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RESULTS OF PULMONARY VALVOTOMY AND INFUNDIBULAR RESECTION IN 100 CASES OF FALLOT'S TETRALOGY

BY

MAURICE CAMPBELL, D.M., F.R.C.P.

D. C. DEUCHAR, M.D., M.R.C.P.

AND

Sir RUSSELL BROCK, M.S., F.R.C.S.

From the Cardiac Department and the Thoracic Surgical Unit, Guy's Hospital

We recently reported the results of Blalock–Taussig operations in 200 patients with morbus caeruleus, 165 of whom had Fallot's tetralogy (Campbell and Deuchar, 1953). We wish to add a parallel series of 100 patients operated on by Brock's direct methods, and a more detailed follow-up and analysis of the 61 operated on at Guy's Hospital up to the end of 1952; 12 others have been operated on at Guy's Hospital during 1953, and the remaining 27 at the Brompton Hospital either for or in conjunction with Dr. Paul Wood. The first attempts at direct relief of pulmonary stenosis by valvotomy were reported by Brock (1948) and by Brock and Campbell (1950a), the latter paper including an account of 15 patients in whom the valvular stenosis was part of Fallot's tetralogy. Infundibular resections were first reported by Brock (1949) and by Brock and Campbell (1950b), who described the results obtained in 11 patients.

Our purpose is to report the subsequent progress of these early patients and the results in those who have been operated on since. Valvotomy only was carried out in 37, infundibular resection only in 45, and a combined operation in 18 in which the stenosis was valvular and infundibular: sometimes these have been grouped with those who had valvotomy as there were too few for separate analysis. All these patients were thought to have Fallot's tetralogy. Two (Cases V65 and 26*) had already had a Blalock operation which had resulted in only moderate improvement.

The 61 patients who had been operated on at Guy's Hospital up to the end of 1952, when the details of the follow-up were arranged, are the only ones included in the full analysis. In 23 the operation was valvotomy, in 25 infundibular resection, and in the other 13 a combined operation.

Age and Sex.—Most of the patients were children. Their age distribution is shown in Table I. Only two were under 5 years of age, nearly a third were between 5 and 9, and nearly a third were between 10 and 15. The youngest was 4 and the oldest 34. Boys and men slightly predominated—33 against 28 girls and women. These figures are very similar to those for the patients who had subclavian–pulmonary anastomosis, but the former were a little older, because preference was being given to those who were older at the time these direct operations were started.

Disability.—This was graded (Campbell, 1948) as IV in 13, III in 28, II in 16, and I in 4 before operation. The disability was on the average a little less than in those who had anastomotic operations. This was because the anastomotic operations started in 1947 and the present ones in 1948, and the most disabled had generally been chosen for operation first. The fact that the patients were older and had survived to this age implies that they had not always been the most severe cases or they would have died sooner, but the older patients chosen for operation were generally losing ground, and sometimes seriously so. We think that the slighter disability and the greater age (with its greater operative risk) balance each other and make the two groups closely comparable. The disability grading in the valvotomy series differs from that in the resection series only by including more patients in grade IV and fewer in grade II.

TABLE I.—*Age Distribution of Patients and Deaths after Operation*

	No. of Cases in Each Age Group					
Age in years:	0–4	5–9	10–14	15–19	20+	Total
Pulmonary valvotomy alone and combined	2	12	9	7	6	36
Infundibular resection	0	7	10	3	5	25
Both operations	2	19	19	10	11	61
Deaths after operation	0	3	2	2	4	11
Proportion of deaths	14%		11%	20%	36%	18%
Proportion of good results	52%		84%	60%	54%	64%

Cardiac Catheterization in Diagnosis

The general findings of catheterization and the value of various special investigations in the diagnosis of morbus caeruleus, and their limitations in the assessment of the results of anastomotic operations, have been discussed (Campbell and Deuchar, 1953). Catheterization has a more valuable place in assessing the haemodynamic changes after direct operations (see later), and has the same value in diagnosis and an added value in elucidating the anatomy of the right ventricular outflow tract, for its precise anatomy is more important to the surgeon than before an anastomotic operation.

Physical signs may be helpful but are not reliable in differentiating valvular and infundibular stenosis. A good angiocardiogram may demonstrate clearly the exact site of the stenosis present in Fallot's tetralogy, but often it does not give a decisive answer or may even lead to a

*Case numbers starting with V indicate those who had valvotomy, and the numbers without a prefix those who had infundibular resection only.

wrong conclusion (Campbell and Hills, 1950; Lowe, 1953; Goodwin *et al.*, 1953); though selective angiocardiography may perhaps succeed more often (Jönsson *et al.*, 1953). Cardiac catheterization has proved more reliable in determining the exact nature of the stenosis. This subject has recently been discussed in detail by Connolly *et al.* (1953), and our findings are in complete accord with theirs.

Briefly the method may be described as follows: the catheter, having been introduced into the pulmonary trunk, is slowly withdrawn while continuous recording of the pressure is taken. Three types of record may then be obtained, depending on the character of the stenosis. (1) A sharp rise in the systolic pressure to the right ventricular systolic pressure as the catheter passes through the valve region indicates a valvular type of stenosis. (2) No change in the systolic pressure with a fall of the diastolic pressure when the catheter passes through the valve, followed by a rise in the systolic to the right ventricular level at the infundibular region, indicates infundibular stenosis. (3) A combined type of record in which the pulmonary arterial tracing gives way at the valve site to the higher systolic and lower diastolic pressure of the infundibular chamber, and a further rise in the systolic pressure to the right ventricular level at the site of the infundibular stenosis indicates the presence of valvular and infundibular stenosis.

Apart from the character of the tracing obtained during ordinary cardiac catheterization, the site of the stenosis can often be identified from its position when the major change in the systolic pressure occurs, if the position of the catheter tip can be observed by radioscopy.

During Operation.—Direct operations are generally performed on patients with simple pulmonary stenosis or Fallot's tetralogy, and the diagnosis can often be made without any special investigations. In cases diagnosed as Fallot's tetralogy the full routine of cardiac catheterization has not been used solely to determine the type of pulmonary stenosis present, but instead it has become our practice to carry out a modified procedure at the time of operation. An initial small cardiotomy incision is made in the right ventricle and a catheter attached to the recording manometer is introduced by the surgeon and passed into the pulmonary trunk, and the procedure is given greater precision by being coupled with direct inspection and palpation of the region by the surgeon. By these means a high degree of accuracy in determining the precise type of the stenosis can be achieved.

When the surgeon has performed the appropriate operation, the pressure records are repeated to determine the effect, and the value of this is emphasized later in the discussion.

Method of Follow-up

This has been carried out in exactly the same way as for those who had anastomotic operations (Campbell and Deuchar, 1953). We have seen most of the patients several times and have tried to see them annually, near the anniversary of their operation, but could not always adhere to this strictly. We have therefore counted the visits between 10 and 21 months as one year; between 22 and 31 months as two years; between 32 and 43 months as three years; and 44 months and over as four years. No patient has been lost sight of, except one who emigrated to Canada 28 months after her operation. In three we have accepted reports and radiographs from their doctors for the follow-up: one of these returned to Africa within a few months of his operation and the other two are in Scotland.

The period of follow-up of the patients who left hospital was as follows—four years, 12; three years, 10; two years, 20; and one year, 8. The assessment of the degree of improvement was made in the same way as for those who had an anastomotic operation. It was made by two of us without any reference to R. C. B., and it has not been very common for a surgeon's results to be judged in this way by physicians.

Results in Early Patients after Infundibular Resection

Before classifying the results, the present condition of the first eight who recovered after infundibular resection is described shortly to give a general picture. The good results of the early survey have been maintained for another three years, though in two patients the heart is larger than one would wish.

Case 1.—A year after operation this patient could walk a mile instead of 100 yards. After five years she is stronger and has walked two miles. She is working as a dressmaker, but is content with a quiet life and has not pushed herself.

Case 2.—A year after operation this patient was leading a normal student life, and was able to dance all evening and to walk five miles, instead of a mile with difficulty. After five years she leads a very active life, but paroxysmal tachycardia troubles her if she does too much. Her cardiothoracic ratio (c.t.r.), which was large before operation, increased soon after (56 to 60%), but not progressively.

Case 3.—This man was at regular work and a year after operation was able to walk four miles, although before it he was getting worse and could not walk more than 100 yards on a good day. After five years he is leading a normal life, working regularly and easily walking five to six miles at the week-end. His heart has not increased in size (Fig. 1). Cardiac catheterization shows that the right-to-left shunt has been reduced and that the pressure in the pulmonary artery has not become too high (see Table VI).

Case 4.—This boy was able to lead a quiet life at school and play cricket a year after operation. After four years he is just as well, but is clumsy and mentally backward, and this prevents greater activity. His heart has not become larger.

Case 6.—This patient had walked three miles and played football a year after operation. After four years he is just as active and works as a shop assistant; he is ready for football and other games in addition to his day's work. There is no undue increase in the size of his heart.

Case 7.—A year after operation this patient could walk four miles. During the next two years he played football and became an enthusiastic cyclist. Although he felt as well as ever, we thought that he was doing too much and that the heart was too large (c.t.r. 48 to 58%) (see Fig. 2). He has given up the long-distance cycling and football, but leads a normal life and plays cricket, and after four years the heart is a little smaller (56%, see later). Cardiac catheterization shows that his right-to-left shunt has been reversed, the arterial O_2 saturation is 95% instead of 72%, and the pulmonary pressure is still low (18/7).

Case 8.—A year after operation this patient could walk two miles and do light work for half a day. Either from gaining confidence or from real progressive improvement, she now, after four years, does a full day's work in a shop and can dance afterwards; she can walk two to three miles, which is all she wishes, at the week-end. There is no undue enlargement of the heart.

Case 9.—A year after operation this patient had lost her attacks of faintness and could walk two miles. After four years the result is excellent: she is leading an active life at school and doing all she wants, without undue enlargement of the heart.

Classification of Results

The classification of the patients after operation is shown in Table II. Very few who survived obtained no benefit. Generally speaking, the results of valvotomy and of infundibular resection are very similar, and are comparable to those of anastomotic operations (Campbell and Deuchar, 1953; Taussig and Bauersfield, 1953), though some significant differences are referred to later. The results of the two direct operations for Fallot's tetralogy are considered together, though the illustrative cases are from those who

had valvotomy, seeing that examples of infundibular resection have just been described.

TABLE II.—*Results of Valvotomy and Infundibular Resection in Fallot's Tetralogy*

Result of Operation	First 61 Guy's Cases		Total 100 Cases (Percentages)				Anastomotic Operations for Fallot's Tetralogy
	No.	%	Valvotomy Only	Combined Operation	Infundibular Resection	Total Direct Operations	
Very good	28	46	49	39	57	51	54·5
Good	11	18	24	16·5	18	20	23*
Some improvement ..	10	16·5	14	28	7	13	8·5
No improvement or no operation possible	1	1·5	2	—	—	1	5·5
Deaths at or soon after operation	11	18	11	16·5	18	15	8·5
Total No. ..	61	—	37	18	45	100	165

* Includes 3% in which the result was good but the patient has died subsequently.

Group I: Patients with Very Good Operative Results (28)

We have classed a result as very good when the patient can earn his living or attend an ordinary school and can walk three to four miles: he is living a normal life except for the more vigorous activities that are not essential. If he could not walk 100 yards before operation we have classed the result as very good even when he has not reached this standard but can walk a mile.

The proportion with very good results is nearly as high as among those who had anastomotic operations for Fallot's tetralogy; nor was there any great difference between those who had valvotomy and those who had infundibular resection (see Table II). Three examples are quoted.

Case V3.—A girl aged 11 had severe cyanosis and could walk only 100 yards. She improved quickly after operation, and two years later had an almost normal colour and was doing all she wanted at school, including drill but not games (Brock and Campbell, 1950a). She has maintained this progress and works as a telephonist: she can easily walk four miles and can dance most of the evening. She is free from any symptoms and looks a healthy, well-developed girl.

Case V10.—A man aged 22 was less disabled, as he could walk two miles and earn his living as a clerk, but he was deeply cyanosed, with a haemoglobin of 180% and a red-cell count of 9,400,000, so that there seemed a risk of cerebral thrombosis. A year after operation he could lead his previous life easily instead of with difficulty. His improvement has been maintained over the four years and he has been regularly at work and can lead a normal quiet life. His haemoglobin has remained at about 118% instead of 180%.

Case V20.—A boy aged 13 could walk only 100 yards. Though at first he was classed as no more than "improved," three years after operation he leads a life that is almost normal and plays some games, including football—in goal. Contrary to the general rule, his cyanosis, which was only moderate, has not changed much and his haemoglobin has hardly fallen from about 120% in spite of the great improvement.

All these patients had valvotomy, and the last had infundibular resection as well.

Group II: Patients with Good Results (11)

We have been conservative in including cases in the highest class. When a patient falls short of this high standard in some particular but leads a normal quiet life we have recorded the result as good. The good results are much the same as in those who had anastomotic operations. The first patient who had a successful valvotomy for Fallot's tetralogy may be given as an example.

Case V2.—A girl aged 18 could not walk more than 200 yards in summer and rarely went outside in winter: she squatted constantly. Two years after operation she had improved a good

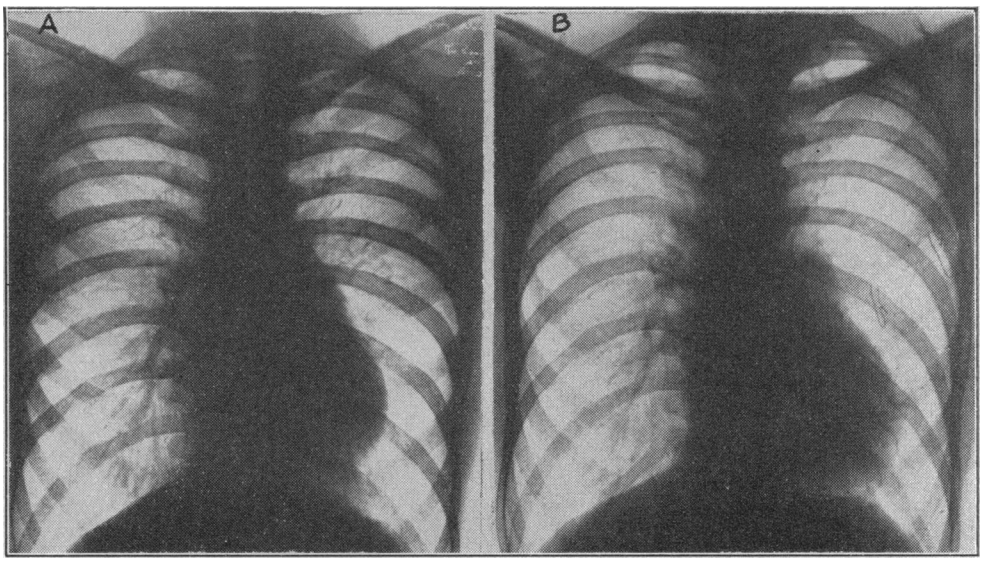

FIG. 1.—Little change in heart size five years after a very successful infundibular resection. (A) Before operation, c.t.r. 46% (11.8:25.4 cm.). (B) Five years after, c.t.r. 47% (12.2:26 cm.). Case 3.

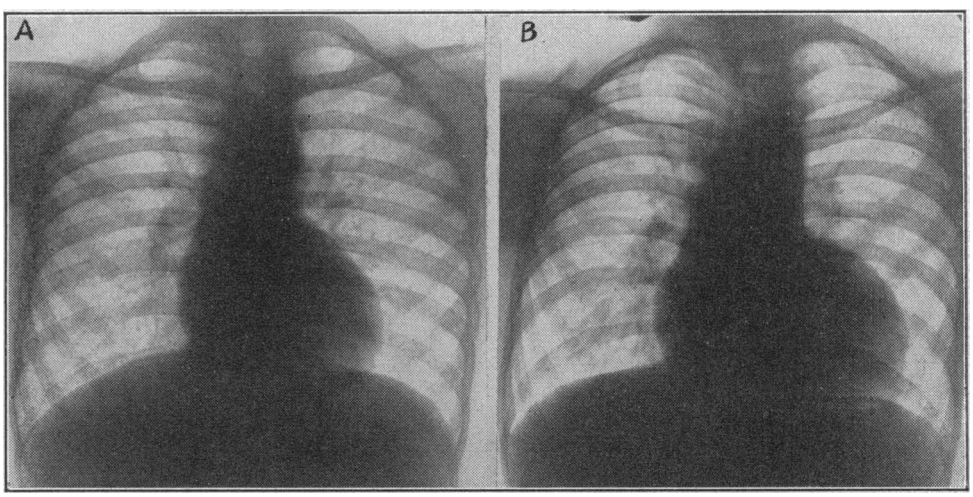

FIG. 2.—An unusual increase in the size of the heart. (A) Before operation, c.t.r. 48% (11:23.2 cm.). (B) Three years after operation, c.t.r. 58% (15:26.2 cm.), associated with rounding of the left border; undue pulsation could be felt in this area. Clinically, he was extremely well, but he was advised to do rather less. Case 7.

deal and could sometimes walk a mile (Brock and Campbell, 1950a). She has steadily improved, more slowly than usual, perhaps because of initial pain in her legs from arterial embolism after the operation. She can walk a mile and lead a quiet life as a musician, travelling to and playing at concerts, and is nearly as good during the winter.

Group III: Patients with Some Improvement (10)

This group contains all those who were still seriously limited in activity but showed real improvement, which sometimes meant a lot to them. It seems most difficult to be sure of a good result after valvotomy (alone or combined with infundibular resection), for there are more such patients classed as "improved" only, perhaps because the importance of an added infundibular stenosis was sometimes missed or not sufficiently appreciated in the early cases.

Case V4.—A woman aged 25 was almost confined to one room. Two years after operation she could walk to the village shops a quarter of a mile from home and was sure this more than compensated her for the disability of the hemiplegia that followed her operation. Without this the result would have been good: but, generally, inclusion in this group is because the operation itself was not as successful as usual.

One patient who was only slightly improved after infundibular resection had recently had an anastomotic operation, and the result is very good.

Group IV: Patients who were Improved but Died Later

No patients have been included in this group, though one (Case 19) who had a very successful infundibular resection and could lead a normal quiet life instead of being almost a complete invalid died nine months after her operation. We have excluded her because she died from Landry's acute ascending myelitis. Her death gave us the chance of seeing a heart after the infundibular resection has healed, and the appearance is most encouraging. The stenotic ring seems to have been removed almost completely and the surface of the infundibulum looks smooth and healthy. We are indebted to Dr. Enticknap for the following histological report. "A scar composed of cellular fibrous tissue runs from pericardium to endocardium, completely separating the muscle on each side: it varies in width from 2 to 5 mm. There is no active inflammation though the scar is not the quiescent hyalinized type that forms in the rectus muscle after laparotomy. There is very little scarring of the pericardium, although a small foreign-body granuloma is present; there is, however, an endocardial scar 1 mm. thick. There are some irregular islands of muscle cells within the scar, and 3 mm. from it there is an area of myocardial degeneration, 1 mm. in diameter, resembling a healed infarct, although patent arterioles traverse it."

Groups V and VI: Patients with No Improvement after Operation or in whom No Operation was Possible

It was possible to perform an operation in every patient, and perhaps this is one advantage of direct over anastomotic operations, though the latter are rarely, if ever, impossible in Fallot's tetralogy.

There was only one patient who gained no benefit, and he had needed valvotomy and infundibular resection; three years later he had an anastomotic operation, with a good result.

Group VII: Patients who Died at or Shortly after Operation

Pulmonary Valvotomy.—Of the first 16 patients with Fallot's tetralogy who had this operation, 3 died (Brock and Campbell, 1950a). Among the next 20 operated on at Guy's Hospital there were two more deaths, so that the operation has become reasonably safe. Considering the severe disability that was often present, 5 deaths in 36 cases cannot be regarded as very high, and the mortality is well under 10% when there are no unfavourable features (see Table II). Two of the five patients were over 20 years of age. All but one died during or very shortly after the operation from cardiac arrest. The youngest, aged 5, was thought to have Fallot's tetralogy but was found *post mortem* to have a single A–V valve and functionally a single ventricle with pulmonary stenosis. The one patient who recovered from the operation but died four months later seemed to be improved at first but was readmitted from convalescence as she had lost ground; in spite of treatment she steadily became worse. At operation some difficulty with the use of the infundibular punch led to its withdrawal in the open position through the cardiotomy incision and to some laceration of the myocardium: it was thought at the time that this was satisfactorily sutured. At necropsy the cause of death was found to be pressure on the root of the pulmonary trunk by a large aneurysm of the right ventricular wall arising at the site of the cardiotomy.

Infundibular Resection.—In spite of the apparent difficulty of such an operation there was only one death in the first eight patients (Brock and Campbell, 1950b). This auspicious beginning was, however, followed by a disappointing period in which five of nine patients died. Fortunately there was no death in the next eight patients, but the total mortality remains higher than for simple valvotomy. The ages of these patients ranged from 8 to 34, but three were 20 or over and the mean age was 19 years. The three eldest all died during or at the end of the operation. The fourth died shortly after, apparently from cardiac arrest, and the fifth died a few hours after with a haematoma under the endocardium of the right ventricular outflow tract which was obstructing the passage of blood to the pulmonary trunk. The sixth developed cardiac arrest during the operation and was successfully resuscitated, but suffered permanent cerebral damage and died twelve days later.

Combined Groups.—In the Guy's Hospital combined series of both direct operations the mortality was 18%, but this was lower in the whole series (see Table II). Disability in these cases was much the same as for the survivors. The haemoglobin before operation ranged from 102 to 172%, with a mean of 134%, which is little higher than for all the survivors. The size of the heart was not a deciding factor, for the c.t.r. ranged from 48 to 61% with a mean value of 51%, which is only slightly higher than that for the rest of the series. The only heart where it exceeded 55% (c.t.r. 61%) was in the patient with a single A–V valve—the only one who was known not to have uncomplicated Fallot's tetralogy. The figures are not large enough for separate analysis of the different operations by age, but the operative mortality increased with age, being 12% in those of 14 and under, 20% from 15 to 19 years, and 36% in those over 20 years (see Table I). Two of these patients, aged 28 and 34, were operated on because they had become very disabled after many years of reasonable activity.

Objective Effects of the Operation

In describing the results of the Blalock–Taussig operation we discussed the reduced cyanosis and clubbing, the reduction in polycythaemia, the increase of the heart size, the widened systemic pulse pressure, and the continuous murmur. The last two are peculiar to the creation of the anastomosis. The other changes are reflections of the general improvement that follows an increase in pulmonary blood flow, and are therefore, not surprisingly, found in the present series also.

Changes in Physical Signs.—The continuous murmur provides a reliable auscultatory sign that the anastomosis is working. After valvotomy or infundibular resection there is no comparable sign. A successful result may be followed by a louder murmur and a coarser thrill, but often there is no decisive change. Nor was there any consistent change in the pulmonary second sound, though sometimes it was rather louder after operation. Only three patients developed a diastolic murmur. In one of these (Case 21, see later) the shunt was completely reversed, and the diastolic murmur, which was maximal in the mitral area, was thought

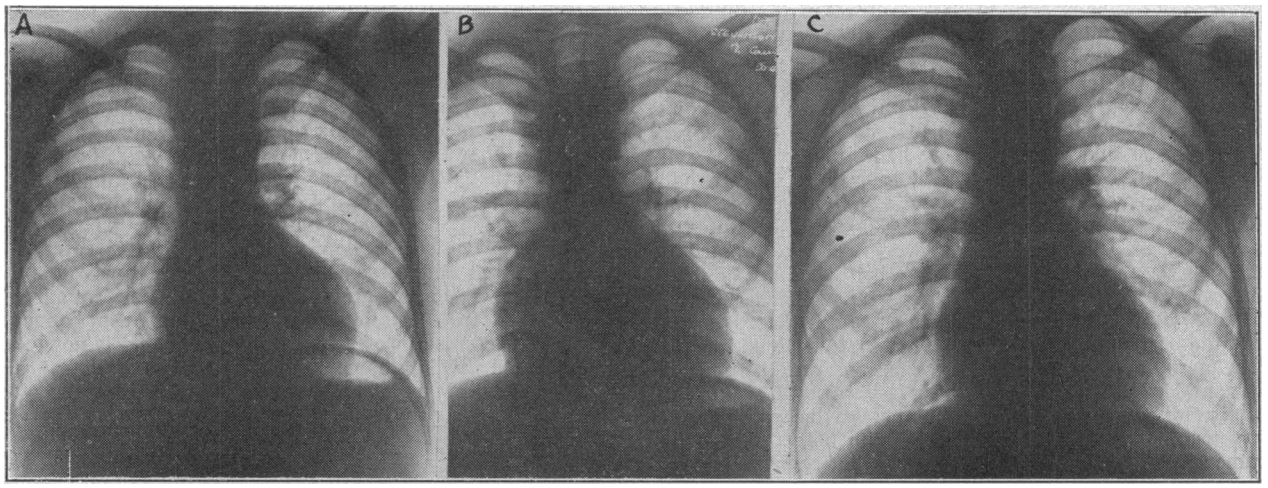

FIG. 3.—Increase of heart size with the development of pulmonary regurgitation after pulmonary valvotomy. (A) Before operation, c.t.r. 51%. (B) A year after, when he was found to have pulmonary regurgitation with moderate increase, c.t.r. 57%. (C) Three years after, with the heart somewhat smaller though he had continued a normal life with some games at school, c.t.r. 53%. Case V25.

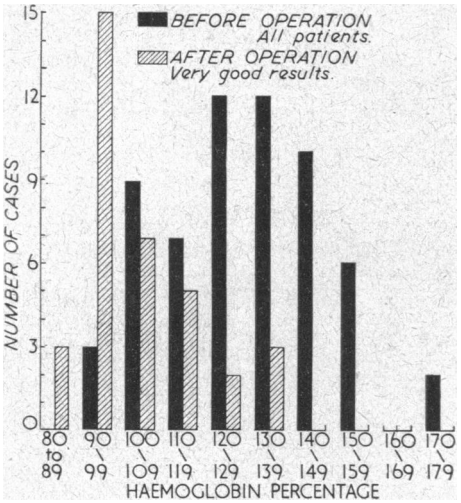

FIG. 4.—Frequency distribution of the haemoglobin percentages in all patients before operation and in those with very good results after operation. Before, the majority were between 120 and 160%. After, the majority were between 90 and 120%. The figures are almost the same as for those who had anastomotic operations. (100% = 15.6 g. per 100 ml.)

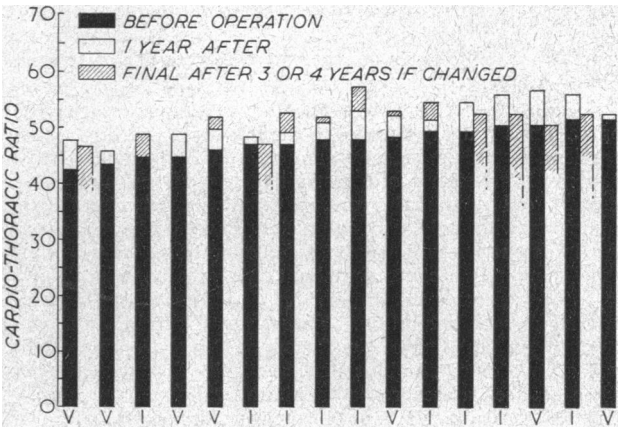

FIG. 5.—Heart size as measured by the c.t.r. before and after operation. The first 16 patients with very good results, all followed for three years or more, have been arranged according to the initial size of their heart. The unshaded area above each black column shows the increase in size within the first year. The lightly shaded area above this shows the increase during the subsequent two or three years, but it was never large and often there was no further increase and sometimes a decrease shown by the shaded column on the right.

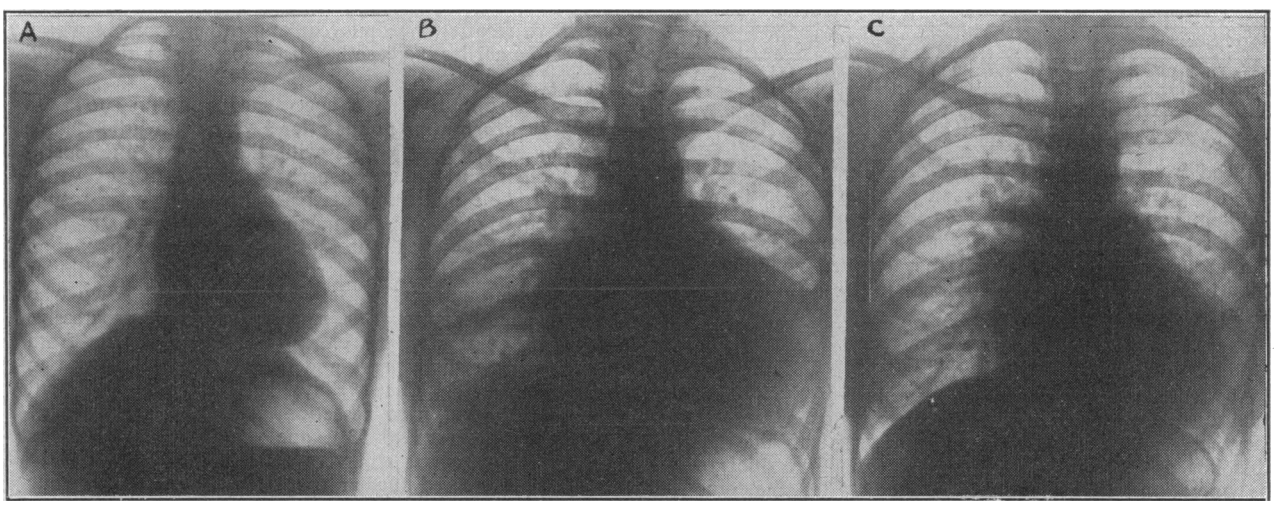

FIG. 6.—Gross increase in heart size after infundibular resection in a patient in whom the right-to-left shunt was reversed. (A) Before operation, c.t.r. 48%. (B) Eight months after operation, showing great increase in the lung markings and in the size of the heart, c.t.r. 67%. (C) Eighteen months after operation, showing some reduction in heart size with a less active life, c.t.r. 64%. Case 21.

to be functional and of the type often heard with septal defects. The other two were thought to have developed pulmonary regurgitation after valvotomy.

Pulmonary Regurgitation.—When valvotomy was under consideration the production of pulmonary regurgitation was one of the things that were feared. When we reported the results in the first 33 cases we had not seen this complication; but we have since seen it four times, though only twice in patients with Fallot's tetralogy. One of these was found to have pulmonary regurgitation when he was seen a year after operation: he was very well and wanted to add rugger and swimming to his other school games, but this was not allowed, as his heart size had increased (c.t.r. 51 to 57%) (see Fig. 3). After three years he keeps as well and the heart has become smaller (53%), but a loud regurgitant murmur is still present. In the second case the murmur was noticed almost at once after the operation: he was improved both as regards his colour and his activity, and has maintained this for two years; the heart quickly became larger (c.t.r. 48 to 57%), but has not changed further.

Pulse Pressure.—There was no significant change in the pulse pressure after operation, and this might be expected. Only one patient has shown an increase of as much as 15 mm., and this was associated with a general rise of blood pressure (95/65 to 135/90) during the five years he was under observation. After Blalock–Taussig operations a few patients, presumably those with the largest anastomotic blood flows, showed an increase of pulse pressure of 15 mm. Hg or more.

Cyanosis and Clubbing.—The improved colour after the operation is roughly parallel to the improved capacity. This applies to both the resection and valvotomy groups. Three patients from each group lost all their cyanosis, and many showed only minimal cyanosis even with exercise. This compares with only two completely devoid of cyanosis in the larger series with anastomotic operations. The difference is mainly because the shunt was greatly reduced and in some patients even reversed so that there was a normal arterial oxygen saturation. There was a parallel improvement in the clubbing of the fingers and in the cyanosis. In one or two cases clubbing has practically disappeared even when assessed as severe before the operation—for example, Case V35, Table VI. A change of this degree was not observed in the anastomotic series.

Reduction in Polycythaemia.—The fall in the haemoglobin percentage resulting from a successful operation is shown in Table III. The mean haemoglobin percentage is

TABLE III.—*Reduction of Haemoglobin after Operation*

	Result of Operation			
	Very Good	Good	Some Improvement	Death
No. of cases	27	8	10	11
Mean Hb before operation (%) ..	130·5	124	135	134
Mean Hb after operation (%) ..	103·5	101	111	—

100% haemoglobin = 15·6 g. per 100 ml.

reduced from 130 to 103% for the very good results. The range in the whole series before operation and in the very good and good results after operation is shown in Fig. 4. These findings are for the valvotomy and infundibular resection groups, combined because they showed no difference. They bear a remarkable resemblance to those found for the anastomotic series.

Increase of Heart Size

An anastomotic operation creates what is virtually an artificial ductus, and so was expected to, and in fact often does, produce some increase in the size of the heart. This has sometimes been used as a basis for criticism of the operation. In our follow-up study after anastomotic operations such enlargement was not often a cause for anxiety. We hoped at first that the direct operations would benefit the patient without making the heart larger, and, indeed, that they might make it smaller owing to the relief of the stenosis. It was found, however, that direct operations for the stenosis in Fallot's tetralogy caused some increase in the heart size very similar in degree and range to that following anastomotic operations (Fig. 5).

Our findings are given in two tables, which show the change in size related to the clinical result of operation (Table IV) and the changes in successive years in the patients obtaining very good or good results (Table V). There was no significant difference between those who had infundibular resection and those who had pulmonary valvotomy, and the figures are remarkably similar to the corresponding ones from the anastomotic series. Here enlargement cannot be due to the creation of an artificial ductus and is not the result of the cardiotomy scar, as patients not achieving a good result show no change (Table IV). Presumably it

TABLE IV.—*Heart Size Before and After Direct Operation*

		Cardiothoracic Ratios				
		Very Good Results	Good Results	Some Improvement	Deaths	All Cases
Before operation	Mean	% 49·1	% 48·4	% 49	% 51·3	% 49·4
	Range	43–56	42–56	41–59	48–61	41–61
After operation ..	Mean	52·7	52·5	49·9	—	—
	Range	46–61	46–57	41–56	—	—

TABLE V.—*Average Heart Size Each Year after Direct Operations (Very Good and Good Results Combined)*

No. of Cases	Cardiothoracic Ratio					
	Before Operation	Less than 6 Months After	1 Year After	2 Years After	3 Years After	4 Years After
	%	%	%	%	%	%
9	49·6	53·2	52·5	52·5	53	53·2
8	47·6	51·7	51·5	51·1	50·8	—
10	50·9	55·3	54·7	54·1	—	—
6	48·0	54·3	53·9	—	—	—

reflects the increased ventricular volume needed for the increased cardiac output that results from the greater pulmonary blood flow even at rest and more so during the greater physical exertion that can now be attempted. If this is correct it is not surprising that the changes should be, on the whole, about the same in both types of operation.

The heart size before operation, one year after, and three or more years after in the 16 cases that achieved a very good result and have been followed for that length of time is shown in Fig. 5. Comparison of this diagram with the similar one we have published for the anastomotic series shows rather fewer patients in whom there has been any great increase after the first year and rather more in whom some of the earlier increase has been lost during the following years.

The average c.t.r. after a successful operation shows an increase of nearly four points after a year, with little change subsequently (Table V). As with the anastomotic operations, these main features conceal a wide range of variations, and some indication of this in the very good results is given in Fig. 5. As the mean increase was about four points we have picked out all those patients showing an increase of six points or more—four in the infundibular resection series and six in the valvotomy series. Two who achieved good results after resection showed progressive increase of heart size, the c.t.r. increasing gradually from 47 to 53% over three years and from 43 to 51% over two years respectively. Case 7 (see Table VI), an excellent result after infundibular resection, had an initial c.t.r. of 48%, which increased to 53% one year after: three years after operation he was still very good in every way except that it had increased further to 58% (Fig. 2). After four years with a rather less active life it is only 56%, but there is still visible and palpable pulsation over the left border

of the heart that might suggest some dilatation at the site of the cardiotomy scar. In the fourth (Case 21, see below) the initial c.t.r. increased during the first six months from 48 to 67%, which made us anxious lest she should develop cardiac failure; but fortunately it has decreased to 64% a year after (Fig. 6) and to 61% two years after operation.

Six of the patients in the valvotomy group have shown an increase of between six and nine points, but none more than this. Four of these have shown a progressive increase, the cardiothoracic ratio having increased from 50 to 57% after four years, from 46 to 52% after three years, from 48 to 54% after two years, and from 49 to 57% after two years. The other two have shown a large initial increase that has not been progressive—from 48 to 57% and from 53 to 58%—this being partly due to the development of pulmonary regurgitation in the former. Those who have shown a progressive increase in the heart size are counterbalanced by those in whom an initial increase is subsequently, at least partly, reversed.

In four of these ten the heart was small enough before operation to leave the patients with a c.t.r. still between 52 and 54%. In six, however, it is now larger and between 57 and 64%, and in two of these (Cases 7 and 21), and in these two only, the large size and the unusual degree of pulsation give us some anxiety about their future although the shunt has been reversed and the clinical result is excellent.

The results were much the same in the anastomotic series, where in 20 of the 200 the increase of the heart size was 6 points or more. In 10 of these the heart was small enough before operation to leave them with a c.t.r. still between 52 and 55%. In the other 10 (three of whom had lesions more complex than Fallot's tetralogy) the c.t.r. is between 57 and 67%, and in two or three of these the size or the progressive increase makes us anxious about their future.

Progress after Operation

The improvement may come more slowly after direct than after anastomotic operations. After an anastomosis one generally has a good idea of the result within a day or two, and certainly before the patient leaves hospital, apart from those few in whom poor muscular development prevents the improvement becoming manifest as quickly as this. And, apart from symptomatic improvement, the presence of a loud anastomotic murmur is generally a reliable guide.

Sometimes the improvement can be recognized equally early after direct operations, but not always. Eight of the 61 patients were thought to have gained little or no benefit when they left hospital, but after six or twelve months they had improved much more, often to reach the highest group. This is easier to understand after infundibular resection, for 2 of the 25 patients were thought at first to have slight improvement only but later reached the best group. It was, however, even commoner after valvotomy—6 of the 36 gaining their main improvement some months later: two of these actually left hospital classed as failures but later achieved good results. In addition there were four who showed some progressive improvement for a year or more, but this may have been due to their gaining confidence in their increased capacity.

Post-operative Complications.—Patients after cardiotomy have been kept in bed longer, generally for three weeks. There is often some pericardial effusion which makes the cardiac shadow still larger than it would be, but this generally resolves quickly, and only two or three patients have needed paracentesis of the pericardium. The effusion is generally sterile—either from the start or as a result of treatment with antibiotics—and has rarely led to any difficulty. Immediate complications have been uncommon. A few patients have developed congestive failure, but it has cleared up spontaneously or with digitalis after a few weeks at the longest.

Bacterial endocarditis and cerebral abscess have not so far occurred in any of these patients, though they must remain a possible risk. Only one developed a cerebral thrombosis after operation.

Electrocardiographic Changes during and after Direct Operations

All these patients had right axis deviation and right ventricular preponderance, as shown by the high R/S ratio in leads V_1 or occasionally only in V_3R. Four of them showed the pattern of severe right ventricular strain that is much commoner with pulmonary stenosis with a closed ventricular septum, when T was deeply inverted in V_1 to V_4 or even further to the left.

In Fallot's tetralogy one cannot expect diminution of the preponderance of the right ventricle, as it is still in communication with the left ventricle and working against the systemic pressure. There has, in fact, been no such diminution after direct operations any more than after anastomotic operations. It is more likely to increase after some years, as the patient leads a more active life and makes a greater demand on his heart, but the extent to which this has happened does not seem to be of clinical significance so far.

The changes after pulmonary valvotomy and after infundibular resection were analysed separately, but as no difference was found the figures have been combined.

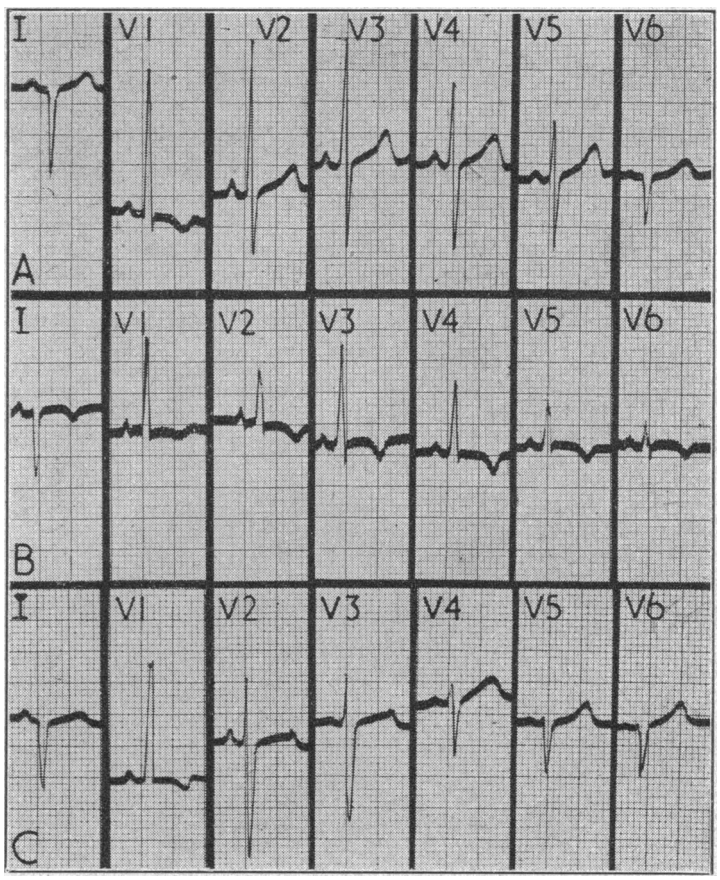

FIG. 7.—Characteristic T-wave changes in leads I and V_2 to V_6 after infundibular resection and valvotomy. (A) Before operation with right ventricular preponderance only. (B) Eighteen days after, showing T inversion in leads I and from V_1 to V_6. (C) Two years after, showing return towards normal, though in V_2 and V_3 T is still rather smaller and slow rising with a peak at the end. Case V65.

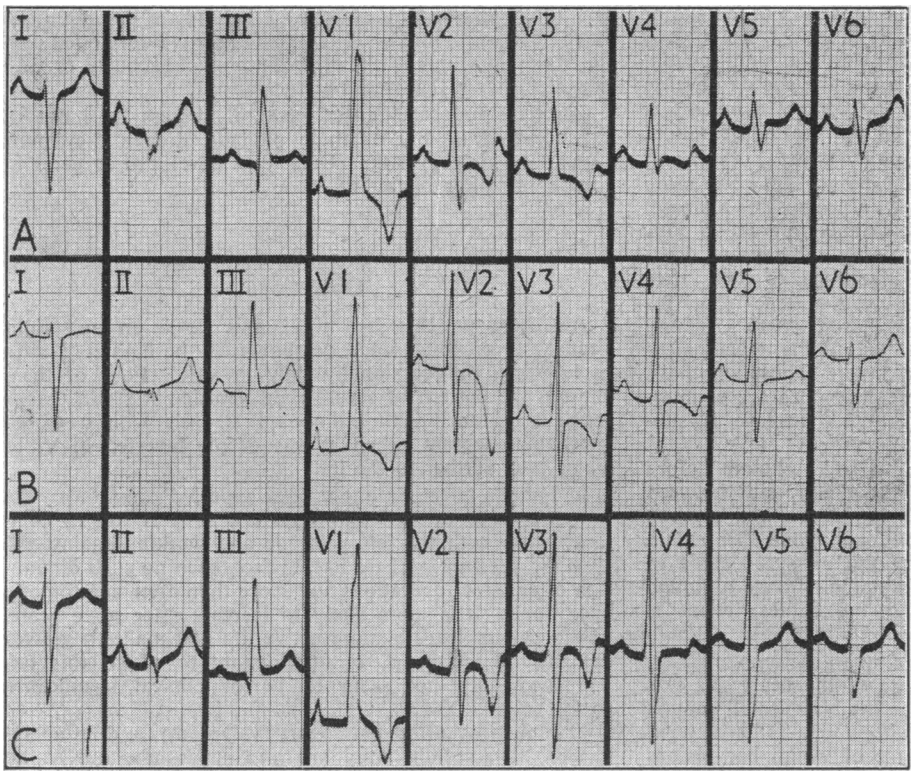

FIG. 8.—Diminution of T_1 and increased T inversion in the chest leads after infundibular resection, without much recovery two years later. (A) Before operation. (B) 21 days after infundibular resection. (C) 18 months after with recovery in V_4 only. Case V62.

Changes During the Operation

Continuous electrocardiograms have been taken during most of these operations and the findings have been described (Campbell and Reynolds, 1954). Changes in the pacemaker, nodal rhythms, A–V dissociation, ventricular extrasystoles, and short paroxysms of ventricular tachycardia were all common : heart-block and ventricular fibrillation were seen occasionally, but only rarely in patients who recovered. Apart from these changes of rhythm, bundle-branch block and S–T depression were common, but disappeared before the end of the operation or soon after. These changes have no direct relationship with the ones that follow the operation.

Early Changes after Operation

Brock and Campbell (1950b) described the changes that are generally seen after the right ventricle had been incised—changes similar to those seen after muscle injury. Subsequent records strengthen the view that these changes are a regular feature. For the first week after the operation no change is seen. Cove-shaped S–T waves with T inversion in lead I and reciprocal changes in lead III appear during the second or third week and increase in degree during the third and fourth weeks (Figs. 7 and 8, and Figs. 12 to 14 of Brock and Campbell, 1950b). During the fifth or sometimes not till the eighth week these changes are stationary. Thereafter, most often about the sixth or eighth weeks they gradually diminish, and have disappeared in the standard leads three or four months after operation. The inversion is greater (10 mm. or more) and lasts longest in the chest leads, especially V_2 and V_5, or even V_6. There are, however, no Q waves.

The more detailed findings on which these general conclusions are based follow. We have not many records taken early after operation, but 12 taken between 3 and 14 days after operation show no changes in the standard leads, though they may start earlier in the chest leads. There were 22 cases in which the changes were first seen in the second week, 15 in which they were seen in the third week, and 4 in which they were seen in the fourth week. The earlier dates are probably more accurate because usually there was no record to show that the change had not started sooner. T changes were still progressive during the third week in 12 and during the fourth week in 8 cases. Reversal of these changes and some return towards normal started in the fourth, fifth, or sixth week (seven cases), but more often in the seventh or eighth weeks.

All the 39 patients in whom records were available showed some of these changes. T_1 became smaller or flat in 10 but was not proved to become inverted, though it may have been at a time we had no records: in 6 of these 10, T was deeply inverted in the chest leads V_2 to V_4 or V_5, and in four it was biphasic.

Later Changes

These changes regress from the sixth to the eighth week after operation and generally disappear from the standard leads by three or four months. Occasionally T_1 may remain rather lower, but it has never remained flat or inverted for more than six months except in Case V 10, whose severe pain in the chest after operation seems likely to have been caused by a small cardiac infarct, though at the time it was attributed to a pulmonary embolism. Regression towards normal starts about the same time in the chest leads but is less often complete.

Recovery was nearly complete in 20 or 42 patients from two to four years after operation, though sometimes the T waves were smaller in leads V_2 and V_3. In 22 there were persistent changes, T in V_2 and V_3 and sometimes V_4 remaining inverted (nine cases) or biphasic (six cases) or slow-rising with a late peak (four cases). Some of the T waves are very similar in shape to those described by Evans and McRae (1952) as the lesser cardiographic signs of cardiac pain, and the late-rising peaked T wave is similar to the notched T waves (Dressler *et al.*, 1951). In the last three of the 22 patients the persistent changes were more severe. In Case V3, recovery was complete two years after operation, but five years after, when she was leading an active life almost without symptoms or undue enlargement of the heart, T had become deeply inverted from V_1 to V_4 (Fig. 9): there was no significant change in the standard leads. In the other two, also very good results, the T inversion has shown little tendency to disappear. In Case 2 T was still deeply, instead of slightly, inverted in V_1 to V_3, and flat in V_4 four years after operation, though the standard leads had returned to normal (Fig. 10). In Case 7 the chest leads had recovered at eight months, but three years after operation, when he had increased his activity greatly and was thought to have been doing too much, his heart was too large and T was inverted from V_1 to V_3 (Fig. 11). Here, too, the post-operative changes have disappeared, but evidence of right ventricular strain is developing. Clinically these three patients have achieved very good results, but the deep T inversion in the chest leads is disappointing; although at present it is not reflected in any clinical signs, it must be unfavourable for prognosis.

T-wave Changes after Anastomotic Operations

These late changes after direct operations have led us to re-examine the records after anastomotic operations, although earlier (Baker *et al.*, 1949) we had not been impressed by any cardiographic changes. A certain number of records three to six years after a subclavian–pulmonary anastomosis do show similar late changes. Of 42 early cases, unselected except that only good results were included, there were nine in which T was inverted from V_1 to V_3 and often to V_4, and in nine it was somewhat biphasic in V_2 and V_3. In the remaining 24 there was no change, though, of course, they still show right ventricular preponderance. These proportions are not very different from what has been found after direct operations.

Increasing right ventricular strain and T inversion might perhaps be expected in the most successful cases in which the degree of activity, the pulmonary blood flow, and the size of the heart show the greatest increase. There was some correlation, but it was not very close. In 6 of the 17 with inverted or biphasic T waves the heart was larger than was usual, but this was not so in the remaining 11. In two of the three with the greatest degree of inversion among the patients who had direct operations the heart was also unusually large, but not in the third. However, among the other 11 with inverted or biphasic T waves there were only two in whom it was larger than was usual.

It looks as if a successful result with a much increased pulmonary blood flow and a capacity for a much more active life is a partial but by no means the whole explanation of these cardiographic changes, as it is with an undue increase in the size of the heart.

Results of Cardiac Catheterization after Operation

Cardiac catheterization has a more useful place in assessing the results after direct than after anastomotic operations, and it has been carried out on selected cases to show the haemodynamic changes which are summarized in Table VI. We have not, however, used it as a routine to assess the results of the operation, for this is best done by clinical judgment of the patient's increased capacity.

The degree of change observed correlates well with the subjective improvement noticed by the patient. Where the operation has produced obvious benefit the right-to-left shunt is generally found to be reduced. This is shown by reduction of the cyanosis and by increase of the arterial O_2 saturation from an average of 78 to 91% and in three cases to normal values of 95% or above, a figure rarely, if ever, reached after anastomotic operations.

The pressure relationships between the right ventricle, the aorta, and the pulmonary trunk are not much changed. In Fallot's tetralogy the right ventricular systolic pressure tends to be fixed near the systemic arterial level because of the ventricular septal defect and overriding aorta. It is perhaps more surprising that the pulmonary pressure is not raised after partial relief of the stenosis and the increased pulmonary flow. It is well known that the pulmonary arterial pressure is largely independent of the pulmonary blood flow, but relief of the valvular stenosis might allow the high right ventricular pressure to be transmitted to the pulmonary trunk, and this has been urged as a criticism of direct operations. In fact, the average pulmonary pressure was 16/6 before and 14/4 mm. Hg after operation (excluding Case 21): the stenosis has been relieved enough to increase the pulmonary flow but not enough to lead to an equalization of systolic pressures.

Calculation of systemic and pulmonary blood flows is less accurate than the preceding figures but gives a good guide to the changes. The systemic flow is on the average unchanged. This is as one would expect, for in most forms of congenital heart disease the systemic blood pressure and flow appear to be maintained near normal and to be independent of changes in the pulmonary circulation (Deuchar and Knebel, 1952). The average pulmonary flow, on the other hand, is increased from 3.1 to 4.9 litres. If it is expressed as a percentage of the systemic flow it is increased from about half to about the same as the systemic flow; this high average covers a wide range and includes the very large—sometimes too large—pulmonary flows in the four patients with the most striking changes after operation.

The findings in these four with extremely good functional results are of great interest (Cases V35, 7, V54, and 21; see Table VI). The right-to-left shunt has been not merely

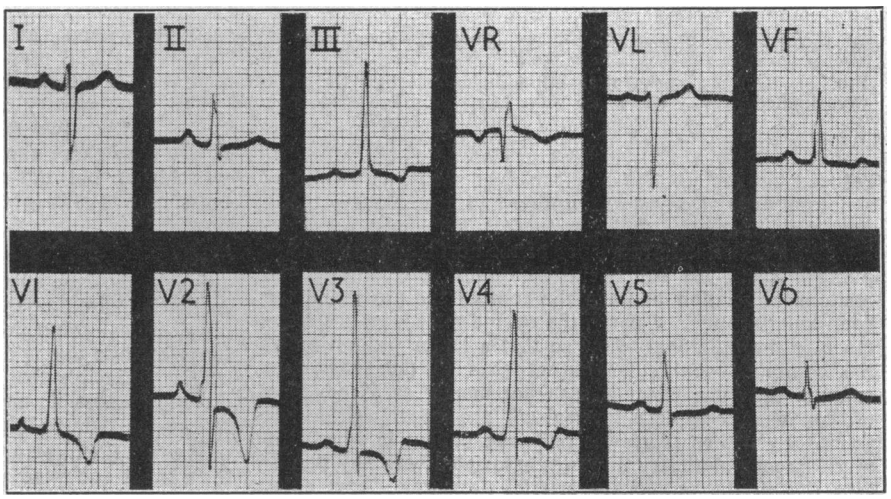

FIG. 9.—Increasing right ventricular strain five years after pulmonary valvotomy for Fallot's tetralogy. Two years after operation there was no more than right ventricular preponderance. Now, although she is very fit and leading an active life, the T waves have become deeply inverted in V_2 to V_3 and biphasic in V_4. Case V3.

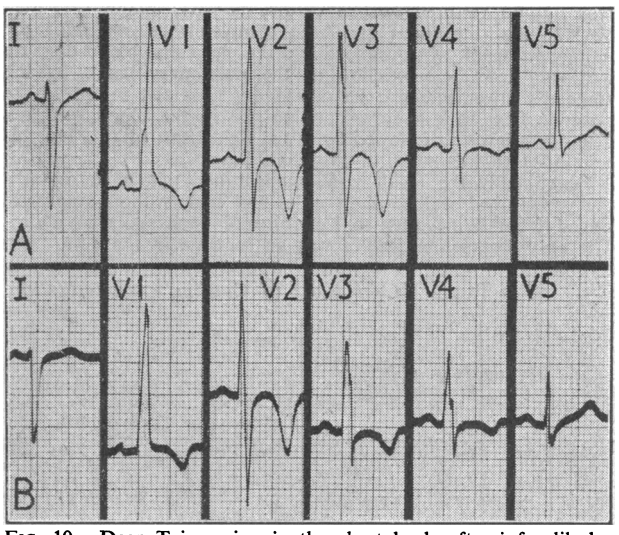

FIG. 10.—Deep T inversion in the chest leads after infundibular resection that changed only slightly during the next four years. (A) A year after, there is much more T inversion in the chest leads to V_1 to V_4 than before operation or even a month after it. (B) Four years after, T is still inverted from V_1 to V_4 but the very deep inversion is only seen in V_2. Case 2.

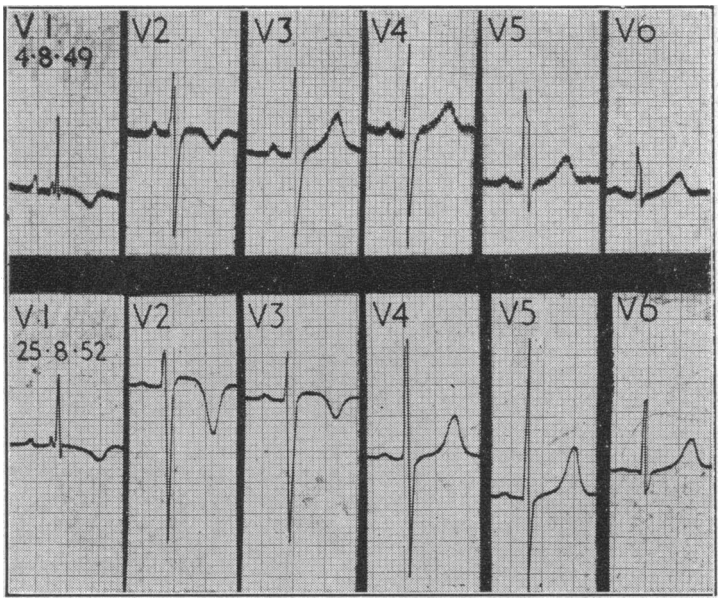

FIG. 11.—(A) Six weeks after infundibular resection the typical changes were limited to V_2. (B) Three years afterwards T was much more deeply inverted in V_2 and V_3. Case 7.

reduced but replaced by a left-to-right shunt, as shown by a normal arterial oxygen saturation and a pulmonary blood flow now in excess of the systemic. This must be determined by the relative resistance of the aortic and pulmonary outflow tracts, for the operation cannot have altered the anatomical relation between the root of the aorta and the ventricular septum. Clearly, the operation reduces the resistance to the pulmonary flow so that a larger proportion of the combined ventricular output goes to the lungs. In extreme cases the effect is seen not merely as a reduction of, but as a complete reversal of, the usual right-to-left shunt. Even then there was only one patient in whom the much larger pulmonary flow was associated with any significant rise in the pulmonary arterial pressure. Short notes about her follow.

Case 21, aged 16, had Fallot's tetralogy with moderate disability and cyanosis. Infundibular resection was performed successfully, but almost at once ventricular fibrillation occurred: resuscitation restored normal cardiac activity, and it was then obvious that the shunt had been completely reversed, for the pulmonary trunk was distended and the peripheral blood pressure was very low. Constriction of the pulmonary trunk by the surgeon's finger reduced the pulmonary flow and improved the systemic flow with a corresponding rise in the blood pressure. The operation was followed by initial right heart failure, but this responded to treatment.

Functionally the result was excellent and within six months the patient had walked eight miles and had (without approval) cycled from Winchester to London and back again in a day. The only disquieting feature was an increase in the c.t.r. from 49 to 68% (Fig. 6), but this diminished later. Cardiac catheterization showed that the shunt was completely reversed (arterial O_2 saturation 98% instead of 86%), so that the pulmonary flow was now more than twice as large as the systemic, instead of being about half as large. The pulmonary arterial pressure was increased from 14/7 to 38/12 mm. Hg. In the light of what was seen at operation this probably represents a maintenance of pulmonary peripheral resistance as a means of preserving an adequate systemic circulation when the pulmonary stenotic resistance has been greatly reduced. The pulmonary pressure may possibly rise further, even enough to cause a reversal of the shunt again, but this seems unlikely.

One other patient of Dr. Paul Wood's operated on at the Brompton—one of four who have had catheterization after operation—showed very similar changes. The clinical result was good and the arterial O_2 saturation was increased from 87 to 96%, but there was a left-to-right shunt of 5 litres. The systolic pressure in the right ventricle was lowered by only 5 mm., but the pulmonary arterial pressure rose from 12/3 to 38/20 mm. Hg. A second also had a moderate left-to-right shunt without an undue increase in the pulmonary arterial pressure (25/12), but for some reason the O_2 saturation in the peripheral artery and in the pulmonary vein was recorded as 88%. In the other two the results were substantially the same as those shown in Table VI; the arterial oxygen was higher but not normal, and the pulmonary arterial pressure was still low in spite of the increased pulmonary flow.

Discussion

Inevitably there must be some comparison between anastomotic and direct operations. The former follow the sound physiological principle of increasing the blood flow to the lungs because this is defective. The latter follow the sound surgical principle that an obstruction should be relieved as directly as possible and have the added advantage that they reduce the right-to-left shunt.

The excellent results of anastomotic operations led to their rapid and wide acceptance, all the more so as at first there was no alternative: they still seem to be preferred by most surgeons. Since that time safe intracardiac surgery has established itself as a daily routine, and in many countries vigorous efforts are being made to develop this new therapeutic weapon as quickly as possible.

The direct operations, although often approved in principle, have not been practised in large numbers. Most surgeons and cardiologists are still reluctant to accept them, because they fear a high mortality, distrust what they call a "blind operation," and are not convinced that good results can be achieved. An overall mortality of 15% is not unreasonable and certainly not prohibitive, for it is no higher than that found in the earlier series of anastomotic operations. Good results can be expected in most cases, as shown by the figures that have been given.

TABLE VI.—*Results of Cardiac Catheterization in Fallot's Tetralogy After Direct Operations*

Case No.	Sex and Age	Type of Stenosis	Condition after Operation	Pressure: mm. Hg from Mid-axillary Line				Systemic Blood Flow (litres/min.)		Pulmonary Blood Flow						Arterial Oxygen Saturation	
				Right Ventricle		Pulmon. Trunk				(litres/min.)		Litres/ sq.m./min.		As Percentage Systemic Flow			
				Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
V24	M11	Inf.+V.	No change	81/4	92/2	14/0	10/4	—	4·0	—	2·9	—	2·2	—	73%	88%	87%
V67	M19	V.	Improved	82/0	80/–2	13/4	10/0	7·0	8·1	3·6	6·1	2·2	3·2	51%	75%	82%	89%
V4	F23	V.	,,	53*	40*	13*	11*	—	—	—	—	—	—	—	—	77%	88%
V32	F18	V.	Very good	36*	33*	9*	7*	4·3	7·7	2·2	3·4	1·5	2·3	51%	48%	69%	84%
V29	F17	V.+Inf.	,,	—	110/0	—	12/3	—	4·4	—	2·9	—	2·1	—	66%	—	85%
8	F20	Inf.	,,	100/6	106/2	12/6	12/4	4·0	3·4	2·5	2·6	1·7	1·8	62%	80%	74%	86%
V10	M22	V.	,,	45*	100/8	16*	17/2	5·1	3·7	2·1	3·2	1·5	2·2	39%	87%	79%	92%
3	M24	Inf.	,,	—	85/10	—	28/4	—	4·0	—	4·8	—	2·9	—	120%	75%	90%
V35	M14	V.	,,	103/0	88/4	16/7	24/9	5·1	4·5	2·8	6·2	1·9	4·2	55%	138%	81%	93%
7	M12	Inf.	,,	85/0	145/5	—	18/7	—	3·6	?	5·6	?	3·9	30%	156%	72%	95%
V54	F14	Inf.+V.	,,	132/11	116/0	27/13	15/5	7·3	5·2	5·2	7·9	3·3	5·1	34%	152%	87%	97%
21	F16	Inf.	,,	114/?	100/5	14/7	38/12	—	3·6	?	7·5	?	6·2	57%	208%	86%	98%

* Mean pressures.

Our present technique, although admittedly restricted and not "open," is certainly not "blind." By complete exposure and external examination of the heart and great vessels at operation a high standard of diagnosis is reached, and is both amplified and verified by direct pressure readings made in the various parts of the pulmonary outflow tract. In this way the presence of one or two stenoses and their exact level and relative importance can be accurately and quickly assessed. When necessary a finger is introduced into the right ventricle and further information is obtained. The obstruction or obstructions are then relieved by a simple technique consisting of incision and splitting the stenosed valve and punch resection of the infundibular stenosis. Not until electromanometric records show that the stenosis has been adequately relieved is the operation concluded. This may involve the introduction of instruments ten or twelve times. Our present technique has evolved from the experience gained in over 100 direct operations of this type and explains why the results, both in low mortality and in good function, are better now than formerly. Failures to-day are rare and some of the earlier ones were due to lack of skill in doing the operation well or in recognizing the presence of infundibular stenosis when valvular stenosis had been relieved.

The right-to-left shunt can be lessened or corrected or even overcorrected. We have ample evidence of this clinically and from cardiac catheterization. The shunt is changed as a result of the lessening of the pulmonary stenosis, and as more blood goes to the lungs less is diverted into the aorta. Indeed, without careful electromanometric control throughout the operation it is easy to relieve the stenosis too effectively and thus cause a left-to-right shunt and too large a pulmonary blood flow. With a bolder attack on the stenosis it has been increasingly important to try to avoid overcorrection, and in some cases we have done too much. This, again, has been put forward as an objection to the direct operation, that one would produce an Eisenmenger's complex. So far this has not occurred, although occasionally the pulmonary blood flow has been increased too much (as, indeed, it may be after an anastomosis). Here again we are dealing only with a technical problem, albeit a big one, and not a principle. In contrast it seems that some surgeons do not use careful electromanometric control in these operations and so may give incomplete relief of the stenosis—often only introducing and withdrawing rapidly a single instrument. They do not check the final pressure changes. In our practice to-day the direct operations are reasonably efficient from the technical point of view but are not complete or entirely satisfactory. We think that the principle behind them—namely, relief of the obstruction—is a sound one, that technical limitations are temporary and can be conquered, and that the only thing that could prevent their development and wide acceptance would be a failure of technical improvement. The next and imminent advance in cardiac surgery is the establishment as a safe routine of direct vision operating within the "dry" heart. We have already found in patients operated on since this series that by this technique and using hypothermia the obstructions can be quickly located by sight and relieved under direct vision. The same principles obtain; their technical achievement is simply to be more effective.

These practical considerations do not present the whole story of direct relief of pulmonary stenosis in Fallot's tetralogy. There is the principle behind the direct operations which attempt anatomical relief of the obstruction. By this two things are achieved—an increase of blood flow to the lungs and a physiological correction of the right-to-left shunt. It does nothing anatomically to the ventricular septal defect or the overriding aorta. The fear of overcorrection of the shunt and the blood flow to the lungs is determined by our present technical inability to correct the ventricular septal defect and the overriding aorta. Once it becomes possible to achieve this, the objection to a too generous relief of the stenosis falls to the ground.

Admittedly, the closure of the septal defect is a difficult technical step and one that may often be unattainable. Equally certainly it must and will be achieved in many cases, and we shall then move nearer to our ideal of trying to correct the whole of the cardiac abnormality; we shall be able to tell some of our patients that they have in truth been cured and that their heart is now as near normal as may be. We shall be relieved of the uncertainty of the later prognosis that must obtain when the septal defect persists and a shunt is still present (after either a direct or an indirect operation), and when the heart may become too large, as has been found sometimes after both types of procedure. However, if we are to draw nearer to this ideal and if we are ever to achieve it, we can never do so by using only the anastomotic operations, but must use and develop the direct operations: herein lies a further justification for their use even though they may carry with them greater anxiety and responsibility in the course of their application and evolution.

Summary and Conclusions

We have reported the results in 100 patients with Fallot's tetralogy operated on by Brock's direct methods. Forty-five had infundibular resection only; all the others had pulmonary valvotomy, but 18 needed infundibular resection as well. We have re-examined and analysed most fully the first 61 who were operated on at Guy's Hospital, and have assessed the degree of improvement in the same way as in the parallel series of patients who had anastomotic operations, almost always subclavian–pulmonary anastomosis.

Both these direct operations can produce excellent results which last at least for the period of observation and seem likely to last much longer, judging by the present condition of the patients. Two-thirds of them have obtained good or very good results, which means that they are leading a quiet life that is nearly normal. One-sixth show some improvement but nothing like the standard of the good results. The remaining sixth died as the result of the operation.

In most particulars there was not much difference between the results of these two operations for Fallot's tetralogy, but valvotomy, with a gross mortality of 11%, seems reasonably safe, and infundibular resection, with, as might be expected, a higher mortality of 18%, seems more dangerous. Another difference is that infundibular resection rarely fails to produce a good result in those who survive, while after valvotomy, alone or combined, there are a larger proportion who show only slight or moderate improvement. Sometimes one cannot be sure of the degree of improvement at first, and we have been disappointed when the patient left hospital, only to find six or twelve months later that he had obtained an excellent result: this, however, is not usual.

The improvement in what these patients can do is as great as after anastomotic operations. In addition, there is the same reduction in their cyanosis and in the polycythaemia and haemoglobin percentage, the mean in those with good and very good results falling from 128 to 103%. The improvement in the colour and in the clubbing of the fingers may be even greater than after anastomotic operations, and some patients lose all their cyanosis at rest and a few even after exertion. In these, catheterization shows that the oxygen saturation of the arterial blood has become normal and that their right-to-left shunt has been not only diminished but reversed.

The heart tends to become larger after direct as after anastomotic operations, the cardiothoracic ratio rising from a mean of about 49 to 53.5% within a few months of operation and remaining at or a little below this level during the next few years. When the clinical result is particularly good and the cyanosis is abolished, the heart may increase in size more than usual, as after an unusually large anastomosis. It would be optimistic to expect the improvement that follows either of these operations without some increase in the size of the heart, because the right ventricle is still working against the systemic pressure and the patient is leading a much more active life. It means that in the patients with the best results the doctor should act as a restraining influence, persuading them to lead a reasonably quiet life if they wish to keep their improvement as long as possible.

It has been suggested as a criticism that direct relief of the stenosis will raise the pulmonary pressure and produce a condition like Eisenmenger's complex. This is not so. Even when the blood flow to the lungs is greatly increased and the patient can do much more, the stenosis has not been relieved so completely that the high pressure of the right ventricle is transmitted to the pulmonary trunk. In most cases, although the larger pulmonary flow and the condition of the pulmonary artery felt at operation and seen on radioscopy all show that the obstruction is less, catheterization shows that there is still a large pressure gradient across the site of the stenosis. In one patient only—one who can do all she wants and is acyanotic, with her right-to-left shunt reversed—there is some rise of pressure in the pulmonary trunk, but the increase is not very great.

The striking improvement as the result of increasing, directly or indirectly, the blood flow to the lungs has perhaps overemphasized the stenosis and drawn attention away from the ventricular septal defect and the overriding aorta. The improvement in the cyanosis shows that the venous shunt to the aorta is much less, and this has been confirmed by catheterization in several cases, though, of course, the pressure in the right ventricle remains about the same. But, so long as the ventricular septal defect remains, the right ventricle will have increased work and will be exposed to the risk of strain.

Future difficulties, however, are no reason for withholding the great advantages that anastomotic and direct operation can give, though clearly the treatment of Fallot's tetralogy will not be ideal until the ventricular septal defect can be closed.

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SOME NEUROPHYSIOLOGICAL ASPECTS OF SEROTONIN

BY

D. W. WOOLLEY, M.D., Ph.D.

AND

E. SHAW, Ph.D.

From the Rockefeller Institute for Medical Research, New York

During the past few years a number of investigations have revealed that serotonin is of importance in the functioning of the autonomic and central nervous systems, and that the neurogenic behaviour of animals can be profoundly influenced by pharmacological agents which interfere with the action of this compound. The purpose of this paper is to summarize several of these findings.

The existence of serotonin was discovered only a few years ago as a result of two quite independent lines of work. Rapport, Green, and Page (1948) attempted the isolation of the vasoconstrictor which has long been known to form in mammalian serum when blood clots. They succeeded in crystallizing the substance present in serum which exerted this effect on the vascular bed and named it "serotonin." Rapport (1949) continued the study of the chemical nature of the active substance, and was able to deduce that it was 5-hydroxytryptamine (see Fig. 1). The correctness of this formulation was confirmed by Hamlin and Fischer (1951) and by Speeter *et al.* (1951), who synthesized 5-hydroxytryptamine and showed that it was identical with the naturally occurring substance.

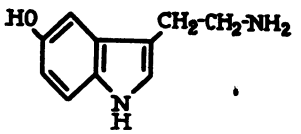

FIG. 1.—Structure of serotonin.

While the work on the identification of the vasoconstrictor of serum was being done, Erspamer (1940), in Italy, had been investigating a constituent of animal tissues which he had named "enteramine." This material occurred in gastric and enteric mucosa of mammals, and in the skin and salivary glands of such lower forms as toads, salamanders, and octopi (Erspamer, 1952; Erspamer and Vialli, 1952). The distinctive staining properties of the argentaffin cells of gastric mucosa were attributed to this substance, and these staining properties were used to follow it in early attempts at isolation. Pharmacological properties of crude extracts containing enteramine were found in that such extracts caused various smooth muscles to contract. Such properties led Erspamer to the view that the active agent was a hormone. Using pharmacological tests and colour reactions as guides, Erspamer and Asero (1952) were able to isolate a pure compound from the salivary glands of the octopus. This compound was found to be 5-hydroxytryptamine, identical with serotonin.

Action on Smooth Muscle

The early work on serotonin, or enteramine, had clearly indicated that it caused smooth muscles to contract. As soon as abundant material became available through chemical synthesis a variety of pharmacological effects of it began to be reported. Thus, segments of carotid arteries of sheep (Reid and Rand, 1952; Woolley