ACTIVE IMMUNISATION AGAINST THE STREPTOCOCCUS SCARLATINÆ.

By R. T. JACKSON.

ACTIVE immunisation against scarlatina is now a frequent procedure, and in this report are set out the results obtained in a boarding school in Dublin during the period from September, 1931, to June, 1936. During this period active immunisation was carried out against both scarlatina and diphtheria.

Method.—In September, 1931, all the resident pupils were Dick-tested, and all positive reactors were immunised; in the following September they were re-tested. In subsequent years all new boys were Dick-tested on their entry in September, and all positive reactors were immunised and re-tested twelve months later. All boys found to be still Dick-positive twelve months after their immunisation were given another course and subsequently re-tested after a further twelve months.

In all, 221 boys were Dick-tested, with the results shown in Table I.

Total Dick-tested	No Positive	%	No. Negative	%
221	83	37·5	138	62·5

When the boys are divided into groups according to their duration in the school the following figures emerge:

Boys 1-5 years resident	Dick-positive	Dick-negative
75	25, i.e. 33·3%	50, i.e. 66·6%

New Boys	Dick-positive	Dick-negative
146	58, i.e. 39·7%	88, i.e. 60·3%

From this it appears that the herd immunity of the community was slight, as the percentage of new boys positive only differs by 6.4 from the percentage of positives in the group one to five years resident. Dudley found a high herd immunity in the boys of the Greenwich Hospital School against diphtheria. This was not found in these boys, who were of almost the same ages as Dudley's group.

To immunise the boys they were given six injections of toxin at weekly intervals, the doses being 500, 1,250, 2,500, 5,000, 10,000 and 25,000 skin test doses, or 44,250 skin test doses in all.

Considerable deliberation on the question of the dosage took place before this schedule was adopted. In the year 1931 considerable variation existed as to the size and frequency of the doses recommended. Thus Nabarro and Signy recommended 39,500 skin test doses in all as adequate. Bousfield gave 16,875 as a sufficient total dosage.

Benson (Edinburgh) advised a total dosage of 26,500 skin test doses.

Dick and Dick suggested that a maximum dosage of 18,000 skin test doses given in five weekly doses was satisfactory.

Hence it was thought that 44,250 skin test doses should be adequate, and this dosage was adopted. Subsequently much larger doses have been used and the Dicks now recommend that the last two doses should consist of 25,000 and 50,000 skin test doses of toxin.

Reactions.—Of the boys under 14 years of age only one developed a reaction. This was a boy, aged 12 years, who after receiving 5,000 skin test doses as his second dose developed what O'Brien describes as miniature scarlet fever. (The boy received this as his second dose because he had absented himself on the occasions when he should have received the two intervening doses). Forty-eight hours after the injection he developed a sore throat with bright red injection of the fauces and uvula, erythematous rash, and pyrexia of 100°F. In 3 or 4 days he was well. Dick-tested twelve months later he was strongly positive. He then received the full ordinary course of injections and became Dick-negative.

It is interesting to note that Nabarro and Signy state that these individuals need no more immunisation as they have developed a very high degree of immunity from the miniature scarlet fever. O'Brien is more cautious; he states that "there are no accurate figures to show what percentage of these patients rapidly become Dick-negative, as after scarlet fever. My impression is that the percentage is high."

Of the boys over 14 years of age, 25 in number, 8 developed reactions after one or more of the doses; none were severe, and no boy was prevented from following the usual routine of school life.

The following are the figures for the group immunised and subsequently re-tested twelve months later.

Total	Rendered negative	Remained positive
74	63, or 85%	11, or 15%

In addition 9 boys were immunised in September, 1935, and will not be re-tested till September, 1936.

All went well in the school till the terms January to June, 1936: during this period an epidemic of scarlet fever of exceptional severity was prevalent in the City of Dublin.

Before considering the events of this period it is well to consider the composition of the school in January, 1936. It was as follows:

Boys tested and found Dick-negative (received no immunisation)	77
Boys found to be Dick-positive, given 44,250 skin test doses, converted to Dick-negative	31
Boys found to be Dick-positive, given two courses, i.e. 88,500 skin test doses converted to negative	4
Boys Dick-positive in September, 1935, given 44,250 skin test doses, not yet re-tested	9
TOTAL	121

Between January and June, 1936, 24 boys developed illnesses believed to be due to infection by the hæmolytic streptococcus of scarlatina.

These cases can be grouped as follows:

I.	Sore throat without rash or complications	10 cases.
II.	Otitis media	2 cases.
III.	Arthritis	1 case.
IV.	Cervical adenitis	4 cases.
V.	Streptococcic septicæmia	1 case.
VI.	Sore throat with rash	5 cases.
VII.	Erythema nodosum	1 case.
	TOTAL	24 cases.

At this stage it is best to give the clinical details of these 24 cases and then to consider the evidence that they were of scarlatinal origin.

Group I.—Sore throat without rash or complication.

(1) D.A. 20/10/'32. Dick test positive.
Received 44,250 skin test doses.
September, 1933. Dick test positive.
Received another 44,250 skin test doses.
September, 1934. Dick test negative.
15/2/'36. Complaining of headache, vomiting, sore throat and pains in legs.
T. 102·4° F. P. 96. R. 22.
Throat showed bright red injection of fauces and palate.
No membrane or exudate.
Throat and other symptoms cleared up in four days.

(2) T.H.W. 20/9/'34. Dick test positive.
Received 44,250 skin test doses.
September, 1935. Dick test negative.
7/3/'36. Complaining of headache, vomiting and sore throat.
T. 101° F. P. 100. R. 20.
Throat showed bright injection of fauces and uvula.
No membrane or exudate.
Throat cleared up in three days.

(3) H.R. 3/11/'31. Dick test negative.
25/3/'36. Complaining of sore throat and headache.
T.P.R. Normal.
Throat showed bright red injection of fauces.
This cleared up in two days.

(4) J.F.H. 24/9/'35. Dick test positive.
Received 44,250 skin test doses.
25/2/'36. Complaining of headache, vomiting, pain in back and sore throat.
T. 102° F. P. 98. R. 22.
Throat showed red injection of fauces and uvula.
This cleared up in six days. No complications.

(5) S.J.T. 20/9/'34. Dick test negative.
25/3/'36. Complaining of headache, sore throat.
T. 100° F. P. 90. R. 22.
Throat showed bright red injection of fauces.
Well in two days.
Contacts in home developed typical scarlatina.

(6) T.P.S.W. September, 1933. Dick test negative.
26/3/'36. Complaining of sore throat, headache and malaise.
T. 99·4° F. P. 100. R. 22.
Throat: bright red injection of fauces.
Well in four days.

(7) D.M. 3/11/'31. Dick test positive.
Received 44,250 skin test doses.
September, 1932. Dick test negative.
28/4/'36. Complaining of sore throat, headache and vomiting.
T. 101·6° F. P. 100. R. 22.
Throat showed red injection of fauces and palate.
This cleared up in six days.
Contacts in home developed typical scarlatina.

(8) J.A.W. 20/10/'32. Dick test negative.
20/5/'36. Complaining of headache, vomiting and sore throat.
T. 101·4° F. P. 100. R. 22.
Bright red flush on fauces and palate.
This cleared up in six days.

(9) G.B.J. 28/9/'35. Dick test negative.
26/3/'36. Complaining of headache, vomiting and sore throat.
T. 100·6° F.
Throat showed red flush of fauces and palate.
This cleared up in seven days.

(10) J.H. 24/9/'35. Dick test negative.
17/2/'36. Complaining of headache and sore throat.
T. 102·6° F. P. 104. R. 24.
Throat: bright red flush of fauces.
Convalescent in five days.

Group II.—Otitis Media.

(1) G.B. 20/9/'34. Dick test negative.
13/3/'36. Complaining of pain in right ear.
T. 101·4° F. P. 90. R. 22.
Purulent otorrhœa 48 hours later.
Pus on culture grew streptococcus hæmolyticus in pure culture.

(2) B.H. 20/9/'34. Dick test negative.
6/3/'36. Complaining of pain in both ears.
T. 100·6° F. P. 100.
7/3/'36. Right ear discharging.
Pus on culture grew streptococcus hæmolyticus in pure culture.

Group III.—Arthritis.

(1) R.K.H. September, 1934. Dick test positive.
Received 44,250 skin test doses.
September, 1935. Dick test negative.
20/3/'36. Complaining of pain and swelling in right knee.
T. 101° F. P. 116. R. 22.
Knee swollen with increased fluid.
24/3/'36. Complaining of pain in left ankle and swelling.
Right knee not so painful or swollen.
Treated with salicylates with satisfactory results.

Group IV.—Cervical Adenitis.

(1) R.G. September, 1931. Dick test positive.
Received 44,250 skin test doses.
September, 1932. Dick test negative.
31/3/'36. Complaining of headache, malaise and pyrexia.
T. 101° F.
3/4/'36. Swelling of glands in upper portion of anterior triangle of neck on left side.
4/4/'36. Swelling fluctuating.
6/4/'36. Incised. Pus found. Discharged 26/4/'36.
Culture showed hæmolytic streptococci.

(2) C.H. September, 1931. Dick test negative.
10/2/'36. Complaining of cold in head, sore throat.
T. 99–101° F. for two days.
12/2/'36. Adenitis right side of neck.
13/2/'36. Incision and drainage.
Pus grew hæmolytic streptococci.
Discharged 27/2/'36.

(3) J.S. September, 1933. Dick test negative.
23/3/'36. Complaining of headache, nausea, enlarged glands in neck.
Throat bright red flush. No rash.
Pyrexia. 99° F.–102° F. for seven days.
Glands did not suppurate, but gradually subsided.

(4) J.A.K.N. September, 1934. Dick test positive.
Received 44,250 skin test doses.
September, 1935. Dick test negative.
11/3/'36. Complaining of chilliness, pain in head and legs.
T. 101° F. P. 100. R. 22.
16/3/'36. Complaining of swelling in left side of neck.
T. 101° F.–103° F.
25/3/'36. Gland incised, local anæsthesia.
Pus cultured: hæmolytic streptococci.

Group V.—Streptococcic Septicaemia.

(1) W.N.C.B. September, 1933. Dick test negative.
21/3/'36. Complaining of tiredness, chilliness and pain in back.
T. 102° F. P. 116. R. 22. No localising signs.
23/3/'36. Small area of dullness at apex of left axilla with normal breath sounds.
T. 104° F. P. 103. R. 36.
24/3/'36. Dull area greatly increased, loss of breath sounds; paracentesis; pus found.
Rib resection and drainage.
All went well till 11/4/'36 when temperature rose to 101° F.
Swelling and tenderness of left buttock.
Incision and drainage of pus.
Convalescence henceforth uneventful.
Pus from empyema: pure culture of hæmolytic streptococci.
Pus from buttock: pure culture of hæmolytic streptococci.

Group V I.—Sore Throat with Rash.

(1) F.E. September, 1934. Dick test positive.
Received 44,250 skin test doses.
September, 1935. Dick test negative.
20/2/'36. Complaining of slight sore throat.
T. 99·8° F. P. 100. R. 24.
Throat: some redness with exudation on tonsils.
No erythema of uvula.
21/2/'36. Patches of bright erythema on front of chest and abdomen. Disappeared in 48 hours.

(2) C.O'D. September, 1934. Dick test positive.
Received 44,250 skin test doses.
September, 1925. Dick test negative.
19/2/'36. Complaining of sore throat, headache and pyrexia.
T. 100·2° F. P. 96.
Temperature came down to normal on 5th day.
Rash: small areas of erythema on trunk and limbs. Rash disappeared in 48 hours.

(3) F.C. September, 1931. Dick test negative.
30/4/'36. Typical scarlatina with rash, etc.
Admitted to Cork Street Fever Hospital.

(4) S.S. September, 1933. Dick test positive.
Received 44,250 skin test doses.
September, 1934. Dick test negative.
7/4/'36. Complaining of mild sore throat. T.P.R. normal.
Slight erythema on upper limbs and chest for 24 hours.
No complications.
Contacts in his home developed typical scarlatina.

(5) J.T. 20/10/'32. Dick test negative.
14/4/'36. Developed typical scarlatina with sore throat, pyrexia and rash.

Group V I I.—Erythema Nodosum.

(1) B.McD. 20/9/'34. Dick test negative.
23/3/'36. Complaining of painful red spots on legs.
T. 100·2° F. P. 90. R. 22.
Typical erythema nodosum.
No rash or sore throat. No complications.
No evidence of active tuberculous focus.
Spots disappeared in about two weeks.

In addition to these cases the Matron and one of the Assistant Masters developed typical severe scarlatina in February, 1936.

Now to consider why it was concluded that these cases were due to scarlatina infection. This is best considered from three points of view:

(1) The fact that the matron, one assistant master and two of the boys developed typical clinical scarlatina may be taken as evidence that scarlatinal infection was present in the school during the period under review.

(2) Two of the cases with sore throat but no rash were allowed home for the Easter holidays, and within five days of their arrival home contacts had developed typical scarlatina.

(3) The cultural evidence: all the cases that developed purulent discharges grew hæmolytic streptococci on culture.

For these reasons it may be reasonably assumed that the cases were due to infection with the streptococcus hæmolyticus of scarlatina.

Now to summarise the facts: In the period January to May, 1936, the school consisted of 121 boys, of whom 112 were known to have been Dick-negative at some previous date and of 9 boys who had received 44,250 skin test doses of toxin in the previous September. In this community there occurred 24 cases of infection with the streptococcus of scarlatina.

Discussion.

In an attempt to explain this disappointing result many factors must be considered: the question of adequate dosage, the division of the signs and symptoms of scarlatina into two groups (toxic and invasive), and the question of the specificity of the streptococcus of scarlatina.

Firstly, as regards dosage, it must be noted that the doses given did convert the Dick-positive reactors into negative reactors, though a few had to have two courses of injections; also 9 boys out of 74 developed reactions with the doses used, and presumably a larger number would have occurred if the doses had been larger. This in itself would be a great disadvantage to immunisation.

Secondly, to discuss the question of the different types of symp-

toms and complications in scarlatina: many observers consider that there are two distinct groups of symptoms; one due to the toxins (exotoxin mainly), the other due to the actual invasion of the tissues by the streptococcus. In the former group would be placed the rash, the erythematous flush on fauces and uvula, the general toxæmia and perhaps the nephritis. The latter group would include the adenitis, arthritis, otitis media and the septicæmic signs and symptoms.

If this be true it would appear that the immunisation affords some protection against the toxic symptoms and complications, but little if any against the invasive manifestations. This is surely a very unsatisfactory state of affairs, for the first sign of anything amiss in a protected community may be the development of cases of severe invasive complications: whereas had the community not been protected these cases would have developed ordinary scarlatina, and the incidence of complications would have been greatly reduced by rest in bed and other forms of treatment.

Thirdly, the question of the specificity of the streptococcus of scarlatina is an interesting and at the same time a difficult one. Most clinicians agree that they see cases of typical scarlatinal throats that do not develop rashes, yet seem to give rise to ordinary scarlatina in contacts. On the other hand Okell states " that the erythrogenic toxins of streptococci from the most diverse sources in human disease are immunologically identical ".

This is at variance with the opinions of Coffy and Wadsworth, who state that the exotoxins from different strains of S. pyogenes differ not only quantitatively but also qualitatively.

Considering the facts recorded in this report, it would appear to be the case that the boys were protected against a strain of streptococcus but not against the particular strain of organism that was responsible for the severe epidemic in Dublin in 1936.

Finally, was the immunisation worth while? It should be noted that in a severe epidemic many of the fatal cases are due to severe toxæmia at the onset, and it is a matter for speculation as to what number of severe toxæmic cases would have occurred had the community not been protected against the symptoms due to the exotoxin.

It should be clearly realised by anyone undertaking the immunisation of a community that little if any protection against the invasive symptoms and complications will be obtained.

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