It is considered that the results recorded in the case of A.P.T. dosage may well have a bearing on the most effective usage of antigens in the case of other diseases.

I wish to express my gratitude to Dr. A. Anderson (M.O.H., borough of Heston and Isleworth) for many facilities, much helpful discussion, and the verification of statistical evidence; to Sir Wilson Jameson and Prof. G. S. Wilson for procuring further supplies of the correct batch of Squibb A.P.T., so essential for the main investigation; to the Wellcome Physiological Research Laboratories for generous supplies of A.P.T. of known Lf value; to Dr. Percival Hartley for estimation of Lf values of certain batches of A.P.T.; and to Sir John Ledingham, Dr. Hartley, Dr. G. F. Petrie, Dr. H. Schütze, and Dr. H. J. Parish for reading the manuscript and for helpful comment.

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DURATION OF ARTIFICIAL ACTIVE IMMUNITY AGAINST DIPHTHERIA

BY

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The areas covered by this report comprise the Cuckfield Rural District, the Cuckfield Urban District, and the Burgess Hill Urban District. In 1936 one of us (W. B. S.) started a campaign to immunize all children between 1 and 15 years against diphtheria. In 1940 a report (cf. Stott and Duke, 1940) was published on this undertaking, which at the time had obtained unique success, particularly among the least accessible section of the population, the "under-fives." Now that the records for over six years are available the time seems ripe to attempt to find an answer to the oft-repeated question, by doctors and parents alike: How long does immunity last? Before presenting the actual figures it will be well to discuss certain points that materially affect their interpretation.

Although two of the districts are nominally urban, in neither of these do the conditions approach those obtaining in our big cities, where, as is well known, a considerable degree of natural immunity to diphtheria occurs among the children. The local incidence of diphtheria up to date (July 31, 1943) is as follows:

Incidence of Diphtheria

Council	Totals for 8 years																										
	1936			1937			1938			1939			1940			1941			1942			1943			Totals for 8 years		
	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c
C.R.D.C.	0	0	2	1	1	20	0	1	6	5	0	1	0	0	1	0	1	0	1	0	0	5	10	9	10	14	9
C.U.D.C.	1	1	1	0	0	2	0	0	7	5	0	0	2	0	1	0	0	0	2	3	1	1	11	14	9	1	0
B.H.U.D.C.	0	0	1	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	3	1	0	0	0

(a="Under-fives"; b=School-children; c=Over 16.)

1 4 b and 2 c in one cottage; 3 b previously immunized.

2 b and 2 c " " ; 2 b " "

3 In an institution.

None of the other cases had previously been immunized.

Total Rates per 1,000 Population

Council	1936	1937	1938	1939	1940	1941	1942	1943
C.R.D.C.	0.1	0.2	0.1	0.5	0.05	0.05	0.1	0
C.U.D.C.	0.2	0.1	0	0.9	0.1	0.1	0	0.6
B.H.U.D.C.	0.1	0.3	0	0.1	0	0	0	0

There was only one death—that of a non-immunized youth aged 17. From the above it is evident that cases of indigenous diphtheria are rare throughout the three areas.

Percentage of Children (1 to 15 Years) Immunized

Council	1936	1937	1938	1939	1940	1941	1942	1943
C.R.D.C.	Negligible	72	77	91	91	96	95	95
C.U.D.C.	"	64	69	92	92	95	97	97
B.H.U.D.C.	"	18	23	90	90	94	96	96

In Sept., 1939, occurred an event of considerable epidemiological importance—the sudden influx of mothers and children evacuated from the Greater London area. The majority of these children were unaccompanied by their parents, and by far the greater proportion of the "evacuees" were billeted on the local inhabitants. Since their first arrival the numbers have fluctuated, a definite rise occurring in 1941.

In the course of this report "natural immunity" denotes immunity gained without deliberate injection of antigen, the latter process being referred to throughout as "immunization." A "pre-Schick test" is one carried out before immunization; a "post-Schick," one done not less than three months after the end of the course. "Positive" and "negative" indicate respectively the presence and absence of a reaction—i.e., failure or success.

Procedure

In order to test sufficient numbers of children in schools scattered over a wide area it was necessary to modify the ordinary procedure. Each child who had at some time previous been immunized and proved Schick-negative received a toxin test only, and no control. At first, when the test was read the control was then performed on all reactors, but the number of pseudo-reactions so revealed was negligible and the control test was finally dropped from the routine (cf. Fulton *et al.*, 1942). It has been found advisable to read the test after seven days, and not earlier as sometimes recommended. All testing was carried out by one of us (H. L. D.). All positives immediately received a supplementary inoculation of antigen. The following points are to be borne in mind in examining the figures:

1. All the children had had at least one negative test not less than three months after the end of the immunizing course.
2. None is included whose first post-Schick test was positive. These primary failures are relatively very few in number (2%, see below), and all received at once a supplementary dose of antigen: in the overwhelming majority of cases this is sufficient.
3. Each child is counted in one year-group only.
4. All children in the 6- and 5-year groups, and many in the 4-year group, had received three injections of T.A.F. at intervals of 14 and 21 days. This antigen proved highly satisfactory, giving 98% successes. The others received A.P.T., the 2-year group mainly the Burroughs Wellcome brand. As Bousfield has so clearly shown, to use an unsatisfactory antigen is merely to deceive the public and play into the hands of the cranks.

Results

The results of the inquiry are as follows:

Years after End of Course	Total Tested	No. Positive	% Positive
6	579	105	18
5	164	41	25
4	588	91	15
3	522	65	12
2	354	14	4

Into this series may be inserted the result of testing, in 1941, 1,000 children two and a half years after immunization with T.A.F., 7% being found positive. As a basic comparison there is also the much greater number of routine tests applied to every child three to six months after the conclusion of its course, when only 2% were positive—an observation that at once disposes of the strange theory that immunization is ineffective in a diphtheria-free area. This last figure relates to both T.A.F. and A.P.T., the latter antigen producing slightly the better results. Apart, therefore, from the statistically inadequate 5-year sample, these figures indicate a steady loss of immunity with the passage of time, and the consequent importance of retesting all children some two years after the completion of their course of immunization. There is little difference between the sexes in their response to antigen. At the schools where the tests were carried out 51% were boys and 49% girls. Of the positives 58% were boys.

An incalculable factor in the interpretation of these figures is the degree to which natural immunizing processes operate in the community under observation. It is well known that among the children of large cities natural processes may result in a high proportion—50 to 70%—of school-children becoming naturally Schick-negative. Samples of the Greater London

evacuee children tested soon after their arrival in our areas yielded much the same results. In sharp contrast a small sample of local children tested at the outset of the campaign in 1936 showed an extremely low percentage of natural Schick-negatives, and among the "under-fives" local experience has failed to reveal any evidence of natural immunizing processes. This is indeed to be expected from the rarity of diphtheria and the essentially rural character of the environment. On the other hand, certain feebly positive children, when tested again six months or more later and without any further treatment, were found to have become negative. The small amount of toxin introduced during the test may contribute to this result, as also may intercurrent disease and fluctuations in the general health. But the considerable changes in the hygienic adjustments of the community that have taken place during the last few years can hardly have failed to affect the oecology of the diphtheria bacillus in these areas. Year by year as the campaign progresses a large body of potential carriers is forming among the locally immunized children, and this has doubtless already built up the naturally or artificially acquired level of immunity and thus serves as a buffer against the large-scale introduction of new sources of infection. It seems probable, therefore, that natural processes are at work, though probably to a limited extent, among our local children at the present time.

What they style the "carrier menace" is a favourite target for the opponents of immunization. These people seem unable to grasp that immunization does not confer protection directly against the bacillus itself, but against its toxin, which causes the symptoms. Once this result is attained the child is at liberty to develop, according to his resources, an antibacterial immunity. Naively enough, these leave-it-to-Nature enthusiasts, while roundly abusing the immunized carrier, alternately extol and conveniently ignore, according to the angle of their attack, the great body of naturally immune town children, all likewise potential carriers of the bacillus. They ignore, too, the value of a high carrier rate in a completely immunized child community as a beneficent factor in maintaining the immunity level.

It is evident that special importance attaches to post-Schick reactors, whether primary or secondary. We have always kept the cards of these children in a special section labelled "Post-Schick Positive," where they remain even after secondary treatment has rendered them negative.

There is no doubt that certain rare children are difficult to immunize and that success is adversely affected by tuberculosis, illness, and poor general condition at the time of treatment. There is also no doubt that local reactions are commoner after A.P.T. than after T.A.F., especially in children over 8 years of age and in girls with well-developed arms. Cold saline compresses are apparently the best treatment. The dosage we use is 0.3 and 0.5 c.cm. A.P.T., and a slightly smaller first dose in children over 8.

Summary

An account has been given of an investigation into the duration of artificial immunity against diphtheria in a country area with a child population (1 to 15 years) of 9,600, 95% of whom had been immunized.

Over 3,000 children were Schick-tested two to six years after completion of a course of immunization. None of these was positive when tested three to six months after the course.

The figures indicate that the number of treated children who lose their immunity to diphtheria increases steadily with the passing of time, rising from 4% after two years to 18% after six years.

The figures should be compared with the results obtained by the routine testing, three to six months after the completion of the course, of all inoculated children—i.e., 2% primary failures.

Certain factors having a possible bearing on the results are discussed, such as the number of notified cases of diphtheria from 1936 to July, 1943 (54), 30 of whom were under 16 years of age.

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Deaths from motor accidents throughout the United States in the first six months of 1943 totalled 10,030, a reduction of 41% from the total of the comparative period in 1941 before the outbreak of the war and 32% in 1942.

GUNSHOT WOUND OF THE INNOMINATE ARTERY

BY

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The following case of spontaneous arrest of haemorrhage from a through-and-through wound of the bifurcation of the innominate artery with resultant hemiplegia from cerebral ischaemia presents several interesting features.

Clinical History of Case

An American rear gunner aged 23 was injured in a plane by an enemy cannon-shell fragment at about 7.30 o'clock in the morning. He collapsed shortly after the injury, and was given first-aid treatment by his captain, who administered two tablets of benzedrine, which helped to revive him; morphine was thought to be inadvisable. A very difficult return journey ensued, with a "belly landing" and only one engine working; he was then conveyed nearly 30 miles by ambulance, to be admitted to hospital at 1 p.m.

On admission he was severely shocked; the front of his voluminous flying kit was soaked with blood, but there was no active haemorrhage. He was conscious, but had moments of confusion; he complained of a feeling of pins-and-needles in his left wrist and hand, which he could not move. There was a round wound half an inch in diameter just above the midpoint of the left clavicle, with some swelling in the deep tissues. Blood pressure was 90/?, and the pulse rate 48, irregular. There was no obvious haemothorax or paralysis elsewhere, but he was too shocked to undress, and resuscitation with serum was started.

One hour later a blood count showed 3,600,000 red cells and 67% Hb. Blood was now being transfused. At this time he was complaining of paraesthesia in the whole of the left arm, and in view of the left brachial monoplegia a provisional diagnosis was made of possible left brachial plexus lesion due to transverse passage of the shot. A radiograph taken through his clothes revealed a cuboidal metal foreign body, 1 c.cm. in size, behind the right side of the manubrium sterni at the level of the first chondro-sternal junction; this caused revision of the diagnosis to possible carotid arterial spasm with cerebral monoplegia. A general neurological examination was still not possible, but no abnormality was noted in the legs. The pupils were normal after allowing for the effects of morphine.

At 4 p.m. he was becoming increasingly confused and disoriented and was not responding to resuscitation, but no active haemorrhage was detected. A small dose of intravenous pentothal was given to enable his flying kit to be removed by the use of scissors and wire clippers in view of the use of electric warming devices. A radiograph of the chest now showed no abnormality. At 5.30 p.m. intermittent tonic contractions of the left arm occurred and his left leg was partly paralysed. He was becoming increasingly restless and at times lapsed into coma. His pupils were dilated and reacted sluggishly; the right disk was paler than the left and the vessels appeared somewhat contracted. There was an extensor plantar response on the left, with ankle clonus; abdominal reflexes were absent, and it was obvious that a progressively severe cerebral ischaemia was present over the right hemisphere. Blood pressure was 110/45; pulse 80.

It was evident that unless the carotid arterial spasm could be relieved the cerebral damage would be fatal: no carotid or temporal pulse could be detected on the right side, and arteriotomy or novocain blockage of the periarterial sympathetics was considered justifiable.

Operation

This was performed at 8 p.m. under intratracheal anaesthesia. A transverse incision above the right clavicle enclosing the wound, with a vertical extension up the sterno-mastoid muscle, gave adequate exposure of the common carotid. The sheath was infiltrated with blood and the artery was small in calibre owing to spasm. It was traced down, and further exposure was obtained by medial reflection of the sterno-mastoid and pretracheal muscles. The wound-track was traced downwards to the back of the sterno-clavicular joint, and the common carotid was visible up to the bifurcation of the innominate; it was still in spasm though a slight pulsation was felt. At the innominate bifurcation a blue-domed clot was seen on the anterior surface, and it was evident that a puncture had occurred at this site. The innominate artery had to be controlled, and accordingly the inner third of the clavicle was divided and resected with a small portion of the manubrium sterni. Exposure of the innominate was now sufficient to allow it to be gently cleared for the passage of a tape ligature, but at this stage the clot shifted and severe haemorrhage from the bifurcation had to be controlled