AN INQUIRY INTO THE INCIDENCE OF CROSS-INFECTIONS, COMPLICATIONS AND RETURN CASES IN SCARLET FEVER*

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INTRODUCTION

Within recent years considerable attention has been paid to the epidemiology of scarlet fever and other infections due to *Streptococcus pyogenes*. This organism has been shown to be very widely distributed in the community, both associated with disease and in apparently healthy carriers. Nevertheless, it particularly lends itself to study owing to the ease with which strains can be isolated and subdivided serologically into a number of types. In this paper an account is given of observations made by three laboratories in widely separated parts of the country. Certain aspects of the epidemiology of scarlet fever have been studied and observations made over the same period of time in a similar manner, so that results can be compared and contrasted.

PROCEDURE AND TECHNIQUE

The investigation was carried out by the Emergency Public Health Laboratories at Oxford, Cambridge and Cardiff in co-operation with the corresponding three isolation hospitals and public health departments. The general procedure adopted at each centre was the same, although there were minor differences in detail. Each case of scarlet fever admitted to hospital was investigated if the initial diagnosis was later confirmed clinically. However, not every notified case was admitted to hospital, as a varying proportion were nursed at home. A number of cases have also had to be omitted from the final analysis of the results, because for various reasons they were not sufficiently followed up. Most of the patients came from the immediate locality, although the Cambridge Borough Isolation Hospital in addition served the surrounding rural area within a radius of about 20 miles. The investigation was continued for 2 years, between 1 January 1941 and 31 December 1942, but Oxford unfortunately was forced to discontinue its observations between 1 January and 23 June 1942 owing to shortage of health visitors.

When a case of scarlet fever was notified the procedure was as follows. The patient was transferred to the isolation hospital, and nose and throat

swabs were taken as soon as possible after admission. The patient's home was visited immediately by a health visitor (at Oxford this visit was made within 7 days of the patient's admission to hospital) and nose and throat swabs were taken from all the members of the household. Subsequently weekly swabs (nose and throat) were taken from the patient while in hospital. Immediately the patient was discharged the home was again visited and swabs were taken from the convalescent domiciliary patient and from all members of the household. This swabbing was repeated once weekly for the next 3 weeks. While the patient was in hospital a record was kept of the clinical condition and progress with particular reference to the incidence of complications. Attention was also paid to the rest of the patient's household and a watch was kept for any return cases of scarlet fever. It was not, however, possible in all cases to investigate home contacts or to follow up the convalescent patient after discharge from hospital.

Clinical, epidemiological and bacteriological information was recorded on printed cards. For each patient three different cards were used, each of a distinctive colour. One was filled in by the isolation hospital and recorded the patient's name, address, age, sex and hospital serial number, the dates of onset of the disease, admission to and discharge from hospital, an assessment of the severity of the disease, the treatment, the nature and date of onset of any complications and the condition of the nose, throat, ears and skin on discharge. The dates and results of any swabs taken in hospital were also entered on the card. A second card was filled in by the health visitor. This gave details of the patient's school or place of employment, the name of the retailer of milk and the names of other cases of scarlet fever in contact with the patient with the dates of onset of their infections. The dates of swabs taken from home and other contacts, and from the patient himself after discharge, were also entered, with notes as to their health at the time of swabbing. The third card was completed by the laboratory and contained the results of bacteriological examinations. For each swab received from the patient

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* A report to the Medical Research Council.

or his contacts the serial number of the specimen, the presence or absence of haemolytic streptococci, the approximate proportion and macroscopic appearance of the colonies of haemolytic streptococci and their serological group and type were entered. Each patient was given a serial number in order to assist the sorting of the cards.

When received by the laboratory swabs were plated out on horse-blood agar and the plates were examined for haemolytic streptococci after 24 hr. incubation at 37° C. At the beginning of the investigation plates were only incubated aerobically, but attempts were made later in each of the laboratories to increase the proportion of positive isolations by other cultural methods. It was found that anaerobic cultivation sometimes led to the isolation of haemolytic streptococci when the aerobic plates were negative. Blood plates or glucose broth containing 1 in 500,000 parts gentian violet (Garrod, 1942) and incubated aerobically

and Cambridge are very similar. Haemolytic streptococci were isolated from about 80 % of cases; Cardiff with 67 % had less success. It is probable that the proportion of cases in which haemolytic streptococci can be demonstrated by culture largely depends on the efficiency with which the swabbing is performed. Where swabs were repeated, either immediately or during the first 8 days of the patient's stay in hospital, that is before cross-infection was likely to have occurred, they were frequently found to be positive when the admission swabs had been negative. In the fifth column of Table 1 the number of these additional positives is given and their inclusion in the total raises the percentage of positive isolations to 81·9 % within 8 days of admission. There were forty-four (6·8 %) patients from whom haemolytic streptococci were never at any time isolated throughout their stay in hospital.

At Cambridge swabs were taken from nose and

Table 1. *Presence of haemolytic streptococci (group A) in swabs taken on admission to hospital or within 1 week of admission*

Centre	Total no. of cases	Cases positive *Str. pyogenes* on admission		No. of additional cases positive *Str. pyogenes* within 8 days of admission	Cases negative *Str. pyogenes* throughout stay in hospital	
		No.	%		No.	%
Oxford*	181	145	80·1	5	14	7·7
Cambridge	230	184	80·0	13	15	6·5
Cardiff	237	159	67·1	25	15	6·3
Total	648	488	75·3	43	44	6·8

* Four cases omitted because of insufficient data.

gave additional positive isolations, especially from nasal swabs in which staphylococci were predominant. From plates which showed haemolytic streptococci one colony was picked off, grouped and typed. Two or more colonies were picked off where they were of different colonial appearance. Grouping was carried out by Fuller's method (1938) or by Fry's modification (1940) of the original Lancefield technique. Serological typing by Griffith's slide-agglutination technique (1926, 1934) was attempted on all strains of haemolytic streptococci found to belong to group A.

THE PRESENCE OF HAEMOLYTIC STREPTO- COCCI IN NOSE AND THROAT ON AD- MISSION TO HOSPITAL

A total of 648 cases of scarlet fever were investigated by the three laboratories. Table 1 shows the number and percentage of cases from which haemolytic streptococci of group A were isolated from swabs taken immediately after the patient's admission to hospital. It will be noted that the results for Oxford

throat in ten consecutive patients with scarlet fever, every 4 hr. during the first 24 hr. in hospital. The results demonstrated the probability of sampling errors, as in only one case were haemolytic streptococci isolated at every swabbing. In three of the cases the throat was persistently negative.

In nearly every series of consecutive cases of scarlet fever from which nose and throat swabs have been examined for haemolytic streptococci (Gunn & Griffith, 1928; Brown & Allison, 1935a; Griffith & Allison, 1936; de Waal, 1940), there has been a small percentage, varying from 3 to 12 %, yielding negative results even on repeated examination. This may in part be due to inaccessibility of the organisms at the site of invasion or to the presence of a primary focus elsewhere in the body. However, in this series, known cases of surgical scarlet fever were very few. Attention has recently been drawn to non-haemolytic, or feebly haemolytic, strains of group A streptococci and such strains are liable to be missed during the routine examination of blood agar plates (Colebrook, Elliott, Maxted, Morley & Mortell, 1942). Reference has already been made to the

increased number of successful isolations obtained when anaerobic cultivation and culture on media containing 1 in 500,000 gentian violet were employed.

In order to discover if the proportion of cases from which haemolytic streptococci could be isolated depended on how early in the disease the swabs were taken, the percentage of positive isolations has been considered in relation to the day of the disease on which the initial swabs were taken. Analysis of the figures in 3-day periods during the first fortnight did not reveal any significant differences.

de Waal (1940, 1941) had a similar experience in Edinburgh. Fourteen other different types accounted for the rest of the cases of scarlet fever. Only two of these, namely types 11 and 8/25, were at all common. In addition a proportion of strains (9·2 %) could not be typed serologically.

If the distribution of types is considered separately for each centre, certain minor differences are apparent. More than half of the cases (51·7 %) in Oxford were due to the one type 4/24 (75 cases out of 145). Otherwise only type 2 with nineteen cases was at all common, while types 1 and 3 were very infrequent. Cambridge found the common types

Table 2. *Distribution of serological types of* Str. pyogenes *isolated from cases of scarlet fever*

Serological type	Oxford	Cambridge	Cardiff	Total	% of total
4/24	75	23	18	116	23·6 ⎫
3	4	51	12	67	13·6 ⎬ 49·6
1	3	34	24	61	12·4 ⎭
11	7	14	28	49	10·0
8/25	3	18	18	39	7·9
2	19	14	3	36	7·3
14/R 491*	6	6	6	18	3·7
22	5	8	3	16	3·3
15/17/23/26	6	2	4	12	2·4
27	5	0	2	7	1·4
12	3	1	1	5	1·2
Imp. 19*	0	0	5	5	1·0
13/B 3264*	0	3	1	4	0·8
6	1	1	1	3	0·6
18	0	(?) 2	1	3	0·6
5	0	1	2	3	0·6
29	0	1	0	1	0·2
30	0	0	1	1	0·2
Types not identified	8	5	32	45	9·2
Total	145	184	162	491	100·0

* Provisional serological types.

From three of the Cardiff swabs two different types were isolated from the same swab.

N.B. Certain serological types (e.g. 4/24 and 8/25) are bracketed together. They often share common antigens and it is frequently difficult or impossible to identify them separately.

DISTRIBUTION OF SEROLOGICAL TYPES

Attempts were made to establish the serological type of all strains of group A streptococci isolated. The results are given in Table 2. It will be noted that almost 50 % of the total cases were due to types 1, 3 and 4/24. If the percentage of cases due to type 2, which itself was a less common cause of the disease than the three types already mentioned, is included, then 56·9 % of cases were due to types 1–4. The predominance of these four types has been noted in previous investigations made in this country. Griffith & Allison (1936), in the course of investigations made over a number of years in London, found that between 50 and 76 % of cases of scarlet fever were due to these four types.

to be those already mentioned as occurring most frequently in the whole investigation. Type 3 was the most frequent followed by types 1, 4/24, 8/25, 11 and 2 in that order. Cardiff found the same common types with the exception of type 2 which was rare; type 11 predominated, followed by types 1, 4/24, 8/25 and 3 in that order.

The incidence of the different serological types was studied in greater detail at Cardiff by considering the weekly isolations of serological types in relation to the weekly incidence of scarlet fever notified in Cardiff City over the whole 2-year period. It was noted that type 1 was found in January and March 1941, but was not encountered again until the last three months of 1942. This reappearance coincided with a steep rise in the incidence of scarlet fever in the borough and type 1 was found

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responsible for a large proportion of the cases. The findings with type 3 were similar. It was found in January and February 1941, and then not met with again until December 1942. These results are in contrast to those with types 4/24, 8/25 and 11. Cases due to these three types occurred in groups throughout the whole 2 years. They appeared to be endemic types giving rise to a large proportion of scarlet fever cases in the district. The marked increase of scarlet fever prevalence in the last 3 months of 1942 was brought about not only by the many cases of type 1 scarlet fever, but also by an increase in all the other common types. In addition a number of cases were due to types only rarely found (e.g. types 2, 5, 12, 22, 27).

patients for medical reasons such as the incidence of complications, or according to the home conditions.

In Table 3 the cases are grouped according to whether or not they were complicated or cross-infected, and the average length of stay in hospital is given for each group. Patients without complications or cross-infections stayed in hospital on an average for 28·0 days. The occurrence of a complication lengthened the stay in hospital to an average of 38·1 days. For the complicated cases which were not cross-infected the average stay was 33·4 days, but if the complicated case was cross-infected as well the average stay was 42·3 days. The average stay for all cross-infected cases was 37·6 days. Thus

Table 3. *Average length of stay in hospital*

	Oxford*		Cambridge		Cardiff†		Total cases	
Type of case	No. of cases	Average stay in hospital in days	No. of cases	Average stay in hospital in days	No. of cases	Average stay in hospital in days	No. of cases	Average stay in hospital in days
All cases	167	27·5	230	24·3	197	40·6	594	30·6
No complications or cross-infections	126	26·9	164	22·7	122	36·4	412	28·0
All complicated cases	31	29·7	30	37·6	31	46·9	92	38·1
Complicated but not cross-infected	22	29·6	23	28·3	20	43·5	65	33·4
Complicated and cross-infected	9	29·9	7	41·4	11	53·0	27	42·3
All cross-infected cases	19	28·5	43	27·1	55	49·0	117	37·6
Cross-infected but not complicated	10	27·3	36	26·6	44	48·0	90	37·2

* Excluding six cases retained in hospital for administrative reasons and twelve cases discharged prematurely because of bed shortage.

† A number of cases omitted because of incomplete data.

LENGTH OF STAY IN HOSPITAL

The average number of days, based on all cases in the series, for which patients were kept in hospital was 30·6 (Table 3), but the averages for the individual isolation hospitals differed considerably. Oxford and Cambridge kept their patients in hospital for about the same period, namely averages of 27·5 and 24·3 days respectively; Cardiff, on the other hand, retained their patients for an average of 40·6 days.

This longer stay in hospital at Cardiff appeared to result from administrative routine, for even patients who showed no evidence clinically of complications, or bacteriologically of cross-infection, were kept in hospital for 36·4 days, compared with 26·9 days at Oxford and 22·7 days at Cambridge. It must be emphasized that at none of the hospitals was the time of discharge decided by the bacteriological findings. Each hospital had its own administrative routine which was varied for individual

it was found that the occurrence of a complication or cross-infection lengthened the average stay in hospital and that the stay was considerably lengthened for complicated cases which were cross-infected in addition. These findings were true for each of the centres, but at Oxford the differences were small; they were most marked at Cardiff.

INCIDENCE OF COMPLICATIONS

The incidence of complications at the three centres is shown in Table 4. In the whole series 16·4 % of cases were noted to have suffered from complications. The incidence was highest at Oxford with 20 % and lowest at Cambridge with 13·0 %. In Table 5 are listed the complications diagnosed by each centre. In this investigation cervical adenitis was not regarded as a complication unless well-marked enlargement of the cervical lymph nodes occurred during the course of the disease accompanied by suppuration or by a secondary rise in

temperature without other symptoms or signs. It is possible that the clinical assessment of complications at the three hospitals was made differently, but the figures as they stand do not suggest that the longer stay in hospital at Cardiff affected the incidence of complications. Previous observations have suggested a higher incidence in hospitals where the patients were kept in hospital longer (Parsons, 1927). The time in weeks after admission at which complications occurred is shown in Table 6. Less than one-third (29·6%) of the complicated cases were found to have been cross-infected (Table 4).

INCIDENCE OF CROSS-INFECTION

The incidence of cross-infection acquired in hospital is shown in Table 7. Cross-infection was assumed to have occurred when haemolytic streptococci of a type different from that originally present were found later in either the nose or throat swab. In the whole series 20·1% of cases were found to have been cross-infected in hospital, but the individual results at the three centres were very different. Oxford with 13·5% had the smallest incidence of cross-infection. Cambridge had a higher rate of

Table 4. *Incidence of complications*

| | | Total cases with complications | | Cases with complications | | | |
| | | | | Who were not cross-infected | | Who were also cross-infected | |
Centre	Total cases	No.	%	No.	%	No.	%
Oxford	185	37	20·0	26	70·3	11	29·7
Cambridge	230	30	13·0	23	76·7	7	23·3
Cardiff	197	31	15·7	20	64·5	11	35·5
Total	612	98	16·4	69	70·4	29	29·6

Table 5. *Distribution of complications*

Complication	Oxford	Cambridge	Cardiff	Total
Cervical adenitis	9	4	8	21
Otitis media	7	12	8	27
Rhinitis	4	0	4	·8
Septic tonsilitis, and quinsy	4	2	0	6
Septic spots, whitlows	6	0	3	9
Albuminuria, nephritis	0	1	5	6
Rheumatism, arthritis, joint pains	3	5	3	11
Relapse	1	7	3	11
Secondary rise in temperature	4	4	0	8
Vaginal discharge	2	0	0	2
Gastro-enteritis	2	0	0	2

Table 6. *Time of onset of complications*

Centre	1st week	2nd week	3rd week	4th week	Later than 4th week
Oxford	8	15	9	7	3
Cambridge*	11	6	6	4	1
Cardiff	12	3	4	6	6
Total	31	24	19	17	10

* Two cases omitted by Cambridge because of incomplete data.

18·7% and Cardiff was even higher at 27·9%. It has already been noted that Cardiff retained the patients in hospital longer as a routine and it is possible that this longer stay in hospital is partly responsible for the increased cross-infection rate. There is confirmation for this suggestion in an analysis of the intervals after admission at which each cross-infection was found to have occurred (Table 8). At Cardiff thirty-eight out of the seventy-nine cross-infections (48·1%) occurred after the 4th week, whereas at the other two centres the peak of the incidence of cross-infection was during the 3rd week. A factor that may have influenced the low cross-infection rate at Oxford was that over half their cases were originally infected by the same serological type (type 4/24). This must have reduced the diversity of types among the patients admitted and nursed in their wards, with a corresponding reduction in the risk of cross-infection.

The risks of cross-infection with different serological types of haemolytic streptococci are now well recognized (Allison & Brown, 1937; Stalker, Whatley & Wright, 1942) and the dangers attendant on the nursing of scarlet fever cases in open wards have been pointed out. In this series less than one-third (23·6%) of the cross-infected cases suffered from complications (Table 7) and, as already pointed out (Table 4), of the complicated cases only 29·6% were found to be cross-infected. Sometimes otorrhoea was due to a cross-infecting type, but often it was caused by the primary infecting type. These results are thus different from those obtained in previously reported investigations. Allison & Brown

(1937) in particular have stressed the importance of cross-infection in causing complications; for instance, in eighteen (54·5 %) of thirty-three patients cross-infection was accompanied by manifest evidence of disease.

Follow-up of the patients after discharge home showed that a proportion of them acquired infection with a fresh serological type (Table 9). The proportion varied at the three centres. It was 8·6 % at Cambridge and 14·7 % at Oxford; at Cardiff the percentage was even higher at 18·7 %. It was also noted by Cardiff that cross-infections after discharge occurred more frequently in patients who had already been cross-infected in hospital than in those who had not. Of thirty-three patients who were

were cross-infected more than once with different serological types. Out of sixty-three cross-infected patients (cross-infected either in hospital or after return home) twenty-five (39·7 %) were cross-infected more than once. One patient was cross-infected four times and eight patients three times.

The serological types responsible for the cross-infections were analysed. Type 4/24 was the commonest cross-infecting type as it was also the commonest primary infecting type. In fact the six types that head the list of primary infecting types were also the commonest causes of cross-infection with one exception; type 11 was less common as a cross-infecting type whereas type 12 was much more common. The position of type 12 among the six

Table 7. *Incidence of cross-infections acquired in hospital*

| | | | | Cases with cross-infections | | | | |
| | | Total cases with cross-infections | | Who had no complications | | Who also had complications | | Total no. of cross-infections |
Centre	Total	No.	%	No.	%	No.	%	
Oxford	185	25	13·5	14	56·0	11	44·0	26
Cambridge	230	43	18·7	36	83·7	7	16·3	44
Cardiff	197	55	27·9	44	80·0	11	20·0	79
Total	612	123	20·1	94	76·4	29	23·6	149

Table 8. *Time of onset of cross-infection*

Centre	1st week	2nd week	3rd week	4th week	Later than 4th week
Oxford	1	4	11	8	2
Cambridge	9	11	10	10	4
Cardiff	2	14	13	12	38
Total	12	29	34	30	44

Table 9. *Cross-infections acquired after return home*

Centre	Total cases investigated	No. of cases cross-infected	% of cases cross-infected	No. of cross-infections
Oxford	116	17	14·7	18
Cambridge	58	5	8·6	5
Cardiff	91	17	18·7	20
Total	265	39	15·1	43

Only cases included which were investigated sufficiently after discharge home.

cross-infected in hospital and were followed up afterwards, nine (27·3 %) acquired another serological type after return home, whereas of fifty-eight patients not already cross-infected only eight (17·4 %) were cross-infected after discharge. Another finding by Cardiff not noted by the other laboratories was the frequency with which patients

commonest cross-infecting types was due to the number of times (eleven) it gave rise to cross-infections in Cardiff. Yet in Cardiff it was found only once as the primary cause of scarlet fever.

PRESENCE OF HAEMOLYTIC STREPTOCOCCI IN THE NASO-PHARYNX ON DISCHARGE FROM HOSPITAL

In Table 10 are given the number and percentage of cases of scarlet fever in which haemolytic streptococci were found in swabs taken shortly before discharge. Only patients whose swabs were taken within 2 weeks of discharge are included in these figures and a small number of cases have had to be omitted where this information was not available. The figures are based on the total cases, that is, including those patients whose swabs on admission to hospital were negative for haemolytic streptococci; some of these had negative swabs throughout their stay in hospital. Though these patients are included, as many as 60·3 % of the patients still had haemolytic streptococci in their swabs on discharge from hospital. The figures for the three centres varied from 64·8 % at Cambridge to 57–58 % at Oxford and Cardiff.

The cases still carrying haemolytic streptococci on discharge have been analysed further according to whether the haemolytic streptococci were the primary or cross-infecting types. The high proportion

Table 1. *Results of agglutination tests, cloacal swabs, cultural examination of eggs and bacteriological findings at autopsy of survivors from an outbreak of* Salmonella thompson *infection in chicks*

Bird no.	8 Titre H	8 O	8 Cloacal swab	9 Titre H	9 O	9 Cloacal swab	10 Titre H	10 O	10 Cloacal swab	11 Titre H	11 O	11 Cloacal swab	12 Titre H	12 O	12 Cloacal swab	13 Titre H	13 O	13 Cloacal swab	14 Titre H	14 O	14 Cloacal swab	15 Titre H	15 O	15 Cloacal swab	16 Titre H	16 O	16 Cloacal swab	18 Titre H	18 O	18 Cloacal swab	K/D	No. of blood tests	No. of positive blood tests (H or O)	Cloacal swabs Total	Cloacal swabs No. infected	No. of eggs examined	No. of eggs infected	Bacteriological findings at autopsy
Birds giving positive reaction to blood tests or positive cloacal swabs																																						
3301	1:187·5	0	Pos.	0	0	Pos.	0	1:17·5	Pos.	0	0	Neg.	1:17·5	0	Neg.	0	0	Pos.	0	0	Pos.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	3	10	5	60	None	*S. thompson* ex gall bladder
3303	0	0	Neg.	0	0	Neg.	1:87	0	Neg.	0	0	Neg.	1:75	0	Neg.	0	0	Pos.	0	0	Neg.	0	0	Neg.	1:35	0	Neg.	0	0	Neg.	K.	10	3	10	1	48	None	Neg.
3305	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	1:37·5	0	Neg.	0	0	Pos.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	1	10	1	84	None	Neg.
3318	0	0	Neg.	0	0	Neg.	0	0	Neg.	1:75	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	1	10	None	2	None	Neg.
3397	0	0	Neg.	0	0	Neg.	1:17·5	1:35	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	1	10	None	28	None	Neg.
3335	0	0	Neg.	0	0	Neg.	0	0	Neg.	1:75	0	Neg.	1:17·5	0	Neg.	0	0	Neg.	1:75	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	3	10	None	30	None	Neg.
3307	0	0	Neg.	0	0	Neg.	1:87·5	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	1:75	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	2	10	None	70	None	Neg.
3336	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	1:17·5	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	1	10	None	6	None	*S. thompson* ex caecum
3319	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Pos.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	None	10	1	8	None	Neg.
3308	0	0	Neg.	0	0	Pos.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	None	10	1	55	None	Neg.
3338	0	0	Neg.	0	0	Neg.	0	1:25	Neg.	1:50	0	Neg.	0	0	Neg.	0	0	Pos.	1:25	0	Neg.	D.	—	—	—	—	—	—	—	—		7	3	7	1	0	None	Neg.
3339	0	0	Neg.	0	0	Neg.	1:25	0	Neg.	1:35	1:17·5	Neg.	1:25	0	Neg.	0	0	Pos.	0	0	Neg.	D.	—	—	—	—	—	—	—	—		7	4	7	1	61	None	Neg.
3362	0	0	Neg.	0	0	Neg.	1:25	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	D.	—	—	—	—	—	—	—	—		7	1	7	None	21	None	Neg.
3334	0	0	Neg.	0	0	Neg.	0	0	Neg.	1:37·5	0	Neg.	1:35	0	Neg.	0	0	Neg.	0	0	Neg.	1:25	0	Neg.	D.	—	—	—	—	—		8	3	8	None	0	None	Neg.
3321	1:35	0	Neg.	0	0	Neg.	0	1:35	Neg.	D.	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—		3	2	3	None	0	None	Neg.
3332	0	0	Pos.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Pos.	0	0	Neg.	0	0	Neg.	D.	—	—	—	—	—		8	None	8	2	26	None	Neg.
3393	0	0	Neg.	0	0	Neg.	1:50	0	Neg.	1:37·5	0	Neg.	0	0	Neg.	0	0	Neg.	1:25	0	Neg.	1:35	0	Neg.	1:50	0	Neg.	D.	—	—	—		9	5	9	None	44	None	Neg.
Birds negative to tests and swabs																																						
3000	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	None	10	None	35	1 (shell)	Neg.
3360	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	None	10	None	2	None	Neg.
3304	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	10	None	10	None	10	None	Neg.
3317	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	D.	—	—		9	None	9	None	18	None	Neg.
3320	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	D.	—	—	—	—	—	—	—	—		8	None	8	None	0	None	Neg.
3313	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	D.	—	—	—	—	—	—	—	—		8	None	8	None	0	None	Neg.
3337	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	D.	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—		4	None	4	None	0	None	Neg.
Totals																																208	33	208	13	608	1	2
Untrapped eggs																																				166	9	
Total eggs																																				774	10	
Control pullets																																						
3018	Not tested						0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	8	None	8	None	2	None	Neg.
3019	Not tested						0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	8	None	8	None	11	None	Neg.
3020	Not tested						0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	8	None	8	None	2	None	Neg.
3021	Not tested						1:17·5	0	Neg.	1:50	0	Neg.	0	0	Neg.	1:50	0	Neg.	1:75	0	Neg.	0	0	Neg.	0	0	Neg.	1:25	0	Neg.	K.	8	5	8	None	23	None	Neg.
3022	Not tested						0	0	Neg.	0	0	Neg.	0	0	Neg.	1:25	0	Neg.	1:25	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	8	1	8	None	0	None	Neg.
3023	Not tested						0	0	Neg.	1:37·5	1:17·5	Neg.	0	0	Neg.	0	0	Neg.	1:37·5	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	8	2	8	None	29	None	Neg.
Control cockerels																																						
Cock 1							Not tested												0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	3	None	3	None	—	—	Neg.
Cock 2							Not tested												0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	3	None	3	None	—	—	Neg.
Cock 3							Not tested												0	0	Neg.	0	0	Neg.	0	0	Neg.	0	0	Neg.	K.	3	None	3	None	—	—	Neg.
Total																																63	5	63	None	67	None	Neg.

D. = Died. K. = Killed. Figures in titre column = End-point. Pos. = Infected. Neg. = Not infected.

of cross-infecting strains in the patients discharged at Cardiff compared with Oxford and Cambridge is probably dependent upon the increased incidence of cross-infection there, itself associated with the longer stay in hospital.

RETURN CASES

In spite of the fact that almost two-thirds of the patients discharged from hospital were known to be still carrying haemolytic streptococci in their nasopharynx, return cases were very few. There were only eleven return cases from among members of the patients' households and an additional four from among other known close contacts (Table 11). However, of these cases one was shown to be caused by a different type of *Str. pyogenes* from that infecting the original patient. It was not therefore a true return case although coming within the usually accepted definition. If this case is excluded the number of primary cases which produced return cases was eleven, that is an infecting case rate of 1·7 % in the 652 cases investigated. It has already

Information concerning the primary cases which had given rise to return cases has been examined to discover any possible factors that may have led to the transmission of the infection. The total number of cases is too small for any detailed analysis to be made but the facts available do not suggest any special factors responsible. No particular serological type or types appear to have caused the return cases. Only three out of the eleven strains were types that had been acquired by the primary case as a result of cross-infection. Few of the primary cases had suffered from complications. Particular attention was paid to the condition of the nasopharynx on discharge and after return home, to discover any unhealthy condition which might have caused the patients to disseminate streptococci in their environment. One child was found to have rhinitis but in the others no abnormality was noted except for some tonsilar enlargement in two cases. Four of the eleven infecting patients still had positive nasal swabs on discharge, but only one was a particularly heavy carrier of haemolytic strepto-

Table 10. *Presence of* Str. pyogenes *in swabs on discharge*

Centre	Total cases investigated	Total positive on discharge		Carrying primary infecting type		Carrying cross-infecting type	
		No.	%	No.	%	No.	%
Oxford	180	103	57·2	87	84·5	16	15·5
Cambridge	230	149	64·8	120	80·5	29	19·5
Cardiff	194	112	57·7	68	60·7	44	39·3
Total	604	364	60·3	275	75·5	89	24·5

Table 11. *Incidence of return cases*

Centre	Total cases* investigated	No. of return cases	Primary cases producing return cases	
			No.	%
Oxford	185	10†	8	4·3
Cambridge	230	3‡	2	0·9
Cardiff	237	1§	1§	0·4
Total	652	14	11	1·7

* Total cases in the series; not all the patients and their contacts were followed up afterwards.

† Six were in home contacts and four were close contacts (children playing together).

‡ Only return cases in home contacts were noted.

§ One additional case of scarlet fever occurred in household immediately after patient's return home, but due to a serological type different from that infecting the primary case.

been pointed out when considering the incidence of cross-infection after discharge that not all of the cases in the series were followed up thoroughly after discharge, but it is probable that if they had given rise to return cases this would have been noted.

cocci. Five of the primary cases had negative nose and throat swabs on discharge and in one instance the facts are of interest.

A mother developed scarlet fever a few days after the return home of her two children. They had been admitted to hospital 7 weeks previously and both had given consistently negative swabs for 6 weeks before the mother developed the disease. There are various possibilities as to the source of her infection. One of the children may have been a carrier although undetected by swabbing. The mother herself may have harboured the organisms, although not at first acquiring scarlet fever. She had, however, negative swabs at the time her children were admitted to hospital. Possibly there may have existed some other source of infection, such as a carrier among other contacts of the family not resident in the house, or the mother may have infected herself with streptococci that had persisted alive in the dried state in dust, etc.

All the primary infecting cases were children, their ages being between 4 and 9 years with the exception of two younger children, one of 2 months and another of 2 years. Most of the return cases

were children, but two were adults, mothers of the primary cases. The time interval that elapsed between the return home of the primary case and the onset of the disease in the return case varied between 2 days and 3 weeks.

LENGTH OF CARRIER STATE

The data about patients who on admission to hospital had haemolytic streptococci present in their nose and throat swabs have been examined to establish the length of time for which they remained carriers of haemolytic streptococci. It was not found possible to express the length of the carrier state as a mean, because with a number of patients routine weekly swabbing ceased before negative swabs were obtained; these patients were on the whole those who remained carriers longest.

negative swab. It undoubtedly reduced the percentage of positives in the later weeks, but, on the other hand, omission of cases with only one final negative swab would have meant some degree of artificial selection of cases. Patients from whom no final negative swabs were obtained are included in the totals as positives only for those weeks when their swabs were examined. Thus the total of cases examined in the first week of the disease includes all cases in the series, but the total for subsequent weeks becomes progressively less as cases are excluded whose swabbing ceased before they yielded negative swabs.

Non-cross-infected patients and cross-infected patients are considered separately in Table 12 for comparison. The figures from all three centres have been combined as the numbers from each are too

Table 12. *Proportion of naso-pharyngeal carriers of* Str. pyogenes *during the disease and convalescence*

	Non-cross-infected patients			Cross-infected patients		
Week of disease	Total no. of patients	No. of patients still carrying *Str. pyogenes*	% of patients still carrying *Str. pyogenes*	Total no. of patients	No. of patients still carrying *Str. pyogenes*	% of patients still carrying *Str. pyogenes*
1	348	344	98·9	118	118	100·0
2	348	310	89·1	118	115	97·5
3	347	279	80·4	117	112	95·7
4	323	219	67·8	117	107	91·5
5	251	125	49·8	106	86	81·1
6	227	82	37·0	86	58	67·4
7	217	58	26·7	80	44	55·0
8	209	36	17·2	79	37	46·8
9	198	22	11·1	68	21	30·9
10	188	6	3·2	62	16	25·8
11	—	—	—	58	8	13·8

There were eighty-seven cases (Oxford 22, Cambridge 39, Cardiff 26) from which only one final negative swab was obtained; few cases had as many as three. Each week of the disease has therefore been considered separately and the number of patients found to have become free of haemolytic streptococci and the number still carrying haemolytic streptococci counted. Thus the percentages still carrying haemolytic streptococci each week have been calculated (Table 12). Patients from whom at least one final swabbing (nose and throat) was negative are included in the totals for each week from the first to the eleventh week. They are included as positives for the weeks they were found to be positive and as negatives for all the weeks subsequently. If a patient first had positive swabs, then became negative and subsequently had a positive swab again he was included as a positive for each week until one or more final negatives were obtained. This method was adopted because a relatively large number of cases had only one final

small to be analysed separately. Owing to the failure to obtain more than one final negative swab in so many cases it is not possible to use the figures for detailed statistical analysis. The figures do, however, clearly demonstrate that cross-infected patients on the average carry haemolytic streptococci for a longer period.

THE PRESENCE OF HAEMOLYTIC STREPTO-COCCI IN THE NASO-PHARYNX OF HOME CONTACTS

When a patient was admitted to hospital with scarlet fever all home contacts when possible were swabbed to discover if they were carrying haemolytic streptococci. One or more contacts of 25·5 % of cases were found to be carrying the same type of streptococcus as the patient; out of a total of 813 contacts swabbed 104 (12·8 %) carried the same type (Table 13). Analysis of the figures for each centre separately showed that at Oxford the pro-

portion of positive contacts was smaller than at the other two centres. The distribution of serological types, where patient and contact both had the same type, was not significantly different from that for the series as a whole.

Cambridge and Cardiff also followed up the contacts after the patient's discharge from hospital. The contacts were swabbed immediately after the patient's discharge and at weekly intervals after-

hospital. The number of such contacts noted at Cambridge was twelve and at Cardiff one.

The age distribution of the contacts who acquired the same type of streptococcus as the patient, either primary or cross-infecting, after his return home, is shown in Table 15. Of 124 contacts eighty-three (66·9 %) were under 15 years of age. Owing to the small numbers in each group the figures for Cambridge and Cardiff are included together.

Table 13. *Swabbing of home contacts made at the time of admission of patient to hospital*

Centre	No. of cases whose contacts were swabbed	Cases at least one of whose contacts carried same type of *Str. pyogenes* as patient		No. of contacts swabbed	Contacts with same type of *Str. pyogenes* as patient	
		No.	%		No.	%
Oxford	103	21	20·4	361	27	7·5
Cambridge	83	26	31·3	262	50	19·1
Cardiff	57	15	26·3	190	27	14·2
Total	243	62	25·5	813	104	12·8

Instances excluded where a second case occurred in the same house soon after the first case.

Table 14. *Swabbing of contacts after patient's return home*

Centre	No. of cases whose contacts were swabbed	No. of cases whose contacts carried primary infecting type	No. of cases whose contacts carried patient's cross-infecting type	Total cases whose contacts carried same type as patient		No. of contacts swabbed	Contacts with same type as patient	
				No.	%		No.	%
Cambridge	58	31	7	38	65·5	126	31	24·6
Cardiff	43	11	8	18*	41·9	151	37	24·5
Total	101	42	15	56	55·5	277	68	24·6

* Includes one case where contacts had both primary and cross-infecting types.
Table based only on cases whose contacts were satisfactorily followed up. A few cases excluded where contacts had strains of haemolytic streptococci which could not be typed.

wards for 3 weeks. It was found that one or more contacts of 55·5 % of patients had in at least one swab a type of haemolytic streptococcus known to have been harboured by the patient at some time or other while in hospital (Table 14). The type may have been the primary infecting type or one acquired as a result of cross-infection. Sometimes swabs from the patient himself were no longer positive when the contacts were first noted to be infected. At Cambridge most of the types were those which had given rise to the primary infection in the patient; but at Cardiff a large proportion of the types were those which had been acquired as a result of cross-infection. The higher incidence of cross-infection in Cardiff has already been noted. Some of the contacts found to be harbouring the patient's primary infecting type after he returned home had also been carrying that type when swabbed at the time of the patient's admission to

Table 15. *Age distribution of* 124 *home contacts of fifty-six patients harbouring the same type of* Str. pyogenes *as the patient after his return home*

Age of contact in years	No. of contacts
0–	28
5–	40
10–	15
15–	2
20 and over	39

SEROLOGICAL TYPES FOUND IN CASES OF UPPER RESPIRATORY INFECTION OTHER THAN SCARLET FEVER

During 1941 and 1942, while this investigation on scarlet fever was proceeding, Cambridge made a survey of the serological types of haemolytic streptococci present in acute streptococcal infections of the upper respiratory tract other than

scarlet fever. All nose and throat swabs received for the routine bacteriological diagnosis of diphtheria, streptococcal tonsilitis, Vincent's angina, etc., were streaked on to horse-blood agar plates; the plates were examined after over-night incubation. If haemolytic streptococci were present in large numbers a single colony was picked off and the strain was grouped and typed. The results of typing 326 strains of group A streptococci are shown in Table 16. For purposes of comparison the number and percentage of times each of the types was isolated at Cambridge from cases of scarlet fever

Table 16. *Distribution at Cambridge of serological types of* Str. pyogenes *giving rise to upper respiratory infection, not scarlet fever, compared to those producing scarlet fever*

Serological type	Strains from cases of upper respiratory infection		Strains from cases of scarlet fever	
	No.	%	No.	%
11	50	15·3	14	7·8
4/24	42	12·9	23	12·8
3	39	12·0	51	28·5
1	38	11·7	34	19·0
8/25	34	10·4	18	10·1
2	31	9·5	14	7·8
12	23	7·1	1	0·6
22	18	5·5	8	4·5
28	13	4·0	—	—
5/27	13	4·0	1	0·6
15/17/23/26	10	3·1	2	1·1
13/B 3264	7	2·1	3	1·6
6	6	1·8	1	0·6
14/R 491	2	0·6	6	3·3
?18	—	—	2	1·1
29	—	—	1	0·6
Total	326	100·0	179	100·0

are included in the table. It will be noted that the common types found associated with upper respiratory infections are those most frequently found causing scarlet fever although there are considerable differences in the actual incidences. Type 12 in particular was significantly more common in upper respiratory infection than in scarlet fever. Cardiff also found type 12 to be one of the commonest types encountered in routine diagnosis, although it was a rare cause of scarlet fever. It was more common as a cause of cross-infection in scarlet fever and was frequently found in the swabs of contacts. Type 12 accounted for five (10 %) out of fifty strains of *Str. pyogenes* isolated from contacts of scarlet fever patients in whom the carrier strain belonged to a type different from that harboured by the patient. These observations are in conformity with the findings of Schwentker, Janney & Gordon (1943) in their investigations into the epidemiology

of scarlet fever in Roumania. The serological types giving rise to scarlet fever in a district are those most commonly found in carriers and giving rise to other forms of streptococcal infection; on the other hand, there are types which may be commonly found in other streptococcal infections but only rarely appear capable of causing scarlet fever.

DISCUSSION

Although it now seems firmly established that infection by group A haemolytic streptococci is responsible for the vast majority of cases of scarlet fever, previous investigations have shown that from a small proportion of cases even repeated nose and throat swabs fail to reveal haemolytic streptococci. In this series haemolytic streptococci were demonstrated in the swabs of 75·3 % of cases on admission. When swabbing was repeated during the first week after admission additional positives were found so that 8 days after admission the percentage of positives had increased to 81·9 %. There were, however, 6·8 % of cases from which haemolytic streptococci were at no time isolated throughout their stay in hospital.

The distribution of serological types of *Str. pyogenes* found to be responsible for scarlet fever in Oxford, Cambridge and Cardiff is in accordance with previous observations made in the British Isles. Since serological typing was introduced in 1926 it has been found each year that at least half the infections have been due to types 1 to 4. Observations have now been published from London, Edinburgh, Oxford, Cambridge and Cardiff. It thus appears that these types are responsible for the majority of cases of endemic scarlet fever in this country. In this series the only other common types have been types 11 and 8/25. At one or other time or locality one or more types predominate; other types may tend to disappear temporarily. For instance, it was noted that type 1 was not isolated from cases in Cardiff for more than a year. It then reappeared in association with a marked increase in scarlet fever notified in the borough and was responsible for a large proportion of the cases. But other common types also shared in the increased incidence and occasional cases were found to be due to types not previously encountered. The occurrence of these uncommon types is of interest; only one or two infections may be found to be due to them over a 2-year period. Reservoirs of these types must exist in the community; the strains are apparently erythrogenic but some factor such as lack of invasive power of the organism retards their diffusion among the population. At both Cardiff and Cambridge it was noted that type 12 was a rare cause of scarlet fever but was common in other streptococcal infections and among carriers. It thus appears to be at the present

time an example of a strain that is fully infective and invasive and yet has feeble erythrogenic powers. With this exception it was observed in a district that the common types causing scarlet fever were also the commonest types giving rise to other forms of streptococcal infection of the respiratory tract.

Unfortunately swabbing of many patients was not continued until three consecutive negative swabs were obtained and thus it was not possible to estimate accurately the rate at which cases became free of haemolytic streptococci. It was, however, clear that cross-infected cases remained carriers longer than non-cross-infected. At the time of discharge nearly two-thirds of the patients still had positive swabs. Nevertheless, there were in the whole series only fourteen return cases, infected by the same serological type as the original case, from among the patient's own household or other close contacts (return case rate of 2·1 %). These had followed the return home of eleven primary infecting cases (infecting case rate of 1·7 %). These figures can be compared with those given by Brown & Allison (1935b) after an investigation in London. They reported a return case rate of 4·9 % which was in accordance with a rate of between 4 and 5 % noted over a number of years. The infecting case rate was 3·7 %. They found as many as 82·8 % of patients to be still carrying *Str. pyogenes* when discharged from hospital, the usual duration of stay in hospital being from 4 to 8 weeks. There was definitely a higher incidence of cases giving rise to return cases among those yielding the more profuse growths of streptococci from their swabs. However, the factors which determine the incidence of return cases need further elucidation. Unfortunately in the investigation described here the fourteen return cases are too few for a satisfactory analysis to be made, but the data available do not reveal any peculiarities of the infecting organism or primary infecting case. No particular serological type of streptococcus was responsible and types acquired by cross-infection in hospital were not more common than in the whole series. Complications and unhealthy conditions of the upper respiratory tract were not particularly common among the infecting cases. Among the eleven cases there were five that had given negative swabs on discharge. The others were carriers; three had both nose and throat swabs positive, two throat only and one nose only. Evidence has been accumulating recently that nasal carriers of *Str. pyogenes* are those particularly liable to contaminate their environment and cause cross-infection (Hamburger, Johnson & Hamburger, 1945a, b). It is therefore of interest that only 34 % of the infecting cases were proved to be nasal carriers.

In this series it was found that 20 % of patients became cross-infected in hospital with a different serological type of streptococcus. This can be compared with the experience of Allison & Brown (1937), who found the incidence of cross-infection in a London fever hospital to be 70 %. However, in a more recent survey in London, Stalker, Whatley & Wright (1942) obtained results similar to those reported here; there was an incidence of 22·6 % cross-infections in an open ward and 20·3 % in a bed-isolation unit. The lower incidence of cross-infection in the more recent surveys compared with that of Allison & Brown is of interest. It may be that the demonstration of the importance of cross-infection has led to the introduction of improved technique and methods into the practice of fever hospitals, thus reducing cross-infection. Since the beginning of the century there has been in this country a continuous decline in the clinical severity and in the mortality of scarlet fever. This decline has become marked during the last two decades and the apparent decrease in virulence of the infecting organisms together with the advent and widespread use of sulphonamides may provide an explanation of the decrease in the incidence of manifest, as distinct from latent, cross-infection. But probably there are other reasons for the differences in results, particularly at Oxford, Cambridge and Cardiff, where the conditions are very different from those obtaining in London. In London the fever hospitals serve a much larger population, where scarlet fever is endemic; whereas in this investigation the wards were sometimes only partly filled. The difference in incidence of cross-infection at Oxford and Cardiff has been noted; at the former centre it was 13·5 % and at the latter 27·9 %. At Oxford the wards were mostly single-bed cubicles and the hospital was usually only partly filled. At Cardiff most of the patients were nursed in large open wards. Scarlet fever was prevalent in the borough, particularly in the last few months of the investigation, so that the wards were kept filled. There were also other differences. More than half the cases at Oxford were due to one serological type; the diversity of types among the hospital patients was thus reduced. On the other hand Cardiff as a routine kept their patients in hospital longer than the 4 weeks which was the average stay in hospital at Oxford and Cambridge. That this increased the liability to cross-infection is shown by the fact that nearly half (48·1 %) the cross-infections at Cardiff occurred after the fourth week.

Table 4 shows that in the present inquiry 16·4 % of the cases suffered from complications, and that the majority (70·4 %) of complications occurred in patients who were not cross-infected, thus indicating the greater relative importance of the primary infecting strain of *Str. pyogenes* as the cause of complications. These findings are very different

from those of Allison & Brown (1937) who in a smaller series of cases reported the occurrence of complications in 42·6 % of their cases, with only 10 % of the complications in patients who were not cross-infected; their findings stressed the importance of cross-infecting strains as causes of complications. The difference in the conclusions arrived at in these two investigations is so striking that some explanation is desirable. Table 6 shows that out of a total of 101 cases with complications fifty-five occurred during the first 2 weeks in hospital, the period when the great majority of complications are caused by the primary infecting strain of *Str. pyogenes*. Again, Table 7 shows a low incidence (20·1 %) of cross-infections and that only twenty-nine (23·6 %) of the cross-infected cases developed complications. This latter figure does not mean that all the complications in cross-infected cases were caused by the cross-infecting organisms. Analysis of data giving the times of occurrence of cross-infection in individual patients week by week (Table 8) and the times of onset of complications in the same patients frequently showed, for example, that a patient developed some complication due to the primary infecting type during the first or second week in hospital, but cross-infection without further complications did not appear until the third week or later. It was found that only one cross-infected patient (8·3 %) developed complications due to the cross-infecting strain during the first week in hospital, three (10·3 %) during the second week, nine (26·5 %) during the third week, three (10 %) during the fourth week and seven (15·9 %) during the fifth week and later, a total of twenty-three. In the remaining six patients who were cross-infected (Table 7) the complications were caused by the primary infecting strains. These figures show that the real danger period for complications due to cross-infecting strains is from the third week onwards. The low incidence of complications in all cases and the remarkably small percentage of cross-infected cases developing complications due to the cross-infecting strain suggest that while the infecting organism is capable of giving rise to complications during the early stages of the disease, its virulence decreases rapidly, rendering it less able to implant itself in the upper respiratory tract of another patient and no longer sufficiently invasive to produce manifest evidence of disease when transmitted to another patient in the ward.

After the patients' discharge 24·6 % of 277 home contacts were found to be latently infected with the patient's strain of streptococcus and 54·8 % of these were under 10 years of age when susceptibility to scarlet fever was highest. Nevertheless, the return case rate was low and direct infection of contacts infrequent. This may be explained by a general decrease in invasive power of the strains of *Str.*

pyogenes responsible for the milder type of scarlet fever now prevalent in this country. It has been suggested that the normal course of events in a patient with scarlet fever infected with a single strain of *Str. pyogenes* is that the invasive power of the organism gradually decreases as the patient reaches convalescence about the third week. From then onwards there is risk of cross-infection with strains from more recently admitted acute cases; these fresh strains acquired by the convalescent patient again require a few weeks for their invasive powers to decrease. Table 10 shows that 60·3 % of patients were still carrying *Str. pyogenes* when discharged from hospital, but 75·5 % of these were harbouring the primary infecting type, the invasive powers of which were probably decreased.

The hypothesis of the decrease in the invasive power of *Str. pyogenes* in the otherwise healthy upper respiratory tract of the individual patient finds some support in the recent work of Lancefield (1940) who showed that the type specific 'M' antigen of *Str. pyogenes* was an important factor in the virulence of the organism, strains in which no 'M' was present being devoid of virulence or ability to stimulate the production of protective antibodies. Experience has shown that the majority of strains of *Str. pyogenes* isolated from acute cases of infection possess the 'M' factor, while strains isolated from asymptomatic carriers or contacts of these cases have frequently been found to possess little or no 'M' substance as shown by precipitin tests with anti-'M' sera.

An interesting point arises out of a comparison of the results of swabbing home contacts carried out at the time of admission of the patient to hospital and after the patient's return home (Tables 13 and 14). It was found that 104 (12·8 %) of 813 home contacts of 243 patients harboured the same type of *Str. pyogenes* as the patient at the time of the latter's admission to hospital and sixty-eight (24·6 %) of 277 home contacts harboured the same type as the patient when the swabbing was carried out after the latter's return home. In other words there were proportionately twice as many home contacts harbouring *Str. pyogenes* after the patient's return home as at the time of his admission to hospital, and Table 16 shows that 67 % of 124 contacts were under 15 years of age, and 44·3 % were of school age. These findings lend support to the view of Paul (1938 *a, b*) in his arguments against the exclusion of contacts from school, as nearly twice as many home contacts of school age harbour *Str. pyogenes* after the patient's return home as at the time of his admission to hospital, and yet the former are allowed to attend school while the latter are excluded for one week after removal of the patient to hospital.

The increasing risk of cross-infection the longer

the stay in hospital and the fact that in the present inquiry the great majority of complications were caused by the primary infecting strains of *Str. pyogenes* early in the disease, strongly support, from the bacteriological point of view, the early discharge from hospital of patients convalescent from scarlet fever. The uncomplicated case should be returned home not later than 3 weeks after admission to hospital (including the usual 2 days' notice to parents) and earlier if possible. This has been common practice in many infectious diseases hospitals for some years, and should become universal. Parents are now accustomed to expect early release from hospital in straightforward un-complicated cases, and the belief in the infectivity of the desquamation scales of 'peeling' cases is almost dead. It is desirable to make a final urinary examination for the presence of albumin on the morning of discharge, and if the patient is discharged earlier than the third week, another examination should be made by the patient's practitioner a few days after discharge.

SUMMARY

A simultaneous investigation into certain epidemio-logical aspects of scarlet fever was carried out over a 2-year period at Oxford, Cambridge and Cardiff. The results obtained at the three centres are com-pared and contrasted.

Nose and throat swabs were taken from 648 patients on admission to hospital; group A haemo-lytic streptococci were demonstrated in the swabs of 75·3 %. Eight days after admission 81·9 % had given positive swabs.

Serological typing showed that 56·9 % of strains were types 1–4. The only other common types were types 11 and 8/25.

The average length of stay in hospital was estimated for all cases, divided into groups according to whether or not they had suffered from complica-tions or been cross-infected. The average for the whole series was 30·6 days; this was increased to 33·4 days for all complicated cases and to 37·6 days for all those cross-infected. It was longest (42·3 days) when there were both complications and cross-infections.

The incidence of cross-infection with fresh sero-logical types of haemolytic streptococci was noted both in hospital and for the first 3 weeks after discharge. In the whole series 20·1 % of cases were cross-infected in hospital. The cross-infection rate was highest at Cardiff (27·9 %) and lowest at Oxford (13·5 %). Of the 123 cross-infected cases, complica-tions occurred in 23·6 %.

A total of ninety-eight patients (16·4 %) suffered from complications; in twenty-three of these (23·4 %) complications were attributed to cross-infecting strains.

Nose and throat swabs were taken from all patients shortly before discharge; 60·3 % were still carrying haemolytic streptococci.

Data were obtained regarding the rate at which cases became free of haemolytic streptococci. By the 10th week of the disease only 3·2 % of those who had not been cross-infected were carrying streptococci. Cross-infected patients were slower in becoming negative; at the 10th week 25·8 % were still carriers.

There were fourteen return cases (return case rate 2·1 %) following the return home of eleven primary cases (infecting case rate 1·7 %).

Swabbing of home contacts at the time of the patient's admission to hospital showed that one or more contacts of 25·5 % of cases carried in their naso-pharynx the same type of haemolytic strepto-cocci as that infecting the patient; 12·8 % of the contacts swabbed were positive. During the first 3 weeks after discharge 24·6 % of contacts, that is one or more contacts of 55·5 % of cases, carried a type that had been harboured by the patient while in hospital.

It was noted that in a particular area the common types that gave rise to scarlet fever also commonly caused other streptococcal infections of the upper respiratory tract. Type 12, however, though fre-quently found in other streptococcal infections and in healthy carriers, appeared only rarely to cause scarlet fever.

It is suggested that the low incidence of complica-tions, less intimate relationship between complica-tions and cross-infections and low return case rate found in this investigation, as compared to earlier observations made in England, are associated with lowered virulence and invasive powers of the strains of *Str. pyogenes* responsible for the much milder scarlet fever now prevalent.

The bacteriological findings confirm the wisdom of modern fever hospital practice of early discharge from hospital. It is suggested that discharge within 3 weeks should be the universally adopted rule.

REFERENCES

ALLISON, V. D. & BROWN, W. A. (1937). *J. Hyg., Camb.,* **37**, 153.

BROWN, W. A. & ALLISON, V. D. (1935*a*). *Brit. med. J.* **2**, 1249.

BROWN, W. A. & ALLISON, V. D. (1935*b*). *J. Hyg., Camb.,* **35**, 283.

COLEBROOK, L. ELLIOTT, S. D., MAXTED, W. R., MORLEY, C. W. & MORTELL, M. (1942). *Lancet,* **2**, 30.

DE WAAL, H. L. (1940). *J. Hyg., Camb.,* **40**, 172.

DE WAAL, H. L. (1941). *J. Hyg., Camb.,* **41**, 65.

FRY, R. M. (1940). *Monthly Progress Report, Emergency Public Health Laboratory Service (Medical Research Council),* September, p. 14.

FULLER, A. T. (1938). *Brit. J. exp. Path.* **19**, 130.

GARROD, L. P. (1942). *Brit. med. J.* **1**, 290.

GRIFFITH, F. (1926). *J. Hyg., Camb.,* **25**, 385.

GRIFFITH, F. (1934). *J. Hyg., Camb.,* **34**, 542.

GRIFFITH, F. & ALLISON, V. D. (1936). *Report, Chief Medical Officer of the Ministry of Health,* p. 214.

GUNN, W. & GRIFFITH, F. (1928). *J. Hyg., Camb.,* **28**, 250.

HAMBURGER, M., JOHNSON, M. G. & HAMBURGER, V. (1945*a*). *J. infect. Dis.* **77**, 68.

HAMBURGER, M., JOHNSON, M. G. & HAMBURGER, V. (1945*b*). *J. infect. Dis.* **77**, 96.

LANCEFIELD, R. C. (1940). *J. exp. Med.* **71**, 521.

PARSONS, A. C. (1927). *Ministry of Health, Reports on Public Health and Medical Subjects,* no. 35.

PAUL, H. (1938*a*). *Public Health,* **51**, 203.

PAUL, H. (1938*b*). *The Practitioner,* **141**, 79.

SCHWENTKER, F. F., JANNEY, J. H. & GORDON, J. E. (1943). *Amer. J. Hyg.* **38**, 27.

STALKER, W. S., WHATLEY, E. & WRIGHT, J. (1942). *J. Hyg., Camb.,* **42**, 231.

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