of the individual that is at fault. I have notes on a subject who was repeatedly and painfully immunized with T.A.F. because of so-called positive reactions; at last, failing to get a "negative," a blood antitoxin titration revealed the presence of between 5 and 10 units of antitoxin per c.cm.! It is an important though secondary function of the Schick test to detect these sensitive persons, and for this reason the test with control should not be omitted in the older groups.

It is probable that all pseudo-reactors are Schick-negative. I have never seen, at any rate in an adult, an undoubted combined or pseudo-positive reaction. In a series of 51 pseudo-reactors 48 were definite pseudo-negatives, and in 3 I queried the possibility of the reading being a combined one.

Conclusion

As a result of this experience with A.P.T. covering several years, and on consideration of the experimental tests detailed, I would suggest that nurses can be immunized with that antigen without undue risk of reaction. The one thing to guard against is the unnecessary immunization of pseudo-reactors. I am inclined to think, in view of what Fulton *et al.* say, together with my own experience of 0.3-c.cm. doses, that an initial dose of 0.5 c.cm. is not necessary. Schick-positive adults will be efficiently immunized, where it is considered desirable to do so, by giving 0.2 c.cm. and 0.5 c.cm. of A.P.T. with a four-weeks interval. In other words, one method, the efficiency of which has been proved beyond doubt, should be used for both children and adults.

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DIPHTHERIA IMMUNIZATION IN A METROPOLITAN BOROUGH

BY

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Until very recently London as a whole held an unenviable record as compared with some provincial towns and cities in the matter of diphtheria immunization. Hence there are comparatively few figures available of reasonably large-scale analyses of the state of natural immunity as shown by the Schick test of the child population in the various parts of London—which might be expected to exhibit their own peculiarities—and of the various responses to different immunizing agents. It was therefore considered that some recent figures relating to a large and fairly representative London borough might be of special interest.

In the early part of 1937 an immunization scheme was started, based on the following principles: (1) Immunization of children 7 years of age and under with alum-precipitated toxoid (A.P.T.) in 2 doses. (2) Immunization of children over this age (except in a few special cases) with toxoid-antitoxin floccules (T.A.F.) in 3 doses. (3) Primary Schick tests for children of 7 years and upwards. (4) Post-Schick tests for all immunized cases. These particular methods were adopted in the light of local factors which made it especially desirable that the number of immunizing attendances should be reduced so far as was possible, but bearing in mind also that reactions following injection should be at an absolute minimum and that the immunizing process should have a very high degree of effectiveness.

The progress of diphtheria immunization was completely suspended for the early part of the war. Figures for the last complete pre-war year, 1938, and for the first full war year, 1941, have been analysed, and their results are as follows.

Primary Schick-test Rates

Islington is a densely populated borough (acreage 3,092; Registrar-General's estimated population, mid-1938—292,300), with the greatest density in the south and south-west. It was not practicable, for the purpose of this analysis, to separate children living in different parts of the borough. The figures given are for girls and boys, and do not include children with a previous history of diphtheria or of diphtheria immunization.

It will be noted that the average Schick-positive rates for 1938 and 1941 approximate each other very closely, and are considerably lower than those given by Wilson and others (Fulton *et al.*, 1942) for Oxfordshire, etc. (77.9%, excluding children under 5 years), and Lewis (1941) for Croydon (76.4%). It will also be noted that although at 5 years the Schick-positive rate for 1941 does not differ greatly from Wilson's (85.5%), the decrease during school years as shown in Table I is very much more rapid, the rate standing at a little over 40% for Islington at 14 years, but still at the high figure of 70.4% for the counties. The rates in Table I, however, approximate

TABLE I

Age (Years)	Children Tested in 1938			Children Tested in 1941		
	No. Tested	No. Positive	% Positive	No. Tested	No. Positive	% Positive
5 & 6	11	6	54.5	283	250	88.3
7	31	24	77.4	233	186	79.8
8	80	59	73.8	217	170	78.4
9	81	60	74.0	319	220	68.9
10	87	53	60.9	306	187	61.1
11	69	45	65.2	292	193	66.1
12	32	14	43.75	313	155	49.5
13	28	16	57.2	256	122	47.7
14	18	8	44.5	206	85	41.7
Totals..	437	285	65.2	2,425	1,568	64.7

rather more closely to those given by Lewis for schools of high diphtheria incidence, and in this connexion it may be stated that the diphtheria incidence in 1938 for this borough was about 7 per 1,000 school children and 8 per 1,000 children from 1 to 15 years of age.

The anomalies in some of the age groups, particularly the 5- and 6-year-olds in 1938, are obviously due to the small numbers in these groups.

For purposes of comparison with other boroughs I have included the figures for Kensington and for Heston and Isleworth (Table II), for which figures I am indebted to Dr. Bousfield, and also to Dr. Anderson, medical officer of health, Heston and Isleworth, and to Dr. Fenton, medical officer of health, Kensington. Since the Kensington work and a good deal of the Heston and Isleworth work were both done by Dr. Bousfield, individual differences should not affect the figures.

TABLE II.—Primary Schick-test Rates (1941)

Age (Years)	Kensington			Heston and Isleworth		
	No. Tested	No. Positive	% Positive	No. Tested	No. Positive	% Positive
5	45	37	82.2	228	221	97.0
6	55	36	65.4	167	154	92.3
7	66	44	66.6	131	120	91.6
8	70	40	57.1	126	116	92.9
9	74	43	58.1	101	85	84.2
10	91	54	59.3	117	91	77.8
11	70	35	50.0	99	79	79.8
12	60	28	46.6	58	49	84.5
13	62	25	40.3	55	43	78.2
14 & over	11	5	45.4	29	19	65.5
Totals..	604	347	57.45	1,111	977	87.9

Results of Immunization by A.P.T. and T.A.F.

Although A.P.T. for children under 7 years and T.A.F. for children over 7 years were the immunizing agents of choice, there were some slight differences in dosage for the years 1938 and 1941, respectively.

TABLE III

	A.P.T. Dosage			T.A.F. Dosage			
	1st	2nd	Interval	1st	2nd	3rd	Interval
1938 ..	0.1 c.cm.	0.5 c.cm.	2 weeks	1 c.cm.	1 c.cm.	1.2 c.cm.	2 weeks
1941 ..	0.2 c.cm.	0.5 c.cm.	2 ..	1 c.cm.	1 c.cm.	1.5 c.cm.	2 ..

A.P.T. for 1938 and for 1941 were not obtained from the same sources, but T.A.F. was supplied by the same firm throughout.

The great majority of the post-Schick tests were performed between the thirteenth and twentieth weeks after the final immunizing injection. All Schick tests are read on the seventh day.

TABLE IV.—Rates for 1938

	No Primary Schick	Primary Schick-positive	No. Positive after Immunizing	Schick-conversion Rate	Schick-negative Rate
Immunized with A.P.T.	—	227	10	95.6%	—
Immunized with T.A.F.	551	—	5	—	99.1%
Immunized with T.A.F. ...	—	23	2	91.3%	—

TABLE V.—Rates for 1941

Age (Years)	Immunized with A.P.T.				Immunized with T.A.F.	
	No Primary Schick	Positive after Immunizing	Primary Schick-positive	Positive after Immunizing	All Primary Positive	Positive after Immunizing
1	184					
2	275	2				
3	205	1	1			
4	180	1	3			
5	143	1	55		1	
6	70		132		4	
7	36	1	141	1	10	
8	15		88	1	41	
9	6		24	1	135	
10	2		7		134	
11	4				132	2
12	1				119	1
13					97	
14					43	
	1,121	6	451	3	716	3
	Schick-neg. rate 99.5%		Schick-conversion rate 99.3%		Schick-conversion rate 99.6%	

The above results compare very well with the most favourable ones obtained by other investigators, both for A.P.T. and for T.A.F. Published results for A.P.T. were recently summarized in tabular form (Fulton *et al.*, 1942).

Discussion

I. Dosage Interval

Although laboratory immunological considerations appear to favour a four-weekly or greater interval between doses, it is felt that in some districts mothers are more likely to bring their children for completion of immunization if the interval between doses is as short as possible, and that fortnightly appointments are much more likely to be kept than monthly ones. This is particularly important with children up to 5 who are not under school or nursery control or in residential institutions. Bousfield has stressed this point. If with suitable antigen Schick-negative or Schick-conversion rates of over 99% can be obtained, there would appear to be no valid objection in practice to a fortnightly interval between injections beyond the unconfirmed possibility of a higher relapse rate at a later stage. When results of this order are obtained with a short interval, the evidence that the same antigen when given at longer intervals in comparable cases will materially affect the respective Schick-relapse rates must for the present be considered inconclusive.

II. Primary Schick Test

The age of 7 years was arbitrarily chosen some time ago, pending the collection of further data on the Schick state of the child population locally, as a period when the proportion of Schick-negatives might show signs of rising appreciably. The Schick tests performed so far indicate, as summarized in Table I, that the proportion of Schick-negatives rises to about one-third at over 9 years of age.

Lewis states: "It has been calculated that when the probable number of Schick-negative reactions is 25% . . . then it will mean considerable extra time, much inconvenience, and the unnecessary use of prophylactic, if wholesale inoculation is carried out, irrespective of immunity state." Lewis does not mention the basis of this calculation, but if we consider the problem only as it affects attendances, and assuming that two-dose A.P.T. is the immunizing agent and a post-Schick test is done in every case, then out of every 100 cases, if 33 are primary negative and the remainder positive, 67 will make 5 attendances each—amounting to 335—and 33 will make 2 attendances each—amounting to 66; giving a total of 401

attendances. If no primary Schick test is performed, then 100 cases will make 4 attendances each—that is, 400 attendances. Accordingly, if the primary Schick-negative rate rises above 33% there will be a saving on attendances, but not otherwise, on the above assumptions for immunizing procedure.

From this point of view, therefore, primary Schick-testing may be dispensed with if the Schick-positives are likely to be more than two-thirds of the total group, or below the age of 9 years if the rates determined in Table I are applicable to other areas. If no primary tests are performed above this age there will be unnecessary attendances, and material used, in increasing proportions as the age groups rise.

The above factors deal only with considerations of mass immunization. From the point of view of the individual parent or the child to be immunized, it might be preferable to be given a 1 in 4 or even 1 in 5 chance of not undergoing a complete immunizing course with a possible post-Schick later on.

A further advantage of performing primary Schick tests for higher age groups is that arising from Wilson's conclusion that Schick-negative children of any age, or Schick-positive children of 10 years of age or over, may respond to A.P.T. with severe reactions. This point must be given particular emphasis where there is a high proportion of Schick-negative reactors among the older age groups at school, such as is shown in Table I, and where such consequences, occurring in considerable numbers, would tend to discourage a mass-immunization campaign. A primary Schick test therefore has the additional advantage of selecting the most probable A.P.T. reactors.

III. Post-Schick Tests

It may appear unnecessary, once preliminary investigations have established satisfactory results, to continue post-Schick testing when the Schick-negative and conversion rates are in the region of 99%. Batches of antigens may differ considerably in their immunizing powers, however, and post-Schick sampling therefore seems necessary as a minimal precautionary measure. Further investigation appears desirable as to the optimum proportion which should be sampled, so that poor batches may be detected with reasonable certainty at an early stage. It would not be an easy matter at the present time in some parts of London to recall children in satisfactory numbers for further immunization three, four, or five months after their original immunization with a poor immunizing agent. Provided that time, staff, and material are available, and until antigen variability per unit volume is eliminated, it would seem a safer procedure to post-Schick-test all those immunized. Otherwise risks are run which must be recognized.

IV. Immunization with T.A.F.

Very satisfactory Schick-conversion rates have been effected with T.A.F. for older children. The administration of 1 c.cm., 1 c.cm., and 1.5 c.cm. was made consequent upon observations by Bousfield, using a variation of the final dose. No single moderate or severe local or general reaction has been reported, and in only a very few instances was the medical officer informed at the following clinic that after the previous attendance there had been a little local tenderness around the site of injection but with no subsequent physical signs.

It cannot perhaps be said that the use of T.A.F. is absolutely necessary for older children, but it is a very satisfactory antigen to use. Wilson and his co-workers note that severe reactions with A.P.T. will be more frequently encountered in Schick-positive children of 10 years of age or over, and that 42% of Schick-positives showed some degree of local reaction to A.P.T. Lewis mentions that when the primary dose of A.P.T. causes a reaction it might be wiser to withhold the second injection of A.P.T. and substitute three T.A.F. injections of 1 c.cm. each. Such a procedure would appear likely to substitute four immunizing injections in a considerable number of older children in place of the two originally planned, and these children would also have experienced the discomfort of a reaction.

If it is particularly desired to avoid reactions in older children it is suggested that T.A.F. as a routine immunizing agent might be restricted to children over 10 years of age.

Summary

A series of children in a London borough from 1 to 15 years of age were immunized and in part primary Schick-tested. The results for two recent complete years, 1938 and 1941, have been given.

Of 437 children of school age tested in 1938, 65.2% were primary Schick-positive. The corresponding numbers for 1941 were 64.7% positive out of 2,425. Over four-fifths of the children were positive at school-entry age, but only a little over two-fifths were found positive at school-leaving age.

A.P.T. given in doses of 0.1 c.cm. and 0.5 c.cm. with a fortnight's interval produced a Schick-conversion rate of 95.6% and a Schick-negative rate of 99.1%. A.P.T. similarly administered in doses of 0.2 c.cm. and 0.5 c.cm. gave a Schick-conversion rate of 99.3% and a Schick-negative rate of 99.5%. T.A.F. given in three fortnightly doses of 1 c.cm., 1 c.cm., and 1.2 c.cm. produced a Schick-conversion rate of 91.3% (23 cases only), and in fortnightly doses of 1 c.cm., 1 c.cm., 1.5 c.cm., a Schick-conversion rate of 99.6%.

Provided a suitable antigen is given in appropriate doses, no practical immunological disadvantage is apparent if an interval of two weeks between doses is employed because it is administratively advantageous locally instead of four weeks.

With A.P.T. in two doses as the antigen, clinic visits will be saved if primary Schick tests are performed in all cases when the expectation of natural immunes is more than one-third of the total for the age groups concerned. In a typical London borough this can be expected from the age of 9 years onwards. The selection of the primary Schick-negatives when they form a considerable proportion of all children also assists in eliminating or indicating (if it is desired to give a single safeguarding injection) the most probable sufferers of local reactions to A.P.T.

In view of the existing variability of the same types of antigens, post-Schick-testing or, as a minimum, post-Schick-sampling is necessary.

Diphtheria immunization clinic work for 1938 was carried out by the author, and for parts of the year by Drs. D. S. Murray and K. M. Hirst. The bulk of the 1941 clinic work was done by Dr. H. W. Swann, to whom appreciation is due for his careful work and enthusiasm, and the remainder by Dr. Mary Adams. Thanks are also due to Mr. D. A. Owen, clerk in the Public Health Department, for his conscientious maintenance of records and clinic arrangements generally. Thanks are also expressed to Drs. Bousfield, Anderson, and Fenton.

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PROGNOSTIC VALUE OF THE BLOOD SEDIMENTATION RATE IN PULMONARY TUBERCULOSIS

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During the past twenty years the estimation of the sedimentation rate of the red blood corpuscles has gradually become established as part of the routine examination of patients suffering from pulmonary tuberculosis. The test has been thoroughly investigated, and a vast amount of literature describing the results has been published. It is claimed that the test has a definite value as a guide to the reaction of the patient to his disease, and, in brief, it is thought that a rising B.S.R. denotes that the condition of a patient suffering from pulmonary tuberculosis is deteriorating while a steadily falling or consistently normal result indicates that he is improving.

The literature was studied by us with great interest, and for some time the test was performed regularly on all in-patients

of this sanatorium, the results being considered in conjunction with serial x-ray films and the usual clinical observations and data. It may be stated at this point that it is our practice to radiograph our patients at monthly intervals, especially during the early months of their treatment. After prolonged investigation we came to the conclusion that while the claims regarding the test were, broadly speaking, true, it was not of great value from the point of view of the hospital or sanatorium physician, whose patients were under close observation, as the test did not give any information which could not be obtained from the usual routine methods and serial x-ray films. Furthermore, the test would have to be performed at regular and frequent intervals on every patient, involving an amount of time and work not commensurate with the value of the information procured. It was also observed that the test was not 100% efficient and that in some cases the results could be misleading. It was possible to observe a patient with obviously progressive disease (as shown by serial x-ray examination) but whose B.S.R. remained unchanged and within normal limits. Conversely, patients with lesions known to have been static over long periods often produced a persistently abnormal B.S.R.

Although these results suggested that the test was not of great value in assessing the progress of patients under institutional conditions, it was thought that it might be of more use when the patient was not in a hospital or sanatorium and in consequence not under such close observation and supervision by his physician. Accordingly the investigation was repeated on the patients attending our out-patient clinics; but again no evidence was obtained that the B.S.R. was superior to the usual examinations in indicating the progress of the disease or evidence of relapse. In addition one was apt to be misled by the alteration in the reading that followed any intercurrent infection which the patient had forgotten or had not thought worthy of mention.

As a result of these investigations we considered that the B.S.R. was of only limited value as an index of progress in a case of pulmonary tuberculosis and could not supersede any of the usual methods of examination. But we had noted that the B.S.R. did alter with the different pathological phases of the disease, and therefore thought it might be worth while to examine the test from a different point of view—namely, from the more remote, as opposed to the immediate, prognosis.

Observations Made

For this purpose B.S.R. estimations were done on admission and on discharge on all patients coming into this sanatorium during a period of nearly 3 years (1936-9). These values were recorded on separate cards for each patient, together with the name, age, sex, date of admission and discharge, the Ministry of Health classification of the state of the disease, the extent of lung involved as disclosed by x-ray examination, and, from the follow-up department of the hospital, the condition of the patient at the latest known date, under the headings "Alive and Working," "Alive," or "Dead."

It will be observed that the data are limited to patients who were discharged, and do not include those dying during their treatment in the sanatorium, for whom only the B.S.R. at entry would be known. But our concern, as stated above, is with the relationship—if any—between the B.S.R. and the state of health subsequent to discharge: the deaths in the sanatorium are for this purpose irrelevant. In all, 630 patients (292 males and 338 females) were discharged between Jan. 1, 1937, and June 30, 1939, their dates of admission lying between Jan. 1, 1936, and June 30, 1939, and their average stay in the sanatorium being 148 days for males and 141 days for females (round these averages there naturally was much variation). These numbers were clearly too small to allow the B.S.R. to be related to the subsequent history of patients of different ages as well as of each sex. Division by sex was clearly necessary, but age, as statistical analysis showed, was not an important factor. In the treatment of the material no differentiation by age has therefore been made. The percentage-age distribution of the patients was, in fact, as follows:

	10—	20—	30—	40—	50+
Males	7	41	33	16	3
Females	18	52	25	4	1

The history of these patients between discharge and the end of April, 1940, was known for variable lengths of time, and