EPIDEMIOLOGY OF HAEMOLYTIC STREPTOCOCCAL INFECTION IN RELATION TO ACUTE RHEUMATISM

II. EPIDEMIC RHEUMATISM

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(With 1 Figure in the Text)

Introduction

Although multiple cases of acute rheumatism have been observed to follow waves of streptococcal infection in institutions (see Green, p. 369) there is doubt as to whether acute rheumatism itself becomes epidemic under such circumstances or whether the element of infectivity lies in the preliminary throat infection as concluded by Sheldon (1931).

The occurrence of acute rheumatism in a training centre to an extent which reached epidemic proportions was therefore of interest. Reference has already been made to this epidemic (Green, 1941) in relation to the control of acute rheumatism in the recruit.

Personnel in training centre Ac.

The bulk of the personnel consisted of youths aged 15–17 years who had all passed a routine medical examination on admission. The youths were divisible into two classes, viz. 300 apprentices and 900 boys. Apprentices were added to the establishment in large classes of 60–70 youths every term, while boys were joined at the rate of 30–35 every week until the end of July 1938 when recruiting ceased.

The establishment was opened in the spring of 1937 and the population steadily increased by the incoming recruits, as shown in Fig. 1, until the spring term of 1938. By that time, some of the boys had completed their training period of 12 months and left the establishment. The average population during the period of observation numbered 1300, although the total entries were approximately 1900.

History of outbreak

Acute tonsillitis appeared in epidemic form in the autumn of 1937 and persisted throughout the 1937–8 session. In the earliest stages of the wave of streptococcal infection which preceded the appearance of rheumatism, periodic examination of cases of tonsillitis and upper respiratory infection invariably indicated that haemolytic streptococci were responsible. Out of 126 swabs so taken, 112 were positive for this organism. The combined figure for throat infections was taken as a rough index of total haemolytic streptococcal infection, and in the full period of observation this total reached 1466 cases while 162 cases of acute rheumatism and 132 cases of scarlatina were notified.

During the epidemic the severity of acute rheumatism varied from the hyperpyrexial polyarthritis of text-book description to less striking cases in which the initial diagnosis was difficult. Thus, some cases had little or no fever and only transient, indefinite joint pains, accompanied by an abnormal sedimentation rate and electrocardiographic changes.

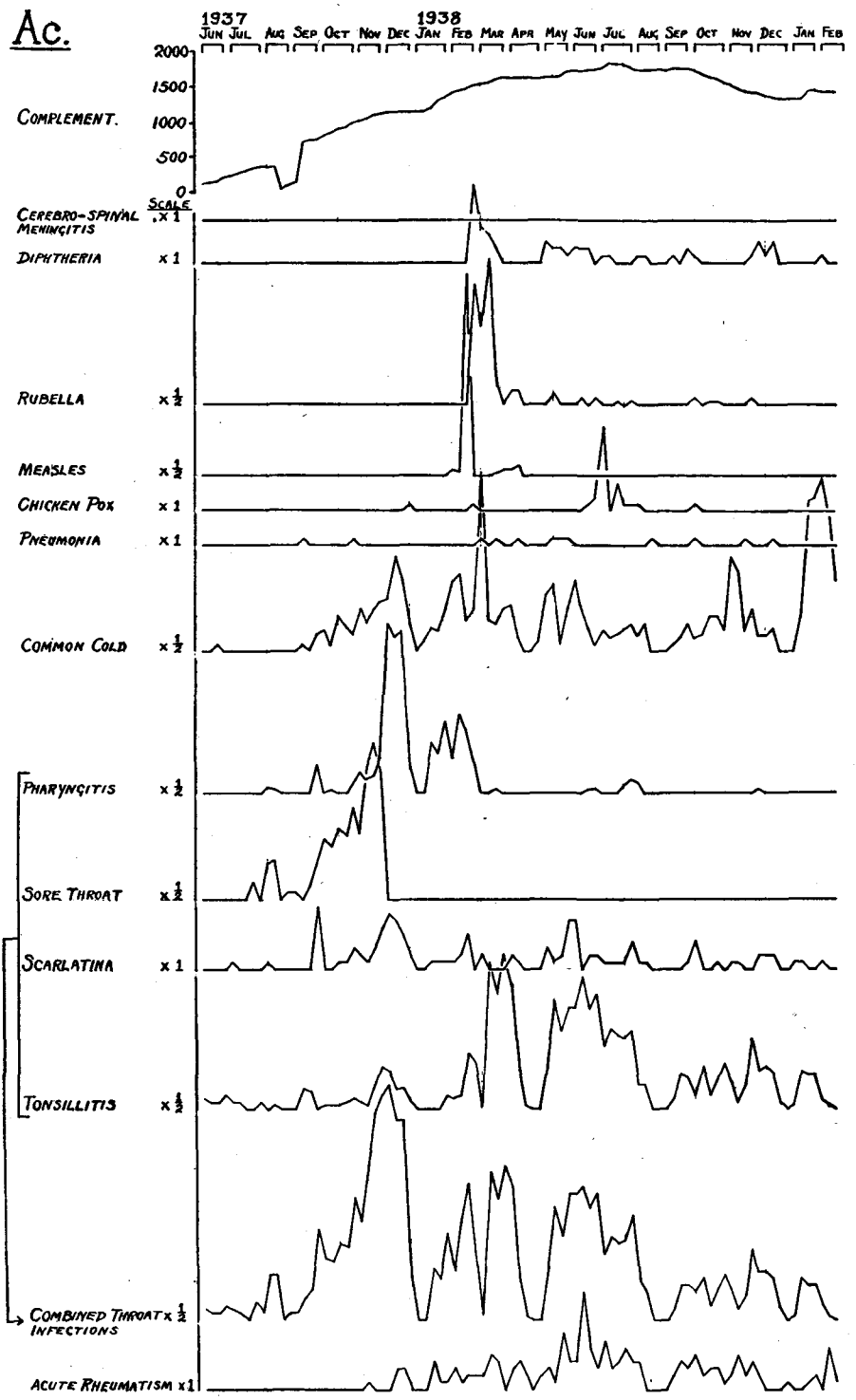

Fig. 1. Showing the incidence of various infections and of acute rheumatism in training centre Ac.

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Some of the most severe cases of carditis occurred in boys whose illness was apyrexial throughout its course, while in a few instances, pancarditis developed in the absence of any definite premonitory symptoms or signs. The insistence of the clinical triad of fever, joint pains and carditis in each case would therefore have excluded some of the most characteristic end-lesions of rheumatism. Nor was the therapeutic test of the relief of pain by massive dosage with salicylates completely satisfactory, as this failed to influence the course of the disease in some cases and certainly did not prevent relapses. Accordingly, the criteria adopted for a diagnosis of acute rheumatism were first, the evidence of acute infection as shown by pyrexia or increased sedimentation rate, followed by joint manifestations with or without carditis.

The monthly case returns for scarlatina, combined throat infections and acute rheumatism are indicated in Table 1, and a pictorial representation of the epidemic is given by

Table 1. *Showing the monthly incidence of acute rheumatism, scarlatina and combined throat infections in training centre Ac. from September* 1937 *to February* 1939

Month	Age of centre in months	Acute rheumatism	Scarlatina	Combined throat infections	Month	Age of centre in months	Acute rheumatism	Scarlatina	Combined throat infections
Sept.	4	0	13	43	July	14	23	1	118
Oct.	5	0	6	113	Aug.	15	2	1	17
Nov.	6	1	16	194	Sept.	16	9	8	43
Dec.	7	6	25	193	Oct.	17	14	5	46
Jan.	8	7	6	52	Nov.	18	13	2	39
Feb.	9	7	16	104	Dec.	19	3	6	44
Mar.	10	14	2	122	Jan.	20	3	2	33
Apr.	11	8	1	51	Feb.	21	6	1	5
May	12	19	18	107		Total	162	142	1466
June	13	27	13	142					

Fig. 1. The latter shows how the combined throat infections increased weekly from the beginning of the autumn term of 1937 until the dispersal of the community for Christmas leave. Towards the end of the term, scarlatina showed a peak, although cases had occurred intermittently during the term. The first case of rheumatism was noted in the week ending 13 November, but it was not until the end of term that several cases appeared simultaneously. The marked reduction in the attack rate of throat infections due to dispersal was evident in the first 2 weeks of the spring term, but there was still a considerable number of cases. These rapidly increased as the term progressed and continued until the Easter vacation. Fewer cases of scarlatina occurred in this term, but cases of acute rheumatism were very numerous throughout, the total being thirty-four. The summer term opened with an immediate recrudescence of streptococcal infection which reached its zenith early in the term and then became less intense. Scarlatina was again prevalent, particularly in the earlier part of the term. Rheumatism reached its greatest incidence during this term, the total number of cases being more than double that of the previous term. The graph indicates that in the latter half of the term the disease became less frequent. The incidence of throat infections declined during the following autumn and spring terms, and there was a corresponding reduction in acute rheumatism though many cases appeared, probably as an after-effect of the preceding terms.

Incidence of rheumatism and scarlatina in relation to period of admission

The effect of time on the incidence of rheumatism and scarlatina was noted as in Table 2. Details of the later cases in the series were not available, but the majority were examined, including all those in the epidemic period. So far as acute rheumatism was concerned, it will be seen that the largest number of cases, viz. 46·5%, occurred in individuals within 3 months of entry. Of these, 19·3% were in the first 6 weeks and 27·2% in the second half of the 3-month period.

Table 2. *Showing the monthly distribution of scarlatina and acute rheumatism in relation to the length of time after admission to the training centre Ac.*

Month	Age of centre months	No. of weeks between admission and onset of disease					Total no. of cases per month
		1–6	7–13	14–26	27–39	40–52	
		Acute rheumatism, absolute number of cases					
Nov.	6	1	0	0	0	0	1
Dec.	7	3	3	0	0	0	6
Jan.	8	0	3	2	2	0	7
Feb.	9	0	2	3	2	0	7
Mar.	10	1	5	6	2	0	14
Apr.	11	0	4	2	2	0	8
May	12	1	3	6	8	1	19
June	13	9	4	7	5	2	27
July	14	6	7	9	1	0	23
Aug. part	15	1	0	1	0	0	2
	Total	22	31	36	22	3	114
Percentage totals		19·3	27·2	31·6	19·3	2·6	100·0
		Scarlatina, absolute number of cases					
Sept.	4	9	3	1	0	0	13
Oct.	5	5	1	0	0	0	6
Nov.	6	10	3	3	0	0	16
Dec.	7	8	9	7	1	0	25
Jan.	8	1	2	1	2	0	6
Feb.	9	10	1	2	2	1	16
Mar.	10	1	0	1	0	0	2
Apr.	11	0	0	0	1	0	1
May	12	10	2	4	2	0	18
June	13	9	2	2	0	0	13
July	14	1	0	0	0	0	1
Aug.	15	1	0	0	0	0	1
Sept.	16	4	0	4	0	0	8
	Total	69	23	25	8	1	126
Percentage totals		54·8	18·3	19·8	6·4	0·9	100

During the epidemic in May, June and July, the proportion of new recruits, involved within 6 weeks of entry, was increased, although many cases appeared in youths who had been in the institution for several months. The total figures indicated that the chances of contracting rheumatism, in relation to time of exposure to the environment, increased up to 6 months and then decreased.

On the other hand, 73·1% of scarlatinal cases occurred within 3 months of entry. Of these, 54·8% were in the first 6 weeks and 18·3% in the second half of the 3-month period. The total figures indicate that the greatest risk of developing scarlatina was in the first few weeks of entry, but that infection may still occur after as long a period of exposure as 6 months.

Type of acute rheumatism

Clinical records were available for cases occurring up to the end of the summer term in 1938 when the acute rheumatic cases, fulfilling the criteria already detailed for the establishment of a diagnosis, totalled 114. Of these, 104 had pyrexia, 97 developed joint pains and 102 showed evidence of carditis, so that the majority exhibited the clinical triad of joint pains, pyrexia and carditis. When last surveyed the position as regards the features of the clinical lesions was as follows:

No carditis	12	Deaths (cardiac failure)	1
Temporary murmurs	27	Pericarditis	8
Cases in which a mitral systolic murmur developed and has persisted in the absence of any other signs of organic damage ...	31	Aortic reflux	4
		Mitral reflux (11 of these appear now to be developing some stenosis)	26
		Established mitral stenosis	11

Thus forty-nine cases exhibited one or other of the more grave lesions typical of rheumatic fever.

Incidence of rheumatism, etc., in the various divisions of the institution

The institution was divided into five divisions, of which the apprentices formed division E while the boys made up the remaining four, A, B, C and D. Each division consisted of some 300 boys and was further subdivided into six groups of about fifty boys. The youths of one group slept in the same dormitory and ate at the same tables. The various groups of a division, however, occupied as far as possible the dormitories of one section of the institution. The youths of one division worked as a unit, so that there was a certain amount of separation of the divisions from each other. This particularly applied to the apprentices who worked during the day in a building remote from the living quarters. The divisions could not, however, be considered as entirely separate populations within the establishment.

In Table 3 are shown the incidences of tonsillitis, rheumatic fever and scarlatina in the divisions. In addition are shown the cases which occurred among boys who had recently joined but had not been assigned to a division. A period of 4–6 weeks was spent in a preliminary course before admission to a division. The number of new entries and boys in preliminary courses averaged 196, but this was a variable figure.

It may be seen that rheumatic fever occurred in all the divisions with approximately the same attack rate, and the same was true of the streptococcal infections, save that scarlatina was much more frequent in the D and E divisions and in the preliminary boys. Beyond noting the high frequency of both rheumatic fever and streptococcal infections in divisions and groups, the examination of the distribution of cases rendered no further assistance in the correlation of incidence.

Incidence of acute rheumatism and recruiting locality

Youths were drawn to the establishment from all over England but the majority were from the North Midlands and from Scotland, as shown in Table 4, which includes all admissions to the end of August 1938.

The incidence of rheumatism in youths from certain grouped areas is shown in Table 5. Northumberland and Durham were considered as one area on account of the similarity in the economic and industrial conditions in the two counties, and because many of the

Table 3. *Showing the distribution of acute rheumatism, scarlatina and upper respiratory infection in the divisions and groups of training centre Ac.*

Division	Group	No. of cases: Rheumatism		Scarlatina		Respiratory infections	
A	1	19	1	5	1	178	35
	2		1		2		43
	3		6		1		36
	4		4		0		39
	5		1		1		20
	6		6		0		14
B	1	21	2	5	1	243	53
	2		2		0		54
	3		0		4		61
	4		3		0		33
	5		6		0		23
	6		8		0		19
C	1	17	3	11	1	212	55
	2		5		8		58
	3		2		0		34
	4		1		0		21
	5		0		1		27
	6		6		1		17
D	1	16	2	17	2	246	55
	2		3		4		75
	3		3		2		48
	4		3		3		25
	5		3		5		28
	6		2		1		15
E	1	22	1	26	5	225	22
	2		5		7		29
	3		3		1		34
	4		4		4		55
	5		3		7		47
	6		6		2		38
Preliminary boys not assigned to a division		19		48		450	

youths came from districts in Tyneside between the two counties. The heavy incidence amongst the boys from Tyneside was significantly greater than that of the remainder, as the following analysis shows:

All admissions:
Total number of youths 1806
Total number of cases of rheumatism 114
Case incidence per 1000 = 63·0

Tyneside admissions:
Total number of youths 385
Total number of cases of rheumatism 39
Case incidence per 1000 = 101·3

All admissions omitting those from Tyneside:
Total number of youths 1421
Total number of cases of rheumatism 75
Case incidence per 1000 = 52·8

Therefore the incidence in Tyneside youths was almost double that in the remainder. The next highest incidence was recorded in the youths from Yorkshire but was not significantly different from that of the remaining youths, the respective figures per 1000 being 59·6 and 63·6.

The reasons for this are controversial, but it may be recalled that Northumberland and Durham show the highest mortality rate in the country, being much higher than the

average for England and Wales, as shown by the following extract from the Registrar-General's Report for 1931:

	Mortality rates for male lives			
Age	England and Wales	Northumberland and Durham	Scotland	Glasgow
16	0·00227	0·00319	0·00232	0·00303
17	0·00259	0·00366	0·00262	0·00334
18	0·00284	0·00405	0·00289	0·00352
19	0·00302	0·00433	0·00310	0·00367
20	0·00316	0·00457	0·00326	0·00379

Table 4. *Showing the numbers of youths admitted to training centre Ac. from various localities from May* 1937 *to August* 1938

Durham	261	Leicester	143
Lancashire	195	Dumfries	
Yorkshire	151	Mull and Argyll	
Lanark	134	Wigtown	
Northumberland	124	Donegal	
Lothian	95	Tyrone	
Antrim	85	Suffolk	
Aberdeen	66	Buckingham	
Fife	58	Warwick	
Hampshire	55	Clare	
Forfarshire	43	Monmouth	
Devon	38	Stafford	
Cornwall	36	Oxford	
Cumberland	31	Kinross	
Aryshire	21	Peebles	
Renfrew	18	Elgin	
Surrey	18	Caithness	
Nottingham	17	Kincardine	
Londonderry	16	Dumbarton	
Cork	16	Selkirk	
Lincoln	14	Kirkcudbright	
Derby	14	Monaghan	
Perth	14	Gloucester	
Berwick	13	Isle of Man	
Co. Down	12	Middlesex	
Glamorgan	12	Roxburgh	
Dublin	11	Wexford	
Essex	11	Sligo	
Kent	11	Flint	
Somerset	11	Hereford	
Dorset	11	Westmorland	
Stirling	11	Wiltshire	
Sussex	10	Northampton	
Denbigh	10	Norfolk	
Ross and Cromarty	10	Pembroke	
Inverness	10	Sutherland	
		Nairn	
		Banff	
		Skye	

Table 5. *Showing the incidence of acute rheumatism in youths recruited from certain grouped areas*

		Acute rheumatism	
District	No. of youths	No. of cases	Percentage of youths from the district
Northumberland and Durham	385	39	10·13
Lancashire	195	9	4·61
Yorkshire	151	9	5·96
Lanarkshire	134	6	4·47
Non-industrial areas	937	51	5·44

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As is well known, Tyneside was for years one of the worst of the depressed areas, and the high incidence of rheumatism in recruits from this area was probably a reflexion of abnormal economic and environmental circumstances.

Discussion

The occurrence of an outbreak of acute rheumatism of epidemic proportions in a community, which had been recently surveyed and considered healthy, has been shown to be correlated with widespread infection by haemolytic streptococci. As regards the streptococcal aetiology of rheumatism it is important to consider to what extent primary infection was encountered, as contrasted with a recrudescence of existing infection. It may be reasonably presumed that obvious rheumatic stigmata were eliminated at the entrance examination. Clinical experience has proved that latent infection readily escapes detection at such an examination no matter how thoroughly it is conducted. However, it was most unlikely that all the cases which subsequently appeared were of this type, and an attack rate of 63 per 1000 was certain evidence that primary infections were taking place. Granted this was the case then the association with haemolytic streptococcal infection assumed much greater significance. That this correlation was not exact did not, in itself, exclude streptococcal infection as a primary factor in the causation of rheumatism. Considering the analogy of another disease spread by droplet infection and which may be sporadic or epidemic in distribution, namely, cerebro-spinal fever, the same absence of correlation between known contact with the causative agent and the incidence of cases has been noted. Thus Dudley (1934) showed that, in a large community, a carrier rate of 50% for agglutinable *N. meningitidis* persisted for over 12 months, but no cases of cerebro-spinal fever appeared in the community. On the other hand, in another community with six cases of meningitis, the carrier rate was only 5%. By contrast, Glover (1920) had found that the carrier rate was in the region of 70% when cerebro-spinal fever outbreaks were imminent or present. There is apparently no simple rule governing the relationship between carrier rates and the appearance of clinical cases, the varying factor which complicates the issue being the herd immunity of the exposed population. Although analogy is a dangerous form of reasoning, the possibility that a similar factor is in operation when rheumatism follows streptococcal infection must be considered.

Of particular importance was the observation that a significantly high proportion of the cases occurred in boys from the Tyneside area. In the absence of notification returns for rheumatism, the incidence in boys from this area as compared with the rest of the country is not known. As there is significantly greater infection with *B. tuberculosis* in this community, the assumption is that rheumatism will also be more frequent. The higher proportion of cases among boys coming from the Tyneside area may therefore be explained by a greater degree of latent infection. For the reasons stated it was unlikely that more than a fraction of the difference could be explained in this way, and the additional factor was most likely to be the greater susceptibility of Tyneside youths when exposed to an environment suitable for contracting infection.

The shape of the term curves for combined throat infections and scarlatina in Fig. 1 suggested the following hypothesis. The steady upward climb of the former in the first term was an index of the increasing virulence of the haemolytic *Streptococcus* as a result of passage through the community, culminating in the appearance of multiple cases of scarlatina. Despite the reduction in incidence at the start of the second term due to the

dispersal of the population, the epidemic rapidly regained its former strength by reason of the increased virulence of the infecting organism. The 'weeding-out' of scarlatinal susceptibles during the first term was indicated by the lowered figures in the second term. At the start of the third term, the increased virulence of the organism maintained the number of clinical cases at a high level, but an important antagonizing factor came into play, namely, the increasing immunity of the community. Although scarlatina was more frequent in this term, the majority of the cases were in new entries who had recently joined and had not experienced the immunizing action of the previous terms.

The shape of the rheumatism curve was quite different and suggested that the incidence of this condition was influenced by the immune state of the community. By the summer of 1938 the community was thoroughly saturated with haemolytic streptococci, and the attack rate was so high that few persons escaped one or more attack of naso-pharyngeal infection. With few exceptions all those who developed rheumatism had two or more attacks of throat infection before the onset, or else the second attack of throat infection coincided with the appearance of joint manifestations.

A marked difference in the incidence of rheumatism and scarlatina in relation to time of exposure to the environment of the institution was demonstrated which again indicated that a different mechanism was at work if the haemolytic *Streptococcus* was alone responsible for acute rheumatism as well as scarlatina. An analogous difference was observed in the incidence of scarlatina and tonsillitis, which was known to be of haemolytic streptococcal origin in practically all cases. The latter difference was due largely to the variation in antitoxin immunity of the exposed herd, produced by the periodic introduction of fresh susceptibles. It is interesting to note that the curve for rheumatism in Fig. 1 was much closer to that of tonsillitis than was the curve for scarlatina.

CONCLUSIONS

1. An epidemic, in a semi-closed community, of upper respiratory infection due to *Streptococcus haemolyticus*, and followed by acute rheumatism, is described.

2. In the period of observation the average population was 1300, although the total entries were approximately 1900; 1466 cases of throat infection occurred which included 132 cases of scarlatina; 162 cases of acute rheumatism were notified in the same period.

3. Rheumatism in youths from Tyneside was significantly more frequent than in the rest of the community, the incidence per 1000 being 101·3 and 52·8 respectively.

4. Of scarlatinal cases 73·1% developed within 3 months of entry, 54·8% being in the first 6 weeks and 18·3% in the following 6 weeks: 46·4% of rheumatic cases were within 3 months of entry, only 18·4% being in the first 6 weeks and 28·4% in the following 6 weeks.

5. This difference in distribution is discussed in relation to the mechanism of acute rheumatism.

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