SCHICK RELAPSE AFTER DIPHTHERIA

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Second attacks of most infectious diseases are somewhat rare. A history of a previous infection in a child suffering from a typical attack of measles raises grave doubt as to the correctness of the earlier diagnosis. Similarly, infection with chicken-pox, rubella, variola, mumps, and the organisms of the enteric group confers an immunity which, if not lifelong, is of many years' duration. Even vaccinia confers sufficient immunity to exert some protective effect for a period as long as the average expectation of life at birth (Hanna, 1913).

The position with regard to scarlet fever and diphtheria is not nearly so clear-cut. Second attacks of both diseases undoubtedly occur. Rolleston (1929) found that of 3,000 cases of diphtheria forty (1.3 per cent.) had relapses and sixty-seven (2.2 per cent.) gave a history of a previous attack. Fortunately we have in the Dick and Schick tests yard-sticks which may be used as a measure of the relative immunity conferred by the primary infection. While we cannot say that a Dick-negative person is unable to contract scarlet fever or that a Schick-negative person is unable to contract diphtheria, we know that they are much less liable to do so than a corresponding Dick-positive or Schick-positive person. We know, too, that even if they are so unfortunate as to contract either disease their chances of rapid uncomplicated recovery are very much greater than those of the Dick-positive or Schick-positive person.

The object of this investigation was to form some idea of the frequency with which cases reverted to Schick-positiveness six or more weeks after an attack of diphtheria. All the patients received serum, and so they must at some time during their illness have been Schick-negative either actively, as a result of their own antitoxin, or passively, as the result of the antitoxin administered. Schick (1911) himself noted the rapid disappearance of antitoxin after an attack in some cases. Dudley (1923) reported that of fifty cases of clinical diphtheria occurring at the Royal Naval School, Greenwich, eight were still Schick-positive or gave a positive combined reaction three to six months after an attack. He did not encounter a second case in any boy who had had a previous attack, in spite of prolonged exposure to infection under ideal circumstances for its spread. He deduced, therefore, that "one attack of diphtheria confers immunity in the vast majority of instances, even if the Schick reaction remains positive."

However true this statement may be, the practitioner in charge of a Schick-positive case of clinical diphtheria cannot excuse a delay in giving serum even though he may be sure that the patient has had a previous attack. His duty is too plain to be avoided. The theories of sub-immunity developed by Glenny (1925), however accurate they may be in the mass, cannot be relied upon in any individual case, for clearly if a patient's circulating antitoxin is less than the amount required to render him Schick-negative we have no ready method of finding out whether he is only just susceptible or entirely unprotected. Delay may do no harm or may be dangerous, none can say which. Treatment on these lines becomes a gamble.

The Investigation

Eighty-seven entirely unselected cases of diphtheria were Schick-tested six or more weeks after a definite clinical attack. The diagnosis was confirmed bacteriologically in every case. Nine gave a positive reaction. They were retested with the same result. Seventy-one were females, of whom seven were positive, and sixteen were males, of whom two were positive. The age distribution was as follows:

	0-2 years	2-5 years	5-10 years	10 years or over
Number of cases ..	1	17	48	21
Positive reactors ..	—	1	6	2

It was thought that perhaps the day of disease on admission, which was also the day on which serum was given, might be in some way connected with the Schick relapse. The cases were grouped:

	Day of admission		
	1st and 2nd	3rd to 5th	6th day and over
Number admitted	20	47	20
Number positive	3	4	2

They were also grouped according to the localization of the disease:

	Faucial	Nasal	Combined Faucial and Nasal
Number of cases	51	10	26
Positive reactors	7	—	2

and again according to the dosage of serum employed:

	Dose in thousands of units		
	2-8	12-32	32-216
Number of cases	50	22	15
Positive reactors	5	3	1

The Schick test was performed between the sixth and twelfth weeks in seventy-one cases, seven of these being positive, and between the twelfth and twenty-fourth weeks in sixteen cases, with two positive results. Paralysis occurred in thirty-one cases. Only one of these was later found to be Schick-positive. No paralysis occurred in the other fifty-six cases, and eight of these were later Schick-positive.

The Schick-Positive Carrier

One Schick-positive patient had had a previous attack twelve months before. Three had virulent diphtheria bacilli in their throats at the time they were Schick-tested, yet none had any clinical evidence of the disease. One of the three, who had been a chronic carrier for nearly three months, developed a second attack in the twenty-fourth week. She received 2,000 units of antitoxin.

The criteria adopted for the diagnosis of a second attack were the presence of a clinically diphtheritic lesion in the nose or throat, a Schick-positive reaction in the patient, and the bacteriological finding of virulent diphtheria bacilli in the swabs taken from the lesion. The fact that other organisms were found in the cultures was not held to affect the diagnosis, for more often than not it is the rule to find in association with the causative bacillus other

bacteria, notably streptococci and less frequently Vincent's organisms, in any series of diphtheria patients. Pure cultures of diphtheria bacilli are obtained from carriers rather than from cases. Indeed, the associated organisms or secondary invaders may so overwhelm the cultures obtained from the most severe of infections that a second or third swab has to be taken to establish a bacteriological diagnosis the clinical counterpart of which has never for a moment been in doubt.

These three cases raise again the question of the Schick-positive carrier. Dudley (1923) says that so far as his experience goes the Schick-positive carrier is unknown. How, then, is a susceptible individual to obtain natural immunity except by an attack of the disease? That some do obtain it by another way is obvious, for how otherwise could 70 to 80 per cent. of adults have become insusceptible? Not all nor even the majority of them have had a clinical attack of diphtheria. Surely at one time in their history they must have been at least temporary carriers of small numbers of virulent diphtheria bacilli.

Immunization of the Schick-positive cases was carried out in six instances. Two doses of alum toxoid were used on four occasions and three doses of toxoid-antitoxin mixture on the other two occasions with complete success. It is strange to reflect that active immunity may be more readily produced by artificial than by natural means.

Summary and Conclusions

The results of Schick-testing a series of patients six or more weeks after an attack of diphtheria are reported. These results have suggested the following conclusions:

1. That after an attack of diphtheria, irrespective of its severity, about 10 per cent. of persons remain potentially susceptible.
2. That the chance of remaining susceptible is not diminished by delayed administration of serum.
3. That immunity is either developed early—that is, before the sixth week—or not at all.
4. That cases developing paralysis would appear generally to have acquired immunity.
5. That cases which do not develop a natural immunity as the result of infection respond satisfactorily to active artificial immunization.

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In the twelve months September 30, 1936, to September 30, 1937, eighty-seven students received training in the medical side of missionary work abroad at Livingstone College. The annual report contains numerous personal tributes to the practical value of this training, which is available for all Christian missionary students without any denominational discrimination. There was a small financial deficit on the year's working, due in large measure to a fall in the amount received from the students' fees. The number of students, it is mentioned, has slightly increased, but the majority in that year only came for short periods. The report contains also the speech delivered at the Commemoration Day meeting in June, 1937, by Mr. W. A. Cadbury, relating to his work in Northern India. The volume of testimonies to the usefulness of the curriculum at Livingstone College shows how missionaries thus trained can be of the greatest value in parts of the world where ordinary medical assistance is scanty.

Clinical Memoranda

"Mixed Tumour" of the Lip: Report of Two Cases

After reading Mr. R. Pilcher's article in the *British Medical Journal* of May 8, 1937 (p. 967), I feel that the following two similar cases of "mixed tumour" of the lip are worth recording. Case II came to my notice a few weeks following the appearance of Mr. Pilcher's article; the other was encountered in 1935.

CASE I

A Chinese woman, aged 24, had had a swelling on the right side of the lip for four years. The tumour was oval, about the size of a walnut, and quite firm.

Histologically the tumour consisted of a fibrous tissue stroma in which were strands of epithelial cells, most of them in alveolar formation, and some appeared to be lining the lymph spaces. Small dark epithelial cells with hyperchromatic nuclei arranged in solid masses were also in evidence. In various areas mucoid and osteoid tissue as well as hyaline material were seen. Lymphocytic infiltration was pronounced in various parts of the tumour.

CASE II

This patient, a Chinese woman aged 36, had had a painless slow-growing swelling on the upper lip for thirteen and a half years. There was no history of trauma, the swelling having first started as a small reddish nodule, growing very gradually. On examination it was found to be hard, pedunculated, and freely movable. It was covered by a tense skin, and several prominent vessels could be seen on its surface. Its under-surface was continuous with the mucous membrane of the lip. The removal of the tumour was followed by a skin graft.

The specimen was oval in shape and about 3 by 2.5 cm. It was firm, encapsulated, and covered by skin. On section it showed a white and opaque smooth surface, containing several small yellowish areas.

The histological report was as follows: "Section shows acini and solid clumps of epithelial cells lying in a fibrous connective-tissue stroma, which in places appears myxomatous. The acini are lined with low cubical or flattened epithelium. Their contents appear pink-staining and homogeneous. Some of the acini are dilated and cystic. The solid masses, with their closely packed cells and a tendency to form cell nests in the centre, present a striking resemblance to squamous epithelium. Distributed in the stroma are seen cartilage-like areas and foci of lymphocytic infiltration."

These two cases were encountered in the course of the routine examination of biopsy material submitted by the University Surgical Clinic. Reports of similar cases in other parts of China are lacking.

I am much indebted to Professor K. H. Digby for the clinical reports.

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A Case of "Mixed Tumour" of the Upper Lip

I was greatly interested in the case of "mixed tumour" of the lip reported by Mr. Robin Pilcher in your issue for May 8, 1937. By a coincidence it so happened that on the day on which I read his report an almost exactly similar case was in my wards awaiting operation.