REINFECTION AS A CAUSE OF COMPLICATIONS AND
RELAPSES IN SCARLET FEVER WARDS

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INTRODUCTION

IN isolation hospital practice one of the accidents liable to cause administrative difficulty is the occurrence of “cross-infection”, defined as the acquisition by a patient, admitted with an infectious disease A, of another infectious disease B. But it has not been realized until recently that cross-infection with haemolytic streptococci was constantly occurring in scarlatinal wards and was responsible for second attacks of scarlet fever, usually described as relapses, and for the majority of the late complications—adenitis, rhinitis, otitis media, etc.—which have such serious consequences. Since such scarlatinal cross-infection is a second infection specifically identical with the first we have applied to it the special term of “reinfection”.

The suspicion that such “reinfection” was happening has no doubt given rise to the practice at some hospitals of keeping acute and convalescent patients apart by using “acute” wards and “convalescent” wards. All cases of scarlet fever are admitted into the “acute” ward, and after the acute stage of the disease is passed they are transferred to the “convalescent” ward. Should a convalescent patient subsequently develop complications, particularly those of a suppurative nature, he is transferred back to the acute

ward. This practice, based on the theory that late complications are due to cross-infection, has not had much success in reducing their incidence.

The identification of multiple serological types of *Streptococcus pyogenes* by Griffith (1926, 1927, 1935) has made possible the more exact study of the epidemiology of infections with this organism. As a result of this work, followed by that of Gunn & Griffith (1928), Allison & Gunn (1929, 1932) and Brown & Allison (1935), it is now possible to have a clear conception of what is meant by the term "reinfection" as applied to scarlet fever. When a patient suffering from scarlet fever is admitted to hospital, he is infected with a particular serological type of *Str. pyogenes*, and during his stay in hospital he may become secondarily infected or reinfected by a different serological type of the same organism from another patient in the ward. In a previous study (1935) of carriers and return cases in scarlet fever, we suggested that secondary cervical adenitis was probably caused by reinfection of the throat by a different serological type of *Str. pyogenes* from that which caused the primary attack of scarlet fever. In the present investigation we have studied the conditions and frequency of occurrence of reinfection as shown by change of type of *Str. pyogenes* found in the nose or throat and their relationship to late complications and relapses. Our observations have been made on cases of scarlet fever nursed in multiple-bed wards as well as on cases nursed in cubicles or single-bed wards.

BACTERIOLOGICAL EVIDENCE OF REINFECTION

The occurrence of secondary infecting types of *Str. pyogenes* in scarlet fever patients, nursed in multiple-bed wards, has already been shown by Gunn & Griffith (1928) and Allison & Gunn (1929, 1932). In the present investigation, swabs were taken from the nose and throat of 100 patients on admission to hospital and again on discharge, after being nursed by the ward isolation method, and the serological type of *Str. pyogenes* obtained on each occasion was determined. The results are summarized as follows:

<i>One hundred scarlet fever patients swabbed (nose and throat) on admission and on discharge and the type of Str. pyogenes present identified serologically</i>									
No. of patients carrying on discharge a serological type of <i>Str. pyogenes</i> different from that found on admission	...	...	...	...	...	...	...	...	57
No. of patients from whom were isolated on admission and on discharge <i>Str. pyogenes</i> belonging to one and the same serological type...	...	...	...	...	...	...	...	...	27
No. of patients whose swabs proved negative for <i>Str. pyogenes</i> on discharge	...	...	...	...	...	...	...	...	13
No. of patients from whom were isolated on admission and on discharge <i>Str. pyogenes</i> which could not be identified serologically	...	...	...	...	...	...	...	...	3
Total									100

The findings are in agreement with the earlier observations and indicate the occurrence of a considerable amount of reinfection among scarlet fever

patients nursed together in large wards, the more so as the above figures do not take into account reinfections which may have occurred while the patients were in the ward but which disappeared prior to the swabbing on discharge. The possible explanations of the change of the serological type of *Str. pyogenes* in a single case have already been discussed by Gunn & Griffith (1928) and Allison & Gunn (1932) and there seems to be no reasonable grounds for doubting that it is due to reinfection and not to transmutation of type. Further evidence in support of this view is afforded by the results of swabbing twice weekly, from admission until discharge, the nose and throat of sixteen scarlet fever patients nursed in separate cubicles. All these patients, with one exception, were found to harbour only the primary infecting type of *Str. pyogenes* throughout their period of isolation; the exception was a patient from whom two different serological types were isolated on admission, one of which was not found after the first swabbing until late in convalescence when it was again found present in moderate numbers, while the other type, presumed to be the cause of the scarlet fever, disappeared.

The study by one of us (V. D. A.) of an outbreak of scarlet fever conveyed by a single milk supply and hence uniform in its "type" provided additional confirmation. The outbreak was caused by *Str. pyogenes* type 1, which was isolated from all of twenty-three patients examined and from one of the milkers and his family. Eight of these patients were nursed together in one ward which contained no other patients, and nasal and throat swabs were taken from them weekly from admission until discharge. The ward staff was also swabbed weekly in order to trace the source of any reinfection which might occur. Convalescence was uninterrupted and no reinfections occurred, the same serological type, type 1, alone being isolated throughout the illness.

The bacteriological evidence is thus clear that reinfection, i.e. infection with a serological type of *Str. pyogenes* different from that causing the primary disease, occurs in a large proportion of scarlet fever patients nursed in multiple-bed wards. Such reinfection does not occur among patients nursed in single-bed wards. In patients all infected with the same serological type and nursed together in multiple-bed wards, transference of infection may and probably does occur but is not perceptible by bacteriological methods and shows no clinical evidence of its occurrence.

SCOPE OF INVESTIGATION AND TECHNIQUE

Gunn & Griffith (1928) and Allison & Gunn (1929, 1932) have drawn attention to the observation that the occurrence of complications such as tonsillitis, rhinitis or otitis in scarlet fever is often associated with the appearance in the throat, nose or ear of a fresh type of *Str. pyogenes*, and in several instances the discovery of the new type coincided with the occurrence of a relapse which exhibited all the typical signs of a fresh attack of scarlet fever including the rash.

The opening of an additional ward for scarlet fever patients in the Brook Hospital, L.C.C., during the height of an epidemic gave us the opportunity of studying this question, free from the difficulties experienced when the investigation is begun in a ward containing patients who have been isolated for varying periods. These difficulties are due to (1) the inability (*a*) to determine whether the serological types of *Str. pyogenes* isolated from patients who have been in the ward some time are primary or secondary infecting types, and hence (*b*) to prove their causal relationship to complications present and to fix the time of their occurrence; (2) the irregular admission of new patients as beds fall vacant; in other words it is like commencing to read a book at the third or fourth chapter, not knowing what has been written before.

The newly opened ward contained twenty-two beds and one cot. The beds were filled with fresh acute cases of scarlet fever admitted over a period of 48 hours. The cot contained the healthy 5 months old baby of a nursing mother admitted to the ward with scarlet fever. Cultures were made from swabs from the nose and throat and from inflammatory exudate when present, of all patients on admission and thereafter twice weekly until discharge. The medical, nursing and cleansing staff of the ward was also swabbed, nose and throat, once weekly throughout the period of the investigation in order that no unsuspected source of reinfection might be overlooked.

Too much stress cannot be laid on the importance of taking swabs carefully; experience has shown that careless swabbing is often the reason for variable results obtained in the laboratory. This applies in greater measure to routine swabbing than to an organized investigation such as the present, in which all swabs were taken personally by one of us (W. A. B.). The fauces were first inspected to decide the best site for application of the swab, in order that reliable results might be obtained. The swab was then well rubbed over and into the selected site, care being taken to avoid contact with other parts of the fauces or mouth.

The swabs were cultured on plates containing a thin layer of 5 per cent horse-blood agar over a layer of plain nutrient agar as recommended by Griffith (1935) and incubated for 18 hours at 37° C. When haemolytic streptococci were present colonies were picked off for subculture and serological typing. Careful examination was made of all positive plates with a view to isolating and identifying more than one serological type of *Str. pyogenes* from individual plates, as evidence of multiple infection. For this purpose the colonies of haemolytic streptococci on a plate were examined with the hand-lens and low-power binocular microscope as to size (small, medium, large), outline (round, crenated or irregular), elevation (flat, domed, contoured, heaped), reflexion of light (shiny, semi-matt, matt), consistency (watery, soft, coherent) and size and intensity of haemolytic zone. Colonies on individual plates differing in one or more of these characteristics were picked off for serological typing. In addition three colonies were examined serologically from plates on which no differences in colony appearance were noted. In

spite of these precautions, it cannot be denied that the appearance of a fresh type may have been missed on occasion, or that the disappearance of the primary infecting type may have been recorded too soon.

In the ward the patients were carefully observed and the time and date of appearance of any untoward signs or symptoms or the occurrence and nature of complications were noted. In order to eliminate unconscious bias the bacteriological examinations and clinical observations were made independently and correlation of the findings was made at a later period. The admission, treatment and discharge of the patients were therefore based solely on clinical grounds.

TABULATION AND DISCUSSION OF FINDINGS

The observations extended over a period of 13 weeks when the ward was again closed as the epidemic waned. In all, forty-nine patients were under investigation during this period and Table I shows the serological types of *Str. pyogenes* isolated as a result of the twice weekly examinations, from admission until discharge, of swabs from nose, throat and lesions with discharges where possible.

To save space the results of swabs from the different sources are not given separately, but an asterisk against the type number in the table indicates the presence of otitis media with a positive ear swab. The serological type number of the primary infecting strain in each case is printed in italics, while the serological type of the reinfecting strain(s) is shown in clarendon. The numbered notes give the results of clinical observation; the occurrence of complicating signs or symptoms and their date of appearance are indicated by figures against the serological type numbers in the appropriate columns of the table. The figures in the first column refer to the numbers given to the beds in the ward and are followed by the letters "a", "b", or "c", according as the patient was the first, second or third occupant of the bed dating from the time of opening of the ward.

Patient 23*a* was the healthy infant, already referred to, which was being nursed by its mother, 7*a*, who was admitted with a typical attack of scarlet fever. It will be noted that haemolytic streptococci were not isolated from the baby's nose or throat till the end of the second week, when it was found to be carrying type 4, the same serological type which caused the mother's infection, although it did not at any time throughout its stay in hospital show any clinical evidence of infection. Another patient, 14*b*, also with a type 4 infection was transferred to another ward during the first week with a super-added attack of chicken-pox, after having been swabbed only twice. These two patients, 23*a* and 14*b*, may therefore be justifiably disregarded when considering the question of reinfection in the ward.

It will be noted that swabs from patient 21*a* remained negative throughout the period of his detention in hospital, although he passed through a typical

attack of scarlet fever. This patient was admitted with an abscess on the right leg which cleared up under treatment. Unfortunately we omitted to take swabs from the abscess, but this case was probably one of "surgical" scarlet fever. It will be further observed that patient 2*a* yielded a negative first swab and that the first two swabs from patient 22*a* were negative; the serological types (4 and 11) found later are those which experience has shown on occasion to yield colonies on blood agar plates with very weak or absent zones of haemolysis, and it is possible they were missed at the earlier examinations. In this connexion patient 11*a* is of interest, in that there were no haemolytic colonies in cultures on blood agar from the first swabs, but examination of the plate showed numerous colonies which possessed the characteristics (opaque, matt, very irregular outline) frequently assumed by strains of *Str. pyogenes* belonging to types 4, 8 and 11. Serological examination of subcultures from these colonies showed them to be *Str. pyogenes* type 4; a small, weakly haemolytic zone round the colonies appeared after incubation at 37° C. for 3 days, while deep colonies in blood agar showed haemolysis in 24 hours. Subsequent swabs from this patient yielded cultures possessing the same characteristics.

Of the forty-seven patients under consideration, only fourteen harboured no serological type of *Str. pyogenes* other than the primary infecting type throughout their period of detention in hospital. The remaining thirty-three patients (70·2 per cent) became reinfected in the ward with one or more fresh serological types of *Str. pyogenes*. The duration of the secondary infection varied in different patients from a few days to several weeks. Moreover, it may be noted that no fresh serological type appeared to have been introduced to the ward from extraneous sources, all the serological types found as secondary invaders being also the cause of infection, primary or secondary, in one or more patients in the ward at the material time.

CLINICAL SIGNS IN RELATION TO REINFECTION WITH *STR. PYOGENES*

The forty-seven patients were classified as follows, according to the absence or occurrence of reinfection and of complications:

	Patients	
(1) No reinfection, no complications	12	29·8 per cent
(2) No reinfection, complications present	2	
(3) Reinfection, no complications	15	70·2 per cent
(4) Reinfections and complications both present	18	
	<hr/> Total 47	

The first group in which the disease ran an uneventful course calls for no comment. Of the two patients in the second group, one (10*a*) showed on the seventh day after admission to hospital an albuminuria which lasted for 4 days, the other (9*b*) developed on the twenty-first day a right otitis externa which lasted for 3 days; it may be observed that it is unlikely that either of these complications are such as could have been caused by reinfection. One patient

(19a), however, placed in the fourth group (*vide infra*) belongs also to this group on account of bilateral otitis occurring at the beginning of the second week; this was the only patient to show complications directly attributable to local proliferation of the primary infecting strain of *Str. pyogenes*. The third group shows that reinfection occurred in quite a high proportion (32 per cent) of the patients without giving rise to clinical signs and that such reinfection is discovered only by repeated bacteriological and serological examination of cultures from swabs. The fourth group of eighteen patients (38.3 per cent) in whom both reinfection and complications occurred is the most important from the point of view of the present enquiry. The patients in this group are as follows (see Table I): 8a, 11a, 15a, 18a, 19a, 1b, 10b, 2b, 18b, 20b, 5b, 7b, 17b, 8b, 14c, 4b, 6c and 9c. A study of the table will show that there was a close time relationship between the discovery of the reinfecting strain and the occurrence of complicating signs or symptoms. In every instance the discovery of a reinfecting type coincided with the appearance of clinical signs within a period of 72 hours before or after swabbing. The time relationship would probably have been even closer, if daily swabbing had been carried out. One patient, 19a, already mentioned, is placed in this group on account of multiple reinfections and complications.

The clinical evidence associated with reinfection varied greatly in different patients and included signs ranging from increased pulse rate for 48 hours, slight rise of temperature for 24 hours to coryza, tonsilitis, cervical adenitis, otorrhoea or the complete clinical picture of scarlet fever (10b and 18b).

A consideration of the third and fourth groups shows that reinfection may be "manifest" or "latent" to use the terms of Okell & Elliott (1936) for patients with or without clinical consequences respectively. It is known that certain serological types, e.g. 4, 8, 11, etc., have in the past been associated with a very mild form of scarlet fever and a resultant low degree of immunity. Gunn & Griffith (1928) found that 58.3 per cent of twelve patients infected with *Str. pyogenes*, type 4, were still Dick-positive reactors on discharge from hospital on an average 5.75 weeks after admission. Gunn and Allison (unpublished) found that, out of nine patients infected with *Str. pyogenes*, type 4, four who were not reinfected during their stay in hospital still gave Dick-positive reactions on discharge; the other five patients who all had complications associated with reinfection while still in the Dick-positive state eventually gave Dick-negative reactions. Patients primarily infected with such types are probably more susceptible to "manifest" reinfection in the ward by serological types, e.g. types 1 and 2, found in other patients and associated with the more severe forms of the disease and more likely to give clinical evidence. On the other hand, patients primarily infected with types 1 and 2 probably develop a higher degree of immunity, and while they may become reinfected with other serological types, clinical evidence of such reinfection is not so frequently observed. We feel that the occurrence and degree of clinical manifestation when a patient is reinfected depends upon the solidity of the

immunity, antitoxic and antibacterial, built up as a result of infection by the primary type, and on the dose and virulence of the reinfecting strain. Differences in antigenic constitution of the various serological types are also probably factors in the solidity of the immunity produced by infection.

Weekly swabs from the ward staff showed that seven out of the ten members harboured *Str. pyogenes* on two or more occasions during the investigation, only three having negative swabs throughout. Three members of the nursing staff were persistent carriers, swabs being positive eleven times out of twelve, nine times out of twelve, and nine times out of nine, respectively. The two latter nurses were the only ones to show reinfection, one changing from type 1 to an unidentified type with no clinical incident, and the other changing from type 11 to type 3 during the sixth week coincident with an attack of acute tonsilitis, which necessitated her being warded for 4 days. This nurse may have derived her infection either from patient 11*a* who had a double otorrhoea due to infection with type 3, or from patient 1*b* who had a rise of temperature and sore throat with cervical adenitis due to reinfection with types 1 and 3; at the time of her reinfection she was in contact with both these patients in the discharge of her duties.

RELATION OF THE DISAPPEARANCE OF THE PRIMARY INFECTING STRAINS TO THE APPEARANCE OF REINFECTING STRAINS

The persistence of the primary infecting strain of *Str. pyogenes* in the nose, throat or complicating discharges of the forty-seven patients under investigation in Table I varied from 1 week (14*c*) to 7 weeks (19*a*) after admission to hospital and the average time of disappearance of the organism for all patients was 2.6 weeks. The time of appearance of reinfecting strains in the nose or throat of the patients varied from the end of the first and beginning of the second weeks (2*a*, 3*a*, 8*a*, 15*a*, 10*b*, 20*b*, 14*c* and 9*c*) to the end of the fourth week (3*b* and 8*b*) after admission to hospital and the average time of appearance of fresh types in the thirty-three patients who were reinfected was 2.4 weeks. The earliest times of isolation of the reinfecting strains in the thirty-three patients was as follows: first week, one patient; second week, eleven patients; third week, seventeen patients; fourth week, four patients. In the group of eighteen patients who were reinfected and also showed clinical signs of reinfection, the average time of appearance of the complicating signs was 2.6 weeks; the earliest appearance of clinical evidence of reinfection confirmed by the bacteriological findings was during the first week (14*c*) and the latest was 5.5 weeks (17*b*) after admission to hospital.

On the basis of these findings and of our investigation of cubicle-nursed patients it is probably correct to say that (*a*) complications due to the primary infecting strain of *Str. pyogenes* are much less common than those due to subsequent reinfection and, when they occur, they do so within the first 2 weeks of the disease; this view can only be confirmed by careful observation of a

considerable number of patients nursed either in cubicles or in single-bed wards; (b) over 90 per cent of complications appearing during the third week of hospitalization and subsequently are due to a reinfecting strain of *Str. pyogenes*. We are unable to throw any light on the relationship, if any, of reinfection to nephritis or late albuminuria. The time of occurrence of albuminuria in case 10a did not correspond to the usual period of onset of nephritis or late albuminuria.

We confirmed the previous findings of Allison & Gunn (1929) that when a reinfecting type was found in the nose or throat it was usually isolated on two or more consecutive occasions; also that the appearance of the fresh type was almost invariably accompanied by a considerable increase in the proportion of colonies of *Str. pyogenes* relative to colonies of other bacteria present on the culture plates. The reinfections appeared first in throat cultures and were usually followed by the appearance in a few days of the reinfecting strain in nasal cultures, again associated with an increase in the proportion of colonies of haemolytic streptococci.

PATHS OF REINFECTION

It will be seen from Table I that out of thirty-three patients in whom a reinfecting type was found, no less than twelve (36·4 per cent) showed the fresh type for the first time within the first 2 weeks of admission to hospital, that is to say at a time when they were still confined to bed. Theoretically patients may become reinfected in the wards in various ways: (1) via the air in dry dust particles; the possibility that this may occur has been shown by Cruickshank (1935), White (1936) and more recently by Brown & Allison (1937) who demonstrated that *Str. pyogenes* is abundant in the air of scarlet fever wards and it cannot be denied that such air may be a source of infection; (2) by droplet infection, e.g. coughing and sneezing; (3) by direct contact—conveyance by contact of patient with patient; (4) by indirect contact (a) through an intermediary such as a nurse or doctor themselves harbouring streptococci or conveying infection from patient to patient; this has repeatedly been shown to occur in infections due to *Str. pyogenes*, more particularly in relation to outbreaks of puerperal fever (Colebrook, 1935), (b) via toys, handkerchiefs, etc.; Brown & Allison (1937) have isolated multiple serological types of *Str. pyogenes* from toys, pencils, swabs of dining table and utensils, and lockers in scarlet fever wards; (5) by true carriers among the staff. In the present state of knowledge (2) and (3) seem to be the most frequent modes of transmission of reinfection. Patients reinfected in this way may be (a) still confined to bed, but visited by other patients who are convalescent and up; direct contact under such circumstances probably accounts for most cases of reinfection occurring among patients in bed during the first 2 or 3 weeks in hospital; (b) convalescent and up, playing and mingling with the other convalescent patients; members of this group may reinfect each other or be themselves reinfected as the result of visiting acute cases still in bed.

MULTIPLE REINFECTION WITH *STR. PYOGENES*

Table II shows the serological types primarily infecting the forty-seven patients, the number of patients (fourteen) who were not reinfected in hospital, and those reinfected with one or more types (thirty-three). It will be noted that a second type appeared in twenty-one cases, a third in eight cases, a

Table II. *Classification of forty-seven scarlet fever patients according to the serological type of the primary infecting strain of Str. pyogenes and the occurrence of reinfection*

Primary infecting type	No. of patients with no evidence of reinfection	No. of patients reinfected with one or more types of <i>Str. pyogenes</i>				Total reinfected	Total cases
		One type	Two types	Three types	Four types		
1	1	2	1	—	1	4	5
2	2	2	—	—	—	2	4
3	1	9	2	1	1	13	14
4	8	3	3	—	—	6	14
5	—	1	—	—	—	1	1
6	—	1	1	—	—	2	2
8	—	1	—	—	—	1	1
11	1	—	—	—	1	1	2
14	—	1	—	—	—	1	1
22	—	—	1	—	—	1	1
27	—	1	—	—	—	1	1
?	1	—	—	—	—	—	1
Total	14	21	8	1	3	33	47
Percentage	29.8	44.7	17.0	2.1	6.4	70.2	

? = one case of ? "surgical" scarlet fever. No *Str. pyogenes* isolated from nose or throat.

fourth in one case and a fifth in three cases. This contrasts strongly with the regular isolation of one serological type throughout the illness from patients nursed in cubicles or single-bed wards and indicates the potentialities for the spread of reinfection in multiple-bed wards.

Clinical and bacteriological observations on patients in this series as well as observations made over a long period suggest that some patients appear to be much more susceptible to reinfection than others. Three patients in this series were reinfected on no less than four occasions, each time with a different serological type, recalling the description by the mother of the child who "picks up everything that is going".

CARRIER RATE ON DISCHARGE

Of the forty-seven patients, forty (85 per cent) were still carriers¹ of *Str. pyogenes* on discharge from hospital, much the same figure as that (82.8 per cent carriers on discharge) found by Brown & Allison (1935) in a much larger series of cases. In the small series of sixteen cubicle-nursed cases already

¹ As there is at present no laboratory criterion for the virulence of *Str. pyogenes*, the term "carrier" indicates only that the patient is harbouring the organism and not necessarily that he is capable of transmitting the infection to others. It has already been shown (Brown & Allison, 1935) that although over 80 per cent of patients, convalescent from scarlet fever, harbour *Str. pyogenes* on discharge from hospital the return case rate is only about 4 per cent.

referred to, twelve (75 per cent) were still streptococcal carriers on discharge. These figures, while suggesting that cubicle isolation does not appreciably reduce the carrier rate on discharge, are much too small to support a firm conclusion. The persistence of haemolytic streptococci in cubicle-nursed patients may be due in part to confinement in small cells with no facilities for exercise in the open air.

It is interesting to note in comparison with the figures on p. 154 that twenty-nine (61·7 per cent) of the forty-seven patients were carrying on discharge a serological type of *Str. pyogenes* different from that found on admission. The difference between this figure and the total number of reinfected patients (thirty-three) is accounted for by two patients who were reinfected but yielded negative swabs on discharge and two who were reinfected but yielded on discharge the primary infecting type only.

BACTERIOLOGICAL EVIDENCE OF THE SPREAD OF REINFECTION BY A SINGLE TYPE OF *STR. PYOGENES*

The spread of reinfection in a multiple-bed ward is well exemplified by patient 4*b* in Table I, admitted at the beginning of the sixth week of the investigation. This patient was found to be suffering from scarlet fever due to *Str. pyogenes*, type 5, and until his admission type 5 had not on any occasion been isolated from any of the patients as either primary or secondary infecting agent, nor had it been isolated from any member of the ward staff.

One week later (seventh week), another patient, 7*b*, was found to be reinfected with type 5, coincident with the occurrence of coryza lasting for 4 days. The primary infecting strain (type 3) was not again isolated from this patient and the reinfecting type persisted until his discharge from hospital 3 weeks later.

During the eighth week, it will be seen that three more patients, 19*a*, 1*b* and 14*c*, became reinfected with type 5; the only one of these three patients to show any "manifest" evidence of reinfection was 1*b* with a temperature of 99° C. lasting for 36 hours. In the meantime the patient 4*b*, originally infected with type 5 and responsible for its introduction into the ward, became reinfected with type 2 showing "manifest" evidence of reinfection, and type 5 was not again isolated from him.

In the ninth week patient 19*a* was no longer a carrier of type 5 and 4*b* was discharged convalescent.

During the tenth week, two more patients, 13*b* and 5*c* were found to be reinfected with type 5. The reinfection in these two patients was latent and both were still carriers of the organism on discharge from hospital, 1 day and 2½ weeks later respectively.

Patient 4*b* was thus responsible, directly or indirectly, for the reinfection of six other patients in the ward, the reinfections being "manifest" in two cases and "latent" in the remaining four. The train of events is illuminating as

showing that the *Str. pyogenes* from a single patient may by transference continue to reinfect other patients even when the former is no longer carrying the organism and has been discharged from hospital.

REINFECTION AND RELAPSES

Table I shows that in this series there occurred two instances of "relapse", viz. 18*b* and 4*b*, in which the patients had second attacks of clinical scarlet fever, in both cases coinciding with the isolation of fresh serological types from the throat. Gunn & Griffith (1928) have reported three such cases, while the present authors have also made observations in three further cases occurring in the course of recent investigations. Gunn and Allison (unpublished) have similarly investigated two cases. The findings in these ten cases, all investigated bacteriologically, are shown in Table III.

Table III. *Bacteriological findings in ten cases of "relapse" in scarlet fever*

Observers	Case no.	Onset of relapse: period of hospitalization Week	Serological type of <i>Str. pyogenes</i> causing	
			Primary infection	Relapse
Brown & Allison	18 <i>b</i>	4th	4	2
	4 <i>b</i>	3rd	5	2
	573	5th	H	1
	R. 57	3rd	4	1
	234 A	4th	H	4
Gunn & Griffith	1	5th	4	3
	2	5th	4	2
	3	5th	H ¹	H ¹
Gunn and Allison	5	5th	H ²	H ²
	26	3rd	H ³	H ³

H = unidentified type.

H¹, H², H³. These strains were found to differ serologically; the reinfecting strains produced toxins many times more potent than those from the primary infecting strains.

The chief points of interest are that in all ten cases the patients were being nursed in multiple-bed wards and the occurrence of relapse was in each case associated with the appearance in the throat of a fresh serological type of *Str. pyogenes*. The onset of the relapses occurred between the third and fifth weeks of hospital isolation, half of them arising during the fifth week.

In observations made on patients nursed in single-bed wards and in multiple-bed wards confined to patients all infected with the same serological type, no relapses have occurred. Lichtenstein (1931) found in a series of 171 patients treated in an isolation pavilion in either single or double-bed wards that no relapses occurred among patients who were nursed alone for the duration of the disease or among patients of the same family rooming together; in these latter instances the patients were probably infected with the same serological type of *Str. pyogenes*. In the isolation pavilion, Lichtenstein had ten cases of "relapse" and in each instance the relapse appeared in patients

who were in the same room with another patient. In a control series of 171 patients nursed in a multiple-bed ward there were during the same period twenty-one relapses. It may be accepted therefore that relapses in scarlet fever are produced by reinfection with a different serological type of *Str. pyogenes* from that causing the primary disease.

The chief clinical sign classifying a patient as a case of "relapse" is the appearance of the rash accompanied by the red sore throat and temperature, the rash especially being evidence of the toxigenic factor as distinct from the invasive factor of the reinfecting strain. It is noteworthy that the reinfecting strain is as a rule many times more potent as a toxin producer than the strain causing the primary infection (Gunn & Griffith, 1928; Allison & Gunn, 1929, 1932). We have already mentioned that *Str. pyogenes*, type 4, has in the past been associated with a very mild form of scarlet fever with an ill-defined, transient rash and very slow production of antitoxic immunity. Toxins prepared from type 4 strains were found to possess a very low degree of potency when compared by skin test with the toxins produced by the other epidemic strains, types 1, 2 and 3. Table III shows that in four cases the primary infecting strain belonged to type 4, and in none of the other six did the primary strains belong to the epidemic types 1, 2 or 3. On the other hand these types were the cause of the relapse in six of the cases and in three of the others the reinfecting strains produced more potent toxins than the primary infecting strains. It is suggested therefore that the rash in cases of "relapse" is due to reinfection with a serological type, producing a toxin more potent than and possibly differing qualitatively (Gunn & Allison, 1932) from that produced by the primary infecting strain. Slow production of antitoxic immunity by the patient is probably an additional factor in the production of the clinical picture.

DISCUSSION

There has been a growing tendency in recent years both in this country and abroad to review the methods of dealing with scarlet fever in infectious diseases hospitals. The main trend has been in the direction of decreasing as far as possible the period of isolation in hospital and increasing the proportion of cubicles or bed-isolation accommodation. The principal reason for this has been the admitted failure of hospital isolation to check the incidence of the disease in spite of the fact that the figures of mortality and complications have been steadily falling. This fall is largely owing to the mildness of the disease in this country during the last two decades.

One of the chief factors militating against early discharge of scarlatinal convalescents is the occurrence of complications which prolong infectivity and add considerably to the period of isolation. Parsons (1927) found that in every isolation hospital considered in his investigation the majority of complications occurred during the third week of isolation and in most hospitals it was the fourth week during which the next highest incidence occurred. In the present investigation, out of forty-seven patients complications occurred

in twenty and in eighteen of these the complications were associated with reinfecting types of *Str. pyogenes*. The times of appearance of the complications in these eighteen patients were: first week, one; second week, six; third week, eight; fourth week, two; fifth week, nil; sixth week, one. As has been shown, secondary infection with or without complications shows the same periodicity, with the main incidence during the third week (seventeen out of thirty-three), the period at which the patient is, as a rule, convalescent and recovering from his primary infection.

In his report on the control and treatment of scarlet fever Parsons compared the percentage incidence of complications in "long-stay" and "short-stay" hospitals and showed that the advantages appeared to be in favour of the "short-stay" hospitals. In the present enquiry the average period of detention in hospital of the forty-seven patients was 33·4 days, which places them in the "short-stay" category. In spite of the shortened period of isolation, thirty-three (70·2 per cent) of the patients were reinfecting and more than half (eighteen) of these showed manifest evidence of reinfection, which was as a rule mild. Therefore in order to prevent such reinfection, with its inevitable trail of prolonged invalidity and added expense, something more is required than mere reduction in the period of isolation.

It has already been shown that it is possible for infection with haemolytic streptococci to be carried in the air (Cruickshank, 1935; White, 1936; Brown & Allison, 1937), but it is generally agreed that infection by contact is probably the chief mode of spread. Contact infection may be direct from patient to patient, or indirectly conveyed by the nursing staff, thermometers, toys, eating utensils, etc. The first desideratum therefore, in addition to the basal requirements of adequate bed-spacing and ventilation, towards preventing reinfection by haemolytic streptococci is improvement of the training and technique of the nursing staff. The belief current among the nursing and medical staffs of many isolation hospitals that no special precautionary measures are necessary to prevent reinfection of one patient by another or by the nurse's hands, etc., in a multiple-bed ward, because "they are all scarlet fever" must be discarded. Each patient should be treated as a separate infection, highly prone to reinfect other patients in the ward or be himself reinfecting. In many isolation hospitals, in multiple-bed wards where patients all infected with the same disease, e.g. scarlet fever, are being nursed, it is uncommon for the nursing staff to wash their hands or carry out disinfectant measures between attending one patient and proceeding to the next. It is not sufficient to disinfect the hands only after attending to patients with complicating discharges such as otitis media or rhinorrhoea, as the haemolytic streptococci are probably present on the patient's face, hands, handkerchief and bedclothes even in uncomplicated cases.

Probably the most important mode of spread of reinfection in scarlet fever is by direct contact from patient to patient. The natural sociability of children with close contact and free interchange of toys, handkerchiefs, eating utensils,

etc., renders them particularly likely to reinfect each other. This is a problem of considerable administrative difficulty and calls for a consideration of the various methods in use of nursing patients in isolation hospitals. Investigations in recent years by Gunn & Griffith (1928), Gunn & Allison (1929), Lichtenstein (1931) and Brown & Allison (1935) have shown the degree of reinfection which occurs in multiple-bed wards devoted to scarlet fever. It is probably not going too far to say that the large multiple-bed ward for nursing patients infected with *Str. pyogenes* has had its day. The system of special wards for the segregation and treatment of acute and convalescent or complicated and uncomplicated cases of scarlet fever, while it may reduce slightly the incidence of reinfection by keeping patients with infective discharges apart from the clean cases, will not solve the problem of reinfection owing to (a) the diversity of serological types of *Str. pyogenes*, and (b) the intimate association of convalescent patients. The systems of barrier-nursing and bed-isolation in multiple-bed wards requires an intelligent nursing staff with good technique and unremitting attention, and while they are to be recommended where patients must be nursed in multiple-bed wards, they are open to the same criticisms as the former methods, in that they break down when the patients are convalescent and up, owing to the great difficulty of preventing contact. We have used the terms "barrier-nursing" and "bed-isolation" synonymously, applied to scarlet fever, as among any group of scarlet fever patients there are almost certainly individuals really suffering from specifically different infections. The last system of nursing for consideration is that of single-bed wards or cubicle-isolation, and the success of Lichtenstein's (1931) experiments in nursing scarlet fever by this method have already been mentioned. In the small series of cubicle-nursed patients which we have investigated the results showed that no reinfection occurred, and confirm Lichtenstein's finding that "relapses" only occurred in patients nursed in the general ward or in patients who shared a room with one or more other patients.

We are therefore driven to the conclusion in agreement with Hobday (1936) that the ideal accommodation for patients in isolation hospitals is the single-bed ward or cubicle for each patient. The main objection to this system is financial—cost of building, increased space required and increase of nursing staff. Small units of four beds would probably be of considerable value in decreasing reinfection, especially if children of the same family infected at the same time or patients from the same local epidemic, e.g. institutional outbreaks, and presumably therefore all infected with the same serological type of *Str. pyogenes*, could be nursed together as suggested by Lichtenstein. Another alternative would be the setting aside of small wards, containing about eight beds, for patients who are all infected with the same serological type of *Str. pyogenes*; three or four units of this type would be required according to the number of epidemic types of *Str. pyogenes* prevailing locally. Patients would in the first instance be admitted to the general ward and barrier-nursed, swabs would be taken from the nose and throat or other focus

of infection, e.g. burn, wound, etc., the serological type of *Str. pyogenes* identified and the patient would then be transferred to the "type" ward. Sporadic cases infected by the less common serological types would, if possible, be nursed in single-bed wards or, if this were not feasible, they could be barrier-nursed in the general ward; an additional improvement would be the use of large screens to segregate patients in the general ward.

The recent investigations of Okell & Elliott (1936), on the spread of infection with haemolytic streptococci in oto-rhinological wards, show that it is not only in isolation hospitals that such cross-infection occurs and that there is need for similar precautions in general hospitals. Their recommendations for the prevention of the spread of infection are well worthy of study. Clinical, bacteriological and epidemiological investigations in recent years, and especially the work of Glover & Griffith (1931) have shown that the exanthem of scarlet fever is only one manifestation of a widely differing group of infections which may be caused by *Str. pyogenes*. Throat infection with this organism may range from healthy carrier through mild pharyngeal catarrh or acute tonsillitis to the complete clinical picture of scarlet fever and its complications and, in any epidemic due to one serological type, the cases will provide examples covering the whole range of clinical differentiation.

The present investigations have been on a comparatively small number of patients, but the conclusions derived from them are supported by the findings and experience of various workers during the last 10 years. Multiplication and extension of these enquiries are necessary not so much to confirm the results, but rather to help in the formulation of improved methods of nursing patients infected with *Str. pyogenes* so as to prevent transfer of the infection to others.

SUMMARY

1. The term "reinfection" has been defined as the secondary infection of a scarlet fever patient during hospitalization with *Str. pyogenes* belonging to a serologically different type from that producing the primary infection.

2. Of forty-seven scarlet fever patients nursed in a multiple-bed ward and swabbed twice weekly during their period of isolation, thirty-three (70.2 per cent) became reinfected with a serological type of *Str. pyogenes* different from that causing the primary disease.

3. In fifteen out of the thirty-three patients reinfected, the reinfection was "latent", i.e. gave rise to no clinical signs, while in the remaining eighteen the reinfection was "manifest", i.e. was accompanied by clinical signs or complications.

4. Patients nursed in cubicles or in a ward confined to infections with a single serological type did not show reinfection; their convalescence was progressive and there were no late complications.

5. The majority of complications occurring during the third week of hospitalization and subsequently, in multiple-bed wards devoted to scarlet fever, are due to reinfection.

6. Most reinfections occur during the third week in hospital at a time when patients are as a rule convalescent from their primary infection.

7. The most frequent mode of transmission of reinfection appears to be by direct contact of patient with patient.

8. Ten instances of "relapse" in scarlet fever (only three in the present series) are quoted; in all of them the patients were nursed in multiple-bed wards. In each instance the "relapse" coincided with the isolation of a fresh serological type of *Str. pyogenes* from the throat, and must therefore be regarded as a second attack of scarlet fever.

9. The various systems of nursing patients in isolation hospitals are discussed and it is suggested that scarlet fever patients should be cubicle-nursed if possible. Failing this they should be nursed by the bed-isolation method in multiple-bed wards. By setting aside small wards it might be possible to keep together patients who are all infected by the same serological type of *Str. pyogenes*; the number of such wards would vary with the number (usually three or four) of epidemic types current at the time.

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