THE SURGICAL TREATMENT OF MAL-FORMATIONS OF THE HEART

IN WHICH THERE IS PULMONARY STENOSIS OR PULMONARY ATRESIA

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Heretofore there has been no satisfactory treatment for pulmonary stenosis and pulmonary atresia. A "blue" baby with a malformed heart was considered beyond the reach of surgical aid. During the past three months we have operated on 3 children with severe degrees of pulmonary stenosis and each of the patients appears to be greatly benefited. In the second and third cases, in which there was deep persistent cyanosis, the cyanosis has greatly diminished or has disappeared and the general condition of the patients is proportionally improved. The results are sufficiently encouraging to warrant an early report.

The operation here reported and the studies leading thereto were undertaken with the conviction that even though the structure of the heart was grossly abnormal, in many instances it might be possible to alter the course of the circulation in such a manner as to lessen the cyanosis and the resultant disability. It is important to emphasize the fact that it is not the cyanosis, per se, which does harm. Nevertheless, since cyanosis is a striking manifestation of the underlying anoxemia and the compensatory polycythemia, a brief discussion of the causes of cyanosis and the factors operative in congenital malformations of the heart is essential in order to understand the principles underlying the present operation.

Cyanosis is due to the presence of reduced hemoglobin in the circulating blood. It is a well established fact that there must be at least 5 Gm. of reduced hemoglobin per hundred cubic centimeters of circulating blood for cyanosis to become apparent. It has long been recognized that one of the principal factors in the production of cyanosis in malformations of the heart is the direct shunting of venous blood into the systemic circulation. Lundsgaard and Van Slyke in their classicstudies on the causes of cyanosis showed that there were four important factors in the production of cyanosis: the height of the hemoglobin, the volume of the venous blood shunted into the systemic circulation, the rate of utilization of oxygen by the peripheral tissues and the extent of the aeration of the blood in the lungs. Their studies demonstrated the great importance of pulmonary factors. The extent of the oxygenation of the blood in the lungs clearly depends on the vital capacity of the individual, the rate of the flow of blood through the lungs, the partial pressure of the oxygen in the inspired air and also on specific pulmonary factors, which these authors designated as the α factor. These investigators showed that in most, if not in all, cases in which there was a pronounced polycythemia, secondary changes occurred in the lungs of such a nature that all of the blood that passed through the lungs was no longer in effective contact with the oxygen in the

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1. Lundsgaard, C., and Van Slyke, D. D.: Cyanosis, Medical Monographs, vol. 2, Baltimore, Williams and Wilkins Company, 1923.

alveoli. The importance of this factor can be demonstrated by the prolonged inhalation of oxygen. almost every case in which there is polycythemia, cyanosis can be greatly lessened by the prolonged inhalation of oxygen. The fact that all of the blood which circulated through the lungs is not fully oxygenated made it seem improbable that if more blood circulated through the lungs a larger proportion of the blood would be oxygenated. Thus the demonstration of the a factor completely overshadowed another vitally important factor, namely the volume of blood which reaches the lungs for aeration.1a

Expressed in the simplest terms, the circulation of the blood through the lungs after birth is essential for life; any one deprived of such circulation dies. Indeed there is a point at which, even though none of the other pulmonary factors are operative in the production of cyanosis and all of the blood that passes through the lungs is fully oxygenated, the volume of blood that reaches the lungs for aeration and hence the volume of oxygenated blood returned to the systemic circulation is insufficient for the maintenance of life. For example, in all cases of pulmonary atresia in which the circulation to the lungs is by way of the ductus arteriosus the closure of the ductus arteriosus renders the condition incompatible with life.

Undoubtedly the importance of the diminution of flow of blood to the lungs has not been fully appreciated, mainly because studies on the nature of cyanosis have been made on older children and young adults, and it is only when this factor is not of vital importance that the individual has survived to that age. All infants with pulmonary atresia with or without a right ventricle and with or without dextroposition of the aorta, in whom the closure of the ductus arteriosus cuts off the circulation to the lungs, die at an early age. In cases of complete pulmonary atresia death occurs before the complete cessation of circulation of blood through the lungs; hence in such cases there is always slight patency of the ductus arteriosus. In cases of a tetralogy of Fallot with an extreme pulmonary stenosis, the ductus arteriosus may become entirely obliterated before death.

There are two different types of congenital malformations which illustrate the importance of the volume of the pulmonary circulation in the production of cyanosis. The first is that of a single ventricle with a rudimentary outlet chamber in which it is common to find that one great vessel is given off from the common ventricle and one from the rudimentary outlet chamber. Usually the vessel which arises from the common ventricle is of normal size and that from the rudimentary outlet chamber is diminutive in size.2 If the great vessels occupy their normal positions, the aorta arises from the common ventricle and is of large caliber, whereas the pulmonary artery which arises from the rudimentary outlet chamber is of small caliber. Under such circumstances a large volume of blood goes to the systemic circulation and only a small volume of blood goes to the lungs. Consequently a large volume of unoxygenated blood is mixed with a small volume of oxygenated blood and cyanosis is intense.3 When, however, the great vessels are transposed and the pulmonary artery is large and the aorta is small, a large volume of blood goes to the lungs for aeration. Under these circumstances a large

The relative importance of this factor and of the α factor will be discussed in a forthcoming paper by Taussig and Blalock.
 Taussig, H. B.: Clinical Analysis of Congenital Malformations of the Heart, to be published by the Commonwealth Fund, New York.
 Taussig, H. B.: A Single Ventricle with a Diminutive Outlet Chamber, J. Tech. Meth. & Bull. I. A. M. M. 19: 120-127, 1939.

volume of oxygenated blood is mixed with a relatively small volume of venous blood and cyanosis is minimal or absent, as in the case reported by Glendy and White.4

The same phenomenon is also seen in cases of truncus arteriosus. When the pulmonary arteries are given off directly from the aorta there is adequate circulation to the lungs, and cyanosis is minimal or absent. In contrast to this, if the pulmonary artery fails to arise from the heart or connect with the aorta and the circulation to the lungs is by way of the bronchial arteries only a small volume of blood reaches the lungs for aeration, and cyanosis is intense.

The importance of adequate circulation to the lungs is further illustrated in the anomalies of the venous return in which all of the pulmonary veins drain into the right auricle; consequently within this chamber there is complete admixture of venous and arterial blood. In such cases a large volume of blood goes to the lungs for aeration and a large volume of oxygenated blood is

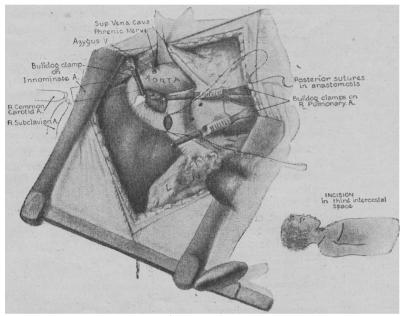


Fig. 1.—General exposure of the operative field on the right side. The end of the innominate artery is being anastomosed to the side of the right pulmonary artery. The posterior row of sutures is complete. The anterior row has not been inserted.

returned to the right auricle. There is great right-sided cardiac enlargement but no cyanosis until the terminal collapse of the circulation.6

These observations clearly indicate that many gross malformations of the heart are compatible with life provided there is adequate circulation to the lungs, and furthermore that lack of circulation to the lungs is the primary cause of death in many infants with congenital malformations of the heart. Furthermore, one of us (H. B. T.) has seen several infants with pulmonary stenosis in whom cyanosis was not apparent until the ductus arteriosus closed. In other words, there was no "visible" cyanosis while the circulation to the lungs was adequate. It was an appreciation of these facts (H. B. T.), together with an extensive previous experience with the experimental use of large arteries for the purpose of conducting blood to sites not usually supplied by such vessels, that led to the development of the clinical work recorded in this paper.

The feasibility of anastomosing a systemic artery to one of the pulmonary arteries in experimental animals has been demonstrated by Levy and Blalock.7 As far as we are aware, this was the first time that both the course and the function of a large artery were altered. Similar experimental alterations were produced subsequently by Eppinger, Burwell and Gross 8 and by Leeds.9 Blalock and Park 10 have reported the suturing of the severed proximal end of the subclavian artery to the aorta as a means for conducting blood beyond the point of an experimental coarctation of the aorta. In unreported observations by Kieffer and Blalock the divided proximal end of the splenic artery has been connected to the distal end of the divided left renal artery and there has been no evidence of renal failure even though the right kidney was removed. In other words, arterial anastomoses have been performed in

animals for the purpose of conducting blood to sites other than those ordinarily supplied

by these vessels.

Before undertaking the operations on patients, many experiments were performed in an effort to produce pulmonic stenosis in dogs. This work met with little success. Finally, in an effort to cause a significant decrease in the oxygen saturation of arterial blood, one or more lobes of the lungs were removed from each side of the chest, and the main arteries and veins of these lobes were connected end to end by suture. In other words, bilateral pulmonary arteriovenous fistulas were produced. These procedures resulted in some instances in a pronounced reduction in the oxygen saturation of the arterial blood. As the result of an artificial patent ductus arteriosus made in two such experiments, there was a significant increase in the arterial oxygen saturation. Although this experimentally produced condition is quite different from that seen in patients, it is of interest that the making of an anastomosis between systemic and pulmonary arteries caused an increase in the oxygen saturation of the arterial blood despite the

fact that several lobes of the lungs had been removed. Since the present operation was devised to compensate for an inadequate flow of blood to the lungs, it seemed desirable that the anastomosis be made in such a manner that the blood from the systemic artery would be able to reach both lungs. It is obvious that the suture anastomosis could not be made to the main pulmonary artery since occlusion of this vessel for more than a few minutes causes death. It appeared, therefore, that the anastomosis should be made just distal to the division of the main pulmonary artery and, furthermore, that the side of the chosen vessel should be used in order that the blood might flow to both lungs.

It was our original idea that the subclavian artery would be the ideal systemic vessel and that after division

^{4.} Glendy, Margaret M.; Glendy, R. E., and White, P. D.: Cor Biatriatum Triloculare, Am. Heart J. 28: 395-401, 1944.
5. Taussig, H. B.: Clinical Findings in Cases of Truncus Arteriosus, to be published.
6. Taussig, H. B.: Clinical and Pathological Findings in the Anomaly of Venous Return in Which All of the Pulmonary Venus Drain into the Right Auricle, to be published.

^{7.} Levy, S. E., and Blalock, A.: Experimental Observations on the Effects of Connecting by Suture the Left Main Pulmonary Artery to the Systemic Circulation, J. Thoracic Surg. 8: 525-530, 1939.

8. Eppinger, Eugene C.; Burwell, C. Sidney, and Gross, Robert E.: The Effects of the Patent Ductus Arteriosus on the Circulation, J. Clin. Investigation 20: 127-143 (March) 1941.

9. Leeds, S. E.: The Effects of Occlusion of Experimental Chronic Patent Ductus Arteriosus on the Cardiac Output, Pulse and Blood Pressure of Dogs, Am. J. Physiol. 139: 451-459 (July) 1943.

10. Blalock, A., and Park, E. A.: The Surgical Treatment of Experimental Coarctation (Atresia) of the Aorta, Ann. Surg. 119: 445-456 (March) 1944.

of this artery its proximal end should be anastomosed to the side of the left pulmonary artery. The fortunate experience to be reported in regard to the second patient has led us to prefer the use of the innominate artery in patients with a severe degree of anoxemia. This patient had a right aortic arch, and the innominate artery was directed to the left side of the chest and neck.

Although there were slight variations in each of the operations, the major features were as follows: Light general anesthesia was produced by the inhalation of ether or cyclopropane. The patient was placed on the table on his back with a slight elevation of that side of the chest which was to be exposed. The patient's arms were strapped in place along his sides. The opera-

tion was performed on the right or left side depending on the position of the great vessels and the artery to be used in the anastomosis. The incision was made in the third interspace and extended from the lateral border of the sternum to the axillary line. The pleural cavity was entered and the third and fourth costal cartilages were divided. A rib spreader was introduced and a good exposure of the upper half of the pleural cavity was obtained. This area is shown in figure 1. The right or left pulmonary artery was then exposed and the vessel was dissected from the adjacent tissues for as great a distance as possible. This was more difficult on the right side than on the left and it was necessary to ligate and divide the azygos vein and to retract the superior vena cava medially. Nothing further was done to the pulmonary artery at this time. Attention was then focused on the systemic artery which was to be anastomosed to one of the pulmonary arteries. The subclavian or innominate artery was dissected free of the adjacent tissues and the vessel chosen was occluded temporarily at the point where it arose from the aorta by the use of a bulldog arterial clamp. In cases in which the innominate artery was chosen, its branches (subclavian and common carotid) were ligated at their origins and the innominate artery was cut across just proximal to the ligatures. In the 1 case in which the left subclavian artery was used for the anastomosis to the pulmonary circulation it was necessary to divide the thyrocervical trunk, the vertebral artery and the internal mammary artery in order to gain access to a sufficient length of the vessel. After the

removal of some of the adventitia from the systemic vessel the pulmonary artery was further prepared for the anastomosis. A bulldog arterial clamp was placed on the left or right pulmonary artery just distal to the point of division of the main pulmonary artery. A second bulldog arterial clamp was placed on the left or right pulmonary artery just proximal to the point where the vessel gave off a branch to the upper lobe of the lung. A transverse opening was made into the side of the pulmonary artery approximately midway between these two arterial clamps. This opening was of about the same diameter as that of the end of the systemic vessel which was to be anastomosed to it. It must be emphasized that the pulmonary artery was

not occluded until all preparations for the anastomotic procedure had been made.

The anastomosis between the end of the systemic artery and the side of the pulmonary artery was carried out in the following manner: Fine silk on a curved needle was used as suture material. Before placing the posterior row of sutures, a stay suture was placed at one end. This was followed by the insertion of a running suture, which was not drawn taut until the greater part of the posterior row had been placed. The stay suture was then tied and the running suture was in turn tied to the stay suture. The posterior row was completed and was tied to another stay suture. The anterior row consisted of a simple through and through

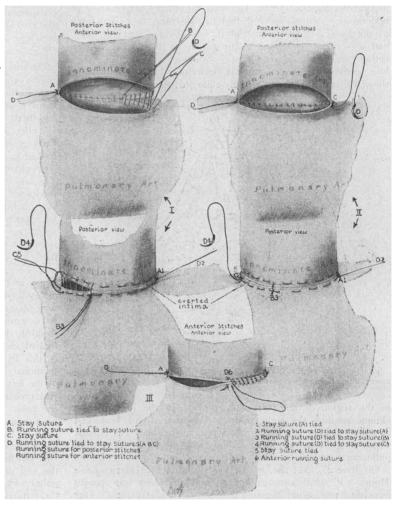


Fig. 2.—Details of the method by which the end of a systemic artery is anastomosed to the side of one of the pulmonary arteries.

continuous suture which approximated intima to intima. The anastomosis is shown diagrammatically in figure 2. The bulldog clamps were then removed from the pulmonary artery, and this was followed by removal of the clamp from the systemic vessel. If bleeding from the suture line did not cease spontaneously, it was stopped by the use of additional sutures. The lung was reexpanded and the incision in the chest wall was closed. Two encircling sutures of braided silk were used for approximating the third and fourth ribs. The soft tissues of the chest wall were closed in multiple layers with interrupted silk sutures.

There follows a detailed report of the 3 cases in which such an operation has been performed.

REPORT OF CASES

Case 1.¹¹—History.—E. M. S., a girl, was born prematurely in the obstetric service of the Johns Hopkins Hospital on Aug. 3, 1943. Her birth weight was 1,105 Gm. A systolic murmur was noted shortly after birth. Slight cyanosis was noted on the fourth and fifth days of life; this subsequently disappeared. The baby gained weight slowly and was finally discharged at 4 months of age weighing 2,900 Gm. After discharge the baby was followed in the dispensary. She was at first thought to have a simple interventricular septal defect, because the heart was normal in size and there was no cyanosis.

At 8 months of age the baby had her first attack of cyanosis, which occurred after eating. It was then for the first time that we thought she had a tetralogy of Fallot and not a simple interventricular septal defect. It soon became evident that cyanosis was increasing. It seemed probable that this increase in cyanosis was due to the fact that the ductus arteriosus was undergoing obliteration and thereby lessening the circulation to the lungs. By March 1944 it was obvious that the baby had a serious congenital malformation of the heart. After eating she would become deeply cyanotic, roll up her eyes, lose consciousness and appear extremely ill. Fluoroscopy showed that the heart was slightly enlarged; there was no fulness

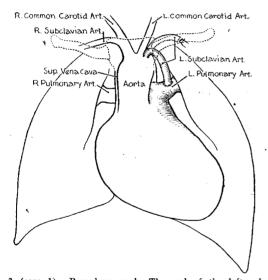


Fig. 3 (case 1).—Procedure used. The end of the left subclavian artery was anastomosed to the side of the left pulmonary artery.

in the region of the pulmonary conus. In the left anterior oblique position the right ventricle appeared slightly enlarged and the pulmonary window was abnormally clear. The clinical diagnosis was tetralogy of Fallot with a severe degree of pulmonary stenosis.

On June 25, 1944 she was first admitted to the Harriet Lane Home. Physical examination showed that she was poorly nourished and poorly developed. She had a glassy stare. Her lips were cyanotic. The heart was slightly enlarged and there was a harsh systolic murmur best heard along the left sternal border. The liver was at the costal margin. The baby was given oxygen and phenobarbital but remained very irritable and would become intensely cyanotic when taken out of the oxygen tent. During her three weeks' stay in the hospital she gained 200 Gm. and weighed 4.66 Kg. on discharge. She was sent home because it was felt that her condition was hopeless.

She was followed in the cardiac clinic for three months, during which time she showed increasing cyanosis and failed to gain weight. She was readmitted on October 17 because of increasing spells of cyanosis, coma and great venous distention of the head and body.

The weight on admission was 4.6 Kg. The venous distention was so great that the possibility of a subdural hydroma or hematoma was considered. Subdural tap was performed, with

the removal of 8 cc. of clear fluid from the right side and a small amount of bloody fluid from the left.

The size of the heart as seen in the anteroposterior view was essentially the same as noted previously. There was still a harsh systolic murmur. In the left anterior oblique position the contour of the heart appeared as a little round ball with a narrow aorta and a clear pulmonary window (fig. 4); this, we believe, is characteristic of a very severe tetralogy of Fallot with a functional pulmonary atresia, that is, a pulmonary stenosis which is so extreme that the condition is not long compatible with life. It was questioned at that time whether in addition to the malformation of the heart she suffered from mental retardation.

During the next six weeks she refused most of her feedings; she lost weight and just before operation weighed only 4 Kg. The red blood cell count, which had been 7,000,000 on admission, had fallen to 5,000,000. Cyanosis was proportionally less conspicuous; indeed, at times while lying quietly, cyanosis was not visible. The clinical diagnosis was again tetralogy of Fallot which was so severe that the baby's condition was becoming critical.

Operation.—This was performed on November 29. The procedure consisted in the anastomosis of the divided proximal end of the left subclavian artery to the side of the left pulmonary artery, as shown diagrammatically in figure 3. The anesthetic agent was administered by Dr. Merel Harmel.

Under ether and oxygen anesthesia, administered by the open method, an incision was made on the left side of the chest extending from the edge of the sternum to the axillary line. The pleural cavity was entered through the third interspace. The left lung appeared normal. No thrill was felt on palpating the heart and pulmonary artery. The left pulmonary artery was identified and was dissected free of the neighboring tissues. It appeared to be of normal size. The superior pulmonary vein, on the other hand, seemed considerably smaller than normal. The left subclavian artery was identified and was The left subclavian artery was identified and was dissected free of the neighboring tissues. In order to secure access to a sufficient length of this vessel it was necessary to ligate and divide the vertebral artery, the internal mammary artery and the thyrocervical axis. A bulldog arterial clamp was placed on the subclavian artery at a point just distal to its origin from the aorta. The subclavian artery was ligated distal to the point at which the thyrocervical trunk had been ligated and divided, and the vessel was cut across just proximal to this ligature. Two bulldog clamps were placed on the left pulmonary artery, the first clamp being placed at the origin of the left pulmonary artery and the second clamp being placed just proximal to the point where the pulmonary artery entered the lung. There was ample space between these two clamps for our purpose. A small transverse incision was made in the wall of the pulmonary artery at a point approximately equidistant between the two clamps. By the use of china beaded silk on fine needles an anastomosis was performed between the end of the left subclavian artery and the side of the left pulmonary artery. There was practically no bleeding following the removal of the clamps.

From a technical point of view the anastomosis seemed to be satisfactory. The main cause for concern was the small size of the left subclavian artery. It was somewhat disturbing that one could not feel a thrill in the pulmonary artery. We were confident, however, that the anastomosis was patent. A small quantity of sulfanilamide was placed in the left pleural cavity and the incision in the chest wall was closed. The patient was given 200 cc. of isotonic solution of sodium chloride and 50 cc. of blood during the operative procedure. The operation required slightly less than an hour and a half and the left pulmonary artery was occluded for approximately thirty minutes. The patient's condition at the end of the operation seemed moderately good.

Postoperative Course.—This was stormy. The patient's left arm and hand were observed frequently. The radial pulse was not palpable and this extremity was cooler than the opposite one, but it was apparent that the circulation was adequate to maintain life of the part. The child suffered from repeated bilateral pneumothoraces, and frequent aspirations were required.

^{11.} This case was discussed briefly at the meeting of the Southern Surgical Association, Dec. 5, 1944, in a paper by Dr. Arthur Blakemore,

Probably the pneumothorax on the right was due to the use of too great pressure in the reexpansion of the left lung at the completion of the operative procedure. As it was found to be a positive pressure pneumothorax, constant suction was exerted through a needle inserted into the right pleural cavity. Had it not been for the excellent care given by the pediatric house staff, particularly Dr. Kaye, Dr. Whitemore, Dr. Steinheimer, Dr. Hammond, Dr. Gilger and Dr. Helfrick, in all probability the child's life would not have been saved.

The child's condition began to improve two weeks after operation. Thereafter further aspirations of the pleural cavity were not required. The occasions on which the patient would become cyanotic became less frequent. Otitis media developed and responded to treatment. The systolic murmur became somewhat louder, but a continuous murmur could not be heard in the pulmonary area.

The patient was discharged from the hospital on Jan. 25, 1945, almost two months after the day of operation. Her condition was considerably better than it had been before operation. More recent follow-up studies have shown that she is gaining weight and that she is only occasionally cyanotic. If the cyanosis increases, it may be necessary to perform a similar operation on the opposite side. Roentgenograms of the patient's heart both before and after operation are shown in figure 4.

It is unfortunate that we do not have a quantitative degree of improvement such as might have been afforded by determinations of the oxygen saturation of the arterial blood. In

view of the small size of the child we did not feel warranted in doing arterial punctures. The clinical improvement, however, has been striking. The baby takes her feedings well, is alert and active and has gained a kilogram in weight (that is, 25 per cent of her former body weight).

Case 2.—History.—B. R., a white girl born July 9, 1933, was first seen at the Harriet Lane Home at 9 years of age, referred by Dr. Dexter Levy of Buffalo. The patient was cyanotic at birth. The birth weight was 6½ pounds (2,955 Gm.). She was breast fed for six months. In infancy she gained extremely slowly. She

had erysipelas at $1\frac{1}{2}$ years of age, a septic sore throat at $4\frac{1}{2}$ years of age, chickenpox at 7 years, measles at 8 years and mumps at 9 years.

The patient was first seen in the Harriet Lane Home on Feb. 13, 1943. She was intensely cyanotic, became dyspneic on slight exertion and would constantly squat to get her breath. There was intense cyanosis and clubbing of the fingers and the toes. The buccal mucous membranes were of a deep mulberry color. There was suffusion of the conjunctiva. The chest was barrel shaped. Her heart was within normal limits in size. There was no thrill over the precordium. On auscultation there was a harsh systolic murmur which was maximal low down in the third and fourth interspaces. The murmur was much louder in the recumbent position than in the erect position, and louder when she bent forward than when she tried to sit erect. The murmur was not widely transmitted and was not audible in the back. The second sound at the base was pure. The lungs were clear. The liver was at the costal margin and the spleen was not palpable. The femoral arteries were readily palpable. The extremities, as previously mentioned, showed intense cyanosis and pronounced clubbing. At this time she climbed half a flight of stairs and walked, almost ran, leaning forward, 60 feet to her room, and then fell forward on the bed and lay in a knee-chest position, panting heavily and without speaking for half an hour.

The red blood cell count was 8,700,000; the hemoglobin was 25 Gm.; the hematocrit reading was 78.

The electrocardiogram showed a normal sinus mechanism, PR interval of 0.16 second, normal upright T waves in all four leads, and considerable right axis deviation.

X-ray examination and fluoroscopy showed the heart to be of normal size with a concave curve at the base to the left

of the sternum (fig. 6). To the right of the sternum the superior vena cava cast a wide ribbon-like shadow. After the administration of barium, the aorta was seen to indent the esophagus to the left on its right margin. Examination in the left anterior oblique position showed that the right ventricle was not greatly enlarged; indeed, the left ventricle appeared larger than the right ventricle. The esophagus was seen to be indented by the aorta in the left anterior oblique position; in the right anterior oblique position its descent was independent of the aorta. There was no enlargement of the left auricle.

The clinical diagnosis was an extreme tetralogy of Fallot with a right aortic arch.

On Jan. 6, 1945 the patient returned for a check-up and because her parents wished to discuss the possibility of operation. The physical findings were essentially the same as previously noted but she was even more severely incapacitated. She could not walk 30 feet without exhaustion, and she panted when she moved from a wheel chair to the examining table. The fluoroscopic findings were essentially the same as noted previously except that the shadows at the hili of the lungs were more conspicuous. There were, however, no pulsations visible in this region.

The patient returned on January 29. Studies on the arterial blood are recorded in table 1.

A sample of venous blood showed that the red blood cell count was 7,500,000, the hemoglobin was 24 Gm., the hematocrit

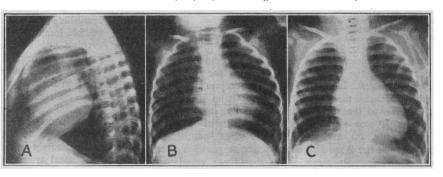


Fig. 4 (case 1).—Appearance before and after operation: A, left anterior oblique view before operation; B, anteroposterior view before operation; C, anteroposterior view after operation.

reading was 71 (Wintrobe) and the white blood cell count was 5,200. The electrocardiogram was essentially the same as that taken in 1943. A roentgenogram of the heart showed a small heart with a right aortic arch. The maximal right diameter was 4 cm. and the maximal left was 7 cm. The total transverse diameter was 26 cm. The cardiothoracic ratio was 42.4.

Operation.—This was performed on February 3. The procedure consisted in anastomosing the divided proximal end of

Table 1.—Studies on Arterial Blood (Case 2)

Dates	Arterial Oxygen Content, Volumes per Cent	Arterial Oxygen Capacity, Volumes per Cent	Arterial Oxygen Saturation, per Cent	Arterial Car- bon Dioxide Content, Volumes per Cent
2/ 1/45	11.7	32.3	36.3	34.9
2/ 3/45	Innominate a	rtery anastom	osed to left pu	lmonary artery
2/12/45	20.3	27.5	73.8	37.8
3/ 1/45	19.8	23.9	82.8	37.2

the innominate artery to the side of the left pulmonary artery. This is shown diagrammatically in figure 5. The anesthetic agent was administered by Dr. Austin Lamont.

Cyclopropane with a high percentage of oxygen was administered through an endotracheal tube. The incision extended from the left costal margin to the anterior axillary line. The pleural cavity was entered through the third interspace. There were no adhesions between the lung and the chest wall, and the lung looked normal. Although the surgeon had been informed by his pediatric colleague that this patient almost

certainly had a right aortic arch, no special thought was given to the fact, and it caused some surprise when it was noted that the aorta was not on the left side. It was fortunate, however, that the incision had been made on the left because this allowed the use of the innominate artery rather than the subclavian artery. There was a very tortuous artery, which

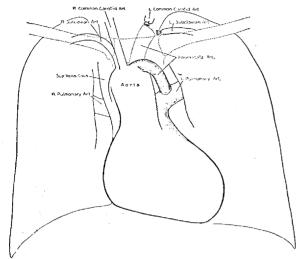


Fig. 5 (case 2).—Procedure used. The patient had a right aortic arch, and the innominate artery was directed to the left. The end of the innominate artery was anastomosed to the side of the left pulmonary artery.

was lying anterior to the vertebral column and which appeared to run from the region of the hilus of the lung toward the upper part of the left pleural cavity. Compression of this vessel indicated that the blood was flowing from above downward. It is believed that this vessel was a large accessory bronchial artery. It was estimated that the lumen of this artery was approximately 3 mm. in diameter. Still another abnormal finding was the large size of the posterior portions of the intercostal arteries. It seems likely that these vessels were also supplying blood to the hilus of the lung. The evidence of extensive collateral circulation led us to believe that we were probably dealing with a case of complete pulmonary atresia.

The innominate artery was located and dissected free of the surrounding tissues. The encouragement of the first assistant, Dr. William Longmire, played no small part in the continued effort to find a large systemic artery. A bulldog arterial clamp was placed on the innominate just distal to its origin from the aorta. The subclavian and common carotid arteries were ligated near their points of origin from the innominate. The innominate artery was divided just proximal to these ligatures. It was estimated that the diameter of the lumen of the innominate artery was approximately 1.3 cm. The left main pulmonary artery was then prepared for the anastomosis. A bulldog clamp was placed just distal to the origin of this vessel from the main pulmonary artery, and a second clamp was placed proximal to its entrance into the lung. A transverse opening was made into the lumen of the vessel midway between the two clamps. A suture anastomosis was performed between the end of the innominate artery and the side of the left pulmonary artery. The length of time that the left pulmonary artery was occluded was fifty to sixty minutes. The bulldog clamps were removed. There was bleeding from one point, which was controlled by an additional suture. An easily palpable thrill was felt in the pulmonary artery both proximal and distal to the anastomosis. The pulmonary artery seemed to be considerably larger than before this new current of systemic blood was admitted to it. The systemic arterial pressure was 110 systolic and 70 diastolic at the time that the arterial clamps were removed. Immediately following the removal of the clamps the systemic pressure declined 30 mm. of mercury. followed a rise in systolic pressure of 20 mm. of mercury, but the pressure then declined gradually during the next thirty minutes until it reached 60 systolic and 30 diastolic. The pulse rate during this time rose from 72 to 120 per minute.

After the completion of the anastomosis and the removal of the clamps, several grams of sulfanilamide were placed in the pleural cavity. The left lung was partially inflated by the use of positive pressure, and the incision in the chest wall was closed. The patient was given a slow continuous intravenous drip of isotonic solution of sodium chloride during the operation and her condition at the end of the operation appeared to be satisfactory.

The operation required two hours and forty minutes. A considerable part of this time was consumed in studying the tortuous vessel which was seen above the hilus of the lung and also in trying to locate the innominate artery.

The patient awakened from the anesthesia a short time after the closure of the incision. She could move the left arm without difficulty. The left arm and hand were slightly cooler than the right, but it was evident that the circulation was adequate to maintain life. There was no evidence of a cerebral disturbance as the result of the ligation of the common carotid. No pulse could be felt in the left arm or the left side of the neck and face.

Postoperative Course.-This was smooth. There was no vomiting following operation, and fluids were taken by mouth. She was placed in an oxygen tent. The administration of penicillin was started immediately after operation and was continued for nine days. The left pleural cavity was aspirated twenty-four hours after operation; 250 cc. of air and 70 cc. of blood were removed. There were no other thoracenteses. Although a thrill was palpable at the site of the anastomosis immediately on release of the bulldog clamps, no murmur was audible immediately after the chest was closed. By the second evening a faint diastolic murmur was audible over the base and at the apex. By the third postoperative day an extraordinarily loud continuous murmur was audible throughout the chest on both the right and the left side. The oral administration of dicumarol was begun on the fourth postoperative day; 50 to 200 mg. was given daily for several weeks. Prothrombin determinations were performed daily. The dose of dicumarol was such as to keep the clotting time of the patient's blood approximately twice that of the normal control.

Femoral arterial punctures were performed on the ninth and twenty-sixth postoperative days. The results of the analyses are given in table 1. Before operation the red blood cell count was 7,500,000, the hemoglobin 24 Gm. and the hematocrit reading 71. Three days after operation the red blood cell count had decreased to 6,000,000, the hemoglobin to 19 Gm. and the hematocrit reading to 61. By the twenty-first day the red blood cell count was 6,000,000, the hemoglobin was 17.5 Gm. and the hematocrit reading was 55.

A roentgenogram of the heart taken ten days after operation showed that the heart had increased in size; that taken twenty-one days after operation revealed no further increase in size.

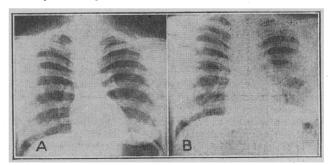


Fig. 6 (case 2).—Heart A, before operation and B, one month after operation.

Indeed, the heart was a trifle smaller than on the previous date. Roentgenograms of the heart before and after operation are shown in figure 6. Before operation the cardiothoracic ratio was 42.4 and three weeks after operation it was 44.7. The electrocardiogram showed no change (fig. 7). The stethocardiogram showed a continuous murmur (fig. 8). There was a significant increase in the pulse pressure. The preoperative arterial pressure had been 110 systolic and 90 diastolic. On

the thirty-seventh postoperative day the arterial pressure was 98 systolic and 66 diastolic.

An appreciable diminution in the cyanosis of the lips and fingernails was apparent several days after operation. The patient was allowed to walk, beginning two and a half weeks after operation. This exercise resulted in a slight increase

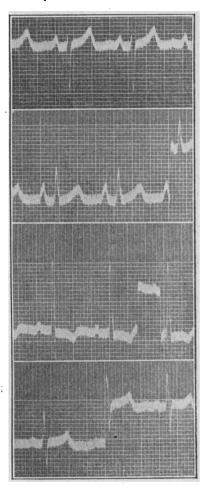


Fig. 7 (case 2).—Electrocardiogram.

in the cvanosis, but it was evident that cyanosis was much less than it had been preoperatively. By the end of the third week she could walk 60 feet in an erect posture without panting, whereas before operation, stooping and leaning forward, she could walk only 30 feet and would then stop and pant. There has been a slow but steady recession of the clubbing of the fingers and toes. The patient was discharged from the hospital on the thirty-eighth postoperative day.

Case 3.—History.—
M. M., a boy born
July 15, 1938, was first
seen at the Harriet
Lane Home at 8
months of age with
the complaint of heart
trouble.

The family history is of importance in that the maternal grandfather was known to have heart trouble and had had a heart murmur throughout his life. The mother's brother

The mother's brother and sister are both reported to have dextrocardia; both have refused examination.

The past history stated that the patient was a full term baby. The birth weight was 6½ pounds (2,955 Gm.). Development was slow; he held his head up at 5 months and sat alone at 6½ months. At 8 months the patient weighed 13½ pounds (6 Kg.). When lying quietly he showed slight persistent cyanosis, which became intense when he cried. On examination of the heart there was no thrill but a very definite systolic murmur, which was audible all over the precordium and well heard in the back. Fluoroscopy showed that the heart was within normal limits in size. There was a wide shadow above the heart which was interpreted as a large thymus. There was no fulness of the pulmonary conus, and the shadow at the base of the heart was concave. The clinical diagnosis was tetralogy of Fallot.

The patient was followed in the cardiac clinic until January 1940, when the family moved to California. They returned to Baltimore in the fall of 1944 and the patient was again brought to the clinic on September 29. At that time the boy, 6 years of age, was thin and undernourished, intensely cyanotic and dyspneic on slight exertion. The temperature was 99.2 F., weight 34½ pounds (15.6 Kg.), height 42 inches (107 cm.), pulse 140, respirations 20 and blood pressure 90 systolic and 60 diastolic.

There was manifest suffusion of the conjunctiva. The lips were purple and the buccal mucous membranes were a deep mulberry color. The teeth were in bad condition; the tonsils

were not unduly enlarged. The chest was barrel shaped. The increase in the size of the heart was in proportion to the growth of the child. There was a systolic thrill at the apex and a harsh systolic murmur, which was maximal along the left sternal border in the third interspace. The second sound at the base of the heart was clear but not accentuated. The lungs were clear. The liver was at the costal margin; the spleen was not palpable. The femoral arterial pulsations were easily felt. The extremities showed deep cyanosis and pronounced clubbing. Although the patient had learned to walk by November 1944, he was so incapacitated that he was unable to walk and even refused to try to take a few steps. The diagnosis was tetralogy of Fallot with a severe degree of pulmonary stenosis.

The patient was referred to the dental clinic, where several teeth were extracted. Sulfadiazine was given for two days. One month later the patient returned to the cardiac clinic with a rectal temperature of 100.4 F. and with numerous petechiae on his legs, which the mother said were of two days' duration. A blood culture taken at this time was sterile and no further petechiae appeared.

Table 2.—Studies on Arterial Blood (Case 3)

Dates	Arterial Oxygen Content, Volumes per Cent	Arterial Oxygen Capacity, Volumes per Cent	Arterial Oxygen Satu- ration, per Cent	Arterial Carbon Dioxide Content, Volumes per Cent	Comment
2/ 8/45	7.3	31.2	23.4	27.5	Patient struggling
2/ 9/45	10.7	30.2	85.5	29.3	Patient quiet
2/10/45	Innomin	ate artery a	nastomose	d to right	pulmonary artery
2/19/45	17.7	22.2	79.7	37.4	Patient crying
3/ 6/45	17.7	21.1	83.8	35.2	Patient quiet

The family was desirous of prompt operation and the patient was admitted to the hospital on Feb. 7, 1945. The results of analyses of blood obtained by arterial puncture are shown in table 2. With venous blood the red blood cell count was 10,000,000, the hemoglobin 26 Gm. and the hematocrit reading 81. The patient continued to have a daily elevation of temperature.

An electrocardiogram showed a normal sinus mechanism, a normal PR interval of 16, high P waves in L₂, and normal upright T waves in leads 1, 2 and 4, and T₃ inverted and an apparent right axis deviation.

X-ray examination (fig. 10) showed that the maximal right diameter of the heart was 2.1 cm., the maximal left 7 cm. and the total transverse diameter 18.8 cm.; the cardiothoracic ratio was 47.5. There was no fulness of the pulmonary conus. Fluoroscopy showed that the aorta descended on the left, and there were no visible pulsations in the lung fields.

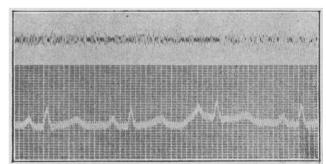


Fig. 8 (case 2).—Stethocardiogram.

Operation.—This was performed on February 10. The procedure consisted in anastomosing the divided proximal end of the innominate artery to the side of the right pulmonary artery. This is shown diagrammatically in figure 9. The anesthetic agent was administered by Dr. Merel Harmel.

Anesthesia was produced by cyclopropane with a high concentration of oxygen. It is of interest that the patient's color was much better under anesthesia than it had been previously.

This patient did not have a right aortic arch. In view of the great improvement in the second case we wished to use the innominate artery, and therefore the incision was made on the right side. There were no adhesions between the lung and the chest wall, and the lung appeared normal. The right upper lobe was retracted downward and the azygos vein was visual-

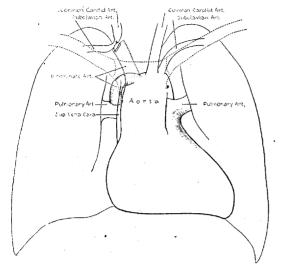


Fig. 9 (case 3).—Procedure used. The end of the innominate artery was anastomosed to the side of the right pulmonary artery.

ized. It was doubly ligated and divided. The superior vena cava and phrenic nerve were retracted medially, and the artery to the right upper lobe of the lung was seen. This was followed medially and the main right pulmonary artery was exposed. This exposure was considerably more difficult than that on the left side. Attention was then turned to the innominate artery. By dissecting under and medial to the superior vena cava the innominate artery was exposed and was dissected free of the surrounding tissues. This vessel was occluded temporarily by the use of a lung tourniquet which was equipped with a catheter overlying a piece of braided silk. The subclavian artery and the common carotid artery were ligated just distal to their origins from the innominate artery. The innominate artery was cut across proximal to these ligatures. Two bulldog clamps were placed on the right main pulmonary artery, and a transverse incision was made into the vessel between these clamps. The proximal bulldog clamp was not of sufficient length to secure entire control of the flow of blood. This resulted in a moderate loss of blood, and another clamp was substituted

With 5-0 silk on a small curved needle an anastomosis was made between the divided proximal end of the innominate artery and the side of the right main pulmonary artery. This anastomosis was more difficult than that in the previous cases because the exposure was less satisfactory. Following the removal of the bulldog clamps from the pulmonary artery there was a rather copious flow of blood from one point along the anterior row of sutures. The clamps were reapplied, and this opening was closed with a mattress suture. Subsequent removal of the clamps did not result in further bleeding. The patient's condition up to the time of this blood loss had been excellent. Occlusion of the right pulmonary artery had not seemed to increase the cyanosis. There was an increase in the cyanosis and a decline in pressure when this loss of blood occurred. It was estimated that at least 250 cc. of blood was lost.

The anastomosis seemed to be a satisfactory one. An easily palpable thrill could be felt in the pulmonary artery both proximal and distal to the anastomosis. It was estimated that the lumen of the innominate artery was slightly less than 1 centimeter in diameter. The right lung was partially inflated and the incision in the chest wall was closed.

The patient received 500 cc. of a mixture of isotonic solution of sodium chloride and glucose and 200 cc. of plasma during the operative procedure. The operation required a total of three hours, the greater part of this time being consumed in

making the anastomosis. It was obvious that a better instrument for occluding the pulmonary artery proximal to the site of the anastomosis is needed. The right pulmonary artery was occluded for approximately ninety minutes.

The patient's condition at the completion of the operation was very good. He was conscious a few minutes after the incision had been closed, was asking for water and was moving his right arm. This arm was slightly cooler than the left. Pulsations could not be felt in the right arm or in the right side of the neck and the face. There was, however, no evidence of cerebral damage, and it was obvious that the circulation of the arm was adequate to maintain life.

Postoperative Course.—This was remarkably smooth. The patient was placed in an oxygen tent for several days. The circulation to the right arm remained adequate. Aspiration of the chest was not necessary. Immediately after operation the child's color improved. It was seen on the fourth post-operative day when the administration of oxygen was discontinued that the cyanosis of the lips had disappeared. The cyanosis of the fingertips decreased more slowly. The administration of penicillin was started the day before the operation and was continued for three weeks postoperatively. Dicumarol was given by mouth, beginning on the third postoperative day. The usual daily administration was 25 mg. Prothrombin determinations were performed daily, and the drug was continued for three weeks.

Although a thrill was palpable at the site of the anastomosis after the arterial clamps had been released, no murmur was audible immediately after the chest had been closed. By the first evening a faint murmur was audible, which gradually increased in intensity. By the fourth postoperative day a continuous murmur was audible over the site of the anastomosis and posteriorly throughout both lungs.

The child's compensation has remained excellent. In contrast to a preoperative arterial pressure of 85 systolic and 65 diastolic, the arterial pressure postoperatively was usually 106 systolic and 52 diastolic. The heart increased somewhat in size during the first ten days after operation, but there did not appear to be a further increase in the subsequent two weeks. Roentgenograms of the heart both before and after operation are shown in figure 10.

Arterial punctures were performed on the 9th and 24th postoperative days. The results of the analyses are given in table 2. On comparing the preoperative studies with those performed twenty-four days after operation, samples of venous blood showed that the red blood cell count decreased from 10,000,000 to 6,000,000, the hemoglobin from 26 to 20 Gm. and the hematocrit reading from 81 to 53 (Wintrobe).

The patient had had a preoperative daily elevation of temperature to 100 F., and this continued for three weeks after operation. For this reason he was not allowed out of bed

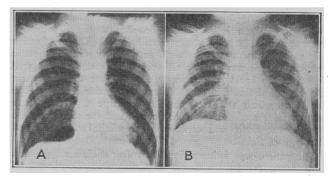


Fig. 10 (case 3).—Heart A, before operation and B, two weeks after operation.

despite his vigorous protests until three and a half weeks after operation. When permitted to do so, the child walked 40 feet with ease. He was then allowed to be up for several hours each day and has walked and played in his room. He did not develop either cyanosis or dyspnea on this activity. The patient was discharged from the hospital on the thirty-eighth postoperative day.

COMMENT

Each of these 3 patients suffered from such a severe degree of pulmonary stenosis that there was inadequate circulation to the lungs. Although the three operations differed in detail, in each instance the operation greatly increased the volume of blood which reached the lungs.

In the first case the end of the left subclavian artery was anastomosed to the side of the left pulmonary artery. As the baby was small and weak, extensive laboratory studies were not performed. Before operation the baby had been steadily losing ground. She had ceased to be able to sit alone; she had refused her feedings and had lost weight. The red blood cell count had declined from 7,000,000 to 5,000,000; consequently the cyanosis had diminished considerably. After operation her clinical improvement was remarkable. The appetite improved, she gained weight and she is now starting to learn to walk.

The second patient had a right aortic arch; hence it was possible to anastomose the innominate artery to the left pulmonary artery. The patient was deeply cyanotic and severely incapacitated and could not walk 30 feet without panting. Two and a half weeks after operation she walked 60 feet, rested a short time and walked 60 feet back to her room and sat down quietly. The seriousness of her condition and the extent of the improvement are shown by the changes in the oxygen saturation of the arterial blood, which was 36.3 per cent before operation and which rose to 82.8 per cent three weeks subsequently. The red blood cell count dropped from 7,500,000 to 6,000,000, the hemoglobin from 24 Gm. to 17.5 Gm. and the hematocrit reading from 71 to 55.

The success of the second operation led us to perform the same operation in the third case. Since the aorta was in the normal position, in order to use the innominate artery the operation was performed on the right side. The end of the innominate artery was anastomosed to the side of the right pulmonary artery. The patient was younger, and improvement was even more dramatic. Before operation he was intensely cyanotic, the lips were a dark purple, and the child was unable to take even a few steps. The day after operation he lay in an oxygen tent with cherry red lips. When taken out of the tent his color remained good. His disposition has changed from that of a miserable whining child to a happy smiling boy. We were slow to permit him to walk because of a persistent low grade fever, but at the end of the third postoperative week he could walk 40 feet without panting and without becoming cyanotic. The oxygen saturation of the arterial blood rose from 35.5 to 79.7 per cent in nine days, and it reached a saturation of 83.8 per cent twenty-four days after operation. The red blood cell count fell from 10,000,000 to 6,000,000; the hemoglobin decreased from 26 Gm. to 20 Gm. and the hematocrit reading from 81 to 53.

There are a number of features of the operative procedure which merit discussion. We were fearful that an intensely cyanotic child would not tolerate a long operative procedure in which it was necessary to open the pleural cavity and to occlude temporarily one of the pulmonary arteries. For this reason our first clinical attempt to increase the circulation to the lungs was postponed almost a year after it was decided that the procedure was a sound one, with the hope that some method of administering oxygen in addition to inhalation might prove satisfactory. This seemed particularly important since it was obvious that a new and

untried procedure should be performed first on patients with a severe degree of anoxemia whose outlook without aid of some sort was hopeless. Although the use of intravenous oxygen has been reported by Ziegler ¹² and may prove to be of benefit in this operation, it was impossible during wartime to procure the necessary equipment. Therefore this method could not be studied.

From our limited experience it appears that this type of patient can tolerate the use of inhalation agents for general anesthesia. We have been fortunate in this respect in that the anesthetic agents were chosen and administered expertly by Dr. Austin Lamont and Dr. Merel Harmel.¹³ The first of these 3 patients was only 14 months of age and weighed less than 9 pounds. Ether by the open drip method was used during the major part of the procedure for the reason that a sufficiently small closed system was not available. In the anesthetization of the second and third patients, cyclopropane with a high concentration of oxygen was employed. Fortunately the administration of oxygen apparently increased the oxygen content of the arterial blood and cyanosis was definitely lessened. Although in only 1 patient was there any serious hemorrhage, the precaution was taken of having both blood and plasma readily available. Indeed, a slow continuous drip of plasma is advisable so that at a moment's notice if necessary the patient can be given large quantities of plasma. With these precautions no great difficulty was encountered in spite of the fact that two of the three operations required three hours.

The next question which arose was whether a patient who was already suffering from a severe degree of anoxemia would tolerate the occlusion of one of the main pulmonary arteries for the period during which the anastomosis was being performed. These periods of occlusion were approximately thirty, sixty and ninety minutes in the three operations. It is a remarkable fact that the cyanosis did not appear to be greatly increased during the occlusion period. It may be that the decreased flow of blood to the lungs caused by the congenital deformity rendered it possible for the opposite artery and lung to utilize this reduced volume almost as effectively as could the two lungs. Be that as it may, the 3 children tolerated occlusion of the left or the right main pulmonary artery for periods ranging from approximately thirty to ninety minutes.

Another question which arose was whether ligation and division of the left subclavian artery or the innominate artery would result in serious impairment of the circulation to the arm and the brain. In most instances heretofore these vessels have been occluded because of preexisting disease such as aneurysm, and it is possible under such circumstances that there has been a prolonged stimulus for the formation of collateral arterial pathways. It was gratifying, therefore, to note in our patients that there was little evidence of impairment of circulation to the parts deprived of their major arterial pathway. It is true that the pulse was absent for some time postoperatively and the part was slightly cooler than that of the opposite part of the body, but immediately after operation it was evident that the circulation was adequate to maintain life of the part. It may prove desirable to perform an upper dorsal sympathectomy at the time of operation. This would not add to the gravity of the operative procedure, since one has an excellent exposure of this region in perform-

^{12.} Ziegler, E. E.: Intravenous Administration of Oxygen, J. Lab. & Clin. Med. 27: 223-232 (Nov.) 1941.
13. Drs. Lamont and Harmel will deal with this subject in a subsequent communication.

ing the arterial anastomosis. In future cases the circulation of the arm will be studied more carefully.

The operation has not been attempted before on patients and there are many operative as well as clinical features which are still under investigation. The first of these is concerned with the type of anastomosis which is to be performed. This will undoubtedly depend on many factors, especially the age of the patient and the degree of anoxemia. As stated previously, in our patients the anastomosis was performed between the end of the subclavian artery or innominate artery and the side of the left or right pulmonary artery. This type of anastomosis appears to be sound in that it allows the blood to flow from the systemic circulation to both lungs. The fact that the continuous murmur which results from the operation is readily audible on both sides of the chest indicates that the anastomosis does direct blood to both lungs. It was this type of anastomosis which was used by Eppinger, Burwell and Gross 8 in their studies on the cardiac output of dogs with an artificial ductus arteriosus.

The easiest of the end to side arterial anastomoses in this region is that between the end of the left subclavian artery and the side of the left pulmonary artery. On the other hand, the subclavian artery is so small in an infant that the chances of the occurrence of thrombosis at the anastomotic site are great. This is particularly true if the patient has extreme polycythemia. Even though the anastomosis remains patent, the size of the vessel is a limiting factor in the flow of blood to the lungs which may not be sufficient to overcome the high degree of anoxemia from which some of these patients suffer. In an older patient with only a moderate degree of cyanosis the subclavian artery would appear to be the ideal vessel. The left common carotid is somewhat larger than the left subclavian artery, and its employment under some circumstances seems to be warranted. When dealing with the degree of anoxemia which was present in our patients, the innominate artery is much to be preferred to the left subclavian artery or the left common carotid artery. The performance of the anastomosis is not very difficult when the left pulmonary artery can be used. The anastomosis of the innominate artery to the left pulmonary artery is possible only in patients with a right aortic arch and hence an innominate artery on the left. With the innominate artery in its normal position the anastomosis of this vessel to the right pulmonary artery is more difficult because so much of the latter artery lies behind the aorta and the superior vena cava. Improvements in the designs of instruments will facilitate this procedure.

It is important to bear in mind that the degree of impairment in the flow of blood to the lungs varies from patient to patient, and the selection of the vessel to be used depends on the extent of the need of the patient for an increase in the circulation to the lungs. Experimental observations and clinical trial and error will undoubtedly shed additional light on this subject. It is obvious that the vessel chosen and the size of the anastomosis itself should not be larger than is necessary for the relief of anoxemia because of the danger associated with excessive shunting of blood to the lungs.

There are other methods in addition to union of an end of a systemic artery to the side of a pulmonary artery by which an anastomosis between the two circulations may be made. Included among these are (1) anastomosis of the divided proximal end of one of the vessels which arise from the aortic arch (innominate,

left common carotid, left subclavian) to the divided distal end of one of the two pulmonary arteries, (2) anastomosis of the divided proximal end of the subclavian artery or the common carotid artery to the divided proximal end of the pulmonary artery to an upper lobe of one of the lungs, (3) anastomosis of the side of the aorta to the side of the left pulmonary artery and (4) anastomosis of the side of the aorta to the side of the left pulmonary artery. These will be considered in the order in which they are enumerated.

The results of the use of the first method, in which the divided proximal end of the left subclavian artery is anastomosed to the divided distal end of the left main pulmonary artery, were reported in 1939 by Levy and Blalock.7 It was stated that "dogs which have been observed for several months following this procedure appear entirely normal. The left lung was aerated and the respiratory movements were unaltered. The systemic arterial blood pressure was not affected by this operation. The blood pressure in the pulmonary artery only a short distance beyond the anastomosis was less than half of that in the systemic arteries. This was due to the relatively low peripheral resistance in the pulmonary bed. Since only arterial blood entered the left lung, the quantity of oxygen consumed by this lung was very small. However, when anoxemia was caused, a larger quantity of oxygen was taken up by the incompletely oxygenated arterial blood. The left lung appeared pinker than the right on gross examination during life. Microscopic examination revealed no noteworthy alteration in either the left pulmonary artery Some of these animals have now been observed over periods ranging up to six years. The only disturbing finding has been that a few of the animals at autopsy have shown a thickening of the left pulmonary artery. It was noted by Dr. Arnold Rich that this was found only in instances in which the anastomotic site was partially occluded as a result of thrombosis. The discrepancy in the size of the left subclavian artery and that of the left pulmonary_artery may have accounted in part for this finding. Furthermore, this discrepancy in size may be responsible in part for the sudden diminution in the arterial pressure just beyond the point of anastomosis. At any rate, it is improbable that the anastomosis of the subclavian artery to the end of the left pulmonary artery would be the procedure of choice in the treatment of pulmonic stenosis. If this type of anastomosis should be performed, the innominate artery would be a better choice than the subclavian because it is more nearly the size of the pulmonary artery. It may be found that an end to end anastomosis is more apt to remain patent than an end to side one; certainly it is technically easier to perform. If, in the process of performing an anastomosis between the end of the innominate artery and the side of one of the pulmonary arteries, the latter vessel should be torn beyond repair, it should be borne in mind that an anastomosis may still be performed between the end of the innominate and the distal end of the pulmonary artery. Experimental studies are being carried out on the relative virtues of end to end and end to side anastomoses.

A second alternative method consists in anastomosing the proximal end of the divided subclavian or carotid artery to the proximal end of the divided pulmonary artery to one of the upper lobes. Since it is technically easier to perform an end to end than an end to side anastomosis, one may consider the advisability of using this procedure for a patient with only a slight degree of cyanosis. The proximal end of the pulmonary artery is specified because this would conceivably allow blood to gain access to all the lobes except the one supplied by the artery which was used for the anastomosis. This procedure has been performed in the laboratory and is not difficult.

The third possible operative procedure is concerned with an anastomosis of the side of the aorta to the side of the left pulmonary artery. That such a procedure is possible in dogs has been shown by Leeds 9 in his studies on patent ductus arteriosus. We considered the use of this method in our patients but were discouraged by the experience of Blalock and Park 10 in studies on experimental coarctation of the aorta. In these experiments the aorta was divided just distal to the ligamentum arteriosum, the two ends of the aorta were closed, the left subclavian artery was divided at some distance from the arch of the aorta, and the proximal end of the divided subclavian artery was anastomosed to the side. of the distal end of the aorta just below the point at which it had been divided. Thus the subclavian artery was used for the conduction of blood beyond the point of division of the aorta. The discouraging feature of these experiments was that in approximately half of the animals the hind legs were paralyzed at the completion of the operative procedure. In 1 dog in which we occluded the aorta for forty minutes for the purpose of making an anastomosis between the side of the aorta and the side of the left pulmonary artery the hind legs became paralyzed. It is impossible to make an accurate anastomosis between the aorta and the left pulmonary artery without interrupting temporarily the circulation through the two vessels. We were fearful of causing a paralysis of the lower extremities and hence did not use this method with our patients. Another difficulty associated with the use of the aorta is that its walls are thick and rather friable and it is difficult to obtain an accurate approximation of the intimal surfaces.

The fourth method to be considered is that of an anastomosis of the aorta and the main pulmonary artery. It is obvious that occlusion of these vessels for the length of time that is required for an open suture anastomosis would result in death. If such a union was to be secured, it would have to be done by some other method. Fortunately the first portions of the medial walls of the aorta and the pulmonary artery are intimately adherent to each other. The ascending aorta and the main pulmonary artery are contained within the pericardial cavity and are enclosed in a tube of serous pericardium common to the two vessels. have been able to produce a fistula between the two vessels in dogs by inflicting a stab wound in this region. The knife blade was introduced through the opposite free wall of the pulmonary artery, the walls of the pulmonary artery and aorta which were in intimate contact were pierced, the knife was withdrawn, and the opening in the free side of the pulmonary artery was closed by sutures. The establishment of the fistula required only a few seconds. This method is mentioned because it may be necessary to use the major blood vessels and to employ considerable speed if newborn infants with pulmonary stenosis or atresia are to be saved. It would not be at all surprising if this experimental method should prove to be a useful one in patients.

It remains to be proved whether a communication between the two circulations should be brought about by direct anastomoses between blood vessels such as we have employed or by the use of tubes such as those devised for other purposes by Blakemore, Lord and Stefko.¹⁴ It is our impression that the suture method is preferable when it can be accomplished without undue tension. This method obviates the necessity for leaving a large foreign body in the tissues; furthermore, there is at least a possibility that the opening will increase in size with the growth of the child. Studies on the latter point are in progress. These comments are in no sense a criticism of the Blakemore method, which is of great value in those instances in which part of a blood vessel has been destroyed and the ends cannot be united by direct suture.

One of the possible complications which causes concern is the danger of thrombosis at the anastomotic site. The improvement of our 3 patients indicates that thrombosis has not occurred. Furthermore, in cases 2 and 3 loud continuous murmurs developed after operation. As mentioned previously, partial occlusion of the anastomotic site has been found in some of the dogs in which such anastomoses were performed. Partial occlusion of the opening and emboli in the lungs were found at autopsy in 1 animal in which the end of the subclavian artery had been anastomosed to the side of the left pulmonary artery. This experiment was complicated by the previous creation of bilateral pulmonary arteriovenous fistulas. The sizes of the vessels used and the size of the communication between the two vessels are, of course, of prime importance in the determination of whether or not the opening will remain patent. This consideration is another point in favor of using a large vessel such as the innominate artery. Because of the difference in pressure on the two sides of the anastomotic site between the systemic and pulmonary circulations, it would be more likely that such an anastomosis would remain open than communications of similar size between two systemic arteries or two systemic veins.

As previously stated, most patients with the type of malformation of the heart under consideration have a decided polycythemia and an increased viscosity of This condition undoubtedly increases the the blood. danger of thrombosis. Indeed, cerebral thromboses are of not infrequent occurrence in these patients. Therefore the question arose as to whether these patients should receive heparin shortly after the termination of the operation. After much deliberation it was decided that the possible dangers were greater than the possible advantages. This opinion, however, is subject to change. By way of compromise, it was decided to give dicumarol during the period of convalescence. Therefore, beginning respectively on the fourth and third postoperative days the second and third patients were given dicumarol in small quantities. Prothrombin determinations were made daily and the dose of dicumarol was regulated so as to keep the clotting time approximately double that of the normal control. This medication was continued for a period of approximately three weeks. It is impossible to state whether this therapy has been of importance in the maintenance of the patency of the

In order to understand the changes produced by the operation and its application to other malformations, it is essential to understand the nature of this malformation and the course of the circulation. The four features which constitute the tetralogy of Fallot are pulmonary stenosis, dextroposition of the aorta, an inter-

^{14.} Blakemore, A. H.; Lord, J. W., Jr., and Stefko, P. L.: Restoration of Blood Flow in Damaged Arteries: Further Studies on Nonsuture Method of Blood Vessel Anastomosis, Ann. Surg. 117: 481-497, 1943.

ventricular septal defect and right ventricular hypertrophy. The pulmonary stenosis consists in a narrowing of the pulmonary orifice, and it is usual to find that the constriction also involves the pulmonary conus of the right ventricle. Dextroposition of the aorta means that the aorta rises from the left ventricle and partially overrides the right ventricle. Whenever this occurs. the aortic septum cannot meet the ventricular septum; consequently there is a high ventricular septal defect. Such is the nature of an interventricular septal defect in the tetralogy of Fallot. The malformation renders it difficult for the blood to be expelled from the right ventricle; hence there is hypertrophy of that chamber. The structure of the heart and the course of the circulation are diagrammatically shown in figure 11.

The degree of incapacity in a tetralogy of Fallot depends on the severity of the pulmonary stenosis and the degree of the overriding of the aorta. It is well known in cases in which the pulmonary stenosis is not extreme that the malformation is compatible with relative longevity. However, with extreme degrees of pulmonary stenosis and greatly diminished circulation

Fig. 11. Diagram of the course of the circulation in the tetralogy of Fallot. In this malformation there is pulmonary stenosis, the aorta is dextroposed and hence receives blood from both ventricles, the ductus arteriosus undergoes normal obliteration and the foramen ovale is closed. The blood from the right auricle flows into the right ventricle; hence part of the blood is pumped through the stenosed pulmonary orifice into the pulmonary artery and part of the blood is pumped directly into the aorta. Only that portion of the blood from the right ventricle which is pumped into the pulmonary artery goes to the lungs for aeration and is returned to the left auricle and the left ventricle. All of the blood from the left ventricle and some of the blood from the right ventricle is pumped out into the aorta to the systemic circulation and is returned by the superior vena cava and the inferior vena cava to the right auricle. There the cycle starts again.

to the lungs, the condition causes severe incapacity and death occurs at an early age.

The anastomosis of the innominate artery to the pulmonary artery directs a large volume of blood from the systemic circulation into the pulmonary circulation. By this means the volume of blood which reaches the lungs for aeration is increased; it follows that a greater volume of oxygenated blood is returned by the pulmonary veins to the left auricle and the left ventricle; consequently a greater volume of oxygenated blood is pumped out into the systemic circulation. As some blood from the aorta is diverted to the pulmonary circulation, the volume of blood to the systemic circulation is decreased

and less blood is returned to the right auricle and the right ventricle. Thus the volume of blood which is returned to the right ventricle is lessened and that which is returned to the left side of the heart is increased. The alteration in the course of the circulation as influenced by the operation is shown in figure. 12.

In short, the operation enables some blood to bypass the obstruction to the pulmonary circulation. Hence the operation should be of value in all malformations in which the primary difficulty is due to lack of adequate circulation of the blood to the lungs; that is, in all cases of the tetralogy of Fallot and complete pulmonary atresia, in cases in which the right ventricle is absent or defective in its development, in cases of truncus arteriosus with bronchial arteries, or even a single ventricle with a rudimentary outlet chamber in which the pulmonary artery is diminutive in size.

Complete pulmonary atresia is, of course, compatible with life only as long as the ductus arteriosus remains open unless the bronchial arteries dilate and establish sufficient collateral circulation for the maintenance of life. This, we believe, happened in case 2, as at operation large aberrant vessels were found in the region of the hilus of the left lung. However, in the great majority of cases of pulmonary atresia the closure of the ductus arteriosus is so rapid that adequate collateral circulation does not develop and consequently the condition is fatal in early infancy. In all such cases the operation, if performed early, may be life saving. The same is true in cases of a defective development of the right ventricle in which all of the blood from the right auricle is directed to the left auricle and hence to the left ventricle and out by way of the aorta, and the only circulation to the lungs is by way of the ductus arteriosus.15 The operation should be equally valuable in cases of truncus arteriosus with bronchial arteries because the bronchial arteries never become sufficiently large to provide adequate circulation to the lungs.

In every instance there is, of course, an admixture of venous and arterial blood. It would be impossible, therefore, to bring the oxygen saturation of the arterial blood to normal; nevertheless, it is conceivably possible to bring the oxygen saturation of the arterial blood sufficiently high so that there would be no "visible" cyanosis. Certainly in the 2 older children there has been an increase in the oxygen content of the arterial blood, a decrease in the oxygen capacity, an increase in the oxygen saturation of the arterial blood, a decrease in the red blood cell count, a diminution in the hemoglobin and the hematocrit reading, a striking decrease in the patients' disability and a great improvement in the patients' ability to exercise.

In cases of the tetralogy of Fallot the heart is either normal in size or relatively small. Following the creation of an artificial ductus, the increased volume of blood which reaches the pulmonary circulation undoubtedly

increases the work of the left side of the heart. our patients the heart has definitely increased in size but compensation thus far has remained excellent. Sir Thomas Lewis 16 has emphasized that in cases of coarctation of the aorta prolonged overwork does not cause cardiac failure. Palmer 17 in his studies on cardiac enlargement showed that, in essential hypertension, cardiac enlargement occurs with the gradual rise in blood pressure and that progressive enlargement does not easily occur after the blood pressure level has become stabilized. Therefore it is our hope and expectation that in this operation, although the heart immediately increases in size in response to the altered blood flow, the condition will not lead to progressive cardiac enlargement. It is encouraging that in both cases 2 and 3, although the heart increased in size in the first

ten days, there was no further increase in the second

ten days.

^{15.} Taussig, H. B.: The Clinical and Pathological Findings in Congenital Malformations of the Heart Due to Defective Development of the Right Ventricle Associated with Tricuspid Atresia or Hypoplasia, Bull. Johns Hopkins Hosp. **59**: 435-445, 1936.

16. Lewis, T.: Material Relating to Coarctation of the Aorta of the Adult Type, Heart **16**: 205-261, 1933.

17. Palmer, J. H.: The Development of Cardiac Enlargement in Diease of the Heart: A Radiological Study, Medical Research Council Special Report Series, No. 222, 1937.

It is important to emphasize that the operation is not of value to all patients with persistent cyanosis. It is of value only in malformations in which the primary difficulty is lack of circulation to the lungs. The operation would be of no use in cases of complete transposition of the great vessels or in the so-called "tetralogy of Fallot of the Eisenmenger type" and probably not in aortic atresia.

In complete transposition of the great vessels the pulmonary artery arises from the left ventricle and the aorta from the right ventricle. The blood from the left ventricle is pumped out through the pulmonary artery to the lungs and is returned by the pulmonary veins to the left auricle and thence to the left ventricle. The blood from the right side of the heart is pumped out into the aorta to the systemic circulation and is returned by the superior vena cava and the inferior vena cava to the right auricle and the right ventricle. The primary difficulty in this malformation is not in the volume of blood which reaches the lungs but in the mechanism by which the blood which has been oxygenated in the lungs can reach the systemic circulation.

In the Eisenmenger complex cyanosis appears to be due to secondary changes in the alveolar wall or in the pulmonary vascular bed of such a nature as to hinder the aeration of the blood as it passes through the lungs; it is even possible that the high pressure in the lesser circulation may increase the right to left shunt and thereby increase the volume of reduced hemoglobin in the arterial blood. In any event, in this malformation there is no lack of circulation to the lungs and, furthermore, only rarely, if ever, is there deep cyanosis in early childhood.

In aortic atresia ¹⁸ not only is there difficulty in pumping blood to the systemic circulation but also the blood which does reach the systemic circulation is pumped through the ductus arteriosus before it has been to the lungs for aeration. Under such circumstances the creation of an additional ductus arteriosus would act to direct a larger volume of blood to the body; but it must be borne in mind that this blood has the same oxygen content as that directed to the lungs.

It is worthy of note in almost all patients with much polycythemia that all of the blood which circulates through the lungs is no longer fully oxygenated. Whether the size of the capillary bed in the lungs varies with the plasma volume and not with the number of red blood cells is not known, but there is clear evidence to show that even in patients in whom the primary difficulty is lack of circulation to the lungs the oxygen saturation of the arterial blood can be appreciably raised by the prolonged inhalation of a high concentration of oxygen. The potency of this factor was demonstrated by the great improvement in the peripheral cyanosis during operation when the patients were receiving oxygen. The importance of the volume of blood which reaches the lungs for aeration is demonstrated in our patients by the extent of the rise in the oxygen saturation of the arterial blood which resulted from the operation; in 1 instance it rose from 36.3 to 82.8 per cent and in the other from 35.5 to 83.8 per cent.

It may be that, with prolonged meager flow of blood to the lungs, secondary changes occur so that the pulmonary capillary bed is no longer capable of complete expansion and restoration to normal. Our 6 year old child showed prompter improvement than did the 12

year old girl. Hence the operation may prove less beneficial to older persons than to young children. For this reason the ideal age for operation appears to be after the systemic pressure has risen sufficiently high to permit the continuous flow of blood from the aorta to the pulmonary artery and before the condition has persisted long enough to cause irreversible changes in the lungs. We believe that the optimal age of patients is probably between 4 and 6 years; however, in all cases in which the closure of the ductus arteriosus renders the malformation incompatible with life the operation must be performed in early infancy.

Since the operation should be of value to all patients in whom the primary difficulty is lack of circulation to the lungs, it behooves the clinician to recognize this condition. The two outstanding features, both of which should be present, are (1) roentgenographic evidence that the pulmonary artery is diminutive in size and (2) clinical and roentgenographic evidence of absence of congestion in the lung fields.

The size of the normal pulmonary artery is not difficult to determine by roentgenography. The striking

feature in the roentgenogram is the absence of the fulness of the normal pulmonary conus. The shadow at the base of the heart to the left of the sternum is concave and not convex. A concave shadow in this region in patients with persistent cyanosis always means that the pulmonary artery is misplaced, absent or diminutive in size.2 When the pulmonary artery is absent or diminutive in size, there is the additional finding in the left anterior oblique position of an abnormally clear pulmonary window.2

Absence of clinical and x-ray evidence of congestion in the lungs is highly important in reaching a decision. When circulation to the lungs is inadequate, the diminished blood flow to the lungs lessens the chances of congestion in the lungs and congestion rarely occurs.² When

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Fig. 12.—Diagram of the course of the circulation in the tetralogy of Fallot after the anastomosis of the innominate artery to the pulmonary artery. Under these circumstances the blood from the right auricle flows into the right ventricle and, as before, part of the blood from the right ventricle is pumped directly into the aorta. Now, in addition to the blood which is pumped through the pulmonary orifice into the pulmonary artery, some of the blood from the aorta is diverted through the anastomosis to the lungs. Thus the volume of blood which reaches the lungs is increased and the volume of oxygenated blood which is returned to the left auricle and the left ventricle is proportionately increased. All of the blood from the left ventricle and also some blood from the right ventricle is pumped into the aorta. Some of the blood from the aorta is directed to the lungs, and the remainder goes to the systemic circulation and is returned by the superior vena cava and the inferior vena cava and the inferior vena cava and the right side of the heart receives less. The operation has bypassed the obstruction in the circulation of the blood to the lungs.

congestion does occur, it suggests that the circulation to the lungs is adequate or excessive. The operation should never be attempted when x-ray exam-

^{18.} Taussig, H. B.: Clinical and Pathological Findings in Aortic Atresia or Marked Hypoplasia of the Aorta at Its Base, Bull. Johns Hopkins Hospital, to be published.

^{19.} The following discussion is based mainly on original unreported observations which are dealt with in detail in chapters II and III of Taussig's forthcoming book on "The Clinical Analysis of Congenital Malformations of the Heart," to be published by the Commonwealth Fund.

ination shows a prominent pulmonary conus or when there are pulsations at the hili of the lungs. These pulsations should be looked for by careful fluoroscopic examination after one's eyes are fully accommodated.

Virtually the only malformation in which there is absence of the normal shadow cast by the pulmonary artery in the presence of adequate circulation to the lungs is complete transposition of the great vessels. In this condition the pulmonary artery lies behind the aorta; therefore, in the anteroposterior view there is a narrow aortic shadow and a concave curve at the base of the heart to the left of the sternum. In the left anterior oblique position the two vessels lie side by side; hence the shadow cast by the great vessels increases in width ²⁰ and the pulmonary window is not abnormally clear. The condition does not cause pulsation at the hili of the lungs but frequently leads to congestion in the lung fields. These observations, together with evidence of relatively rapid progressive cardiac enlargement,2 should aid in the establishment of the correct diagnosis.

The operation should be performed on the right or left side, depending on which vessel is to be used and on which side the aorta descends. Furthermore, it is important to bear in mind that the occurrence of a right aortic arch is by no means rare in congenital malformations of the heart which cause persistent cyanosis. Bedford and Parkinson 21 have shown that the determination of the course of the aorta is not difficult, provided fluoroscopy is carefully performed and the esophagus delineated with a barium opaque mixture. Normally the aortic knob is visible on the left, the esophagus lies in the midline and is indented by the aorta on the left margin, and in the right anterior oblique position the esophagus is seen to be slightly displaced backward by the aorta. In cases of a right aortic arch the aortic knob frequently is hidden within the shadow cast by the superior vena cava. In the anteroposterior view the esophagus is indented on the right and is displaced backward in the left anterior oblique position.

It remains to be seen whether these patients will develop heart failure. Even if this occurs, the intervening period appears to be one of great clinical improve-It may well be that, if more patients with congenital malformations of the heart survive, more will develop subacute bacterial endocarditis. Certain it is that there is nothing in persistent cyanosis which renders an individual immune from subacute bacterial endocarditis. The condition is less frequently encountered in cyanotic persons only because a comparatively small number of patients survive long enough to be liable to contract the disease. The fear of subacute bacterial endocarditis in the future is no justification for allowing a patient to die of anoxemia in the present. Even the possibility of future cardiac failure does not weigh heavily against present extreme incapacity and the danger of early death from anoxemia or cerebral thrombosis.

SUMMARY

An operation for increasing the flow of blood through the lungs and thereby reducing the cyanosis in patients with congenital malformations of the heart consists in making an anastomosis between a branch of the aorta and one of the pulmonary arteries; in other words, the creation of an artificial ductus arteriosus. Thus far the procedure has been carried out on only 3 children, each of whom had a severe degree of anoxemia. Clinical evidence of improvement has been striking and includes a pronounced decrease in the intensity of the cyanosis, a decrease in dyspnea and an increase in tolerance to exercise. In the 2 cases in which such laboratory studies were performed there has been a decline in the red blood cell count, in the hemoglobin and in the hematocrit reading, an increase in the oxygen content of the arterial blood, a fall in the oxygen capacity, and most significantly a decided rise in the oxygen saturation of the arterial blood.

The types of abnormalities which should be benefited by this operation are the tetralogy of Fallot, pulmonary atresia with or without dextroposition of the aorta and with or without defective development of the right ventricle, a truncus arteriosus with bronchial arteries. and a single ventricle with a rudimentary outlet chamber in which the pulmonary artery is diminutive in size. The operation is indicated only when there is clinical and radiologic evidence of a decrease in the pulmonary blood flow. The operation is not indicated in cases of complete transposition of the great vessels or in the so-called "tetralogy of Fallot of the Eisenmenger type," and probably not in aortic atresia. It must be emphasized that the operation should not be performed when studies reveal a prominent pulmonary conus or pulsations at the hili of the lungs.

Council on Physical Medicine

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HOWARD A. CARTER, Secretary.

THERAPEUTIC AND REMEDIAL EXERCISES

FRANK H. EWERHARDT, M.D. st. louis

It is my purpose to confine myself to the practical application of physical exercise as related to the health of the human body rather than to discuss problems involved in the physiology of exercise.¹

Almost all of the bodily movements done by a normal person throughout the day's routine, such as sitting, walking, eating and dressing, consist essentially of a successive recurrence of simple reflex acts. However, the matter of learning new movements has an entirely different significance and involves a review of the phenomenon of muscular control. It is interesting to syllogize on the subject of what happens when a boy learns to swim, a girl to knit or an athlete to pole vault. The answer is found in an understanding of the classification, action and coordination of muscles.

Skeletal muscles are classified as prime movers (protagonists or agonists), antagonists and synergists or fixers.

^{20.} Taussig, H. B.: Complete Transposition of the Great Vessels, Am. Heart J. 16:728-733, 1938.
21. Bedford, D. E., and Parkinson, J.: Right-Sided Acrtic Arch, Brit. J. Radiol. 9:776-798, 1936.

^{1.} For studies on the physiology of exercise the reader is referred to Lipovetz (Applied Physiology of Exercise, Minneapolis, Burgess Publishing Company), who concisely interprets studies on the phenomenon of muscle contractions; the chemical changes of contraction; the phenomenon of muscular action, control and movement; equilibrium, postural tonus and tonus reflexes; nerve mechanism of the heart; innervation and chemistry of respiration, and the localization of brain function and the process of learning.