# THE DICK TEST IN SCARLET FEVER.

THESIS

submitted for the

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# I N T R O D U C T I O N.

Scarlet Fever still ranks as an important cause of death and debility in the community. It affects a larger number of the population than any other of the common notifiable diseases. During the past few years it has shown a steady decline in severity as indicated by the case mortality but it has not exhibited a similar tendency in incidence. Indeed, reference to the Report of the Ministry of Health for England and Wales for 1925 shows that during a few years previous to that date there was a slight increase in its incidence. The mortality is highest during the first year of life and thereafter shows a steady decline. The importance of its complications, particularly otitis media, as a factor militating against the later efficiency and health of the individual has long been recognised. The ordinary methods of prophylaxis, such as notification and isolation, have been shown to have little or no effect on the incidence of the disease. Any procedure then which can diminish the incidence of Scarlet Fever in the general population and particularly in the early years of life must be considered

as important.

Recent years have seen important advances in our knowledge of Scarlet Fever. After many previous attempts by other workers G. H. and G. F. Dick of America succeeded in 1923 in producing experimental Scarlet Fever in a volunteer by swabbing his throat with a culture of haemolytic streptococci which they had isolated in apparently pure culture from the septic finger of a nurse suffering from the disease. Later they demonstrated that these streptococci produced what they considered to be a soluble toxin, and that this 'toxin' could be used in suitable dilution as a test of susceptibility to the disease. Working on the analogy of the skin test introduced in 1913 by Schick of Vienna for susceptibility to Diphtheria, they published in January, 1924, their first paper on this aspect of the subject. The test they employed is now generally referred to as the Dick test.

This thesis embodies the results obtained from the use of the Dick test in Acute, Convalescent and Recovered cases of Scarlet Fever. The investigation was carried out in the County Fever Hospital, Motherwell, during the winter of 1926-1927. I am much indebted to Dr. John Reid, the medical superintendent of the County Fever Hospital, Motherwell, for

facilities provided and for much helpful criticism given during the course of this investigation.

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## The Relationship of the Streptococci to Scarlet Fever.

The relationship of an organism to a disease can be established by the fulfilling of Koch's canons. The first of Koch's postulates which requires the constant presence of the microbe in all cases of the disease has been confirmed many times with regard to the Streptococcus and Scarlet Fever. Thus Loeffler in 1884, drew attention to the haemolytic streptococci which are almost invariably present in the throat of acutely ill Scarlet Fever patients. Klein in 1887, from investigations of milk-borne epidemics of Scarlet Fever, expressed the view that streptococci had an etiological relationship to Scarlet Fever. In 1895 Marmorek, and later Moser in 1902, produced antistreptococcic sera to strains isolated from cases of Scarlet Fever and reported good results from the therapeutic use of these sera in cases of Scarlet Fever. Their work was confirmed by Rossiwall and Schick in 1905. Savchenko demonstrated in 1905 that Scarlatinal streptococci produce a potent exotoxin while Gabritschewsky in the same year immunised children with a Scarlatinal streptococcus vaccine. The potency of this vaccine was demonstrated by Polotevkeva in 1921. The following extract from Muir and Ritchie's Manual of Bacteriology, 1919, sums up the knowledge of the relationship of streptococci to

Scarlet Fever at that date.

"At present no definite opinion can be expressed as to the etiological relation of streptococci to Scarlet Fever. We can only say that streptococci are almost invariably present in the fauces and that to them many of the complications of the disease are due. The streptococcus conglomeratus (anginosus) is specially abundant as a rule, though it also occurs in other acute catarrhal states. In fact, Gordon found that the types of streptococci in the throat in Scarlet Fever, correspond with those met with in normal conditions. Mair has recently isolated an organism to which he has given the name Diplococcus Scarlatinae. He obtained it from the throat in over 80% of cases of Scarlet Fever. From experiments on monkeys and on other grounds he considers that it probably has an etiological relationship to Scarlet Fever."

In 1923 we find the following statement in the third edition of Kolmer: "the virus of Scarlet Fever is unknown; those patients who are overwhelmed and prostrated at the very onset are probably intoxicated with the true scarlatinal virus and streptococci are probably the most important bacteria of secondary infection." This view of the virus of Scarlet Fever being other than the streptococcus is still

maintained by some continental workers, notably di Cristina and Caronia.

Notwithstanding the importance of the work done by these and other workers the causal relationship of the streptococcus to Scarlet Fever was not established until the work of the Dicks in 1923 and after.

It is interesting to note that the experimental Scarlet Fever produced by the Dicks in 1923 was due to a streptococcus obtained not from the throat but from the finger of a nurse suffering from the disease. The following is a summary of their original and now historic paper.

'A nurse developed Scarlet Fever. Two days previously she had a septic finger. A few drops of pus were obtained from the finger on the second day of disease. Gram, Levaditi and Giemsa stains were made of the smear. Polymorphs, Gram positive cocci and Gram positive diphtheroids were found. Anaerobic sheep's blood agar plates showed colonies of haemolytic streptococci and a few colonies of diphtheroids. Pure colonies of the streptococci were obtained by plating out single colonies.

Cultures of the streptococci were smeared on the throats of five volunteers. Three were negative. One had sore throat and fever without rash. One smeared with a three weeks' culture developed typical mild Scarlet Fever. Further

cultures were made on a partly bouillon and partly agar medium and passed through a Berkefeld filter. The filtrate was sterile and did not affect volunteers when swabbed on the throat. The culture was swabbed on the throats of those who had not reacted to the filtrate and showed two well and two sore throats and one Scarlet Fever. The conclusions they came to were:

1. Two cases of Scarlet Fever caused by Streptococcus haemolyticus or by unrecognised organisms associated with it.
2. If this unrecognised organism was present it did not pass through a Berkefeld filter.
3. Conclusion not justified that all cases of Scarlet Fever are caused by streptococcus haemolyticus.

The further work of the Dicks demonstrated that the filtrate mentioned above contained a toxic substance which in appropriate dilution could be used for skin tests. The toxicity of this filtrate was neutralised by serum obtained from convalescent Scarlet Fever patients. Persons showing a positive skin test, when injected with the filtrate developed scarlatiniform symptoms, and the skin test became negative. They immunised a horse against this filtrate which they regarded as a true toxin and produced an anti-

toxin which could be concentrated in the usual manner. The exact nature of this 'toxin' is not yet rightly understood. It presents certain differences from other bacterial exotoxins, being very thermostabile and non-toxic to animals. It has therefore been suggested that the Dick test and the rash in Scarlet Fever are simply phenomena of hypersensitiveness to the proteins of streptococcus haemolyticus. In this connection it is of interest to note that Besseman from his observations on the use of the Dick test in Belgium states that the age group for susceptibility to Scarlet Fever corresponds to that for hypersensitivity to ordinary proteins and Gorter and De Korte come to the conclusion that the Dick test material was different in nature from the exotoxin of Diphtheria and was "something not a toxin".

Experimental work on the streptococci of Scarlet Fever has been mainly concerned with their classification and identification. So far attempts to classify them into one serological group have been unsuccessful although various workers have claimed to have done this at different times.

The earliest attempts were those of Moser in 1902, and a little later of Moser and von Pirquet (1903). They prepared agglutinating sera by inoculating horses with strains of scarlet fever streptococci and found that these strains

were agglutinated specifically, whereas haemolytic streptococci from other sources were not. Aronson (1903) and Neufeld (1903) came to the conclusion that it was not possible to differentiate between types of haemolytic streptococci by means of the agglutination reaction. Weaver (1904) found that the agglutinative reaction produced in types of streptococci from Scarlet Fever patients by sera obtained from these cases was in no way specific and could not be of any value in diagnosis. The work of Moser and von Pirquet was confirmed by Rossiwall and Schick (1905). Favourable results of the agglutination tests with the serum of an immunised sheep were reported by Ruediger (1906) and with the serum of an immunised rabbit by Nakayma (1919). In 1920 Bliss found that of twenty-five strains of haemolytic streptococci obtained from the throats of patients suffering from Scarlet Fever, twenty were agglutinated at equal titres by a serum prepared by immunising a rabbit with an individual strain. No agglutination was obtained with these twenty strains when tested with sera obtained against strains of streptococci from other sources. Gordon (1921) examined nineteen strains of haemolytic streptococci isolated from cases of Scarlet Fever and found they were identical in their agglutination and absorption reactions. Tunnicliff (1922)

found this too in seventy-two strains from seventy-five cases of Scarlet Fever. Bliss (1922) confirmed his previous work and found that twenty out of twenty-four strains were agglutinated specifically by anti-scarlatinal sera. Both Gordon and Bliss concluded that the streptococci of Scarlet Fever belonged to a single serological group. Stevens and Dochez (1924) as a result of their observations on streptococci obtained from forty cases of Scarlet Fever early in the disease and later on, formed the opinion that the strains of haemolytic streptococci associated with Scarlet Fever are closely related biologically and probably constitute a single group. Eagles (1924) found that nineteen strains of streptococcus scarlatinae could all be placed in one group by the agglutination test. Dick and Dick found no cross- agglutination between the two strains of haemolytic streptococci with which they produced experimental Scarlet Fever although these two strains differed in their action on mannite. They emphasise the importance of toxin formation as a means of differentiating the true streptococcus scarlatinae. The lowest results recorded recently were those obtained by Williams in 1925. She found that, out of seventy strains tested only 30% fell into one serological group. Of the others, 63% were not classified

serologically.

Smith of Aberdeen (1926) examined the streptococci obtained from the throats of two hundred and ten cases of Scarlet Fever. He obtained haemolytic streptococci from 92% of cases in the first two days of disease. These strains fell into two main serological groups. This work was confirmed later by Griffith (1926). Smith also observed that strains obtained from members of the same family usually were of the same serological group and that strains obtained from cases in small isolated outbreaks were also of the same serological type. Griffith found that some puerperal strains conformed to the chief Scarlatinal types.

James (1926) from his investigations into the relationship of the streptococci to Scarlet Fever does not confirm the claim made by Dick and Dick as to the specificity of the streptococci causing Scarlet Fever. He found that 56.6% of them fall into one of three main types. The other 43.4% were not classified. He advances the hypothesis that Scarlet Fever may be caused by several serologically distinct types of Streptococcus and that there may be considerable variation in the incidence of types in different parts of the world. He confirms the main hypothesis that streptococci, though not necessarily identical in type, are the direct etiological factor in Scarlet Fever.

Tunnicliff (1926) has lately advocated opsonin tests as giving quicker results than either agglutination or toxin tests. The absence of a rapid means of identifying the streptococci of Scarlet Fever has for long been a hindrance ~~to its use~~ for diagnostic and other purposes.

Various observers have reported the finding of streptococcus scarlatinae in situations other than the throat of an acutely ill Scarlet Fever patient. Thus the Dicks first obtained it from the finger of a nurse suffering from the disease. Tunnicliff and others have found it in the discharges of Scarlet Fever convalescents up till the sixth week. Smith states that the specific streptococcus of Scarlet Fever can be found in at least four clinical diseases other than scarlet fever, namely, Tonsillitis, Erysipelas, Puerperal Fever and Broncho-Pneumonia. Stevens and Dochez point out that Sore Throat due to the streptococcus scarlatinae may occur in patients who have had Scarlet Fever and that protection against the toxin does not imply protection against infection by the organism. In this connection it is interesting to note the high incidence of Sore Throat among nurses in Aberdeen immunised against the toxin of Scarlet Fever, (Kinloch). Nicholls, (1926) at Yale, has demonstrated the presence of Streptococcus Scarlatinae in a notable proportion of patients suffering from some mani-

festation of that organism other than clinical Scarlet Fever. These patients usually had been exposed intimately to Scarlet Fever. Though they were protected against the soluble toxin of Streptococcus scarlatinae they were not protected against local infection by that organism. These observations throw interesting light on the problems of immunity to Scarlet Fever and must have an important bearing on future investigations into its epidemiology.

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## The Work of the Dicks.

I have mentioned that the Dicks originated the skin test for susceptibility to Scarlet Fever. The test is an intradermal one with a minute dose of toxin. They used the soluble filtrate, (= exotoxin), of a broth culture of the organisms causing experimental Scarlet Fever. This filtrate was diluted 1 in 1000 in sterile salt solution. They injected 0.1 c.c. of this dilution into the skin on the anterior surface of the forearm and a careful watch was kept for the appearance of a reaction. The presence of a positive reaction was indicated by redness and swelling round the area of inoculation. The positive reactions usually began to appear about four to six hours after the injection as a small circular area of erythema which increased in size and intensity up till eighteen to thirty-six hours after being given. After reaching a maximum in thirty-six hours the reactions in most cases rapidly subsided, even the most strongly positive fading in forty-eight hours, leaving a faint yellow area. Sometimes this area desquamated in the week or ten days following the test. They classified their results as negative, where no reaction ocurred; and as strongly positive, positive and slightly

positive in the others, depending on the degree, size, time of appearance and duration of the erythema. Frequently the redness was associated with some swelling. The details of their classification made at the end of twenty-four hours is now given.

Slightly Positive - a faint red area, less than 2 cms. in diameter and with no swelling or tenderness.

Positive - red area 1.5 cms. to 3 cms. in diameter with some swelling and tenderness.

Strongly Positive - red area more than 3 cms. in diameter with swelling and tenderness. Frequently it was as big as 5.7 cms.

Negative - site of injection only showing point of needle or a linear streak along the course of the needle.

The following table gives the results of their first series of cases with the type of patient on whom the test was performed.

| | Number of Cases | Negative Result | Slightly Positive | Positive | Strongly Positive |
|---|---|---|---|---|---|
| Convalescent Scarlet Fever Patients | 65 | 62 | 3 | - | - |
| Patients with a History of Scarlet Fever | 16 | 15 | - | - | 1* |
| Patients with no History of Scarlet Fever | 72 | 35 | 7 | 17 | 13 |

* A young man with a doubtful history of Scarlet Fever in childhood.

To exclude the possibility of the reaction being caused by foreign proteins in the culture medium they injected into the positive cases undiluted fluid from a sterile culture medium. The results were negative. It was observed that several of the convalescent Scarlet Fever patients giving negative results, at the same time had positive Schick reactions thus showing that the Dick result was not due to an inability of the skin to react.

As further evidence of the specific relation of the test to Scarlet Fever they mixed the filtrate with an equal volume of serum from a convalescent patient and comparing the results obtained in a positive reactor with this mixture heated for thirty minutes with that of a mixture, heated for thirty minutes, of filtrate and salt solution, they found that the filtrate and salt solution showed positive while the filtrate and serum solution showed negative results. Two of the positive reactors developed Scarlet Fever subsequantly and the reaction in each instance during convalescence was negative.

They concluded that the skin test described bore a specific relation to immunity to Scarlet Fever.

In February, 1924, Dochez and Sherman reported experiments on the lower animals with the haemolytic strepto-

coccus. Their object was the production of a serum which might counteract the disease in the human subject. They advanced the hypothesis that the disease resembles Diphtheria in that the infection is a local one in the throat with the production of toxins which are absorbed and produce the rash and general symptoms. As a result of these experiments a serum was obtained which possessed the capacity of blanching the Scarlet Fever rash locally, and when used therapeutically, of causing a marked amelioration of all the symptoms. No conclusive evidence was obtained of the production of a soluble toxin in vitro, although they believed that both immunity in man and experimental immunity developed in animals were due to the presence of antitoxins.

In the same Journal the Dicks reported observations on the production of immunity by injection of the toxic filtrate. Persons reacting positively to their skin test were given various doses of toxic filtrate and the resulting negative reaction showed the production of immunity. They concluded that the immunity developed was for a true toxin and not for a filterable virus on the following grounds:-

1. The short interval between the injection of the filtrate and the development of symptoms compared with the longer interval found in the experimental production of

Scarlet Fever.

2. The resistance of the filtrate to heat at temperatures which ordinarily kill bacteria.

3. The more rapid disappearance of the symptoms.

These observations would point to a marked resemblance between the Schick test and the Dick test in that they are both skin reactions to a minute dose of a toxin produced by the specific organism.

Branch and Edwards reported observations on the use of the Dick test in one hundred and forty-eight patients. In this series they used as a control in every case the toxic filtrate heated for one hour at 90°C and in no instance was there a positive reaction. Their actual figures will be referred to later, but the conclusion they reached was that the Dick test had a specific relationship to Scarlet Fever. Zingher, working independently, showed that the age-group percentage susceptibility to Scarlet Fever as shown by the Dick test corresponded closely to results obtained by the Schick test for susceptibility to Diphtheria. He concluded that the Dick test bore a specific relationship to immunity to Scarlet Fever. The control used by these workers is the one now generally employed and the terminology

which they used was that which has been in vogue now for some time with regard to the Schick test, namely:-

Negative - no reaction showing, or a red streak along the needle track on either arm.

Pseudo and Negative - a reaction showing both with the toxin and with the control but in which the toxin reaction is not greater than the control reaction.

Positive - a reaction of 3 cms. or more due to the toxin and no reaction from the control.

Slight Positive - a reaction less than 3 cms. but not less than 1.5 cms. on the toxin arm and no reaction from the control.

Pseudo and Positive - a reaction with both the toxin and the control but in which the toxin reaction is greater than the control reaction.

In August, 1924, Zingher published results from the use of the Dick test in Acute and Convalescent cases of Scarlet Fever and I will have occasion to refer to this article later as the work done by myself was on similar lines. In this country the first notable contributions to the subject were by Ker and McCartney of Edinburgh along with McGarrity of Cardiff, and a little later by Okell and

and Parish of the Wellcome Research Laboratory and Harries and his co-workers in Birmingham. The results obtained by these and various subsequent authors will be referred to, where necessary, later.

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Materials and Technique used in the Dick Test in the present Research.

The material used was the "Wellcome" Brand Diluted Scarlet Fever Toxin (Test) and Heated Scarlet Fever Toxin (Control). The test consists of an intradermal injection of 0.2 c.c. of a 1 in 1000 dilution of filtrate obtained from a broth culture of the Streptococcus scarlatinae. This material was sent to Motherwell regularly twice a week and was used immediately. Where occasion required, an additional supply apart from the bi-weekly order was obtained so that fresh reliable material was always available for use. In every case a control was used. This control was the toxin of the test heated so as to destroy its specific toxicity.

In doing the Dick test, accuracy is essential. Each case must get the same amount of toxin, which must be given intradermally. The same applies to the control. To achieve this object a finely graduated syringe with a sharp closely-fitting needle is essential. The arm is swabbed with Methylated Spirit. Holding the syringe parallel to the arm, the needle is inserted "into" the skin for a distance of half an inch. The bevelled opening of the needle should look upwards. The fluid is now injected by applying steady

pressure to the piston of the syringe. A definite white button-like elevation of the superficial layers of the skin is seen to form. Then the needle is withdrawn slowly. The sharpness of the needle, the steady pressure used in injecting the fluid and the slowness of the withdrawal are all necessary for the accurate performance of the test. Occasionally a small venule is punctured, in which case the needle is withdrawn and the test repeated in a different place. It is easy, especially in very young children, to go through the skin and introduce the fluid subcutaneously. Two things combine to produce this, namely, the delicacy of the skin in a young child and the fact that he or she is liable to move the arm at the moment of injection. With the help of a nurse and a little practice this difficulty is overcome. I have frequently in such a case pushed the needle a little further in an upward direction through the deepest layers of the skin and given the fluid intradermally in this fashion. The two criteria for successful performance are the feeling of resistance when injecting the fluid and the appearance of a well-defined white area immediately afterwards.

The white area in the majority of cases disappears in

a few minutes, to be followed in the course of six to twelve hours by a deep red colouration of ½ - 1 inch in diameter in the positive and pseudo cases. The reaction seldom persists for more than forty-eight hours, and in the majority of cases leaves no trace behind it. In some instances a small yellowish-brown area may be visible for a few days, but no desquamation such as is seen after the Schick test is noticed. Although I have done more than two thousand Dick tests, I have only seen one case of septic infection at the site of inoculation. It is advisable to use a different syringe and needle for the test and for the control.

There is a large group of patients who were treated with Anti-Scarlatinal serum. This was supplied by Messrs. Burroughs, Wellcome & Company, and was obtained from a horse immunised against the specific Scarlet Fever organisms and toxins. No known method has been found of titrating this serum in the same way as Anti-Diphtheritic Serum can be titrated, although recent work by Okell and Parish is hopeful in this direction. At the commencement of this investigation every case of Scarlet Fever, no matter how mild, was being given 10 c.c.s of this unconcen-

trated Anti-Scarlatinal Serum on admission to hospital. This amount of serum has been defined as sufficient to turn a Dick-positive reactor into a Dick-negative reactor within twenty-four hours of its administration. This routine treatment was delayed by one day to allow of the Dick test being performed and the result interpreted before the administration of serum. Patients, who, on clinical grounds, required a larger dose of serum, were given it. After a time the routine administration of serum was stopped and only those patients were given serum who, on clinical grounds required it.

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## Summary of the Work done.

The work falls naturally into two divisions.

(1) One hundred and fifty-two patients admitted to Motherwell Fever Hospital with Scarlet Fever in the ten weeks prior to 1st January, 1927, were Dick tested on admission and at weekly intervals until their dismissal from hospital. These cases were all treated with Anti-Scarlatinal Serum.

(2) Eighty~~-five~~ SEVEN patients admitted to Motherwell Fever Hospital with Scarlet Fever in the first ten weeks of 1927 were Dick tested on admission and at weekly intervals until their dismissal from hospital. These cases were not treated with Anti-Scarlatinal Serum.

Both of these divisions represent the total Scarlet Fever admissions to Motherwell Fever Hospital for their corresponding period. The prevalence of Scarlet Fever was considerably less throughout the second period. The cases were in no way selected and the type of disease was the same throughout the investigation.

It was determined to investigate the Dick test in patients who had been in Motherwell Fever Hospital with

Scarlet Fever at some previous date.

(1) Seventy-six patients who had Scarlet Fever nine months previously were Dick-tested. These cases had all been treated with Anti-Scarlatinal Serum.

(2) Eighty-three patients who had Scarlet Fever five years previously were Dick-tested. These cases had not been treated with Anti-Scarlatinal Serum.

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## Dick Tests on Admission.

The rash in Scarlet Fever is an important and early feature of the disease. In the majority of cases its appearance settles the diagnosis. According to the view put forward by recent workers the rash is the response of the skin, and in particular a dilatation of the skin capillaries, to the exotoxin of the Streptococcus Scarlatinae. The Dick test, consisting of an intradermal injection of this exotoxin, can be regarded as a localised infection with the Scarlet Fever toxin. In other words, the rash in Scarlet Fever is a'universal Dick Test'.

Altogether two hundred and seventy-three cases of Scarlet Fever were Dick tested on admission to hospital. The day of disease on admission varied from the first day to the fourth week, although the majority (92.5%) were admitted during the first week of illness. The results obtained are given in the table below. Here, as elsewhere in this paper, the pseudo and positive reactors are given separately but in drawing up percentages are included among the positive reactors. This follows the practice of previous workers and allows of comparison with their figures.

The Dick test in 273 cases of Scarlet Fever on admission.

| Day of Disease. | 1 | 2 | 3 | 4 | 5 | 6 | 7-14 | 14 onwards |
|---|---|---|---|---|---|---|---|---|
| Total cases. | 15 | 69 | 64 | 53 | 36 | 11 | 16 | 9 |
| Number Positive. | 8 | 49 | 43 | 34 | 18 | 6 | 9 | 4 |
| Number Negative. | 6 | 18 | 17 | 17 | 15 | 3 | 7 | 5 |
| Number Pseudo & Positive. | 1 | 2 | 4 | 2 | 3 | 2 | - | - |
| Per Cent Positive. | 60 | 73.5 | 72.3 | 68 | 58.4 | 72.7 | 58 | 45.5 |

This table shows that, with the exception of the first day, there is a large percentage positive early in the disease and that this percentage declines steadily until the sixth day after which the numbers are too small to allow of trustworthy conclusions. Zingher found that all his cases of Scarlet Fever who were Dick tested on the first day of disease were positive and that 98% of cases were positive during the first five days of disease. Rosen and Korobicina

from observations made on one hundred and twenty-three cases found that 82.5% were positive on the second and third day of disease, and 74.1% on the fourth day of disease, 50% on the fifth day of disease, and 44.9% on the fourth to the tenth day.

In this country the earliest observations were those of Ker and his co-workers. They obtained 73.9% of positives during the first three days and 68.6% in the period three to six days. In his paper on the subject Ker noted the disparity between his results and those of Zingher; he attributed this disparity to various causes but especially to the greater dilution of toxin which he himself used. Lees, in an outbreak of Scarlet Fever in a school in Minnesota found that fifteen out of forty-eight boys who developed Scarlet Fever gave a negative Dick test at the onset of symptoms. He used ten times the strength of toxin to retest contacts and did not find more positive reactions; he came to the conclusion that in this particular outbreak he was dealing with more than one strain of toxin. Smith and Taylor reported the results obtained with the Dick test in one hundred and seventy cases of Scarlet Fever early in the disease. They obtained 86.3% posi-

tive in the first two days, 70% in the third, 60% in the fourth day and 52.9% in the fifth day. They remarked in their paper that the test would be more valuable when a method of more accurate standardisation of the toxin had been evolved.

It is interesting to note that Ker gives also as part explanation of his smaller percentage of positives that the history of the day of onset of the disease is not always reliable. Perhaps he had this in mind when he grouped together his cases Dick tested during the first three days of illness. However, it has been observed, as in the outbreak recorded by Lees, that, even under the most strict conditions a certain proportion of cases give a negative Dick Test on their first day of illness.

The rash in Scarlet Fever varies greatly in different cases. It may be absent, slight and transient, or well-marked and lasting. Some workers, as, for example Sutherland of Monsall, have noticed that a bright rash may obscure a positive Dick Test. I have seen this in a few of my cases and noted that in others with a bright rash the positive Dick Test has been indicated by an intensification of the rash at the site of injection. In making an abstract

of cases according to their degree of rash the following figures are obtained.

| | Pos. | Neg. | % Pos. |
|---|---|---|---|
| Bright Rash | 81 | 54 | 60 |
| Faint Rash | 69 | 24 | 74 |

While the larger percentage of positive reactions among those with faint rashes is probably due in part to the greater ease with which a positive reaction is manifested, yet in these cases the milder nature of the infection may also allow a larger proportion of positive reactions.

My conclusions from this part of the work are:-

1. The Dick Test has a specific relationship to Scarlet Fever.
2. A positive Dick Test is more common than a negative Dick Test in the first six days of Scarlet Fever.
3. A negative Dick Test in a case of doubtful Scarlet Fever, early in the disease, does not exclude a diagnosis of Scarlet Fever.

4. A bright rash may obscure a positive reaction.

5. That more accurate standardisation of the toxin is necessary before complete reliability can be placed on results obtained from its use.

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## CASES NOT TREATED BY SERUM.

The work of this section falls naturally into two parts.

1. Eighty-three patients who had suffered from Scarlet Fever in 1922 were Dick tested.

2. Eighty-seven patients admitted to Motherwell Fever Hospital with Scarlet Fever during the first ten weeks of the year 1927 were Dick tested on admission and at weekly intervals until their dismissal from hospital.

1. A certain number of cases notified as Scarlet Fever are found after residence in hospital to suffer from some other disease such as Tonsillitis or Sore Throat. Thus, as will be found in my appendix, there were fifty-four such cases admitted to Motherwell Fever Hospital during the winter of 1926-27. These patients were treated in the isolation wards of the hospital and were dismissed, usually three weeks later, once a diagnosis other than Scarlet Fever had been made. But the important point is that, to a proportion of these patients and to their relatives, the disease has been Scarlet Fever; so that, in after years, these patients would give a history of Scarlet Fever when, in reality, they had never suffered from that disease. It was for this reason

that care was taken in this series of eighty-three cases to ascertain, by reference to hospital records, that the attack of Scarlet Fever in each case was undoubted. Rosen and Korobicina call attention to this in one of their papers. Other workers on the results obtained from the Dick Test in patients with a 'history' of Scarlet Fever have not stated that they took similar precautions.

The following table gives the results of the Dick Tests in these eighty-three patients. Their ages ranged from seven years to twenty-nine years. The type of disease was severe in one, moderate in three and mild in seventy-nine cases.

| Type of Disease | Number of cases | Result of Dick Test. Pos. | Neg. | Percentage Pos. |
|---|---|---|---|---|
| Mild | 79 | - | 79 | None |
| Moderate | 3 | - | 3 | None |
| Severe | 1 | - | 1 | None |

It is seen, therefore, that all of these cases are Dick negative indicating the presence in their body fluids of antitoxins to the Streptococcus Scarlatinae and showing that they are no longer susceptible to Scarlet Fever. This is in

agreement with the well-known fact that one attack of Scarlet Fever, in the majority of cases, protects the individual against a second attack. Kinloch and his co-workers found that 10% of persons with a 'history' of Scarlet Fever gave a positive reaction. Dick and Dick in a series of 204 cases who had previously suffered from Scarlet Fever found 9.3% positive. They do not state however if the history of Scarlet Fever was verified in the same way as in this series. In their first paper the Dicks found the test negative in fifteen out of sixteen cases. In the remaining case which was positive they note that the history of Scarlet Fever was doubtful. Rosen and Korobicina in a series of one hundred and eleven cases with a history of Scarlet Fever obtained 23.4% of positives. However in another series of fourteen persons in whom the history was verified they found that two only were positive and that these two had suffered from Scarlet Fever twenty and thirty-five years previously. It would seem therefore that where a history of Scarlet Fever is verified the Dick reaction is negative in practically every case, thus indicating immunity to Scarlet Fever.

2. In this series of eighty-seven cases the ages ranged

from one year to twenty-eight years. There were fifty-eight females and twenty-nine males; the type of disease was severe in one, moderate in five, and mild in eighty-one. More than half of these patients were not in hospital after the sixth week. The following table gives the results of the weekly Dick tests in these patients.

Weekly Dick Tests in Patients not treated by Serum.

| Week of Illness. | 1st Week. | 2nd Week. | 3rd Week. | 4th Week. | 5th Week. | 6th Week. | 7th Week. |
|---|---|---|---|---|---|---|---|
| Number Positive | 49 | 28 | 21 | 16 | 21 | 11 | 6 |
| Number Slightly Positive | - | 3 | 2 | 2 | 1 | 3 | 2 |
| Number Pseudo & Positive | 6 | 1 | 1 | 3 | 1 | - | - |
| Number Negative & Pseudo Negative | 24 | 50 | 60 | 66 | 62 | 52 | 34 |
| Percentage Positive | 69.6 | 39.02 | 28.57 | 24.13 | 27.06 | 21.21 | 19.05 |
| Percentage Negative | 30.4 | 60.98 | 71.43 | 75.87 | 72.94 | 78.79 | 80.95 |

This table shows that there is a decline in the number of positive reactions from the first week onwards and that this decline is most marked between the first and second weeks. There is a slight and temporary increase in the number of positives during the fifth week. This will be explained later.

These figures indicate a steady increase in immunity. A detailed analysis does not prove this for the individual. There are wide variations from the patient who is negative on the second day of illness to the patient who never becomes negative during his seven weeks residence in hospital. By sub-dividing these eighty-seven cases into groups according to the variations in their reactions to the Dick Test the following are obtained.

GROUP A. consists of thirty-six cases positive on admission, subsequently becoming negative and remaining so.

GROUP B. consists of twelve cases positive on admission and remaining positive until dismissal from hospital.

GROUP C. is made up of nineteen cases negative on admission and remaining so until dismissal from hospital.

GROUP D. is an irregular group of twenty cases characterised by becoming Dick Positive after having been Dick negative.

GROUP A. Of these thirty-six cases thirty-three were admitted during their first week of disease, two in the second week and one in the third week. Twenty-five of them were negative in the second week and thirty-one in the third week while the remainder became negative by the fifth week. This means that these patients developed their immunity while in hospital although it developed more rapidly in some than in others.

GROUP B. All of the twelve patients were admitted during the first week of disease. Ten of them were mild cases, and two of moderate severity. Seven were dismissed from hospital before the sixth week and two of them remained until the seventh week. From my observations on the patients who had Scarlet Fever five years ago it can be assumed that these twelve patients will develop their antitoxic immunity at some time after leaving hospital. This implies that a positive Dick Test during convalescence from Scarlet Fever does not indicate an inability to develop immunity to the disease at a later date. While Branch and Edwards found no positive reactions among sixty-five cases of Scarlet Fever in convalescence, Ker found 7.3% positive and Rosen and Korobicina 17.2%. Zingher in his series of one hundred and seventy

cases had twelve who were persistent Positive Dick reactors. In some of these he regarded the diagnosis of Scarlet Fever as doubtful and he suggests as an explanation of the others that there may be occasional strains of haemolytic streptococci causing Scarlet Fever which produce different toxins.

GROUP C. Sixteen of nineteen cases negative on admission and negative throughout their illness were admitted to hospital during the first week of disease. One patient was discharged from hospital in the fifth week, one in the sixth week, four in the eighth week, while one remained until the tenth week. Probably some of these cases were Dick positive before contracting Scarlet Fever and rapidly became Dick Negative. Others may have been Dick negative before their attack of Scarlet Fever. They may have had enough antitoxin to render them Dick negative and yet not enough to protect them against Scarlet Fever. This has been recorded by various authors. Robertson reports a case occurring in an epidemic, Nobel and Orel report one case seen by themselves and publish records of another case. The following case observed by myself in Motherwell Fever Hospital presents some interesting features.

Nurse C. age 19 years was Dick-tested and found to be negative. Two months later she was again Dick-tested and was

again negative. Three weeks later she took a typical attack of Scarlet Fever. The Dick test was negative on the first day of her illness and again on the third day. It is interesting to note that the Schultz-Charlton test was positive on the first day of disease. The tongue peeled and she desquamated as in typical Scarlet Fever. Throughout her illness there was no elevation of temperature and very little constitutional disturbance. She was again Dick-tested on the forty-sixth day of her illness and was negative. The note on her chart is "true Scarlet Fever in spite of the Dick Tests."

Points of interest in this case are:-

1. Twice found to be Dick negative before the attack of Scarlet Fever.
2. Dick negative on the first day and again on the third day of disease.
3. Dick negative in the last week of illness.
4. Schultz-Charlton reaction positive on the first day of illness
5. No elevation of temperature and mild symptoms.

Lees, in the paper which I mentioned previously, found

that fifteen negative Dick reactors developed Scarlet Fever. He used toxin supplied by two different manufacturers and the results were alike in each case. In other thirty-five Dick negative reactors he used ten times the strength of toxin employed in the ordinary skin test and there was no difference in the results. From this observation he considered that the fault did not lie in the strength of toxin employed but rather in the variety of toxin. The Dicks have pointed out that there is much variability in the potency of toxin produced by different strains of the haemolytic streptococcus and that this may account for the different results obtained by various observers. Lees remarked that in any epidemic it would greatly enhance the value of the test if the exact variety of toxin responsible for the symptoms of Scarlet Fever in that epidemic, could be ascertained. At present the fact that a person Dick negative may yet be susceptible to Scarlet Fever minimises greatly the value of the test both as an indication of susceptibility and as an aid in diagnosis.

GROUP D. In groups A and C it was seen that patients, when once they became Dick negative, remained so. The twenty

cases belonging to this group have as their important feature a Dick positive reaction following on a Dick negative. Seven patients were Dick negative and thirteen were Dick positive on admission. Of the seven patients Dick negative on admission three became positive and remained so whilst the other four became positive during the second and third weeks and then became negative again. An analysis of the thirteen cases positive on admission and thereafter irregular in their Dick response will be given now. Giuffré has reported two cases similar to these thirteen.

Analysis of Thirteen Cases Positive on Admission.

| WEEK | 1st | 2nd | 3rd | 4th | 5th | 6th | 7th | 8th | 9th | 10th | 11th | 12th | 13th | 14th |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case 1 | + | − | + | + | + | | | | | | | | | |
| " 2 | + | + | − | − | + | + | | | | | | | | |
| " 3 | + | − | + | + | + | + | + | | | | | | | |
| " 4 | + | − | − | + | + | + sl | + sl | + sl | + sl | + sl | + | + | | |
| " 5 | + | − | − | + | + | − | + sl | − | | | | | | |
| " 6 | + | + | + | − | + | + | − | + | + | + | + ps | + ps | + ps | − |
| " 7 | + | − | − | + sl | − | − | | | | | | | | |
| " 8 | + | − | + sl | + | + | + | + | + | + | + | + | + | | |
| " 9 | + | − | − | − | − | + sl | sl | | | | | | | |
| " 10 | + | + | + ps | − | − | − | + | | | | | | | |
| " 11 | + | + | + | − | + | − | − | − | − | | | | | |
| " 12 | | | + | − | + | + | + | + | + | + | | | | |
| " 13 | | | + | + | + | + | + | + X | + | − | − | − | − | + |

X indicates occurrence of attack of scarlet fever while in hospital.
+ sl = slightly positive.
+ ps = pseudo and positive.

This table shows that eleven of these patients were admitted in the first week and two in the third week of the disease.

The general inference to be drawn from the results of the Dick Tests in these twenty patients is that the amount of antitoxin present in the blood varies in these patients from week to week. Blake and Trask have shown that the amount of toxin present in the blood in the early stages of Scarlet Fever varies greatly in different cases, and that clinical estimation of the amount of toxaemia is subject to considerable error. Lindsay and his co-workers have shown that the amount of natural antitoxin present in the blood of convalescent cases of Scarlet Fever varies greatly in different individuals, while Henry and Lewis found that the amount of antitoxin present in the blood of Scarlet Fever patients is considerably greater than in normal 'resistent' controls. The exact mechanism of antitoxin formation is not yet fully understood. It is known that the amount of antitoxin formed may be much greater than the amount of toxin injected. Non-specific substances such as the metallic salts have the power when injected of stimulating the production of antibodies. It would appear therefore that the formation of antitoxin is not a simple reaction but more of the nature

of a secretion. The results of the weekly Dick tests in these twenty patients would seem to indicate that in these cases at least the production of antibodies is not a steady progression. It is difficult to explain why the development of antitoxin is apparently regular in some cases and irregular in others. However, there is one clinical feature of this group of twenty cases which is interesting and suggestive. The percentage of complications is higher in this group than in any of the others. There is no suggestion that the patient is Dick positive, and, therefore presumably more susceptible, before the onset of a complication. Indeed, as I will show later, there is no apparent connection between the Dick test, before or after a complication, and the incidence of that complication. But I do suggest that the variation in the amount of antitoxin present in the patient's blood and the high incidence of complications in these patients may both be evidence of a general defect in the defensive qualities of the patient.

The last two cases (Nos. 12 and 13) in the preceding table are of special interest. They were sisters admitted desquamating and in the third week of their illness, to a

Scarlet Fever Ward. They were both Dick positive on admission. The following week No.12 was Dick negative while No. 13 was Dick positive. No. 12 became positive again the following week and remained so until dismissal from hospital in the tenth week. No. 13 had an attack of typical Scarlet Fever while in the ward. Her history is as follows:-

On admission in the third week of her illness her general condition was good with normal pulse and temperature. She was desquamating generally but particularly typically on the hands. The Dick Test was positive on admission and for the ensuing four weeks. The following week, the eighth of her disease and the fifth of her residence in hospital, she was again Dick Positive. Next day an urticarial rash developed on the arms and legs. This rash varied in intensity. The temperature rose to 99.4°F. and the pulse rate to 120 per minute. The following day the rash was scarlatiniform in character and the patient complained of sore throat which was red. The temperature rose to 102°F. and the pulse rate to 134 per minute. Next day the tongue began to peel, the rash to subside and the temperature to fall by lysis. Two days later she was again Dick tested,

i.e. exactly six days from her previous Dick test. The result was positive. "Papillae on tongue still prominent but general condition better" is the note on her chart two days later. Seven days from her latest Dick test she was again Dick tested and found to be negative. Her three succeeding weekly tests were all negative but the next and last before dismissal from hospital was positive. Typical desquamation commenced for the second time, on the twelfth day of this attack.

Points of interest in this case are:-

1. Admitted with typical desquamation in the third week of disease.
2. Dick positive on admission and for the ensuing four weeks.
3. Dick positive in the fifth week of her residence in hospital; this was followed next day by an urticarial rash and then within a few hours by an attack of typical Scarlet Fever.
4. Dick test positive on the fifth day of her second attack.
5. Dick test becoming negative in the second, third, fourth and fifth weeks of this attack.

6. Dick test becoming positive again before dismissal from hospital in the sixth week of her second attack.
7. That her sister whose second Dick test was negative and who was exposed to infection in the same way did not develop Scarlet Fever.
8. That they were both Dick positive on dismissal from hospital.

Goodall in a recent discussion stated that even in cases with most typical desquamation, unless there is a history of sore throat with a rash some short time previously, it is not safe to diagnose Scarlet Fever. However, keeping in view this statement of Goodall's, the opinion arrived at in Motherwell Fever Hospital with regard to these sisters was that the original attack was genuine. It may safely be assumed that the original attack of Scarlet Fever was mild. The most important feature of these two cases is their response to the Dick Test during their second week in hospital. The sister who had enough antitoxin in her blood to render her Dick negative, if only for one week, did not develop Scarlet Fever. It is probable that her response to the

original infection was better. Whether this was due to some individual peculiarity or to her original infection having been more severe than that of her sister it was not possible to determine. It will be observed that altogether No.13 had six Dick tests at weekly intervals before she developed Scarlet Fever. With regard to the view held by some authors that the Dick test and the rash in Scarlet Fever are phenomena of hypersensitiveness to the proteins of Streptococcus haemolyticus, the occurrence of an urticarial rash immediately prior to the attack of Scarlet Fever is interesting. Although I have Dick-tested many patients at weekly intervals for six weeks and more, this is the only case in which I observed the occurrence of an urticarial rash or a second attack of Scarlet Fever.

My conclusions from this section of the work are:-

1. The majority of patients become Dick negative during an attack of Scarlet Fever.
2. The majority of those who become Dick negative remain so.
3. The development of antitoxic immunity is regular in most individuals but varies in rate in different individuals.

4. In a proportion of cases (23%) the development of antitoxic immunity is not a steady progression.
5. A negative Dick test early in and during an attack of Scarlet Fever may be due to the patient being Dick negative before contracting the disease.
6. After a considerable interval of time (five years) antitoxic immunity becomes finally established in patients with a definite history of Scarlet Fever.
7. That the mechanism of immunity to Scarlet Fever is not yet fully understood.

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## Cases Treated by Serum.

The investigation into the Dick test in these patients took the same form as in those cases not treated by Anti-Scarlatinal Serum.

(1) Seventy-six persons who had been in hospital early in 1926 with Scarlet Fever and who had been treated by Anti-Scarlatinal serum were Dick-tested.

(2) One hundred and fifty-two patients who were admitted to hospital with Scarlet Fever in the ten weeks prior to January, 1927, were Dick-tested on admission. Anti-Scarlatinal serum was given next day and they were Dick-tested every week until their dismissal from hospital.

(1) The use of Anti-Scarlatinal serum only began in Motherwell Fever Hospital in 1926 so that in investigating the Dick test in old cases of Scarlet Fever who had been treated by serum this group automatically selected itself. However, in all of these cases a period of nine months had elapsed since their attack of Scarlet Fever and the in-

vestigation of their Dick response. Although the time difference between this series and the corresponding series of cases not treated by serum does not allow us to compare these two series strictly, yet they are sufficiently similar to allow of some useful inferences being drawn. As in the corresponding group of patients not treated with serum the attack of Scarlet Fever was verified by reference to the hospital records in each case.

Two of these cases had severe attacks of Scarlet Fever, seventeen had moderate attacks and fifty-seven were mild. All the mild cases had been given 10 c.cs. of Unconcentrated Anti-Scarlatinal Serum while the rest were given larger doses than this. The results of the Dick tests are shown in the following table:-

| No. of Cases. | Type of Disease. | Result of Dick Test | |
|---|---|---|---|
| | | Positive | Negative |
| 2 | Severe | - | 2 |
| 17 | Moderate | 3 | 14 |
| 57 | Mild | 5 | 52 |
| Total 76 | - | 8 | 68 |

In 10.52% of these cases an attack of Scarlet Fever had not rendered them Dick negative when tested nine months later. Zingher states that immunity to Scarlet Fever is mainly antitoxic and not to any extent antibacterial. These patients have not developed their antitoxic immunity. At least the positive Dick test indicates that they have not developed enough antitoxin to render them Dick negative although they may have developed enough to protect them against another attack of Scarlet Fever. Davies of Yale from his investigations on a similar group of cases considers that there may be some disadvantage in the use of Anti-Scarlatinal Serum from the point of view of subsequent immunity to the disease. The injection of Anti-Scarlatinal Serum early in the disease neutralises the toxins which are causing the symptoms. While it neutralises the toxins and improves the patients' general condition it also removes the stimulus which induces his permanent immunity. It is too soon yet to say whether or not this is the case since the therapeutic use of Anti-Scarlatinal Serum is very recent. It may be that second attacks of Scarlet Fever will become more frequent and that the security which an attack of

Scarlet Fever almost invariably conferred in former days will be lessened.. From this point of view the following case is of special interest.

A little girl, five years of age, was admitted to Motherwell Fever Hospital with Scarlet Fever on the 21st July, 1926. It was her third day of disease. The rash was faint and the tongue peeled. The day after admission 10 c.cs. of unconcentrated Anti-Scarlatinal Serum were given intra-muscularly. Her subsequent clinical history was uneventful except for the development of an urticarial serum rash in the seoond week. She desquamated on the eleventh day and was dismissed on the thirty-ninth day. The type of disease was mild and there were no Dick tests performed. Exactly four months later she was again admitted with Scarlet Fever. It was the second day of illness; the temperature was 104° F., pulse rate 140 per minute and her general condition very poor. The rash was ill-developed and the tongue was peeling. She was so ill that 20 c.cs. of Anti-Scarlatinal Serum was given at the same time as she was Dick tested. She was Dick negative and remained so every week until dismissed from hospital on the 44th day of

disease. A marked improvement was noted after the administration of serum. She made a good recovery. Desquamation began on the tenth day of her illness. The type of disease was severe.

This was the only case of a second attack of Scarlet Fever admitted to Motherwell Fever Hospital during the winter of 1926-27. On both occasions the attack was undoubted. Points of interest in this case are:-

1. Second attack of Scarlet Fever a short time (four months) after the first.
2. Second attack more severe than the first.
3. Anti-Scarlatinal Serum administered on the occasion of her first attack.

Second attacks of Scarlet Fever are very rare and when they do occur are usually milder than the first attack. Evidently, in the case of this child, the primary attack conferred only a very slight immunity; an immunity so slight that her second attack was much more severe than her first. There were more than six hundred cases of Scarlet Fever in Motherwell Fever Hospital in 1926 who were treated with Anti-Scarlatinal Serum. This is the only patient who returned

with a second attack. It is too early yet to look for confirmation of any hypothesis based on a single case.

(2) In this series of 152 cases there are eleven cases of severe infection, sixteen moderate cases and the remaining one hundred and twenty-five are mild cases. There are sixty-three males and eighty-nine females and the ages range from one year to thirty-six years. In one hundred and thirty patients the amount of serum administered was 10 c.cs. unconcentrated. Of the remaining sixteen who had more serum than this six received more than twenty-five c.cs. unconcentrated. In all of these cases the result of the Dick test on admission was obtained before serum was given.

Table of weekly Dick tests in Scarlet Fever patients treated by Anti-Scarlatinal Serum.

| Week of Disease | 1st | 2nd | 3rd | 4th | 5th | 6th | 7th |
|---|---|---|---|---|---|---|---|
| Number of Positives | 91 | 16 | 17 | 17 | 27 | 24 | 21 |
| Number of Pseudo and Positives | 9 | 1 | 3 | 4 | 9 | 6 | 2 |
| Number of slightly positives | - | 1 | 4 | 4 | 4 | 4 | 2 |
| Number of negative and Pseudo Negatives | 44 | 133 | 128 | 127 | 100 | 72 | 37 |
| Percentage of Positives | 69.4 | 11.92 | 15.78 | 16.44 | 28.57 | 32.02 | 40.32 |
| Percentage of Negatives | 30.6 | 88.08 | 84.22 | 83.56 | 71.43 | 67.98 | 59.68 |

The two striking features in this table are the large decrease in the number of positive reactions from the first to the second week, and the gradual increase in the number of positives from the second week onwards. Both of these may be attributed to the administration of the anti-scarlatinal serum. The passive immunity conferred by the serum is lost more quickly in some patients than in others. The smallest amount of serum (10 c.cs. unconcentrated) given to these patients has been defined as sufficient to convert a Dick positive reactor into a Dick negative reactor within 24 hours. There is a definite proportion (12% in this series) who lose their passive immunity before the second week. Trask has shown that the amount of circulating toxin early in Scarlet Fever varies greatly in similar cases. It is probable that in some of these cases the amount of antitoxin given in the serum was neutralised by the circulating toxins.

Between the second and third weeks 4% of patients lose their passive immunity without having developed enough antitoxin in their own to render them Dick negative. When no antitoxin is given the production of antibodies begins very early in the disease. Thus Zingher found that patients

usually developed enough antitoxin by the eighth or tenth day of disease to render them Dick negative. There are thus two sources of this antitoxin and it can be assumed that as the passive immunity is being lost the active immunity is being acquired in the majority of cases. It is reasonable to suppose that these two processes are equally balanced between the third and fourth weeks; that the loss of passive immunity is greater than the development of acquired immunity from the fourth week onwards and particularly so between the fourth and fifth weeks.

A detailed analysis shows that these patients vary in their response to the Dick Test and can be discussed under four main groups as in the series of cases not treated by serum.

Group A. is composed of sixty-two patients Dick positive on admission, subsequently becoming negative and remaining so.

Group B. consists of four cases positive on admission and who remained positive throughout their residence in hospital.

Group C. comprises twenty-nine cases Dick-negative on admission and who remained Dick negative while in

hospital,

Group D. has as its distinctive feature in each patient, a Dick positive reaction following on a Dick negative one. There are fifty-seven cases in this group.

Group A. is the largest group. All of these sixty-two cases except three are negative by the second week. The administration of serum was largely responsible for this, but in the later weeks after passive immunity is lost active immunity must be held responsible for the negative reactions. It is impossible to say from these data where in any particular case the one factor became subordinate to the other. It can be said that in some of these cases the immunity conferred by serum did not interfere with the natural development of immunity. In some it induced a negative Dick test earlier than would have occurred if they had had to rely on the acquirement of their own immunity.

Group B. These four cases were admitted during the first week of their illness. All had mild attacks and were given the smallest dose of serum used in this investigation. The immunity given to them by the serum passed off before the second week and their active immunity had not developed up till the time of their dismissal from hospital. It is possible

too, that the amount of antitoxin given was more than neutralised by the circulating toxin. I have shown that out of eighty-seven cases not treated by anti-scarlatinal serum, there were twelve persistent positive reactors. The much smaller percentage of cases in this group of serum-treated cases is due to the serum having induced a passive immunity which persisted long enough to give them a negative Dick Test at least in the second week of illness.

Group C. Of these twenty-nine patients three had severe infections, four moderate and twenty-two had a mild attack. All, except one, were admitted in the first week of disease. It is interesting to note that the Schultz-Charlton reaction was positive in four and negative in three cases, all of whom had very bright rashes. I have pointed out in the corresponding group of cases not treated by serum that the negative Dick Test so early in the disease, while it may be evidence of a rapid development of immunity, may also be due to these patients being Dick negative before contracting Scarlet Fever. The ratio of this group to the whole series corresponds in both serum-treated and non-serum treated patients, so that it might be inferred that in these patients

the administration of serum does not interfere with the natural development of immunity.

Group D. In this group of fifty-seven cases characterised by becoming Dick positive after having been Dick negative, there are eighteen who were Dick negative on admission to hospital. Of these eighteen, twelve became positive for one week only, (the fifth week in six instances) and were again negative on dismissal from hospital. The other six cases were positive when dismissed from hospital, three of them having become positive in the fifth week. Thirty-nine cases were positive on admission to hospital. Fifty-two out of the fifty-seven cases were admitted to hospital in the first week of illness.

I have indicated already that the effect of the administration of serum is shown by the large number of negative Dick reactions in the second week of disease. This immunity is a passive one as is proved by many of these patients becoming positive in later weeks and particularly in the fifth week. I have already demonstrated in Groups A. and C. that some patients develop their own immunity

independently of the immunity conferred by anti-scarlatinal serum. These two groups correspond to the two similar groups in the series of cases not treated by serum. Group B. on the other hand, is much smaller in the serum-treated series than in the other. We now find that Group D. is correspondingly increased in the serum series. The anti-scarlatinal serum has interfered with the natural development of immunity in a definite proportion of cases. It can at least be said that the passive immunity conferred by serum has delayed the natural development of immunity. Since the immediate effect of the administration of serum on the Dick reaction persists in a large number of cases till shortly before their dismissal from hospital its more remote effect is difficult to estimate. It is found for instance, that of fifteen cases in this group remaining in hospital after the seventh week, ten show more than one weekly variation in their Dick reaction, thus indicating that the natural development of immunity is not a steady progression in these patients. This would suggest that the development of acquired immunity besides being delayed may be interfered with in a more positive manner. However, the small number of

cases remaining in hospital after the seventh week is too small to allow of very reliable inferences in regard to subsequent natural development of immunity in serum treated cases as a whole. It is interesting to note that, as in the corresponding group of the non-serum series, the percentage of complications was highest in this group.

My conclusions from this section of the work are:-

1. The administration of Anti-Scarlatinal Serum quickly turns a Dick positive into a Dick negative reactor.
2. The passive immunity conferred by the serum passes off very quickly in some patients and probably in most by the fifth week.
3. The giving of serum not only delays but may also interfere with the steady development of acquired immunity.
4. Since 10% of serum-treated cases are Dick-positive nine months after leaving hospital, it is possible that the administration of Anti-Scarlatinal serum may prevent altogether the development of acquired immunity and so render these individuals liable to a second attack of Scarlet Fever.

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## Influence of the Incidence of Complications on the Weekly Dick Tests.

Complications in Scarlet Fever have been regarded for many years as secondary invasion of specific tissues by pyogenic organisms particularly streptococci. That these streptococci may be in some cases the organisms now regarded as the cause of the disease is undoubted. Thus the Dicks first produced experimental Scarlet Fever by a streptococcus from the septic finger of a nurse suffering from the disease. Also the rôle of the discharges from the complications of Scarlet Fever in harbouring the infective organisms has been varified by various workers. Tunnicliff states that the haemolytic streptococcus cannot be recovered from a Scarlet Fever patient after the first two weeks except from the discharges. She also states that probably complications arising after the third week are not due to the specific organism. The general resistance of the patient has been lowered by the Scarlet Fever infection and this allows of secondary invasion by other organisms. There are undoubtedly other

local factors, anatomical and pathological, which influence the site of a complication. A good example of the latter is seen in the frequency with which quiescent lesions, such as an otitis media or an adenitis may become lighted up with the onset of Scarlet Fever.

In the series of eighty-seven patients who were not treated by serum twenty-seven had complications. A slight degree of adenitis or of rhinitis early in the disease have not been considered as complications but rather as part of the clinical picture of Scarlet Fever. Some of these patients had more than one complication. It has not been considered necessary in the following analysis of these cases to specify the type of complication as the investigation is concerned solely with the reaction of the patient to the Dick test and the influence, if any, of the incidence of complications on that reaction.

Analysis of Complications in eighty-seven Patients not treated by Anti-Scarlatinal Serum.

| Group | A. | B. | C. | D. | TOTALS |
|---|---|---|---|---|---|
| Total Cases | 36 | 12 | 19 | 20 | 87 |
| No. of cases with compli-cations. | 8 | 3 | 5 | 11 | 27 |
| Percen-tage of cases with com-plica-tions. | 22 | 25 | 26 | 55 | 31.03 |
| Result of Dick Test immed-iately before and immed-iately after the onset of the compli-cation. | Neg. before and after in 6 cases. Pos. before and neg. after in 2. | Pos. before and after in three cases. | Neg. before and after in five cases. | Pos. before and after in 7 cases. Neg. before and after in 2 cases. Pos. before and neg. after in 1 cases. Neg. before and Pos. after in 1 case. | Pos. before and after in 10 cases. Neg. before and after in 13 cases. Pos. before and Neg. after in 3 cases. Neg. before and Pos. after in 1 case. |

In only four cases was there any change noted in the Dick response before and after the onset of a complication. Thirteen patients were Dick positive before the incidence of the complication and only three of these became Dick negative afterwards. Fourteen patients were Dick negative before and only one of these was Dick positive afterwards. It is obvious then that the onset of a complication bears no apparent relation to the amount of antibodies present in the blood immediately before and that in the big majority of cases it has no obvious effect on the Dick response of the patient immediately afterwards. It is possible that, in the three patients who were Dick positive before and subsequently became Dick negative, the complications in these cases were due to the specific streptococcus and its toxins, although the absence of bacteriological proof of this hypothesis is a serious drawback.

There is a much greater percentage of complications in Group D. than in any of the others. As I have pointed out elsewhere the characteristic of this group is the irregular production of antitoxin in response to the scarlatinal infection. It is possible that this variability in response

to the Scarlet Fever virus is evidence of a weakness in the mechanism for the production of antibodies generally. These patients then may be said to have a naturally defective mechanism for the formation of antibodies and the irregular nature of their response to the Dick Test and the high incidence of complications may both be evidence of this defect.

In the series of one hundred and fifty-two cases treated by serum the complications were similar to those in the non-serum group. In addition a large proportion of these cases suffered from serum phenomena, particularly rashes. This latter complication has been included in a special table as it is not an infection in the usual sense of the word.

Analysis of Complications in 152 patients treated by Anti-Scarlatinal Serum and excluding Serum phenomena.

| Group | A. | B. | C. | D. | TOTALS |
|---|---|---|---|---|---|
| Total Cases | 62 | 4 | 29 | 57 | 152 |
| No. of cases with complications. | 18 | 1 | 7 | 23 | 49 |
| Percentage of cases with complications. | 28 | 25 | 24.1 | 40.3 | 32.2 |
| Result of the Dick Test immediately before and immediately after the onset of the complication. | Pos. before and after in 1 case. Neg. before and after in 13 cases. Pos. before and neg. after in 4 cases. | Pos. before and after in 1 case. | Neg. before and after in 7 cases. | Pos. before and after in 4 cases. Neg. before and after in 15 cases. Pos. before and Neg. after in 2 cases. Neg. before and Pos. after in 4 cases. | Pos. before and after in 6 cases. Neg. before and after in 35 cases. Pos. before and Neg. after in 6 cases. Neg. before and pos. after in 4 cases. |

The higher incidence of complications in Group D. in this series is again evident although it is not quite so marked a feature as in the corresponding group of cases not treated by serum. In thirty-five out of forty-nine cases the Dick test was negative before and after the onset of the complication. This must be attributed to the passive immunity conferred by the anti-scarlatinal serum. Apart from this, the observations made on the incidence of complications in the non-serum treated group apply equally well here.

Some patients in both of these series developed more than one complication and it is interesting to note that the Dick tests before and after the onset of one complication may be totally different from the tests before and after a subsequent complication. Thus one case had double otitis media in the second week, the Dick test being positive before and negative afterwards. In the sixth week the same patient developed cellulitis of the neck and the Dick test was negative before and positive afterwards.

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Analysis of Serum Phenomena in Relation to the Dick Test.

| Group | A. | B. | C. | D. | TOTALS |
|---|---|---|---|---|---|
| Total Cases | 62 | 4 | 29 | 57 | 152 |
| No. of cases with Serum Phenomena | 22 | 1 | 7 | 24 | 54 |
| Percentage of cases with Serum Phenomena | 35.48 | 25 | 25.51 | 42.1 | 35.52. |
| Result of the Dick Test immediately before and immediately after the onset of the complication. | Pos. before and after in 2 cases. Neg. before and after in 17 cases. Pos. before and neg. after in 3 cases. | Pos. before and after in 1 case. | Neg. before and after in 7 cases. | Pos. before and after in 3 cases. Neg. before and after in 9 cases. Pos. before and neg. after in 4 cases. Neg. before and pos. after in 8 cases. | Pos. before and after in 6 cases. Neg. before and after in 33 cases. Pos. before and neg. after in 7 cases. Neg. before and pos. after in 8 cases. |

From this table it is seen that there is no obvious connection between the Dick Test and the onset of a serum reaction. Nearly all of these serum reactions had as part of the picture a rash which was usually urticarial in type. In cases where this rash was recurrent I have observed that the Dick Test before and after the first appearance may be quite different from the Dick Test before and after the recurrence. There is no evidence from these observations that a Dick Test may induce a rash or that the incidence of a rash may alter the patient's reaction to the Dick Test. There is a slightly higher percentage of cases with serum rashes in Group D. than in any of the others, although this is not so marked as in the table of the incidence of complications. In only four out of these fifty-four cases was there a larger amount than 10 c.cs. unconcentrated anti-scarlatinal serum given.

My conclusions from this part of the work are:-

1. There is no connection between the Dick Test immediately before or after a complication and the onset of that complication.
2. The higher incidence of complications and the irregular

nature of the response to the Dick Test in Group D. may both be due to a natural defect in the patient's resistance to infection.

3. There is no obvious connection between the Dick test and the incidence of serum reactions.

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Comparison of Serum and Non-Serum treated Cases.

This comparison does not include any discussion of the therapeutic value of Anti-Scarlatinal serum.

In both of these series of cases the percentage of positive reactions on admission to hospital is approximately the same. Then there is a decline in the percentage of positives in both in the second week. This decline is much more marked in the series of serum-treated cases than in the other, and is due to the administration of serum. After the second week while this decline continues in the non-serum series it is replaced in the serum-treated cases by an incline indicating an increase in the number of positives in successive weeks. This is well shown by a graph (see Graph 1). The explanation of this is that the passive immunity conferred by the serum is being lost more rapidly than the active immunity is being developed.

The slight increase in the percentage of positive results obtained in the fifth week in the non-serum treated series is due to the large number of positive reactions obtained that week in the group of patients with an irregular response to the Dick test and is probably fortuitous. The

marked increase in the percentage of positives in the fifth week in the serum series is due to the loss of passive immunity at that time by a large number of cases.

While less than 20% of patients not treated by serum are positive in the seventh week there are 40% for the corresponding week in the serum treated series. This indicates that the serum has at least delayed the natural development of immunity.

These two series can be conveniently sub-divided into groups according to the variation in their weekly response to the Dick test.

Table showing groups in the Serum and Non-Serum Series.

| Group | A | B | C | D | Total |
|---|---|---|---|---|---|
| Non-Serum Series | 36 | 12 | 19 | 20 | 87 |
| Percentage of total Non-Serum cases | 41.4 | 13.8 | 22.35 | 22.9 | |
| Serum Series | 62 | 4 | 29 | 57 | 152 |
| Percentage of total Serum Cases | 40.3 | 2.6 | 18.85 | 37.5 | |

The largest group (A) 40% in each series, consists of those cases Dick positive on admission who developed their immunity while in hospital in a steady manner. The difference between those two groups in the speed of this development is well shown in Graph 2. This indicates that the early immunity conferred by serum did not influence the subsequent development of acquired immunity in these cases.

Group C. is approximately the same in each series and shows that in a certain proportion of cases Dick negative either before or very early in Scarlet Fever the administration of serum does not interfere with the retaining of their immunity.

The most striking differences occur in Groups B. and D. The loss in group B. of the serum series is counterbalanced by a gain in Group D. This is explained by the administration of serum conferring an early passive immunity in patients who would otherwise be persistently positive reactors and the subsequent loss of this passive immunity not being replaced by the development of acquired immunity. It is obvious then that the administration of serum in a proportion of positive reactors only delays

their subsequent development of acquired immunity.

In pursuing the investigation of these two series of cases still further and Dick-testing them a considerable time after leaving hospital there is a definite proportion of positive reactors among the patients formerly treated by serum and none among those not treated by serum. This would suggest that the administration of serum has interfered with their development of immunity. This view is further strengthened by the case recorded earlier in this paper of the only patient who had a second attack of Scarlet Fever after leaving hospital being one who had been treated by serum earlier in the year.

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## Summary and Conclusions.

It has long been recognised that streptococci have some relationship to Scarlet Fever but until the work of the Dicks no convincing evidence that the streptococcus was the primary etiological factor had been adduced. Their discovery, too, of a soluble exotoxin able to produce clinical Scarlet Fever marks an epoch in the history of our knowledge of the disease.

The material in this thesis includes practically all cases of Scarlet Fever admitted to Motherwell Fever Hospital during the winter 1926-27 so that any selection of cases was avoided. Care was taken in every case to ascertain on clinical grounds that the attack of Scarlet Fever was genuine.

The investigation was concerned with the reaction of these Scarlet Fever patients to the Dick test which was performed.

a) On admission to hospital.
b) At weekly intervals during their stay in hospital,
c) In a series of cases dismissed from hospital some time previously.

No such systematic investigation has been discovered in a review of the current literature on the subject.

The cases were divided into two main sections.

1. Those patients who were treated by Anti-Scarlatinal Serum.

2. Those patients who were not treated by Anti-Scarlatinal Serum.

A comparison of the reactions of these two groups has been made.

The results obtained from the use of the Dick test early in Scarlet Fever have in general confirmed those obtained by other observers. The percentage of positive results obtained however is not sufficient to be of much aid in diagnosis. Correspondingly the large percentage of negatives obtained in convalescence has been observed but here again the figure is not high enough to permit of very great stress being laid on this in diagnosis.

The results obtained from the weekly Dick tests throw interesting light on the development of immunity to Scarlet Fever. They show that a definite proportion of individuals do not develop their antitoxic immunity in a

steady manner. These figures also show that any conclusion based on the result of the Dick test in a patient at any particular week of the disease is liable to be fallacious. In this section also I have confirmed the observation of previous observers as to a negative Dick test in the normal individual not always indicating immunity to Scarlet Fever. The general effect of serum in promoting a rapid passive immunity and the short duration of this immunity have been noted. It has also been demonstrated that the administration of serum at least delays the development of acquired immunity in a proportion of cases and may also interfere with its more permanent development.

In all cases with a reliable 'history' of Scarlet Fever the Dick test has been found negative except in those cases treated by serum. The view that the use of anti-scarlatinal serum may have a deleterious effect on the development of permanent immunity receives some support from the foregoing observation and from the record of the only case admitted to Motherwell Fever Hospital during the time of this investigation with a second

attack of Scarlet Fever being a patient who had been treated by serum in the primary attack.

There is no apparent connection between the results of the Dick tests either immediately before or after the incidence of a complication or a serum reaction and that complication or serum reaction.

Lastly, attention has been drawn to the comments of various workers as to the need for standardisation of the Dick test and that until this has been done satisfactorily the Dick test cannot be regarded with relation to Scarlet Fever as reliable as the Schick test is regarded with relation to Diphtheria.

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Appendix. I.

The Dick Test in Patients Suffering from some Disease other Than Scarlet Fever.

Every patient, notified as suffering from Scarlet Fever or Diphtheria and admitted to the County Fever Hospital, Motherwell during the winter of 1926-27, was Dick tested. The Dick tests in the patients with proved Scarlet Fever I have already discussed. In addition there were fifty-four patients, notified as suffering from Scarlet Fever, in whom this diagnosis was changed after residence in hospital. In twenty-four of these the Dick test was positive. Two-hundred and sixty eight patients, notified as suffering from Diphtheria, were admitted to hospital. In forty-two of these the diagnosis of Diphtheria was changed after residence in hospital. In none of these forty-two patients was the diagnosis changed to Scarlet Fever. By combining these groups, one large group of three hundred and twenty-two patients, suffering from some disease other than Scarlet Fever is obtained.

Thirty-nine of these three hundred and twenty-two patients gave a history of Scarlet Fever. The Dick test was positive in six of these. I have mentioned previously the importance of verifying a history of Scarlet Fever. It was decided to do this in the case of these six patients who were Dick positive.

Two of them had had Scarlet Fever in 1919 and 1920 respectively and had been treated at home so that the history of Scarlet Fever could not be verified by reference to hospital records. One had been in Motherwell Fever Hospital with Scarlet Fever in 1920. By consulting the hospital record of this patient it was found that the history of Scarlet Fever was not upheld. The patient had been notified as suffering from Scarlet Fever, but after residence in hospital this diagnosis had not been confirmed. Of the remaining three patients one is included in my series of serum-treated cases who were Dick tested every week during residence in hospital. She had been Dick-positive too before her dismissal from hospital two months previously. The other two patients had had Scarlet Fever in 1923 and 1925 respectively. It is interesting to note that both of these had been treated while in hospital with an anti-streptococcus Vaccine. These six cases illustrate the difficulty of making sure of a "history of Scarlet Fever". In one the history was not true and in two it could not be verified.

The following table gives the results of the Dick tests in the two hundred and eighty-three patients who did not give a "history of Scarlet Fever."

| Disease. | Number of Cases. | Number showing Positive Dick Tests. | % age with Positive Dick Tests. |
|---|---|---|---|
| Diphtheria | 194 | 88 | 45.3 |
| Sore Throat and Tonsillitis. | 73 | 31 | 42.6 |
| Tonsillar Abscess. | 2 | - | Nil. |
| Glandular Abscess. | 1 | 1 | 100% |
| Rhinitis. | 1 | - | Nil. |
| Nephritis. | 1 | - | Nil. |
| Otitis Media. | 2 | - | Nil. |
| Miscellaneous. | 9 | 4 | 44.4 |

Various authors have mentioned the importance of Dick testing patients suffering from Diphtheria. They point out its value in the case of an outbreak of Scarlet Fever in a Diphtheria ward. Sutherland of Monsall found that in three hundred and fifty-four Diphtheria patients 55·9% gave a positive Dick test. Although all Diphtheria patients in Motherwell Fever Hospital during the winter of 1926-27 were Dick tested, it was impossible to prove its value as an indication of susceptibility since no epidemic

of Scarlet Fever occurred in a Diphtheria ward during that period.

Zingher investigated the Dick reactions in four thousand five hundred and seventy normal individuals. He found that susceptibility to Scarlet Fever according to age-groups corresponded to susceptibility to Diphtheria in the same way. A similar investigation on one thousand five hundred people selected at random was carried out by Kinloch and his co-workers in Aberdeen. I have given below the results obtained by these workers and have arranged my own two hundred and eighty-three patients, suffering from some disease other than Scarlet Fever, in the same way.

The Dick Test at Different Age Groups - Zingher.

| Age. | 6-12 mths | 1-2 yrs | 2-3 yrs | 3-4 yrs | 4-5 yrs | 5-10 yrs. | 10-15 yrs | 15-20 yrs | 20 yrs up |
|---|---|---|---|---|---|---|---|---|---|
| Number tested. | 42 | 123 | 140 | 207 | 237 | 1475 | 1690 | 285 | 342 |
| Number Dick Pos. | 27 | 87 | 95 | 123 | 100 | 522 | 430 | 75 | 61 |
| % age Dick Pos. | 64.2 | 70.7 | 67.8 | 59.4 | 46.4 | 35.4 | 25.4 | 26.3 | 17.9 |

From an investigation of the Dick test in mothers and babies Zingher came to the conclusion that there was a maternal transmission of Scarlet Fever antitoxin and that this protected most children during the first year of life and probably all during the first six months of life.

The Dick Test at Different Age-Groups - Kinloch ¥

| Age. | 0-5 yrs. | 5-10 yrs | 10-15 yrs | 15-20 yrs | 20-25 yrs | 25 yrs upwards. |
|---|---|---|---|---|---|---|
| Number tested. | 63 | 610 | 644 | 199 | 44 | 8 |
| % age Dick Pos. | 96.4 | 81.2 | 65.5 | 60.8 | 52.4 | 27.7 |

¥ Including 121 persons with a history of Scarlet Fever.

The Dick test at different age-groups in persons suffering from some disease other than Scarlet Fever - myself.

| Age | 6-12 mths | 1-2 yrs | 2-3 yrs | 3-4 yrs | 4-5 yrs | 5-10 yrs | 10-15 yrs | 15-20 yrs | 20 yrs upwards |
|---|---|---|---|---|---|---|---|---|---|
| Number tested. | 6 | 14 | 21 | 25 | 26 | 117 | 52 | 10 | 12 |
| Number Dick Pos. | 4 | 7 | 15 | 12 | 12 | 63 | 9 | 1 | 1 |
| % Age Dick Pos. | 66.6 | 50 | 71.4 | 48 | 46.15 | 53.8 | 17.3 | 10 | 8.3 |

Since the individuals Dick-tested by myself were not normal and since their numbers are so small a strict comparison is not justifiable. The figures obtained by myself approximate more closely to Zingher's than do those obtained by Kinloch. Both Zingher and Kinloch found a higher percentage of positive reactions among patients of better social standing. Most of my patients were drawn from industrial and mining areas so that this too may account for the general low percentage of positive reactions

obtained by myself.

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## Appendix II.

The following tables contain the main features of the serum and non-serum treated patients who were Dick-tested every week.

### Eighty-seven Patients not treated with Serum.

Type of Rash.

| | A. | B. | C. | D. | Totals. |
|---|---|---|---|---|---|
| Bright. | 12 | 3 | 7 | 7 | 29 |
| Faint. | 15 | 7 | 5 | 9 | 36 |
| Negative. | 9 | 2 | 7 | 4 | 22 |
| Totals. | 36 | 12 | 19 | 20 | 87 |

Type of Disease.

| | A. | B. | C. | D. | Totals. |
|---|---|---|---|---|---|
| Severe. | - | - | - | 1 | 1 |
| Moderate | 1 | 2 | - | 2 | 5 |
| Mild. | 35 | 10 | 19 | 17 | 81. |
| Totals. | 36 | 12 | 19 | 20 | 87 |

Ages of Patients.

| | A | B | C | D |
|---|---|---|---|---|
| Highest | 28 | 13 | 23 | 21 |
| Lowest | 3 | 1 | 3 | 1 |
| Average | 12.9 | 5.3 | 9.3 | 7.58 |

Sexes of Patients.

| | A | B | C | D | Totals |
|---|---|---|---|---|---|
| Males | 12 | 4 | 7 | 6 | 29 |
| Females | 24 | 8 | 12 | 14 | 58 |
| Totals | 36 | 12 | 19 | 20 | 87 |

Degree of Desquamation.

| | A | B | C | D | Totals |
|---|---|---|---|---|---|
| Well-marked | 33 | 10 | 19 | 19 | 81 |
| Not marked | 3 | 2 | - | 1 | 6 |
| Totals | 36 | 12 | 19 | 20 | 87 |

## One Hundred and Fifty-two Patients Treated with Serum.

### Type of Rash.

| | A. | B. | C. | D. | Totals. |
|---|---|---|---|---|---|
| Bright. | 38 | 1 | 20 | 30 | 89 |
| Faint. | 20 | 1 | 6 | 15 | 42 |
| Negative. | 4 | 2 | 3 | 12 | 21 |
| Totals. | 62 | 4 | 29 | 57 | 152 |

### Type of Disease.

| | A. | B. | C. | D. | Totals. |
|---|---|---|---|---|---|
| Severe. | 2 | - | 3 | 6 | 11 |
| Moderate. | 4 | - | 4 | 8 | 16 |
| Mild. | 56 | 4 | 22 | 43 | 125 |
| Totals. | 62 | 4 | 29 | 57 | 152 |

### Ages of Patients.

| | A. | B. | C. | D. | |
|---|---|---|---|---|---|
| Highest. | 36 | 9 | 17 | 14 | |
| Lowest. | 2 | 4 | 2 | 1 | |
| Average. | 8.92 | 6.5 | 8.51 | 5.88 | |

## Sex of Patients.

| | A. | B. | C. | D. | Totals. |
|---|---|---|---|---|---|
| Males. | 25 | 1 | 14 | 23 | 63 |
| Females. | 37 | 3 | 15 | 34 | 89 |
| Totals. | 62 | 4 | 29 | 57 | 152 |

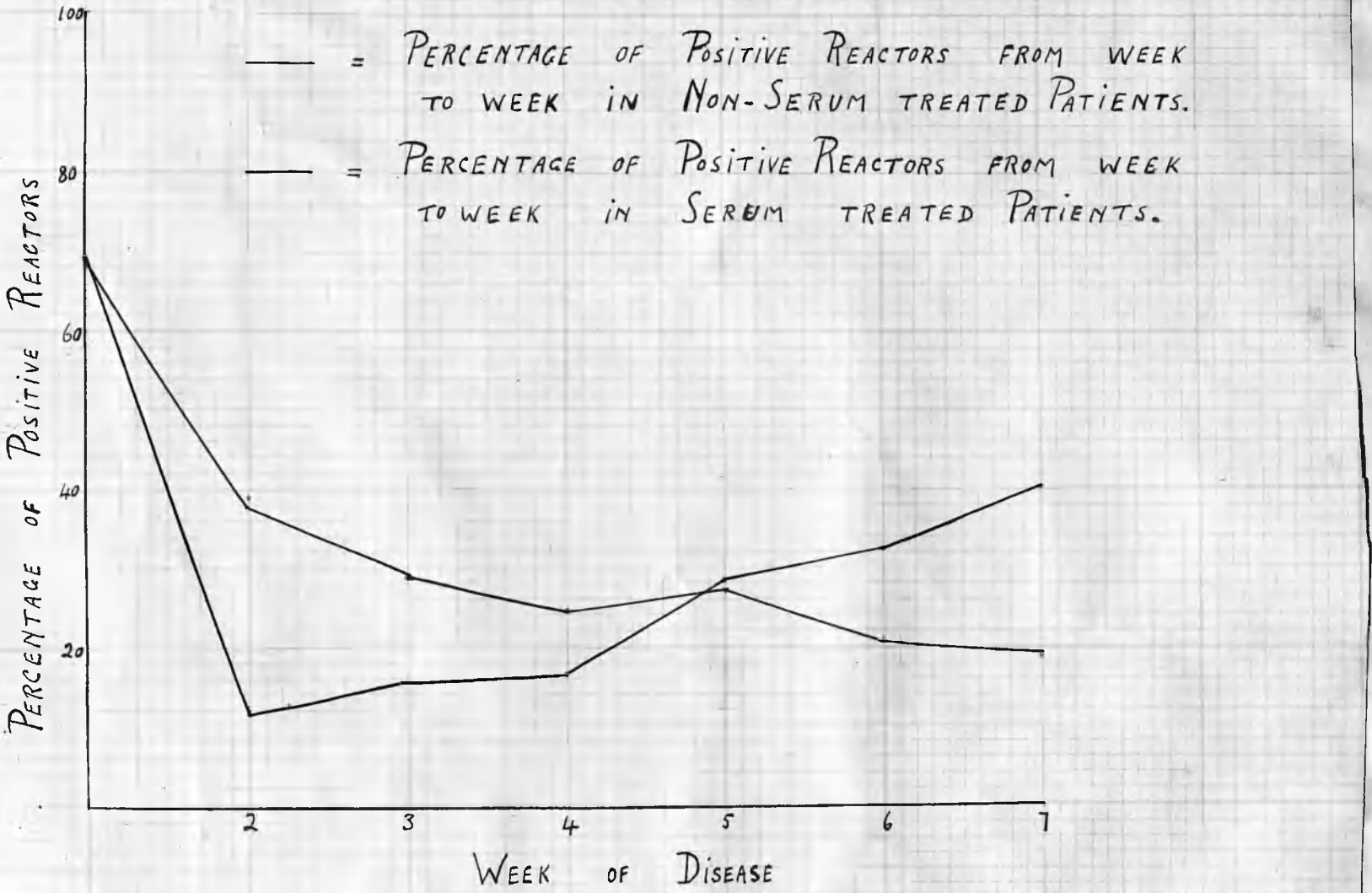
## Degree of Desquamation.

| | A. | B. | C. | D. | Totals. |
|---|---|---|---|---|---|
| Well-marked | 55 | 3 | 24 | 47 | 129 |
| Not marked. | 7 | 1 | 5 | 10 | 23 |
| Totals. | 62 | 4 | 29 | 57 | 152 |

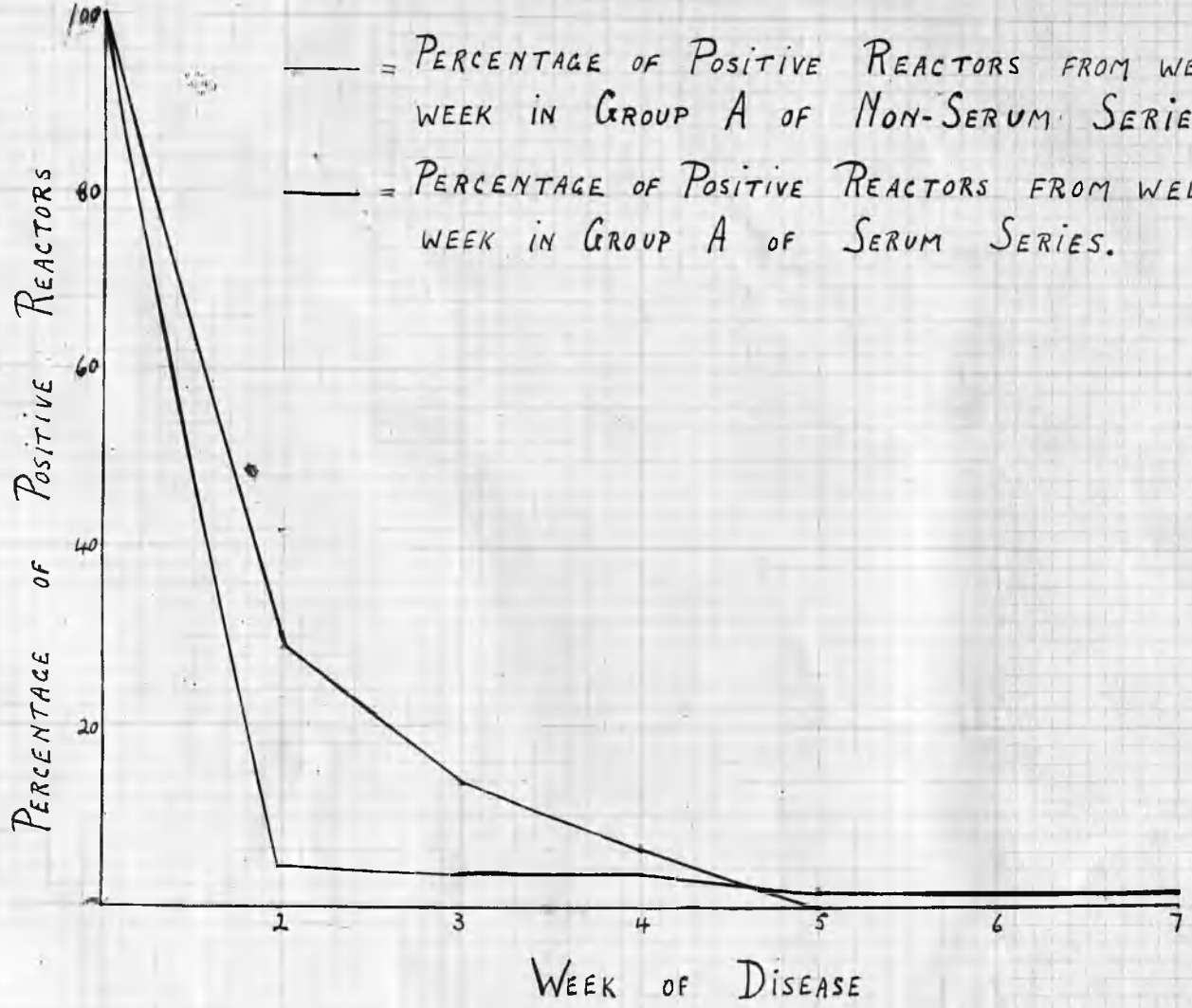
## Amount of Anti-Scarlatinal Serum Administered.

| | A. | B. | C. | D. | Totals. |
|---|---|---|---|---|---|
| 10. ccs. unconcen-trated. | 60 | 4 | 22 | 50 | 136 |
| 10-25 ccs. unconcen-trated. | 1 | - | 4 | 5 | 10 |
| Over 25ccs. unconcen-trated. | 1 | - | 3 | 2 | 6 |
| Totals. | 62 | 4 | 29 | 57 | 152 |

Graph. 1.


—— = Percentage of Positive Reactors from week to week in Non-Serum treated Patients.
—— = Percentage of Positive Reactors from week to week in Serum treated Patients.
Percentage of Positive Reactors
100
80
60
40
20
2
3
4
5
6
7
Week of Disease

Graph 2.




——— = PERCENTAGE OF POSITIVE REACTORS FROM WEEK TO WEEK IN GROUP A OF NON-SERUM SERIES.

——— = PERCENTAGE OF POSITIVE REACTORS FROM WEEK TO WEEK IN GROUP A OF SERUM SERIES.