

CONTROL OF SCARLET FEVER BY ACTIVE IMMUNISATION.

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THIS paper deals with the result obtained after testing, by the "Dick" method, the susceptibility of a series of adults to scarlet fever toxin. The toxin used was produced by the Wellcome Physiological Research Laboratory. While various strengths of solutions were tried to begin with from 1:2500 to 1:250, no advantage was found to result from the use of a solution stronger or weaker than 1:1000. The tests were, therefore, carried out with the standard "Dick" toxin as supplied by this firm.

Until the beginning of 1928 the regulations of the Glasgow Royal Infirmary laid it down that, in the event of the occurrence of a case of scarlet fever, the ward in which the case occurred was closed for the admission or discharge of patients for the recognised period. After June, 1928, a different procedure obtained. On the removal of a case of scarlatina to the Infectious Diseases Hospital, all the occupants of the ward in which the case occurred were tested with "Dick" toxin. Nurses and ward-maids as well as patients were tested and those who were "Dick" positive were given serum. After June also, it was decided to "Dick" test all the nurses starting as probationers before they began their ward work. Those who were "Dick" positive were offered immunisation by scarlet fever toxin, graduated doses up to 20,000 s.t.d.¹ being considered necessary for this. The initial dose was 500 s.t.d. and this dose was doubled weekly till 20,000 s.t.d. was reached. In several cases there was a local reaction with stiffness, redness and slight heat, but seldom was the general reaction more than mild, with a temperature of over 99° F. and headache for a few hours. In two cases, vomiting occurred but never did a rash appear or desquamation. The injections of toxin were all given intramuscularly into the deltoid in the morning, the nurses carrying on with their work. Any nurses who were unfit were required to report the morning after injection, but this happened so infrequently that it was exceptional.

Since the Royal Infirmary is a general hospital, cases of scarlet fever are occasionally admitted during the incubation period, while sometimes patients acquire scarlatina from visitors to the Hospital. As the number of cases in the Hospital was small no effort was made to keep records of those "Dicked" in the wards, but complete records have been kept of all the nurses who were tested. Although the total numbers are small records of the general health of the cases during the last 3½ years show one or two points worth bringing out.

"Dick" positives among the pupil nurses were treated along with "Dick"

¹ s.t.d. denotes skin test doses throughout.

positives among any who had been in contact with cases in the wards. Two or three months later the pupil nurses were all retested and positives were again retested in 6 months time. The nurses came mostly from Glasgow or the West Highlands, and this analysis was undertaken to ascertain whether those who were town-bred presented any different features from those reared in the country. The ages varied from 19 to 21. Few of them had had previous fever training.

Toyoda, Moriwaki and Futagi (1930) state that the weaker the reaction of an individual to scarlet toxin the more simple the type of disease he is likely to develop; among their "Dick" negatives there were no deaths and no complications; 0.4 per cent. of their "Dick" negative children took scarlet fever; while among the strongly positive 7.6 per cent. took scarlet fever. Toyoda and Futagi (1930) state that of 305 contacts 14 per cent. of the "Dick" negatives took scarlet fever, while 86 per cent. of the "Dick" positives developed the disease. Toyoda, Moriwaki, Futagi and Okamoto (1930), in yet another paper, report that of 200 contacts 43 were "Dick" positive. Of these, 23 per cent. took scarlet fever, but of the 157 who were "Dick" negative none contracted scarlatina.

The Dicks (1929) state that they have not seen a case of scarlet fever among 20,856 "Dick" negatives nor among 11,584 "Dick" positives who were immunised. They immunised 1191 students and staff of a fever hospital and no case occurred.

Benson (1925) reduced the scarlet fever incidence among the Staff in the Edinburgh Fever Hospital from 8.59 to 0.67 per cent. by active immunisation. In the London Fever Hospital no case has occurred among the "Dick" negatives or among those who were immunised.

This paper deals with the period 1928-31, during which time 393 nurses were "Dick" tested and their after history investigated. 23 per cent. were found to give a positive reaction and, among those who gave no reaction, no cases of scarlet fever occurred. 50 per cent. of the negative reactors were retested in 3-6 months and in no case did a negative ever become positive.

From 1920 to 1927 there was an annual average of 3.2 cases of scarlet fever from the nursing staff of 400. In the four years 1928-31 we had eight cases altogether; three of these had not been "Dicked," while the remaining five were "Dick" positive. The details are as follows:

1928. *One case*, A.G., a senior nurse, who had not previously been "Dick" tested.

1929. *Two cases*, M.N. and C.C., one had not been "Dick" tested. The other was "Dick" positive and had had a course of 10,000 s.t.d., but had not been "re-Dicked." She had a typical average attack of simple scarlet fever; she recovered rapidly and had no complications.

1930. *Four cases.* (1) M.G. gave an ambiguous reaction, on being tested on admission only a faint blush of 1 cm. diameter occurred. She was re-tested

after two months, gave the same reaction and developed scarlet fever three weeks later. She had a moderately severe attack and received 20 c.c. of serum.

(2) T.G. was positive, was given toxin up to 10,000 s.t.d. and when "re-Dicked" gave a doubtful reaction. Two months later she developed an average attack of simple scarlet fever without complications.

(3) M.M., who had been in the Hospital for a couple of years, had not been "Dicked."

(4) H.L. was a charge Sister. The first time she was tested on 6. iii. 28 the reaction was strongly positive. Serum was administered since she was a contact. Unfortunately a degree of anaphylaxis of the delayed type developed and she refused to be actively immunised by toxin. On 10. x. 29 scarlet fever again broke out in her ward and again she gave a positive reaction. This time, in view of the previous experience, no serum was given. In December, 1930, she developed scarlet fever though the source of infection could not be discovered. She had a severe attack of simple scarlet fever with marked pyrexia. 20 c.c. of serum were administered and there were no complications.

1931. *One case*, E.B. This nurse came to Hospital on 10. iv. 29 and was "Dick" positive. After receiving 10,000 s.t.d. she left before being "re-Dicked." When she returned 6 months later she was overlooked as she was no longer a pupil nurse. She had a severe attack with slight adenitis and arthritis and was given serum.

It is gratifying to notice (*a*) that no "Dick" negative reactor has developed scarlet fever—this supports the accepted finding—and (*b*) that no case among those who were treated efficiently developed scarlatina, *i.e.* among those who received up to 20,000 s.t.d. and became "Dick" negative.

I have found a case can be made "Dick" negative, but that subsequently it may become positive. This occurred in 5 per cent. of our cases, but in none of these did scarlet fever subsequently develop. We had, however, three cases of scarlet fever among those who were treated with toxin (two of them remained "Dick" positive; while the third developed scarlet fever before she was "re-Dicked").

Toyoda, Moriwaki and Futagi have separated the toxin of scarlet fever streptococcus into an "endotoxin" (heat-stabile, characteristic of the whole streptococcal group) and an "exotoxin" (heat-labile, the true "Dick" toxin). The latter is the toxin which is used to increase the immunity against scarlet fever for it is peculiar to the group of haemolytic streptococci of scarlet fever, erysipelas and puerperal sepsis, particularly the first. Toyoda and his colleagues have found that the number of "Dick" positives remaining positive even after efficient treatment is 10–15 per cent. (our figure is 12·5 per cent.). They divide this group up into six sub-groups:

- (1) Positive to exotoxin and "Dick" toxin and negative to endotoxin.
- (2) Positive to all three.

- (3) Positive to endotoxin and "Dick" toxin and negative to exotoxin.
- (4) Positive to endotoxin and negative to others.
- (5) Negative to all.
- (6) Positive to "Dick" toxin only.

They state that the 32.7 per cent. of people who have had scarlet fever are positive to endotoxin and only 3 per cent. to exotoxin. They also state that the efficiently treated who are still "Dick" positive are Schultz-Charlton negative (therefore immune to scarlet fever) and if re-tested with pure exotoxin would be negative. Unfortunately, I had no facilities for trying the Schultz-Charlton reaction, but note that three of our cases were treated with doses up to 10,000 s.t.d., and yet developed scarlet fever, though mildly. This may be due to giving only 10,000 s.t.d. Latterly, we gave 20,000 s.t.d. and, so far, no case has developed, but this may be due to chance.

Table I.

		Total number of nurses "Dicked" from 1928 to 1931 393						
		"Dick" negative 298						
		"Dick" positive 95						
Previous history of scarlet fever was obtained in 114 cases of which three still gave a positive "Dick" reaction.								
		Total	Scarlet fever positive	Scarlet fever negative	"Dick" reaction		"Dick" negative Scarlet	
					Negative	Positive	Positive	Negative
Town-bred		197	67	129	149	48	67 (44 %)	85
Country-bred		196	47	149	149	47	47 (32 %)	102
					Scarlet positive		History of sore throats	
"Dick" negative		298			37 %		27 %	
"Dick" positive		95			3 %		15 %	
Scarlet positive. Sore throat positive								46
" " " negative								68
" " negative. " " "								228
" " " positive								51
i.e. 40 % of scarlet fever cases suffered from sore throats compared with only 18 % of non-scarlet.								
"Dick" positive. Scarlet negative. Sore throats positive								14
" " " negative								78
" " negative. " " positive								37
" " " negative								150
i.e. 15 % of "Dick" positives have had sore throats compared with 20 % of "Dick" negative.								

In Table I the results of the investigation are analysed. Note (a) 2.6 per cent. of the number who had a history of scarlet fever still gave a positive "Dick" reaction, and (b) the incidence of scarlatina is greater in the town than in the country though the percentage of "Dick" positive reactors from both the town and country is the same.

Table II gives the figures of the "Dick" positive cases which were investigated. Note that (a) 20 per cent. of the untreated cases, and (b) a similar percentage of the treated cases which did not become "Dick" negative developed scarlet fever.

One point has come out in the investigation over which there has been

controversy. There has not been any increase in sore throats of streptococcal nature among those immunised.

From the figures in Table I, one would conclude that those brought up in the town and exposed to greater risks of scarlet fever infection should show a higher percentage of "Dick" negatives than the country-bred. This does not obtain, for equal numbers from both groups were found to be "Dick" negative. Again, 40 per cent. of those who had had scarlatina gave histories of sore throats while only 18 per cent. of non-scarlet cases suffered from such a condition. 15 per cent. of "Dick" positive and 20 per cent. "Dick" negative reactors had sore throats. There is therefore, slight support for the belief that recurring sore throats tend to an increase in immunity towards haemolytic streptococci. In taking the histories of the cases, great difficulty was ex-

Table II. *Result of treatment of 95 positive less 16 who left before they were "re-Dicked" after treatment.*

		Subsequently developing scarlet
"Dick" positive becoming negative	55 (69 %)	Nil
" remaining so	10 (12.5 %)	2 (20 %)
" becoming negative and later positive again	4 (5 %)	Nil
" untreated for various reasons	5 (6 %)	1 (20 %)
Doubtfully negative and untreated	5 (6 %)	1 (20 %)
Total	79	

Table III.

	Haemolytic Streptococci Positive (%)
(1) "Dick" positive, 56	29
(2) " " negative, 144	23

perienced in defining what was meant by sore throats; diphtheria and simple hypertrophied tonsils were excluded.

I felt that this factor should be investigated a little further. Work was therefore started on the bacterial flora of a series of tonsils which were removed at the Cumberland Infirmary, Ear, Nose and Throat Department. I managed to "Dick" test 200 children and subsequently to obtain their freshly removed tonsils. For examination, the tonsils were washed in several changes of sterile saline, split open with a sterile razor and the deep tonsillar substance cultured on blood agar plates.

Table IV shows the result of the bacteriological investigation. There was a high incidence of staphylococcal and catarrhalis infections, 55 per cent. of the tonsils harboured streptococci, the percentage of those being infected with the haemolytic variety being 26. In only three cases did haemolytic and non-haemolytic strains occur together. Haemolytic streptococcal colonies were examined microscopically and evidence of true haemolysis tested by 5 per cent. suspension of human blood corpuscles. Among the same children (age 4-14 years), 28 per cent. were "Dick" positive.

From the figures in Table III, it would appear that haemolytic strepto-

cocci in the throat, even when not of the scarlet fever group, produce sufficient local reaction and general immunity to give a "Dick" negative reaction. This assumes, of course, that only 30 per cent. of the children have had scarlet fever, for the area drained by the Cumberland Infirmary is largely rural and therefore the percentage of scarlet fever should not be higher than this, at this age—see Table I.

Apart from the actual occurrence of scarlet fever it would appear that it is the repeated slight infections of the throat by haemolytic streptococci which reduce the incidence of "Dick" positive reactors from 90–100 per cent. in infants up to 12 months old, to 30 per cent. among children of 8 years old.

It would almost seem a justifiable procedure to advocate the inoculation of a fixed quantity of scarlet fever stock toxin into all children at an early age and so reduce the liability to scarlet fever and other streptococcal infections of the throat.

One or two other points of passing interest emerge. While a "Dick" positive reactor may become "Dick" negative and subsequently "Dick" positive, he does not become infected with scarlet fever. This seems to support the view that the toxin has two independent fractions, a heat-labile and a heat-stabile, and that the second "Dick" positive reaction is due to endotoxin. This, however, does not account for the 12 per cent. of cases which did not become "Dick" negative, two of which subsequently developed scarlet fever. At the same time, it is noticeable that serum offers complete, though transient, protection, for we had no case of scarlet fever among all the contacts, nurses or patients who were given serum. Moreover, when those who have been treated with toxin develop scarlet fever the severity of the illness is mitigated.

Table IV. *Analysis of bacterial flora of 259 tonsils.*

	Positive	%	Negative	%
Pus	39	15	220	85
Haemolytic Streptococci	70	27	189	73
Non-haemolytic Streptococci	73	28	186	72
Pneumococci	41	16	218	84
Staphylococci	175	68	84	32
Neisseria catarrhalis	193	75	66	25
Diphtheroids	29	11	230	89

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