AN INVESTIGATION

INTO THE RELATIONSHIP BETWEEN THE

BACTERIOLOGICAL FINDINGS AND THE

"RETURN CASE" IN SCARLET FEVER

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

INTRODUCTION

In isolation hospital practice when patients are admitted suffering from a disease of known organismal origin, before discharge from hospital is permitted examination is usually made in order to determine whether the infecting organism is any longer present. Thus if diphtheria be taken as an example, faucial and nasal swabs are examined as a routine measure for the presence or absence of C. diphtheriae. Likewise in the enteric group of diseases, stools are examined bacteriologically and if found to be still harbouring the particular pathogen, the patient from whom they came is detained in hospital maybe for a considerable period of time until the organism is found to be no longer present. This procedure is done in order that so far as is possible no patient, having suffered from an infectious disease, shall be permitted knowingly to resume his normal duties while still a potential danger to his fellow-citizens.

Cases of infectious disease occurring in a household, a member of which has recently returned from hospital suffering from the same disease, are known as 'return cases'. Such have been more accurately defined by the Society of Medical Officers of Health in the following terms: Return cases may be defined as "cases occurring in the same house or elsewhere, and

apparently traceable to the person released within a period of not less than twenty-four hours, and not more than twenty-eight days after his return or release from isolation."

The two most common infectious diseases in which return cases are of frequent occurrence are probably diphtheria and scarlet fever. In the former disease when a patient has been admitted to hospital suffering from it, before he is discharged as free from infection, faucial and nasal swabs are examined for the presence of the organism while in the latter disease no such precaution is usually taken. To-day, of the two diseases mentioned, diphtheria is by far the greater killing disease but nevertheless scarlet fever can be a very unpleasant disease, and it is our bounden duty to endeavour so far as we can to prevent it, and therefore any step which might lessen the number of return cases would be a welcome one.

In the annual health reports of the Medical Officer of Health of the Borough of Willesden for the years 1934 and 1935 the following table shows the numbers of return cases of scarlet fever which arose.

	1934	1935
Number of infecting cases giving rise to return cases not longer than 28 days after release from isolation.	38	23
Number of return cases they gave rise to.	36	30
Number of infecting cases per cent of total hospital cases.	3.8	5.3
Number of return cases per cent of total hospital cases.	4.9	6.9
Total number of hospital cases.	741	433

It is thus seen that in the small hospital of the Borough of Willesden (190 beds) the return case rate in two consecutive years varied from 4.9% to 6.9%. This variation seems to be found in most hospitals in this country and also on the Continent of Europe.

For some years past the organism responsible for scarlet fever has been suspected to be a streptococcus, although scientific proof was lacking until 1931 when Dick and Dick proved conclusively that such indeed was the case.

In the following small group of 106 cases of scarlet fever, which I have investigated, an attempt has been made to determine the following:

(1) Is it a practicable routine in fever hospital practice to isolate haemolytic streptococci from the throats of patients suffering from undoubted attacks of scarlet fever?

(2) If this is the case, to endeavour to determine the average length of time the organisms could be found in the throat.

(3) To determine the relationship, if any, between the bacteriological findings and any return cases which might arise.

The cases investigated have all been clinical cases of scarlet fever treated in the wards of the Borough of Willesden's Isolation Hospital, and no case which was in any way of doubtful diagnosis is included. On admission, a swab was taken from the tonsillar regions and from any nasal or aural discharge present in addition, and plated on blood agar. Thereafter swabs were

taken at intervals of seven days until the patient was discharged from hospital; the question of whether or not he was fit for discharge was entirely estimated on clinical examination, irrespective of the bacteriological results obtained.

BACTERIOLOGY OF THE STREPTOCOCCUS (and CLASSIFICATION)

The term Streptococcus is given to organisms of spherical shape which have a tendency to grow in chains, either long or short, or in pairs.

The Committee of American Bacteriologists separated the pneumococcus from the main group by forming a genus Diplococcus c̄ D.pneumoniae as the type species but responsible opinion in this country considers that this is not desirable. With this I am in agreement as will be seen later when classification of the streptococci is considered.

A description of the generic characters of the streptococcus is given as follows by Topley and Wilson (Principles of Bacteriology and Immunology, 1936).

"Definition - Streptococcus.

"Spherical or ovoid cells, arranged in short or long chains, or in pairs. Usually non-motile. Non-sporing. Most species Gramnegative. Some species form capsules. Growth tends to be relatively slight on artificial media, and some species grow poorly in the absence of added native protein. Several species produce characteristic changes in media containing blood. Various carbohydrates are fermented with the production of acid.

Most species fail to liquefy gelatin. Most species are aerobic and facultatively anaerobic; some are anaerobic. Many species are normally parasitic on man or animals; some species are highly pathogenic, and some produce soluble toxins.

"Type species. Streptococcus pyogenes."

In the classification of the streptococci many attempts have been made. Classification has been attempted on the criterion of morphology - on length of chain - but this failed. It has also been tried based on the fermentation reactions of the streptococcus to various sugars notably lactose, salicin (which are fermented), and mannitol, raffinose, or inulin (which are not fermented).

This method to-day is rather used as evidence of a confirmatory nature than for primary differentiation.

Bile solubility, the decolorizing or not of a dilution of methylene blue added to milk, and heat resistance have also been tried, but they too are rather used as auxiliary evidence than in primary identification.

Classification based on changes produced in blood.

When certain strains of streptococci are grown on blood agar plates it is found that some of them have the power of producing clear zones of lysis while other strains have the power of producing areas of a greenish discoloration surrounding them. Other strains again are unable to produce any area of lysis whatever.

Brown, (J.H.Brown, Monogr. Rockefeller Inst. Med. Res.No.9,

1919) in a monograph in 1919 describes four different types of reaction in blood agar plates.

"α. A somewhat greenish discoloration and partial haemolysis of the blood corpuscles immediately surrounding the colony, forming a rather indefinitely bounded zone 1-2 m.m. in diameter, outside of which is a second, narrow, clearer, not discoloured zone. Under the microscope many corpuscles are seen in the inner zone and these are obviously discoloured, the discoloration varying in degree with different strains of streptococci. Very few corpuscles remain in the outer, clearer zone; and these are never discoloured. These typical appearances may fail to appear after 24 hours', or even after 48 hours' incubation, at the end of which time the narrow outer zone of haemolysis may not have developed. In such cases this zone makes its appearance during the subsequent 24 hours in the ice chest. If a plate, which has developed the typical appearances, is re-incubated for 24–48 hours, and then placed in the ice chest for a further 24 hours, a double series of rings will frequently develop, so that the colony is surrounded by a hazy discoloured ring, a clear haemolysed ring, and a second clear ring. By repeating the whole process it is sometimes possible to develop three or more series of such rings.

"β. The colonies are surrounded by sharply defined, clear, colourless zones of haemolysis, 2-4 m.m. in diameter. Under the microscope no corpuscles can be seen within this zone. The zones of β-haemolysis develop more rapidly than those of

the α-type. They are often well developed after 18 hours' incubation. They extend slightly between the 24th and 48th hour, but show no qualitative changes. They undergo no alteration or extension during the subsequent 24 hours in the ice chest.

"γ The colonies develop in blood agar without any change in the surrounding medium."

It will therefore be appreciated that this criterion serves a very useful method of primary identification and is the method used by the writer in this investigation.

The terms α- and β-haemolysis are now generally used in bacteriology; the α-haemolytic strain is exemplified in Str. viridans and Str.pneumoniae while the β-haemolytic strain is usually regarded as a haemolytic streptococcus.

The γ-strain includes those strains of streptococci which cause no change in blood agar and the term "indifferent streptococci" is sometimes used in referring to them.

For practical purposes this method of classification can be summarised as follows:

(1) Haemolytic streptococci - these producing β-haemolysis on blood agar plates.

(2) Streptococci giving α-haemolysis.

(3) Streptococci having no action on blood agar.

The further subdivision of these groups has proved to be extremely difficult and the technique now employed requires considerable experience and skill. In the case of Str.pneumoniae it was discovered quite early that this organism could be sub-

divided into three types leaving a fourth group which contained a large number unclassified. Two different groups of workers - Dochez and Avery in America, and Lister in South Africa - using a similar technique, viz. direct agglutination and agglutination absorption proved quite conclusively that pneumococci isolated from cases of human pneumonia could be divided into three well differentiated types, leaving a large heterogeneous group unclassified. The American workers called them Types I, II, and III and Group IV, while Lister labelled his with letters instead of numbers. Further work by Cooper in 1929 (J.Exp.Med. 40,609) has shown that there are in this heterogeneous group 29 new antigenic types making a total of 32 antigenically different types of pneumococci.

"A further advance was made in the study of the antigenic structure of the pneumococci and of bacteria in general when Avery, Heidelberger, and their colleagues attacked the problem of antigenic structure from the chemical side." (Topley and Wilson, p.444.)

These workers found that the components of the capsules of pneumococci could be separated into complex polysaccharides by a complicated chemical process, and that these polysaccharides could be used (when used in solution) to determine type-specificity of pneumococci with great accuracy in high dilution.

Topley and Wilson give an excellent description of the picture of the antigenic structure of the species Str.pneumonia which I quote:

"There is a central protoplasmic portion of the cell which, in its antigenic relationships, is neither species nor type-specific. Situated probably at the cell surface, there is another component, mainly carbohydrate in nature but containing nitrogen and phosphorus that is specific for Str.pneumoniae as a species. External to this, in the normal smooth forms, there is a capsule composed wholly or in part of a polysaccharide that is specific for each pneumococcal type. There are, we must suppose, at least 32 of these capsular polysaccharides within the pneumococcal species; probably there are more. The virulence, and the antigenic behaviour of the intact pneumococcal cells are, it should be noted, determined by these capsular antigenic components, so that they are of particular importance to the medical bacteriologist."

The antigenic structure of the haemolytic streptococcus is much more difficult. This appears to be due to two main reasons viz:

(a) using the definition previously given - the occurrence of β-haemolysis on a blood agar plate - are included not one, but several species.

(b) the technical difficulties of antigenic analysis are far greater than in the case of the pneumococcus.

Previously, in the attempts to classify the haemolytic streptococcus, the same technique, namely agglutination and agglutination absorption, was employed as in the study of the antigenic structure of the pneumococcus, and it appears that the preparation of a satisfactory suspension of the haemolytic

streptococcus under study is well nigh impossible owing to auto-agglutination in saline. F.Griffith (J.Hyg.Camb. 1926, 35) has isolated 27 types of pathogenic haemolytic streptococci to man using this technique.

Lancefield (J.Exp.Med. 1928, 1934, 47, 59) has evolved a new technique which appears to have enormous possibilities though, as will be appreciated, is a highly skilled one and beyond the resources of the ordinary laboratory worker.

This consists in preparing an extract from dried bacteria which have been pulverised in a ball mill and then boiled in a water bath for 15 minutes with N/20 HCl and thereafter neutralising with NaOH. This preparation of the bacteria is suspended in saline and to it is added an immune serum which has been previously put up against (i.e. absorbed by) heterologous strains of haemolytic streptococci.

In a series of articles (the summaries of which I quote below) Lancefield found in her extracts two non-type specific substances in addition to a type-specific substance. The non-type-specific substances consisted of (a) a carbohydrate substance which she has labelled C-substance, and (b) a nucleo-protein which she called the P-substance.

The type-specific substance was a protein and this she called M-substance.

SUMMARY I. Lancefield R.C., J.Exp.Med., 1928, 102.

1. HCl extracts of Str.haemolyticus contain type-specific as well as non-type-specific substances. The precipitates formed by these crude extracts with homologous anti-bacterial serum are flocculent, while those obtained with heterologous serum are usually disc-shaped.

2. The type-specific substance may be detected by the use of anti-bacterial sera absorbed with heterologous strains of haemolytic streptococci. Such absorbed sera are type-specific: they are precipitated only by extracts of strains of the homologous type.

3. Any heterologous strains of haemolytic streptococcus absorbs the antibodies for all other heterologous strains but homologous strains absorb type-specific antibodies as well.

4. Three strains did not yield a type-specific substance; and it seems probable that they had lost this function because of long-continued cultivation in artificial media.

5. Classification based on the precipitin test with absorbed serum agrees with that previously determined by agglutination and protection tests. The method is, therefore, applicable to the problem of classification of the haemolytic streptococci.

In a further article Miss Lancefield investigates further the chemical and immunological characteristics of the type-specific substance (M) of streptococcus haemolyticus.

SUMMARY II. Lancefield R.C., J.Exp.Med., 1928, p.479.

1. A summary of the evidence for the protein nature of this substance follows:

   (a) It is precipitated by the usual protein precipitants such as, dilute alcohol, dilute acetic acid, picric acid.

   (b) It contains 14% protein nitrogen after considerable purification.

   (c) It is progressively destroyed by removal of the NH_2 group by treatment with nitrous acid.

   (d) It is completely and readily digested by trypsin and by pepsin.

2. "Purified" extracts react in relatively high dilution with homologous anti-bacterial sera, but do not precipitate most heterologous anti-bacterial sera or sera potent in non-type-specific antibodies for the group reactive nucleo-protein P or for the species specific probable carbohydrate C.

Attempts to immunise rabbits with the type-specific protein have been unsuccessful, with simple salt-solution extracts of streptococci as well as with purified solutions. This protein therefore seems to have the characteristics of a haptene. The type-specific substance (M) is contrasted with the so-called nucleo-protein (P) which shows group relationships with nucleo-proteins of related species and is the only fraction of haemolytic streptococcus extracts so far obtained which, after separation from the bacterial cell, is a true antigen leading to antibody production when injected into rabbits.

In a third article R.C.Lancefield investigates more fully the chemical and immunological characteristics of the species-specific substance (C) of streptococcus haemolyticus.

1.(a) It seems to be a carbohydrate because considerably purified preparations of C resisted prolonged tryptic and peptic digestion and were negative for the ordinary protein colour tests but gave positive Molisch reactions to the limit of the precipitin titre . . .

(b) The C substance forms precipitates with anti-bacterial sera prepared against heterologous, as well as against homologous haemolytic streptococci.

(c) The C substance is probably a haptene.

In Miss Lancefield's earlier observations as quoted above on the C substance, she used haemolytic streptococci of human origin only but later investigation in which strains from a variety of sources, human and animal, were included showed that this component (C) was <u>not</u> shared by haemolytic streptococci as a class, but served to differentiate them into several well defined groups with a definite correlation between antigenic type and natural habitat.

Thus, using the C substance to define the group, and M substance to define the type in the group, Lancefield has been able to differentiate over 20 different haemolytic streptococci belonging to Group A. These organisms have been obtained from human sources, mainly from cases of acute infection.

The organisms of the second group (B) were derived from various animals, mainly from cases of bovine mastitis.

49 strains falling into the third group (C) were derived

from various other animals all suffering from definite infection (guinea-pig, rabbit, horse, fox, pig, and fowl).

8 strains falling into a fourth group (D) were derived from cheese and human faeces.

3 strains falling into a fifth group (E) were obtained from certified milk.

In Miss Lancefield's opinion, which is shared now by most authorities, only haemolytic streptococci belonging to Group A are capable of producing human infection.

HISTORY OF SCARLATINA.

Most authorities appear to agree that the disease was unknown to the writers of the classics of antiquity and give credit to Ingrassias of Palermo for giving the first description of scarlet fever about the middle of the sixteenth century. From that time until the end of the eighteenth century, scarlatina became recognised as a clinical entity though there does appear to have been some difficulty in the differentiation of the more malignant types with severe anginal signs with diphtheria.

Since recognition, as mentioned earlier, the disease has gone through many cycles being at times very malignant and at other times very mild. At the present day the type of the disease met with is exceedingly mild and indeed in the year 1936 in the Borough of Willesden's Isolation Hospital out of nearly 500 cases treated in the wards, there have been no deaths at all.

BACTERIOLOGY OF SCARLET FEVER.

In 1887 while investigating the cause of an epidemic of scarlet fever at Hendon, Klein came to the conclusion that streptococci which he isolated from the udders of the cows supplying the milk were the organisms responsible. Since then many writers have recorded the finding in the throats of infected persons of long chained streptococci but there has been great hesitation in accepting the association as cause and effect. For many years the organisms obtained from the throats were regarded as being mere secondary invaders, although it was agreed by most authorities that streptococci were found in such complications as rhinitis and otitis media.

Most authorities agree that for a particular organism to be accepted as the cause of a certain disease, a series of conditions must be fulfilled. Such conditions are usually termed "Koch's Postulates", and although I have been unable to find in any textbook of bacteriology Koch's original statement, they run in general terms as follows:

1. The organism should be found in all cases of the disease in question.

2. The organism should be cultivated outside the body in artificial media in pure culture.

3. The organism once isolated in pure culture should be able to reproduce the disease in susceptible animals.

Koch died in 1910 and since then bacteriology has made great progress; so to-day in addition to these criteria must be added a fourth "postulate" viz, the demonstration of specific antibodies in the blood of an infected man or animal.

When we come to apply these criteria individually to the theory that a haemolytic streptococcus is the organism responsible for scarlet fever we must come to the conclusion that such indeed is not theory but fact.

1. That Str. pyogenes can be recovered from the throats of patients with scarlet fever in almost 100% of cases has been shown many times and reference to any of the standard textbooks on infectious disease gives many examples. As will be shown at a later stage in this thesis a haemolytic streptococcus can be recovered in almost 100% of cases.

2 & 3. For the proof of the criteria that the suspected

organism should be cultivated outside the body in artificial media in pure culture and that once isolated, should be able to reproduce the disease in susceptible animals, the most conclusive demonstration is that of the Dick brothers (1921, J.Amer.Med.Ass., 77, 782). In 1921 they attempted to reproduce scarlet fever in a series of human volunteers by inoculating the throats of the volunteers with organisms isolated from scarlatinal patients including haemolytic streptococci but failed. But in 1923 they did succeed in reproducing it. This time they used a strain of Str. pyogenes which had been isolated from pus from the finger of a nurse who had been nursing a case of scarlet fever now convalescent, and who was now suffering herself from surgical scarlet fever. Using five volunteers who were inoculated by swabbing the fauces with a broth culture of the organism, Dick and Dick (1924a J.Amer.Med.Ass., 82, 265; 1924b, Ibid 83, 84) succeeded in giving one of the five a typical attack of scarlet fever. As a control, five other volunteers were swabbed with filtrates from the broth cultures and showed no reaction but later, when swabbed with the cultures themselves, one of the five again developed scarlatina.

4. In order to prove that infection with the Str.haemolyticus will result in the development of specific antibodies in the blood, consideration of the blanching phenomenon first described by Schultz and Charlton and usually described as their best is necessary. These workers noticed that if 1 c.c. of "normal" human serum was injected into the skin of a patient showing the

characteristic punctate erythematous rash of scarlet fever, a blanching of the skin in the immediate neighbourhood of the injection resulted. And moreover, if human serum from a patient just convalescent from scarlet fever was used a similar result was obtained. However, if serum was used from a patient who was at the height of an attack then no blanching resulted. Later, it was found that normal horse serum, or diphtheria anti-toxin, did not possess the property of blanching, but that the serum of horses immunised with a toxin of Str. pyogenes did possess the property of blanching as described by Schultz and Charlton. The next fact for consideration is that described by Mair (Lancet 1923, ii, 1390) who demonstrated that the serum of a child gave a negative Schultz-Charlton reaction before an attack of scarlet fever and a positive reaction after convalescence, and he also showed that sera obtained from young children who had not gone through an attack of scarlet fever gave a greater percentage of negative reactions than sera from apparently normal adults.

His view that a positive reaction is due to the development of a specific anti-toxin which on injection intradermally neutralises the toxin present in the skin of the scarlet fever patient with the result that blanching at the site occurs.

Due consideration of the data given above will, I think, show that infection with the Str.pyogenes in time gives rise to the production of specific antibodies. Mair's demonstration cited above, coupled with the fact that serum from a horse which

has previously been immunised with a stain of Str.pyogenes is exceedingly strong evidence, that such indeed is the case.

The bacteriological evidence that Str.pyogenes is indeed the organism responsible for the disease scarlatina is therefore complete and recognition of it will explain in large measure the different clinical manifestations of the disease, and will also make more clear many phenomena which previously were just accepted as fact.

But before discussing the clinical signs and symptoms, there is one other point which can be most conveniently examined in this section. I refer to the erythrogenic toxin.

Dick and Dick (J.Amer.Med.Ass., 1924(a)(b), 1925(a)(b)) demonstrated that filtrates of broth cultures of the Str.pyogenes when injected intradermally into some people contained a toxin which produced an erythematous reaction. These individuals were normal persons who had never had an attack of scarlet fever. If small doses - 0.1 c.c. of a 1:1000 dilution of filtrate - were injected intradermally, a local reaction resulted, while if larger doses were administered there occurred a general reaction with fever, nausea, vomiting, and a generalised punctate erythematous rash. In other words, the patient had suffered from an attack of scarlet fever without being actually infected with the organism.

Such attacks of "miniature scarlet fever" have been described in the medical press when occasionally occurring during immunisation with the usual doses of toxin.

Reference to textbooks of bacteriology written about 10 years ago, shows that this scarlatinal toxin was at first regarded as a characteristic and distinctive product of a single organism called the Str.haemolyticus which was regarded then as the causative organism. But, as shown previously in this thesis, such a state of affairs is not to-day considered to be the case. The evidence at present available tends to support the following conclusions.

The production of an exotoxin which in man gives rise to a punctate erythematous rash is not confined to a single organism, the Str.haemolyticus, but rather to the group of haemolytic streptococci now generally referred to as Str.pyogenes, e.g. Griffiths (J. Hyg. Camb. 1934, 32, 542) differentiated 27 types of haemolytic streptococci but found that types 1, 2, and 3 were the ones most frequently isolated from cases of scarlet fever.

It is also to be noted that the administration of anti-toxin to patients suffering from scarlet fever with typical skin manifestations is followed within 24 hours by the fading of the rash.

It would appear, therefore, that there is little difference in the quality of the exotoxin produced by antigenically different organisms but rather that some organisms produce an exotoxin in greater quantity or of greater strength than others, and therefore give rise more constantly to skin manifestations in man.

CLINICAL SCARLET FEVER.

If a textbook on general medicine or a textbook on infectious diseases be referred to it will be found that scarlet fever is defined in terms like the following:

Scarlatina is an acute specific, infectious disease due to a streptococcus and characterised by a sudden onset with fever, headache, vomiting, and sore throat, followed on the second day by a generalised punctate erythematous rash which later gives rise to desquamation and is frequently complicated by cervical adenitis or abscess formation, otitis media, and nephritis.

In 1899 "The Infectious Disease (Notification) Act" became law in England and Wales, and included amongst other infectious diseases scarlet fever in the schedule of compulsory notifiable diseases, and provided a penalty of 40/- for failure to notify. To the clinician, therefore, the presence of the "punctate erythematous rash" is the acid test as to whether or not a patient is notified to the public health authorities as suffering from scarlet fever. In the majority of cases, once notified, such a case is removed to the appropriate isolation hospital and detained there for a period of some weeks.

In the present survey the patients under investigation had all been officially notified by their own doctor as cases of scarlatina, and were treated throughout in the scarlet fever wards of the hospital. They were therefore clinical cases of the type of scarlet fever found in London (Willesden) in 1936-37.

A brief clinical description follows:

On admission they showed a punctate erythematous rash on trunk and limbs. This rash varied considerably in intensity, in some being very bright and in others not so bright, but in all there was no doubt about its presence. The face usually showed the typical malar flush with circumoral pallor.

Sore throat was complained of in all but a very few cases and on examination the fauces showed engorgement to a greater or lesser extent. In a few cases exudate was present on one or other tonsil but this was exceptional.

Tongue was not normal. The majority of cases being admitted to hospital on the same day as the rash had appeared, the tongue was covered with a white fur, the papilla engorged and showing through the fur - i.e. the white strawberry tongue. But in a few cases delay had occurred in notifying and they were admitted about the fourth day of the disease when the fur had stripped to a greater or lesser extent, and the acute faucial engorgement becoming less marked, i.e. the red strawberry tongue.

Pyrexia was usually present on admission, it being of moderate extent - 100° to 101°F - usually falling to normal within 24 to 48 hours and in the absence of complications

remaining thus until discharge.

In all cases the treatment, apart from general nursing treatment, consisted in the intramuscular injection of 10 c.c. scarlatinal anti-toxin (P.D.& Co.). This was invariably followed within 12 to 24 hours with the fading of the rash, though in some cases faucial engorgement with sore throat persisted for a day or two longer. Those patients who were old enough were given gargles with the commoner gargles e.g. Glyc-thymol Co., while the younger patients had their throats painted with Mandl's paint.

No deaths whatsoever occurred, and the complications encountered were for the most part the minor ones such as rhinitis, adenitis, and otitis media. Two cases of otitis media went on further to mastoiditis, the radical operation being performed in the treatment. No deaths occurred in the series.

PREPARATION OF MEDIA.

Throughout the present investigation the method used in the culture of organisms from the throats of patients has been inoculation of blood agar plates and incubation thereafter at 37°C. Blood agar was prepared in the following way:

To 1 litre of hot water (not sterile) is added 10 grams of "Lab.Lemco" (the meat extract prepared by Messrs Oxo Ltd.), 1% peptone, and 0.5% salt.

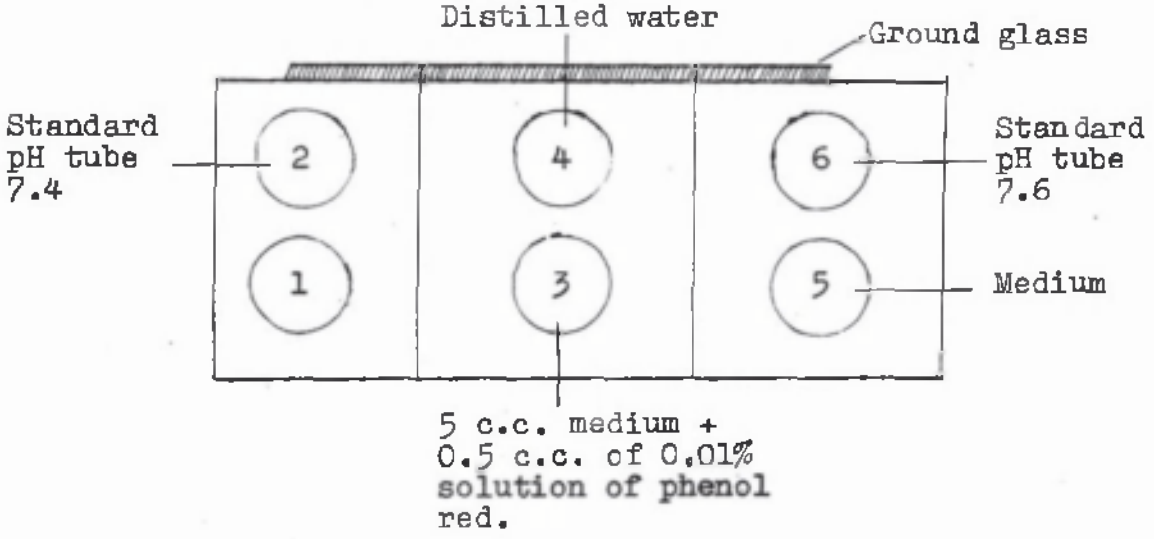
N/1 NaOH is then added to the mixture until the reaction is slightly alkaline to phenolphthalein. This is done by taking a sample of the solution e.g. 10 c.c., adding two drops phenolphthalein and noting the amount of normal NaOH required to turn the solution a faint pink. From this the amount of N. NaOH required for 1 litre is calculated, and added.

The alkaline broth is now steamed for 45 minutes in the steam steriliser in order to precipitate the phosphates, and afterwards filtered through ordinary filter paper [Whatman's No.1] and allowed to cool. The solution now is clear and slightly brownish in colour.

The next step is the standardisation of the broth solution to pH 7.5, and in the media used in the present investigation the colorimetric method was used. The set of standards used were purchased commercially and were solutions of fixed and known hydrogen-ion concentration to each of which had been added

a definite amount of the indicator - phenol red.

In standardising the broth, therefore, a small quantity e.g. 5 c.c. is taken and to it is added 0.5 c.c. of 0.01% solution of phenol red. This is titrated with N/20 HCl until the colour obtained matches the standard. A plan of the comparator rack is given below.



It is found easier to bring the solution to a colour midway between two standard colours than to make an exact match of two tints and so in this investigation the pH of the broth has always been brought to midway between the standard colours of pH 7.4 and pH 7.6 i.e. 7.5 approximately.

Also, since the broth is coloured slightly brown both standards must be viewed with a background of broth in order that the solution being titrated can be compensated for.

From the readings obtained from this sample it can be easily calculated how much N/20 HCl it will be necessary to add to the bulk broth in order to bring it to pH 7.5.

To the broth so prepared is added 2% agar powder. The mixture is now heated in the steam steriliser for approximately 1 hour until the agar is dissolved. When dissolved it is cooled to 55°C and the switched whites of 2 eggs added (to 1 litre). This is then sterilised in the autoclave at 5 lbs pressure for 1 hour.

The sterilised agar broth medium is now filtered through Chardin filter paper being kept at approximately 55°C meantime; and in this investigation in order to maintain sterility, the now filtered sterile agar broth medium was run into sterile bottles of 1 ounce capacity with screw tops.

These bottles of sterilised nutrient agar are once again autoclaved at 5 lbs pressure for ½ hour, cooled, and incubated at 37°C for 24 hours, and if found after examination to be sterile are stored until required for use. The usual amount of nutrient agar run into each bottle was 12 c.c.

PREPARATION OF BLOOD AGAR.

The blood used in culturing streptococci throughout this investigation was obtained by aspirating from the veins of human volunteers. Usually about 50 c.c. was withdrawn at a time under sterile conditions and immediately injected into a sterile bottle containing a small quantity of sodium citrate solution and capped with a rubber cap.

The nutrient agar is heated until liquid and then poured into a sterile Petri dish. When cooled to about 55°C, 1 c.c. blood is

allowed to run on to the top of the agar and the whole then allowed to cool till solid. Using this technique, blood plates of fairly good quality were obtained. They were stored until required in metal containers, and they in turn were stored in a refrigerator.

From 50 c.c. blood, 45 to 48 plates could usually be made. It was found that if more than that number were prepared, before they were used they had to be rejected owing to contamination. The usual contaminant was moulds.

INOCULATION OF PLATES.

For convenience and economy, the Petri dish containing blood agar was divided into two equal parts and then the swabs gently smeared on to a small part of the media in each half. Thereafter plating took place by means of a platinum wire using successive strokes. By this means, individual colonies were easily obtained.

INCUBATION.

The plates so inoculated were immediately placed in a hot air incubator at 37°C and examined after 24 hours. If after inspection colonies were seen surrounded by an area of β-haemolysis no further incubation was done, and the presence of haemolytic streptococci confirmed by microscopical examination after staining with Gram's stain.

If, however, no haemolysis was noted after 24 hours' incubation, the plate was left in the incubator for a further

period of 24 hours and then inspected. If no haemolysis was observed after this period, haemolytic streptococci were presumed absent. If, however, colonies were present showing β-haemolysis, these were stained and examined as previously described.

CLINICAL

In the pages which follow, details are given in tabular form of the results obtained from the examination of 106 patients each of whom suffered a typical attack of scarlet fever. Faucial swabs were taken immediately on admission and again at 7-day intervals, and examined for streptococci showing the β-type of haemolysis as previously described. On the development of any complication, e.g. otitis media, swabs were immediately taken and examined also at weekly intervals for the organism present.

From the results obtained it will be seen that in 94.34% of the cases streptococci giving the β-type of haemolysis were isolated from the faucial swabs.

From the results obtained from the swabs taken at weekly intervals, and using the common statistical method of frequency distribution, the average length of time that such organisms were to be found in the throat swabs was calculated and this was found to be 15.4 days.

	Male	Female	Total
Total number examined	58	48	106
Number + on admission	53	47	100
" " after 1st week	40	34	74
" " " 2nd "	24	19	43
" " " 3rd "	17	15	32
" " " 4th "	13	6	19
" " over 4 weeks	7	1	8

These 8 consisted of:

	Reg.No.	Days in hospital	Weeks +	Complications	If - on discharge
1	178	38	5	Albuminuria	+ on discharge
2	211	63	8	Adenitis: Rhinitis	- on discharge
3	216	141	5	Abscess of thigh (staphylococcal)	- on discharge
4	265	59	5	Albuminuria. Septic finger.	- on discharge
5	273	62	8	2nd attack. Septic finger.	+ on discharge
6	377	65	6	Otitis media. Mastoid.	- on discharge
7	383	38	5	Nil	+ on discharge
8	1234	35	5	Nil	+ on discharge

Number of cases negative throughout = 5. [Note all negative on admission were negative throughout illness.]

The following table indicates the complications met with in the series:

Uncomplicated	76.4%
Complicated	
(a) Otitis media	3.8%
(b) Mastoiditis	1.9%
(c) Nephritis	0.9%
(d) Albuminuria	3.8%
(e) Rhinitis	11.3%
(f) Other sepsis	1.9%
(g) 2nd attack while in hospital	1.9%
(h) Adenitis	4.7%
Average stay in hospital	30.4 days
Deaths	-

Of 106 cases examined on admission, each one showing the typical clinical signs of scarlet fever, 100 of the swabs revealed the presence of streptococci giving the β-type of haemolysis when grown on blood agar, i.e. 94.34%.

These 100 cases were distributed as follows:

Number	of	cases	with	+	swabs	on admission	=	100
"	"	"	"	"	"	after 1 week	=	74
"	"	"	"	"	"	" 2 weeks	=	43
"	"	"	"	"	"	" 3 weeks	=	32
"	"	"	"	"	"	" 4 weeks	=	19
"	"	"	"	"	"	over 4 weeks	=	8

From these figures the true mean was calculated indicating the average duration of haemolytic streptococci in the throat. Thus:

Number of days	Frequency	Deviation from arbitrary mean	Weighted deviations
+ after 7 days	74	- 1	- 74
+ after 14 days	41	0	0
+ after 21 days	32	+ 1	+ 32
+ after 28 days	19	+ 2	+ 38
+ over 28 days	8	+ 3	+ 24

+ Products = 94 - Products = 74

Difference = + 20

Therefore c, or average deviation from arbitrary mean is equal to 20, divided by 100 (the total number of cases) which is 0.2.

And as the actual interval is 7 days the average deviation from the arbitrary mean is 0.2 x 7 = 1.4. Therefore the actual or true mean is 14 + 1.4 days which therefore is 15.4 days.

i.e. The average duration of haemolytic streptococci in the throat is 15.4 days.

Average duration in hospital = 30.4 days.

Below is given a table showing the number of cases with a positive faucial swab on discharge and indicating any complication present with the number of swabs taken and their results.

Registered Number	Sex	Age	Days in hospital	Result of swabs on discharge	Complications	Swab results from complications	Return case
178	M	7	38	+ F	Albuminuria	-	Yes. Brother admitted notified scarlet fever 24 days later. Diagnosed tonsillitis but haemolytic streps grown.
273	M	4	62	+ F - N	2nd attack. Rhinitis	3 + nasal swabs followed by 2 - prior to discharge	No.
337	M	11	30	+ F	Adenitis	-	No.
383	M	4	38	+ F - N	Rhinitis. Adenitis	2 + nasal, then 3 - nasal	Returned himself in 29 days with tonsillitis + haemolytic streps
384	M	18	23	+ F	None	-	No.
426	M	6	27	+ F	None	-	Yes. Sister aged 23 years 16 days later. Typical scarlet.
479	M	24	25	+ F	None	-	No.
1199	M	6	26	+ F	None	-	No.
185	F	5	29	+ F	None	-	Yes. Sister aged 4 9 days later with typical scarlet fever
238	F	6	29	+ F	None	-	No.
260	F	6	31	+ F	None	-	No.
1214	F	32	24	+ F	None	-	No.
1234	F	8½	34	+ F	None	-	No.

In addition to the 4 return cases which arose from these 13 patients who gave positive faucial swabs on their discharge from hospital, other return cases arose of which details are available.

Case A. When commencing this investigation it was decided to swab all cases admitted, after a certain date, to the scarlet fever wards on admission, and not to swab those patients who were already admitted up to that date. The case about to be described, therefore, although an in-patient at the time of the commencement of the series, did not have faucial swabs examined during his residence in hospital.

The patient, a boy aged 5 years, was admitted to hospital on 7th February 1936 suffering from a typical mild attack of scarlet fever, and was discharged 29 days later on 6th March 1936. He suffered from no complications.

On 15th March 1936, i.e. 9 days later, his sister aged $2\frac{10}{12}$ years was admitted with scarlet fever. A health visitor brought the child responsible for the return case up to hospital for examination on the 16th March, and a faucial swab taken on that date revealed the presence of haemolytic streptococci, although clinical examination showed him to be apparently well and without any discharge of a muco-purulent character from nose or ears.

In the figures given later, this case is included as the conclusion which one had to come to was that the original case had been discharged from hospital while still in an infectious

state and because of this, had been responsible for the transmission of the disease to his sister.

Case B. Dr. A. N. Mathias of Harlesden, the private practitioner in charge of the family has very kindly supplied me with information of the previous medical history and relevant details of the present medical history in the following case.

David P. aged 8 years was admitted to a private nursing home in the company of his younger brother Nigel P. aged 4 years on October 20th 1936, to have tonsillectomy performed. The past medical history of David P. is largely one of illnesses attributable to streptococcal infection, and at the age of 4 years he developed acute rheumatic endocarditis which has left him with a permanent cardiac lesion. In August 1936 he developed acute otitis media, also streptococcal (no mention of haemolysis), which led to mastoiditis requiring operation.

Tonsillectomy was successfully performed on both children on 21st October 1936, and on 25th October David developed a rise of temperature with vomiting followed in a few hours with the development of a scarlatiniform rash. The R.M.O. in the home diagnosed the rash as being due to senna and therefore did not notify it as scarlet fever, but nevertheless he administered a prophylactic dose of 5 c.c. scarlet fever antitoxin to all the other children in the ward, including Nigel, the younger brother.

Both children returned home on November 10th, David being kept isolated in bed in a room by himself and being nursed by his aunt, Violet P. aged 27 years. On November 18th this young

woman was admitted to this hospital suffering from scarlet fever. Swabs from the fauces revealed the presence of haemolytic streptococci. She was discharged from hospital on 10th December. Concurrently with his aunt's return home, Nigel P. was permitted to play with his brother, and on 12th December he (Nigel) was admitted to hospital with scarlet fever.

Swabs from the throats of both David P. and Violet P. were taken by Dr. Mathias and examined by the writer and revealed the presence of haemolytic streptococci in the former but not in the latter.

On December 18th a domestic servant, Eliz. W. employed in the household, was admitted with scarlet fever and here also haemolytic streptococci were found in the fauces. All these patients were repeatedly swabbed for the presence of the organisms while in hospital, and the results obtained are tabulated herewith. In the case of David P. swabs of the tonsilar regions were taken by Dr. Mathias at intervals and examined by myself. The results also are tabulated below.

David P.

Date	Result
14.12.36	+
27.12.36	+
7. 1.37	+
16. 1.37	+
29. 1.37	-
5. 2.37	-
12. 2.37	-

Nigel P.

Date	Result
12.12.36	+
19.12.36	+
26.12.36	-
2. 1.37	-
9. 1.37	-
12. 1.37	-

Violet P.
aet.27.

Date	Result
18.11.36	+
25.11.36	+
2.12.36	-
9.12.36	-
14.12.36	-

Eliz. W.
aet.21.

Date	Result
18.12.36	+
25.12.36	-
1. 1.37	-
8. 1.37	-

In addition to these undoubted cases of scarlet fever which arose in the household, there were several cases of tonsillitis. The grandmother who lives with the family developed an acute tonsillitis, and so also did an uncle who although not resident in the house spent a great deal of his spare time there. Both these throats showed a rapid improve-

ment under treatment with 'Prontosil'.

The conclusion which one is forced to arrive at is that David P. originally suffered from an undiagnosed attack of scarlet fever and was responsible for 3 attacks of the disease in different members of the household, and in addition two cases of tonsillitis which although no swabs were taken I am convinced were due to infection with a haemolytic streptococcus. It is possible that the onset of the disease in Nigel was due to infection from his aunt, but the fact that the swab from her throat revealed no haemolytic streptococci, while that from his brother David was strongly positive, rather points to the latter being the true infecting person.

It is interesting to observe that although Nigel received 5 c.c. scarlet fever antitoxin prophylactically on 25th October he did not develop a rash until 12th December, i.e. fully 7 weeks later. It is probable that the explanation lies in the fact that the artificial immunity conferred by the antitoxin had been lost in that period and contact with his brother being resumed, he developed the disease. As to the source of the original infection in David P. speculations were made whether he had in turn been infected by another child in the home or whether the operation of tonsillectomy had resulted in a wound through which absorption of toxins had taken place from streptococci which had previously been lying dormant.

Case C. The third case which I should like to describe is that of a return case arising from a boy who had been in hospital for 59 days.

W.B. aet 7 years was admitted to hospital on 3.3.36 with scarlet fever. In addition to the punctate erythematous rash there were numerous septic spots on the trunk and face and forehead. A swab taken from the throat and from pus obtained from the spots all resulted in a profuse growth of haemolytic streptococci when inoculated on to a blood agar plate. The child developed complications in the form of cervical adenitis, albuminuria and a septic finger (like a whitlow), all of which had cleared up when he was discharged from hospital on 1.5.36 i.e. 59 days later.

On 30.5.36, i.e. 29 days after discharge, his sister, aged 9 years, was admitted to hospital also suffering from scarlet fever.

The dates of the swabs taken, their source and the results obtained are indicated in the following table:

Date	Source	Result (Haemolytic streptococci)
3.3.36	Faucial	+
	Pus from septic spots	+
10.3.36	Faucial	+
18.3.36	Faucial	+
25.3.36	Faucial	+
1.4.36	Faucial	−
1.4.36	FINGER	+
8.4.36	Faucial	+
15.4.36	Faucial	−
23.4.36	Faucial	−
30.4.36	Faucial	−
30.4.36	NASAL	−

Clinical examination of W.B. on 31.5.36 revealed the Fauces to be normal, no discharge from nose or ears, no septic spots present, and no haemolytic streptococci were obtained from the fauces on culture.

Commentary

In this case there is an infection not only of the fauces but also of the subcutaneous tissues with haemolytic streptococci resulting in complications both of a toxic and of a bacterial nature. Five weeks elapsed before haemolytic streptococci were absent from the throat and thereafter three consecutive swabs taken at weekly intervals were negative to the organism. In spite of these findings I am inclined to the view that W.B. was responsible for the infection of his sister because of the massiveness of his original infection and the long duration of the infectivity in hospital, though it may be that the sister was infected from another source in the course of her everyday duties.

This case is not included in the tabulation of the return cases in view of the negative swab results, and also because 29 days had elapsed and not the 28 days recognised in the definition of a return case.

The final results are, therefore, that of 15 patients who were found on examination to be harbouring haemolytic streptococci, 6 of them gave rise to return cases within the meaning of the definition; and 1 patient who before discharge from hospital had been found to be negative on 3 occasions to the organisms

gave rise probably to 1 case of scarlet fever which strictly speaking could not be called a "return case".

The details of these six cases, and the return cases to which they gave rise I give below.

Case 1.

Registered No. Sex Age	Dates of swabs taken and results	Complications	Return case
178 Male aged 7 years	14.2.36 + 21.2.36 + 28.2.36 + 6.3.36 + 13.3.36 + 20.3.36 +	None	Brother aet 9 years 24 days later, admitted with tonsillitis from which haemolytic streptococci were obtained. No rash.

Case 2.

Registered No. Sex Age	Dates of swabs taken and results	Complications & swab results	Return case
383 Male aged 4 years	27.3.36 + 3.4.36 + 10.4.36 + 17.4.36 - 23.4.36 + 1.5.36 +	Rhinitis 3.4.36 + 10.4.36 + 17.4.36 - 23.4.36 - 1.5.36 -	Patient returned 27 days later with acute haemolytic streptococcal tonsillitis and no rash.

Case 3.

Registered No. Sex Age	Dates of swabs taken and results	Complications	Return case
426 Male aged 6 years	3.4.36 + 11.4.36 - 18.4.36 + 25.4.36 + 1.5.36 +	None	Sister aged 23 years admitted 16 days later. Swab revealed haemolytic streptococci

Case 4.

Registered No. Sex Age	Dates of swabs taken and results	Complications	Return case
185 Female aged 5 years	15.2.36 + 22.2.36 + 29.2.36 + 7.3.36 + 13.3.36 +	None	Sister aged 4 years admitted 9 days later. Swab (faucial) revealed haemolytic streptococci.

Case 5.

Sex Age	Swabs taken and result	Complications	Return case
Male aged 5 years	Faucial swab after discharge + from hospital	None	Sister aged $2\frac{10}{12}$ admitted 9 days later. Faucial swab revealed haemolytic streptococci

Case 6.

Sex Age	Swabs taken and result	Complications	Return cases
D.P. Male aged 8 years	14.12.36 + 27.12.36 + 7. 1.37 + 16. 1.37 + 29. 1.37 - 5. 2.37 - 12. 2.37 -	None	1. Violet P. aged 27 years admitted with scarlet fever. Faucial swab + for haemolytic streptococci. 2. Nigel P. aged 4 years admitted scarlet Faucial swab + 3. Eliz.Walters aged 21 years admitted with scarlet. Faucial swab + for haemolytic streptococci.

DISCUSSION

1. This series confirms the findings of other workers that a haemolytic streptococcus can be found in the throats of almost 100% of cases of Scarlet Fever. Although only 94% of the cases investigated in this group gave a positive result, I am convinced that in a more fully equipped laboratory, and with the services of a trained bacteriologist available, the percentage would more and more approach 100%. The preparation of the media used was found to be one of the greatest difficulties, and undoubtedly a person more fully trained than the writer in such matters would obtain a better result.

Topley and Wilson (Principles of Bacteriology and Immunology, p.1548) record the frequency of certain bacteria in the nasopharynx, nose, tonsils, and oral cavity as found in an investigation among a sample of the general population in Manchester from 1925 to 1927. Haemolytic streptococci were found in the nasopharynx in amounts varying from 5.84% to 11.90%. It would appear, therefore, that the finding of haemolytic streptococci in the throat of a person suspected to be suffering from scarlet fever could be a useful adjuvant in arriving at a diagnosis, provided that the organism found was "grouped", using the Lancefield technique.

The problem of what exactly constitutes "scarlet fever" would appear to become more complicated as our knowledge of the

etiology of the disease and the bacteriology of the streptococcus increases. So far as the law is concerned, the presence of a punctate erythematous rash is the determining criterion. But to the clinician, experience goes to show that infection with a haemolytic streptococcus can in one case result in a follicular tonsillitis only and in a second case to follicular tonsillitis with a punctate erythematous rash. The latter individual is accordingly notified to the public health authorities as suffering from scarlet fever and is isolated for a period of time in hospital while the former goes about as usual and can infect others. In some this infection results in tonsillitis with a rash, i.e. scarlet fever; while in others no rash results. Dr. Hilda M. Woods (M.R.C., Special Report Series No.180) has pointed out that the statistical evidence that isolation has had any appreciable effect upon either the prevalence or the mortality of scarlet fever during the last twenty-five years is unconvincing. The explanation of this probably lies in the fact that while only those patients with a rash are removed to hospital, other persons suffering from a haemolytic streptococcal tonsillitis without a rash are permitted to walk about in an infectious state and thus keep spreading the disease. It must also be remembered that the carrier state can exist in scarlet fever as in other bacterial illnesses.

In latter years, great prominence has been given to puerperal septicaemia as a cause of maternal mortality and morbidity, and all recent work goes to show that a haemolytic

streptococcus is in the majority of cases the responsible organism. In the light of our present knowledge of the haemolytic streptococcus, patchy and inadequate as it is, the etiology of puerperal scarlet fever can be more easily understood. It seems logical to assume that the lodgement in the vagina or uterus of the organism from the throat of an attendant in the labour room can easily lead, through the absorption of either the organism or the erythrogenic toxin which it is capable of elaborating, to septicaemia or puerperal scarlet fever. Bacteriological examination of the throats of doctors, nurses, or medical students working in maternity hospitals, for the presence of haemolytic streptococci prior to attendance at a confinement seems to be indicated in safeguarding the health and maybe lives of young mothers in view of the ubiquity of the organism. Such a step would not be possible as a routine measure outside institutions. The prophylactic use of masks has, of course, been a routine measure for some time past in maternity hospitals.

2. Banks (Jour. of Hyg., 1933, xxxiii, 282) has recorded his observations on a large number of cases of scarlet fever which he treated by intravenous injection of anti-scarlatinal serum. He states as the advantages of the intravenous route that the temperature falls by crisis in six to twelve hours, that the rash fades in twelve to twenty-four hours, and that desquamation is usually absent if the serum is given not later than the third day of the disease.

In the present group of cases under review, all received 10 c.c. anti-scarlatinal serum (P.D. & Co.) intramuscularly. Although no actual note was made regarding the manner in which the temperature fell or the presence or absence of desquamation, the general impression on clinical observation was that they behaved in a way similar to Banks' series.

Dr. Banks also points out as another advantage of the intravenous route that the typical case "may be discharged from hospital after 8-10 days or a few days longer if it is considered advisable that the patient should remain in hospital over the period of the serum rash". The average duration in hospital was 16.6 days, as some of his patients developed complications.

In the small group under review by the writer, the average duration of haemolytic streptococci in the throat was 15.4 days, although quite a proportion of the uncomplicated cases gave negative swabs after the first week. This figure of 15.4 days compares favourably with Dr. Banks' 16.6 days, and the fact that he was able to discharge his cases in that period without any increase in his return case rate, can probably be explained by the fact that in the average case by that time haemolytic streptococci would be absent from the throats irrespective of the manner in which the anti-serum was administered. When it is noted that Dr. Banks had 3 cases which developed severe anaphylactic reactions before completion of the intravenous injection, one is inclined to the view that any slight advantage

in the intravenous route over the intramuscular, is overshadowed by the ever present danger of acute anaphylactic shock.

3. Regarding the general incidence of return cases J.D.Rolleston (Brit. Jour. Chil. Dis. XXIX, 1932, 91) states that this varies considerably in different hospitals from 0% to 6.9%. In the hospital to which the writer is attached at present, the figure varies from year to year. Thus in 1934 the percentage was 4.9 and in 1935 6.9.

In the present series no attempt has been made to determine the actual percentage of return cases as illustrative cases have been included which occurred both before the commencement and after the finish of the short series.

Continuing his observations in the same article, Rolleston regards the discharges from nose, throat and ear to be the main source of the infection in return cases with desquamation of no importance at all. Most observers will agree with this, and in the present series haemolytic streptococci were found in such discharges in almost 100% of cases at some time or other. The fact that a greater number of return cases occur in the colder seasons of the year is probably explained by the greater incidence of catarrh of the upper respiratory passages during these times.

On the other hand, Rolleston in the hospital in which he is medical superintendent does not use the examination for haemolytic streptococci in the nose and throat swabs as a criterion of freedom from infection, and states in the same article as his

reasons for not so doing "the enormous amount of labour and expense involved by its routine employment and by the discordant results reported by various observers."

From the results obtained in this small number of cases it would appear that in the majority of return cases the presumed infecting person was discharged while still harbouring a haemolytic streptococcus in his throat. Strictly speaking one should not assume that such an organism is responsible for return cases without first of all determining the group to which it belongs, using Lancefield's technique; but for practical routine investigation, if a patient has suffered from clinical scarlet fever and before being discharged from hospital it is discovered that he still harbours a haemolytic streptotoccus in his fauces or nose, it appears to be a fair assumption that such an organism was the one originally responsible for his disease and therefore liable to cause the disease in another person susceptible to it.

In the diphtheria wards of most infectious diseases hospitals no patient is discharged while still harbouring virulent C.diphtheriae. As a routine, therefore, swabs are taken and examined for organisms showing the morphological characters of C.diphtheriae, and if such are found over a period of weeks (the exact number of weeks depending on the case) it is the practice of the authorities in the hospital to which the writer is at present attached to have the organism examined for 'virulence' by a professional bacteriologist. In this way the

occurrence of return cases is reduced to a minimum.

For the reasons which I have endeavoured to explain above, the conclusion to which I am drawn is that return cases of scarlet fever could be appreciably diminished by the use of a routine bacteriological investigation of the throat and nose for the presence therein of haemolytic streptococci. Should the swab be persistently positive after 28 to 30 days in hospital and the clinical examination of the patient reveal no abnormality before further detention as a 'carrier' is insisted on, the organism found could be grouped. The routine procedure, therefore, in the two diseases would tend to become very similar. With some practice the making of blood agar media should become easier. Blood can usually be obtained in sufficient quantities by vein puncture of adult patients already in the hospital. During this present series blood was always obtained from patients in hospital except on one occasion when 50 c.c. had to be purchased from a proprietary firm. The expense therefore was not great although in the cases of larger hospitals dealing with one thousand and over admissions per annum, considerably more blood would be required. This could probably best be obtained by vein puncture of a rabbit or other laboratory animal.

4. The average duration in hospital of the present group was 30.4 days. At the First Congress of the International Association of Preventive Paediatrics held at the Hague in 1931 a discussion on return cases of scarlet fever and their prevention was held (Brit.Jour.Child.Dis., 1931, XXVIII, 314).

The speakers were mostly convinced that the average duration in hospital should be 28 days for mild cases of scarlet fever and longer for complicated ones, the exact length of time being determined by the clinical condition. Most of them were against the use of the swab result as a criterion of freedom from infection and advocated individual attention, functional disinfection (i.e. frequent baths, sufficient supply of clean linen) and as much fresh air as possible as the only reliable means of prevention of return cases.

All of my patients received treatment along such lines and yet return cases still arose. If the case of the child David P. is considered it seems possible that had he been isolated in the first instance and detained in isolation till bacteriologically safe for discharge along the lines I have indicated, the three return cases to which he gave rise might never have arisen, and it is also interesting to note that although three months have passed at the time of writing since the third negative swab was obtained there have been no other cases either of scarlet fever or of tonsillitis in the household.

Unquestionably there are many cases of inconsistency in the use of the bacteriological test, particularly if too great a reliance is placed on it, and the general clinical condition of the patient is undoubtedly the most reliable criterion, but nevertheless the results in my opinion do tend to show that a certain proportion of return cases of scarlet fever could be prevented by a greater use of the bacteriological facilities

available. Once a diagnosis of scarlet fever is made on the clinical evidence and notified as we are required by law to do before release from isolation either in hospital or private house, two negative swabs from throat and nose taken at weekly intervals should be obtained. By such a measure I am convinced that return cases of scarlet fever could be appreciably diminished.

SUMMARY OF CONCLUSIONS

1. It is practicable as a routine measure and without the help of any special apparatus to isolate haemolytic streptococci from the throats of almost 100% of cases of scarlet fever.

2. The average length of time the organisms can be found in the throat is 15.4 days.

3. Some patients in whose nasopharynx haemolytic streptococci are found prior to discharge from hospital do give rise to return cases of scarlet fever while others with a similar positive bacteriological result do not give rise to return cases. In spite of these discordant results I am convinced that if swabbing were made a routine measure an appreciable percentage of return cases of scarlet fever could be prevented.

4. No appreciable advantage is obtained by the intravenous administration of anti-serum over the intramuscular.