termination only that part of the pancreas embraced by the concavity of the duodenum appeared to remain. No subsequent sequela referable to the spleen made me regret the decision to conserve that organ, despite the surgical interference with both its arterial and its venous blood supply. The patient continued in excellent health until the autumn of 1938—that is, 11 years—when the possibility of a recurrence suggested itself. *Just over 13 years after the removal of the tumour* he died from undoubted abdominal malignancy—probably a late metastasis of the original tumour.

Case 8: A Calcified Mass embedded in the Pancreas and compressing the Common Bile Duct; Removal of Mass together with Portion of Head of Pancreas.—A stoker 49 years of age with jaundice of 4 months' duration; rather poor physique. Two-stage operation after modern pre-operative measures. *Cholecysto-gastrostomy*; at operation a firm mass was palpated in the head of the pancreas near the ampulla, and was regarded as confirmatory of the accuracy of the pre-operative diagnosis of ampullary cancer. *Second operation*, undertaken 6 weeks later: The second part of the duodenum was mobilized and the mass approached from behind. The tumour was found embedded in the substance of the head of the pancreas in intimate proximity to the retroduodenal and pancreatic portion of the common duct, and was removed from the pancreas with some of the gland tissue. On section the tumour was found to consist largely of calcareous material, possibly a mass of agminated calcified tuberculous glands. There was perhaps some justification for the mistake in diagnosis, but at least the patient is to be congratulated on the pathological nature of the compressing mechanism, which before this experience I might have seriously doubted.

Prof. C. F. W. Illingworth has had two admirable unpublished cases in which a successful radical two-stage operation for cancer of the pancreatic head was performed, and which I had the good fortune to see in Glasgow some months ago. My friend Victor Hurley of Melbourne told me that he had successfully removed a malignant tumour from the head of the pancreas by a retroduodenal approach, without removing the duodenum or bile duct. Rodney Maingot's (1941) excellent case is the first truly radical and successful case to be reported in Britain.

Some new growths of the ampullary region are apparently radiosensitive. Upcott (1935) performed a local excision of an ampullary growth and introduced radium on a probe down the common duct; the patient was well *15 years later*. Sampson Handley (quoted by Upcott, 1935), employing 6 mg. of radium for 5 days, was able to report 3 cases free from recurrences for 10 months, 2 years, and *14 years*, respectively. Sir James Walton (1939a) reported two successful cases of resection of the common bile duct for cancer in his Bradshaw Lecture of 1939, but amid the wealth of surgical experience and skill contained in this address these two cases deserve special mention lest they escape notice. Mr. C. E. Kindersley of Bath had also a successful case of resection of the junction of the cystic and common bile duct; this patient has survived several years.

Of *transduodenal resection of the duodenal end* of the common bile duct, my friend Mr. David Ligat of Hastings, operating at Middlesex Hospital in 1916 during the last war, had a successful case, the patient living *nearly five years* before ultimately dying of obvious malignant recurrence in the liver. This man had been jaundiced for 4 or 5 months, and the extrahepatic ducts were enormous.

These cases have been reported in the hope that the younger generation of surgeons may be encouraged to attempt to cure and not merely to palliate. The natural history of ampullary and pancreatic tumours justifies more vigorous surgical effort, and the end-results of the cancer surgery of this region should compensate the operator for his enterprise.

The concluding part of the Lecture will appear, with a list of references, in next week's issue.

The plan for fusion recommended by the Council of the Incorporated Association of Hospital Officers and of the Incorporated Association of Clerks and Stewards of Mental Hospitals has been adopted by extraordinary general meetings of both associations. Accordingly, from Oct. 1 next the two bodies will be amalgamated under the title of the Incorporated Association of Hospital Administrators, and membership will be open to all duly qualified lay hospital administrators.

DIPHTHERIA IMMUNIZATION OF ADULTS

BY

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The admirable paper by Fulton *et al.* (1942) has, with convincing proof, laid down a highly efficient routine for the immunization of children with alum-precipitated toxoid (A.P.T.). The dosage of 0.2 c.cm. followed by a second dose of 0.5 c.cm. at an interval of not less than 4 weeks has received the approval of the Chief Medical Officer to the Ministry of Health in his letter to all medical officers of health dated May 8, 1942. It is safe to assume that such a method will become routine and will at last lead to satisfactory immunization in this country. Provided we can rely on the antigen, the checking of which is the concern of the issuing and controlling laboratories, we now have an efficient and simplified diphtheria prophylaxis. Schick-testing can be dispensed with and records can be reduced to the insertion of a batch number and two dates upon a card. Whether this work be done in a consulting-room, a child welfare clinic, or a school will matter little. The aim now should be to get over 80% of children under 10 years of age treated in this manner.

At the same time the Chief Medical Officer to the Ministry, in another letter, advised that nurses in general hospitals who are Schick-positive should be immunized with toxoid-antitoxin floccules (T.A.F.), 3 doses of 1 c.cm. being injected at intervals of 3 weeks. The reason given for this recommendation is that T.A.F. tends to give rise to less reaction than does A.P.T.

Fulton *et al.* in their paper state that above the age of 18 years the number of subjects tested (20) was too small to enable them to obtain a reliable figure for the Schick-conversion rate. This encourages me to add as a small contribution the figures I have collected during the past 9 years in the course of immunizing the staff at the Hull City Hospital. Though not large they have been carefully compiled, and all testing, readings, and injections have been done personally. All persons in the group are more than 16 years of age, and the great majority between 18 and 20. Most are nursing and domestic staff at the hospital, but occasional visitors, medical and otherwise, have been included.

After various experiences with other antigens since 1922, including T.A.M. and F.T., I began to use T.A.F. in 1933, giving 3 injections at monthly intervals and Schick-retesting 4 weeks after the last dose. The Schick-conversion rate was not good, and largely for this reason I turned to A.P.T. in March, 1935, giving 0.3 c.cm., followed after 4 weeks or a little longer by 0.3 c.cm., with a Schick-retest one month later. Originally I had intended to give 0.25 c.cm. and 0.25 c.cm., but there was always enough in a 0.5-c.cm. ampoule to give two doses of 0.3 c.cm. to two subjects, so it seemed a pity to waste antigen. The Schick-conversion rate rose to 100%. I get no severe reactions, and the method, except for an increase to 0.5 c.cm. for both doses in 1940, has been in use since. In 1936 I began to give a single dose of 0.3 c.cm. of A.P.T. to Schick-negative reactors if they did not have a pseudo-reaction, and have continued that procedure, increasing the dose to 0.5 c.cm. in 1940. The results are summarized in Table I. The details given in this Table suggest that the T.A.F. used in 1933 was a weak antigen and that it was considerably improved in the following year. Despite this improvement, the T.A.F. results as a whole were poor (Schick-conversion rate 78%). The excellent results with A.P.T. were so soon apparent that there was no question of return to the older antigen. I would regard any such return as a regression.

Reactions

There were no severe reactions in any of the 388 adults immunized. I have notes of only 5 moderate local reactions—4 with A.P.T. and 1 with T.A.F. One of the 4 A.P.T. reactors was a pseudo-negative who was given 0.1 c.cm. of A.P.T. as a detector dose. Some local reactions have doubtless

TABLE I.—*Diphtheria Immunization of Adults at Hull City Hospital, Cottingham*

Year	Schick		No. Immunized and Retested	Antigen	Schick Retests		No. originally Schick-neg. given 1 dose A.P.T.
	Neg.	Pos.			Neg.	Pos.	
1933	44	47	32	1 c.cm. T.A.F. 4 weeks	19	13	
1934	59	36	27	1 c.cm. T.A.F. 4 weeks	26	1	
1935	32	29	4	1 c.cm. T.A.F.	4	0	
			20		20	0	
1936	25	20	17		17	0	5 (0.3 c.cm.)
1937	37	41	36	0.3 c.cm. A.P.T. 4 weeks	36	0	24 "
1938	60	23	18	0.3 c.cm. A.P.T.	18	0	43 "
1939	44	26	25		25	0	36 "
			15		15	0	27 "
1940	51	24	5	0.5 c.cm. A.P.T. 4 weeks	5	0	18 (0.5 c.cm.)
1941	35	15	11	0.5 c.cm. A.P.T.	11	0	25 "
	387	261	210	T.A.F.: 63 A.P.T.: 147	147	14	178

occurred and not been reported; anything severe would have been. No time off duty has been lost owing to reaction and nothing has required treatment.

In this connexion it might be as well to add that the skin was cleansed with ether on a small swab, both injections were made into the triceps of the left arm, the syringes were all-glass 1 c.cm. dry (hot-air) sterilized, and the stainless-steel needles for injection were of the same small type as that used for the Schick test. The needles were also hot-air-sterilized. Each dose was given from a sealed glass ampoule opened at the time. The syringes are kept for the one purpose sterile in Petri dishes. All antigens employed were "Wellcome" products as ordinarily issued.

When persons are immunized with T.A.F. they are rendered serum-sensitive in consequence of the antitoxin fraction in the antigen. It is difficult to assess the degree of such sensitization, but I have noted in 2 cases that nurses who had received T.A.F. had greatly accentuated serum sickness, amounting almost to anaphylactic phenomena, when given therapeutic sera months after their immunization. Since the introduction of refined (protein-digest) therapeutic sera almost the only cases of serum sickness I see in hospital are in children who have been immunized with T.A.F. Is not the presence of an antitoxin fraction in any material for active immunization an anomaly? With the remarkable results now obtained with A.P.T. surely we may say that the weaker antitoxin-containing antigens are becoming obsolete.

Subjects who are most likely to have severe reactions are those who give pseudo-negative reactions to the Schick test. I have not as a rule given a "reinforcing" dose of A.P.T. to such subjects. These pseudo-negatives are, however, excellent material for testing reactions, and 6 of my nursing staff who

TABLE II.—*Experimental Test of T.A.F. (Right Arm) and A.P.T. (Left Arm) on Sensitive (Schick-pseudo-negative) Subjects*

Subject	Hours after Inoc.	Head-ache	Mal-aise	Temp.	Pain		Tender-ness		Red-ness		Indura-tion	
					R	L	R	L	R	L	R	L
A	24	No	No	N	+	+	++	—	30	25	+	+
	48				+	+	+	—	50	60	+	++
	72				—	—	—	—	fading	—	—	—
	24				+	+	++	++	20	30	+	++
B	48	Yes	Yes	101°	+	++	+	++	70	80	+	++
	72				—	—	—	—	fading	—	+	++
	24				+	+	++	++	10	10	+	+
	48				+	+	++	++	60	10	++	—
C	72	"	"	N	—	—	+	++	fading	—	++	—
	24				—	—	—	—	5	8	—	—
	48				—	—	+	++	20	30	—	—
	72				s	s	+	++	fading	—	±	—
D	24	No	"	N	—	—	±	+	15	20	±	—
	48				s	s	±	+	50	70	+	++
	72				—	—	±	+	fading	—	±	—
	24				—	—	±	+	8	20	±	—
E	48	Yes	"	N	—	++	±	++	10	60	—	++
	72				—	—	—	—	fading	—	±	—
	24				s	s	—	+	—	—	±	—
	48				—	—	—	—	—	—	±	—
F	72	"	"	N	—	—	—	—	—	—	±	—
	24				—	—	—	—	—	—	±	—
	48				—	—	—	—	—	—	±	—
	72				—	—	—	—	—	—	±	—

R=right arm. L=left arm. ±=very slight. +=slight. ++=moderate. s=stiffness rather than pain. The long diameter of redness is shown in mm.

fall into this group kindly offered themselves as experimental animals. They were injected in the left arm, using the usual technique, with 0.1 c.cm. of A.P.T., and in the right arm with 0.1 c.cm. of T.A.F. They were closely observed at 12, 24, and 48 hours, and at 3 and 7 days. General and local reactions were most marked at between 36 and 48 hours; the visible signs were most obvious at 48 hours, after which, except in 2 cases, they began to subside. The results are summarized in Table II.

The 7-day readings were as follows: A, D, E—small painless nodules in left arm only; B, F—induration and sterile abscess in left arm; C—small painless nodule in left arm; slight right axillary adenitis.

It will be seen that in 5 out of the 6 cases there was more local reaction with A.P.T. than with T.A.F. In 4 subjects local signs were subsiding by the third day, except that the left arms had the small nodule of infiltration that is usual with this antigen. Three of the reactions could be classed as moderately severe. All were feeling well by the third day despite their local signs. No member was off duty; in 2 subjects the headaches were severe enough to need acetyl-salicylic acid. Two volunteered the statement that their "worst" arms were not so bad as when they had had anti-enteric vaccine, and the others when asked about this stated quite definitely that that was their experience also. It must be noted that the dose of A.P.T. was an effective immunizing one, while that of the T.A.F. was a tenth of the recommended dose.

At 7 days 3 had nodules in the left arm without pain or tenderness, but 3 presented definite signs, of which more must be said. Subjects B and C were very sensitive. At 36 hours B had to keep her arms folded to minimize axillary pain, which was similar on both sides. At 48 hours the redness of the left arm showed double zoning with approximate diameters of 30 mm. for the inner zone and 80 mm. for the outer; but she felt much better generally than 12 hours previously. She was able to use her arms quite comfortably at 3 days. At 7 days the left arm still showed moderate induration and swelling. There was a superficial abscess from which 2 to 3 c.cm. of pus was withdrawn by aspiration. Culture on blood-agar plate and into infusion broth gave no growth.

Subject C was the only one who showed more reaction with T.A.F. than with A.P.T. She had general symptoms, headache, shivering, and a feeling of sickness at 48 hours, and did not eat her breakfast. At 48 hours both arms were equally tender, although there was much more swelling and redness on the right. At 7 days, on the right side there was slight axillary adenitis but no pain or tenderness at the injection site, on the left side a small nodule at the site without pain or tenderness. This nurse had reacted markedly to anti-enteric vaccines in March, 1941, was in bed and off duty for a day then, and volunteered the statement that her arm was much worse than either was now. She affords an excellent example of what I believe to be generally true, that it is the individual rather than the antigen or its dose that is the chief factor in these reaction phenomena.

Subject F, though her symptoms were not so pronounced during the first 3 days, showed redness, tenderness, induration, and sterile abscess formation in the left arm at 7 days. Two or three c.cm. of pus was aspirated, and this gave no growth when inoculated into broth and on to a blood-agar plate. There was no pain, local or axillary, and no adenitis. On the eleventh day a small incision was made and about 20 c.cm. of pus evacuated.

Discussion

My impression in reviewing these experimental tests is that I have been right in not giving A.P.T. to pseudo-reactors. Until now I have never seen sterile abscess formation, though I was aware it had been reported. Such cases were probably similar to these—pseudo-reactors who had been given A.P.T.: the remedy is, not to use T.A.F., which will give a strong though in most cases a lesser reaction, but not to immunize pseudo-reactors at all. Here I must plead for a careful reading of the Schick tests: the arms must be seen at 24 hours and at 7 days by one who has had some experience of reading the reaction; otherwise pseudo-reactors will be read as positive, and results obtained similar to those in this short experimental series, to the discredit of the antigen when it is the selection

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.

REFERENCE

Fulton, F., Moore, B., Taylor, J., Wells, A. Q., and Wilson, G. S. (1942). *British Medical Journal*, 1, 315, 349.

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.