THE SEROLOGICAL TYPES OF HAEMOLYTIC STREPTOCOCCI IN RELATION TO THE EPIDEMIOLOGY OF SCARLET FEVER AND ITS COMPLICATIONS

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(With 1 Figure in the Text)

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Introduction

As early as 1903 Hektoen reported the isolation of streptococci from the blood in 12 % of scarlet-fever patients. The work of Gabritschewsky (1907) on the immunizing effects of streptococcal vaccine against infections by this organism, of Moser (1902), some years before, on the therapeutic action of anti-scarlatinal serum in the human disease, of Krumwiede, Nicoll & Pratt (1914), who recorded a case of scarlet fever in a technician, after accidentally sucking into her mouth a suspension of living haemolytic streptococci, and finally that of Schultz & Charlton (1918), and of Dick and Dick (1921, 1924*a*, *b*, 1925*a*, *b*),

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on the action of immune serum and of toxic filtrates of haemolytic streptococci when injected intradermally, all aided in establishing the view that scarlet fever is due to streptococci of the haemolytic type.

The results of the early attempts at classifying the haemolytic streptococci are much at variance with one another. Of the methods devised for such a classification, that based on the agglutination reaction has found most favour. As early as 1902 Moser & von Pirquet arrived at the conclusion that the strains found in scarlet fever formed a distinct serological group. This was confirmed by Meyer (1902), Rossiwall & Schick (1905). After this initial work little attention was paid to the serological classification of the haemolytic streptococci until the subject was once more opened up by Dochez, Avery & Lancefield (1919). They showed by means of the agglutination reaction that these organisms could be subdivided into at least four types. The following year Tunnicliff (1920) and Bliss (1920) and, later, Gordon (1921), found that at least 80% of scarlet-fever strains were of one serological type. This observation did not remain unchallenged. Williams *et al.* (1924) showed that several types existed, and the one most frequently found constituted only 15% of all the strains examined. The importance of his work was enhanced by the discovery that strains, identical with those found in scarlet fever, were responsible for other infections, such as puerperal fever and erysipelas.

These observations were confirmed by other observers (Smith, 1926, 1927; MacLachlan & Mackie, 1928). About the same time Griffith (1926) examined, by means of slide-agglutination, a hundred strains from scarlet-fever patients, and found that the majority could be classified into four types. The following year (1927) he published a comprehensive monograph, and produced evidence that 60% of all strains found in acute scarlet fever belonged to one or other of these types. He has now extended his classification to include thirty types which he regards as of epidemiological significance.

Griffith's slide-agglutination method of typing haemolytic streptococci, in which absorbed antisera are used, has in fact made it possible to type the majority of the haemolytic streptococci found in human lesions.

Lancefield (1928) demonstrated the presence of a specific substance of carbohydrate nature in haemolytic streptococci, and later developed a method of grouping these organisms, based on the precipitin test. A general agreement between her system and Griffith's has been shown to exist (Swift, Lancefield & Goodner, 1935). Thus, Lancefield (1933) has made it possible to identify the strains which are commonly pathogenic to man (group A), and it has been found that most of Griffith's types are included in this group (Pauli & Coburn, 1937). The four exceptions are types 7, 16, 20, 21. Of these, type 16 belongs to Lancefield's group G and the others to group C.

One of the main difficulties encountered in the agglutination test with streptococci is the spontaneous clumping which the organisms tend to undergo. This problem has been investigated by numerous workers (Dochez *et al.* 1919; Bliss, 1922; Durand & Sedallion, 1925; Rosner, 1928; Tunnicliff, 1922; Gordon,

1921; Shipley, 1924; Smith, 1926; James, 1926; Noble, 1927; Stevens & Dochez, 1926; Spicer, 1930; Williams & Gurley, 1932; MacLachlan & Mackie, 1928; Gunn & Griffith, 1928; Allison, 1931; and Mueller & Klise, 1932). Although the various methods recommended by these workers have been to a certain extent successful, they have not solved the problem. Their variety indicates the difficulty experienced in obtaining homogeneous suspensions.

Of all the methods adopted for classification of the haemolytic streptococci Griffith's slide-agglutination remains the most practicable for epidemiological work. It is rapid and simple, and the results are fairly constant.

The serological investigation of the types concerned in small epidemics of scarlet fever had been studied by Glover & Griffith (1931) and Griffith (1934), but the first investigation on a large scale was carried out by Green (1937) during the epidemic of 1933 in Edinburgh. He found that Griffith's types 1–5 were the epidemiological strains, among which type 5 predominated. Recently, Neisser (1939) has carried out a survey of 1211 strains of haemolytic streptococci found in scarlet fever, puerperal fever and vulvo-vaginitis.

The typing of haemolytic streptococci has also made it possible to obtain a clearer understanding of the significance of cross-infection among scarlet-fever patients. When a patient is admitted into a ward he is infected with a particular serological type of haemolytic streptococcus, and during his stay in hospital may become secondarily infected or reinfected by a different type of this organism from other patients in the ward.

That a change of type may occur in the throat of a scarlet-fever patient, after he has been in hospital for some time, was observed by Gunn & Griffith (1928) and by Allison & Brown (1937), and that the change of type in a particular patient is not likely to be due to transmutation of the original strain has been indicated by the same workers.

The problem of air-borne infection by haemolytic streptococci was investigated by Cruickshank (1935), White (1936) and Brown & Allison (1937). Brown & Allison showed that 70·2 % of scarlet-fever patients in hospital became secondarily infected with a type of haemolytic streptococcus which differed from the type originally present. They further showed that the majority of complications in large wards, devoted to scarlet fever, are due to reinfection, and that most of the complications occur during the third week, when the majority of the patients are convalescent. Their assumption is that most of the complications arise from direct contact.

The carrier problem has received much attention. Williams *et al.* (1924) noted that after 30 days in hospital only 20 % of convalescents were carriers. Kirkbride & Wheeler (1930) found that between 50 and 60 % were carriers after the same period. Gunn & Griffith (1928) found 49 % of carriers, while Brown & Allison (1935) found that 82·8 % of all patients were carriers, irrespective of the length of hospitalization. Kirkbride & Wheeler made the important observation that little difference in virulence was found between strains of haemolytic streptococci isolated from acute and convalescent cases. With

regard to "return" cases Brown & Allison observed that a correlation existed between the degree of streptococcal infection of cases leaving hospital and the "return" case rate. This was found to be 3 % in mild and moderate, but 6 % in heavy and very heavy infection.

The object of this paper is to record the results of a systematic study of the serological types of haemolytic streptococci in a large series of cases of scarlet fever and in the complications with particular reference to the epidemiological analysis of this infection.

METHODS

(*a*) *Preparation of type-specific antisera*

Type-specific antisera were prepared by inoculating rabbits with vaccines of representative strains of Griffith's thirty types of haemolytic streptococci. Formolized vaccines were used in such a concentration that 1 c.c. of the vaccine corresponded to 20 c.c. of an 18 hr. broth culture of the organisms. The injections were given for three consecutive days each week until test bleedings showed the serum to possess a sufficiently high titre when tested with the specific strains. The initial doses were small (0·05–0·1 c.c.) and were given subcutaneously; the later doses, given intravenously, were increased to 0·75–1 c.c. A fixed scheme for the increase of dosage was found impracticable; the best method was to increase the doses rapidly as long as the rabbits remained healthy and maintained their weight. The time taken to obtain satisfactory sera varied from 3 to 8 weeks.

It was found that the longer the time taken to immunize the rabbits the more likely were group agglutinins to be found in the antisera.

The method of preparing the agglutinating sera differed somewhat from that recommended by Griffith (1934). The standard he aimed at was that a small loopful of a 1 in 5 dilution of the serum, which had been absorbed with a mixture of known heterologous strains to remove group agglutinins, should give rapid flocculation with a drop of the homologous suspension on a slide.

The method adopted in this study was as follows:

(*a*) To a drop of a heavy suspension of the type-specific haemolytic streptococcus on a slide was added a small loopful of the corresponding serum. If rapid agglutination did not occur the serum was discarded and the rabbit was given a further course of injections. Trial bleedings showed when a sufficiently high titre in the serum had been reached. If after repeated trials the agglutinating effect of the serum remained low, fresh vaccine was prepared or a new rabbit was injected.

(*b*) If, however, marked agglutination took place on the slide the serum was regarded as suitable for further treatment.

(*c*) It was then tested with the rest of Griffith's thirty type strains and any cross-agglutination noted. This test was carried out with all thirty sera, and considerable cross-reaction was noted.

(*d*) The serum was added drop by drop to a small test-tube containing 2 c.c. of normal saline. After the addition of each drop the agglutinating power of the saline-serum mixture was tested. When this was found to be satisfactory (i.e.—when the organisms on the slide were rapidly agglutinated) the diluted serum was tested with the other twenty-nine type suspensions. With a number of types (2, 6, 7, 8, 10, 13, 16, 18, 21, 27, 28, 30) cross-reaction no longer occurred, and therefore with them no absorption was necessary.

Since the titres of the various sera differed considerably, the number of drops added to the 2 c.c. of saline varied correspondingly. The titre seemed to bear little relation to the cross-agglutination. For example, in the types 8 and 22 antisera, five drops were added to

the 2 c.c. of saline. Both showed marked cross-agglutination before dilution, but, though the end-titres of both antisera were 1:640, after dilution cross-reactions with type 8 were absent and with type 22 still marked.

(*e*) *Absorption of heterologous agglutinins.* From this stage the preparation of type-specific antisera was similar to Griffith's simplified method.

A type 3 strain was grown on blood-agar to which had been added 10% of type 3 antiserum. Opaque and clear colonies were formed. A clear colony (non-specific) was transplanted into digest broth which was then incubated for 18 hr. 0·5 c.c. of the serum, which gave cross-reactions, was diluted 1:5 with saline, and to it was added the deposit of 400–500 c.c. of a broth culture of type 3 (non-specific). It was incubated in a water-bath at 37° C. for a few hours and then left at room temperature for 24 hr. Thereafter it was centrifuged and the supernatant serum again tested for type specificity. No group agglutinins were detected except with types 11, 15, 17 and 19. After a second absorption of these sera, in a similar manner, only type 17 serum was found to give a slight cross-reaction with the type 15 organism. A third absorption did not remove this. In types 11 and 19 sera over-absorption had occurred with a marked decrease of specific agglutinating power, and so fresh sera had to be absorbed.

(*f*) *Pooling the sera.* Pooled sera were prepared by mixing 0·5 c.c. of each of five type-sera and adding to these the deposits of 2 l. of digest broth culture of non-specific type 3.

It must be observed that type 3 serum was absorbed by strains of types 1, 2, 4 and 19, and in the pooled serum 1–5, type 3 serum was not added till after absorption, and then only as the absorbed serum.

(*b*) *Technique of typing*

The method of typing strains of haemolytic streptococci was similar to that described by Griffith (1934). To obtain suitable homogeneous suspensions certain modifications were, however, adopted:

(*a*) Some of the organisms were transferred from a pure culture on a blood-agar plate to a small tube half filled (3 c.c.) with horse-muscle digest-broth, to which had been added 3 % of ascitic fluid.

(*b*) This was incubated for 5 hr. and afterwards observed at hourly intervals. As soon as a tube showed clouding it was removed and left in a rack at room temperature for 12–24 hr.

(*c*) After this period the tubes showed slight increase of growth. Those which yielded a homogeneous suspension were ready for typing. The tubes with deposits and clear supernatant fluid were agitated in front of a light. A shot-silk appearance in the medium indicated that they were also suitable for typing. The other tubes were granular and had to be further treated.

(*d*) Each granular growth was plated out on blood-agar to see if a pure culture was being dealt with. Cultures were also made in the following three media: horse-muscle digest-broth, the same medium with 6 % rabbit serum added, and undiluted ascitic fluid. The procedure of incubation was the same as before.

By these means 93 % of cultures gave uniform suspensions.

The reason for leaving the organisms at room temperature for 12–24 hr. was that this procedure appeared to increase the type-specificity. (Confusion is apt to arise unless it is remembered that decrease of type-specificity occurs when the organisms are incubated at 37° C. for 24 hr. or longer.)

Of the 7 % granular growths remaining no amount of subculturing in various media produced homogeneous suspensions. Some of these growths were, however, made homogeneous by plunging a red-hot loop into the centrifuged deposit of organisms. In some cases this had to be repeated a number of times. It was, however, found that in these cases where agglutination occurred on adding antisera, it was markedly delayed and not complete.

(*c*) *Methods of isolating haemolytic streptococci from cases*

All cases of scarlet fever were swabbed as soon as possible after their entry into the hospital. Fortunately, night admissions in the Edinburgh City Fever Hospital are rare, and so most of the swabs were obtained shortly after the patients entered the wards.

The following was the routine procedure adopted in most cases:

(i) On entry, two swabs were taken—throat and nasal. In those cases which were admitted with complications (e.g. otorrhoea, sepsis, etc.) a third swab was taken, if discharges were present.

(ii) All cases were examined daily, and when they developed complications swabs were again taken.

When swabbing throats, an attempt was made to rub the swab over both tonsils. For the nose thinner swabs gave better results, for they could be inserted deeper into the nares.

(iii) All swabs were plated out on blood-agar plates, which were incubated for 16–18 hr., the optimum time for the formation of the best discrete colonies.

Colonies were then picked off and subcultured on blood-agar plates, which were incubated for 12–14 hr.

From this stage the procedure was that described in section (*b*).

Record of scarlet-fever cases investigated

The number of cases of scarlet fever examined is given in Table 1, of complications in Table 2, and of the haemolytic streptococci isolated in Table 3.

Table 1. *Cases of scarlet fever examined*

Date	Total entries	Total no. swabbed	Total no. with complications	Total complications swabbed
1937 Sept.	177	177	34	34
Oct.	254	254	63	63
Nov.	248	248	73	73
Dec.	217	217	65	65
1938 Jan.	160	160	48	48
Feb.	142	142	57	57
Mar.	133	133	45	45
Apr.	111	20	32	—
May	131	20	52	—
June	101	101	29	29
July	83	20	21	—
Aug.	78	20	24	—
Sept.	94	94	24	24
Oct.	89	89	19	19
Nov.	76	76	14	14
Dec.	75	20	—	—
1939 Jan.	—	20	—	—
Feb.	—	20	—	—
Totals	2169	1831	600	471

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Table 2. *Complications*

	Nephritis	Arthritis	Otorrhoea	Adenitis	Rhinitis	Endo-carditis	Vaginitis	Total no. of com-plications
1937 Sept.	1	3	11	23	10	0	1	49
Oct.	0	7	18	40	16	1	1	83
Nov.	1	8	24	44	14	1	1	93
Dec.	0	6	21	38	12	0	2	79
1938 Jan.	0	6	15	22	17	0	4	64
Feb.	3	7	10	27	22	1	3	73
Mar.	0	4	9	27	14	0	0	55*
Apr.	0	4	11	20	8	0	0	43
May	2	2	13	45	12	0	4	78
June	0	4	4	16	7	0	3	34
July	0	2	4	11	1	4	0	22
Aug.	0	3	5	8	12	0	2	31†
Sept.	2	2	9	12	8	0	0	33
Oct.	0	1	7	11	5	0	1	25
Nov.	0	2	2	7	6	0	0	17
	9	61	163	351	164	7	22	779

* Sinusitis 1. † H.S. Empyema 1.

The number 779 does not indicate the number of patients; one patient may have had two or more complications. The number of patients who developed complications was 600 as indicated in Table 1.

Table 3. *Showing types of haemolytic streptococci found each month in scarlet-fever cases*

	Total no. of cases swabbed showing haemolytic streptococci positive															
	1937 Sept.	Oct.	Nov.	Dec.	1938 Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	1939 Jan.
	154	215	211	209	154	137	129	20	20	96	20	20	89	85	74	20	20
Types																	
1	47	126	143	107	98	90	76	13	11	39	7	5	32	18	10	2	2
2	10	13	19	19	13	13	16	1	2	20	2	1	6	4	1	1	0
3	1	4	5	15	10	8	12	0	0	1	1	0	0	0	0	0	0
4	19	7	2	16	3	1	0	1	1	16	5	8	27	40	43	13	12
6	3	1	0	2	0	0	0	0	0	0	0	0	3	7	4	1	0
8	10	6	3	7	2	1	0	0	0	0	0	0	2	3	4	0	0
11	5	4	0	4	0	1	0	0	1	1	0	0	0	0	0	0	0
15	8	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
22	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25	2	3	1	0	0	0	0	1	2	3	1	2	0	0	0	0	0
27	2	3	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0
28	1	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Untyped	43	41	34	38	28	22	25	4	2	16	4	4	19	13	12	2	5

These figures may be better appreciated in the following graph and summary.

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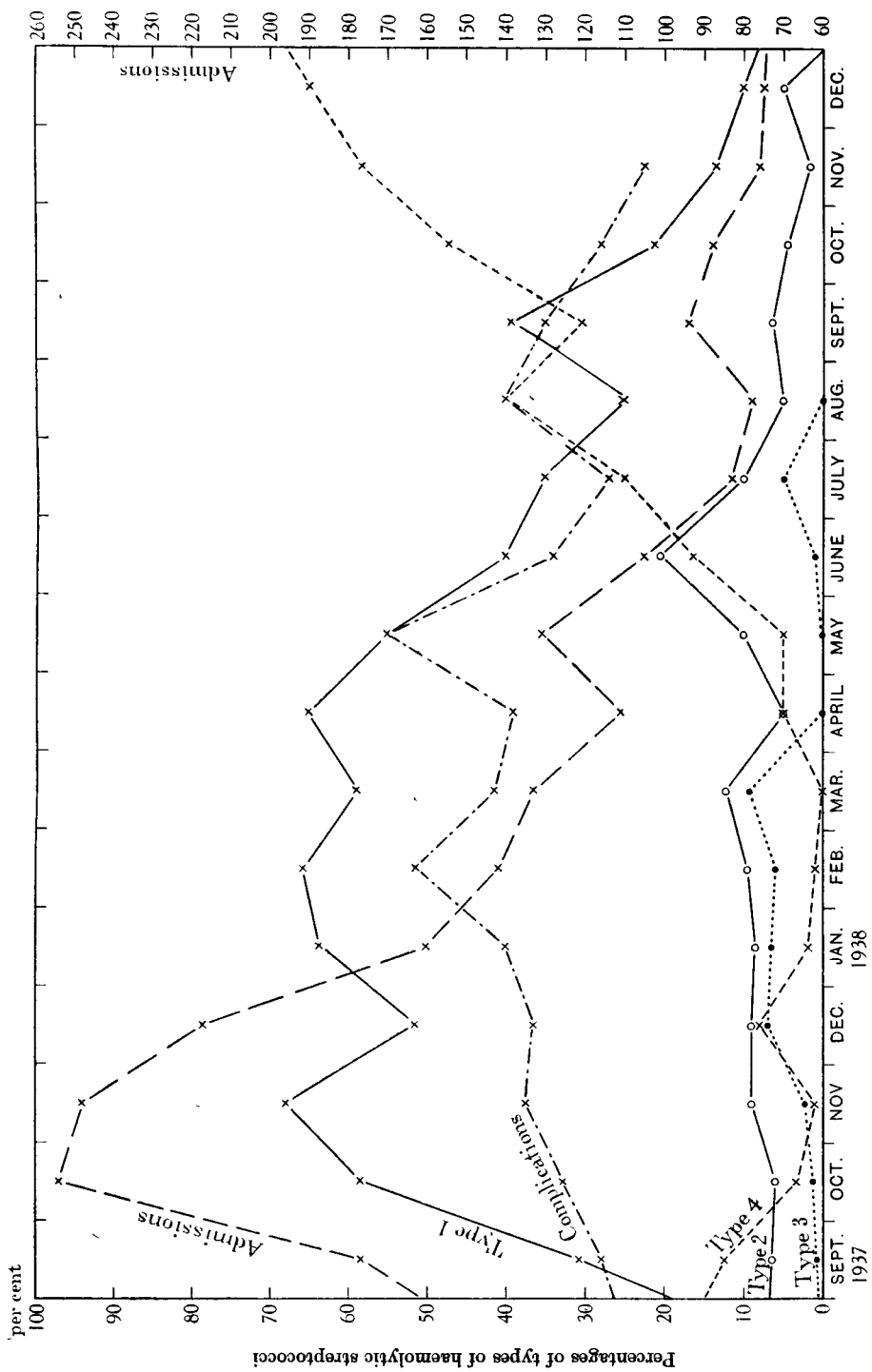

Chart showing percentages of epidemiological types of haemolytic streptococci and total number of admissions to hospital.

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Summary of Tables 1–3

1 September 1937 to 31 December 1938.

Number of scarlet-fever admissions	2169	
Total number of complications (including more than one complication in certain cases)	779	(35·9%)
Number of cases showing complications	600	(27·7%)
Number of scarlet-fever cases swabbed (including January and February 1939)	1831	
Number of cases with complications swabbed	471	
Total number of cases showing positive haemolytic streptococci swabs	1664	(96·6%)

Number of strains typed out of a total of 1664 was 1352, i.e. 81·3%.

Of the 2169 cases of scarlet fever 1253 were between the ages of 5 and 14, and of those 909 occurred during the first 5 years of school attendance.

The serological identity of the haemolytic streptococci in the throats and noses of scarlet-fever cases

The throat and nose of each case admitted was swabbed in order to ascertain the differences, if any, in the strains present.

From 25 October to 18 December 1937, 415 cases of scarlet fever were swabbed within a few hours of admission. If a case had been in hospital for more than 4 hr. it was regarded as unsuitable for investigation, because haemolytic streptococci from the air might have been inhaled.

The results obtained were as follows:

(1) Of the 415 cases swabbed, 366 (88·2%) had haemolytic streptococci either in the throat or the nose. All negative cases were swabbed on the following day, which increased the positive swabs by 35 and brought the percentage to 96·6. These cases were, however, not included in the investigation.

Only the 366 cases are therefore considered.

(2) In 115 cases both the nose and the throat gave positive swabs, in general the throat swabs giving better growth of haemolytic streptococci.

(3) In nine cases (2·5%) the nasal swab was positive, but the throat swab negative.

(4) 242 nasal swabs were negative.

(5) Total number of positive throat swabs was 357 and of nasal swabs 124.

The 366 strains were divided as follows: type 1, 241; type 2, 30; type 3, 7; type 4, 5; type 8, 8; type 11, 4; type 15, 5; type 25, 4; and untyped, 62.

On only two cases did the strains (230) isolated from the throat and nose of 115 cases differ in type, though in nineteen of these cases the haemolytic streptococci isolated could not be typed, and were assumed to be identical. In one of the two cases mentioned the culture from the throat belonged to type 2 and that from the nose could not be typed owing to granularity but may have been type 2, and in the other the throat gave type 1 and the nose type 11. In the latter it is unknown which of the two types was the primary organism.

It seems therefore that in 99 % or more of early cases of scarlet fever the haemolytic streptococci in the nose and throat are of the same type.

This conclusion was accepted, and from 20 December 1937 throat swabs only were taken. The possible error thus introduced in typing was probably slight.

THE IDENTITY OF SEPARATE COLONY CULTURES OF HAEMOLYTIC STREPTOCOCCI ISOLATED FROM THE THROAT IN EARLY CASES OF SCARLET FEVER

In this enquiry an attempt was made to determine whether there occurred more than one type of haemolytic streptococcus in the throat swabs of individual patients.

Twelve cases of scarlet fever were swabbed on admission. Eight of the most suitable plates, showing numerous discrete colonies of haemolytic streptococci, were chosen and six of the morphologically most varied colonies picked off from each plate. In each case the same type only occurred.

Table 4. *Types of haemolytic streptococci in individual cases*

	Colonies						
Case	1	2	3	4	5	6	
1	1	1	1	1	1	1	
2	1	1	1	1	1	1	
3	8	8	8	8	8	8	
4	1	1	1	1	1	1	
5	—	—	—	—	—	—	(untyped)
6	2	2	2	2	2	2	
7	3	3	3	3	3	3	
8	1	1	1	1	1	1	

A blood plate inoculated from a throat swab taken from a patient, who was isolated in a separate room, was particularly interesting since it showed an almost pure culture of haemolytic streptococci. The colonies, however, differed. Some appeared moist and opaque with a large zone of haemolysis round them, others were small, smooth and had only a narrow, clear zone of haemolysis. A third variety of colony had a rough umbilicated appearance, and the haemolytic area was poorly defined and irregular. Three subcultures of each form of colony were made and later typed. All proved to be type 2.

Nineteen other cases were swabbed, and as many colonies as appeared to be different were picked off from each plate, subcultured and typed. The results are given in Table 5.

Excluding the four cases in which the organisms could not be typed owing to the granularity of the suspensions, each case showed the same type in all the colonies, except case 26, which yielded types 1 and 24. This patient had entered hospital with a high temperature and had received 20 c.c. of scarlet-fever antitoxin. He made an uneventful recovery, and swabs were taken four times, at weekly intervals. On the first occasion type 1 only was found, on the second both types were again present, and on the third and fourth (before leaving hospital) only type 24.

Table 5. *Showing results of typing morphological different colonies from individual cases*

	Colonies										
Case	1	2	3	4	5	6	7	8	9	10	11
10	2	2	2	2	2	2	.	.	.	.	.
11	—	—	—	—	—	—	—	—	—	—	—
12	—	—	—	—	—	—	—	—	.	.	.
13	1	1	1	1	1	1	1	1	1	1	1
14	1	1	1	1	1	1	1	1	1	1	1
15	1	1	1	1	1	1	1	1	1	1	1
16	23	23	23	23	23	23	.	.	.	.	.
17	1	1	1	1	1	1	1	1	1	1	.
18	—	—	—	—	.	.	.	.	.	.	.
19	1	1	1	1	1	1	1	1	1	1	.
20	1	1	1	.	.	.	.	.	.	.	.
21	2	2	2	2	2	2	2	2	.	.	.
22	1	1	1	1	.	.	.	.	.	.	.
23	4	4	4	4	4	4	4	4	4	4	4
24	1	1	1	1	.	.	.	.	.	.	.
25	—	—	—	—	—	—	—	.	.	.	.
26	1	1	1	24	24	24	24	24	24	24	24
27	3	3	3	3	3	3	3	3	.	.	.
28	2	2	.	.	.	.	.	.	.	.	.

Type 24, as far as could be ascertained, has not previously been associated with scarlet fever. It has been found as a normal commensal in throats and in cases of sore throat in patients convalescent from rheumatic fever. It is of interest to note also that no other cases of scarlet fever with this type have been observed in Edinburgh, nor was it present in any cases showing complications.

If we can exclude this case these observations all point to the probability that most cases of scarlet fever are individually due to only one type of haemolytic streptococcus.

The practice adopted after this was to take only one swab, on admission to hospital, and to pick off only one colony for typing purposes. If this was negative a second was taken, and if the second was negative a third.

Occurrence of different types of haemolytic streptococci in the throats of scarlet-fever cases after a period of residence in hospital

This investigation was carried out to ascertain whether any cases, which had been in the wards for some time, carried more than one type of haemolytic streptococcus in their throats.

On one day all the patients in a ward were swabbed with positive results. Most of the patients had been in hospital for over 2 weeks, and therefore a considerable amount of cross-infection must have occurred. The ward was particularly suitable for this enquiry, because it went under quarantine the next day for chicken-pox, and also because a high percentage of cases showed complications.

From each of the plates a number of colonies (four to fifteen) were picked off and subcultured. In the plates with many colonies, an attempt was made to select the most different. All these were typed.

This procedure was repeated on two other occasions. The results of these three investigations are shown in Table 6.

Table 6. *Showing the results of examining the throats of patients after a period of residence in hospital*

No. of patient	Type on admission	Complications	Types of haemolytic streptococci present on		
			17. xii. 37	29. xii. 37	7. i. 38
29	1	Late adenitis	4, 2	2	None
30	—	,,	1, 4	4	4, 27
31	27	Otorrhoea	4	4, —	—
32	1	Intercurrent chicken-pox	1	None	None
33	4		4	Discharged	
34	1		1	1	Discharged
35	1		1, 8	Discharged	
36	4		4	Discharged	
37	2	Adenitis	2, 4	4	4
38	1	,,	1, 4	4	4
39	1	Otorrhoea and adenitis	1, 4	4	None
40	1	Otitis media	4	None	None
41	8	Adenitis	1	1, 4	1
42	1	Otitis media	27	27	27, 1
43	1	Adenitis and intercurrent chicken-pox	27, 1	27	27
44	—		1	None	1
45	1		—	4	4, 6(?)
46	—	Rhinitis and adenitis	4, 2	4	None
47	4		1, 8, 4	8	8, 27
48	2	Intercurrent chicken-pox	2	—	27, —
49	—	,,	—	—	None
50	3	,,	3	1	1
51	1		1, 4	4	4, —
52	1		—	—	1, —
53	6		6	6	6

(A dash [—] indicates that the organism could not be typed.)

It is evident that a considerable amount of cross-infection occurred among the patients of this ward. The problem under immediate consideration, however, was whether scarlet-fever patients, after continued residence in a ward, harboured at any particular time more than one type of haemolytic streptococcus in their throats. The results showed that this was the case. In only six of the twenty-five cases did the original type persist alone. In no case were more than three types shown to exist in the throat at any particular time. It must, however, be noted that, at the most, only fifteen colonies were taken from each plate, and that a greater number might have shown even more types in individual patients.

A point which appears to be of some interest is that once a new type occurred in the throat of a patient it tended to persist, either alone or in

conjunction with the original type. When a third type occurred its appearance was either temporary, or if it persisted the other types disappeared. A good example of this was seen in patient no. 3. In turn, type 27 was replaced by type 4. Later 4 was associated with an unknown strain (—), which in turn replaced type 4.

The occurrence of a single type of haemolytic streptococcus in scarlet-fever patients on the first day of a complication

From the data just recorded it seemed at first sight that in future investigation of cross-infections in wards, and of complications among the patients, the additional labour of typing numerous colonies from each plate would be entailed. The following observations, however, showed that this was unnecessary.

A number of cases were swabbed as soon as any clinical manifestations of complications became evident. The cases were divided into the following two categories: (1) those showing complications accompanied by discharges; (2) those showing complications unaccompanied by discharges.

(1) *Complications with discharges*

(*a*) J. W. Age 3½ years. Admitted 5 January 1938. Type 1. Complication, vaginitis. 1 February 1938.

On 30 January 1938 there was a rise of the pulse rate to 114. The following day a slight vaginal discharge was observed. Swabs were taken and a number of colonies were typed.

			Types of haemolytic streptococci											
Date		Colonies ...	1	2	3	4	5	6	7	8	9	10	11	12
31. i. 38	Vagina	Type	4	4	4	4	4	4	4	.	.	.	.	.
	Throat	,,	4	4	4	4	4	4	4	4	4	.	.	.
4. ii. 38	Vagina	,,	4	4	4	4	4	4	4	4	4	4	4	4
	Throat	,,	No streptococci present											

(*b*) J. K. Age 1 year. Admitted 5 January 1938. Type 1. Complication, rhinitis. 22 January 1938.

On the 22nd the temperature rose from an average of 97 to 98·4° F. and pulse rate to 120. Rhinitis was observed.

			Types of haemolytic streptococci											
Date		Colonies ...	1	2	3	4	5	6	7	8	9	10	11	12
22. i. 38	Nose	Type	4	4	4	4	4	4	4	4	4	4	4	4
	Throat	,,	4	4	4	4	4	4	4	4	4	4	.	.
	Nose	,,	4	4	4	4	4	4	4	4	.	.	.	.
	Throat	,,	4	4	4	4	4	4	4	4	4	.	.	.
28. i. 38	Nose	,,	4	4	4	4	4	1	1	1	1	1	1	1
	Throat	,,	4	4	1	1	1	1	1	1	1	1	1	1
2. ii. 38	Nose	,,	1	1	1	1	1	1	8?	8?	.	.	.	.
	Throat	,,	1	1	1	1	1	1	1	1	1	1	.	.
10. ii. 38	Nose	,,	1	1	1	1	1	1	1	8	8	8	8	8
	Throat	,,	1	1	1	1	1	1	1	1	1	1	8	8

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(*c*) E. C. Age 2½ years. Admitted 13 January 1938. Type 2. Complication, rhinitis. 4 February 1938.

This patient had been circumcized at a general hospital on 10 January 1938. On 11 January 1938 the rash appeared.

On admission a swab was taken from the penis which showed type 2; the throat swab was negative.

			Types of haemolytic streptococci											
Date		Colonies ...	1	2	3	4	5	6	7	8	9	10	11	12
13. i. 38	Throat	Type	No haemolytic streptococci present											
	Penis	,,	2	2	.	.	.	.	.	.	.	.	.	.
4. ii. 38	Throat	,,	4	4	4	4	4	4	4	4	4	4	4	4
	Nose	,,	4	4	4	4	4	4	4	4	.	.	.	.
14. ii. 38	Throat	,,	4	4	4	4	4	4	4	4	.	.	.	.
	Nose	,,	4	4	4	4	4	4	4	4	.	.	.	.
23. ii. 38	Throat	,,	4	4	4	4	1	1	1	1	1	1	1	1
	Nose	,,	1	1	1	1	1	1	1	1	.	.	.	.
23. iii. 38	Throat	,,	1	1	1	1	1	1	1	1	2	2	.	.
	Nose	,,	1	1	1	1	1	1	.	.	.	.	.	.
14. iv. 38	Throat	,,	2	2	2	2	2	.	.	.	.	.	.	.
	Nose	,,	No haemolytic streptococci found											

(*d*) I. McI. Age 5½ years. Admitted 16 January 1938. Type 1. Complication, tonsillitis. 1 February 1938.

			Types of haemolytic streptococci											
Date		Colonies ...	1	2	3	4	5	6	7	8	9	10	11	12
1. ii. 38	Throat	Type	25	25	25	25	25	25	25	25	25	25	25	25
2. ii. 38	,,	,,	25	25	25	25	25	25	25	1?	.	.	.	.
3. ii. 38	,,	,,	25	25	25	25	25	25	25	25	25	25	.	.
5. ii. 38	,,	,,	25	25	25	25	25	25	.	.	.	.	.	.
7. ii. 38	,,	,,	25	25	1	1	1	1	1	1	1	1	1	1
10. ii. 38	,,	,,	1	1	1	1	1	1	1	1	.	.	.	.
11. ii. 38	,,	,,	1	1	1	1	1	1	1	1	1	25	.	.

(*e*) C. M. Age 8 years. Admitted 20 January 1938. Type 2. Complications: otorrhoea (L.), 22 January 1938; mastoiditis (L.), 1 February 1938; otitis (R.), 11 February 1938.

			Types of haemolytic streptococci											
Date		Colonies ...	1	2	3	4	5	6	7	8	9	10	11	12
22. i. 38	Throat	Type	3	3	3	3	3	3	3	3	3	3	3	3
	Ear (L.)	,,	3	3	3	3	3	3	3	3	3	3	3	3
26. i. 38	Throat	,,	3	3	3	3	3	3	3	3	.	.	.	.
	Ear (L.)	,,	3	3	3	3	3	3	3	3	3	3	3	3
30. i. 38	Throat	,,	3	3	3	3	3	1	1	1	1	1	.	.
	Ear (L.)	,,	3	3	3	3	3	3	3	3	3	3	3	3
1. ii. 38	Throat	,,	1	1	1	1	1	1	1	1	3	.	.	.
	Mastoid (L.)	,,	3	3	3	3	3	3	3	3	3	3	3	3
11. ii. 38	Throat	Type	8	8	8	8	8	8	8	8	8	8	8	8
	Ear (R.)	,,	8	8	8	8	8	8	8	8	.	.	.	.
	Ear (L.)	,,	3	3	3	3	3	3	3	3	3	3	3	3
26. ii. 38	Throat	,,	4	4	4	4	4	.	.	.	.	.	.	.
	Ear (R.)	,,	4	4	4	4	4	4	4	4	4	4	4	4
	Ear (L.)	,,	No haemolytic streptococci found											
26. iii. 38	Throat	,,	1	1	1	1	1	4	4	4	4	.	.	.
	Ear (R.)	,,	4	4	4	4	.	.	.	.	.	.	.	.
	Ear (L.)	,,	No haemolytic streptococci found											
26. iv. 38	Throat	,,	4	4	4	—	—	—	—	.	.	.	.	.
	Ear (R.)	,,	4	4	4	4	4	4	4	4	4	.	.	.
	Ear (L.)	,,	No haemolytic streptococci found											

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(2) *Complications without discharges*

(*a*) A. W. Age 27 years. Admitted 6 January 1938. Type 1. Complication, arthritis. 17 January 1938.

The patient was admitted with rhinitis. The nasal swab gave the same type as the throat swab.

The temperature was normal by 13 January 1938.

On 17 January 1938 he complained of slight pains in back and neck. On 20 January 1938, polyarthritis and temperature 100·2.

			Types of haemolytic streptococci											
Date		Colonies ...	1	2	3	4	5	6	7	8	9	10	11	12
17. i. 38	Throat	Type	1	1	3	3	3	3	.	.	.	.	.	.
20. i. 38	,,	,,	3	3	3	3	3	3	3	3	3	3	3	3
25. i. 38	,,	,,	3	3	3	3	3	3	3	3	3	.	.	.
10. ii. 38	,,	,,	2	2	2	2	2	2	2	3	.	.	.	.

(*b*) R. C. Age 9 years. Admitted 12 January 1938. Complication, adenitis (L.). 17 January 1938.

			Types of haemolytic streptococci											
Date		Colonies ...	1	2	3	4	5	6	7	8	9	10	11	12
17. i. 38	Throat	Type	2	2	2	2	2	2	2	2	2	2	.	.
18. i. 38	,,	,,	2	2	2	2	2	2	2	2	2	2	2	2
19. i. 38	,,	,,	2	2	2	2	2	.	.	.	.	.	.	.
20. i. 38	,,	,,	2	2	2	2	2	2	2	2	8	.	.	.
21. i. 38	,,	,,	2	2	2	2	8	8	8	8	8	8	8	8
22. i. 38	,,	,,	2	2	2	2	2	2	8	8	.	.	.	.
23. i. 38	,,	,,	2	2	8	8	8	8	8	8	8	8	.	.
24. i. 38	,,	,,	8	8	8	8	8	8	8	8	2	2	.	.
25. i. 38	,,	,,	8	8	8	8	8	8	8	8	8	8	8	.
26. i. 38	,,	,,	1	1	1	1	1	1	1	8	8	.	.	.
27. i. 38	,,	,,	1	1	2	2	2	2	2	2	.	.	.	.
28. i. 38	,,	,,	1	1	1	1	1	1	1	1	1	1	1	1
29. i. 38	,,	,,	1	1	1	1	1	1	1	.	.	.	.	.

It will be observed that in all the cases examined there was present in each only one type of haemolytic streptococcus on the day the complication became manifest.[1]

This suggests that the type of haemolytic streptococcus found in the discharge or throat is the type causing the complication.

From this stage onwards only one colony was picked and typed from each swab culture.

[1] In cases 1 (*e*) and 2 (*a*) this statement at first sight does not apply. Case 1 (*e*) showed two types on the 1 February 1938 and 11 February 1938 respectively (1 and 3, and 8 and 3). It will, however, be observed that the individual swabs of the discharges showed only one type, viz. mastoid (L.), type 3; ear (R.), type 8. Case 2 (*a*) had arthritic pains on 17 January 1938. On that day types 1 and 3 were present in the throat. The arthritis, however, at this stage was not accompanied by any temperature. This only occurred on 20 January 1938, and on that day type 3 only was found.

DATA COLLECTED FROM THE TYPING OF HAEMOLYTIC STREPTOCOCCI OBTAINED BY THE DAILY SWABBING OF ALL PATIENTS IN A SINGLE WARD OVER A PERIOD OF 45 DAYS

In this investigation a single ward was selected and swabs were taken daily of all the patients. This was done, first, to ascertain the effects of the introduction into the ward of new types of haemolytic streptococci and, secondly, to ascertain how long new types were present in the throats of the patients before they produced complications, if any.

From the beginning of March to 15 April all the cases within this ward were swabbed daily, and the haemolytic streptococci, when present, typed.

When discharges occurred in the cases showing complications, cultures were made from these (not from throat swabs). When no discharges were present, the ordinary throat swab was taken. Table 7 summarizes the results and shows that:

(1) After the patient entered the ward the type of haemolytic streptococcus which caused the scarlet fever persisted for an average of 9 days (limits 2 to 16) in the throat before it was replaced temporarily or permanently.

(2) When the original type produced a complication, as in cases 11, 39, 47, 49, it persisted for a longer period, which sometimes extended throughout the illness.

(3) Of the eight cases who were swabbed and typed daily from admission to discharge from hospital, only two did not show, at some period, any cross-infection.

(4) Of the fifty-five cases observed, thirty-seven yielded two or more types of haemolytic streptococci at various times. Of all the cases one showed no haemolytic streptococci, seventeen one type, twenty-two two types, eight three types, six four types and one five types. A considerable amount of cross-infection therefore occurred in the wards.

(5) Two or three days before the onset of the clinical manifestations of complications there were present in the throats of the patients the same types afterwards found to be responsible for the complications. It therefore appears that an incubation period of 2–3 days (extremes 1–4) was necessary before the new strains of streptococci produced complications.

(6) In the majority of patients, before new strains became established in their throats, a period of some days elapsed during which the previous strains appeared to decrease or die out. In cases 4, 6, 9, 15, 26, 28, etc., however, one type was suddenly replaced by another.

(7) After 3 weeks in hospital the number of positive swabs in each case steadily decreased. Negative swabs, however, did not altogether exclude the presence of the type last found in the throat. In case 6, for example, seven negative swabs were followed by a reappearance of type 4; then another five negative swabs were followed by its reappearance. In case 26 six negative

Table 7. *Showing the results of daily swabbing of all patients in a ward*

No. of patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55
Type on admission	1	1	3	–	1	2	0	1	1	1	4	1	–	4	1	1	–	–	1	1	1	3	–	1	4	1	0	1	1	1	1	–	1	–	2	1	2	1	3	3	1	–	1	1	1	0	1	3	1	4	1	1	1	1	4	1
1938																																																								
2 Mar.	1	4	0	1	0	2	0	2	2	0	4	1	–	4	1	1	–	1	1	1	3	–	1	4	1	0	1	1	1	1	–	1	–																							
3	1	0	0	6	0	2	0	2	2	0	**4**	1	–	4	1	1	–	1	1	1	3	–	1	4	1	0	1	1	1	1	–	**1**	–	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
4	1	0	1	6	0	2	0	2	2	0	4	1	–	0	1	1	–	0	1	0	3	–	1	4	1	0	1	1	1	0	–	1	–	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
5	D	0	1	6	0	2	0	1	3	1	4	1	–	4	1	0	–	0	1	1	3	–	1	4	1	0	1	1	1	1	–	1	–	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
6	.	0	1	6	0	2	0	1	3	1	4	1	–	0	1	0	–	1	1	3	3	–	0	4	1	0	1	1	0	–	0	0	–	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
7	.	**0**	1	6	–	2	0	1	3	1	**4**	1	–	0	1	**0**	–	–	1	1	3	–	0	4	1	3	1	1	1	–	–	1	–	2	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
8	.	4	1	–	–	2	0	1	3	0	4	0	–	0	1	0	–	–	1	1	3	–	1	4	1	3	1	1	1	–	–	1	–	2	1	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
9	.	0	0	–	–	4	0	0	**3**	1	0	0	–	4	–	0	–	0	0	1	0	–	–	4	1	**3**	1	1	1	–	0	3	0	0	1	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
10	.	0	1	–	–	4	0	1	3	0	4	0	–	4	–	0	–	0	0	0	0	–	–	4	1	3	1	11	0	–	0	**3**	–	2	1	2	1	3	3	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
11	.	0	1	–	–	**4**	0	1	3	1	0	0	–	4	–	0	–	1	1	1	0	0	0	4	1	3	1	11	0	3	–	3	3	2	1	2	1	3	3	1	–	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
12	.	D	D	–	–	4	D	D	3	D	0	0	–	4	–	0	–	1	0	0	0	0	0	1	3	1	**11**	0	3	–	3	3	2	1	2	1	3	0	1	–	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
13	.	.	.	–	–	4	.	.	0	.	0	0	–	4	–	0	–	0	1	1	0	1	–	0	1	11	0	11	0	0	–	3	0	2	1	0	1	3	**3**	1	–	1	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
14	.	.	.	–	4	4	.	.	3	.	4	0	–	4	–	11	–	0	1	1	0	0	0	0	1	11	1	11	0	0	0	3	0	2	1	2	1	11	**3**	1	–	1	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
15	.	.	.	–	0	4	.	.	D	.	4	D	–	D	–	11	–	3?	0	1	0	0	1	4	1	11	1	11	0	0	–	3	0	0	1	–	1	11	3	1	0	1	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
16	.	.	.	–	0	4	.	.	A	.	0	.	–	.	–	11	–	1	υ	0	0	4	1	0	1	11	0	11	0	3	–	3	0	0	1	0	11	**11**	0	1	0	1	0	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
17	.	.	.	–	0	4	.	.	.	.	0	.	0	.	–	0	–	1	0	0	0	4	1	0	1	11	0	11	0	0	–	3	0	2	1	0	**11**	11	0	1	–	1	0	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
18	.	.	.	–	1	4	.	.	.	.	0	.	–	.	–	0	–	1	0	0	0	4	0	0	1	**11**	0	11	0	0	–	3	1	2	1	11	11	11	0	1	–	0	4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
19	.	.	.	1	1	4	.	.	.	.	4	.	–	.	–	11	–	D	1	D	0	4	4	0	1	11	0	11	0	1	0	3	0	0	1	11	11	11	3	1	–	1	4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
20	.	.	.	1	1	4	.	.	.	.	0	.	0	.	–	0	–	.	11	.	0	**4**	4	4	1	11	0	11	0	1	–	3	–	0	1	0	11	11	3	1	0	1	**4**	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
21	.	.	.	1	1	4	.	.	.	.	0	.	0	.	–	0	–	1	.	–	4	4	0	0	11	0	11	4	1	0	3	0	0	1	0	11	11	3	1	–	1	4	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
22	.	.	.	1	1	4	.	.	.	.	11	.	0	.	–	0	–	.	0	.	–	4	**4**	0	1	11	0	11	4	1	0	3	0	3	1	0	11	11	3	1	–	1	4	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
23	.	.	.	1	1	4	.	.	.	.	4	.	0	.	4	0	0	.	1	.	–	4	4	0	0	11	0	11	4	1	0	0	0	0	1	2	11	11	3	1	–	1	4	0	0	1	3	.	.	.	.	.	.	.	.	.
24	.	.	.	1	1	4	.	.	.	.	4	.	0	.	–	0	–	.	1	.	–	4	4	0	1	11	0	0	4	0	0	3	0	0	1	2	11	0	3	1	–	1	4	2	0	1	3	.	.	.	.	.	.	.	.	.
25	.	.	.	1	1	0	.	.	.	.	0	.	–	.	–	4	0	–	1	.	–	**4**	4	0	1	11	0	11	**4**	1	0	0	0	0	1	2	11	11	0	10?	0	1	4	2	–	1	3	1	.	.	.	.	.	.	.	.	.
26	.	.	.	1	1	4	.	.	.	.	0	.	0	.	4	0	0	.	D	.	–	4	4	0	D	0	D	0	4	0	0	0	0	4?	0	0	11	0	3	1	0	0	4	0	0	1	3	1	4	.	.	.	.	.	.	.
27	.	.	.	0	1	4	.	.	.	.	0	.	0	.	4	0	–	.	.	.	–	4	3	0	.	11	.	0	4	0	0	0	0	0	1	2	11	1	0	0	0	0	4	1	0	1	**3**	1	4	1	1	.	.	.	.	.
28	.	.	.	0	1	4	.	.	.	.	4	.	0	.	**4**	0	–	.	.	.	–	0	3	0	.	0	.	1	4	0	0	0	0	0	1	2	0	11	0	1	1	0	4	1	–	1	3	1	4	1	1	1	.	.	.
29	.	.	.	0	1	4	.	.	.	.	D	.	0	.	.	D	–	.	.	.	–	0	3	D	.	0	.	0	4	D	D	3	D	0	1	2	0	0	0	1	0	1	4	1	0	1	3	0	**4**	0	1	1	1	.	.
30	.	.	.	1	1	0	.	.	.	.	R	.	0	.	.	.	–	.	.	.	–	1	**3**	.	.	0	.	0	4	.	.	3	.	0	1	2	11	1	1?	1	1	0	4	1	0	0	3	1	**4**	1	1	1	1	4	1
31	.	.	.	**1**	1	0	.	.	.	.	.	.	0	.	.	.	–	.	.	.	–	1	3	.	.	0	.	0	4	.	.	0	.	0	1	0	0	1	0	0	1	1	4	1	0	1	3	1	4	1	1	0	1	4	1
1 Apr.	.	.	.	1	1	0	.	.	.	.	.	.	0	.	N	.	–	.	.	.	–	0	3	.	.	0	.	0	4	.	.	3	.	0	1	2	0	1	0	0	0	1	4	1	0	1	3	1	4	1	1	0	0	4	1
2	.	.	.	D	1	0	.	.	.	.	.	.	0	.	A	.	–	.	.	.	0	1	3	.	.	0	.	D	4	.	.	0	.	0	D	2	0	0	0	0	0	1	4	0	0	1	0	4	4	4	1	0	1	1
3	.	.	.	.	0	0	.	.	.	.	.	.	1	.	P	.	0	.	.	.	–	1	3	.	.	11	.	A	4	.	.	0	.	1	.	2	0	0	0	0	–	0	4	11	0	0	3	0	4	4	1	4	1	**4**	1
4	.	.	.	.	1	0	.	.	.	.	.	.	0	.	.	0	.	.	.	.	–	0	3	.	.	0	.	.	4	.	.	0	.	0	.	2	0	1	1	0	–	0	4	0	0	2	3	0	4	0	0	4	1	4	1
5	.	.	.	.	1	0	.	.	.	.	.	.	D	.	*died*	.	0	.	.	.	0	1	3	.	.	D	.	.	4	.	.	2	.	D	.	D	D	0	0	0	D	1	4	0	0	2	3	0	4	0	1	0	0	4	1
6	.	.	.	.	0	4	.	.	.	.	.	.	.	.	.	1	.	.	.	.	0	1	3	.	.	R	.	.	0	.	.	2	.	.	.	.	R	0	0	1	.	1	4	0	0	2	0	0	4	1	1	0	0	4	1
7	.	.	.	.	0	0	.	.	.	.	.	.	.	.	.	1	.	.	.	.	–	1	3	.	.	.	.	.	4	.	.	0	.	.	.	.	.	0	0	1	.	1	4	11	0	2	0	0	4	1	1	6	1	1	4
8	.	.	.	.	1	0	.	.	.	.	.	.	.	.	.	D	.	.	.	.	–	1	3	.	.	.	.	.	0	.	.	0	.	.	.	.	.	1	0	0	.	1	4	11	0	2	0	0	4	1	1	6	1	4	0
9	.	.	.	.	D	0	.	.	.	.	.	.	.	.	.	.	.	.	.	.	–	0	3	.	.	.	.	.	0	.	.	0	.	.	.	.	.	D	D	0	.	D	4	11	0	0	3	1	4	0	1	**6**	6	4	1
10	.	.	.	.	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0	1	3	.	.	.	.	.	0	.	.	11	.	.	.	.	.	A	A	0	.	.	0	0	0	0	3	1	4	0	1	6	1	4	1
11	.	.	.	.	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0	1	0	.	.	.	.	.	4	.	.	11	.	.	.	.	.	.	R	0	.	.	4	0	0	11	0	0	4	0	1	**6**	1	4	0
12	.	.	.	.	.	4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0	1	3	.	.	.	.	.	D	.	.	0	.	.	.	.	.	.	.	11	.	.	4	0	0	11	0	0	4	6	1	6	0	4	0
13	.	.	.	.	.	4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0	1	0	.	.	.	.	.	R	.	.	0	.	.	.	.	.	.	.	11	.	.	4	0	6	0	3	0	4	6	1	6	1	4	0
14	.	.	.	.	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.	.	–	1	0	.	.	.	.	.	.	.	.	0	.	.	.	.	.	.	.	0	.	.	4	0	6	0	0	1	4	0	1	6	1	0	0
15	.	.	.	.	.	0	.	.	.	.	.	.	.	.	.	.	.	.	.	.	–	1	3	.	.	.	.	.	.	.	.	0	.	.	.	.	.	.	.	0	.	.	0	1	6	6	0	1	4	1	1	0	1	4	0
	.	.	.	.	.	R	.	.	.	.	.	.	.	.	.	.	.	.	.	.	N	N	Re	.	.	.	.	.	.	.	.	F	.	.	.	.	.	.	.	R	.	.	.	.	.	.	.	A	.	A	.	.	A	A	.	.
	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	R	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	R	.	.

The figures in black represent the type present on the days the complication was first noted. D = Dates on which the patients were discharged from the hospital. — = Strain could not be typed. 0 = Negative swabs. R = Rhinitis, N = Nephritis, A = Adenitis. P = Pneumonia. Re = Relapse. F = Multiple furunculosis.

swabs were obtained before type 11 again reappeared. Another good example is case 31.

Such a recurrence of a type might possibly be accounted for by re-infection with the same type, and in order to obtain some information on the subject an investigation was made on a patient with type 1 placed in a cubicle by herself. Daily swabs were taken with the following results: 1, 1, 1, 1, 0, 1, 1, 0, 0, 1, 1, 1, 1, 1, 1, 0, 0, 0, 1, 1, 1, 0, 0, 0, 0, 1, 0.

This single case gave sufficient evidence that three or four negative throat swabs do not exclude the possibility that a positive throat swab containing the type last found may be obtained later.

(8) With regard to the types of haemolytic streptococci which were found to produce complications, type 3 accounted for six, type 4 for eight, type 6 for one, type 11 for three, and untyped strains for three.

(9) The untyped strains are interesting. Case 22 developed nephritis and an unknown strain was isolated from the urine. Case 15, a week later, also developed nephritis associated with an unknown strain, and similarly with case 21, who had haematuria 12 days after the last case. Nephritis associated with known strains was not observed. It is doubtful, however, what significance can be attached to these findings.

(10) Case 15 was also interesting. An unknown type appeared on the eighth day, and 3 days later produced nephritis, and right- and left-sided adenitis 3 days later. For 5 days the patient appeared to improve, but the unknown strain persisted. A sudden rise of temperature to 102° F. then occurred, and signs of broncho-pneumonia supervened. As the illness became more severe type 4 made its appearance along with the unknown strain. A few days before death type 4 alone was found. After death swabs were taken from the larynx and trachea. Forty colonies were picked off of which thirty-three colonies belonged to type 4, six to an unknown type, and one to type 11.

This is the only case that was met with throughout this work which had three types of haemolytic streptococcus present in the throat at the same time.

(11) It is difficult to account for the sudden outbreak of type 6 cross-infections after 7 April 1938. Six cases were infected by this type within the course of a week. The last occasion when type 6 was found was on 7 March 1938 in case 4. As the case, however, remained in the ward till 2 April 1938, there is the possibility that this type was still being dispersed through the ward. On the other hand, it may have been carried into the ward by the nursing staff.

COMPARISON OF TYPES OF HAEMOLYTIC STREPTOCOCCI IN COMPLICATIONS WITH THOSE OF THE PRIMARY INFECTING ORGANISMS IN SCARLET FEVER

The following observations were made to ascertain whether any correlation existed between particular types of haemolytic streptococci and complications in scarlet fever. All cases from 1 September 1937 to 31 March 1938, 1–30 June

1938, and 1 September to 30 November 1938, were swabbed on admission and again when complications occurred.

In these periods 471 patients developed complications. Positive swabs were given, and 455 complications occurred in 366 out of the first 384 of these.

The strains of haemolytic streptococci found in the 455 complications are given in Table 8.

Table 8. *Showing types of streptococci and other organisms in 455 complications occurring in 366 patients*

Types	No. of complications	%
1	99	21·9
2	49	11·9
3	31	6·8
4	93	20·4
6	13	2·9
8	8	1·9
11	12	2·6
15	17	3·7
23	4	0·9
25	4	0·9
27	9	1·9
28	6	1·3
Staph. aureus	7	1·5
Strept. viridans	4	0·9
Mixed infections	19	4·1
B. coli	4	0·9
Untyped haem. strept.	76	17·7
	455	

(1) Of the complications 280 were produced by a type different from that present when the patient entered hospital.

(2) The same type as that present on admission accounted for 92.

(3) Strains which could not be typed, produced 49 of the complications occurring in patients who had untyped strains on entering hospital. These complications, therefore, belong either to (1) or (2).

(4) Bacteria other than streptococci accounted for 34 complications.

Converted into percentages these figures are:

(1) Complication type different from type on admission ... 61·5 %
(2) Complication type same as type on admission ... ... 20·2 %
(3) Untyped strains in both cases ... ... 10·8 %
(4) Complications due to other bacteria ... ... 7·5 %

(5) Of the sixty-three patients who had typed strains in their throats and developed complications before the fifth day thirty-three had the same type in their complications. After the fifth day in the wards there was a steady

increase in the number of complications associated with types of haemolytic streptococci differing from the original ones. Thus after the second week over 90 % of complications were associated with new strains.

This observation is significant for it suggests that the longer the patients remain in the wards the more likely are they to become infected with new strains, which may be responsible for complications. This statement must, however, be qualified, for it was noted that after the patients had been in the wards for some considerable time the throat swabs became increasingly negative as regards haemolytic streptococci, which suggests that, after a longer period of time, the patients exposed to cross-infection, become the more immune to haemolytic streptococci in general.

Table 9 shows the steady decrease of haemolytic streptococci in the throats of uncomplicated cases in various wards during their stay in hospital. Patients leaving hospital before the 29th day and complicated cases with discharges for long periods were not included in this survey. The swabs were taken at the end of each week.

Table 9. *Showing the decrease in haemolytic streptococci in the throats of uncomplicated cases*

Case no.	1st week	2nd week	3rd week	4th week	During 5th week
1	×	×	×	0	0
2	×	×	0	×	0
3	×	×	×	×	×
4	×	0	0	0	0
5	×	×	×	0	×
6	×	×	×	0	0
7	×	×	0	×	0
8	×	×	×	×	0
9	×	0	×	×	×
10	×	×	0	0	0
11	×	0	×	×	×
12	×	×	×	×	0
13	×	×	0	×	0
14	×	×	0	0	×
15	0	×	×	0	×
16	×	×	0	0	0
17	×	×	×	×	0
18	×	×	×	0	0
19	×	×	×	0	0
20	×	×	0	×	0
21	×	0	×	0	×
22	×	0	0	×	0
23	×	×	0	0	×
24	×	×	0	0	0
25	×	×	×	0	0
26	×	×	×	×	0
27	×	×	×	0	0
28	×	×	0	×	×
29	×	×	×	0	×
30	×	×	×	0	0

× = positive and 0 = negative culture.

After the 1st week out of 30 cases 1 was negative.
„ 2nd „ „ 3 were negative
„ 3rd „ „ 8 „
„ 4th „ „ 15 „
„ 5th „ „ 20 „

(6) A classification of the types of haemolytic streptococci found on admission in the 366 cases, and for comparison in a number of uncomplicated cases during the same period is given in Table 10.

Table 10. *Showing types of haemolytic streptococci found on admission in* 366 *cases which developed, and* 932 *cases which did not develop, complications*

Type	No. of patients with complications	%	No. of patients without complications	%
1	221	60·4	515	55·2
2	22	6·0	101	10·8
3	4	1·1	52	5·6
4	31	8·5	33	3·5
8	7	1·9	22	2·4
11	3	0·9	12	1·3
15	1	0·3	12	1·3
22	1	0·3	3	0·3
27	1	0·3	7	0·8
28	1	0·3	2	0·2
Untyped	74	20·2	173	18·6
	366	100·0	932	100·0

The significance of these figures is not quite clear. Table 11, showing the percentages of the first four types which are the most frequent, may be helpful.

Table 11. *Showing the percentages of types* 1–4

Types	Percentage of types on admission in cases later showing complications	Percentage of types in cases when complications arose	Percentage of types in cases without complications
1	60·4	21·9	55·2
2	6·0	11·9	10·8
3	1·1	6·8	5·6
4	8·5	20·4	3·5

Type 1. The percentages of this type on admission in both cases with and without complications were nearly the same (plus-minus 60 %). It was found in 21·9 % of complications. Type 1 does not seem to be responsible for complications to the same extent as the other three types.

Types 2 *and* 3. The percentage occurrence of these types on admission, in patients who later had complications, was low (6·0 and 1·1), but in complications and in uncomplicated cases was high (11·9, 6·8 and 10·8, 5·6). The low percentages in column 1 and the high percentages in columns 2 and 3 appear to indicate that types 2 and 3 were more apt to produce complications than type 1 (but only in those cases which were admitted without this type).

Type 4. Twice the number of cases admitted with this type showed complication later as showed no complications (8·5 %, 3·5 %). It was present in 20·4 % of the complications. Type 4 is particularly interesting, because twenty of the thirty-one cases who were admitted with this strain also developed complications from it, indicating the special liability of the strain to cause complications. Only 3·9 % of cases which did not develop complications were admitted with this type.

From these observations it seems that type 1 is not very liable to cause complications, and that the considerable number associated with it are due to its preponderance in the wards, since it is the primary organism in more than 50 % of the cases admitted.

Types 2 and 3 are more likely to cause complications than type 1, but only in cases not admitted with these types.

Type 4 is specially liable to be the cause of complication accounting for 20·4 % about as many as produced by type 1, which, however, was seven times as common in patients on admission.

Types 8, 11, 15, 22 and 27 fall into the same class as types 2 and 3. They produce from 0·9 to 3·7 % of complications, but most of the complications occur in patients admitted with other types, particularly type 1. Type 15 appears to be slightly more liable to cause complications than the other types.

Type 28 (on the result of an investigation carried out in May 1938) falls into the same class as type 4.

Correlation of bacteriological and clinical findings

(*a*) *Uncomplicated cases*

Of the 1432 cases swabbed during September to December 1937, January to March 1938, and June of the same year, 949 of those which gave positive swabs developed no complications: type 1 was present in 515, type 2 in 101, type 3 in 52, type 4 in 33, type 6 in 6, type 8 in 22, type 11 in 12, type 15 in 12, type 22 in 3, type 23 in 2, type 25 in 9, type 27 in 7, type 28 in 2 and untyped strain in 173.

Patients with types 1, 8, 11 and 25 showed the mildest form of scarlet fever, and their average stay in hospital was 24·8 days.

The average stay in hospital of patients with types 2, 15, 22, 23 and 28 was 27·8 days.

Twelve patients with type 15 remained in hospital for an average period of 30·7 days.

The average stay in hospital of patients with types 3, 4, 6 and 27 was 34 days. It remains evident that type 4 was one of the most pathogenic of those encountered.

(*b*) *Cases developing complications*

Table 12 was constructed to show the relationship between the types and the complications.

This table does not take into account the complications caused by other organisms than haemolytic streptococci.

Adenitis. Of the 404 complications 169 were adenitis. Type 1 produced the greatest number, namely, forty-one. Types 2, 4 and certain unknown strains produced eighty-two examples of adenitis.

Table 12. *Showing the relation between the types and complications*

Type	Ad.	Rh.	Ot.	Ma.	Ar.	Va.	En.	Ne.	Py.	Re.	O.C.	
1	41	19	15	2	11	2	—	—	1	1	My. 2	(2·1%)
	43·2%	20·0%	15·8%	2·1%	11·9%	2·1%	—	—	1·1%	1·1%	LS. 1	(1·1%)
2	27	5	6	—	6	—	—	—	—	1	Pa. 1	(2·2%)
	58·7%	10·9%	13·0%	—	13·0%	—	—	—	—	2·2%		
3	10	5	7	1	3	1	—	—	1	2	Pe. 1	(3·1%)
	31·3%	15·6%	21·9%	3·1%	9·4%	3·1%	—	—	3·1%	6·3%	D. 1	(3·1%)
4	30	15	25	2	8	3	1	1	3	—	Pa. 1	(1·1%)
	32·9%	16·5%	27·5%	2·2%	8·8%	3·3%	1·1%	1·1%	3·3%	—	D. 1	(1·1%)
											Pn. 1	(1·1%)
											LS. 1	(1·1%)
6	6	2	2	—	—	—	—	—	—	—		
	60·0%	20·0%	20·0%	—	—	—	—	—	—	—		
8	4	2	1	—	1	2	—	1	—	—		
	36·4%	18·2%	9·1%	—	9·1%	18·2%	—	9·1%	—	—		
11	6	3	—	—	—	1	—	—	—	1		
	54·5%	27·3%	—	—	—	9·1%	—	—	—	9·1%		
15	7	1	5	1	—	1	—	—	—	—	LS. 1	(6·3%)
	43·8%	6·3%	31·3%	6·3%	—	6·3%	—	—	—	—		
23	—	—	—	—	—	3	—	—	—	—		
	—	—	—	—	—	100·0%	—	—	—	—		
25	2	—	—	—	—	2	—	—	—	—	To. 2	(33·3%)
	33·3%	—	—	—	—	33·3%	—	—	—	—		
27	9	—	—	—	—	—	—	—	—	—		
	100·0%	—	—	—	—	—	—	—	—	—		
28	2	—	—	—	1	—	—	—	—	—	En. 3	(50·0%)
	33·3%	—	—	—	16·7%	—	—	—	—	—		
—	25	13	19	—	3	—	—	3	1	1	D. 1	(1·5%)
	37·3%	19·4%	28·4%	—	4·5%	—	—	4·5%	1·5%	1·5%	To. 1	(1·5%)

Ad. = adenitis; Ot. = otorrhoea; Ar. = arthritis; En. = endocarditis; Rh. = rhinitis; Ma. = mastoiditis; Va. = vaginitis; Ne. = nephritis; Py. = pyrexia; Re. = relapse; O.C. = other complications; My. = myositis; D. = death; To. = tonsillitis; Pn. = pneumonia; LS. = local sepsis; Pa. = peritonsillar abscess; Pe. = pericarditis.

The figures refer to the numbers of complications, and the percentages to occurrence of each type in the complications caused by it.

Type 27 was found only nine times, and always in this complication. After this came type 6 with 60 %, then type 2 with 58·7 % and type 11 with 54·5 %, thereafter types 1, 3, 4, 8, 15, 25 and 28. Of the frequently occurring types, 2 was the most important, for more than half of the complications it produced were adenitis.

Rhinitis. This condition occurred in sixty-five cases and type 1 accounted for nineteen, type 4 for fifteen cases, and unknown strains for thirteen.

Type 11 showed the greatest tendency to produce this complication—27·3 % of all complications due to this type being rhinitis. Thereafter came *type 6 with 20 %, unknown strains with 19·4 %, type 8 with 18·2 %,* and types 4 and 3 with 16·5 and 15·6 % respectively. Of the common types these last two showed the greatest tendency to produce rhinitis.

Otorrhoea occurred in eighty cases, of which twenty-five were due to type 4, nineteen to unknown strains and fifteen to type 1.

Type 15 showed the greatest tendency to produce this complication, 31·3 % of all complications due to this type being otorrhoea. Of the common

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types, 4 is the most important, for 27·5 % of the complications produced by this type were otorrhoea.

Mastoiditis occurred in six cases. Types 1 and 4 being responsible for two cases each, and types 3 and 15 for one case each.

Arthritis occurred in thirty-three cases. Type 1 was responsible for 11, but type 2 showed the greatest tendency to produce this complication.

Vaginitis occurred in fifteen cases. Types 4 and 23 each produced three cases, the latter causing no other complication.

Nephritis occurred in five cases, of which three were due to unknown types, and the other two to types 4 and 8.

Deaths. Three deaths, due to types 3, 4 and an unknown type respectively, occurred. 3·1 % cases with complications due to type 3 died.

The types associated with other complications can be ascertained from the table, and special attention may be drawn to 25 and 28; 50 % of complications due to the latter being enteritis in which blood and mucus were found in the stools. In all three cases the organisms were isolated from the faeces. In many instances small numbers only of cases are dealt with and to arrive at more convincing percentages in these cases it would be necessary to investigate the matter further.

Correlation of type with average stay in hospital

An interesting fact which has come to light in this investigation was that the average stay in hospital of cases with complications varied with the type (Table 13).

Table 13. *Showing the average stay in hospital of cases showing complications associated with each type*

Type	Average stay in hospital days	Type	Average stay in hospital days
3	63·0	Untyped strains	44·3
4	59·4	2	43·2
6	57·5	23	40·2
27	49·9	11	34·7
15	47·7	28	34·7
1	45·1	25	32·5
8	44·7		

Taking all the complications together, we find that the average stay in hospital per case was 52·0 days.

For the period of fifteen months, 1 September 1937 to 30 November 1938, there were 600 cases which developed complications.

The average stay in hospital for cases without complications was 27·3 days. The difference between the two averages, 52·0 and 27·3, is striking. The 600 cases with complications were therefore an additional burden to the hospital to the extent of 14,400 days.

Further observations

A. During the month of May 1938 there were 131 admissions of scarlet-fever cases to the City Fever Hospital, and during the same period there were fifty-two cases who developed complications. The total number of complications were seventy-eight: adenitis, forty-five; otorrhoea, thirteen; rhinitis, twelve; vaginitis, four; nephritis, two; and arthritis, two.

During this period a routine examination of all cases was not being undertaken and only twenty cases were swabbed on admission with the following results: eleven cases showed type 1, two type 2, one case type 4, one case type 11, two cases type 25, one case type 28, two cases an unknown type and one granular.

The types were determined in fifteen of the complications (Table 14).

Table 14. *Showing the types associated with complications in May* 1938

Patient	Admitted	Complication	Type of haemolytic streptococcus
1	11. v. 38	Otorrhoea	28
2	12. v. 38	Rhinitis	—
3	12. v. 38	Otorrhoea	28
4	15. v. 38	Otorrhoea	1
5	15. v. 38	Otorrhoea	28
6	16. v. 38	Otorrhoea	28
7	19. v. 38	Otorrhoea	4
8	22. v. 38	Vaginitis	28
9	23. v. 38	Vaginitis	28
10	23. v. 38	Otorrhoea	4
11	27. v. 38	Adenitis	28
12	28. v. 38	Arthritis of arms	28
13	28. v. 38	Adenitis	0
14	30. v. 38	Adenitis	2
15	31. v. 38	Otorrhoea and vaginitis	28

Of the fourteen complications nine showed type 28 (64·3 %), two type 4, one type 2, one type 1, one an unknown type, and one had a negative throat swab.

Although only a small percentage of the cases with complications were typed, the fact that nine out of the fifteen cases showed complications due to type 28 suggests that the great rise of complications during May was due to an active spread of this type through the scarlet-fever wards of the hospital.

That one of the cases swabbed had this type on admission suggests that other cases with this type may also have entered hospital and caused the spread of complications, from this type, in several of the wards.

The important and interesting question of virulence arises here.

Type 28 had been found in the throats of three patients on admission during the months of September, October and November 1937, and also occurred in six complications—adenitis (two), arthritis (one), enteritis (three).

It might seem difficult to understand how a type of streptococcus which presented the virulence shown by type 28 during the May outburst of complications remained relatively inactive when present in the hospital some months before, but in all probability virulence depends on factors which cannot easily be determined by the usual methods of investigation.

B. During the 3 months, 1 September to 30 November 1938, all admissions were swabbed and 248 out of 259 cases gave positive throat swabs, sixty due to type 1, eleven to type 2, 110 to type 4, fourteen to type 6, nine to type 8, and forty-four to unknown types.

This was almost the reverse of the state of affairs during the same period of 1937, when 316 cases were due to type 1 and twenty-eight to type 4.

During September, October and November 1938, seventy-five complications occurred, in 57 patients, classified as follows: adenitis (five), rhinitis (nineteen), otorrhoea (eighteen), arthritis (three), vaginitis (one), nephritis (two), otitis media (two), pyelitis (one), and relapses (four).

Table 15 compares the numbers of the various types of haemolytic streptococci found on admission and during complications.

Table 15. *Showing types on admission and in complications in May* 1938

Types	No. of cases who developed complications. (Types on admission)	%	No. of complications due to the various types	%
1	24	42·1	10	13·3
2	4	7·0	7	9·3
4	17	29·8	38	50·6
6	0		5	6·7
8	1		4	5·3
22	0		1	1·3
Untyped	8	14·8	8	10·6
Negative swabs	3	5·3	2	2·6
Totals	57		75	

These results may be compared with those obtained from typing the cases without complications.

Of the 259 cases swabbed during September, October and November 1938 202 did not develop complications. Of these thirty-six (17·9 %) were due to type 1, seven (3·6 %) to type 2, ninety-three (46·0 %) to type 4, fourteen (6·9 %) to type 6, eight (3·5 %) to type 8, thirty-six (17·9 %) to unknown types, and eight (3·5 %) had negative swabs.

Of the twenty-four cases which entered hospital with type 1, fifteen developed complications which were due to type 4, apparently indicating that patients admitted with type 1 were particularly liable to complications due to type 4. This susceptibility appears to be of greater importance than the actual pathogenicity of type 4, since out of 202 cases 110 were admitted with type 4 and of these ninety-three remained free from complications. The conclusion therefore is that patients who contract scarlet fever from type 4 are not as

likely to get complications from that type, as those who contract scarlet fever from type 1 and subsequently become infected with type 4.

In other words, it would appear that cases which develop scarlet fever from the more pathogenic types of haemolytic streptococci build up an immunity to those types, and so decrease the possibility of complications with the more virulent as well as with less virulent strains. It is difficult to find another explanation for the relatively low complication rate among patients of the September-December 1938 epidemic, particularly since it is known that type 4 accounted for almost half the number of admissions.

The fact that more than a third of the cases admitted with type 1 and only eight out of 110 cases admitted with type 4 contracted complications with type 4, appears strongly in favour of the above assertion.

A further analysis of the complications shows that types 2, 6, 8, 22 and the untyped strains individually accounted for only a small percentage of the total complications.

Discussion

The typing of all the strains of haemolytic streptococci which are pathogenic to man, is still a matter of considerable difficulty, because there are a number of strains which fail to produce homogeneous suspensions, and are therefore unsuitable for the agglutination method of typing, and because a number of strains which produce suitable suspensions fail to agglutinate with any of the type-specific sera obtained from rabbits prepared from Griffith's thirty types of haemolytic streptococci.

The first difficulty can partly be overcome by suitable cultural methods, which take into account the media for growing the organisms, and the period of incubation of the cultures. The media generally used, with certain modifications, are those specified by Griffith (1934), who advocated that in testing an unknown strain colonies should be taken from primary plate cultures and subcultured in each of the following three media: (1) plain trypsinized meat broth; (2) the same broth with 5 % serum (bovine or horse); (3) the same broth with 5 % ascitic fluid. He mentions further that plain broth cultures are more sensitive to the action of agglutinating sera but more liable to become granular than ascitic fluid broth cultures.

The methods laid down by Griffith were at first adhered to in this investigation, but it was found that certain modifications were advantageous in dealing with large numbers of strains. Instead of employing three media, the organisms were first cultured in only one, namely, a modification of Okell's medium, with 3 % of ascitic fluid added. In this medium 51 % of cultures showed uniform suspensions. All the granular strains were thereafter cultured in three media, ordinary broth, rabbit serum broth, and pure ascitic fluid. By these means 93 % of cultures were rendered suitable for typing.

In agreement with Griffith's (1934) observation, it was found that although the ascitic-broth medium gave the best cultural results, it yielded the highest

percentage of homogeneous suspensions which could not be typed. The latter suspensions were also subcultured in the three media just mentioned, and again tested with the type-specific sera. The fact that an appreciable proportion of the uniform suspensions could not be typed may have been due either because new types were being dealt with or the loss of type specificity by frequent subculturing.

The heaviest growths were obtained in pure ascitic fluid, but they were for the most part highly granular. It appears, therefore, that the addition of excess of broth modifies this tendency. On the other hand the ascitic fluid, which was all obtained from one patient, may have possessed agglutinating powers, apparent only when the fluid was used in the undiluted state.

The time factor has been shown to be of the utmost importance in the preparation of suitable suspensions. After the growth had reached a certain stage it readily became granular if it was left at 37° C. It was, however, found that if the cultures were removed from the incubator as soon as a fairly marked haze appeared in the medium, and left at room temperature for 18–24 hr., the tendency to granular growth did not advance as rapidly. This procedure also appreciably enhanced the type specificity of the organisms. The time taken for the organisms to reach a suitable stage for removal from the incubator was found to be for the most part 6–9 hr. This time was longer the smaller the inoculum. A heavy inoculum was therefore the most suitable.

The number of days spent in hospital by cases of scarlet fever developing complications, in excess of the average, during the period September 1937 to November 1938 was 14,400 days, a heavy additional burden to the hospital authorities, which makes a more comprehensive study of the underlying causes of scarlet-fever complications very desirable.

Complications seem to arise from a number of causes, of which the most important appears to be cross-infection with new strains of haemolytic streptococci. Of all complications 61·5 % have been found to be due to types differing from those present when the patients were admitted to hospital, 20·2 % to the type found on admission, 10·8 % to untypable strains and 7·5 % to other organisms. It would be difficult to determine without laborious investigation, to which of the first two groups the majority of cases due to untypable strains belong.

Since the bulk of the complications are due to cross-infection with new types, this is the problem which deserves most serious consideration. The haemolytic streptococcus may be conveyed from patient to patient by one of four methods, by direct contact, by indirect contact, by fomites and food, and by the air, including in this method droplet infection.

Direct contact seems to play some part in the transmission of streptococci, for many complications arise only after the patients have been allowed up, and come into free contact with one another.

The average times which elapsed before the various complications arose, were as follows: adenitis 11·7 days, rhinitis 14·4 days, otorrhoea 13·8 days,

arthritis 7·8 days, nephritis 18·3 days, peritonsillar abscess 6·1 days, vaginitis 19 days, myositis 5 days, and pyrexia 15·1 days.

These figures, however, are somewhat misleading, since it was found that the highest incidence of complications occurred during the fifth, sixth and seventh days in hospital. Out of 282 complications one complication occurred on the first day, ten on the second, thirty-one on the third, eleven on the fourth, twenty-six on the fifth, twenty-three on the sixth, sixteen on the seventh, eighteen on the eighth, nine on the ninth, nine on the tenth, twelve on the eleventh, fourteen on the twelfth, eight on the thirteenth, seven on the fourteenth, eleven on the fifteenth, five on the sixteenth, nine on the seventeenth, five on the eighteenth, five on the nineteenth, five on the twentieth, eleven on the twenty-first, four on the twenty-second, six on the twenty-third, five on the twenty-fourth, seven on the twenty-fifth, and twenty-four after the twenty-fifth.

Of the 282 complications, 126 occurred before the ninth day, and 185 by the end of the second week. Thus by the time the average patient was allowed up more than half the complications had already occurred.

A number of the ninety-seven complications which occurred after the second week may have been due to contact, but all were not due to contact, for it was shown, in an enquiry not recorded here, that a number of convalescent patients, who were going about the ward, contracted complications almost simultaneously with type 6 streptococcus, and the only source of infection in the ward, at that time, was an isolated cot-patient with rhinitis from whom type 6 had been isolated.

By a series of enquiries it was ascertained that in over 99 % of early cases of scarlet fever the types of haemolytic streptococcus in the nose and throat were the same when both swabs proved positive, and it was concluded that in the great majority of such cases only one type of haemolytic streptococcus is present. It was shown that after some days in the wards the state of affairs was very different, for then more than one type of haemolytic streptococcus could be isolated from the throats of individual patients. This suggests that cross-infection of patients is a common feature in scarlet-fever wards. By daily swabbings of the throats of all the patients in a particular ward over a prolonged period it was shown that most of the cases became infected with new types of haemolytic streptococci. These new types were, in the majority of cases examined, found to be the cause of such complications as occurred.

On the day a complication occurred in cases of scarlet fever, and for 2–3 days preceding it, only one type of haemolytic streptococcus was isolated from the throats of individual patients. At a later date the type originally present might again be found, in which case the strain responsible for the complication tended to disappear.

It appeared that the complications which developed during the first few days in hospital were mostly due to the type of haemolytic streptococcus with which the patient entered hospital, whereas the later complications were for

the most part the result of cross-infection from other cases with new types. It seems possible that this can be explained in terms of immunity: during the early stages of scarlet fever the patient's immunity is low for the aetiological type of haemolytic streptococcus, and complications with that type are most liable to occur. Later the immunity to the original type is high and complications from that type are less liable to occur.

The various types of haemolytic streptococci which were found in scarlet fever appeared to vary in the severity of the scarlet fever they produced. Thus it was found that of the common epidemiological types, 2 and particularly 1, produced a milder form of scarlet fever than 3 and 4. It was observed that cases admitted into hospital with the less pathogenic types were more liable later to develop complications with the more pathogenic types than were the patients admitted with these latter types. Fig. 1 shows that when admissions with type 1 were numerous (end of 1937 and first half of 1938) the complication rate was relatively high (mostly with type 4); whereas when admissions with type 4 were on the increase (end of 1938) the complication rate steadily declined.

Theoretically, therefore, when an epidemic occurs showing mild cases the complication rate should be high provided a highly pathogenic type of haemolytic streptococcus persists among the cases with complications in the wards. Conversely, when the epidemic is accompanied with severe cases the complication rate should be low.

Summary and conclusions

1. The paper records the results of a study of the serological types of haemolytic streptococci in scarlet fever, and their clinical and epidemiological relationships, with particular reference to cross-infection.

2. Tables are given showing statistical records of scarlet-fever cases which were examined bacteriologically in an infectious diseases hospital over a period of 13 months. In all, 1831 cases were studied, including 471 with complications.

3. In 415 cases in which swab cultures were made from the throat and nose on admission, both throat and nasal swabs yielded haemolytic streptococci in 115, and the nasal swab alone in nine cases (2·5 %). The total number of throat swabs giving positive results was 357. In only two cases were different types of haemolytic streptococci found in the throat and nose.

4. Only a single type of haemolytic streptococcus was found to be present in a series of twenty-eight early cases in which many colonies of the primary culture were examined serologically.

5. More than one type of haemolytic streptococcus was found in the throats of a series of twenty-five individual cases during a period of residence in hospital when swabs were plated at weekly intervals, and many colonies examined from each plate. In only six of the twenty-five cases did the original type persist throughout the period of residence in hospital. A new type ap-

peared to replace the original strain. In one case three types of haemolytic streptococci were present in the throat at a particular time.

6. On the day a complication occurred in a scarlet-fever case only a single type of haemolytic streptococcus was found to be present in the throat or discharge. This suggests that the strain responsible for the complication is present before the complication becomes evident.

7. Many colonies from the swab cultures of seven patients, who developed complications, were serologically examined. On the day a complication occurred a single type of haemolytic streptococcus was found present in each case.

8. The swab cultures of all the patients in a ward were examined daily over a period of 45 days. Of fifty-five patients thirty-seven were infected by two or more types of haemolytic streptococci. Of these the original type persisted for an average of 9 days. Two or three days before a complication appeared the responsible type was present in the throat.

9. 455 cases with complications were studied bacteriologically. In thirty-four the complication was due to organisms other than haemolytic streptococci (7·5 %). 280 were due to a type of haemolytic streptococcus other than that with which the patient entered the hospital (61·5 %), whereas only ninety-two were due to the same type (20·2 %). In forty-nine both the original strain of haemolytic streptococcus and that associated with the complication, could not be typed (10·8 %). In patients who had been 2 weeks resident in hospital 90 % of complications were due to new types of streptococci.

10. Tables comparing the types of haemolytic streptococci found on admission and during the first day of a complication are appended. Reference to the types found in cases which did not develop complications is also made.

11. The types of haemolytic streptococci and the severity of the scarlet fever produced by each have been correlated in 949 cases without complications.

12. Records are included of a further series of observations made on 390 cases of scarlet fever occurring at a later date. The types of haemolytic streptococci present were compared with those of the same period in the previous year. While type 1 was the prevalent form in the earlier enquiry, type 4 was the dominant form in the later.

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