Ida and Agnes noticed anything which might have replaced or formed a part of the normal menstrual cycle.

The women were asked if they were worried by the stoppage of periods. Hanna said that she was worried, but that the doctors reassured her. Margret, Agnes, and Emma were not anxious about it, and Emma thought it was "*sehr praktisch*." Hanna and Elli thought that normal sexual desires persisted, and Elli's replies suggested that if she had found a suitable partner she might have had intercourse with him. She was the only one of the four unmarried women who admitted that she was not a virgin before captivity in Russia. Ida was on very good terms during the last year in camp with a German boy aged 18, but the friendship was of an adolescent type and did not advance to sexual intercourse.

Since their return to Germany the two married women had met their husbands and had opportunities for intercourse. Agnes, who had had a number of years of married life before the war, said that, although she was happy to be with her husband again, she was "*zu schwach*" for sexual relations. Emma, who was married (at the age of 33) while her husband was on leave from the Army and had spent only one other short leave with him, said that her relations with him after their four years of being apart were perfectly normal. Margret dismissed the subject by saying that she was too young and that she was not interested in the men in the camps.

Four of the women knew personally women in their camps who became pregnant while they were in captivity, some of the fathers being German prisoners and others Russians of German or other descent. No details of the menstrual history of the women who became pregnant could be obtained. The children were born in the local hospitals, and all the mothers were able to breast-feed their children. Pregnant women received extra food from the sixth month and during lactation, and Elli said the children in her camp looked very bonny. These pregnancies were not the results of rape. All the women agreed that the danger of rape was over as soon as they were "*verladen*" into their cattle-trucks. (The word *verladen*, which was always used by the women when talking about their train journey, is normally never used for human beings but only for cattle and goods.) All the women except Margret were able to avoid rape during the critical first weeks, and regarded this as very good fortune. Margret said she had been raped "only twice"; she did not enlarge on this statement.

The Release from Captivity

During the last year there were rumours in most of the camps that release might be near for women in Group III. Previously only women who were unfit for work had been sent home. Release, when it actually came in July, 1948, was sudden and unexpected. Margret, Agnes, Emma, and Hanna were released because they were in Group III, and Hanna said that she was lucky in that the choice was made according to the classification of March, 1948. She had actually since then considerably improved in health. Elli was released because she had had an accident in her mine at Christmas, 1947. She had broken her collar-bone and two ribs when she was crushed between two trucks. Since then she had been on lighter work and made a good recovery. Ida, who was a Group I worker in the last two years, was sent home because of her dental cyst.

All the women gave a similar account of their return journey. Although they again travelled in cattle-trucks until they reached the border of the Russian zone at Frankfort-on-Oder, the conditions were very much better than on the outward journey, and there were no complaints of ill-treatment. They went from Frankfort-on-Oder to

Göttingen, where they were medically examined. The very great majority of all the women repatriated at this time were dismissed from hospital care or left hospital at Göttingen of their own accord to join relations in the western zones. Twenty-four women who preferred to stay under medical care after meeting their relations were sent to another hospital at the beginning of August, 1948, and the six women questioned belonged to this party.

Finally all the six women were asked what their plans were for the future. Margret hoped that when she was fully recovered she would be able to join her mother, who had come to the British zone and was trying to build up a home again in Hilden, near Düsseldorf. Ida expected to join her mother, now in a village near Krefeld, and had made inquiries about work in a factory where her brother was working. Hanna planned to keep house for her uncle and cousin in the British zone. Elli's family was widely scattered, and she could not decide what she would do. Her mother was still in her old home in Pomerania, and her father, who had been a prisoner of war in England, was working for a farmer in the Ruhr Valley. She had other relations near Münster and she might go to them. The two married women, Agnes and Emma, intended to join their husbands, who were trying to establish themselves in the British zone. They would leave hospital as soon as they felt completely well.

Summary

An account is given of the experiences of six German women who were taken into captivity in Russia. This account was compiled from the information they gave after they had returned to Germany. Great hardships were endured at first, but conditions gradually improved, and the women were in good clinical state on their return.

Menstruation ceased soon after the women were captured, and five of them had amenorrhoea for nearly three years.

P.T.A.P.: THE PRESENT POSITION

BY

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In the prophylaxis of diphtheria A.P.T. has certain drawbacks: it is not constant in its composition and, especially in adults, there may be unpleasant reactions. One of us (L.B.H.), working in the Wright-Fleming Institute of Microbiology, produced a purified diphtheria toxoid which instead of being precipitated by alum was adsorbed on to pure aluminium phosphate—a more suitable compound. To this prophylactic he gave the name P.T.A.P. (signifying *Purified Toxoid precipitated by Aluminium Phosphate*).

In November, 1944, it was decided that the results obtained in guinea-pigs with this new diphtheria prophylactic justified field trials (Holt, 1947). At that time we appreciated that numerous important problems arose in diphtheria prophylaxis regarding which there was very little accurate knowledge. These included: (a) the route of choice for inoculations—subcutaneous or intramuscular; (b) the dose of toxoid (Lf units) administered as adsorbed toxoid for the satisfactory mass immunization of children; and (c) the optimal amount of mineral carrier (AlPO₄) to employ. The new method gave us complete control of the composition of the prophylactic and therefore promised

that these questions could be answered with a measure of reliability not previously obtainable.

In the preliminary trials very small amounts of aluminium phosphate carrier were employed. The results of these trials (Bousfield, 1947a) revealed two important facts: (1) that aluminium phosphate is an extremely suitable vehicle for adsorbing toxoid when used for human prophylaxis, in that local or general reactions were absent or at most trifling; and (2) that the efficiency of the prophylactic, as judged by the Schick conversion rate (S.C.R.) in young children following one inoculation, increased as the amount of phosphate was increased, but without clear-cut evidence of an optimal amount. The amounts of carrier eventually used, and with no untoward reactions, were very much greater than would be considered safe if presented as A.P.T.

As the work progressed it was found that samples of P.T.A.P. having a mineral content of 10–15 mg. AlPO_4 per ml. gave the best Schick conversion rates (dose 0.5 ml.); that this new prophylactic improved in antigenicity on storage (three months) at room temperature (Bousfield, 1947b); and that consecutive batches, chemically almost identical and of the same age, were antigenically the same (Bousfield, Duke, *et al.*, 1948).

We propose here to set forth further details showing the superiority of P.T.A.P. over A.P.T. in the immunizing of children and some further details about its constitution and use.

Uniformity of Antigenicity in Successive Batches of P.T.A.P. and A.P.T.

It has been found that successive batches of A.P.T. sometimes show disturbing variations in efficiency when tested in the field (Bousfield, 1947c).

These variations were greatly reduced by the acceptance in 1942 of more stringent provisional regulations (B.M.J., 1942). Even so, although the new regulations eliminated the grossly inferior products they did not solve the problem of variations in antigenicity. These, of course, are more readily demonstrated when the responses to single inoculations are observed (Bousfield, 1947a).

Evidence showing the degree of antigenic uniformity obtainable with P.T.A.P. has already been published (Bousfield, Duke, *et al.*, 1948), but it may be useful at this stage to recapitulate. In Table I a summary of the results already published is given together with those obtained recently from single inoculations employing six unselected batches of Government issue A.P.T. It will

TABLE I.—Uniformity, and Performance of Six Consecutive Batches of P.T.A.P.* (30 Lf and 10 mg. AlPO_4 /ml.), and of Government Issue A.P.T. (Lf > 50/ml.) Dosage 0.5 ml., Administered Intramuscularly. Children all Schick-positive before Immunization, and Post-Schick-tested Four Weeks After a Single Inoculation.

Batch No.	Post-Schick Results							
	P.T.A.P.				A.P.T.			
	(+)	(–)	Total	S.C.R. %	(+)	(–)	Total	S.C.R. %
1	9	143	152	94.1	11	66	77	85.7
2	5	144	149	96.6	11	87	98	88.8
3	6	149	155	96.1	6	35	41	85.4
4	4	146	150	97.3	22	111	133	83.5
5	4	160	164	97.6	1	28	29	96.6
6	0	141	141	100.0	1	39	40	97.5
Total	28	883	911	96.6	52	366	418	87.5

* Redrawn from Bousfield *et al.*, 1948.

† Two and one-half times the officially recommended first dose for A.P.T.

Statistical Analysis of the Results

	χ^2	df	P
P.T.A.P. ..	9.284	5	>0.10
A.P.T. ..	8.930	5	>0.10
Comparison ..	44.436	1	<0.001

Namely, there is no significant heterogeneity between the six batches in either group, but P.T.A.P. is definitely superior to A.P.T.

be noted that with P.T.A.P. the Schick conversion rate varied from 94.1 to 100%, with an average of 96.6; and the rate for A.P.T. varied from 83.5 to 97.5, with an average of 87.5%. These latter figures were obtained with a dose of 0.5 ml., which is two and a half times the officially recommended first dose.

The differences among the samples of each group are not statistically significant in either case, but the difference between the results obtained with P.T.A.P. and A.P.T. is significant.

Route of Choice

It was thought of some importance to determine whether the immunity response after intramuscular injection differed from that after subcutaneous injection. To answer this question the following evidence may be taken into account: direct observations (Schick conversion rates) made at a fixed time interval on a number of subjects who had been inoculated by one or the other route; the immunity response curves over a period of time following injections by either route; and a combination of the results obtained from the above two methods.

In regard to the first method, samples of P.T.A.P. were employed containing a fixed amount of toxoid (5 Lf in 0.5 ml.) and widely different amounts of aluminium phosphate carrier. The conversion rates were determined 28 days after inoculation. The results, which are summarized in Table II and have their probit analysis depicted in the diagram, show that the intramuscular route gives a significantly better response.

TABLE II.—Comparative Antigenicity of P.T.A.P. of Varying AlPO_4 Content, when Administered Either Subcutaneously or Intramuscularly. (Toxoid Dose Constant at 5 Lf in 0.5 ml. S.C.R. Determined 28 Days After One Inoculation).

Mg. AlPO_4 Injected	Schick Conversion Rate %	
	Subcutaneous Route	Intramuscular Route
1.5	65.6 (93 cases)	87.3 (79 cases)
2.5	83.3 (54 ")	95.2 (83 ")
3.5	85.0 (100 ")	92.7 (82 ")
4.5	—	94.1 (85 ")
5.0	93.3 (45 ")	—
5.5	—	92.9 (55 ")
6.5	—	96.4 (84 ")
7.5	91.5 (47 ")	97.4 (88 ")
	(339 cases)	(556 cases)

Statistical analysis of Comparable Groups					
Mg. AlPO_4 Injected	χ^2	df	P		
1.5 ..	10.949	1	..	<0.001	
2.5 ..	5.346	1	..	<0.05	
3.5 ..	2.605	1	..	<0.20	>0.1
7.5 ..	2.807	1	..	<0.1	>0.05
Total ..	21.707	4	..	<0.001	

Regarding the second method, no data are available concerning the time for maximal Schick conversion rates in children who had received subcutaneous inoculations of either A.P.T. or P.T.A.P. It has been found in guinea-pigs, however, that when A.P.T. or P.T.A.P. is administered subcutaneously the time for maximum antitoxin response was always the same regardless of the amount of mineral carrier employed—namely, 25 to 28 days (Holt, unpublished observations). This was correlated with the time for fibrous encapsulation of the residual mass (nodule formation) to occur—namely, some 7 to 10 days.

Since the time interval for the (sterile) foreign-body reaction in the human is the same or even a little less, it seems justifiable on this point to transfer the evidence direct from the guinea-pig to the child.

When an inoculation is made intramuscularly it would seem reasonable to infer that the continuous movement of the muscle fibres would not only usefully disperse the injected particles but delay or even prevent fibrous

Probit Analysis of the Two Curves

	χ^2	df	P
Homogeneity of subcutaneous series	1.620	3	>0.50
Homogeneity of intramuscular series	2.532	5	>0.70
Parallelism between the two curves	1.724	1	>0.10

Namely, no significant deviation from parallelism.

Both the subcutaneous route and the intramuscular route show a linear dependence on the probit of the response (percentage of Schick negatives) with the logarithm of the dose of carrier, a result analogous to that shown by Carlinfant (1948). The two lines are parallel, and the ratio of potency of the intramuscular to the subcutaneous route is 2.6 with 95% fiducial limits of 1.4 and 5.0; therefore the intramuscular route is definitely superior to the subcutaneous route.

encapsulation. Should this occur the antitoxin response curve to moderately large or large doses of P.T.A.P. or A.P.T. should show a peak value later than 28 days after injection. This was in fact found to be the case.

Three sets of figures are available on this point. The Schick conversion rates after a period of time were observed in children who had received intramuscular inoculations of 0.1 ml. A.P.T. (Lf 50), 0.5 ml. P.T.A.P. (Lf 200, 5 mg. AlPO_4 /ml.), and 0.5 ml. P.T.A.P. (Lf 190, 8 mg. AlPO_4 /ml.). In the case of the very small dose of A.P.T. the conversion rate showed a peak value at the sixth week, and in both cases of P.T.A.P.—where much more carrier was employed—the Schick conversion rate was still rising at the end of twelve weeks (Bousfield, 1947c). These observations show that conversion rates obtained four weeks after an intramuscular injection of P.T.A.P. would have been higher had the tests been carried out at a later date.

This conclusion, now referred back to Table II, means that in the case of the subcutaneous route the conversion rates found represent maximal ones and those for the intramuscular route submaximal.

From all these considerations it is concluded that the intramuscular inoculation of P.T.A.P. containing reasonably large amounts of mineral carrier results in a more complete utilization of the prophylactic than that following subcutaneous inoculation, with its early fibrous encapsulation of much of the material injected.

Optimal Amount of Mineral Carrier

In determining the optimal amount of mineral carrier to employ in young children it is not possible to substitute any animal for the child, and it would be unwise in our present state of knowledge to rely too much on investigations based on a weight-for-weight basis between animal and child. The results already published (Bousfield, 1947a) clearly demonstrate the great part played by the amount of carrier inoculated, and reveal that the best conversion rates are obtained with samples of P.T.A.P. containing 10–15 mg. AlPO_4 per ml. (see Table II). But to be able to say definitely that 15 mg. is better than 10 mg., or vice versa, involves two serious difficulties, as the percentage differences involved are very small. These difficulties are: (a) the rapidly increasing dose of antigen required to immunize the residual less responsive members of a population, and (b) because of this, the necessity for studying really large numbers of cases, if it is sought statistically to substantiate any conclusion drawn, when Schick conversion values greater than 90% are achieved.

With the limitations indicated above borne in mind, the evidence shown in Table VI strongly indicates but does not conclusively prove that P.T.A.P. containing 10 mg. AlPO_4 per ml. is better than an antigen containing 15 mg.

Essential Lf Dosage

In order to answer this problem it was considered necessary to use a rather longer time interval between inoculation and the post-Schick test. It was therefore decided to determine the Schick conversion rate three months after a single intramuscular inoculation of samples of P.T.A.P. each containing 15 mg. AlPO_4 /ml. and different amounts of purified toxoid. The figures obtained from a preliminary test were as shown in Table III.

TABLE III.—Schick Results

Toxoid Injected (Lf)	Three Months After One Intramuscular Injection of 0.5 ml.		
	(–)	(+)	S.C.R. (%)
5	114	6	95
10	123	2	98.4
15	118	5	96
20	124	1	99.2
30	120	4	96.77
Total ...	599	18	97

$$\chi^2 (5 \text{ Lf/the rest}) = 1.8, P = 0.2.$$

These results do not show any statistically significant differences.

This experiment was repeated. For the more recent trials, two similar series of preparations were used, and observations were made at three time intervals—three, six, and fifteen months after injection.

It is clear from the results shown in Table IV that, using a dose of 7.5 mg. of AlPO_4 , the same excellent responses were obtained with amounts of toxoid varying from 10 to 30 Lf. Even with 5 Lf of toxoid the response was not appreciably lowered.

Amounts of toxoid as low as 10 Lf/ml. gave results equally as good as those obtained from the amounts prescribed by the T.S.A. Regulations (50 Lf/ml.). It seems, therefore, that much of the toxoid demanded by the present regulations is wasted when used in P.T.A.P. This is a matter of no small importance economically when toxoid of the quality described is used.

Another point of importance arising from these findings is the persistence of the immunity induced by one dose of P.T.A.P., which suggests that we may in fact be in sight of a single-injection prophylactic against diphtheria.

TABLE IV.—Schick Conversion Rate after One Inoculation of 7.5 mg. of $AlPO_4$, with Varying Amounts of Purified Toxoid (Children Aged 1 Year at Time of Inoculation)

Lf Injected	Schick Failure Rate %		
	Material E.3061		
	After 3 Months	After 6 Months	After 15 Months*
5	5.0 (120)	4.0 (50)	4.08 (47)
10	1.6 (125)	4.1 (49)	4.08 (49)
15	4.06 (125)	1.9 (52)	1.75 (57)
20	0.8 (125)	5.6 (54)	4.76 (63)
30	3.23 (124)	1.8 (58)	3.64 (55)
	619 cases S.C.R. 97.08%	263 cases S.C.R. 96.7%	
Duplicate Material E.3143			
5	5.3 (75)		
10	2.6 (76)		
15	1.4 (72)		
20	1.3 (77)		
30	5.6 (71)		
	(371 cases, S.C.R. 96.7%)		
Materials E.3061 and E.3143 Combined			
5	4.8 (125)		
10	3.2 (125)		
15	1.6 (124)		
20	3.05 (131)		
30	3.9 (129)		
	(634 cases, S.C.R. 96.6%)		

Statistical Analysis of Results E.3061 and E.3143 Combined

χ^2	2.142	df	4	P	0.7
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The results are homogeneous, and no statistical difference exists between the several samples.

* This series, tested 15 months after a single inoculation, is obtained by retesting all the children available who were injected with batch E.3061 and found negative three months later. (Although the antigen in Schick toxin results in a definite second response effect, this is transitory and does not affect the immunity level when the tests are repeated 12 months later. This was shown by the study of a further 239 children, who received the same material and were not post-Schick tested until 12 months after the single inoculation. This group showed an overall conversion rate of 95.4%, which compares with an approximate 93.3% for the group (271 cases) which received the intermediate Schick test.) The findings thus represent the persistence rate of immunity in children who responded to a single inoculation. To get a true picture of the situation in such a group of children as is shown in the results of the three-months test in batch E.3061 at a period of 15 months (assuming that those who failed had not received a further inoculation), it is necessary to add the percentage of failures in the original group to the failures found 15 months after inoculation. If this is done one can say that the expectation in the five groups not post-Schick-tested for 15 months would be approximately:

5 Lf still Schick + at 15 months	9.1%
10 Lf " " " " "	5.7%
15 Lf " " " " "	5.8%
20 Lf " " " " "	5.8%
30 Lf " " " " "	6.9%

With the possible exception of the 5 Lf series, these figures would compare reasonably favourably with those obtained 15 months after the present routine two-injection treatment with A.P.T.

pH of P.T.A.P.

It was noted by Dr. W. B. Stott (M.O.H., Cuckfield) and one of us (G.B.) that during the injection of P.T.A.P. babies showed some signs of temporary discomfort. It was obviously desirable to rectify this if it could be done without affecting the efficiency of the prophylactic.

That the injection of P.T.A.P. in 0.5-ml. doses did cause some pain was confirmed by inoculating a number of adults. The pain, which was trifling and transient, was suspected to be due to the slight acidity of the prophylactic—pH 5–5.2. When the reaction was altered to pH 7, or even to pH 6, and again tested on adults, it was found that, apart from the needle puncture, the injection was painless. It became necessary, therefore, to determine the stability and efficiency of P.T.A.P. prepared in such a way that the final mixture was so nearly neutral that pain was avoided.

A quantity of P.T.A.P. was prepared containing 30 Lf of purified toxoid and 10 mg. $AlPO_4$ per ml.; one part was adjusted to pH 5 as usual and the other to pH 6.5. Both samples were then left at room temperature (20–22° C.) for six months and tested for potency by animal assay as follows: They were each diluted 1 in 60 with physiological saline, and 1-ml. quantities were injected subcutaneously into normal guinea-pigs.

The dose, therefore, was 0.5 Lf and 0.16 mg. of mineral carrier. The animals were bled four weeks later and the

sera from each group pooled. At the same time they were given a second identical inoculation. Two weeks later they were bled again, and the antitoxin titre of each serum was determined. The results obtained are shown in Table V.

TABLE V.—Animal Assay of Acid and Nearly Neutral P.T.A.P., Lf 30, 10 mg. $AlPO_4$ /ml. (Six Months Matured at Room Temperature)

Pig No.	Group A (P.T.A.P., pH 5)	Group B (P.T.A.P., pH 6.5)
	Mean Value 28 days after 1 dose	
	0.2 u./ml.	1.0 u./ml.
Individual Values 14 days after 2nd dose, u./ml. serum		
1	2.5	10
2	0.2	8
3	7.0	7
4	1.5	1.5
5	1.0	3
6	4.0	1.5
7	2.2	4
8	0.1	2
9	5.1	8
10	2	3
11	1.25	2.5
12	2	—
Arithmetic Mean	2.4	4.6
Geometric Mean	1.48	3.4

Statistical Analysis

$$t = \frac{\bar{x}}{\sqrt{\frac{s^2(n_1 + n_2)}{n_1 \cdot n_2}}} = 2.1$$

which, for 21 degrees of freedom, gives a P value of 0.05.

From the figures obtained it seemed probable that the prophylactic at a reaction of pH 6.5 was actually a better antigen than that at pH 5.

For the purpose of determining by *clinical trial* the relative efficiency of nearly neutral and acid P.T.A.P. three preparations were made: (a) P.T.A.P., Lf 30, 10 mg. $AlPO_4$ /ml., pH 6.5; (b) P.T.A.P., Lf 30, 15 mg. $AlPO_4$ /ml., pH 6.5; and (c) P.T.A.P., Lf 30, 10 mg. $AlPO_4$ /ml., pH 5. They were matured for six months at room temperature before use.

As before, Schick-positive children between their first and second birthdays were used. The dose administered was 0.5 ml. intramuscularly, and the Schick conversion rate was observed four weeks later. The "pain factor" was assessed on three grounds—"reaction" to (1) the needle-pain, (2) the actual pressing of the syringe plunger (the inoculation proper), and (3) duration of "reaction" after withdrawal of the needle.

These factors were assessed as carefully as possible and were recorded as +, ++, or +++. The total number of plus signs set down against each preparation was divided by the number of cases observed.

TABLE VI.—Comparison of P.T.A.P. at pH 5 and pH 6.5 (S.C.R. Observed Four Weeks After a Single Intramuscular Inoculation of 0.5 ml.)

Composition of P.T.A.P.			Post-Schick Results			
Lf/ml.	pH	$AlPO_4$ /ml.	(+)	(-)	S.C.R.	"Pain-factor"
A. 30	6.5	10 mg.	2	206	99.0	0.68
B. 30	6.5	15 mg.	10	181	94.8	0.65
C. 30	5.0	10 mg.	4	167	97.7	1.05

Statistical Analysis

I. Series A and B (comparison of the 10- and 15-mg. preparations at pH 6.5):

$$\chi^2 = 4.612; df = 1; P = < 0.05$$

(after Yates's correction for continuity, difference significant at the 5% level).

II. Series A and C (comparison of the pH 5 and pH 6.5 preparations):

$$\chi^2 = 1.47; df = 1; P = 0.25$$

The results, summarized in Table VI, show that there was a greatly reduced overall "reaction" to the pH 6.5

mixtures. Furthermore, they reveal that there was no reduction in potency when such mixtures were used—in fact, the results obtained with the 10 mg./ml. preparation were virtually perfect, and indicated that 10 mg./ml. of aluminium phosphate is optimal.

Résumé, and Conclusion Arising from Latest Findings

It is now four years since field trials on P.T.A.P. were begun. A number of important points had to be unequivocally established. It has been shown that in order to obtain the best results a far greater amount of carrier must be used than would be considered safe if presented as A.P.T. With these very large amounts of carrier the remarkable conversion rates of 97–99% following a single inoculation have been achieved, and this immunity has been shown to persist in 94% of the children for 15 months or more. Of equal importance is the virtual absence of local or general reactions; and not one child in over 6,000 inoculated developed a sterile abscess.

The work progressed in stages. Up to now the optimal amount of mineral carrier has been determined, the route of choice has been found, an approximation of the requisite quantity of purified toxoid has been made, and most of the discomfort of the earlier preparations has been abolished. Also, as a result of improved laboratory technique, the purity of the toxoid employed as routine procedure has been increased to 2,000 Lf/mg. p. N₂ (90% pure toxoid). Toxoid of this purity was used in all the more recent work described above.

On the basis of these findings the composition of P.T.A.P. now prepared is as follows:

AlPO ₄		10 mg./ml.
Toxoid:		
(a) amount		50 Lf per ml. (by law)
(b) purity		2,000 Lf/mg. p. N ₂
NaCl		0.85%
Preservative		0.01% sodium ethyl mercury thiosalicylate
Reaction		pH 6–6.5

The prophylactic is stored at room temperature for three to six months before issue.

Summary

Purified toxoid, aluminium phosphate precipitated (P.T.A.P.), is an accurately standardized diphtheria prophylactic, which in its antigenicity, stability, and freedom from reactions has distinct advantages over alum-precipitated toxoid (A.P.T.).

Study of the results obtained from experimental work and field trials shows that: (a) The optimal amount of mineral carrier for young children is 5 mg. AlPO₄, in a 0.5-ml. dose. (b) Intramuscular inoculations confer appreciably better immunity than do subcutaneous. (c) P.T.A.P. produces a definitely better Schick conversion rate than does A.P.T. A single inoculation of 0.5 ml. P.T.A.P. containing 10 or more Lf units of purified toxoid and 10 mg. AlPO₄ per ml. produces in children a Schick conversion rate of >95% one month after injection. At three and six months the S.C.R. is still over 95%, and has not fallen appreciably even after fifteen months. (d) P.T.A.P., adjusted to pH 6, is an antigen at least as efficient as the earlier more acid (pH 5) preparation, and causes less discomfort on inoculation.

The composition of P.T.A.P., as now prepared, is accurately described.

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A METHOD OF INCREASING THE LUNG BLOOD SUPPLY IN CYANOTIC CONGENITAL HEART DISEASE

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The purpose of this report is to describe an ancillary method of increasing the pulmonary blood supply in patients suffering from congenital cyanotic heart disease in whom the main defect is inadequate blood flow to the lungs. There are already two methods of increasing this blood supply. An anastomosis has been created between a systemic artery and one of the pulmonary arteries (Blalock, 1947; Potts and Gibson, 1948), and valvulotomy has been successfully practised in patients with valvular stenosis (Brock, 1948; Sellors, 1948).

These procedures have improved many seriously incapacitated children. Enthusiasm has been rekindled in a field in which endeavour had almost ceased, and physicians and surgeons have been brought together at a time when "progress" has often led to divergence of paths.

Theoretical Considerations

It has been found that anastomosis or valvulotomy may not be practicable or advisable in every case. There are patients in whom the pulmonary arteries may be absent or too small for any form of anastomosis. The Blalock type of operation may be impossible if the aortic arch lies at the base of the neck or if there is unusual aortic branching.

The clinical condition of some patients is so serious before operation that even the most skilled and experienced surgeon may hesitate to embark upon a procedure which may take many hours to complete. Conversely, some congenital cardiac deformities alter function to such a minor degree that it is unreasonable to undertake an operation of great magnitude. Therefore, if a simple operation could be devised which offered hope of amelioration it might serve a purpose in some cases.

It occurred to one of us (N.R.B.) that a simple alternative method of improving these patients might be to produce vascular pleural adhesions and so to bring blood into the lungs from the parietes. Attempts to revascularize the heart (by omentopexy and similar procedures) have been disappointing, but there are reasons for believing that success might be achieved if the same principles were applied to the lungs. These reasons are:

(a) Some children are born without pulmonary arteries and survive; thus blood from systemic collateral vessels can reach the alveoli.

(b) In patients suffering from pulmonary tuberculosis in whom an artificial pneumothorax has been induced and