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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REFERENCES

- Bousfield, G. (1947a). *Lancet*, **1**, 286.
 — (1947b). *Ibid.*, **2**, 867.
 — (1947c). *Publ. Hlth. Lond.*, **60**, 121.
 — Duke, H. L., et al. (1948). *Med. Off.*, **80**, 145.
British Medical Journal (1942). **1**, 734.
 Carlinfanti, E. (1948). *Lancet*, **2**, 629.
 Holt, L. B. (1947). *Lancet*, **1**, 282.

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

adhesions cauterized it is common to find blood vessels either in the middle of adhesions or, as isolated strands, spanning the pneumothorax from the parietes to the visceral pleura. These vessels carry blood from the extrapleural tissues to the lung and sometimes are the main blood supply to a diseased area: for instance, if vascular adhesions over a large tuberculous cavity situated near the edge of the lung are divided the peripheral wall of the cavity may slough.

(c) At thoracotomy performed on patients suffering from Fallot's tetralogy collateral vessels coming from the mediastinal, the phrenic, and the internal mammary arteries are often seen entering the hilum of the lung. It is well known that in some of these patients death may follow a thoracotomy when an anastomosis could not be achieved, and this may be due to severance of collateral vessels in the course of dissection.

With these points in mind, thoracotomies were performed upon two patients suffering from Fallot's tetralogy, and the experiences obtained gave clinical support to the proposition. The object was to perform a Blalock's operation, but in neither case could the operation be carried out.

The first patient was a small girl. The right chest was opened in the hope that the right subclavian could be anastomosed to the right pulmonary artery. Dense, diffuse vascular adhesions were found, and it was only after these had been divided that the hilum was reached and a very small pulmonary artery isolated. This artery was not clamped, but about twenty minutes later the child died, and at necropsy it was found that the left pleural cavity was obliterated by adhesions and that the left pulmonary artery was also diminutive. Death probably occurred because an important collateral circulation had been removed on the right side as the pleural adhesions were cut to expose the hilum.

The second patient was also a little girl. The aortic arch was high in the mediastinum, and the innominate artery came off so far towards the left side that it was anatomically impossible to approximate the right subclavian to the pulmonary artery. A good deal of dissection in the mediastinum was carried out before the attempt was abandoned, and in the end the mediastinal pleura was not closed because of oozing from the raw surface which was left. After the operation the parents were informed that nothing beneficial had been achieved or could be done; hence it was surprising to find a few months later that the girl was much improved. Before this operation she could walk only 40 to 50 yards (37-46 metres) before becoming severely dyspnoeic, whereas after operation she could walk a mile (1.6 km.). Since then a further operation has been performed on the left side and adhesions have been deliberately created. She can now walk three miles (4.8 km.), has given up her push-chair, and goes to an ordinary school. (See Case 1, below.)

Surgical Technique

After these experiences operations were developed expressly to create vascular adhesions, and they have been practised when, for the reasons already described, systemic pulmonary anastomosis or valvulotomy seemed to be impracticable. The ordinary methods of pleurodesis, such as the injection of a small amount of strong silver nitrate into the pleural cavity or insufflation of iodized talc, were not used, because it was felt that more effective blood vessels would be created if the surface of the lung was brought into direct contact with the vessels in the chest wall. For this reason the first cases were treated by opening both pleural cavities—at separate operations—and removing the parietal pleura from the upper mediastinum, from the dome of the pleura, and from the upper half of the chest. Powdered asbestos (0.4 g.) was

dusted on to the raw surfaces, the chest was closed, and, after instituting temporary drainage, the lung was completely re-expanded.

At each of these operations a fairly extensive examination of the anatomy of the congenital abnormality was undertaken and the pericardium was often opened, but in spite of this the children sustained the procedures well and there has been no mortality. The parietal pleura has not been stripped off the lower part of the chest and the diaphragm, because it was felt that this might reduce the vital capacity too much. We have found that bilateral excision of the pleura actually reduces the vital capacity by about 200 ml. in children under the age of 10 years.

Another type of operation to improve the circulation to the lungs has also been tried. The great omentum has been brought up into the chest and placed in contact with the left lung. The use of the omentum, although attractive in that it carries a large blood supply and can easily be transposed to the lung, is not without theoretical and practical disadvantages. Experience gained in the management of recent chest wounds has shown that whenever a knuckle of omentum passes through a small hole in the diaphragm a diaphragmatic hernia begins to form and steadily increases in size as more and more omentum is insinuated into the pleural cavity. Hence any method of bringing the omentum straight up through a convenient artificial hole in the diaphragm is certain to be complicated by the development of a diaphragmatic hernia. To overcome this the omentum has first been brought up into the upper part of the rectus sheath so that it lies immediately superficial to the muscle fibres of the transversus abdominis and deep to the rectus abdominis. From this point it has been introduced into the left pleural cavity by creating a tunnel in the tissues behind the costal margin and then spread out and stitched in the fissure between the upper and lower lobes of the left lung. As large a surface of the lung as possible has been brought into contact with the omental vessels. Powdered asbestos has been dusted on to the fissural surfaces of the lung before the omentum has been stitched into place.

Results

This communication is a preliminary report and is submitted because the surgery of congenital cyanotic heart disease is progressing so rapidly that ideas and experiences gained from a small group of patients may be useful stepping-stones to better surgical treatment.

Assessing results of operation is a matter of difficulty. The majority of "blue children" lead sheltered lives and their activity is restricted to a degree which is not commensurate with their ability. Hence a stay of a few weeks in hospital, where the services of physiotherapists and occupational therapists are available, almost invariably improves the morale of the patient and increases functional ability. The sensitive, uncommunicative child lying in bed with clubbed fingers hidden under the bedclothes soon becomes active, and tries to play games and to sit at table with the others for meals. These factors must be taken into consideration before increased exercise tolerance can be attributed to the beneficial result of any particular operation, but increased exercise tolerance is an important method of assessing any treatment and it is of course the criterion by which the patient and relatives judge improvement.

Estimations of arterial oxygen saturation provide evidence of improvement if the conditions under which the blood is taken remain comparable and the child is not upset by the procedure. Decrease of polycythaemia and oxygen capacity is good evidence of improvement if enough time is allowed for correction of post-operative anaemia.

Probably the most satisfactory objective evidence is obtained by the measurement of oxygen intake as a percentage of ventilation before and after a standard exercise according to the method of Cournand (Baldwin, Cournand, and Richards, 1948) and Bing (Bing *et al.*, 1947). From the results of this test the pulmonary blood-flow response to effort can be inferred.

In the following case histories it will be seen that only some of these tests have been carried out in the majority of the patients.

Case Histories

Case 1.—A girl aged 8 years suffered from the tetralogy of Fallot. She was very cyanosed and unable to walk up more than one flight of 12 stairs. She squatted frequently and the edges of her frock were soiled and torn. The oxygen capacity was 25.9 vols.%. The aortic arch was so high in the mediastinum that no systemic artery could be brought down to the pulmonary artery. At the first operation, in April, 1948, the right hemithorax and superior mediastinum were explored. No collateral vessels were found. Three months later she was able to walk one mile on the flat. In August, 1948, the upper half of the parietal pleura on the left side was removed and 0.4 g. of asbestos insufflated. By December, 1948, she could walk two to three miles (3.2 to 4.8 km.) on the flat, was able to climb 50 stairs without dyspnoea, and had ceased to squat. Her arterial oxygen saturation was then 80% at rest and 45% after walking up and down three flights of stairs. Oxygen capacity was 23.3 vols.%.

Case 2.—This patient, a girl aged 16 years, had been to an ordinary school but had to be taken there in an invalid chair. She subsequently worked as a bookbinder. She was able to lead only a sedentary life and could not walk up more than one flight of stairs or dance slowly more than once round a ballroom. She suffered from the tetralogy of Fallot, and before the first operation the resting arterial oxygen saturation was 78%. Oxygen capacity was 28.2 vols.%. It was felt that her disability was not of sufficient degree to warrant a major operation. Consequently in May, 1948, a right thoracotomy was performed. A few apical vascular adhesions were present, which were divided when the upper parietal and mediastinal pleurae were removed, and 0.4 g. of asbestos was insufflated over the exposed area. In October, 1948, the same procedure was carried out on the left side. By January, 1949, she was able to walk about 1½ miles (2.4 km.) on the flat and go up three or four flights of stairs, and had attended a dance "without anyone knowing there was anything wrong with me." Her arterial oxygen saturation was then 88% at rest and 60% after walking up three flights of stairs. Oxygen capacity was 23.4 vols.%.

Case 3.—A mentally retarded boy aged 13 years was suffering from pulmonary stenosis and an interventricular septal defect. He was very dyspnoeic after walking 50 yards (46 metres) and when in hospital squatted most of the time. The arterial oxygen saturation was 85% at rest. Oxygen capacity was 20.8 vols.%. Oxygen consumed per litre ventilated was at rest 33.5 ml., after standard exercise 26.7 ml. Carbon dioxide produced per litre ventilated was at rest 26.5 ml., after standard exercise 21 ml. In September, 1948, a right thoracotomy was performed. There were no adhesions and no visible collateral vessels. The upper halves of the parietal and mediastinal pleurae were removed and 0.4 g. of asbestos was insufflated. In November a similar operation was carried out on the left side and in addition an omental graft was brought up to the left lung. By January, 1949, he was able to run up and down six flights of stairs without undue dyspnoea and had entirely given up squatting. Arterial oxygen saturation was then 84.5% at rest and 62.1% after exercise. The oxygen capacity was 21.4 vols.%. Oxygen consumed per litre ventilated was at rest 30 ml., after standard exercise 36 ml. Carbon dioxide produced per litre ventilated was at rest 21.7 ml., after standard exercise 23 ml.

Case 4.—A well-developed girl of 12 years who had been blue from birth was proved by angiocardigraphy to have a common truncus arteriosus and absent pulmonary arteries. She attended an ordinary school and was able to walk about

440 yards (400 metres) slowly on the flat, but was very dyspnoeic after ascending three flights of stairs. The arterial oxygen saturation was 57.5% at rest and 44% after three flights of stairs. Oxygen capacity was 33.3 vols.%. Oxygen consumed per litre ventilated was at rest 18 ml., after standard exercise 14.5 ml. Carbon dioxide produced per litre ventilated was at rest 17.5 ml., after standard exercise 12.5 ml. In November, 1948, a left thoracotomy was performed and the absence of a pulmonary artery on the left side was confirmed. There were a large number of collateral vessels entering the hilum. Pleural adhesions were absent. The omentum was grafted into the interlobar fissure, and the upper half of the parietal pleura was removed, 0.6 g. of asbestos being insufflated over the raw surface. Three months later (i.e., after only one side of the chest had been operated upon) her exercise tolerance had increased by about 50%. The arterial oxygen saturation was then 73% at rest and 46% after three flights of stairs. Oxygen capacity was 25.9 vols.%. Oxygen consumed per litre ventilated was at rest 24.5 ml., after standard exercise 23 ml. Carbon dioxide produced per litre ventilated was at rest 22.7 ml., after standard exercise 18.8 ml.

Case 5.—A timid girl aged 10 years was suffering from Fallot's tetralogy and arachnodactyly. Her deformities were so great that she had been almost constantly bedridden. She became dyspnoeic after struggling along a few steps. Arterial oxygen saturation was 42% at rest. Oxygen capacity was 30.1 vols.%. In May, 1948, the right hemithorax was explored. The innominate artery bifurcated at the base of the neck, and an anastomosis using the right subclavian artery would have been very difficult. No adhesions were present, but there was some collateral circulation. A large area of parietal and mediastinal pleura was removed and 0.4 g. of asbestos insufflated. In August, 1948, a similar operation was performed on the left side. After many months in hospital she was educated to walk, and by January, 1949, she was able to walk about 50 yards unaided. Arterial oxygen saturation was 55% at rest. Oxygen capacity was 25.8 vols.%.

Case 6.—A mentally retarded boy aged 12 years was suffering from Fallot's tetralogy. He had attended an ordinary school, but since 1945 his activities had been so limited by dyspnoea that his attendances became very infrequent. He squatted a great deal and his maximum slow-walking distance was about 100 yards (92 metres). Oxygen capacity was 29.1 vols.%. In July, 1948, a right thoracotomy was performed. There were few collateral vessels and no pleural adhesions. The right subclavian artery was unsuitable for anastomosis because it came from the aortic arch distal to the left subclavian. The pulmonary arteries were very small. Accordingly the right parietal and mediastinal pleurae were extensively removed and 0.4 g. of asbestos was insufflated. A similar operation on the left side was carried out in September, 1948. When seen in February, 1949, he had ceased to squat and his range of activity had increased so that he could walk up 72 stairs or about 440 yards on the flat without discomfort. Oxygen capacity was 22.1 vols.%. His mother reported that she recently went to collect him at school in his wheel-chair, but he had run several hundred yards and arrived home before her.

Conclusion

Judged by clinical means, such as improved exercise tolerance, diminution of cyanosis, and less frequent squatting, it is considered that there have been two good results (Cases 1 and 3) and that three patients have shown considerable improvement (Cases 2, 4, and 6). One patient (Case 5), whose condition was complicated by arachnodactyly, has been educated to walk, but her skeletal deformity is so great that improvement is difficult to assess.

Of the four cases of which there are details of resting arterial oxygen saturation before and after operation significant improvement has occurred in three (Cases 2, 4, and 5) and no change in one (Case 3).

In six patients the blood oxygen capacity was measured before and after operation and was significantly decreased in four. One patient (Case 3), although clinically improved, showed no change in arterial oxygen saturation or oxygen

capacity, but his oxygen intake and carbon dioxide production, measured as a percentage of ventilation, changed from markedly abnormal to normal figures.

The results may be improved after a longer follow-up period than three to four months, but it is thought that as preliminary observations they are encouraging enough to warrant further application of the procedure to patients who for various reasons are unsuitable for the types of surgery already devised.

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REFERENCES

- Baldwin, E. de F., Cournand, A., and Richards, D. W. (1948). *Medicine*, **27**, 243.
 Bing, R. J., Vandam, L. D., and Gray, F. D. (1947). *Bull. Johns Hopk. Hosp.*, **80**, 107, 121, 323; and **81**, 192.
 Blalock, A. (1947). *Lancet*, **2**, 478.
 Brock, R. C. (1948). *British Medical Journal*, **1**, 1121.
 Potts, W. J., and Gibson, S. (1948). *J. Amer. med. Ass.*, **137**, 343.
 Sellors, T. H. (1948). *Lancet*, **1**, 988.

THE ASSOCIATION OF MATERNAL OBESITY, LARGE BABIES, AND DIABETES

BY

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The obstetric histories of the majority of diabetic women are characterized by an abnormally high foetal loss rate before the onset of clinical diabetes (Miller, Hurwitz, and Kuder, 1944; Miller, 1945; Henley, 1947; Gilbert and Dunlop, 1949). The foetal loss rate shows a progressive increase during this period, reaching a maximum in the immediately pre-diabetic phase, and is higher among women developing diabetes before the age of 45 than among those in whom the disease has its onset after this age.

Allen (1939), in reviewing the obstetric histories of diabetic women, noted that a high percentage of large babies were born many years before the onset of clinical diabetes. Further, Miller, Hurwitz, and Kuder (1944) report the incidence of babies with birth weights in excess of 11 lb. (5 kg.) to be as follows; non-diabetic women, 0.07%; pre-diabetic women, 3.9%; and diabetic women, 6.4%. Miller (1945, 1946) surveyed the birth weights of 22 babies born to 16 mothers who eventually developed diabetes after the age of 40. All deliveries were carried out in the hospital at which these women later sought treatment for their diabetes. Of the 22 babies three weighed 5 kg. (11 lb.) or more, six weighed 4.5 kg. (9.9 lb.) or more, and 15 weighed 4 kg. (8.8 lb.) or more. The number of babies in each weight group was 200, 27, and 7 times the expected incidence respectively, which led him to conclude that women developing diabetes after the child-bearing age are recruited almost wholly from the 5-7% of mothers giving birth to babies weighing more than 4 kg. (8.8 lb.). The recent publication of Kriss and Futcher (1948) confirms these observations. These workers report that 58% of their diabetic women had at some time prior to the onset of clinical diabetes given birth to at least one baby of 10 lb. (4.53 kg.) or more in weight. The average "latent period" between the birth of the first of such babies and the development of diabetes was 24.2 years.

Large babies were formerly attributed to maternal hyperglycaemia, resulting in the transfer of an excess of glucose to the foetus. Bill and Posey (1944), Bigby and Jones (1945), and Henley (1947), however, report the delivery of large babies in spite of well-controlled diabetes, and this has also been my experience.

White and Hunt (1943) and White (1946) conclude from observations of diabetic pregnancies that the unusually large babies are accounted for by an excess of chorionic gonadotropin.

Allen (1939) observed a relationship between excessive maternal gain in weight during pregnancy and the birth of large babies. Watts (1935) and others, who injected into pregnant rats what was at that time assumed to be anterior pituitary growth hormone, observed an unusual gain in maternal weight and in foetal size; such findings may in some measure explain Allen's observations. The report of Miller (1946) again suggests the importance of the growth hormone in the production of large babies: he drew attention to the similarity of the splanchnomegaly observed in the babies of diabetic mothers to that found in acromegalic patients.

Young has often stressed the relationship between the growth-promoting and the diabetogenic effects of anterior pituitary extracts. Thus in 1941 he reported that puppies treated for long periods with daily injections of diabetogenic pituitary extract failed to exhibit glycosuria as did adult dogs, but rapidly increased in weight. Diabetes did eventually develop, however, in some of the animals after many months' treatment. Further injections of the anterior pituitary extract produced only a diabetogenic effect, the growth-promoting influence having been lost. Lukens (1946) suggests that diabetes does not result from an excess of any one anterior pituitary hormone but from the combined oversecretion of both the growth and the adrenotropic hormones.

It is thus apparent that maternal obesity, an abnormally high foetal loss rate, and an unusually high incidence of large babies may occur many years before the onset of clinical diabetes, and that the investigation of women with such obstetric histories may show that a considerable proportion of them become diabetic in the course of time. Such a group of women form the basis of the present investigation.

Selection of Patients

Pre-diabetic foetal loss reaches a maximum during the two-year period immediately before the diagnosis of diabetes (Gilbert and Dunlop, 1949). It follows that some of the women who in 1941-3 had abnormal obstetric histories but showed no signs of diabetes might in 1948 have developed this disease.

The obstetric histories of 5,000 women confined in the Simpson Memorial Maternity Pavilion, Edinburgh, between August, 1941, and April, 1943, were therefore examined, and 150 of these were found to have unexplained histories of repeated abortions, miscarriages, intrauterine deaths, neonatal deaths, and babies weighing 10 lb. or more. Mimeographed forms asking for the results of all pregnancies since 1941-3 were sent to these women, but owing to the evanescent nature of Edinburgh's wartime population only 75 replies were received. Thirty-five of these gave histories of one or more normal pregnancies since 1941-3 and were therefore discarded from the investigation. The remaining 40 had either not been pregnant since 1941-3 or had had abnormal pregnancies. Of these it has been possible to examine 21 in hospital, the remaining 19 having declined admission owing to pressing domestic obligations.