the aortic area.

Follow-up: Patient attended for one injection then defaulted until - 23.1.54 he attended the Clinic complaining of dyspnoea on exertion. He was found to have a marked cardiomegally and rate of 110/min. Pulse was regular in rate and rhythm. E.S.R. however was only 8 mm.
There was no evidence of congestive cardiac failure.
X-ray chest confirmed the clinical diagnosis of cardiomegally. E.C.G. normal.

Readmission:

Admitted 23.1.54. Discharged 3.3.54. Days in hospital: 38.

He was readmitted to hospital and confined to bed. Salicylates were not administered, as his E.S.R. remained normal throughout his 38 days in hospital. The cardiomegally decreased. He became symptom free.
Examination of the heart, systolic and diastolic murmurs were present at at both mitral and aortic areas.
Penidural penicillin prophylaxis was continued throughout his stay in hospital.

Condition on Discharge: E.S.R. 3 mm.

Heart: B.P. 130/70.
A.B. 4½" from M.S.L. in 5th L. space. Systolic and diastolic murmurs at aortic area. The latter murmur was propagated down left border of sternum. Systolic and diastolic murmurs were also present at the mitral area. The latter murmur was propagated into the axilla.

Follow-up: Patient continued well and symptom free. He attended for a further 13 Penidural injections. Altogether, the patient received only 18 injections of Penidural penicillin. He stated that he was willing to attend for more but, for private reasons, was unable to do so.

Routine Review: March, 1959 (aged 23 years) - Patient very well. Had had no recurrences of rheumatic fever. Heart well compensated. Patient gave a history of having been admitted to another hospital two months previously with a fairly brisk haematemesis, which he was told was due to a peptic ulcer in the stomach.

On Examination:

Heart: B.P. 130/75. Pulse rate 90/min. Patient excited as usual. A.B. 4½" from M.S.L. in 5th L. space. Presystolic and diastolic murmurs were present at the mitral and aortic areas. The diastolic murmurs were propagated down left border of sternum and to the axilla, respectively.

14. H.G.

Aged 13 years. Male. First attack of rheumatic fever.

Admitted 25.4.53. Discharged 29.9.53. No. of days in hospital: 156.

Complaint: Pains in arms and legs of three weeks' duration.

History: Influenza and sore throat prior to onset of symptoms.

Clinical Examination: T. 99°. P.R. 92/min. Regular. H.B. 70%.
W.B.C. 12,000/c.mm. R.B.C. 3.4M/c.mm. E.S.R. 110 mm.
Right knee was swollen and painful. The left elbow was painful, but not obviously swollen.

Heart: B.P. 130/80.
A.B. 3½" from M.S.L. in 5th L. space. Soft systolic murmur was present at the apex.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - no H.S. grown on culture.

Treatment: 1. Aspirin gr. 15 five times daily.
2. Ferrous Gluconate gr. 10 thrice daily for 14 days.

Progress: Patient's condition improved steadily, and convalescence was uneventful. However on 22.7.53, a diastolic murmur was audible at the apex, and propagated into the axilla. This murmur persisted.

Condition on Discharge: Hb. 100%. W.B.C. 8,600/c.mm. E.S.R. 10 mm.

X-ray Chest: Normal.

E.C.G. Early right axis deviation, suggesting mitral stenosis.

Heart: B.P. 130/80.
A.B. 3½" from M.S.L. in 5th L. space. Systolic and diastolic murmurs were present at the mitral area. The diastolic murmur being propagated into the axilla. The second sound at the pulmonic area was accentuated.

Follow-up: Patient remained well, and in all received 35 injections of Penidural. The expense of bus and tram fares prevented his attending more frequently whilst at school (sometimes he omitted to come every fortnight, but came monthly). On commencing work he was unable to obtain leave of absence to attend. By 28.4.55, there was no diastolic murmur audible.

Routine Review: March, 1959 (aged 19 years) - Patient extremely well.
no /

14. H.G. (Continued).

No further attacks of rheumatic fever.

Heart: B.P. 120/70.
A.B. 3½" from M.S.L. in 5th L. space. Splitting of first sound at mitral area. No diastolic murmur detected, even after exercise.

X-ray Chest: Lung fields normal.
Cardiac size normal.

15. J.B.

Aged 18 years. Male. First attack of rheumatic fever.

Admitted 18.1.54. Discharged 19.4.54. No. of days in hospital: 91.

Complaint: Pains in elbows, knees and ankles of two days' duration.

History: No recent sore throats.
Subject to recurrent attacks of bronchial asthma.
No family history of rheumatic fever.

Clinical Examination: T. 99.9°. P. 96/min. Regular. Hb. 95%.
W.B.C. 4,500/c.mm. E.S.R. 68 mm.
Very flushed. Right knee and left elbow swollen, stiff and painful.

Heart: B.P. 100/60.
A.B. 3½" from M.S.L. in 5th L. space. A systolic murmur and a doubtful diastolic murmur present at the mitral area. There was splitting of 2nd sound at the aortic area.

Examination of urine: Normal.

X-ray Chest: Low grade inflammatory changes in both lower zones. Probably bronchiectasis. Normal cardiac shadow.

E.C.G. Normal.

Laboratory Findings: Throat Swab - No H.S. grown on culture but heavy growth of strep. viridans.
Blood cultures, Agglutination tests } All negative.

Treatment:
1. Aspirin gr. 20 five times daily, later increased to gr. 20 six times daily.
2. Course of Crystalline Penicillin (for a middle ear infection).

Progress: Two days after admission patient's temperature became elevated to 102.8°F. W.B.C. rose to 27,000/c.mm. and E.S.R. to 98 mm. A right middle ear infection was diagnosed. Ten days later, a loud pericardial friction rub was audible all over the precardial area.
A.B. was 4¾" from M.S.L. in 5th L. space. E.S.R. thereupon rose to 112 mm.
Salicylate dosage was then increased, as above.
By 5.3.54, patient's condition had greatly improved.
P.R. was 80/min. and regular in rate and rhythm.
A.B. 4" from M.S.L. in 5th L. space. A systolic murmur was present at the mitral area, and also, when patient was examined in the left lateral position, a mid-diastolic murmur was heard at the mitral area. Later, after the patient's condition improved, a definite diastolic murmur was audible at the mitral area after exercise. Subsequently the patient's convalescence was uneventful.

Condition on /

15. J.B. (Continued).

Condition on Discharge: Hb.96%. W.B.C. 5,000/c.mm. E.S.R. 4 mm.

Heart: B.P. 130/60.
A.B. 3½" from M.S.L. in 5th L. space. Systolic and diastolic murmur at mitral area. The diastolic murmur remained localised.

X-ray Chest: Normal.

E.C.G. Normal.

Follow-up: Patient continued well for three years. He attended the Follow-up Clinic faithfully and in all received 51 injections of Penidural (when he decided that he had had sufficient treatment).
After his 27th injection of Penidural (which had been given regularly), a routine throat swab was cultured, and a heavy growth of H.S. was obtained. He was given a course of Permapen penicillin and a repeat throat swab culture was then made and no H.S. were grown on culture.
The patient was referred to the E.N.T. Department for removal of his tonsils and adenoids, but he declined to have this operation.
Routine X-ray of chest and E.C.G. were both normal.
On 15.3.57 the patient was readmitted with a complaint of generalised joint pains for the previous ten days.

On Readmission: T. 97°. P.R. 80/min. Hb. 110%. W.B.C. 8,000/c.mm. E.S.R. 20 mm.
Patient was found to have a bilateral phlyctenular conjunctivitis. No joint abnormality was present.

Heart: B.P. 120/60.
A.B. 3½" from M.S.L. in 5th L. space.

Throat Swab: A few colonies of H.S. were grown on culture.

X-ray Chest: Normal.

E.C.G. Normal.

Treatment: Consisted of a course of Crystalline Penicillin.

Progress: Patient rapidly became symptom free. Repeat throat swab - no H.S. were grown on culture. After ten days observation, he was discharged well.

Routine Review: March, 1959 (aged 24 years) - Patient continued well and symptom free.

Heart: B.P. 120/75.
A.B. 3½" from M.S.L. in 5th L. space.
Heart sounds pure.

16. J.M.

Aged 21 years. Female. Second attack of rheumatic fever.

Admitted 3.6.54. Discharged 26.7.54. No. of days in hospital: 53.

Complaint: Painful, swollen knees and ankles of four days' duration.

History: Sore throat four weeks prior to admission. Subject to frequent attacks of sore throats during the winter months. Patient states she was in bed for three years with rheumatic fever at age of ten years.
No family history of rheumatic fever.

Clinical Examination: T. 101° F. P.R. 104/min. Regular. Hb. 84%.
W.B.C. 10,200/c.mm. E.S.R. 80 mm.

Heart: B.P. 120/70.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur was audible at mitral area.
Both knees and the left ankle were swollen and painful.

Examination of Urine: Normal.

X-ray Chest: Lung fields clear. Cardiac countour normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture but a heavy growth of strep. viridans was obtained.

Treatment: Aspirin gr. 20 five times daily.

Progress: Patient's condition steadily improved and convalescence was uneventful.

Condition on Discharge: Hb. 84%. W.B.C. 4,200/c.mm. E.S.R. 8 mm.

Heart: B.P. 120/70.
A.B. 3½" from M.S.L. in 5th L. space. Soft systolic murmur audible at apex.

E.C.G. Normal.

Follow-up: Patient returned on only two occasions to the Follow-up Clinic, thereby receiving only 2 injections of Penidural Penicillin. Despite repeated attempts at contacting the patient, she failed to return to the Clinic. Her own doctor was contacted again, in May, 1959, but he had not seen her for the previous two years, but at that time she was well and had had no recurrences of rheumatic fever.
The Executive Council have no trace of her as being on any doctor's list.

17. A.G.

Aged 13 years. Male. Reputed to be his first attack of rheumatic fever.

Admitted 5.2.54. Discharged 19.3.54. No. of days in hospital: 43.

Complaint: Painful swollen ankles of five days' duration.

History: "Running ears" of two months' duration.
No previous sore throat prior to onset of symptoms.
No family history of rheumatic fever.
Admitted from a Borstal school.

Clinical Examination: T. 99°F. P.R. 90/min. Regular.
Hb. 100%. W.B.C. 10,000/c.mm. E.S.R. 25 mm.
Bilateral otitis media present. Both ankles swollen and painful.

Heart: B.P. 110/40.
A.B. 3½" from M.S.L. in 5th L. space. Diffuse and heaving in character. Systolic and diastolic murmurs at aortic and mitral areas. The diastolic murmurs were propagated down left border of sternum and into axilla respectively. Systolic and diastolic murmurs were also present at pulmonary area.

X-ray Chest: Normal.

E.C.G.: Sinus arrhythmia. Left axis deviation.

Laboratory Findings: Throat swab - No H.S. grown on culture.
Blood cultures, Agglutination Tests) Negative.

Treatment: In view of the low E.S.R., patient was treated with bed rest alone. No salicylates were given.

Progress: Patient's condition steadily improved. Convalescence was uneventful.

Condition on Discharge: Hb. 100%. W.B.C. 5,200/c.mm. E.S.R. 5 mm.

E.C.G. Left axis deviation. Sinus arrhythmia.

Heart: B.P. 110/40.
A.B. 3½" from M.S.L. in 5th L. space. Systolic and diastolic murmurs audible at aortic, mitral and pulmonary areas.

Follow-up: Patient remained well and symptom free. It was very difficult to make him attend the Follow-up Clinic. After attending on one occasion, it required the supervision of the Headmaster of the Borstal Institution for a further five attendances. Thereafter, he was discharged from the school and all trace of him was lost for many months. In all, he had 6 injections of Penidural.

Routine Review: /

17. A.G. (Continued).

Routine Review: May, 1959 (aged 19 years) - Knowing the boy's character, several sheriff courts were contacted and ultimately he was traced to the Prison After-Care Council Officer, who states that the boy remains well.
The patient again ignored appeals to attend the Follow-up Clinic.

18. J.J.

Aged 14 years. Female. First attack of rheumatic fever.

Admitted 4.8.56. Discharged 11.10.56. No. of days in hospital: 68.

Complaint: Severe pains in knees and wrists of six days' duration.

History: "Quinsy" throat seven weeks previously, followed two weeks later by Scarlet Fever.

Clinical Examination: T. 99.6°. P.R. 110/min. Hb. 70%.
W.B.C. 11,000/c.mm. E.S.R. 130 mm.
Skin was desquamating in fine scales.
Throat was inflamed around fauces and pharynx.
Both knees and wrists swollen and painful.

Heart: B.P. 110/70.
A.B. impalpable. Soft systolic murmur at mitral and aortic areas.

Examination of Urine: Normal.

X-ray Chest: Normal.

E.C.G.: Normal.

Laboratory Findings: Throat swab - Numerous colonies of H.S. grown on culture.
Blood cultures, Agglutination Tests } Negative.
No lupus Erythematosus cells present.

Treatment:
1. Aspirin gr. 20 five times daily.
2. Course of Crystalline Penicillin.
3. Ferri-et-ammon cit. gr. 30 daily.

Progress: Patient steadily improved, and E.S.R. gradually returned to normal (3 mm.).
On 14.8.54 - a faint mid-diastolic murmur was audible at the mitral area. This however had disappeared by 9.9.56.

Condition on Discharge: Hb. 88%. W.B.C. 5,800/c.mm. E.S.R. 5 mm.

Throat Swab: No H.S. grown on culture.

X-ray Chest: Normal.

Heart: Soft systolic murmur at mitral area.

E.C.G. Normal.

Follow-up: Patient remained well. She was very averse to attending the Follow-up Clinic for Penidural injections but with much persuasion, attended for 7 injections in al, thereafter defaulting. Her mother was contacted without avail.

Routine Review: May, 1959 (aged 18 years) - No trace of the patient could be found as she had left her doctor's practice two years previously.

19. R.S.

Aged 13 years. Male. First attack of rheumatic fever.

Admitted 2.6.54. Discharged 17.8.54. No. of days in hospital: 76.

Complaint: Painful knees and wrists of four days' duration.

History: Tonsillitis four weeks previously.
No family history of rheumatic fever.

Clinical Examination: T. 99.4°F. P.R. 100/min. Regular.
Hb. 70%. W.B.C. 5,800/c.mm. E.S.R. 24 mm.
Right wrist very painful and swollen.

Heart: B.P. 110/60.
A.B. 3" from M.S.L. in 5th L. space. Soft systolic murmur at the mitral area.

X-ray Chest: Normal.

E.C.G. Normal.

Examination of urine: Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture.
Blood cultures } Negative.
Agglutination Tests }

Treatment: Aspirin gr. 20 five times daily. This had to be reduced to gr. 15 five times daily because of nausea and mild tinnitus.

Progress: Two days after admission, the left wrist became swollen and painful. The condition settled fairly quickly; the E.S.R. returning to normal (4 mm.). Convalescence was uneventful.

Follow-up: Patient remained well. He was a faithful attender at the Follow-up Clinic, receiving in all 32 injections of Penidural. He then felt, that as he was so well, he did not require further treatment. His parents agreed with him.

Routine Review: May, 1959 (aged 18 years). Extremely fit and well. Gained two stones in weight over previous two years. Had had no recurrences of symptoms.

Heart: B.P. 140/80.
A.B. impalpable. Soft systolic murmur at mitral area.

20. S.W.

Aged 15 years. Male. First attack of rheumatic fever.

Admitted 29.3.56. Discharged 1.5.56. No. of days in hospital: 33.

Complaint: Pains in knees and ankles of two days' duration.

History: Sore throat three weeks previously. No family history of rheumatic fever.

Clinical Examination: T. 100°F. P.R. 90/min. Regular.
Hb. 93%. W.B.C. 8,950/c.mm. E.S.R. 48 mm.
Throat moderately inflamed.
Both ankles swollen and stiff and painful.

Heart: B.P. 110/80.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at the apex.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - H.S. grown on culture.
Agglutination Tests } Negative.
Paul Bunnell Test }

Treatment: Aspirin gr. 20 five times daily.
Course of Crystalline Penicillin.

Progress: Patient's condition rapidly improved. Convalescence was uneventful.

Condition on Discharge: Hb. 98%. W.B.C. 5,200/c.mm. E.S.R. 3 mm.

Throat Swab: No H.S. grown on culture.

E.C.G. Normal.

Heart: B.P. 110/75.
A.B. 3½" from M.S.L. in 5th L. space.
Sounds pure at all areas.

Follow-up: Patient continued well. He attended in all for 14 injections of Penidural. He stated that he was unable to attend further as this interfered with his work, which entailed a good deal of "over-time". He was also averse to giving up any of his leisure time, which, he said was "little enough".

Routine Review: April, 1959 (aged 18 years) - Patient was extremely fit. Had not had a day's illness since discharge from hospital.

Heart: B.P. 130/80.
A.B. 3½" from M.S.L. in 5th L. space. The first sounds at the mitral and aortic areas were a little accentuated. No cardiac murmurs were present.

21. D.McC.

Aged 17 years. Male. First attack of rheumatic fever.

Admitted 13.4.54. Discharged 7.6.54. No. of days in hospital: 56.

Complaint: Generalised joint pains of four days' duration.

History: Had a "head cold" four weeks previously, but no sore throat.
Subject to frequent attacks of epistaxis.
No family history of rheumatic fever.

Clinical Examination: T. 101°F. P.R. 90/min. Regular.
Hb. 100%. W.B.C. 6,200/c.mm. E.S.R. 45 mm.
Throat mildly inflamed. Left wrist swollen and painful.

Heart: B.P. 140/30.
A.B. $4\frac{3}{4}$" from M.S.L. in 5th L. space. Coarse systolic and early diastolic murmurs at mitral area. Coarse systolic and loud diastolic murmur at aortic area, the diastolic murmur propagated down left border of sternum. Coarse systolic and early diastolic murmurs present at pulmonary area.

Examination of urine: Normal.

X-ray Chest: Normal.

X-ray Screening: Enlargement of left auricle and left ventricle.
Dilation of pulmonary trunk.
Minimal right ventricular enlargement present.
Marked aortic pulsation noted.
No vascular calcification present.
Appearances suggest combined mitral stenosis and aortic incompetence.

E.C.G. Early R. axis deviation.

Laboratory Findings: Throat swab - Numerous colonies of H.S. grown on culture.
Blood cultures - Negative.

Treatment: Disprin gr. 20 six times daily.
Course of Crystalline Penicillin.

Progress: Patient made a steady recovery. Convalescence was uneventful. Arrangements were made for him to have his tonsils and adenoids removed at a later date, but the patient and his parents refused to have the operation performed.

Condition on Discharge: Hb. 98%. W.B.C. 6,200/c.mm. E.S.R. 3 mm.

E.C.G. Early R. axis deviation.

Heart: A.B. $4\frac{1}{2}$" from M.S.L. in 5th L. space.
Systolic /

21. D. McC. (Continued).

Systolic and diastolic murmurs present at mitral, aortic and pulmonary areas.

Follow-up: Patient remained well and symptom free. He attended for only 7 injections of Penidural. He refused to have any further treatment, either by injection or orally, as he did not wish to "feel like an invalid" and different from the "other lads". He also stated that money was deducted from his wages whilst attending hospital.

Routine Review: April, 1959 (aged 22 years) - Patient extremely well. No symptoms whatsoever.

Heart: B.P. 140/35.
A.B. 4¼" from M.S.L. in 5th L. space.
Systolic and diastolic murmurs present at mitral and aortic areas. No other murmurs detected.
No evidence of congestive cardiac failure.

Arrangements were made for him to have an X-ray of chest taken but he did not return to keep the appointment.

22. M. F.

Aged 14 years. Female. Sixth attack of rheumatic fever.

Admitted 27.12.53. Discharged 10.3.54. No. of days in hospital: 53.

Complaint: Pains in arms and legs of two days' duration.
Knees very stiff and painful.

History: "Cold" two weeks previously.
One sister had rheumatic fever, two years previously.

Clinical Examination: T. 100°F. P.R. 110/min. Regular.
Hb. 90%. W.B.C. 15,400/c.mm. E.S.R. 40 mm.
Throat inflamed.
Swelling and stiffness present in both knees.

Heart: B.P. 100/60.
A.B. 3½" from M.S.L. in 5th L. space.
Systolic murmur present at apex.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture.

Treatment: Aspirin gr. 15 five times daily.

Progress: Patient made a steady recovery. Convalescence was uneventful.

Condition on Discharge: Hb. 94%. W.B.C. 5,200/c.mm. E.S.R. 4 mm.

E.C.G. Normal.

Heart: B.P. 100/65. A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur was audible at mitral area.

Follow-up: Patient remained very well. She had no recurrences of rheumatic fever. This patient attended regularly for three injections of Penidural penicillin. A routine throat swab made at her next visit was found to have H.S. present on culture. She was given a course of Permapen Penicillin, whereupon a repeat throat swab was free from presence of H.S. on culture. She received her fourth injection of Penidural and thereafter defaulted. Repeat requests for attendances were made to her without avail. Finally, she phoned to say that her employer did not believe it was necessary for her to attend hospital any longer. She stated that her parents were of the same opinion. Her employer was contacted by letter and the position explained to him. This met with no result.

Routine Review: /

22. M.F. (Continued).

Routine Review: 1959, (aged 20 years) - No trace of the patient could be found, either by contacting her own doctor, or through the Executive Council of the National Health Service. As far as can be ascertained from her previous neighbours, she was very well when last they saw her some 18 months before.

23. T.D.

Aged 12 years. Female. Third attack of rheumatic fever.

Admitted 26.12.55. Discharged 28.1.55. No. of days in hospital: 33.

Complaint: Pains in both legs of four days' duration.
Pain and stiffness of right elbow of one day's duration.

History: No recent sore throat.
Was in hospital for 40 days one year previously for observation but was not considered to have had rheumatic fever.
No family history of rheumatic fever.

Clinical Examination: T. 101.8°. P.R. 132/min. Regular.
Hb. 70%. W.B.C. 14,200/c.mm. E.S.R. 110 mm.
Tonsils enlarged.
Right elbow very swollen and painful even to touch.

Heart: B.P. 100/60.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur at mitral area.
The second sounds at aortic and pulmonic areas were accentuated.

Examination of urine: One red blood cell per high power field was seen. No casts were present. No albumen, pus, bile or sugar were present.

X-ray Chest: Catarrhal changes at both lung bases.
Cardiac outline normal.

E.C.G.: P-R interval at upper limit of normal.

Laboratory Findings: Throat swab - No H.S. were grown on culture.
Catheter specimen of urine - Normal. No growth of organisms obtained on culture.

Treatment:
1. Disprin gr. 20 five times daily.
2. A mixture containing Potassium Citrate and Sodium Bicarbonate containing 30 gr. of each per dose was given four times daily for 10 days because symptoms of salicylism developed (Plasma Salicylates 39 mg.%).
3. Ferrous Gluconate gr. 10 t.d.s. pc.

Progress: Patient's signs and symptoms steadily subsided after commencing treatment. However on 30.12.55, a definite mid-diastolic murmur, best heard in the left lateral position, became audible at the mitral area.

Condition on Discharge: Hb. 98%. W.B.C. 6,000/c.mm. E.S.R. 4 mm.

Heart: B.P. 100/60.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur present at mitral area.

X-ray Chest: /

23. T.D. (Continued).

X-ray Chest: Normal.

E.C.G. Sinus tachycardia.

Follow-up: Patient remained well and symptom free. Tonsils and adenoids were removed three months after discharge. In all, she attended for 16 injections of Penidural Penicillin. Thereafter she defaulted, giving no reason, and ignoring requests to the Clinic.

Routine Review: 1959, (aged 16 years) - Repeated communications were ignored by the patient. Her own doctor was contacted, and he stated that she continues well, has had no recurrences of rheumatic fever, and that her heart sounds were pure at all areas.

PART B.

A description of cases, chosen by random selection to act as controls in the series. They did not receive Penidural Penicillin.

1. E.M.

Aged 13 years. Female. Second attack of chorea.

Admitted 30.6.54. Discharged 31.8.54. Days in hospital: 62.

Complaint: Jerky movements of head, hands and feet of two weeks' duration.

History: Sore throat seven weeks prior to onset of symptoms. The first attack of chorea occurred six months previously. One sister had had rheumatic fever 4 years before.

Clinical Examination: T. 97.4°. P.R. 98/min. Regular.
Hb. 86%. W.B.C. 16,000/c.mm. E.S.R. 28 mm.
Throat was moderately inflamed.
Typical choreiform movements present in hands, feet and head.
Uncontrollable grimaces of face were present.

Heart: B.P. 100/75.
A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space.
A soft systolic murmur and a soft diastolic murmur were present at the mitral area.
There was splitting of the second sound at the aortic area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Sinus arrhythmia.

Laboratory Findings: Throat swab - Numerous colonies of H.S. were grown on culture.

Treatment: Aspirin gr. 15 five times daily.
Phenobarbitone gr. $\frac{1}{2}$ t.i.d.
Course of Crystalline Penicillin.

Progress: Patient's condition steadily improved. Convalescence was uneventful.

Condition on Discharge: All choreiform movements had ceased.
Hb. 94%. W.B.C. 5,200/c.mm. E.S.R. 3 mm.

Heart: /

1. E.M. (Continued).

Heart: B.P. 100/75.
A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space.
A soft mid-diastolic murmur was audible at the mitral area. There were no other adventitae.

X-ray Chest: Normal.

E.C.G. Normal.

Throat Swab: No H.S. were grown on culture.

Follow-up: Patient was reviewed at intervals of six weeks. She remained symptom free.
By April, 1957, no diastolic murmur was audible at the mitral area, even after exercise. The following month she received treatment as an Out-patient at another hospital for a septic hand. A few weeks later she was admitted by her own doctor to a fever hospital with signs and symptoms suggesting meningitis. Her temperature was 101°F; nuchal rigidity was marked and there was a petechial rash on the skin of her abdomen. Lumbar puncture was performed, revealing a purulent fluid, which failed to grow any organism when cultured. Her condition deteriorated rapidly and she died 36 hours after admission.

Summary of Post Mortem Report: This revealed an acute bacterial endocarditis, plus an area of cerebral haemorrhage in the left occipital lobe, which was considered to be probably embolic in origin. As well as the bacterial thrombi present on the mitral valve, firm thrombi were present along the lines of contact of the valve cusps. These had the appearance of an acute rheumatic infection.
A blood culture performed at the time of admission produced a growth of coagulase positive staphylococci.

2. M. McA.

Aged 18 years. Female First attack of rheumatic fever.

Admitted 11.7.54. Discharged 5.10.54. Days in hospital: 86.

Complaint: Flitting pains affecting all joints, of one week's duration.

History: Sore throat one week previously.
One sister had rheumatic fever three years before.

Clinical Examination: T. 101°F. P.R. 130/min. Regular.
Hb. 80%. W.B.C. 12,600/c.mm. E.S.R. 75 mm.
Throat was markedly inflamed. The tonsils were enlarged. Both knees were swollen, stiff and painful.

Heart: B.P. 130/90.
A.B. 3½" from M.S.L. in 5th L. space.
Systolic murmurs were present at mitral and aortic areas.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G.: Normal.

Laboratory Findings: Throat swab - A scanty growth of H.S. appeared on culture.

Treatment: Aspirin gr. 20 five times daily.
Course Crystalline penicillin.
Mixture containing Potassium Citrate and Sodium. Bicarbonate (gr. 30 of each, per dose) was given when symptoms of salicylism appeared (nausea and tinnitus; serum salicylates 41 mg.%).

Progress: Patient's condition steadily improved, convalescence was uneventful. She refused to have arrangements made for removal of tonsils and adenoids.

Condition on Discharge: Hb. 96%, W.B.C. 6,000/c.mm., E.S.R. 5 mm.

Heart: B.P. 130/85.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at all areas.

X-ray Chest: Normal.

E.C.G.: Normal.

Follow-up: Patient failed to attend the Follow-up Clinic, and she was not seen again until 29.12.56, when she was readmitted with a second attack of rheumatic fever.

2nd Admission:

Admitted 29.12.56. Discharged 3.2.56. No. of days in hospital: 63.

Complaint: /

2. M. McA. (Continued).

Complaint:	Pain and swelling of both knees of two weeks' duration.
History:	No recent sore throat on this occasion.
Clinical Examination:	T. 101°F. P.R. 120/min. Regular. Hb. 90%. W.B.C. 5,000/c.mm. E.S.R. 50 mm. Tonsils inflamed. Both knees stiff and swollen.
Heart:	B.P. 130/90. A.B. 4" from M.S.L. in 5th L. space. A loud systolic murmur was audible at all areas.
Examination of urine:	Normal.
X-ray Chest:	Normal.
E.C.G.	Normal.
Laboratory Findings:	Throat swab - No H.S. grown on culture.
Treatment:	Disprin gr. 20 five times daily. Four courses of crystalline penicillin.
Progress:	The patient's condition remained unchanged for two weeks, then she began to improve slowly. However, on four occasions, routine throat swabs revealed a heavy growth of H.S. on culture. Gradually the E.S.R. returned to normal. After 63 days treatment she had her tonsils and adenoids removed.
Condition on Discharge:	Hb. 80%. W.B.C. 5,000/c.mm. E.S.R. 12 mm.
Throat swab:	No H.S. were grown on culture.
Heart:	Blood pressure 130/90. A.B. 3½" from M.S.L. in 5th L. space. A soft systolic murmur was audible at the mitral area only.
E.C.G.	Normal.
Follow-up:	The patient remained well, and was seen at intervals for one year. After this, she defaulted.
Routine Review:	April, 1959 (aged 24 years) - The patient ignored all requests to attend the Clinic. On being contacted, her own doctor stated that she continued well, had remained free from recurrences of rheumatic fever and that she had no cardiac murmurs.

3. W. McK.

Aged 15 years. Male. Second attack of rheumatic fever, and congestive cardiac failure.

Admitted 5.12.53. Discharged 6.6.54. Days in hospital: 181.

Complaint: Flitting joint pains of three days' duration.
Breathlessness and chest pain of two days' duration.

History: No recent sore throat.
Had first attack of rheumatic fever two years previously.
No family history of the disease.

Clinical Examination: An extremely ill boy, dyspnoeic at rest. Jugular venous congestion was marked. Oedema present in face, sacrum and legs.
T. 101°F. P.R. 124/min. Regular. Resp. R. 28/min.
Hb. 72%. W.B.C. 11,200/c.mm. E.S.R. 60 mm.
Left wrist and both knees swollen and extremely painful.

Heart: B.P. 130/40.
A.B. $4\frac{1}{2}$" from M.S.L. in 5th L. space.
At both the mitral and the aortic valves, a prolonged blowing systolic murmur was present, together with a soft diastolic murmur - the mitral diastolic murmur was propagated into the axilla and that at the aortic area was propagated down the left border of the sternum.

Examination of urine: Normal on admission.
Two months later granular casts were present for ten days, and then urine returned to normal.

X-ray Chest: "Cardiac dilatation present. Lungs congested at both bases".

E.C.G.: "Suggestive of mitral stenosis".

Laboratory Findings: Throat swab - No H.S. present on culture.
Blood cultures - persistently negative.
Agglutination tests - negative.
Liver and kidney function tests (including electrolytes) - normal.

Treatment: Aspirin gr. 20 six times daily.
Digoxin 0.25 mg. twice daily.
Mersalyl 2 c.c. thrice weekly.
Ferrous Gluconate gr. 10 thrice daily for four weeks.
Course of crystalline penicillin.
Aureomycin 250 mg. six hourly for seven days.
Patient was nursed in an oxygen tent.

Progress: Progress was very slow indeed.
His temperature continued to rise and fall at intervals of 2-3 days - the chart having a "spiked" appearance.
By 14.5.54 his condition had greatly improved.
A.B. $4\frac{3}{4}$" from M.S.L. in 5th L. space. The cardiac murmurs, /

3. W. McK. (Continued).

murmurs, however, remained unchanged. On this date, treatment with Digoxin and Mersalyl was discontinued. Convalescence then proceeded uneventfully.

Condition on Discharge: Hb. 82%. W.B.C. 6,200/c.mm. E.S.R. 8 mm.

Throat Swab: No H.S. grown on culture.

Heart: B.P. 115/75
A.B. 4¼" from M.S.L. in 5th L. space.
Systolic and diastolic murmurs at mitral and aortic areas.

X-ray Chest: "Generalised cardiac dilatation".

E.C.G.: "Minimal myocardial involvement. Slow conduction through A.V. Bundle".

Follow-up: Patient remained very well until January, 1955, his cardiac condition being fully compensated. Climbing stairs, etc., was of no effort to him. He obtained a post as a tailor's assistant and coped very successfully. However, he was readmitted from the Clinic with a recurrence of rheumatic fever.

2nd Admission:

Admitted 6.1.55. Died 5.2.55. No. of days in hospital: 28.

Complaint: Generalised joint pains of two weeks' duration.
Breathlessness, even at rest, of two weeks' duration.

History: "Chill" with sore throat at onset of symptoms.

Clinical Examination: Pale, dyspnoeic boy. No oedema present.
T. 100°F. P.R. 120/min. Regular.
Hb. 68%. W.B.C. 12,000/c.mm. E.S.R. 35 mm.
Both knees swollen.
Left wrist painful but not swollen.

Heart: B.P. 115/75.
A.B. 5½" from M.S.L. in 6th L. space. Forceful and heaving in character.
Systolic and diastolic murmurs audible at aortic and mitral areas and heard over all the praecordium.

Examination of urine: On admission albumin was present, but no casts or red cells were present on microscopical examination until 2.2.55, when many were present.

X-ray Chest: "Generalised cardiac enlargement with pulmonary venous congestion".

E.C.G.: "Mitral stenosis."

Laboratory Findings: /

3. W. McK. (Continued).

Laboratory Findings: Throat swab - No H.S. grown on culture.
Series of blood cultures persistently negative.

Treatment: Aspirin gr. 20 five times daily.
Digoxin 0.25 mg. 6 hourly for 7 days.
Mersalyl 2 c.c. three times per week.
Aureomycin 500 mg. initially, and 250 mg. 6 hourly for 6 days.

Progress: Patient remained extremely ill, and gradually his condition deteriorated.
E.S.R. rose to 70 mm.
By 21.1.55, there was gross cardiomegally present.
Liver and spleen were both enlarged.
2.2.55. Pericardial friction rub present; this was best heard at the left lower border of the sternum.
Two days later a massive pericardial effusion developed.
Despite all measures, the patient died on 5.2.55.

Summary of Post Mortem Report:

"Examination of the heart valves revealed acute rheumatic lesions.
There was also an incidental subacute phthisis with slight miliary spread."

It was concluded that the condition was an acute exacerbation of chronic rheumatic endocarditis (mitral, aortic and tricuspid valves), with terminal rheumatic pericarditis and heart failure.

4. R.B.

Aged 12 years. Male. First attack of rheumatic fever.

Admitted 29.6.53. Discharged 15.1.54. Days in hospital: 201.

Complaint: Pain and swelling of right knee and left ankle of three days' duration.

History: No history of recent sore throat.
No family history of rheumatism.

Clinical Examination: T. 99° F. P.R. 120/min. Regular.
Hb. 85%. W.B.C. 6,200/c.mm. E.S.R. 46 mm.
Throat inflamed.
Right ankle and left knee swollen.

Heart: B.P. 120/80 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
No murmurs were present, but there was a "roughening" of the first sound at the mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G.: "Sinus tachycardia."

Laboratory Findings: Throat swab - No H.S. grown on culture.

Treatment: Aspirin gr. 15 five times daily.

Progress: Patient responded very slowly to treatment. A slight relapse occurred when he became ambulant for the first time on 23.11.53. The E.S.R. which had returned to normal, again rose to 44 mm. He was returned to bed for a further five weeks, by which time all symptoms had subsided and E.S.R. had returned to normal. He was then allowed to become ambulant with no ill effects. His haemoglobin rose spontaneously to 100%.

Condition on Discharge: Hb. 96%. W.B.C. 5,200/c.mm. E.S.R. 10 mm.
Throat swab - No H.S. grown on culture.

E.C.G. "Sinus tachycardia."

Heart: B.P. 120/80 mm.Hg.
A.B. 3" from M.S.L. in 5th L. space.
Soft systolic murmur was present at the mitral area.
There was splitting of second sound at the mitral area.

Follow-up: Patient remained well, until he appeared at the Clinic on a routine visit, complaining of general malaise. He was readmitted for observation.

2nd Admission:

Date 28.3.54. Discharged 28.4.54. Days in hospital: 31.

Complaint: /

4. R.B. (Continued).

Complaint: General malaise of three days' duration.

History: None of significance.

Clinical Examination: T. 98° F. P.R. 128/min. Regular. R.R. 20/min.
Hb. 96%. W.B.C. 10,000/c.mm. E.S.R. 22 mm.
Throat was not inflamed. No swelling of any joints.

Heart: B.P. 120/70.
A.B. 3¾" from M.S.L. in 5th L. space.
Diffuse and heaving in character.
As before, a systolic murmur was present at the mitral area, but on this occasion, a mid-diastolic murmur was audible at the mitral area.

Examination of urine: Normal.

X-ray Chest: "Normal" on admission.
Two weeks later reported as "showing straightening of the pulmonary bay, suggesting mitral stenosis. No cardiac enlargement noted."

E.C.G. "Sinus tachycardia."

Laboratory Findings: Throat swab - H.S. grown on culture.

Treatment: Bed rest, without salicylates.
Course of crystalline penicillin.

Progress: Pulse rate returned to normal (80/min.) with rest in bed and no salicylate was required. E.S.R. returned to normal within one week. A repeat throat swab had no H.S. present on culture.

Condition on Discharge: Hb. 98%. W.B.C. 7,000/c.mm. E.S.R. 16 mm.

Heart: B.P. 120/75 mm.Hg.
A.B. 3¾" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at the mitral area.
No diastolic murmur was present, even after exercise.

E.C.G. Normal.

X-ray Chest: As before - "straightening of the pulmonary bay."

Follow-up: Patient remained well and continued to be seen at intervals until 1958, when he defaulted.

Routine Review: April, 1959 (aged 18 years) - Patient stated that he felt extremely well and had had no recurrence of symptoms. On examination, however, he was found to have an elevation of blood pressure to 160/110 mm.Hg.
Since he was very much against being admitted to hospital investigations were performed at the Out-patient department.

Heart: /

4. R.B. (Continued).

Heart:	A.B. 3¾" from M.S.L. in 5th L. space. Rate 112/min. and of regular rhythm. A soft systolic murmur was present at the mitral area. No other adventitae were present.
Examination of urine:	Normal.
X-ray Chest:	Normal.
E.C.G.	"Sinus tachycardia."
	Blood urea 33 mg.% (normal 15-40 mg.%). Liver and kidney function tests were normal.
Fundal Examination:	Normal.
Throat Swab:	No H.S. grown on culture.

On a further visit, his B.P. remained elevated - 160/95 mm.Hg. and he again refused admission. The patient then failed to attend for observation but according to his own doctor, he has been symptom free, and working very hard; he had not attended him for further checking of blood pressure, as requested.

5. J. A.

Aged 13 years. Female. First attack of rheumatic fever.

Admitted 29.12.53. Discharged 25.3.54. Days in hospital : 86.

Complaint: Joint pains of three days' duration - "jumping from ankles to knees, to wrists, to elbows".

History: Tonsillitis two months previously.
No family history of rheumatic fever.

Clinical Examination: T. 103° F. P.R. 110/min. Regular.
Hb. 75%. W.B.C. 22,000/c.mm. E.S.R. 125 mm.
Throat was normal.
Both wrists were painful and swollen.

Heart: B.P. 115/70 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was audible in all areas.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G.: "Right axis deviation."

Treatment: Aspirin gr. 15 five times daily.
Ferrous gluconate gr. 10 thrice daily for 14 days.
Course of crystalline penicillin as an "umbrella" for removal of a tooth.

Progress: Patient's condition gradually responded to treatment. Convalescence was uneventful, apart from toothache. The affected tooth was later removed.

Condition on Discharge: Hb. 95%. W.B.C. 7,600/c.mm. E.S.R. 6 mm.

X-ray Chest: Normal.

E.C.G. "Right axis deviation."

Heart: B.P. 115/70 mm.Hg.
A.B. 3½" from mid-sternal line.
A soft systolic murmur was audible at the mitral area only.

Follow-up: Patient attended the Follow-up Clinic on two occasions, and thereafter, failed to attend despite many requests to do so.

Routine Review: May, 1959 (aged 19 years) - She again failed to attend the Clinic. Her own doctor, on being contacted, stated that she was well and symptom free and that her heart was normal, with a soft systolic murmur present at the mitral area only.

6. M.L.

Aged 16 years. Female. First attack of rheumatic fever.

Admitted 29.12.53. Discharged 10.3.54. Days in hospital: 71.

Complaint: Pains in both ankles of six days' duration. Rash on both legs of five days' duration.

History: Influenza and tonsillitis two weeks previously. No family history of rheumatic fever.

Clinical Examination: T. 99.2° F. P.R. 104/min. Regular.
Hb. 80%. W.B.C. 12,300/c.mm. E.S.R. 114 mm.
Throat - normal.
Erythema nodosum lower ⅓ of both legs.
The left wrist and left knee were swollen and painful.

Heart: B.P. 95/65 mm.Hg.
A.B. 4" from M.S.L. in 5th L. space.
Soft systolic murmur was audible at all areas.

Mantoux Test: Negative (both 1/10,000 and 1/1,000 dilutions).

Examination of Urine: Normal.

X-ray Chest: "Congenital abnormality of 8th and 9th right ribs (fusion). Slight congestion at right base."

E.C.G.: "Sinus tachycardia."

Laboratory Findings: Throat swab - No H.S. grown on culture.

Treatment: Aspirin gr. 20 five times daily.

Progress: Patient's condition gradually improved. The erythema nodosum subsided within 10 days of admission. On 24.2.54 a mid-diastolic murmur was audible at the mitral area, but this was not present two weeks later. Convalescence was otherwise uneventful.

Condition on Discharge: Hb. 100%. W.B.C. 9,200/c.mm. E.S.R. 4 mm.

X-ray Chest: Normal (Apart from congenital fusion of 8th and 9th right ribs).

E.C.G. Normal.

Heart: B.P. 100/65 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur present at mitral area.

Follow-up: Patient remained well and symptom free. On one occasion, H.S. were produced on culture of a routine throat swab. After a five day course of Permapen, no H.S. were grown on a repeat throat swab culture.

Routine Review: /

6. M.L. (Continued).

Routine Review: May, 1959 (aged 22 years).
Patient extremely well. Had not had any recurrences of symptoms.

Heart: B.P. 100/65 mm.Hg.
A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space.
Soft systolic murmur at mitral area.

7. M.G.

Aged 16 years. Female. First attack of rheumatic fever.

Admitted 10.2.54. Discharged 21.4.54. Days in hospital : 70.

Complaint: Pains in all joints of four days' duration.

History: Influenza and tonsillitis four weeks previously.
No family history of rheumatic fever.

Clinical Examination: T. 101.3° F. P.R. 100/min. Regular. R.R. 22/min.
Hb. 88%. W.B.C. 15,000/c.mm. E.S.R. 45 mm.
Throat normal.
All joints stiff and painful, but none actually swollen.

Heart: B.P. 115/75 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Rough systolic murmur present at the mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture but numerous colonies of streptococcus viridans were obtained.

Agglutination Tests
Paul Bunnell Test } Negative.

Treatment: Aspirin gr. 20 five times daily.

Progress: Patient responded slowly to treatment. The ventricular systolic murmur at the mitral area became much softer. Convalescence was uneventful.

Condition on Discharge: Hb. 95%. W.B.C. 6,000/c.mm. E.S.R. 4 mm.

X-ray Chest: Normal.

E.C.G. Normal.

Heart: B.P. 115/75 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at the mitral area.

Follow-up: Patient developed "painful knees" some months after discharge, but her E.S.R. was only 4 mm. and the complaint subsided within two days.
Otherwise she remained well and symptom free. A routine throat swab on one occasion revealed H.S. on culture. A repeat swab after a five day course of Permapen had no H.S. present on culture.

Routine Review: May, 1959 (aged 21 years). Patient extremely well. Had not had any recurrences of her symptoms.

Heart: B.P. 115/80. A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur at the mitral area.

8. J.H.

Aged 10 years. Male. First attack of rheumatic fever.

Admitted 10.11.53. Discharged 10.3.54. Days in hospital: 130.

Complaint: Pains in feet, knees and wrists of four days' duration.

History: No recent sore throat.
No family history of rheumatic fever.

Clinical Examination: T. 100° F. P.R. 104/min. H.B. 75%.
W.B.C. 10,500/c.mm. E.S.R. 115 mm.
Both wrists swollen and painful.

Heart: B.P. 95/50 mm.Hg.
A.B. 3½" from M.S.L. in 4th L. space.
Soft systolic murmur at mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G.: Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture.
Blood film - Iron deficiency anaemia.

Treatment: Aspirin gr. 10 five times daily.
Mist. Ferri et. ammonium Citrate gr. 15 thrice daily for 25 days.

Progress: Patient's general condition gradually improved; haemoglobin took some considerable time to return to normal.

5.1.54 X-ray chest revealed slight cardiac enlargement together with some catarrhal bronchitis.

18.1.54 X-ray chest normal.

Condition on Discharge: Hb. 80%. W.B.C. 4,200/c.mm. E.S.R. 9 mm.

Heart: B.P. 95/60 mm.Hg.
A.B. 3½" from M.S.L. in 4th L. space.
Soft systolic murmur at mitral area.

E.C.G. Normal.

Follow-up: Patient remained well and symptom free. Four months after discharge a diastolic murmur was audible at the mitral area, after the patient was exercised and examined whilst lying in the left lateral position. This was not present on the next Clinic visit, six weeks later, nor thereafter. On one occasion, H.S. were isolated from a routine throat swab culture. After a five-day course of "Permapen" penicillin, a repeat throat swab did not reveal the presence of H.S. on culture.

Routine Review: /

8. J.H. (Continued).

Routine Review: May, 1959 (aged 16 years).

Patient remained very well. He had no recurrences of his symptoms.
Gained $1\frac{1}{2}$ stones in weight over previous five years.

Heart: B.P. 100/70 mm.Hg.
A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space.
Soft systolic murmur audible at mitral area.

9. M. McL.

Aged 12 years. Female. First attack of rheumatic fever.

Admitted 18.7.53. Discharged 14.11.53. Days in hospital: 120.

Complaint: Generalised aches and pains, especially in knees and ankles, of two days' duration.

History: No history of recent sore throat.
No family history of rheumatic fever.

Clinical Examination: T. 99° F. P.R. 124/min. Regular.
Hb. 95%. W.B.C. 12,200/c.mm. E.S.R. 109 mm.
Both knees very tender and painful. Right knee swollen.

Heart: B.P. 130/70.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur present at mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture.

Treatment: Aspirin gr. 15 five times daily.
Course of crystalline penicillin (for septic finger during convalescence).

Progress: Patient's progress was slow, but steady improvement occurred. During convalescence she developed a pulp infection which was incised. A swab of pus from this lesion produced a growth of staphylococcous aureus on culture.

Condition on Discharge: Hb. 90%. W.B.C. 6,300/c.mm. E.S.R. 4 mm.

Heart: B.P. 130/70 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur was audible at mitral area.

X-ray chest: Normal.

E.C.G.: "Query left axis deviation."

Follow-up: Patient remained very well, and free from any illness whatsoever.

Routine Review: April, 1959 (aged 18 years).
Patient did not attend for examination despite several requests to do so. On contacting her own doctor, it was ascertained that she kept well and free from recurrences of rheumatic fever. Examination of her heart, when last he saw her some four weeks before, revealed a systolic murmur at the mitral area.

10. C.L.

Aged 13 years. Female. Second attack of rheumatic fever.

Admitted 30.11.53. Discharged 9.4.54. Days in hospital: 130.

Complaint: Flitting joint pains of three weeks' duration. Both hips, both knees and left wrist were most affected.

History: Influenza three weeks prior to onset of symptoms.
No family history of rheumatic fever.

Clinical Examination: T. 100° F. P.R. 104/min. Regular. Hb. 90%.
W.B.C. 15,000/c.mm. E.S.R. 110 mm.
Throat inflamed, but no exudate present.
Cervical glands enlarged.
Right elbow and left wrist were swollen and painful.

Heart: B.P. 120/65 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was present at the mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture but numerous colonies of strep. viridans were present.

Treatment: Aspirin gr. 20 five times daily.
Course of crystalline penicillin (because of inflamed throat).

Progress: Patient's condition was slow to return to normal but convalescence was uneventful.

Condition on Discharge: Hb. 100%. W.B.C. 6,000/c.mm. E.S.R. 9 mm.

Heart: B.P. 120/65 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Heart sounds pure at all areas.

X-ray Chest: Normal.

E.C.G. Normal.

Throat Swab: No H.S. grown on culture.

Follow-up: Patient remained very well and symptom free.
A routine throat swab, however, on 18.1.56, revealed several colonies of H.S. on culture. She was given a course of Permapen penicillin. At the end of this treatment a further throat swab was free from the presence of H.S. on culture.

Routine Review: April, 1959 (aged 19 years) - Patient had remained free from recurrences of rheumatic fever or sore throats.

Heart: B.P. 120/70. A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur audible at mitral area.

11. V.D.

Aged 13 years. Female. First attack of rheumatic fever.

Admitted 26.5.54. Discharged 27.8.54. Days in hospital: 94.

Complaint: Flitting joint pains in knees, ankles and wrists of two weeks' duration.

History: No history of recent sore throat.
No family history of rheumatic fever.

Clinical Examination: T. 99° F. P.R. 100/min. Regular.
Hb. 86%. W.B.C. 9,600/c.mm. E.S.R. 25 mm.
Throat not inflamed.
Both wrists swollen and very painful.
"Sweat" rash on trunk.

Heart: B.P. 125/75 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur present at the mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. "Sinus tachycardia."

Laboratory Findings: Throat swab - No H.S. grown on culture.

Treatment: Aspirin gr. 15 five times daily.

Progress: Patient's condition slowly returned to normal.
Convalescence was uneventful.

Condition on Discharge: Hb. 88%. W.B.C. 7,200/c.mm. E.S.R. 4 mm.

X-ray Chest: Normal.

E.C.G. Normal.

Throat Swab: No H.S. grown on culture.

Heart: B.P. 120/75 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was present at the mitral area.

Follow-up: Patient remained well and symptom free.

Routine Review: April, 1959 (aged 18 years).
Patient very well indeed, remaining free from recurrences of rheumatic fever.

Heart: B.P. 120/80 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur audible at mitral area.

12. D.M.

Aged 13 years. Male. First attack of rheumatic fever.

Admitted 24.2.54. Discharged 5.5.54. Days in hospital: 69.

Complaints: Flitting joint pains, affecting knees, shoulders and ankles of two weeks' duration.

History: Sore throat lasting 10 days, immediately prior to onset of symptoms.
No family history of rheumatic fever despite the fact that he lived in grossly overcrowded conditions, viz. 3 adults and 8 children in one room and kitchen.

Clinical Examination: T. 99° F. P.R. 120/min. Regular. Hb. 100%.
W.B.C. 8,200/c.mm. E.S.R. 38 mm.
Throat not inflamed. Both knees swollen and painful.

Heart: B.P. 115/70 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur present at the mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - No H.S. grown on culture.
Agglutination Test) Negative.
Paul Bunnell Test)

Treatment: Aspirin gr. 15 five times daily.

Progress: Patient's condition slowly returned to normal.
Convalescence was uneventful.

Condition on Discharge: Hb. 90%. W.B.C. 7,300/c.mm. E.S.R. 13 mm.

X-ray Chest: Normal.

E.C.G. Normal.

Throat Swab: No H.S. grown on culture.

Heart: B.P. 115/75 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Soft systolic murmur present at mitral area.

Follow-up: Patient remained well until August, 1954, when he was admitted (together with his sister) to a Fever Hospital with Sonne Dysentry. He remained free from recurrences of rheumatic fever until October 1954, when he attended the Clinic looking rather toxic and complaining of sore throat and painful knees, of three days' duration. He was re-admitted to hospital.

2nd Admission:

Date /

12. D.M. (Continued).

2nd Admission:

Date 13.10.54. Discharged 10.12.54. Days in hospital : 59.

Clinical Examination:	T. 99° F. P.R. 112/min. regular. Hb. 90%. W.B.C. 8,200/c.mm. E.S.R. 35 mm. Throat inflamed, catarrhal sinusitis present. Both knees painful, but only left knee was swollen.
Heart:	B.P. 120/60 mm.Hg. A.B. 3½" from M.S.L. in 5th L. space. Soft systolic murmur present at the mitral area.
Examination of urine:	Normal.
X-ray Chest:	Normal.
X-ray Sinuses:	"Thickening of frontal sinus."
E.C.G.	"Sinus tachycardia."
Laboratory Findings:	Throat swab - No H.S. grown on culture but many colonies of streptococcus viridans appeared.
Treatment:	Aspirin gr. 15 five times daily. Course of crystalline penicillin (for sinusitis).
Progress:	Patient's condition steadily improved. Convalescence was uneventful.
Condition on Discharge:	Hb. 96%. W.B.C. 5,000/c.mm. E.S.R. 14 mm.
X-ray Chest:	Normal.
X-ray Sinuses:	Normal.
E.C.G.	Normal.
Heart:	B.P. 120/65 mm.Hg. A.B. 3½" from M.S.L. in 5th L. space. Soft systolic murmur was audible at the mitral area.
Follow-up:	Patient remained well and symptom free.
Routine Review:	May, 1959 (aged 18 years) - Patient continued free from recurrences of symptoms. Very well indeed.
Heart:	B.P. 120/80 mm.Hg. A.B. 3½" from M.S.L. in 5th L. space. Heart sounds pure at all areas.

13. T.R.

Aged 13 years. Male. First attack of rheumatic fever.

Admitted 8.9.53. Discharged 15.1.54. Days in hospital : 129.

Complaint: Pains in ankles, knees and back, of four days' duration and swollen wrists of two days' duration.

History: A sore throat one week prior to onset of symptoms.
No family history of rheumatic fever.

Clinical Examination: T. 101° F. P.R. 115/min. Regular.
Hb. 98%. W.B.C. 8,800/c.mm. E.S.R. 38 mm.
Both tonsils were enlarged and inflamed, with areas of exudate present.
Both wrists and the left knee were swollen and painful.

Heart: B.P. 140/75 mm.Hg.
A.B. 3" from M.S.L. in 5th L. space.
A soft systolic murmur was present at all areas.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G.: Normal.

Laboratory Findings: Throat swab - No H.S. were grown on culture but numerous colonies of streptococcus viridans were obtained.

Treatment: Aspirin gr. 20 five times daily.
Course of crystalline penicillin (because of the follicular tonsillitis).

Progress: Patient's condition gradually returned to normal. Apart from the occurrence of a mild generalised rash (Erythema Multiforme), which lasted for ten days, convalescence was uneventful.

Condition on Discharge: Hb. 88%. W.B.C. 8,500/c.mm. E.S.R. 2 mm.

X-ray Chest: Normal.

E.C.G.: "Sinus arrhythmia."

Heart: B.P. 140/70 mm.Hg.
A.B. 3" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at the mitral and aortic areas.

Follow-up: Patient remained free from recurrence of rheumatic fever, but gave a history (on several occasions, on routine visits to the Clinic) of recurrent attacks of sore throat, which had been treated by his own doctor with oral penicillin. Tonsils and adenoids were removed in December, 1954. Following this, he remained free from sore /

13. T.R. (Continued).

sore throats. In March, 1957, he was admitted by his own doctor, to a Fever Hospital suffering from pneumonia.

Routine Review: May, 1959 (aged 19 years).
Patient had remained symptom free - looked very well.

Heart: B.P. 140/95 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
Heart sounds were pure at all areas.

14. A.D.

Aged 11 years. Male. First attack of rheumatic fever.

Admitted 12.8.54. Discharged 24.9.54. Days in hospital : 43.

Complaint: Pains in wrists, ankles and knees of 7 days' duration.

History: Acute coryza and sore throat at onset of symptoms.
No family history of rheumatic fever.
Admitted whilst on holiday from England.

Clinical Examination: T. 99.4°F. P.R. 108/min. regular.
Hb. 90%. W.B.C. 8,000/c.mm. E.S.R. 35 mm.
Throat not inflamed. Both ankles were stiff and swollen.

Heart: B.P. 120/80 mm.Hg.
A.B. Diffuse and heaving in 5th L. space.
Loud systolic murmur audible at all cardiac areas.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. "Sinus tachycardia".

Laboratory Findings: Throat swab - No H.S. grown on culture.

Treatment: Aspirin gr. 15 four times daily.

Progress: Patient's condition steadily improved.
Convalescence was uneventful.

Condition on Discharge: Hb. 95%. W.B.C. 8,000/c.mm. E.S.R. 5 mm.

X-ray Chest: Normal.

E.C.G. "Sinus tachycardia".

Heart: B.P. 120/80.
A.B. 3½" from M.S.L. in 5th L. space. No longer diffuse and heaving in character. A soft systolic murmur was audible at the mitral area only.

Follow-up: Patient returned to his home in England but was seen from time to time, when he came back to Glasgow on holiday. He remained well and free from recurrence of his symptoms.

Routine Review: 1959 (aged 16 years).
Despite several letters sent to his parents, and to his own doctor, no information was received about the patient's condition nor his present whereabouts.

15. M.S.

Aged 10 years. Female. First attack of rheumatic fever.

Admitted 18.11.55. Discharged 21.1.56. Days in hospital: 64.

Complaint: Pains in elbows and knees of four days' duration.

History: Sore throat three weeks previously.
No family history of rheumatic fever.

Clinical Examination: T. 99.8° F. P.R. 128/min. regular.
Hb. 75%. W.B.C. 14,600/c.mm. E.S.R. 95 mm.
Throat was not inflamed. Left elbow and right knee were swollen and tender.

Heart: B.P. 120/40 mm.Hg.
A.B. 2¾" from M.S.L. in 5th L. space.
Soft systolic murmur at all areas.
A doubtful 3rd heart sound was present at the mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. "Sinus arrhythmia."

Laboratory Findings: Throat swab - Two colonies of H.S. were grown on culture.

Treatment: Disprin gr. 15 five times daily.
Ferrous Gluconate gr. 5 thrice daily for 16 days.

Progress: Patient's condition gradually returned to normal, but during convalescence she had a fairly brisk epistaxis. At that time, she also complained of tinnitus; the serum salicylate level was 31 mg.%. The symptoms of tinnitus subsided when Disprin dosage was reduced to gr. 5 five times daily.
On 5.11.55 a diastolic murmur was audible at the mitral area.

X-ray Chest: A few days later revealed "mitral configuration with some pulmonary congestion."

Condition on Discharge: Hb. 95%. W.B.C. 7,300/c.mm. E.S.R. 5 mm.

X-ray Chest: "Normal cardiac outline. Lung fields clear."

E.C.G. "Sinus arrhythmia."

Heart: 120/70 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at all areas.

Follow-up: Patient remained well and symptom free. On one occasion a routine throat swab revealed H.S. on culture. A repeat throat swab after a five-day course of "Permapen" penicillin /

15. M.S. (Continued).

penicillin did not reveal H.S. on culture.

Routine Review: May, 1959 (aged 14 years).
Patient was very well. She had not had any recurrence of rheumatic fever, though she gave a history of an attack of acute sore throat several months previously, which had subsided after a course of oral penicillin prescribed by her own doctor. There were no sequelae.

Heart: B.P. 115/75 mm.Hg.
A.B. $3\frac{1}{2}$" from M.S.L. in 5th L. space.
The first sound at the mitral area was accentuated.
A soft systolic murmur was present at the mitral area.
No diastolic murmur was audible even after exercise.

16. J.S.

Aged 11 years. Female. Third attack of rheumatic fever.

Admitted 24.6.54. Discharged 8.9.54. Days in hospital : 76.

Complaint: "Pains jumping from knees to ankles to wrists, of two weeks' duration.

History: Sore throat three weeks previously.
Patient also suffered from idiopathic epilepsy.
Three sisters each had attacks of rheumatic fever, several years before, and at different times.

Clinical Examination: T. 100° F. P.R. 120/min. Regular. Hb. 80%.
W.B.C. 9,000/c.mm. E.S.R. 45 mm.
Throat was not inflamed. Both knees and left wrist were swollen and tender.

Heart: B.P. 90/40 mm.Hg.
A.B. 3" from M.S.L. in 5th L. space.
A soft systolic murmur was present at the mitral area.

Examination of urine: Normal.

X-ray Chest: "Prominence of both lung roots, probably of glandular nature. Cardiac outline normal."

E.C.G. "Normal apart from sinus tachycardia."

Laboratory Findings: Throat Swab - No H.S. present on culture.

Treatment: Aspirin gr. 15 four times daily.
Course of crystalline penicillin (see below).

Progress: Patient's condition gradually improved. The pulse rate returned to normal within 7 days of admission. On 7.8.54 a routine throat swab revealed the presence of H.S. on culture. She was given a course of penicillin, whereupon a repeat throat swab was free from the presence of H.S. on culture. Thereafter the patient made an uneventful recovery. She had no epileptic fits whilst in hospital.

Condition on Discharge: Hb. 80%. W.B.C. 7,000/c.mm. E.S.R. 3 mm.

X-ray Chest: Normal.

E.C.G. Normal.

Heart: B.P. 95/45 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
The second sound at the pulmonic area was accentuated.
There was a soft systolic murmur at the mitral area.

Follow-up: Patient remained well for some months apart from vague pains in her legs, knees and ankles. On each occasion when /

16. J.S. (Continued).

when she complained of this, her E.S.R. was estimated, and found to be normal each time. However, on 15.11.55 she was readmitted for two weeks for observation when she attended the clinic complaining of a headache and joint pains.
The only abnormality found was a mild frontal sinusitis which subsided on treatment with menthol inhalations.
No change was found in her physical condition.
On June, 1956, appendicectomy was performed. From that time she remained well and free from joint pains.

Routine Review: May, 1959 (aged 16 years).
The patient ignored all requests to attend the Clinic for examination. Her own doctor was contacted, and stated that the patient remained well, and had not had any recurrence of rheumatic fever, and that her heart sounds were pure at all areas.

17. R.M.

Aged 16 years. Male. Fourth attack of rheumatic fever.

Admitted 14.4.54. Discharged 30.8.54. Days in hospital : 138.

Complaint: Pains in knees, ankles and elbows of two weeks' duration.

History: No history of recent sore throat.
No family history of rheumatic fever.

Clinical Examination: T. 99.6° F. P.R. 88/min. Regular. Hb. 92%.
W.B.C. 9,000/c.mm. E.S.R. 62 mm.
Throat was not inflamed.
Both ankles were swollen and tender.

Heart: B.P. 100/60 mm.Hg.
A.B. 3¼" from M.S.L. in 5th L. space.
Heart sounds were pure at all areas.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. "Sinus tachycardia."

Laboratory Findings: Throat swab - No H.S. were grown on culture.

Treatment: Aspirin gr. 20 six times daily.

Progress: Patient's condition slowly returned to normal.
Convalescence was uneventful.

Condition on Discharge: Hb. 95%. W.B.C. 4,600/c.mm. E.S.R. 3 mm.

Throat Swab: No H.S. present on culture.

X-ray Chest: Normal.

E.C.G. Normal.

Heart: B.P. 100/60 mm.Hg.
A.B. 3¼" from M.S.L. in 5th L. space.
A soft systolic murmur was present at the mitral area.

Follow-up: Patient remained very well and symptom free. On one occasion a routine throat swab revealed H.S. on culture, but a repeat swab after a five-day course of "Permapen" penicillin revealed no H.S. on culture.

Routine Review: 1956 (aged 21 years). Prior to entering army for national service. Patient remained very well. Had not had any recurrence of rheumatic fever.

Heart: B.P. 105/70 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
A soft systolic murmur was audible at the mitral area.

18. J. McC.

Aged 19 years. Male. First attack of rheumatic fever.

Admitted 17.3.57. Discharged 31.5.57. Days in hospital : 42.

Complaint: Pains in both knees and ankles of four days' duration.

History: Sore throat three weeks previously.
No family history of rheumatic fever.

Clinical Examination: T. 99° F. P.R. 90/min. Regular.
Hb. 100%. W.B.C. 7,600/c.mm. E.S.R. 36 mm.
Throat mildly inflamed. Both knees stiff and painful.

Heart: B.P. 120/65 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
A rough, short, presystolic murmur was present at the mitral area.

Examination of urine: Normal.

X-ray Chest: Normal.

E.C.G. Normal.

Laboratory Findings: Throat swab - Several colonies of H.S. were grown on culture.

Treatment: Disprin gr. 15 five times daily.
Course of crystalline penicillin.

Progress: Patient's condition rapidly returned to normal.
Convalescence was uneventful.

Condition on Discharge: Hb. 100%. W.B.C. 5,200/c.mm. E.S.R. 2 mm.

X-ray Chest: Normal.

E.C.G. Normal.

Heart sounds pure at all areas.

Follow-up: Patient remained very well and symptom free. Three months after discharge - no diastolic murmur was detected.

Routine Review: 1959 (aged 21 years).
Patient very well. Had not had any recurrence of rheumatic fever.
Heart: B.P. 120/65 mm.Hg.
A.B. 3½" from M.S.L. in 5th L. space.
No murmurs present.

19. A.H.

Aged 18 years. Male. Second attack of rheumatic fever.

Admitted 13.7.57. Discharged 27.9.57. Days in hospital : 45.

Complaint: Pains in wrist and knees of three days' duration.

History: Sore throat three weeks prior to onset of symptoms. No family history of rheumatic fever.

Clinical Examination: T. 98° F. P.R. 112/min. Regular.
Hb. 100%. W.B.C. 15,000/c.mm. E.S.R. 87 mm.
Left wrist and right knee swollen and painful.

Heart: B.P. 125/55 mm.Hg.
A.B. 5" from M.S.L. in 5th L. space.
A diastolic thrill was present at the apex.
A rough blowing systolic murmur and a mid-diastolic murmur were audible at the mitral area.
A blowing diastolic murmur was present at the aortic area and was best heard down the left border of sternum.

Examination of urine: Normal.

X-ray Chest: "Generalised cardiac enlargement.
Lung fields normal."

E.C.G. "No definite abnormality present."

Laboratory Findings: Throat swab - Two small colonies of H.S. were grown on culture.
Peripheral blood - No lupus Erythematosus cells were present.

Treatment: Aspirin gr. 20 five times daily.

Progress: Patient's condition slowly returned to normal. Convalescence was uneventful.

Condition on Discharge: Hb. 100%. W.B.C. 7,200/c.mm. E.S.R. 2 mm.

X-ray Chest: "As before - generalised cardiac enlargement present."

E.C.G. "No definite abnormality present."

Heart: B.P. 120/55 mm.Hg.
A.B. 4¾" from M.S.L. in 5th L. space.
A mid-diastolic murmur was audible down left border of sternum.

Follow-up: Patient remained well and symptom free. Tonsils and adenoids were removed six months later.

Routine Review: /

19. A.H. (Continued).

Routine Review: 1959 (aged 20 years).
Patient remained very well and had not had any recurrence of symptoms.

X-ray Chest: "Some generalised cardiomegally still present."

Heart: B.P. 120/55 mm.Hg.
A.B. $4\frac{3}{4}$" from M.S.L. in 5th L. space.
A diastolic thrill was present at apex.
A mid-diastolic murmur was still audible down the left border of sternum.
Other areas were free from adventitae.

DESCRIPTION OF A CASE OF COLLAGEN DISEASE WHICH PRESENTED AS A CASE OF RHEUMATIC FEVER

DESCRIPTION OF A CASE OF COLLAGEN DISEASE WHICH PRESENTED AS A CASE OF ACUTE RHEUMATIC FEVER

The following is an account of a girl aged 15 years, who presented initially as a case of acute rheumatic fever. The course of her illness is described, together with the post-mortem findings.

J. McI. Aged 15 years.

Admitted on 17.5.54. Died on 23.6.54. Days in hospital: 47.

Complaint: Pains in all joints for 5-6 weeks prior to admission. Extreme tiredness for 8 months.

Past History: Diphtheria at age of 3 years.
Scarlet fever at age of 7 years, and again at 13 years.
Tonsils and adenoids removed at age of 5 years.
"Shingles" at age of 7 years.
Corneal ulcers at age of 12 years.

History on Admission: For the previous 8 months, patient had been feeling extremely tired. Menstruation had ceased in November, 1953.
For 5 weeks, she had been experiencing pains in all her joints, but especially her left ankle, both knees, all her fingers and across her shoulders. All these joints were affected together. The pains were not fleeting in character. Prior to the onset of these, she had had a sore throat, and a recurrence of her throat condition occurred three weeks prior to admission. Since November, 1953, she had been losing weight.

Examination: Well-nourished, intelligent girl. Left ankle swollen and painful. Loss of full extension of R. knee and L. elbow. Tongue clean and moist. Teeth in good condition. No lymphadenopathy. No evidence of cyanosis, jaundice, anaemia, oedema, or clubbing of the fingers. No rheumatic nodules. There were multiple warts on both hands, but no evidence of skin rashes, or other cutaneous lesions. Temperature 98° F.
P. 76/min. Resp. 20/min.

Cardiovascular System: B.P. 95/65 mm.Hg.

Apex Beat: 3½" from mid-sternal line in the 5th L. space. Heart borders within normal limits on percussion. Pulse regular /

J. McI. (Continued).

regular in rate and rhythm. A soft systolic murmur was heard at all areas, but no other adventitae were present.

Respiratory System: Trachea was central. Chest moved freely on both sides during respiration. Percussion of lung fields was resonant throughout. Respiratory murmur was vesicular. Vocal fremitus and vocal resonance were equal on both sides. No adventitae were detected.

Abdomen: Soft. Moved freely on respiration. Neither hepatomegally nor splenomegally was present. Neither kidney was palpable. No masses were palpable.

Central Nervous System: Pupils were equal and central. Reacted to light and to accommodation. No nystagmus was elicited. Other cranial nerves were intact. Limb reflexes were all present and physiological. Sensation was normal. There was no upset in balance or co-ordination.

Investigations performed on admission (17.5.54) :-

Hb. 82%.
W.B.C. 8,900/c.mm.
E.S.R. 13 mm. 1st hour.
36 mm. 2nd hour.
(3 days later E.S.R. 68 mm. 1st hour.
90 mm. 2nd hour.)

Throat Swab: Numerous Haemolytic Streptococci were isolated on culture.

Sputum: No Acid - or Alcohol - Fast bacilli seen.

Urine : Normal.

W.R.: Negative.

X-ray Chest: (19.5.54) - "Calcified lesion in left lower zone. No evidence of pulmonary disease. Slight generalised cardiac enlargement present."

X-ray: Knees, hands and ankles - negative.

By 19.5.54: W.B.C. had fallen to 5,400/c.mm. and E.S.R. had fallen to 20 mm. in 1st hour. Patient improved steadily until 5.6.54, when temperature became elevated to 101° F. and W.B.C. increased to 15,000/c.mm.

Differential W.B.C. Neutrophils 76%
Eosinophils 3%
Basophils 2%
Monocytes 1%
Lymphocytes - small 8%
large 10% } 18%

On several occasions, blood specimens were examined and found to be negative for B. Typhosus (H. and O.); B.Para-Typhosus B. (H. and O.); Abortus Fever; and Paul /

J. McI. (Continued).

Paul Bunnell Test was also negative (on several occasions). Blood cultures - negative.
Throat became red and inflamed - but no Haemolytic Streptococci were then grown on culture of throat swab.

Clinical examination of chest on 8.6.54 revealed fluid present at L. base. Patient also developed diarrhoea on this date.

X-ray Chest: (8.6.54) - "Effusion at L. base. ? Tubercular infiltration L. mid-zone."

Sputum: Again negative for Tubercle Bacilli.

Gastric Lavage: Normal. No Tubercle Bacilli revealed.

Mantoux Test: Faintly positive (only erythema present, no ulceration) at dilution of 1/10,000.

Culture of Faeces: No growth of pathogenic organisms.

Pleural Tap: was performed on 8.6.54, and blood-stained, straw-coloured fluid was obtained.
On microscopical examination, a moderate number of small mono-nucleated cells were present. No Tubercle Bacilli or other organisms were seen.

Culture of Pleural Fluid: No growth obtained and culture test for B. Tuberculosis was negative.

Repeat Throat Swab: Again no H.S. grown. (H.S. were only grown on one occasion from the throat of this patient, namely, on admission).

On 9.6.54, patient was examined by Chest Physician who stated, in brief, as follows:-

"Pleural friction rub at both bases. Fluid and crepitations at L. base.
As gastric lavage reveals no Tubercle Bacilli, and as Mantoux Test is not strongly positive, there is no necessity for commencing anti-Tubercular treatment.
It is not possible in this case, to distinguish between rheumatism and tuberculosis."

Joints of both knees remained slightly swollen.

9.6.54: E.S.R. 53 mm. 1st hour. 106 mm. 2nd hour.

14.6.54: E.S.R. 98 mm. 1st hour. 118 mm. 2nd hour.

17.6.54: W.B.C. 9,500/c.mm.

Differential W.B.C. - Neutrophils 58%
Eosinophils 1%
Basophils 2%
Monocytes 1%
Lymphocytes Large 18% } 38%
Small 20% }

J. McI. (Continued).

On 21.6.54: Vesiculated papules appeared on both elbows. Buttocks became inflamed and several ruptured vesicles were present - and these rapidly became black in colour.
Throat once again became inflamed and painful.
That afternoon, the patient was examined by a Dermatologist who stated - "Multiform lesions present on elbows and buttocks. These lesions have necrotic centres. I do not think that they are lesions of Bacterial Endocarditis, but are more in keeping with the skin manifestations of rheumatic fever. I suggest examination of blood for L.E. cells.
Antihistamine treatment would be of benefit in this case."

By this date, patient's general condition had begun to deteriorate steadily.
Cardiac enlargement became obvious clinically - A.B. $4\frac{1}{2}$" from mid-sternal line in 6th L. space. Heart sounds were of poor quality - with a systolic murmur at apex.
Temperature remained elevated - 104° F. at one point.
Cervical glands palpable - both sides of neck.
By evening on 21.6.54, patient complained of pain in epigastric region. She was found to be tender across epigastrium, and especially in L. hypochondrium.
The spleen was not palpable, but there was marked guarding over the splenic region.
Abdomen became distended - with marked flatus present, and percussion note was hyper-resonant.
Examination of central nervous system revealed no nuchal rigidity, or any other abnormality.
On 22.6.54, the patient developed a pericardial friction rub, and signs suggestive of a pericardial effusion appeared. A pericardial "tap" was performed, but no fluid was obtained.
Ankles then became oedematous. Respirations became very distressed. Despite all measures, patient became comatose and died on 23.6.54.

Summary of Treatment:-

On admission, treatment with salicylates was commenced - 20 grains Sodium Salicylate were administered five times daily.

Penicillin 500,000 units (Crystalline) were given every four hours for one week.

On 18.6.54 Aureomycin was commenced, 500 mg. initially, and 250 mg. every six hours thereafter.

On /

J. McI. (Continued).

On 22.6.54 Sodium salicylate was replaced with Disprin 20 grains every six hours, as patient was nauseated. (Plasma salicylates at this point were 38.4 mg.%).

On 22.6.54, Digoxin therapy was also commenced, 0.25 mg. every six hours.

Patient was finally nursed in an oxygen tent. However, she died at 2.40 a.m. on 23.6.54.

This child's illness was long-continued, and not typical of acute rheumatic fever. This made one consider the possibility of Collagen Disease. However, lupus erythematosis cells were not found in the peripheral blood.

Bacterial Endocarditis was also considered in the differential diagnosis, but it was not until 28.6.54, (after further isolation) that a report was received (on blood removed on 22.6.54) that the specimen had grown colonies of streptococcus viridans.

Blood chemistry was normal throughout the patient's illness.

On 28.7.54, a guinea-pig culture of gastric washings was reported to be negative.

Post-Mortem Report:-

Histological examination of pleura, pericardium, spleen and kidneys, showed lesions consistent with a collagen disease of the Lupus Erythematosus type, but not sufficient to clinch the diagnosis, in the absence of cardiac lesions.

The heart at postmortem was free from any lesion, but the myocardium was pale.

APPENDICES A - E.

APPENDIX A.

TABLE I.

Average Rainfall per month: Average days of Fog and Frost per month: As recorded at Springburn and Paisley. Number of cases per month of Acute Rheumatism.

Year	Av. Rainfall in mm.	Days of Ground Frost.	Days of Fog	No. of Cases
1950				
Jan.	84	14	1	11
Feb.	116.5	15	2	5
Mar.	70	8	-	4
Apr.	79.5	13	-	2
May	31.5	1	-	4
June	51.5	-	-	3
July	139	-	-	4
Aug.	128	-	-	4
Sept.	123	-	-	3
Oct.	91.5	5	1	1
Nov.	78	16	2	1
Dec.	39.5	25	2	5
	Total no. of cases for 1950 = 47.			
1951	(Wettest year since 1921).			
Jan.	138	17	2	13
Feb.	74	17	1	8
Mar.	76	18	-	4
Apr.	63.5	16	-	-
May	47	9	-	1
June	62	1	-	-
July	90	-	-	-
Aug.	121.5	-	-	-
Sept.	83	-	-	2
Oct.	24.5	5	1	5
Nov.	164	5	1	5
Dec.	163	13	1	6
	Total no. of cases for 1951 = 44.			

APPENDIX A.

TABLE I. (Contd.)

Year	Av. Rainfall in mm.	Days of Ground Frost	Days of Fog	No. of Cases
1952				
Jan.	126.5	24	2	4
Feb.	39	18	1	7
Mar.	68	9	-	3
Apr.	55	4	-	4
May	56.5	1	-	1
June	74.5	-	-	1
July	130.6	-	-	5
Aug.	92	-	-	3
Sept.	78.5	3	-	4
Oct.	115	7	2	9
Nov.	55	21	2	9
Dec.	101	18	2	9
	Total no. of cases for 1952 = 59			
1953				
Jan.	39	13	3	6
Feb.	38	15	-	7
Mar.	25	6	3	13
Apr.	46	7	-	7
May	59	2	-	6
June	52	-	-	8
July	130.5	-	-	8
Aug.	91	-	-	4
Sept.	104.5	-	-	6
Oct.	67	5	-	4
Nov.	165	4	-	4
Dec.	129	8	2	8
	Total no. of cases for 1953 = 81			
1954				
Jan.	141	14	-	4
Feb.	103.5	13	2	4
Mar.	65.5	8	-	2
Apr.	43.5	12	-	5
May	89	-	-	6
June	86	-	-	6
July	77.5	-	-	7
Aug.	151	-	-	1
Sept.	133	3	-	1
Oct.	246.5	6	1	5
Nov.	173	12	1	1
Dec.	137	9	-	8
	Total no. of cases for 1954 = 50			

APPENDIX A.

TABLE I. (Contd.)

Year	Av. Rainfall in mm.	Days of Ground Frost	Days of Fog	No. of Cases
1955				
Jan.	80.5	19	-	4
Feb.	69.5	25	1	3
Mar.	45	27	2	4
April	46.5	10	-	3
May	87.5	7	-	2
June	57	1	-	3
July	31.5	-	-	6
Aug.	26.5	-	-	-
Sept.	97	-	-	4
Oct.	73.5	11	1	5
Nov.	50	15	-	5
Dec.	166.5	13	1	7
	Total no. of cases for 1955 = 46			
1956				
Jan.	71	20	2	4
Feb.	33	21	1	2
Mar.	61	10	1	7
Apr.	30.4	16	-	5
May	58.5	4	-	3
June	73.6	-	-	3
July	132	-	-	1
Aug.	124.5	1	-	4
Sept.	127	-	-	-
Oct.	78.7	5	1	5
Nov.	43.2	11	1	3
Dec.	122	6	-	2
	Total no. of cases for 1956 = 39			
1957				
Jan.	155	13	-	3
Feb.	81	16	1	1
Mar.	113.5	1	-	2
Apr.	51.4	-	-	1
May	72.4	1	-	4
June	58.6	-	-	2
July	89	-	-	6
Aug.	97.5	-	-	1
Sept.	72	1	-	3
Oct.	108.5	2	-	-
Nov.	40.5	10	3	3
Dec.	144	5	3	2
	Total no. of cases for 1957 = 28			

APPENDIX A.

TABLE I. (Contd.)

Year	Av. Rainfall in mm.	Days of Ground Frost	Days of Fog	No. of Cases
1958				
Jan.	120.8	18	7	2
Feb.	72.6	16	5	-
Mar.	26.9	20	1	3
Apr.	31.2	10	1	-
May	86	6	-	1
June	78.7	-	1	2
July	136	-	-	1
Aug.	134	-	1	2
Sept.	97.4	-	2	2
Oct.	81	3	2	2
Nov.	48	13	8	2
Dec.	117.4	16	7	4
	Total no. of cases for 1958 = 21			
1959				
Jan.	38.3	26	12	1
Feb.	42.4	11	10	1
Mar.	45.7	7	3	5
Apr.	65.5	8	1	3
May	27.4	3	-	-
June	76	-	-	2
July	123.2	-	1	1
Aug.	15.8	-	-	5
Sept.	30.7	-	4	-
Oct.	127.3	2	6	-
Nov.	133.7	10	3	2
Dec.	177.5	9	5	2
	Total no. of cases for 1959 = 22			

APPENDIX A.

TABLE II

POPULATION AND ACREAGE OF THE ELECTORAL WARDS IN GLASGOW AREA

No.	WARD	POPULATION		RESIDENTIAL AREA	
		1951	1958	1951	1958
				(acres)	
1	Shettleston and Tollcross	42,609	46,257	450.68	531.62
2	Parkhead	21,578	18,946	252.66	252.66
3	Dalmarnock	40,621	34,840	134.95	134.95
4	Calton	26,273	22,143	82.37	82.37
5	Mile-end	40,171	34,641	132.57	132.57
6	Dennistoun	26,944	23,911	180.06	180.06
7	Provan	24,235	46,565	333.02	777.38
8	Cowlairs	27,998	24,031	120.65	120.65
9	Springburn	35,659	38,729	236.28	480.97
10	Townhead	35,005	29,483	126.03	126.03
11	Exchange	20,089	16,244	69.18	69.18
12	Anderston	31,902	25,325	103.12	103.12
13	Park	23,758	18,710	166.04	166.04
14	Cowcaddens	27,229	22,067	80.98	80.98
15	Woodside	26,946	21,830	75.47	75.47
16	Ruchill	45,929	49,211	329.90	505.41
17	North Kelvin	25,817	23,102	121.24	121.24
18	Maryhill	25,515	26,467	199.01	241.04
19	Kelvinside	21,032	19,929	407.07	423.07
20	Partick East	23,376	20,013	193.08	193.08
21	Partick West	26,814	24,475	194.16	194.16
22	Whiteinch	23,241	21,438	317.75	317.75
23	Yoker	30,198	27,688	608.97	608.97
24	Knightswood	17,530	42,547	372.63	661.74
25	Hutchesontown	30,965	26,462	86.39	86.39
26	Gorbals	36,648	26,989	112.61	112.61
27	Kingston	26,895	22,207	80.87	80.87
28	Kinning Park	28,124	24,978	135.83	135.83
29	Govan	35,152	30,717	171.30	171.30
30	Fairfield	25,132	22,312	167.67	167.67
31	Craigton	40,448	38,284	908.20	908.20
32	Pollokshields	38,956	42,719	853.83	869.93
33	Camphill	22,529	20,469	257.80	257.80
34	Pollokshaws	39,717	51,471	556.85	678.78
35	Govanhill	26,377	24,142	154.58	154.58
36	Langside	25,578	26,943	372.12	444.26
37	Cathcart	21,787	43,215	556.94	1008.13
	TOTAL:	1,089,767	1,078,400	9702.86	11656.86.

Average population at 1951 Census - 112/Acre
Average population at 1958 Census - 92/Acre

APPENDIX A.

TABLE III.

Population per acre: Number and rate per 1,000 of population of cases of Acute Rheumatism for periods 1950-54 and 1955-59, with resulting change in population and change in incidence rate per 1,000 of the population of the Electoral wards in the Glasgow area.

	1950-54			1955-59			A.	B.
	Population/Acre	No. cases / ward	Rate cases/1,000	Population/Acre	No. cases / ward	Rate cases/1,000	Drop P/acre	Drop R/1,000
1. Shettleston & Tollcross	94	12	.282	87	5	.108	7	.174
2. Parkhead	85	2	.093	75	2	.106	10	-.013
3. Dalmarnock	301	13	.320	258	2	.057	43	.263
4. Calton	320	17	.647	270	7	.316	50	.331
5. Mile-end	302	9	.224	261	4	.115	41	.109
6. Dennistoun	149	3	.111	133	6	.251	16	-.141
7. Provan	73	6	.248	60	8	.172	13	.076
8. Cowlairs	231	7	.250	198	1	.042	33	.208
9. Springburn	151	8	.224	81	1	.026	70	.198
10. Townhead	278	7	.200	234	1	.034	44	.166
11. Exchange	291	10	.498	235	1	.062	56	.436
12. Anderson	310	10	.313	246	5	.197	64	.116
13. Park	143	6	.253	113	1	.053	30	.200
14. Cowcaddens	336	14	.514	272	3	.136	64	.378
15. Woodside	355	14	.520	287	3	.137	68	.383
16. Ruchill	139	19	.414	97	4	.087	42	.333
17. Nr. Kelvin	213	4	.155	191	3	.130	22	.025
18. Maryhill	128	9	.353	110	3	.113	18	.240
19. Kelvinside	52	1	.048	47	1	.050	5	-.002

APPENDIX A.

TABLE III (Contd.).

	1950-54			1955-59			A.	B.
	Population/Acre.	No. cases / ward	Rate Cases/1,000	Population/Acre.	No. cases / ward	Rate Cases/1,000	Drop P/acre	Drop R/1,000
20. Partick East	121	7	.299	103	1	.050	18	.249
21. Partick West	138	7	.261	120	5	.204	18	.057
22. Whiteinch	73	11	.473	67	4	.187	6	.286
23. Yoker	50	17	.563	46	9	.325	4	.238
24. Knightswood	47	6	.342	63	10	.235	-16	.107
25. Hutchesontown	348	24	.775	319	5	.189	29	.586
26. Gorbals	324	10	.273	239	1	.037	85	.236
27. Kingston	332	25	.930	274	3	.135	58	.795
28. Kinning Park	207	4	.142	183	2	.080	24	.062
29. Govan	206	7	.199	180	4	.130	26	.069
30. Fairfield	150	2	.080	133	2	.090	17	-.010
31. Craigton	45	3	.074	42	1	.021	3	.048
32. Pollokshields	47	5	.126	49	2	.047	-2	.079
33. Camphill	87	0	.000	79	1	.049	8	-.049
34. Pollokshaws	70	8	.201	76	2	.039	-6	.162
35. Govanhill	170	8	.303	156	3	.124	14	.179
36. Langside	69	1	.039	59	1	.038	10	.001
37. Cathcart	39	4	.184	43	2	.046	-4	.138

For purposes of representation:-

Increases in Population per Acre are shown as minus quantities.
Increases in Incidence Rate of Cases/1,000 of Population are shown as minus quantities.

The correlation co-efficient of the drop in population and drop of incidence rate of cases over the two periods 1950-54 and 1955-59 was calculated from columns A. and B.

APPENDIX B.

Copy of Proforma issued to parents of all cases of rheumatic fever who had been admitted to Oakbank Hospital

Dear .....

A study of Rheumatic Fever is being carried out, with the hope of finding a way to prevent this disease occurring, or if this is not possible, at least to cut down the number of cases, and prevent any second or further attacks.

As your ..... was in Oakbank Hospital from ..... to ..... with Rheumatic Fever, I should be glad if you would answer the following questions.

Your co-operation in this matter would be greatly appreciated, and I would like to add that all information will be treated with the utmost confidence. No names will be mentioned in the Report, and only Doctors will see the information given.

1. Is ..... well at present? .....
2. Has he/she had any further attacks of rheumatic fever? .....
3. Is he/she subject to sore throats? .....
4. What is his/her occupation at present .....

During the time of .....'s illness:-

5. What was your occupation? .....
6. Total wages coming into the household per week? .....
7. Number of rooms in house? .....
8. Was house damp? .....
9. Number of persons altogether in the house? .....
10. Number of children - up to the age of 21 years? .....
11. Any chronic illness in house? .....
12. Was toilet inside or outside? .....

A stamped, addressed envelope is enclosed for your reply.

I am,

Yours faithfully,

M.B., Ch.B., D.(Obst.), R.C.O.G.

APPENDIX C.

Record of number of injections given at the Follow-up Clinic.

	Name	Attendances	Total.
1.	A.G.	11111111111111111111111111111 11111111111111111111111111111	59
2.	G.A.	11111111111111111	18
3.	I.K.	111111111111111111	19
4.	P.C.	111111	6
5.	S.McC.	11111111111111	14
6.	J.S.	111111111111111111111	21
7.	J.McK.	1111111	7
8.	J.M.H.	11111111111111111111111111111111 1111111111111111111	54
9.	E.M.	111	3
10.	H.McQ.	11111111	8
11.	K.G.	1111111111111111111111111111	30
12.	C.J.	11111111111111111111111111111111 1111111111111111111	54
13.	J.McG.	11111111111111111	18
14.	H.G.	1111111111111111111111111111111111	35
15.	J.B.	111111111111111111111111 111111111111111111111111	51
16.	J.M.	11	2
17.	A.G.	111111	6
18.	J.J.	1111111	7
19.	R.S.	1111111111111111111111111111111	32
20.	S.W.	11111111111111	14
21.	D.McC.	1111111	7
22.	M.F.	1111	4
23.	T.D.	1111111111111111	16

Total number of injections given = 485.

APPENDIX D.

Extract from the Statement prepared by the Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis appointed by the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association (1960).
(As published in Circulation Vol. 21, January, 1960. p. 151).

DIAGNOSIS OF STREPTOCOCCAL INFECTIONS.

The accurate recognition of individual streptococcal infections, their adequate treatment, and the control of epidemics in the community presently offer the first practical means of preventing initial attacks of rheumatic fever.

About half of the streptococcal infections which occur are likely to escape detection because they are asymptomatic or atypical. The other half can often be suspected by their clinical manifestations. However, in the absence of a scarlatinal rash, it is impossible to differentiate streptococcal infections with certainty on clinical grounds alone. Therefore, bacteriological support (by throat culture) of the clinical impression is highly desirable. The following section on diagnosis has been included in order to assist physicians in making a correct diagnosis and assuring adequate treatment.

SYMPTOMS	SIGNS
Sore throat - sudden onset, pain on swallowing.	Red throat
Headache - common.	Exudate - usually present.
Fever - variable, but generally from 101° to 104° F.	Lymphadenopathy - swollen, tender lymph nodes at angle of jaw.
Abdominal pain - more common in children than in adults.	Rash - scarlatiniform, when present, usually diagnostic of a streptococcal infection.
Nausea and vomiting - common, especially in children.	Acute otitis media, Acute sinusitis } frequently due to the streptococcus.

In the absence of the above symptoms and signs, occurrence of any of the following symptoms is usually not associated with a streptococcal infection: simple coryza, hoarseness, cough.

LABORATORY FINDINGS

Throat culture - hemolytic streptococci are almost invariably recovered on culture during acute streptococcal infections. A single well-done culture is usually sufficient, although hemolytic streptococci which are occasionally missed on initial culture may be detected in subsequent cultures.

White blood count - generally over 12,000.

TREATMENT OF STREPTOCOCCAL INFECTIONS

Treatment should be started as soon as possible but the 18 to 24 hour delay entailed in making a diagnosis by awaiting the results of a throat culture does not reduce the efficacy of antibiotic treatment in preventing the occurrence of rheumatic fever.

Penicillin is the drug of choice. Effective blood levels should be maintained for a period of 10 days to prevent rheumatic fever by eradicating the streptococci from the throat. Even with this prolonged treatment, streptococci may sometimes fail to be eradicated, especially when oral therapy is used. If possible, a follow-up culture two days after discontinuing treatment is desirable to ascertain the absence of haemolytic streptococci.

Penicillin may be administered by either intramuscular or oral route. Intramuscular administration is recommended as the method of choice since it ensures adequate blood levels for a sufficient length of time. Oral therapy, by contrast, is dependent upon the co-operation of the patient.

RECOMMENDED TREATMENT SCHEDULES

INTRAMUSCULAR PENICILLIN

Benzathine penicillin G.

Children - one intramuscular injection of 600,000 to 900,000 units. (The larger dose is probably preferable for children over /

ORAL PENICILLIN

Children and adults - 200,000 to 250,000 units three times a day for a full 10 days. Therapy must be continued for the entire 10 days even though the temperature /

over 10 years of age.)

Adults - one intramuscular injection of 900,000 to 1,200,000 units.

or

Procaine penicillin with aluminium monostearate in oil

Children - one intramuscular injection of 300,000 units, every third day for 3 doses.

Adults - one intramuscular injection of 600,000 units, every third day, for 3 doses.

ature returns to normal and the patient is asymptomatic.

OTHER ANTIBIOTICS

Broad-spectrum antibiotics, such as erythromycin and the tetracyclines are useful in patients who are sensitive to penicillin. If given for 10 days, these antibiotics are possibly as effective as oral penicillin in the treatment of streptococcal infections, but are subject to the same uncertainties of administration by the oral route.

CAUTION

The sulfonamide drugs should not be used for the treatment of streptococcal infections. In an established infection, they will not eradicate the streptococcus and therefore will not prevent rheumatic fever. However, the sulfonamides are effective in preventing reinfection and recurrences when administered as continuous prophylaxis to rheumatic subjects. (Please see "Specific Prophylactic Methods", Appendix E. of this work).

Antibiotic troches and lozenges are also inadequate for the treatment of streptococcal infections because they do not eliminate the streptococcus.

PROTECTION OF RHEUMATIC FEVER PATIENTS IN HOSPITAL WARDS

Patients with rheumatic fever or rheumatic heart disease are often exposed to increased hazards in hospital wards as the result of contact with streptococcal carriers or patients with active streptococcal infections.

Patients with inactive rheumatic fever or rheumatic heart disease should be placed on continuous streptococcal prophylaxis on admission to the hospital or as soon thereafter as the diagnosis is established. (See Appendix E. of this work, "Continuous Prophylaxis"). If oral penicillin is used, a dosage of 200,000 to 250,000 units twice a day is preferable.

Patients with acute rheumatic fever should be treated first with therapeutic doses of penicillin to eradicate streptococci.

TREATMENT OF STREPTOCOCCAL INFECTIONS IN RHEUMATIC INDIVIDUALS

When streptococcal infections occur despite prophylactic regimen, or occur in a rheumatic subject who is not receiving continuous prophylaxis, they should be treated promptly and vigorously. At least the maximal dose regimen recommended for treatment of streptococcal infections in the general population (Please see Appendix E. of this work, "General Recommendations) should be employed. Despite optimal therapy, it is sometimes not possible to prevent rheumatic recurrences once streptococcal infections occur in the rheumatic subject.

APPENDIX E.

Extract from the Statement prepared by the Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis appointed by the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association (1960).
(As published in Circulation Vol. 21, January, 1960. p.151)

CONTINUOUS PROPHYLAXIS

Many streptococcal infections occur without producing clinical manifestations. For this reason, prevention of recurrent rheumatic fever must depend on continuous prophylaxis rather than solely on recognition and treatment of acute attacks of streptococcal disease.

GENERAL RECOMMENDATIONS

Who should be given prophylaxis?

In general, all patients who have a well documented history of rheumatic fever or chorea, or who show definite evidence of rheumatic heart disease, should be given continuous prophylaxis.

Although recurrent attacks of rheumatic fever occur at any age, the risk of recurrence decreases with the passage of years. Some physicians may wish to make exceptions to instituting or maintaining prophylaxis in certain of their adult patients, particularly those without heart disease who have had no rheumatic attacks for many years.

How long should prophylaxis be continued?

The risk of acquiring a streptococcal infection and the possi-

bility /

bility of rheumatic fever recurrences continue throughout life. It is, therefore, suggested that the safest general procedure is to continue prophylaxis indefinitely, particularly if rheumatic heart disease is present.

When should prophylactic treatment be initiated?

Active rheumatic fever: Prophylaxis should be initiated as soon as the diagnosis of rheumatic fever is made, or any time thereafter when the patient is first seen. The streptococcus should be eradicated with penicillin (Please see Appendix D. of this work "Recommended Treatment Schedules"), and following this the prophylactic regimen should be instituted.

Inactive rheumatic fever: In inactive rheumatic fever, prophylaxis should be instituted when the patient is first seen.

Should prophylaxis be continued during the summer?

Yes, continuously. Streptococcal infections can occur at any season, although they are more prevalent in the winter.

SPECIFIC PROPHYLACTIC METHODS

Several effective methods of continuous prophylaxis are available, and the physician must decide which is most suitable for an individual patient.

Oral vs. intramuscular route

Oral medication depends on patient co-operation. Most failures occur in patients who fail to ingest the drug regularly. Patients should /

should receive careful and repeated instructions on this point from the physician. Patients who have proved unreliable in taking oral medication should receive long-acting depot penicillin, given intramuscularly once a month.

Penicillin vs. sulfonamides

Sulfadiazine has the advantage of being easy to administer, inexpensive, and effective. Although resistant streptococci have appeared during mass prophylaxis in the armed forces, this is rare in civilian populations.

Penicillin rarely produces serious toxic reactions. It has the further advantage of being bactericidal for group A streptococci, and strains of group A streptococci resistant to penicillin have not been encountered.

BENZATHINE PENICILLIN G - INTRAMUSCULAR

Dosage - 1,200,000 units once a month.

Toxic reactions - Urticaria and angioneurotic edema.

Reactions similar to serum sickness include fever and joint pains and may be mistaken for rheumatic fever.

Some discomfort due to local irritation at the injection site is usual.

A careful history of allergic reactions to penicillin should be obtained. Although many individuals who have had reactions to penicillin may subsequently be able to tolerate the drug, it is safer /

safer not to use penicillin if the reaction has been severe and particularly if angioneurotic edema has occurred.

SULFADIAZINE - ORAL

Dosage - from 0.5 to 1.0 Gm. once a day. The smaller dose is to be used in children under 60 pounds.

Toxic reactions are infrequent and usually minor. In any patient being given sulfonamides, consider all rashes and sore throats as possible toxic reactions, especially if they occur in the first eight weeks. In patients on this prophylactic regimen, it is hazardous to treat toxic reactions or intercurrent infections with sulfonamides.

The chief toxic reactions are:-

Skin eruptions

Morbilliform - continue drug with caution. Urticaria or scarlatiniform rash associated with sore throat or fever - discontinue drug.

Leukopenia

Discontinue drug if white blood count falls below 4,000 and polynuclear neutrophils fall below 35% because of possible agranulocytosis which is often associated with sore throat and a rash. Because of these reactions, weekly white blood counts are advisable for the first two months of prophylaxis. The occurrence of agranulocytosis after eight weeks of continuous prophylaxis with sulfonamides is extremely rare.

PENICILLIN - ORAL

Dosage - 200,000 to 250,000 units once or twice daily. Twice daily is probably more effective.

Toxic reactions - except for local irritation, reactions are similar to those with intramuscular penicillin, but occur less frequently and tend to be less severe. A careful history concerning penicillin allergy should, however, be obtained.

PROPHYLAXIS AGAINST BACTERIAL ENDOCARDITIS

In individuals with rheumatic or congenital heart disease, bacteria may lodge on the heart valves or other parts of the endocardium, producing bacterial endocarditis.

Although transient bacteremia is a rather common phenomenon and may occur after the mere chewing of hard candy or brushing of teeth, it is likely that the number of organisms entering the blood stream is usually relatively low under such circumstances. Transient bacteremia is especially apt to occur after dental extraction or other procedures in which the gums are manipulated, after removal of tonsils and adenoids, and as a consequence of genitourinary operative procedures such as catherization or cystoscopy. It is also probable that delivery is associated with transient bacteremia.

Since patients with rheumatic or congenital heart disease are especially vulnerable to bacterial endocarditis, it is advisable to protect such patients with antimicrobial agents when they are to be subjected /

subjected to any of the above procedures. Some cardiologists are of the opinion that these patients should also receive prophylaxis against bacterial endocarditis when subjected to any surgery involving general anesthesia, or to diagnostic procedures such as cardiac catheterization.

GENERAL RECOMMENDATIONS FOR DENTAL MANIPULATIONS AND ORAL SURGERY

Penicillin is the drug of choice for administration to patients with rheumatic or congenital heart disease undergoing dental manipulations or surgical procedures in the oral cavity.

Although the exact dosage and duration of therapy are empirical, there is some evidence that for effective prophylaxis, reasonably high concentrations of penicillin must be present at the time of these procedures. The dosage regimens employed for long-term prophylaxis against group A streptococci in rheumatic susceptibles are inadequate for preventing bacterial endocarditis. To prevent organisms from lodging in the heart valves or to eradicate them promptly before the formation of a vegetation, high levels of penicillin in the blood over a period of several days after the given procedure are recommended.

Extraction of teeth from badly infected gums is apt to result in more intense bacteremia than when infection is minimal or absent. If prophylaxis is instituted 24 to 48 hours prior to the operative procedure, it may decrease the intensity of bacteremia. Since occult /

occult infection may be present, some workers recommend that treatment always be started several days prior to the operative procedure. On the other hand, some workers have been concerned that pretreatment might lead to the emergence of antibiotic-resistant microorganisms. These would constitute a very difficult therapeutic problem if they implanted in the valves. It has, therefore, been argued that prophylaxis should not be instituted until immediately before the operative procedure.

In view of the lack of definite evidence to support categorically either method, the physician must evaluate the likelihood of infection and decide whether a period of preliminary treatment prior to the operative procedure is indicated. It is emphasised that there is no disagreement regarding the advisability of using antimicrobial agents immediately before and subsequent to the operative procedure.

SUGGESTED TREATMENT SCHEDULES

Two regimens are presented. In one, the intramuscular route is used throughout. In the other, oral therapy is combined with a single injection of penicillin one hour prior to the surgical procedure. Because of practical considerations, some physicians and dentists rely on oral penicillin alone when the full cooperation of the patient is assured. It should be emphasized that these regimens are only empirical guides.

INTRAMUSCULAR REGIMEN

STEP I* Prophylaxis extended to two day period before surgery:

600,000 /

600,000 units of procaine penicillin I.M. on each day.

STEP II. Day of surgery:

600,000 units procaine penicillin I.M. supplemented by 600,000 units of crystalline penicillin I.M., one hour before surgical procedure.

STEP III For two days after surgery:

600,000 units procaine penicillin I.M. each day.

INTRAMUSCULAR PLUS ORAL REGIMEN

STEP I*. Prophylaxis extended to two day period before surgery:

500,000 units of buffered penicillin G or phenoxymethyl penicillin (penicillin V), by mouth four times a day.

STEP II. Day of surgery:

500,000 units of buffered penicillin G or phenoxymethyl penicillin (penicillin V), by mouth four times a day, supplemented by 600,000 units crystalline penicillin I.M. one hour before surgical procedure.

STEP III. For two days after surgery:

500,000 units of buffered penicillin G or phenoxymethyl penicillin (penicillin V), by mouth four times a day.

CONTRAINDICATIONS TO ABOVE REGIMENS.

Sensitivity to penicillin. All patients should be carefully questioned /

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* Step I. may be omitted if desired.

questioned for previous history of penicillin sensitivity. In patients with such a history, even if equivocal, penicillin should not be given. Under such circumstances, erythromycin should be employed in a dose of 250 mg., by mouth four times per day for adults and older children. For small children, a dose of 20 mg. per pound per day, divided into three or four evenly spaced doses, may be used. No dosage should exceed a total of 1 Gm. per day.

FOR OTHER SURGICAL PROCEDURES AND CHILDBIRTH

For childbirth and procedures such as catheterization of the bladder, surgery of the genitourinary tract, or surgery of the lower intestinal tract, the following regimen should be employed:-

In addition to either of the penicillin regimens outlined above, streptomycin should be administered in full dosage for five days, with treatment beginning, when possible, two days prior to the surgical procedure. In patients who are sensitive to penicillin, chloramphenicol may be substituted.

REFERENCES

REFERENCES

American Heart Association; Committees Appointed by the Council on Rheumatic Fever and Congenital Heart Disease. 1953.

"Prevention of Rheumatic Fever". Circulation. 7 : 316.

Aschoff, Ludwig. 1904.

Quoted from - "Heart Disease". 3rd Edition, 1947. p. 330. Ed. Paul D. White. The Macmillan Company, New York.

Ash, R. 1948.

"The First Ten Years of Rheumatic Infection in Childhood". American Heart Journal. 36 : 89.

Baillou, Guillaume. 1762.

"Liber de Rheumatismo. Opera Medica Omnia". De Tournes, Geneva. p. 314.

Bland, E.F., Jones, T.D. 1938.

"Fatal Rheumatic Fever". Arch. Int. Med. 61 : 161.

Bland, E.F., Jones, T.D. 1951.

"Rheumatic Fever and Rheumatic Heart Disease : A Twenty-Year Report of 1,000 Patients Followed Since Childhood". Circulation. 4 : 836.

Bouillaud, Jean. 1836.

"Nouvelle Researches". Paris.
Quoted from - Bywaters, E.G.L. 1950.
"The Relation Between Heart and Joint Disease".
Br. Heart Jour. 12 : 101.

Burke, P.J. 1947.

"Penicillin Prophylaxis in Acute Rheumatism".
Lancet. 1 : 255.

Bywaters /

Bywaters, E.G.L. 1956.

"Treatment of Rheumatic Fever". Symposium on Rheumatic Fever. Circulation. 14 : 1138.

Bywaters, E.G.L., Thomas, G.T. 1958.

"Prevention of Recurrences of Rheumatic Fever". B.M.J. 2 : 350.

Cabot, R.C. 1926.

"Facts on the Heart". W.B. Saunders, Philadelphia.

Chancey, R.L. et al. 1955.

"Studies of Streptococcal Prophylaxis: Comparison of Oral Penicillin and Benzathine Penicillin". Amer. Jour. of Med. Sci. 229 : 165.

Coburn, A.F. 1931.

"Infection in the Rheumatic State". Williams and Wilkins, Baltimore.

Coburn, A.F., and Moore, L.V. 1939.

"The Prophylactic Use of Sulphonilamide in Streptococcal Respiratory Infections, with Especial Reference to Rheumatic Fever". Jour. Clin. Invest. 18 : 147.

Coombs, C.F. 1924.

"Rheumatic Heart Disease". J. Wright and Sons : Bristol. p. 203.

Cope, S., et al. 1960.

"Prophylactic Use of Oral Penicillin in Rheumatic Fever, Chorea and Carditis". B.M.J. 1 : 913.

De Graff, A.C., Lingg, C. 1935.

"Course of Rheumatic Heart Disease in Adults : Influence of Auricular Fibrillation on the Course of Rheumatic Heart Disease". Amer. Ht. Jour. 10 : 459.

Diehl /

Diehl, A.M. et al., 1954.

"Long-Acting Repository Penicillin in the Prophylaxis of Recurrent Rheumatic Fever".
J.A.M.A. 155 : 1466.

Diehl, A.M. et al. 1958.

"Epidemiology of Rheumatic Fever". Am. J. Cardiology. 1 : 423.

Diehl, A.M., Hamilton, T.R. et al. 1956.

"Prevention of Recurrent Rheumatic Fever : Use of Repository Benzathine Penicillin G." South. Med. Jour. 49 : 250.

Ellias, W. et al. 1951.

"N.N'dibenzylethylenediamine Penicillin - a New Repository Form of Penicillin". Antib. and Chem. 1 : 491.

Ernstene, C.A. 1930.

"Erythrocyte Sedimentation, Plasma Fibrinogen, and Leucocytosis, as Indices of Rheumatic Infection".
Amer. Jour. Med. Sci. 180 : 12.

Feinstein, A.R., Spagnuolo, M. 1960.

"Mimetic Features of Rheumatic Fever Recurrences".
New Eng. Jour. Med. 533 : 262.

Findlay, Leanord. 1931.

"The Rheumatic Infection in Childhood".
Ed. Arnold and Co. London. p. 42 and p. 47.

Five Year Report of a Co-operative Clinical Trial of A.C.T.H., Cortisone and Aspirin. 1960.

Joint Report of the Rheumatic Fever Working Party of the Medical Research Council of Great Britain and Sub-Committee of Investigators of the American Council on Rheumatic Fever and Congenital Heart Association.
B.M.J. 2 : 1033.

Further Report of the Rheumatic Fever Committee of the Royal College of Physicians, London. 1957.
Harrison and Sons, Ltd. London.

Hitchins /

Hitchins, R.A.N. 1958.

"Recurrent Attacks of Rheumatic Fever in School Children".
Ann. Rheum. Dis. 17 : 293.

Holt, K.S., Illingworth, R.S., et al. 1954.

"Cortisone and Salicylates in Rheumatic Fever".
Lancet. 2 : 1144.

(Interim) Report of the Rheumatic Fever Committee of the Royal College of Physicians, London. 1947.

Harrison and Sons, Ltd., London.

Joint Report by the Rheumatic Fever Working Party of the Medical Research Council of Great Britain, and the Sub-Committee of Principal Investigators of the American Council on Rheumatic Fever and Congenital Heart Disease, American Heart Association. 1955.

Circulation. 11 : 343. Also B.M.J. 1 : 555.

Kaplan, S. 1958.

"Oral Phenoxymethyl Penicillin Therapy in the Prophylaxis of Recurrent Rheumatic Fever.
Am. Jour. Dis. of Children. 96 : 288.

Keil, H. 1936.

"Remarks on a Disease of the Heart Following Acute Rheumatism: Illustrated by Dissection".
"Bull. Instit. Histor. Med."
John Hopkins Bull. of Med. Hist. 4 : 789.

Kohn, K.H., et al. 1953.

"Prophylaxis of Recurrences of Rheumatic Fever, with Penicillin Given Orally". J.A.M.A. 151 : 347.

Leading Article, British Medical Journal. 1956.

"Prevention of Rheumatic Fever. B.M.J. 1 : 31.

Leading Article, British Medical Journal. 1959.

"Preventing Recurrences of Rheumatic Fever". B.M.J. 1 : 351.

Leading Article, British Medical Journal, 1960.

"Rheumatic Heart Disease in Children". B.M.J. 2 : 1073.

Leff /

Leff, S. 1956.

"Modern Trends in Acute Rheumatism".
Ann. Rheum. Dis. 15 : 33.

Lim, W.N., Wilson, M.S. 1960.

"Comparison of the Recurrence Rate of Rheumatic Carditis Among Children Receiving Penicillin by Mouth Prophylactically, or on Indication".
New Eng. Jour. of Med. 262 : 321.

Lunther, E.G., Franklin, D.Y. 1959.

"Rheumatic Fever Prophylaxis with Benzathine Penicillin G in Wyoming".
Rocky Mountain Med. Jour. Jan. : 37.

Magarey, F.R. 1951.

"The Pathogenesis of Mitral Stenosis".
B.M.J. 1 : 856.

Markowitz, M.D. 1957.

"Observations of an Epidemic of Streptococcal Infections and Recurrences of Rheumatic Fever Among Children Treated with Oral Penicillin".
Paediatrics. 20 : 257.

Markowitz, M.D., et al. 1957.

"A Comparison of Oral and Intramuscular Benzathine Penicillin G for the Prevention of Streptococcal Infections and Recurrences of Rheumatic Fever".
Paediatrics. 19 : 201.

Massell, B.F., Sturgis, B.P. et al. 1951.

"Prevention of Rheumatic Fever by Prompt Penicillin Therapy of Haemolytic Streptococcal Respiratory Infections".
J.A.M.A. 146 : 1469.

Massell, B.F. 1957.

"Prevention of Rheumatic Heart Disease".
The Heart Center Bulletin of St. Francis Hosp. and Sanatorium.
14 : 1.

Miller /

Miller, J.M., 1959.

"Prophylaxis of Rheumatic Fever and Rheumatic Heart Disease".
New Eng. Jour. Med. 260 : 220.

Milton, Saslow, S. 1955.

"Rheumatic Fever - Diagnosis, Prophylaxis and Therapy".
Jour. Am. Med. Assoc. 159 : 653.

Mortimer, E.A., et al. 1958.

"Effect of Penicillin on Acute Rheumatic Fever and Valvular Heart Disease.
Am. Jour. Dis. of Children. 96 : 482.

Mou, T.W. et al. 1960.

"Prevention of Recurrent Rheumatic Fever in Children and Adults with Oral and Repository Penicillin".
Am. Jour. of Med. Sci. 239 : 403.

Parkinson, J. 1945.

"Rheumatic Fever and Rheumatic Heart Disease".
Lancet. 2 : 6378.

Parkinson, J., Hartley, R. 1946.

"Early Diagnosis of Rheumatic Valvular Disease in Recruits".
Brit. Heart Jour. 8 : 212.

Pitcairn, David. 1788.

Quoted from - Wells, Wm. 1812.
"On Rheumatism of the Heart".
Trans. Soc. Improv. Med. and Chir. Knowledge. 3 : 373.

Purdy, Ann. 1957.

"Rheumatic Fever".
"Current Therapy", p.45. Saunders, London.

Putnam, L.E., and Roberts, E.F. 1954.

"Concentrations of Penicillin Following Intramuscular Benzathine Penicillin G".
Antibiotics and Chemotherapy. 4 : 931.

Rantz, L.A., Randall, E., and Rantz, H.H. 1948.

"Anti-Streptolysin 'O' : A Study of This Antibody in Health and in Haemolytic Streptococcus Respiratory Disease in Man".
Am. J. Med. 5 : 3.

Reid, J., Sproul, D.H. 1957.

"Plasma Fibrinogen in Rheumatic Fever".
B.M.J. 1 : 1089.

Report of the Census (Scotland). 1951.

on "Occupations and Industries" (Introduction).
H.M. Stationery Office, London. 4 : xii.

Report of the Committee of the Executive Council of the American Heart Association on the Standards and Criteria for the Programs of Care of Rheumatic Fever and Congenital Heart Disease. 1955.

Modern Concepts of Cardiovascular Disease. 24 : 291.

Report by the Royal Commission, 1917.

quoted from -
"Third Statistical Account of Scotland (Glasgow). 1958.
Cunnison J., Gillfillan, J.B.S. 5 : 465. Collins, Glasgow.

Scott, G.E.M. 1943.

"Rheumatic Infection in Childhood: Survey from the Children's Hospital, Melbourne".
Med. J. Austr. 2 : 309.

Scottish Housing Advisory Committee's Recommendation. 1944.

Quoted from -
Third Statistical Account of Scotland (Glasgow). 1958.
Cunnison, J., Gillfillan, J.B.S. 5 : 467. Collins, Glasgow.

Seal, J.R. 1955.

"Oral Penicillin Prophylaxis of Streptococcal Infection".
Am. Jour. Public Health. 45 : 662.

Sibson /

Sibson, F. 1877.

Reynold's System of Medicine. McMillan, London. 4 : 526.

Statement of the American Heart Association's Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis, Appointed by the Council on Rheumatic Fever and Congenital Heart Disease. 1960.

"Prevention of Rheumatic Fever and Bacterial Endocarditis Through Control of Streptococcal Infections".
Circulation. 21 : 151.

Still, G.F. 1921.

"Social Conditions in Acute Rheumatism in London and Glasgow".
M.R.C. Report. No. 114.

Stollerman, G.H. 1954.

"Antibiotics in Prevention of Rheumatic Fever"
American Journal of Medicine. 17 : 757.

Stollerman, G.H. 1954(a).

"The Prevention of Rheumatic Fever"
American Practitioner and Digest of Treatment. 5 : 589.
Quoted from -
Stollerman, G.H.
"Prevention of Rheumatic Fever".
Bull. New York Acad. of Med. 1955. 31 : 165.

Stollerman, G.H. 1954(b).

"Prevention of Rheumatic Fever"
American Practitioner and Digest of Treatment. 5 : 589.
Quoted from -
Stollerman, G.H.
"Prevention of Rheumatic Fever".
Amer. Jour. of Med. 1954. 17 : 757.

Stollerman, G.H. and Rusoff, J.H. 1952.

"Prophylaxis against Group A Streptococcal Infections in Rheumatic Fever Patients, with a new Repository Penicillin".
J.A.M.A. 150 : 1571.

Stollerman /

Stollerman, G.H., Rusoff, J.H. et al. 1955.

"Prophylaxis Against Group A Streptococci in Rheumatic Fever : Use of Single Monthly Injections of Benzathine Penicillin G."
New Eng. J. Med. 252 : 787.

Symposium of Streptococcal Infections, 1954.
Held at the New York Academy of Medicine.

Ed. by M. McCarty.
Columbia Univ. Press, New York.

Third Statistical Account of Scotland (Glasgow), 1958.

Cunnison, J; Gillfillan, J.B.S. 5 : 590. Collins, Glasgow.

Thomas, C.B., and France, R. 1939.

"A preliminary Report of the Prophylactic Use of Sulphonilamide in Patients Susceptible to Rheumatic Fever".
Bull. John Hopkins Hosp. 64 : 67.

Tweedy, P.S. 1956.

"Pathogenesis of Valvular Thickening in Rheumatic Heart Disease".
Br. Heart Jour. 18 : 173.

Wells, William. 1812.

"On Rheumatism of the Heart".
Trans. Soc. Improv. Med. and Chir. Knowledge. 3 : 373.

Wood, P. 1956.

"Diseases of the Heart and Circulation.
2nd Edition. Eyre and Spottiswoode, London.
(a) p. 495
(b) p. 483
(c) p. 554