THE POSTNATAL DEVELOPMENT

OF THE

HUMAN CARDIAC VENTRICLES

Thesis

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Doctor of Medicine

by

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INTRODUCTION

"It is to be observed, however, that all this is otherwise in the embryo, where there is not such a difference between the two ventricles; but as in a double nut, they are nearly equal in all respects, the apex of the right reaching to the apex of the left, so that the heart presents itself as a sort of double-pointed cone. And this is so, because in the foetus, as already said, whilst the blood is not passing through the lungs from the right to the left cavities of the heart, but flowing by the foramen ovale and ductus arteriosus, directly from the vena cava into the aorta, whence it is distributed to the whole body, both ventricles have in fact the same office to perform, whence their equality of constitution. It is only when the lungs come to be used, and it is requisite that the passages indicated should be blocked up, that the differences in point of strength and other things between the two ventricles begin to be apparent: in the altered circumstances the right has only to throw the blood through the lungs, whilst the left has to impel it through the whole body."

From 'De Motu Cordis et Sanguinis', by William Harvey, published in 1628 at Frankfort-am-Main; as translated by Robert Willis, M.D.

The name of William Harvey is immortal, and it is fitting that a quotation from his epoch-making ' De Motu Cordis et Sanguinis' should preface this thesis. The discoverer of the circulation did not fail to point out the difference between foetal and postnatal conditions of the heart and great vessels. Harvey, however, was not particularly concerned with the problems of the foetal circulation, and devoted only a passing glance to the subject, using foetal conditions to illustrate his general argument about the circulation of the blood.

The subsequent progress of thought on the subject of foetal circulation has been admirably set out in the first chapter of Barclay, Franklin, and Prichard's book 'The Foetal Circulation', published in 1944, but there is no doubt that the major advance since Harvey's time is represented by the cine-radiographic observations made by the authors of this book on the foetal lamb. They provided, for this species, a convincing and complete picture of the pattern of the foetal circulation, together with the changes brought on by allowing the foetus to breathe and by severing the umbilical cord, thus simulating the event of birth. They showed that the via sinistra (foramen ovale) was functionally closed within a few minutes of the onset of respiration, and the ductus arteriosus within a few minutes of severance of the umbilical cord. Until similar experiments are possible in human subjects, no direct evidence of the comparable events at the birth of a human being will be obtained.

One of the last adjustments necessary to convert the foetal cardiovascular system to one which is, in all essentials, a small replica of the adult state, concerns the functional balance between the two ventricles. Many authors have asserted, on somewhat slender evidence, that in foetal life the two ventricles are of equal bulk and that therefore they do the same amount of work. Curiously little attention has been paid to the rate at which this relationship is changed to a functional balance which characterises the normal adult heart. The determination of this rate of change has some importance as a source of indirect evidence about the circulatory events at birth in the human being. An exception to this general neglect is seen in the published statements of Bradley M. Patten, the American embryologist who has contributed much to the study of the foetal human heart. He claimed, as can be seen from the statements quoted on pages 40 and 48 that the investigations of W. Müller (1883) supported his view that the event of birth is but a minor incident in the development of the human cardiovascular system, involving no changes which can in any way be described as revolutionary.

During the course of the present investigation a copy of Wilhelm Müller's book 'Die Massenverhältnisse des menschlichen Herzens' (The Weight Ratios of the Human Heart), which was published in 1883, was obtained. It then became clear that Müller's answer to the problem in question was not that claimed by Patten. However Müller's methods can be quite severely criticized, and his conclusions have therefore to be revised. Müller's own comments seem to have been quite ignored by the numerous authors who have made use of his findings.

A fresh investigation into the rate of change of the ventricular ratio seemed therefore necessary. The facts appear to be in dispute, and the true facts are of importance not only in the study of human birth, but also to the cardiologist interpreting the changes which the normal electrocardiogram undergoes for several years after birth.

PRESENT INVESTIGATION.

(1) Material

Over a period of eighteen months during 1951 and 1952, 237 hearts from infants and children, whose bodies were brought to the Police mortuary in Cape Town, were collected for investigation. The large majority of these deaths were due to natural causes, and in these cases the bodies were only brought to the mortuary because no death certificate was available. In the minority an accident such as overlaying was the cause of death. The series as a whole is representative of the less privileged classes living in and around Cape Town.

In about a quarter of the cases the post-mortem examinations were conducted by the author, who is indebted to the other pathologists working in the mortuary for the remainder. The only selection of material exercised was to avoid cases falling into two categories:

(1) those in which the heart was, or might have been, affected by the disease process causing death. In particular generalised tuberculosis of the lungs had to be avoided; two such cases, early in the series, showed considerable right ventricular hypertrophy. Beyond the two specimens mentioned, it was necessary to exclude only one other specimen, because of congenital cardiac defect; the details of this case are shown on p.13 .

(2) specimens from infants who might have been prematurely born. It was naturally easy to classify the newly born infants, but detection of prematurity in infants of 2 months or more proved very difficult, as it was rare for the parents to know what the weight of the baby had been at birth. In the face of malnutrition and disease, it was clearly useless to rely on the weights of the infants, and there does not seem to be any published guide to the growth in length of infants born prematurely, or to the influence of malnutrition on the growth

in length of the mature infant under six months of age. The decision as to whether a particular infant had or had not been born prematurely therefore often became a matter of judgement on the part of the pathologist concerned, assisted in some cases by the recollections of the parents. These difficulties make it probable that some of the specimens were derived from infants born prematurely, despite efforts to exclude them. On the other hand some cases may have been excluded in error. The difficulties to which this selection gives rise are described on p. 17. The classification of all cases except three was accepted. Each of these three was from a child of three months, which was considered to have been born prematurely on internal evidence of heart weight; the justification for this exclusion will be found detailed on page 13 .

The 234 hearts investigated were distributed in age groups as follows:

PREMATURELY BORN			
Stillborn	11		
Aged 3 days or less	9		
Aged 4 days or more	14		
Total	34		
FULL TERM INFANTS			
Stillborn	15		
Aged 3 days or less	21		
Total	36		
Neonatal period	11		
1 month old	14		
2 months old	15		
3 months old	14		
4 months old	15		
5th and 6th months	18		
7th to 12th months	21		
Second year	22		
Third year	10		
Fourth and subsequent years	24	TOTAL	234

The classification by age was arranged so that the mean age of the specimens grouped, for example, in the class " 2 months old" was approximately 2 months; on the other hand the designation

"Second year" includes all specimens from children dying in that period. The mean age of the 'neonatal' cases was 11 days, with a standard error of 1.9 days.

This study was particularly directed to the series of full term infants and children from birth until three years. The 36 hearts from stillborn infants and those dying in the first three days of life were grouped together as representing conditions at birth; data relating to them are included in the tables and graphs under the heading "Birth".

(2) Method

Collection of specimens. The atria of each heart were freely opened, and as much as possible of the blood and clots washed out from atria and ventricles. The ventricles were not incised. The specimen was labelled with a name and a reference number, but age and other details were deliberately not included on the label. In the case of specimens not personally collected, this information was not sought until the dissection and weighings had been completed. The specimens were stored in 10% formol saline. After 72-96 hours they were removed and dissected according to a uniform plan to be described below. By controlled daily weighings the loss in weight due to storage in 10% formol saline for 3/4 days was found not to exceed 2%, and this was ignored.

Dissection of the heart. Throughout the process of dissection the specimen under investigation was kept moist to avoid the loss of weight caused by drying. The steps of dissection are described below, and illustrated in Fig. 1.

undisturbed pericardium

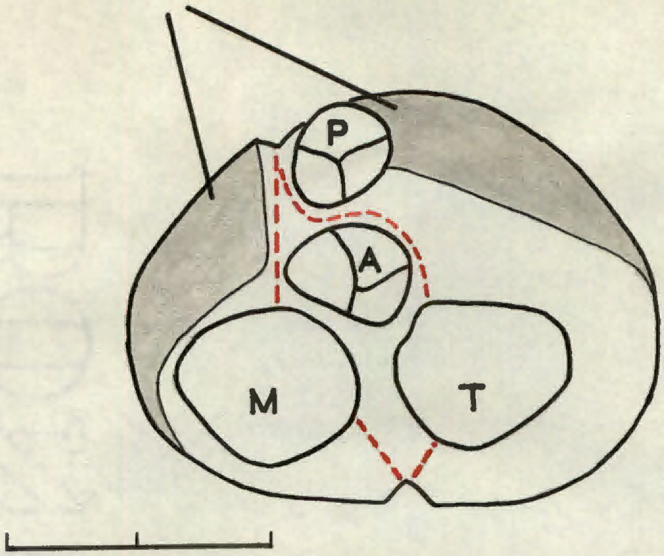


Fig. 1: A diagram of the basal surface of the ventricles of the heart, after removal of the atria and the great vessels; the red lines indicate the lines of division of the ventricular mass. Scale in cm. A, aortic valve. M, mitral orifice. P, pulmonary valve. T, tricuspid orifice.

(1) A narrow strip of pericardium with the underlying vessels was removed from the interventricular grooves on the front and back of the heart; the underlying myocardium was damaged as little as possible. This manoeuvre served to fix the peripheral attachment of the septum, and the division between right and left ventricles, as far as the position of the vessels could be relied on to do so. In practice the interventricular branches of the two coronary arteries were easily defined and marked the division between the ventricles accurately, in most cases; occasionally there was some difficulty on the inferior surface of the heart. No attempt was made to remove other branches of the coronary vessels, and the pericardium was left intact except where it overlay deposits of fat (see par. (4)).

(2) By sharp dissection all fat, vessels, and the attached

atrial walls were removed from the upper surface of each ventricle and from the septum. With experience it was easy to expose with a few strokes of a sharp knife the rounded "shoulder" of ventricular muscle which presents in the atrio-ventricular groove.

(3) The aorta and pulmonary trunk were removed with scissors at their roots; the aorta proximal to the origin of the coronary arteries, and the pulmonary trunk at the limit of the infundibular myocardium - a level easily seen with the naked eye.

(4) Any deposits of sub-pericardial fat were removed with their overlying pericardial covering. The remaining specimen was now separated into right ventricular, septal, and left ventricular portions by the following incisions. The position of these incisions on the basal surface of the ventricular mass is shown in Fig. 1.

(5) With a fine pair of scissors, one blade of which was inserted into the tricuspid opening, the infundibulum of the right ventricle was separated from the aorta. This incision passed usually between the anterior and septal cusps of the tricuspid valve, divided the tendon of the infundibulum (conus tendon), and was prolonged a short way down the anterior interventricular sulcus. The muscle of the infundibulum always separated from the aorta as a complete muscular cylinder, which extended for a short distance below the level of the attachments of the cusps of the pulmonary valve.

(6) An incision was made from the posterior interventricular sulcus into the cavity of the right ventricle in such a way as completely to separate the free wall from the septum. The position of this incision was to some extent controlled by the necessity to insert the knife into the sulcus, but it was possible to incise too deeply into the septum. Consistency is acquired with experience, and the personal error involved is certainly less than the error involved in attempting to separate the left ventricular wall from the septum in a consistent way (see par. 8).

(7) A similar incision made from the anterior interventricular sulcus into the right ventricle divided the last attachment of the right ventricular free wall to the rest of the heart.

(8) From the anterior and posterior interventricular sulci incisions were made into the left ventricle so as to separate its free wall from the septum. These incisions avoided the aorta, the intracardiac portion of which remained with the septal fragment. It was very difficult to make these incisions in a consistent fashion, but as will be shown, the division of the septal fragment from the free wall of the left ventricle by this method can be ignored in analysing the weight ratio of the two ventricles.

(9) From each of the three fragments the cusps of the mitral and tricuspid valves with their chordae tendiniae were dissected away, and the semilunar cusps of the aorta and pulmonary valves were similarly removed. The removal of the anterior cusp of the mitral valve naturally opened the aorta widely, and access to the pulmonary valve was obtained by dividing the muscular cylinder of the infundibulum along a convenient line. The roots of the two great arteries were further trimmed if necessary.

Weighing. Each fragment was shaken free of moisture by hand, and weighed on an ordinary laboratory balance to the nearest 0.1 g. The abbreviations R, L, and S, will be used freely to represent the weights in g. of the three fragments dissected in the way described, and T the total ventricular weight, i.e. R + S + L.

(3) Analysis of Observations

The difficulty of interpreting the mutual relationships of the three quantities R, S, and L naturally resolves itself into a decision about the quantity S. The division of the ventricular mass may be regarded as taking place in two stages: the division of the right ventricular free wall (R) from the remainder (S + L), and the division of the latter into a septal fragment (S) and the left ventricular free wall (L). The present study is closely concerned with the foetal heart, which in comparison with the adult heart, shows a marked right ventricular 'hypertrophy', diminishing after birth at a rate to be demonstrated. It is therefore evident that the ratio R/T, which is a quantitative reflection of the first stage of the division, will provide some clue to this altering relationship.. It remains to be shown whether all, some, or none of the septal fragment should be considered as 'belonging' to the right side, a procedure which might modify the impression given by the R/T proportion alone.

In the present study the proportion S/S+L expresses quantitatively the second stage of the division. This proportion has been worked out to the nearest whole figure of percentage for each specimen, and the mean observation with its standard error computed for each age group. The results of this analysis appear in Table 1.

TABLE 1.

MEAN SEPTAL PROPORTION WITH STANDARD ERRORS

	S/S+L per cent	standard error of the mean
Birth	32.6	0.54
Neonatal	32.7	1.29
1 month old	32.4	0.79
2 months old	32.0	1.03
3 months old	31.1	0.65
4 months old	31.9	1.03
5th & 6th months	32.4	0.65
7th-12th months	31.9	0.55
2nd year	30.8	1.44
3rd year	31.4	1.17
24 specimens from 4-16 years	31.4	0.63
20 specimens from premature infants at birth	32.3	1.23

No figure in this table differs significantly from any other. The inference is clear: in this series of observations the septum (more correctly the septal fragment as divided) follows the free wall of the left ventricle in its increase in weight slavishly, and is not influenced by the behaviour of the right ventricular free wall. In other words the division of septal fragment from left ventricular free wall may safely be ignored, and the change in relationship between right and left ventricles measured by the ratio R/T alone.

It must be clearly understood that the conclusions in the last paragraph do not mean that the septum by its contraction does not assist the right ventricle as well as the left; but simply that the inevitably crude analysis of the structure of the heart which arises from arbitrary cuts dividing its parts cannot detect the functional relationship of the septum and the right ventricle. This must be particularly borne in mind in considering the foetal heart, where the two ventricles are approximately equal in bulk.

As a result of these observations it was decided to analyse in detail the changes in weight of the right ventricular free wall (R), the remainder of the ventricular mass (S+L), and the total ventricular weight (T), with the sole significant relationship R/T%. These accordingly are the quantities reported in the following tables and graphs. The proportion R/T% was calculated to the nearest unit of percentage for each heart. In Table 3 the observations of the proportion S/S+L are reported in greater detail.

(4) Results

The results are reported in Tables 2 and 3, the first dealing with the absolute weights, and the second with the significant proportions. In each table the results are collected in the age groups already described, and opposite each age appear four observations for each quantity measured; the mean, with its standard error (s.e.m.), the range of observations, and the standard deviation (S.D.).

In Table 2 and under R/T in Table 3 there are four ages for which alternative means are offered, in each case after exclusion of one specimen from the group. The justification for the exclusion of these cases, and therefore for preferring the alternative figures, now follows. In each of the four cases the observations made on the excluded specimen are compared with the other members of the group in a manner which should be self-explanatory.

Case (1)

Neonatal period	R	S+L	T	R/T%
serial number 223	10.3	11.0	21.3	48
next highest R value	6.8	9.0	15.8	43
next highest R/T value	4.9	6.0	10.9	45
mean including no. 223	5.6	8.5	14.1	39.2
mean excluding no. 223	5.1	8.3	13.4	38.4

Case (2)

1 month old	R	S+L	T	R/T%
serial number 59	11.0	12.8	23.8	46
next highest R value	6.4	13.4	19.8	32
next highest R/T value	5.9	9.3	15.2	39
mean including no. 59	5.3	11.2	16.5	32.0
mean excluding no. 59	4.9	11.1	16.0	31.0

In both these cases the right ventricular fragment weighs far more than in the other members of the age group. In neither was there any pulmonary stenosis or other congenital cardiac defect which might have explained this hypertrophy, and there was no opportunity of examining the lungs in detail. It may tentatively be surmised that these infants suffered from some form of pulmonary hypertension of early onset. In any case each seems to differ sufficiently from the rest to suggest that it is abnormal, and to justify its exclusion from the group. In Table 2 can be seen the marked reduction in the S.D. values in the R column which the exclusion of the cases occasions.

Case (3)

4 months old	R	S+L	T	R/T%
serial number 13	10.2	20.2	30.4	34
next highest T value	6.5	18.3	24.8	26
next highest R value	6.7	14.8	21.5	31
mean including no. 13	5.3	13.1	18.4	28.8
mean excluding no. 13	5.0	12.6	17.6	28.4

In this case there appears to be a generalised hypertrophy of the ventricular mass, in addition to an unusual preponderance of the right ventricle.

Differences in the T value of 6 g. from the next biggest specimen and 12 g. from the mean value seem sufficient to label the heart abnormal.

Case (4)

5th and 6th months	R	S+L	T	R/T%
serial number 24	2.6	6.9	9.5	27
next smallest T value	3.6	7.9	11.5	31
mean including no. 24	5.3	13.2	18.5	28.8
mean excluding no. 24	5.5	13.6	19.1	28.9

The very small size of this specimen, only 0.6 g. above the minimum T value encountered among the full term infants at birth, suggests that the infant from which the heart came had been prematurely born. It must be admitted that the exclusion of this case does not rest on such firm ground as the three already described. The range of observations is in any case so wide that the exclusion of this one case does not alter the means or deviations very much.

Four other cases were excluded before the tables were compiled, and have been mentioned on pages 4 and 5. The three specimens from the age group <u>three months</u> which were considered premature showed T values of 7.8, 8.3, and 8.8 g. respectively; these figures should be compared with the mean of 18 g. for the other members of the age group, the range of observations extending from 12.8 to 26.2 g. The remaining case, serial number 213, was also from an infant aged 3 months, and gave these results: R 17.6 g., S+L 19.1 g., T 36.7 g., R/T 48%. This was such a gross case of right ventricular hypertrophy that there was never any doubt about excluding this case from the series.

TABLE 2: POSTNATAL DEVELOPMENT OF THE VENTRICLES

Weights in g. of the total ventricular mass and of the parts into which it is divided. R - right ventricular free wall. S - septal fragment. T - total ventricular weight. L - left ventricular free wall.

Age	No.	R				S + L				T			
		mean	s.e.m.	range	S.D.	mean	s.e.m.	range	S.D.	mean	s.e.m.	range	S.D.
Birth	36	6.0	0.26	3.4 - 8.8	1.6	7.5	0.25	5.2 - 11.1	1.5	13.5	0.47	8.9 - 19.4	2.8
Neonatal	11	5.6	0.53	3.7 - 10.3	1.8	8.5	0.44	6.0 - 11.0	1.5	14.1	0.90	10.1 - 21.3	3.0
alternative	10	5.1	0.28	3.7 - 6.8	0.9	8.3	0.41	6.0 - 10.1	1.3	13.4	0.64	10.1 - 15.9	2.0
1 month old	14	5.3	0.48	3.6 - 11.0	1.8	11.2	0.66	7.1 - 14.2	2.5	16.5	0.98	10.7 - 23.8	3.7
alternative	13	4.9	0.21	3.6 - 6.4	0.7	11.1	0.67	7.1 - 12.8	2.5	16.0	0.87	10.7 - 20.7	3.1
2 months old	15	4.7	0.24	3.4 - 6.8	0.9	11.2	0.56	8.4 - 16.2	2.2	15.9	0.86	11.8 - 23.0	3.3
3 months old	14	5.2	0.34	3.5 - 7.6	1.3	12.8	0.83	8.7 - 18.6	3.1	18.0	1.13	12.8 - 26.2	4.2
4 months old	15	5.3	0.43	3.4 - 10.2	1.7	13.1	0.86	8.4 - 20.2	3.3	18.4	1.25	11.8 - 30.4	4.8
alternative	14	5.0	0.28	3.4 - 6.7	1.0	12.6	0.74	8.4 - 18.3	2.8	17.6	0.92	11.8 - 24.8	3.6
5th-6th months	18	5.3	0.34	2.6 - 8.6	1.5	13.2	0.99	6.9 - 16.0	4.2	18.5	1.31	9.5 - 34.6	5.6
alternative	17	5.5	0.33	3.6 - 8.6	1.3	13.6	0.98	7.9 - 26.0	4.1	19.1	1.29	11.5 - 34.6	5.3
7th-12th months	21	5.6	0.34	3.6 - 8.8	1.6	14.6	1.05	8.3 - 26.5	4.8	20.2	1.38	12.1 - 34.9	6.3
2nd year	22	7.9	0.61	4.6 - 12.0	2.9	21.7	1.05	12.3 - 30.8	4.9	29.8	1.39	16.9 - 41.1	6.5
3rd year	10	10.7	0.78	6.9 - 14.6	2.5	26.6	1.17	19.2 - 32.3	3.7	38.3	1.81	31.3 - 47.6	5.7

p.15

TABLE 3: POSTNATAL DEVELOPMENT OF THE VENTRICLES

Weight ratios. R, T, S, L as in Table 2.

Age	R/T% No.	R/T% mean	R/T% s.e.m.	R/T% range	R/T% S.D.	S/S+L% mean	S/S+L% s.e.m.	S/S+L% range	S/S+L% S.D.
Birth	36	44.1	0.61	36 - 53	3.7	32.6	0.54	26 - 42	3.2
Neonatal	11	39.2	1.38	33 - 48	4.6	32.7	1.29	28 - 38	4.3
alternative	10	38.3	1.18	33 - 43	3.7				
1 month old	14	32.0	1.41	25 - 46	5.3	32.4	0.79	29 - 39	2.9
alternative	13	31.0	1.06	25 - 39	3.8				
3 months old	14	28.9	0.69	25 - 35	2.6	31.1	0.65	26 - 36	2.4
4 months old	15	28.8	0.73	26 - 34	2.8	31.9	1.03	25 - 40	4.0
alternative	14	28.4	0.67	26 - 34	2.5				
5th-6th months	18	28.8	0.61	25 - 32	2.6	32.4	0.65	29 - 39	2.8
alternative	17	28.9	0.75	25 - 32	3.1				
7th-12th months	21	28.1	0.56	24 - 31	2.6	31.9	0.55	26 - 37	2.5
2nd year	22	27.4	0.39	24 - 31	1.8	30.8	1.44	24 - 37	6.7
3rd year	10	27.9	1.00	22 - 31	3.2	31.4	1.17	27 - 36	3.7
4 - 16 years	24	27.2	0.44	24 - 33	2.2	31.4	0.63	25 - 37	3.1

(5) Interpretation of the Results

In the following statements about the age changes in the various mean figures, no change has been considered significant unless shown to be so by the 't' test, with a probability limit of 0.05, and most of the changes on which stress will be laid exceed the probability limit of 0.02 or 0.01 by the 't' test. A rough check on the validity of the statements made is available in the standard errors of the means.

T values The total ventricular mass appears, from the figures in Table 5 to increase in a rather irregular step-like fashion. There is little doubt that the irregularities would be smoothed out if the numbers in each group were very much larger. The rate of increase represented by the gain of 2.5 g. on 13.5 (18%) in the first month is greater than at any subsequent period. The same statement can be made about the increase of 4.5 g. (33%) in the first three months. After this point the errors of the means do not seem to justify the drawing of any other than a straight line through the points on the graph (see Fig. 2); in other words from the age of three months onwards the rate of increase in total ventricular weight is probably reasonably steady at about 0.7 g. per month.

S+L values Here the contrast between events in the first month and the subsequent rate of growth is still more striking. A birth weight of 7.5 g. increases to 11.1 g. (48%) in the first month. This spurt rapidly ceases, and after the age of three months the figures seem to show a steady rate of increase of about 0.5 g. per month.

R values There is a sharp reduction of the weight of the right ventricular fragment in the first month amounting to a loss of about 20%. After this the figures remain stable, or increase slightly; the lowest figure in the column, 4.7 g. at 2 months, cannot be distinguished from any which follow until the figure of 5.5 g. at 5-6 months. The birth mean of 6.0 g. is not regained until the second half of the first year, and is first exceeded by the figure for the second year. The last three figures in the column suggest an average rate of growth of just over 0.2 g. per month.

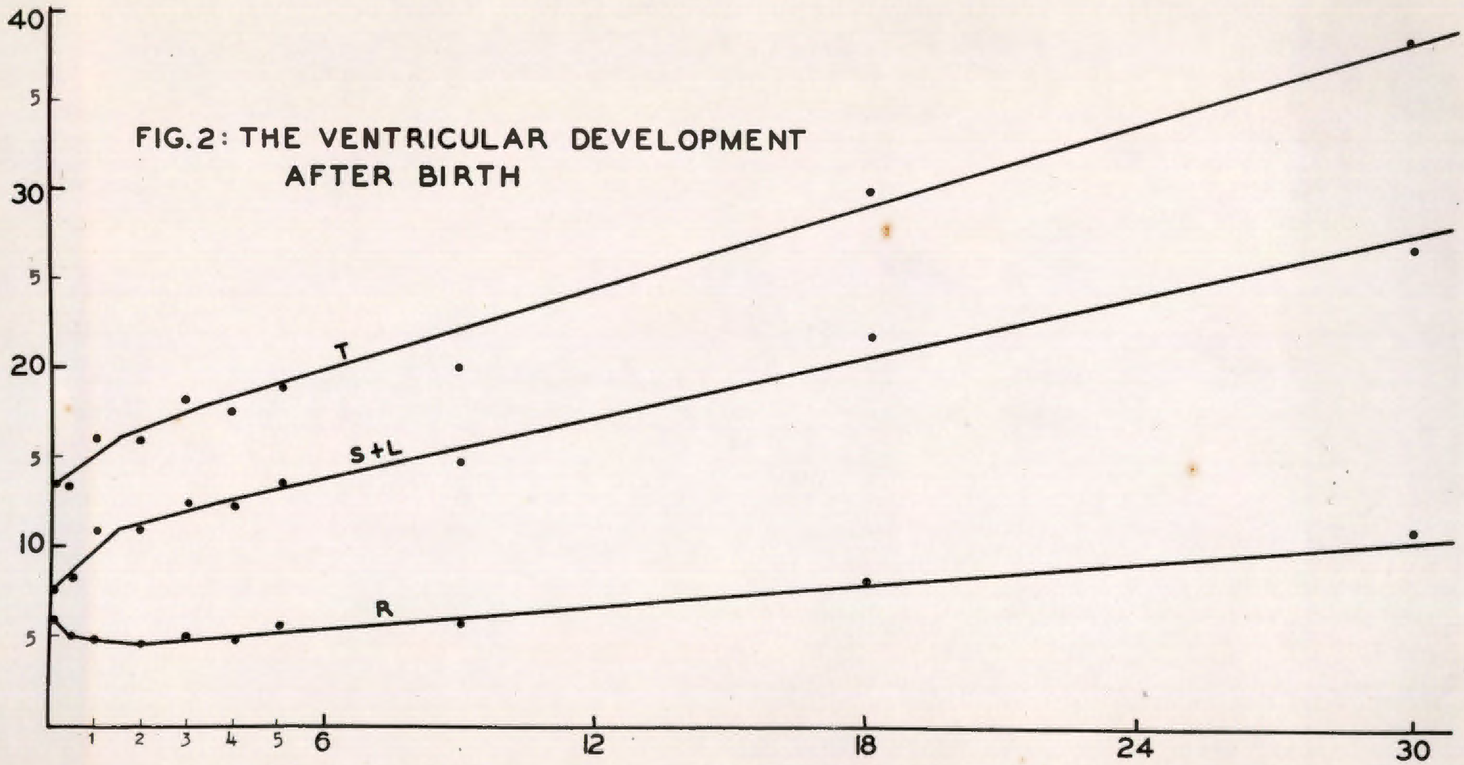
Some doubt may be felt about the validity of the age changes expressed in the last three paragraphs, in view of the arbitrary selection of the postnatal cases in the effort to avoid premature subjects. Thus if too many were excluded the appearance of rapid growth of S L, and also T, in the first three months might be spurious. On the other hand, if premature specimens were included, then the atrophy of the right ventricular free wall might have been exaggerated. However as the two parts into which the ventricular mass was divided move in opposite directions, the one growing rapidly and the other shrinking, the two possible objections to some extent cancel each other. Thus if prematures were included, the rapid increase of S + L would be difficult to account for; and if too many specimens were excluded in error, then the true shrinkage of the right ventricular fragment would be even more striking than it already appears.

The changes in R, S + L, and T values with age are graphically shown in Fig. 2.

R/T values The variation of the observations about the mean figures is much less in the case of the proportions reported in Table 3 than it is in the case of absolute weights in Table 2. The standard deviations in Table 2 average 20% of the mean figures, while the corresponding comparison in Table 3 shows S.D. figures usually about 10% of the mean. In other words the proportionate development of the two ventricles is less variable than their absolute weight; this conclusion is not, perhaps, very surprising, but it does indicate that the methods used do reasonably measure the mutual relationship of right and left ventricles.

Starting with the birth figure of 44%, the R/T figure drops sharply in the first month to 31%. This rapid change of relationship is brought about by the weight changes in opposite directions which have already been demonstrated - the hypertrophy of the septal fragment and the

FIG.2: THE VENTRICULAR DEVELOPMENT AFTER BIRTH



Abscissae: age in months
Ordinates: weights in Gm.

T is the total ventricular mass

R is the free wall of the right ventricle

S+L is the septum and free wall of the left ventricle, i.e. T - R.

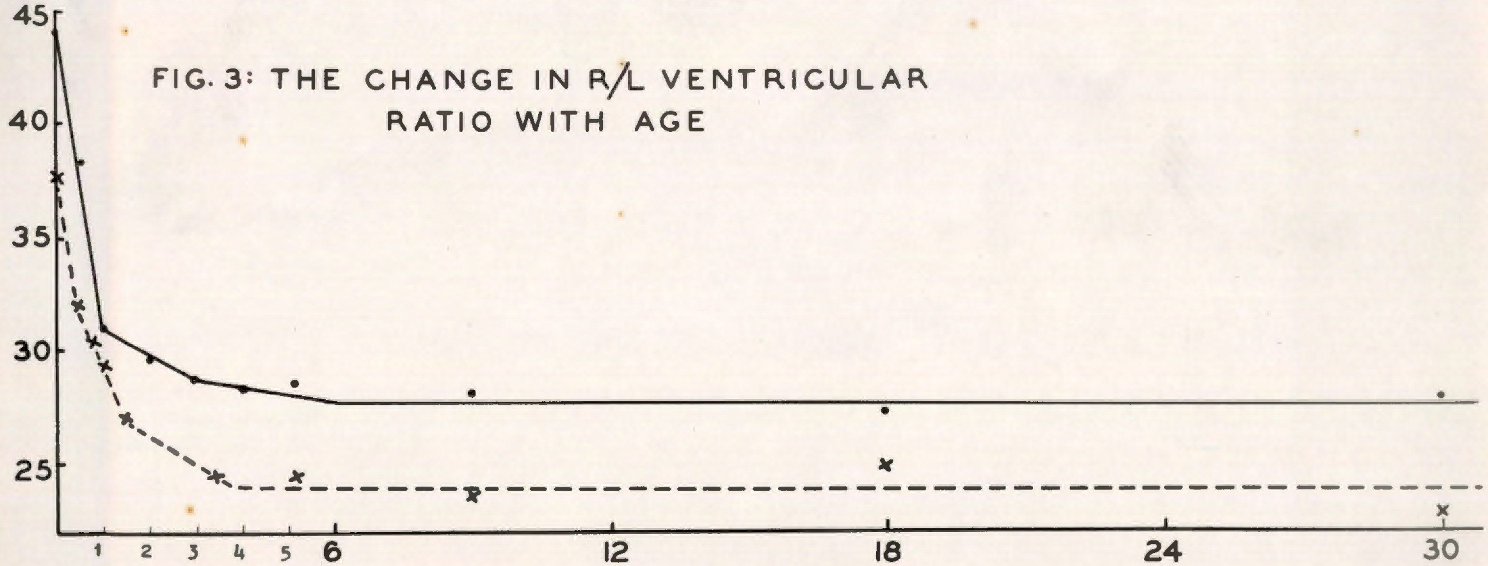
left ventricular free wall combined with the atrophy of the right ventricular free wall. This rate of change in relationship of the two ventricles is not approached in the subsequent months; in fact more than three-quarters of the total change seen in the Table occurs in the first month.

The mean figure of 31% at one month cannot be distinguished statistically from those that follow until the figure of 28.4% at four months. After this point it is possible to demonstrate change only by comparing the 45 cases in the period 3 - 6 months with the 77 cases from the 7 - 12 months and subsequent age periods. The mean figure for the earlier groups is 28.7% and this is found to differ significantly from the mean of 27.6% for the later cases. Stability is reached with the mean figure of 28.1% at 7 - 12 months, because this value cannot be differentiated from the mean figures which follow.

It is possible that an increase in the numbers of hearts examined would show up further slight change with age; with the S.D. figure remaining about 2.5%, more than 60 observations would be necessary in each age group to show up a significant change of 1% in the mean figures, and about 250 observations in each age group to show up a change of 0.5% in the mean figures. From a practical point of view there seems to be no change in the relative development of the two ventricles after the first six months of life .

To recapitulate in round figures, the R/T proportion changes from 44% at birth to a steady level of about 28% in six months. Of the total drop of 16%, 13% is achieved in the first month, a further 2% between one and three months, and the remaining 1% change between three and six months of age. These changes are graphically shown in Fig. 3. Evidence will be presented later that the final level reached is the same as is found in normal adult hearts (page 45).

FIG. 3: THE CHANGE IN R/L VENTRICULAR RATIO WITH AGE



Abscissae: age in months

Ordinates: R/T%
(R is the weight of the right ventricular free wall, and T the total ventricular mass)

——— Figures from present study

– –x– – Figures from W. Müller (1883)

Premature Cases   As mentioned on page 5 , 34 hearts from infants considered to have been born prematurely were also examined. The 20 which were from stillbirths or from infants dying in the first 3 days gave the following R/T figures, which compare reasonably well with the figures under 'Birth' in Table 3:

R/T%	mean	s.e.m.	range	S.D.
Premature infants at birth	42.0	0.99	34 - 48	4.4

Those which survived longer than 3 days were too few to analyse collectively, and are now reported individually:

Premature infants	No.	R/T%
one week old	6	37, 40, 42, 44, 44, 45
two weeks old	1	45
three weeks old	2	30, 34
one month old	1	27
three months old	3	26, 30, 36
four months old	2	29, 33

These figures, for what they are worth, show that the influence of extra-uterine life on the heart is the same for these premature infants as for those born at full term; particularly striking are the values at three weeks and one month old.

THE WORK OF W. MÜLLER

Wilhelm Müller published his book on "Die Massenverhältnisse des menschlichen Herzens" in 1883. The research which this author undertook is still of importance, because the work (on hearts of infants and children) does not appear to have been repeated in the twentieth century. As will be shown, Müller has been much quoted and misquoted by subsequent writers.

(1) Müller's Method and Results

Müller was interested in all aspects of the weight of the heart and its parts, but his ventricular weighings are all that concern the present study. He dissected 35 hearts from foetuses weighing more than 2.5 kg., 91 from infants dying in the neonatal period, 167 from infants dying in the age period 1-12 months, 41 from the 2nd year, 29 from the 3rd year, 36 from the 4th and 5th years, 37 from the 6th to 10th years, and representative numbers from adolescences and adults up to the ninth decade. He dissected the hearts in the fresh state. In order that there should be no doubt as to his procedure, the following quotation shows how he separated the total ventricular mass from the atria, and divided it into three portions, viz. a right ventricular, a left ventricular, and a septal fragment:

> "....wird der rechte Vorhof durch einen von der Mündung der Vena cava inferior zu jener der Vena cava superior geführten Schnitt eröffnet und vom Blut und Gerinnseln gereinigt, hierauf die hintere Wand des rechten Ventrikels unter Durchschneidung des Klappenrings möglichst in der Flucht der Kammerscheidewand von letzterer abgetrennt. Ein zweiter Schnitt trennt von der Lungenarterie ausgehend die vordere Wand des rechten Ventrikels vom Septum und vereinigt sich mit dem ersten an der Spitze des rechten Ventrikels.
>
> Am linken Vorhof werden erst die Einmündungsstellen der rechten, dann jene der linken Lungenvenen

vereinigt und sodann der Vorhof durch einen quer zwischen beiderseitigen Einmündungen verlaufenden Schnitt geöffnet. Hierauf wird die hintere Wand des linken Vorhofs möglichst in der Flucht des Septum vom letzterem abgetrennt und die Abtrennung, unter Durchschneidung des Klappenrings, auf die hintere Wand der linken Ventrikels so fortgesetzt, dass die hintere Papillarmuskel am freien abschnitt bleibt. Der zweite Schnitt wird von der Spitze des linken Ventrikels durch die vordere Wand möglichst in der Flucht des Septum geführt, und mit Vermeidung der Lungenarterie und des linken Herzohrs in die Aorta fortgesetzt. Der vordere Papillarmuskel bleibt dabei gleichfalls am linken Ventrikel. ....

Nach Erhebung der pathologischen Befunde werden die grossen Arterien längs der Ansätze der halbmondförmigen Klappen vom Herzen abgetrennt, hierauf die beiden Vorhöfe im Niveau der Klappenringe von den Kammern, endlich die Vorhofsscheidewand von jener der Kammern, welch' letzterer Akt grössere Vorsicht erheischt."

A translation of this passage runs:

"The right atrium is opened by a cut running from the inferior to the superior vena cava, and cleaned of blood and clots; then the fibrous ring of the tricuspid valve is cut through and the posterior wall of the right ventricle separated from the septum by dividing its wall as close as possible to the line where it joins the septum. A second cut starts from the pulmonary trunk and separates the anterior wall of the right ventricle from the septum, joining the first cut at the apex of the ventricle.

The left atrium is opened first by joining the openings of the right pulmonary veins, and then those of the left side, after which a transverse cut between the two side openings completes the process. Then the posterior wall of the left atrium is separated from the septum as close as possible to where it joins the latter, and the division continued down by a cut running through the fibrous ring of the mitral valve and down the posterior wall of the left ventricle in such a way that the posterior papillary muscle remains with the separated free wall. The second cut starts from the apex of the ventricle, runs up the anterior wall as close as possible to where it joins the septum, and is continued into the aorta; care should be taken to avoid cutting the pulmonary trunk and the auricle of the left atrium. The anterior papillary muscle similarly remains with the separated left ventricle. ...

After the pathological changes have been recorded, the great vessels are separated from the heart along the line of the attachment of the semilunar cusps of the aortic and pulmonary valves; then both atria are cut away from the ventricles at the level of the fibrous rings of the mitral and tricuspid valves. Last of all the atrial septum is cut away from the ventricular septum, a procedure which demands great care."

He was then faced, as all who investigate along these lines must be faced, with the problem of allocating the septal fragment. He decided to investigate its function by examining its change in weight in cases of right and left ventricular hypertrophy. The steps of his argument were as follows:

(a) The average observations in all the adult hearts from the age of 21 to 90 were, in grammes

	R	L	S	L/R
418 males	54.1	100.0	71.8	1.84
318 females	43.9	77.7	56.4	1.77

(b) Taking all cases where L/R was less than 1.4 as representing cases of right ventricular hypertrophy, but excluding male cases where L was less than 81 g. and females where L was less than 63 g. because the 'Atrophy' of the left ventricle represented by these low figures might artificially lower the L/R proportion, average figures were obtained as follows:

Right Ventricular Hypertrophy

	R	L	S
28 males	92.0	99.3	84.9
32 females	79.0	76.6	68.2

If the septal fragment had enlarged in proportion to the increase in the right ventricular free wall, it would have weighed much more than it did; the proportion $\frac{\text{actual increase in septal weight}}{\text{expected increase in septal weight}}$

was .260 in the male series, and .261 in the females.

(c) A similar calculation was applied to cases of left ventricular hypertrophy, defined as cases where L/R exceeded 2.4. No male cases were excluded on account of concomitant 'atrophy' of the right side, but in the females a lower limit of 33 g. was set. The results were

Left Ventricular Hypertrophy

	R	L	S
64 males	53.9	157.5	96.8
36 females	42.9	126.7	77.6

Here the ratio $\frac{\text{actual increase in septal weight}}{\text{expected increase in septal weight}}$ turned out to be .607 in the males and .597 in the females.

(d) There seemed to be good agreement with the findings in the two sexes in both types of hypertrophy, and it was felt that they could be compared in this way:

males .260 / .607 = 1:2.33) average 100 / 231
females .261 / .597 = 1:2.28)

(e) Therefore the functional division of the septal fragment should be
0.6979 S to be added to the left side,
0.3021 S to be added to the right side.

Using the figures derived in this way, Müller applied them to his observations not only on adult hearts, but also on all his foetal, infantile, and childhood specimens. A selection of his summarised findings is presented in Table 4. The headings to the columns are largely self-explanatory. Each figure represents a separate mean observation for all the cases in the appropriate sex and age division. In the fourth and fifth columns of weight observations are seen the corrected R and L figures, after the addition of the septal portions in the stated way, and in the sixth column the mean observation of the proportion: corrected R/corrected L.

TABLE 4: POSTNATAL DEVELOPMENT OF THE VENTRICLES: MÜLLER'S ORIGINAL FIGURES
Weights in g. of the three parts into which the ventricular mass is divided, with Müller's 'functional index'. R, L, S as in Table 2.

	MALES							FEMALES						
	No.	(1) R	(2) L	(3) S	(4) R+ .3021 S	(5) L+ .6979 S	(4)/(5)	No.	(1) R	(2) L	(3) S	(4) R+ .3021 S	(5) L+ .6979 S	(4)/(5)
STILLBORN														
2.5-3 kg.	6	6.02	4.84	4.60	7.40	8.09	.925	7	5.46	4.92	4.43	6.80	8.02	.849
3 kg. & over	15	7.72	5.44	5.40	9.34	9.21	1.007	7	7.14	4.69	5.22	8.71	8.34	1.065
LIVE BORN														
1st week	16	4.85	4.45	4.29	6.14	7.45	.839	17	3.82	3.47	3.26	4.81	5.76	.827
2nd week	13	4.11	4.79	4.09	5.34	7.65	.698	15	4.10	4.53	3.93	5.41	7.28	.733
3rd week	10	4.10	4.93	4.29	5.39	7.95	.680	5	4.04	5.04	4.11	5.27	7.89	.678
4th week	5	4.11	5.83	4.29	5.41	8.83	.635	10	3.44	4.71	3.93	4.63	7.46	.634
2nd month	14	3.09	4.54	3.91	4.28	7.28	.594	14	3.43	5.42	4.34	4.74	8.45	.571
3rd month	14	3.94	6.44	5.06	5.47	9.98	.561	16	3.88	6.41	5.08	5.41	9.96	.545
4-6 months	24	4.68	7.99	6.23	6.55	12.35	.532	20	4.33	7.91	5.62	6.12	11.84	.522
7-12 months	34	5.72	10.68	8.02	8.04	16.31	.502	31	5.77	10.43	7.88	8.45	15.76	.515
2nd year	17	9.00	14.11	11.30	12.42	22.00	.561	24	7.82	13.52	10.00	10.85	20.57	.525
3rd year	13	10.63	23.77	14.42	14.98	32.15	.469	16	9.04	18.26	12.88	12.93	27.24	.473
4-5 years	17	11.07	22.23	17.15	16.24	34.20	.473	19	11.71	21.94	16.22	16.61	33.26	.499
6-10 years	16	17.68	33.98	24.32	25.01	50.97	.487	21	14.31	29.01	21.92	20.93	44.32	.471
11-15 years	8	24.2	44.4	32.5	34.0	67.1	.500	9	20.1	40.9	28.5	28.7	60.8	.467
16-20 years	23	46.0	76.9	57.6	63.4	117.1	.542	13	39.1	73.8	53.3	55.2	111.1	.508

comparison of the figures for the first month of extra-uterine life with those of later foetal life shows that during the first month after birth the right ventricle loses weight, and the left gains weight; loss and gain occur much more rapidly in the first and second weeks than in the third and fourth.

The cause of this change must be that birth relieves the right ventricle of some of its work, while the left ventricle is increasingly loaded..."

p.212 (5) After the pulmonary and systemic circulations are completely separated, which appears to happen at the beginning of the second month of life, an unequal increase in weight of the two ventricles takes place, which continues throughout the remainder of the first year. In this way the permanent proportion between the weights of the two ventricles is first established at a time when independent nourishment has started, and the infant learns to walk upright.

(6) This proportion is expressed by the functional index; from the second year onwards this shows an average figure of 0.507, i.e. the right ventricle weighs about half the left.

(7) The proportion between the two ventricles does not alter with time after the first year. The variations about the average reflected in the tables are naturally explained by individual variation and by the more accidental influence of certain causes of death in the various age periods."

(2) Comment and criticism of Müller's work

Muller's work was very thorough, and is still of great interest. However, he cannot today escape criticism based on modern statistical practice. Such criticism cannot detract from the value of the work Müller did, for statistical analysis of means was not understood in 1880. In fact, since Müller published detailed protocols in his book, a re-analysis of his figures seems the most sensible thing to do. This has been attempted, and the results of the analysis and comparison of the figures with the author's results are given below.

Müller's own comments on these figures, in so far as they help to show the course of the transformation of the foetal ventricular ratio during postnatal life, are again set out in full, as they appear to have been largely ignored by those who have quoted him:

> p.210 "...die Verteilung der Arbeitsleistung auf die beiden Ventrikel eine andre wird, und in der That ergiebt die Vergleichung der Zahlen des ersten Monats des freien Lebens mit jenen des späteren Embryolebens dass der rechten Ventrikel im Verlauf des ersten Monats nach der Geburt an Masse abnimmt, der linke an Masse zunimmt; Ab- und Zunahme erfolgen in der ersten und zweiten Woche rascher als in der dritten und vierten.
>
> Die Ursache der Veränderung kann nur liegen in einer durch die Geburt herbeigeführten Entlastung des rechten, eine zunehmende Belastung des linken Ventrikels........"

> p.212 "(5) Auch nachdem der Abschluss des Lungenkreislaufs vom Körperkreislaufs ein volkommener geworden ist, was zu Anfang des zweiten Lebensmonats der Fall zu sein pflegt, findet eine ungleiche Massenzunahme beide Herzkammern statt, welche sich durch den ganzen Rest des ersten jahres erstreckt, sodat erst um Zeit, in welche gewöhnlich die selbständige Nahrungzufuhr und die Erlernung des aufrechten Ganges fällt, das bleibende Verhältnis zwischen den Muskelmassen der beiden Herzkammern zur Ausbildung gelangt.
>
> (6) Das Verhaltnis findet seinen Ausdruck im functionellen Index; diesen hat vom Zweiten Lebensjahr an im mitten den Wert von 0.507, d.h. der rechter Ventrikel hat annähernd die Hälfte der Masse des linken.
>
> (7) Die weitere zunahme des Alters andert das Verhältnis zwischen rechter und linker herzkammern nicht. Die Abweichungen vom Mittel, welche die Tabelle aufweist, erklaren sich ungezwungen aus der individuellen Variation und aus dem mehr zufalligen Uberwiegen bestimmter Todesursachen in den einzelnen Alterstufen."

A translation runs:

> p.210 "... the sharing of work between the two ventricles is another matter, and indeed

Taking his work at its face value, several criticims are at once apparent. (1) His description of his division of the heart is vague, for example the key words "in der Flucht des Septum" are not precise enough. In particular the cut from the pulmonary trunk down the front wall of the right ventricle is liable to leave quite a portion of the muscular wall of the conus with the septal fragment.

(2) The argument Müller develops about the septal fragment is open to serious objections. The 'average' observations seen in paragraph (a) of the summary of his argument (page 22) cannot be considered as representative of a 'normal' heart, because the series from which they were derived included all the cases of heart disease as well as the hearts from those dying of diseases not affecting the heart. In paragraphs (b) and (c) Müller appears to have selected the cases so as to provide a reasonable comparison between the unaffected ventricle and the 'normal' figures in paragraph (a). In the case of the hearts showing right venticular hypertrophy, inspection of the original findings shows wide variations in the proportions of R, L, and S, to each other, and it would be difficult to show that the small rise in septal weight was outside the limits of observational error combined with variation inherent in the structure of the various hearts; certainly it cannot be done without knowing the variability of observations made on the 'normal' hearts.

(3) Next the argument in paragraph (d) (page 23) cannot be accepted, at any rate in the form in which it is presented. The fact that 0.260 + 0.607 does not equal 1.00 is not discussed.

(4) A theoretical division of the septum derived in this way from a study of adult hearts should not have been applied indiscriminately to foetal and early postnatal hearts. For example, in the hearts from infants dying in the first week the right ventricular fragment outweighs the left, yet because of the unequal division of the septum the proportion right to left ventricle expressed in the ratios in column 6 of the tables amounts to little more than 0.8 .

(5) A further difficulty is apparent when the hearts from early infantile life are compared with those from full-term foetuses weighing 2.5 Kg. or more. For convenience the values of the mean total ventricular mass for the various age groups are set out in Table 5.

TABLE 5
MEAN TOTAL VENTRICULAR MASS
Müller's data

	Age	No.	Wt. in g.
Stillborn	2.5-3 K	13	15.1
	3.0 K & more	22	18.1
Neonatal	1st week	33	12.0
	2nd week	28	12.8
	3rd week	15	13.3
	4th week	15	12.9
Infants	2nd month	28	12.4
	3rd month	30	15.4
	4-6 month	44	18.4
	7-12 month	65	24.3

The figures are derived by weighting the means for the two sexes according to the number of specimens dissected; there was no statistical difference between the sexes except in the specimens from infants dying in the first week, when the original figures were compared by the 't' test. This table makes it clear that a number of hearts from prematurely born infants were included in the series from the early weeks of extra-uterine life. This makes Müller's conclusion about the immediate postnatal events, particularly about loss of weight on the right side, less certain than his statement on p. 210 of his book (quoted on p.25) suggests. In a later section, an attempt has been made to exclude the specimens from obviously premature infants, and this proceeding will be seen to alter the figures considerably (p. 32).

(6) Although Müller's method of analysis of the figures may be open to criticism, the fact that the method was uniformly applied does allow some comparison between the age groups. His own comments are quoted on p. 25. He states that there is a changing relationship

between the right and left ventricles until the end of the first year. Inspection of the tables suggests that he was not justified in distinguishing the figures in the last column for 4-6 months and 7-12 months from those which follow.

In order to know precisely the conclusions which may be legitimately drawn from Müller's 'Functional Index', the mean observation for each age period, with its standard error (s.e.m.), has been calculated from the original figures in Müller's monograph.

TABLE 6
MÜLLER'S FUNCTIONAL INDEX

age	no.	mean	s.e.m.
1st week	33	83.3	2.5
2nd week	28	71.7	1.8
4th week	15	63.4	2.4
2nd month	28	58.2	1.4
3rd month	30	55.3	1.8
4-6 months	44	52.7	1.2
7-12 months	65	50.8	1.0
2nd year	41	54.1	1.9
3rd year	28	47.1	1.1
4-5 years	36	48.7	0.7
6-10 years	37	47.8	0.8
11-15 years	17	48.3	1.5
16-20 years	36	53.0	1.5

The figures published for the two sexes have been pooled, as there appears to be no sexual difference in the figures. The results are seen in Table 6. For convenience the figures representing ventricular proportions have been multiplied by 100, converting them into percentages. The differences between these figures have been tested by the 't' test, using a probability of 0.05 as the significant level. The results show that up to the figures for the 2nd month the obvious decreases in the percentage figures are significant; thereafter there is a measurable change when the figure for the 2nd month is compared with that for 4-6 months. From then on the means appear to vary about a level of approximately 50, without any of the deviations being significant, with the exception of the 2nd year figure, which is significantly higher than the figures before or after it. As Müller himself has written, such a deviation is almost certainly due to the effect of various causes of death on the hearts in the groups, rather than to a normal reversal of the developmental trend.

(3) Re-analysis of Müller's Observations

By tracing the individual specimens through the various sections of Müller's detailed report, it is possible to find out the weight and length of all of the infants from which his specimens were derived. Many of the infants were seen to have been prematurely born when these data were examined. Typical examples were: 2nd week, 41 cm., 1.3 kg.; 4th week, 40 cm., 1.3 kg.; 2nd month, 41 cm., 1.4 kg; 3rd month, 49 cm., 2.0 kg.; 4th month, 53 cm., 1.9 kg. In order to provide a rough comparison between the present study and Müller's cases, it was decided to exclude from Müller's series the more obviously premature cases. To this end a generous lower limit of 2.0 kg. and 45 cm. was used for infants up to 2 months, and the same weight but 50 cm. for the period 3 - 6 months. The object of setting such a low limit as 2.0 kg., was to make every possible allowance for normal loss of weight as well as the effect of malnutrition on infants whose birth weight might have been 2.5 kg. or more. As will be seen from the results, however, there are grounds for thinking that these limits were not nearly severe enough, and that many premature cases remain included in the series. 40 out of 192 postnatal cases in the first six months were excluded from Müller's series on the grounds stated.

The next difficulty arose from the difference in the two methods of dissection of the ventricular mass. This can best be illustrated by showing the mean proportions of the three fragments as separated by Müller, and by comparing these proportions with those derived from the present study. Table 7 presents the mean percentage distribution, to the nearest whole number, of R, S, and L at two representative age periods. As Müller's classification into age categories is not quite the same as that used in the present study, the author's 'Birth' category is compared with Müller's stillborn cases weighing 2.5 to 3.0 kg.

TABLE 7
COMPARISON OF MÜLLER'S AND AUTHOR'S METHODS OF DISSECTION OF VENTRICLES.

	R/T%	S.D.	S/T%	L/T%	S/S L%
Müller's results Stillborn 2.5-3.0 kg.	38	3.5	30	32	48
Present study 'Birth'	44	3.7	18	38	33
Müller's results 7th-12th months	24	3.4	33	43	43
Present study 7th-12th months	28	2.4	23	49	32

It is apparent from these figures that in Müller's method the septal fragment is much larger than in the present study. This might have been expected from his description quoted on page 21, even if it is somewhat vague. It is larger at the expense of both right and left ventricles. The effect of including part of what is considered in the present study to be right ventricular free wall with the septal fragment can be seen in the last column. This shows that by Müller's method there is not the constancy in proportion between the septal fragment and the free wall of the left ventricle which the author found (v. page 10). Direct comparison of the weights of the fragments was therefore out of the question. However, on the assumption that Müller was consistent in his method, it seemed reasonable to enquire whether his figures analysed according to the author's method showed similar growth changes or not. Accordingly R, R/T%, and T values were tabulated for all the cases remaining after exclusion of cases supposed prematurely born in the way described. These figures appear in Table ' on page 32.

p.32

TABLE 8: POSTNATAL DEVELOPMENT OF THE VENTRICLES

Müller's findings corrected by the omission of premature subjects. Weights in g. of the parts into which the ventricular mass is divided with the significant weight ratio. R, T as in Table 2.

Age	No.	R				R/T%				T			
		mean	s.e.m.	range	S.D.	mean	s.e.m.	range	S.D.	mean	s.e.m.	range	S.D.
STILLBORN													
2.5-3 kg.	13	5.7	0.24	4.1 - 7.7	0.8	37.7	1.02	31 - 46	3.6	15.1	0.35	13.4 - 17.4	1.2
3kg.& over	22	7.5	0.46	5.4 -11.8	2.1	41.4	1.01	34 - 51	4.7	18.1	0.77	13.1 - 24.0	3.6
LIVE BORN													
1st week	17	5.9	0.38	3.5 - 8.4	1.6	36.9	1.40	21 - 46	5.8	16.1	0.95	10.3 - 22.7	3.9
2nd week	21	4.5	0.19	2.9 - 6.3	0.8	32.0	0.65	27 - 38	3.0	14.0	0.51	10.3 - 18.3	2.3
3rd week	13	4.2	0.29	2.9 - 6.0	1.4	30.6	0.58	28 - 34	2.0	13.8	0.95	9.9 - 19.7	3.4
4th week	11	4.0	0.22	2.7 - 5.4	0.6	29.5	0.78	24 - 32	2.6	13.5	1.02	9.4 - 20.8	3.4
2nd month	21	3.6	0.13	2.7 - 7.5	0.6	26.9	0.67	24 - 33	3.1	13.4	0.63	9.4 - 19.6	2.9
3rd month	27	4.0	0.22	2.7 - 7.5	1.2	25.7	0.78	19 - 40	4.1	15.8	0.83	10.5 - 28.4	4.1
4th month	19	4.3	0.33	2.6 - 7.7	1.4	24.6	0.81	18 - 32	3.5	17.6	1.21	10.2 - 26.8	5.3
5-6 months	23	4.9	0.31	2.7 - 8.5	1.5	24.6	0.69	20 - 33	3.3	19.9	0.92	11.1 - 26.7	4.4
7-12 months	64	5.8	0.18	2.7 -10.7	1.4	23.7	0.43	16 - 39	3.4	24.5	0.73	11.5 - 38.2	5.8
2nd year	41	8.3	0.50	4.2 -22.0	3.2	25.0	0.72	19 - 38	4.6	32.6	1.25	19.8 - 57.0	8.0
3rd year													
male	13	10.6	0.71	7.7 -15.1	2.6	22.7	0.66	19 - 36	3.6	46.5	2.66	32.0 - 69.6	9.6
female	16	9.0	0.58	6.1 -14.0	2.3					40.2	1.74	33.2 - 53.0	7.0

Comparison of the T values with those from the author's study shown in Table 2 (page 14) shows some puzzling inconsistencies. Some of these may be due to the selection of Müller's postnatal cases being faulty; others are not open to the same explanation. In particular, there is no suggestion of the rapid growth in the first three months which was so obvious in the author's cases.

Turning to the R values, a change not unlike that shown by the author's observations is seen. Comparing the cases for the 2nd week (T 14.0 g.) with those from the 2nd month (T 13.4 g.) there is a significant diminution in the weight of the right ventricular free wall. This does not regain its birth weight until the second half of the first year, and is first exceeded by the figures for the 2nd year. The atrophy is of the same order of magnitude as the author's cases, that is a loss of about 20% to its lowest point at 2 months.

The R/T% figures show, by comparison of the standard deviations, that Müller was about as consistent as the author in dividing up the ventricular mass. Although the figures are throughout lower, for the reasons already explained, there is the same rapid readjustment of the ventricular ratio. There is a decrease of about 10% in the first month from the initial level of approximately 40% After this the rate of change slackens off considerably, and when the figure of 24.6% for the 4th month is reached, no further statistical change is obvious. As might have been expected from the figures analysed on page 29 , the R/T proportion for the 2nd year is higher than the figures before or after it, and but for this figure it might have been possible to show some change after the 4th month. These changes are illustrated graphically in Fig. 3, and the similarity in the proportionate growth change revealed by the two studies is obvious.

Broadly, then, fresh examination of Müller's work by improved statistical technique re-enforces the conclusions reached by the author. The readjustment between the bulk of the right and left ventricles is rapid, the greater part occurring in the first month of life. Finality in this relationship appears to be reached within the first six months. There is a similar reduction in the mass of the right ventricular free wall in the first month or two, which is not restored for nearly a year.

DISCUSSION

(1) The assessment of the Ventricular Ratio

The method of analysis used in the present study, in which the septum is considered as forming a unit with the free wall of the left ventricle, has been justified in a previous section (p. 9). The usefulness of the method is that it allows easy comparison of one heart with another, or of one group of hearts with another. It does not provide a measure of the precise proportion in which the weight of the ventricular myocardium should be divided between right and left sides, and does not in consequence permit a precise estimate of the relative anatomical and functional status of the two ventricles.

Those who have made gravimetric studies of the heart have usually attempted to establish some theoretical rule which would enable them to state a precise ventricular weight ratio, and have commonly proceeded without hesitation on the assumption that such a weight ratio accurately reflects the functional relationship of the two ventricles. Müller's methods have already been described and criticised. Lewis (1914), in a classical study of the effect of ventricular hypertrophy on the electrocardiogram, felt dissatisfied with Müller's account, and adopted a method of division which separated each ventricle from the septum as an intact chamber. He did this because he felt that the trabeculated surfaces of the septum belonged functionally to the side to which they presented. Hermann and Wilson (1922), in a similar study, stated that they were unable to follow the details of Lewis' method, and preferred to partition the septum by dividing it along a white line (seen in successive sections of the septum), which they considered indicated the functional division of the septum. Fulton, Hutchinson and Morgan Jones (1952), in a recent study of ventricular hypertrophy, rejected the methods of their predecessors as difficult to follow and of doubtful theoretical validity. Instead they divided the ventricular mass by a method closely resembling that followed in the present study. Having established a range of observations for normal hearts, they found that in right ventricular hypertrophy the septal fragment hardly ever exceeded its normal range of weight. On the other hand it exceeded the normal limits of its weight in almost all cases of left ventricular hypertrophy. As a result they decided, as in the present study, to consider the septum and free wall of the left ventricle as one part of the heart, to be compared in weight with the free wall of the right ventricle. They made no attempt to establish an absolute weight for the two ventricles.

It is clear that there is no agreed method by which the weight of the two ventricles can be precisely stated. It is doubtful whether any method would survive critical scrutiny. The procedure adopted in the present study is simple and less liable to misinterpretation than those quoted, and is quite capable of being used to compare the ventricular ratio of one heart with that of another heart, or with a normal standard.

Even if some acceptable method of allotting the septal fragment were proposed, theoretical considerations would make it hazardous to base functional conclusions on the anatomical weight ratio so established. The two ventricles are not of the same shape, and it is not permissible to assume that they act as equally efficient pumping units. This may be illustrated by the findings of Fulton et al., in the study mentioned above. For 43 normal hearts from adults under the age of 65, they reported the following weights of the divided ventricular mass (in g.):

	R	S	L	T
Mean	46	39	86	171
Maximum	68	61	123	235
Minimum	23	17	48	88

Taking the mean figures, the weight of the right ventricular free wall is seen to amount to 37% of the weight of the septum and free wall of the left ventricle. This means that the weight of myocardium active on the right side averages over one third of the weight of the left ventricle, if not more. Now direct studies of human ventricular pressures, obtained by the use of the cardiac catheter, have shown that the right ventricle does a fourth part or less of the work of the left, in the normal heart. The discrepancy is obvious, and it is clear that the relative functional status of the two ventricles cannot be accurately assessed by dissection and weighing of the ventricular myocardium.

If these arguments are accepted, it follows that any statement of relative ventricular status, based on dissection of the heart, which is precise will be suspect. On the other hand, a method of dissection, such as that used in the present study, consistently applied, provides a satisfactory means of comparing the relative ventricular status of one heart with another, or with an established normal range of variation.

(2) The foetal ventricular ratio

Many authors have followed Harvey's lead and stated that the two ventricles of the foetal heart are equal in thickness, and have inferred that they are functionally balanced. Müller, whose work has been described, took this view as may be seen from this quotation: "..zur zeit der Reife die zu leistende Arbeit annähernd gleichgförmig auf beide Ventrikel verteilt ist." (..at full term the work of the ventricles is divided about equally). An example of a more modern authority is Professor Brash (1951) who writes, referring to the weight of the parts of the heart, that in the latter part of foetal life the two ventricles are equal.

Two other views, mutually contradictory, have also been put forward. Scammon (1923), for example, stated on Müller's authority that the ratio left/right ventricle was 5/4 at birth. Brock (1932) also quotes the figure 83.3 as Müller's 'functional index' (right/left ventricle) at birth. From Table 4 it will be seen that this is a figure midway between the male and female averages from the first week of life. Both authors treated Müller's figures for the first week as representing birth conditions, and in this way arrived at an opinion not held by Müller himself. In view of the rapid postnatal change in ventricular ratio shown in the present investigation, and confirmed by a re-examination of Müller's findings, it is not surprising that figures derived from the first week should differ from those characteristic of birth. Another author Falk (1901) is quoted as stating that at birth the left ventricular wall weighs about 25% more than the right wall, and is about 50% thicker.

The opposite view is taken by Patten (1930), in the course of an article in which he attacked the idea that the event of birth necessitated radical circulatory adjustments. In a figure accompanying the article he stated that the average weights of the right and left ventricles at birth were 8 and 7 g. respectively. A footnote to the figure explained that "tabulated measurements from a series of over 50 hearts ranging from 15-30 g. show the constancy of the significant relationships here indicated (Patten and Toulmin, 1930)." (The reference indicates a preliminary note of work in progress which was published in that year. The definitive publication has not appeared). In the text Patten stated that "in the fetus... the load of the systemic circuit is shared by the right and left ventricles, and their muscular walls are of about the same thickness, although the total bulk of the right ventricle is a little greater because of its slightly greater capacity".

The objections to precise statements such as those quoted above have already been stated. While precision cannot be expected, an approximation is not ruled out. It is obvious on inspection that the two ventricles in the foetus are more nearly equal in status than they are in the adult. In the present study the free wall of the right ventricle amounted, at the time of birth, to 44% of the total ventricular weight on the average, and in several cases exceeded 50%. The septal fragment in these hearts averaged 18% of the total. If, for argument's sake, the septum were considered to be neutral in status, then half its weight would go to each side. On this assumption the ventricular weight would be divided in the ratio right 53, left 47. Judging simply from appearances during dissection of these hearts, the right ventricle often appears more bulky than the left. These figures show that in late foetal life the weight of the ventricular myocardium is divided about equally between the two sides, although in some cases the musculature of the right ventricle weighs more than that of the left. There is some slight support for the idea that the right ventricle is, on the average, the heavier. The objections to proceeding, without further evidence, from these statements to more precise functional conclusions have already been discussed.

(3) The postnatal transformation of the foetal ventricles

As in the case of the foetal ventricular proportion, many different statements about the postnatal ventricular changes can be found in the literature. Some of these statements are repeated here in order of date of publication.

Sir Thomas Lewis (1914), in an early electrocardiographic study of right and left ventricular hypertrophy, stated that he examined a number of new born children, and found in these subjects that the signs of right sided preponderance of the heart were constant. Moreover in extended observations upon two such children, he saw the curves gradually change until they presented more natural relations at about the third month of extrauterine life. He continued: "Since Müller (1883) has conclusively shown right sided preponderance in the new-born child and its gradual decline towards the third month, the evidence..... became stronger." In a later publication (1920) dealing with the same subject, and referring to his own 1914 work, Lewis again stated that the heart of the child possessed a "relatively heavy right ventricle" from the time of birth up till 3 months after birth, and that the signs of right preponderance were always present at birth, disappearing about the third month of extrauterine life. It can be seen that Lewis did not follow Müller's own statement about the conclusions to be drawn from his investigations.

Scammon (1923), also relying on Müller, stated that the ratio left/right ventricle was 5/4 at birth, 2/1 at the age of two years, and even more at puberty.

Patten (1930), in the article already mentioned, after stating his view of the foetal ventricular ratio,(page 38) continued:

> "..... By three to four months after birth the left ventricular musculature has overtaken the right in response, first, to the progressively increasing return from the lungs, then, as the fetal passages become closed, to the added stimulus of the long systemic route over which the blood must be pumped by the left ventricle alone. In response to this added load the left ventricular weight begins to climb steadily above that of the right, until its full adult degree of preponderance is reached around the seventh year (Müller 1883, Gross,1921)."

It has already been shown that Müller's results do not in fact support a slow change such as Patten described. Gross (1921) printed a page of figures from Müller's book. He copied the figures under R and L (see Table 4) but not the septal weights. In a third column labelled R/L he put Müller's proportional figures from the original sixth column. As he did not explain how this proportion was derived, the printed table is rather confusing. Gross added no comment other than that the figures showed "the gradual and consistent, increasing, postnatal preponderance of the left over the right ventricle as age advances.." It is clear that he cannot be regarded as assisting Patten's argument, as he did no more than quote Müller.

Brock (1932) also made use of Müller's results, and drew from them conclusions which were similar to Patten's. He included two tables showing Müller's results. The first starts:

	Right Ventricle	Left Ventricle
	g.	g.
Newly born	6.14	7.15
4 - 6 months	6.55	12.35
7 -12 months	8.04	16.31

These figures are derived from the 4th and 5th columns of Müller's table for males (see Table 4). Under the heading "Newly born" appear the original figures for the first postnatal week. There is a transcription error in the first line, and the interesting figures from the first three months are omitted. The second table shows R/L ventricular proportions. Brock explained how Müller calculated his ratio, but does not explain Wideroe's method.

	Müller	Wideroe
Birth	83.3	109.0
2 weeks	71.6	88.5
1 month	63.5	72.0
2 months	58.2	65.0
3 months	55.3	62.5
4-6 months	52.4	57.0
7-12 months	53.8	54.5
2nd year	54.3	56.0
4-5 years	48.6	51.4
6-10 years	47.9	50.5
11-15 years	48.4	52.0
16-20 years	52.5	56.5

Brock's comment on these figures runs:

> "...Sie zeigen - in sehr guter Übereinstimmung bei beiden Autoren - folgende Alterskurve:- Nach Umstellung vom fetalen auf den bleibenden Kreislauf bleibt der rechte Ventrikel anfangs ganz hinter dem stark wachsenden linken Ventrikel zurück (Abfall des Relativwertes von 83.3 - 53.3 bzw. 109.0 - 62.5 in den ersten drie Lebensmonaten), weiterhin verschiebt sich das Verhältnis nur noch langsamer zuungunsten des rechten Ventrikels, und mit 6-10 Jahren ist der tiefste Punkt erreicht (Relativwert 47.9 bzw. 50.2), dann holt der rechte Ventrikel im Verhältnis zum linken wieder ein wenig uf...."

A translation of this passage runs:

> "...They show - with close agreement between the two authors - the following age changes: after the change from a foetal to a permanent circulation is achieved the right ventricle lags far behind the strongly growing left ventricle (fall of the proportion from 83.3 - 53.3 in the one case, 109.0 - 62.5 in the other, during the first three months); subsequently the proportion changes more slowly in the same direction, and the lowest point is reached in the period 6 - 10 years (proportion 47.9 in the one, 50.2 in the other). After this the right ventricle regains a little in relationship to the left. .."

Reference to Table 4 shows that the figures in Müller's column are obtained by averaging Müller's male and female mean figures. There are two mistakes - 4-6 months should be 52.7 and 7-12 months 50.8 - and an unfortunate omission - the figure for the 3rd year is 47.1, which would have been the lowest figure in Müller's list and would have destroyed the agreement between the two series which Brock emphasized. But in any case it has already been shown on page 29 that no statistically justifiable difference exists between the figure for 4-6 months and those which follow it. Brock's analysis of Müller's figures must therefore fall away. Some of the figures from Brock's book have been quoted by Smith (1951), whose statements are considered on page. 47.

In 1942 J.A. Keen published planimetric observations on cross sections of foetal and infantile ventricles. This method is open to several criticisms, and too few hearts were examined to permit firm conclusions. Changes in the R/L relationship were observed as early as six days, and there was one specimen from an infant one year old which suggested that the right ventricle was thinned out to a point beyond the ratio seen in adult hearts. This was an isolated observation, and lacks confirmation.

In their book "The Foetal Circulation" Barclay, Franklin and Prichard (1944) devoted little space to postnatal changes in the ventricles. There is no mention of the course of events in the sheep, which was the species on which the brilliant radiological studies were made. For the human subject they quoted J.A. Keen (1942) but criticised his methods. They continued:

> "From other sources comes evidence that the right ventricle retains a foetal dominance for some time from birth, after which the left ventricle predominates for the rest of life in the healthy subject. This evidence is electrocardiographic and anatomical. The electrocardiogram of the human infant exhibits a right axis deviation up to two or three months from birth. For the term "right axis deviation" one can substitute, in this instance, the term "right preponderance" because during the period mentioned the right ventricle actually weighs more than the left ventricle (Lewis 1920). In full-term foetuses, according to Patten (1933), it is 13% heavier. The change to "left preponderance" cannot be regarded as a very immediately post-natal one, but it is necessary to give this brief account of it, as it

may need to be taken into account in connection with the post-natal closures of various foetal blood channels."

The work of Lewis (1920) is quoted on page 40, and it will be seen that he did not write that the right ventricle was absolutely heavier than the left at birth; his words were "relatively heavy", and were meant, presumably, to compare the infantile with the normal adult heart. The contribution of Patten (1933) was to Curtis' Obstetrics, in which he summarises the 1930 conclusions which are mentioned on pages 38 and 40.

Professor Brash (1951), whose statement on the foetal ventricular ratio is quoted on page 38, continued by stating that after birth the left grows more rapidly than the right, until at the end of the second year, a position of stability is gained, when the right is to the left as 1 is to 2, and this proportion is maintained until death.

A typical opinion derived from modern electrocardiographic studies is provided by Alimurung et al. (1951). These authors studied 521 children and observed continuing changes in the normal appearances up to the age of 13 years. In explanation they stated that this gradual change was easily explained by the differences in relative size and thickness between the two ventricles as compared to adult age. For authorities they quoted Brock and Patten, and inferred that a gradual growth change was the main factor causing the gradual electrocardiographic changes which they observed in the children.

The quoted statements indicate a wide variety of opinion on the rate of the postnatal transformation of the ventricular balance. There has been a tendency to read into the published figures such conclusions as seemed to the various authors to agree with their several ideas about the postnatal course of events.

The present investigation, which is supported by a re-analysis of Miller's figures, shows that the period of most rapid change in the ventricular ratio is the first month of life. After this a more gradual change takes place, until at 6 months the left ventricle has reached a degree of preponderance which no longer changes with increasing age. (Table 3 and Fig. 2). The final steady level of mutual ventricular relationship can fortunately be compared with the ratio characteristic of the normal adult heart through the study by Fulton, Hutchinson and Morgan Jones (1952) which has been quoted above. Taking the mean figures which they reported for normal hearts (see page36), the ratio between the weight of the free wall of the right ventricle and the total ventricular weight (R/T) is 26.9%. It has already been mentioned that these authors divided the ventricular myocardium by a method closely resembling that used in the present study. The similarity of methods is illustrated by the figures reproduced in Table 9, where the average proportions of the parts into which the ventricles were divided in the two studies are compared.

TABLE 9
COMPARISON OF METHODS OF DISSECTION OF VENTRICLES
USED BY FULTON ET AL., AND BY THE AUTHOR.

	R/T%	S/T%	L/T%
Fulton et al. (1952):			
43 normal hearts from adult subjects.	26.9	22.8	50.3
Present study:			
24 normal hearts from subjects aged 4 to 16 years.	27.2	22.9	49.9

R - weight of free wall of right ventricle; S - weight of septal fragment; L - weight of free wall of left ventricle; T - total ventricular weight.

It has already been shown that after the age of 6 months, the hearts investigated in the present study showed no change in the degree of left preponderance which was statistically significant. It is obvious that the two R/T figures in Table 9 are almost identical. It is a reasonable conclusion that the ventricular weight ratio reached after six months of life remains characteristic of the rest of childhood, adolescence and normal adult life. In other words, growth of the ventricular mass after six months of age occurs in such a way that the increments to each side are proportionate to their bulk. The slow electrocardiographic changes in childhood which have been referred to on a previous page must be caused by factors other than a change in the ratio of ventricular bulk, at any rate after the first six months of life.

(4) Postnatal atrophy of the right ventricle

A striking feature of the present study is the observation that the right ventricular free wall loses weight after birth, particularly during the first month. The loss amounts to 20%, and this amount is not regained until the end of the first year. On page 25 can be seen the original statement of Müller, who appears to have been the first to observe this phenomenon. Müller's statement has not been quoted, so far as can be discovered, and it is specifically denied in the following passage from Smith (1951). Commenting on a selection of figures reprinted from Brock (1932) (see page 41), he stated:

> "A rapid increase in left ventricular development is apparent. Although in these data the left is from the beginning somewhat larger than the right ventricle, Patten's measurements have shown that the right ventricle may be the larger of the two at birth. In any case, the first few months of life are marked by the ascendancy of the systemic circulation; that this process gets under way within the first two weeks is shown by the figures collected by Brock. No actual decrease in the right heart is part of this process, but the left side grows rapidly, increasing (according to Scammon (1923)) more in thickness of muscle walls than in general expansion."

It is clear that if Smith had consulted Müller's original publication, instead of Brock's quotation of this author, he would have gained a different impression.

Müller's explanation of the atrophy was that immediately after birth the work of the right ventricle was diminished. This conclusion must be endorsed as the only convincing explanation of the facts. The whole process shows that healthy myocardium responds to a diminution of the work it is required to do in the same way as skeletal muscle.

Patten's view that birth has little immediate effect on the foetal cardiovascular system has already been mentioned. His main article was published in 1930, some years before the crucial experiments of Barclay, Franklin, and Prichard on the foetal lamb were performed. Patten's conclusions were partly based on post-mortem observations on the ductus arteriosus and the foramen ovale. This method of study has been strongly attacked by Barclay, Franklin and Prichard (1944). A typical quotation from their book "The Foetal Circulation" runs:

> "...One has, however, constantly to bear in mind that the post-mortem appearance of a vascular channel may be no real guide to its preceding functional state. This proviso applies particularly to those parts of the cardio-vascular system which are more directly concerned with the change-over from the foetal to the postnatal conditions, and it means that large numbers of careful measurements listed in earlier publications may be valueless in the present connection, for they are post-mortem findings and cannot be assumed to be identical with the in vivo measurements."

Patten, however, has not abandoned his point of view, which is restated in his textbook of Human Embryology, published in 1946, and again in a contribution to the tenth edition of Morris' Anatomy, published in 1951. It is worth quoting the relevant portions of this last account, as it indicates a concept with the truth or falsity of which the present study is directly concerned:

> "The profound character of the change, which must inevitably take place immediately following birth in the manner in which the blood is oxygenated, has led to a wide-spread belief that there must be revolutionary changes in the routing of the blood through the heart. As the embryology of the vascular system has been studied more closely from a functional angle, however, it is becoming increasingly clear that the heart and great vessels develop in such a manner that the pumping load on the different parts of the heart remains balanced at all times during foetal life. Moreover the very mechanisms that maintain this cardiac balance during

> intra-uterine life are perfectly adapted to rebalance the circulatory load post-natally without any sudden overloading of previously inactive parts of the vascular system."
>
> And again: "..... with our present knowledge it is quite apparent that the changes in circulation which occur following birth involve no revolutionary changes of the load carried by different parts of the heart. The fact that the pulmonary circulation is already so well developed before birth means that the changes which must occur following birth are far less profound than was formerly believed, and the compensatory mechanisms at the foramen ovale and the ductus arteriosus which have been functioning all during foetal life are entirely competent to effect the final postnatal rebalancing of the circulation with a minimum of functional disturbance."

In the more detailed account in the embryology textbook he explains that "the right ventricle at all times carries its full share of the pumping load. Were this not the case the muscular development of the right ventricle would not be sufficient at the time of birth to meet the load it must carry when the pulmonary circulation becomes functional."

It is clear that if the findings of the present study are accepted, Patten's view of the cardiovascular adjustments at birth can no longer be supported. Far from being insufficiently developed to meet the load of the pulmonary circulation, the right ventricle is found to have developed in the later foetal months to a point where it deals with more work than it is required to do after birth. Nor can any support be given to the idea that the changes in the heart are gradual and extend over years; the change in ventricular proportion can be described by the word revolutionary, as the greater part of the readjustment takes place in the first month of life.

In terms of the work to be done by the two ventricles, the event of birth introduces a dramatic change. The atrophy of the right ventricle in the early postnatal period occurs at a time of vigorous left ventricular growth. It can therefore be concluded with some certainty, that while the burden of work required of the right ventricle is sharply diminished by the event of birth, the left ventricle faces increased tasks, and meets them by rapid growth.

It is naturally tempting to proceed further, and to argue that the dramatic change in ventricular ratio involves the necessity of early functional closure of the ductus arteriosus, which has so convincingly been demonstrated by Barclay, Franklin and Prichard (1944) for the foetal lamb. It does not seem justifiable to argue too far in this direction. All that is necessary to explain the reduction in the bulk of the right ventricle is a reduction in the peripheral resistance against which the chamber has to pump. Such a reduction is known to occur as a result of the expansion of the lungs with the onset of respiration. A patent ductus arteriosus during this period could be expected to lead, as it does when it persists, to leakage from the aorta to the left pulmonary artery, but would not necessarily cause the right ventricle extra work. If and when angio-cardiography becomes possible in newly-born infants, the occurrence or absence of such a leak may be demonstrated, and the question of early functional closure of the ductus finally settled. All that can be asserted is that the right ventricle does not, after birth, continue to pump blood against the peripheral resistance provided by the pressures in the aorta - the flow in the ductus either stops or is reversed. No other conclusion will fit the observed atrophy of the right ventricle in the early postnatal period, occurring at a time of vigorous left ventricular growth.

SUMMARY AND CONCLUSIONS

(1) Anatomical examination of the heart cannot be expected to provide precise estimates of the proportion in which the ventricular myocardium should be divided between right and left sides. Even if this were possible, it does not appear that precise conclusions about the relative amount of work done by the two ventricles can be based on observations of the proportionate ventricular myocardial weight.

(2) Despite these difficulties, it is possible, by suitable dissection and weighing, to compare the degree to which the left (or right) ventricle preponderates in various hearts. By the method used in the present study, the weight of the free wall of the right ventricle is compared with the total ventricular weight, and this method is shown to provide a satisfactory comparative measure of the relative bulk of the two ventricles.

(3) This method of study has been applied to a series of normal hearts from newly born babies, infants, and children. At the time of birth the weight of the myocardium of each ventricle is approximately the same, though in some cases the right ventricle weighs more than the left. Change in this proportion occurs rapidly after birth, so that the left ventricle soon comes to preponderate. The greater part of the total change observed occurs in the first month of life. A slower change proceeds subsequently until the age of six months, by which time the relative development of the two ventricles has reached proportions which remain characteristic of the rest of infancy, childhood, adolescence, and normal adult life.

A re-examination of the results of the investigations of W. Müller (1883) supports the conclusions of the present study. Müller's own conclusions about the postnatal change in ventricular proportions cannot be supported, and those who have quoted results from Müller's work have usually drawn from them conclusions which appear on examination to be even less justified.

(4) During the first month of life the rapid adjustment of ventricular weight ratio results from atrophy of the right ventricle (diminution of the absolute weight of the myocardium of its free wall by about 20%) during a time of rapid left ventricular growth. The loss of weight is not restored until the end of the first year. This observation means that at or very soon after birth circulatory changes occur which radically alter the relative amounts of work performed by the right and left ventricles. The rapid change in ventricular weight ratio does not necessarily imply early cessation of flow through the ductus arteriosus in the human infant, although this explanation must be considered. The right ventricular atrophy does however mean that the flow in the ductus is either reversed or halted.

The published statements of Bradley M. Patten on the circulatory adjustments at and following birth are critically reviewed. The idea that the right ventricle slowly stops pumping blood through the ductus during the early postnatal months is not consistent with the observed atrophy of the right ventricle.

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