XII.—The Development of the Heart in Man. By Prof. D. Waterston, M.D., Bute Medical School, University of St Andrews. (With Eighteen Text-figures and Sixteen Plate-figures.)

(Read July 9, 1917. MS. received December 26, 1917. Issued separately August 1, 1918.)

Introduction.

Examination of living embryos has shown that the heart is a functionally active organ from a very early stage of its development. At all periods of life the result of the functional activity is in essentials the same, viz. the propulsion of the blood in a definite direction through the heart into the vessels arising from it; but the mechanism for effecting this propulsion undergoes profound alterations, and the heart becomes transformed from a simple continuous tube, destitute of valves, whose walls contract in a rhythmic peristaltic wave, into a complex four-chambered organ, divided into right and left portions, which are ultimately completely separated from one another, possessing valves, and contracting not in a peristaltic wave but in alternating consecutive contractions of the atria and ventricles of the right and left sides simultaneously. Coincidently with the changes in the heart itself, profound alterations occur in the vessels leading to and from the heart. In this combination of simultaneous development and functional activity the heart differs from the other organs of the body, and hence its development presents special problems involving the function as well as the structure of the different parts. Our knowledge of the development of the heart in man cannot yet be said to be complete.

The discovery by Kent and His of connections between the atria and ventricles, and that by Keith and Flack of the sinu-atrial node, with the consequent altered views of the mechanism of the heart-beat which are now generally accepted, have imparted a new interest and value to the study of the development of the heart.

The development of the atrio-ventricular bundle has been worked out by Mall, but the records of examination of at all complete series of the hearts of human embryos are as yet scanty. The introduction of the plate method of reconstruction provided a new method of great value to embryologists, particularly in the study of the development of the heart, since without accurate plastic reconstructions it is almost impossible to follow the complex three-dimensional changes which occur, and hence those descriptions alone are of special value in which this method has been employed.

The embryonic material examined in this investigation includes human embryos from 3 mm. to 30 mm. in length (maximum) cut in serial section, and a number of larger embryos.

The principal developmental changes have been completed at the 30-mm. stage, though complete separation of the atria does not occur until birth.

The embryos examined in section include the following specimens :—

1.	Embryo	2W1,	3 mm. in length (maximum).	
2.	,,	S1,	6 ,,	,,
3.	,,	B1,	8 ,,	,,
4.	,,	M1,	9 ,,	,,
5.	,,	S4,	12·5 ,,	,,
6.	,,	B2,	13 ,,	,,
7.	,,		16 ,,	,,
8.	,,	S3,	20 ,,	,,
9.	,,	B3,	22 ,,	,,
10.	,,		30 ,,	,,
11.	,,	E1,	28·5 ,,	,,

All of these embryos showed good histological condition, and most of them almost perfect histological detail.

I am indebted to Prof. SYMINGTON for the embryos B1, B2, and B3, and to Prof. PETER THOMPSON and to Prof. BRYCE respectively for the opportunity of examining and reconstructing from their sections the heart in the embryos 7 and 10 of the list.

In addition, I have examined series of sections of embryos of the cat, guinea-pig, and mouse, and I am greatly indebted to my colleague, Prof. W. C. M'INTOSH, for the opportunity of examining specimens of the adult heart in the shark, dogfish, boa, and crocodile, examination of which gives considerable help in the correct interpretation of the conditions found in different stages of the development of the mammalian heart.

Prof. PETER THOMPSON also kindly allowed me to examine several of his reconstructions of developing hearts, and particularly his model of the 2·5-mm. embryo of R. MEYER'S collection, which is a most valuable specimen.

The earliest stages of the development of the human heart are as yet unknown, as the material necessary for investigating them does not exist in any collection ; but it is presumed that the heart follows the lines of development exhibited in the earliest stages of other mammals, in whom the primitive heart is formed by the fusion of two parallel longitudinal vessels, which unite to form a single tube, receiving at its caudal extremity the afferent veins, and terminating orally in a single vessel, the truncus arteriosus, which divides almost at once into the two ventral aortæ.

The heart tube becomes bent upon itself and twisted into the shape of an S. Alternate dilatations and constrictions make their appearance, so that it comes to show a series of dilatations, viz. the sinus venosus, the atrium, the ventricle, and the "bulbus cordis" in succession from the caudal to the oral end. The atrium and ventricle are joined to one another by a short narrow channel of great importance in the later stages of development, termed the atrial canal. In describing these chambers the terms "proximal" and "distal" may be used, the former indicating the sinus end and the latter the truncus arteriosus end of the heart.

The stage at which the following description begins is that at which the heart has the form of a twisted tube, showing the constrictions and dilatations referred to above.

It is convenient to begin the description of the successive stages by giving an account of the heart in the youngest specimen examined, an embryo of twenty-seven pairs of somites (2W1) (1), maximum length (from sections) about 3 mm., from which models of the heart and trunk at a magnification of 100 and 200 diameters were made.

The larger model of the heart of this embryo is shown in the Plate-fig. 1. Viewed from the front, a portion of the atrium, the atrial canal, the ventricle and "bulbus cordis," leading to the commencement of the truncus arteriosus, are visible. In its general shape the heart bears a resemblance to the model constructed and figured by P. Thompson from the R. Meyer embryo (No. 399) of eighteen pairs of somites (2).

At this stage the heart tube is twisted so that the atrium lies oral and dorsal to the ventricle, the atrial canal lies on the left side, and the ventricle and "bulbus" are sharply bent upon one another. The ventricle lies on the left side and at the apex, and the "bulbus" extends along the right margin and curves orally to the left.

The heart tube has become divided into segments, viz. sinus venosus, atrium, ventricle, and bulbus cordis, separated from one another by constrictions, and the principal bendings have occurred at the constrictions separating these chambers. The sinus venosus and atrium are not sharply bent upon one another, but the atrial canal marks the position of a sharp bend, in an oblique plane, between atrium and ventricle. At the bulbo-ventricular constriction a bend has been formed in an almost vertical plane. The bulbus is slightly curved to the left, and another bend is found at the junction of bulbus and truncus arteriosus.

The terms "ventricle" and "bulbus cordis" are used here following Tandler (3). The terms and the significance of the chambers which they denote are discussed later.

Table I.

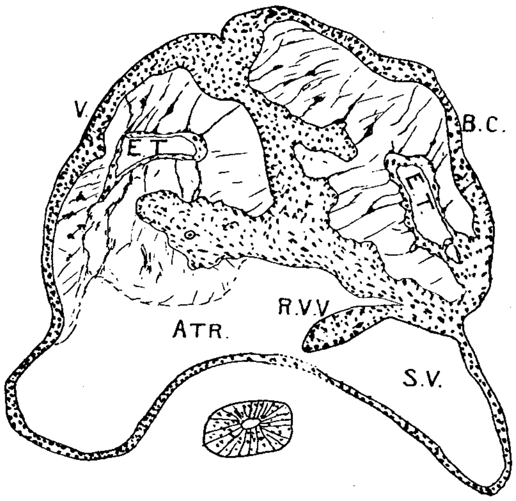
Dimensions of Heart Model of 2W1. × 200.

Vertical height		150 mm.
Transverse width of atrium		85 ,,
Vertical height of atrium		110 ,,
Sinu-atrial orifice, height		50 ,,
Atrial canal, width		15 ,,
Ventricle, dorso-ventral width		70 ,,
,, transverse width		60 ,,
,, thickness of wall		13 ,,
Bulbus cordis, thickness of wall	lower part	13 ,,
	upper ,,	6 ,,

Chambers.—The sinus venosus consists of a short and comparatively narrow transverse portion, and of a right and left horn. The left horn, the smaller of the two, lies in the upper margin of the left portion of the septum transversum, whence the transverse portion passes to the right and terminates in a large right horn, which is partly embedded in the septum transversum and partly has risen out of it.

The right horn of the sinus venosus lies dorsally and to the right of the atrium. It is roughly triangular on section, and its wall is continuous with that of the atrium (text-fig. 1).

Sinu-atrial Orifice.—The communication between sinus and atrium is a vertical slit-like orifice, opening from right to left, and slightly ventrally. The ventral



TEXT-FIG. 1.—Transverse section (slide 103, section 3) of heart of 3-mm. embryo, showing the chambers and the narrow endothelial tube within the myo-epicardial mantle. × 100.

junction of sinus venosus and atrial walls is infolded, forming a prominent right venous valve, but there is no left venous valve.

Atrium.—The atrium is a large, capacious chamber, lying dorsal and oral to the ventricle, and extending at its oral end across the whole width of the heart; the sinu-atrial opening is placed at the dorsal right margin, while the atrial canal opens from the caudal and left ventral corner.

The dorsal wall is incurved towards the cavity, but there is no trace of the atrial septum.

The muscular wall is deficient over a small area of the dorsal wall; the "area interposita" and the myocardial and endocardial walls are in contact. The muscle wall is extremely thin.

Atrial Canal.—This short channel extends from the left ventral and caudal corner of the atrium to the oral left portion of the ventricle. Its width in the model, at 200 diameters magnification, is 15 mm., and it is almost cylindrical.

In this portion is found that separation of the myocardial and epicardial walls by a space containing a loose reticulum of tissue, whose features have been worked out in similar specimens by MALL (4).

The endothelial tube containing the blood stream is a very narrow channel indeed, lying centrally within the lumen of the myocardial wall.

The sub-endocardial reticulum shows no division into separate cushions. It extends uniformly round the lumen of the tube, and is continuous with a similar reticulum in the upper part of the ventricle and in the bulbus.

The next portion of the heart, from the atrial canal to the root of the truncus arteriosus, is divided into two segments, separated from one another by a deep groove which traverses obliquely the ventral surface from the left to the caudal right margin, and is produced by the acute flexion of the heart tube (Plate-fig. 1).

The homologies of these portions and the successive development of each will be traced later; but for the present the proximal limb may be termed the ventricle, while the distal segment is termed the "bulbus cordis."

The ventricle is of the shape of an inverted triangle, the apex forming the apex of the heart. Its muscle wall, of considerably greater thickness than that of the atrium, is reticulated and separated in the greater part from the endothelial tube within by a space containing fine fibrils. Only at the caudally-placed apex are these two walls, myocardium and endocardium, in apposition. The atrial canal opens at the oral left angle, while the exit to the bulbus is at the corresponding oral and right corner.

At the junction of bulbus and ventricle the lumen of the heart tube is narrowed, and a short surface constriction is formed, partially separating them.

From the interior, this separation of bulbus and ventricle is seen to be due to the infolding by the bulbo-ventricular groove of the ventral wall, so that a prominent ridge is formed on the ventral and oral aspect extending to the caudal border of the lumen.

The bulbus cordis possesses a myocardial wall of some thickness, a delicate reticulum, and in the interior a narrow endothelial blood tube.

As in the atrial canal a reticulum of this nature precedes the formation of endocardial cushions, so apparently here also the reticulum precedes the formation of definite bulbar cushions.

The reticulum ceases abruptly at the commencement of the truncus arteriosus, and the endothelial tube widens out to line the external wall; and at this point the muscle wall of the heart ceases abruptly, and is replaced by fibrous tissue on the wall of the truncus arteriosus.

The bulbus is roughly of a triangular outline, for near its middle the oral right wall is considerably distended. It lies in the ventral surface of the atrium.

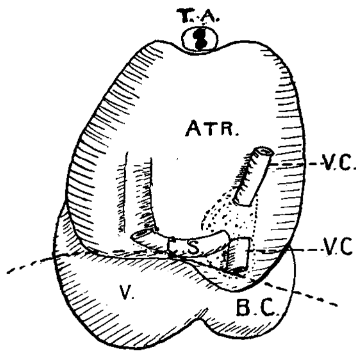
If this specimen be compared with the rather younger embryo heart modelled by THOMPSON (2), a close resemblance of the specimens can be noted, and corresponding divisions of the heart tube are present. In his specimen, however, while the ventricle and bulbus have generally the same features as in mine, their relative position is different—the ventricle lying caudally in his specimen, and the bulbus lying orally, the two chambers separated by a bulbo-ventricular groove which is nearly horizontal in direction.

The condition in my specimen has been reached by a rotation of the bulbo-ventricular groove from the horizontal to the oblique axis, and later specimens show that this rotation is continued until the groove is vertical in direction.

Heart of Embryo S1 (6 mm. in Length).

The external form and the internal structures are shown in Plate-figs. 2, 3, and 4.

At this stage the sinus venosus has risen out of the substance of the septum transversum, and in place of the vitelline and umbilical veins there is a single large



Text-fig. 2.—Dorsal view of heart of 6-mm. embryo.

vessel (vena cava inferior) which opens into the right horn of the sinus venosus. The left duct of Cuvier runs into a comparatively narrow channel, and the transverse portion of the sinus venosus passes along the posterior surface of the heart and opens by a narrow orifice into the right horn. The right horn forms a small chamber, into which opens the right duct of Cuvier and the vena cava inferior. The sinus venosus opens into the atrium by a narrow slit-like orifice, measuring in the model 25 mm. vertically and 5 mm. transversely at its widest part. The sinus wall is smoothly and evenly continued into the atrial wall.

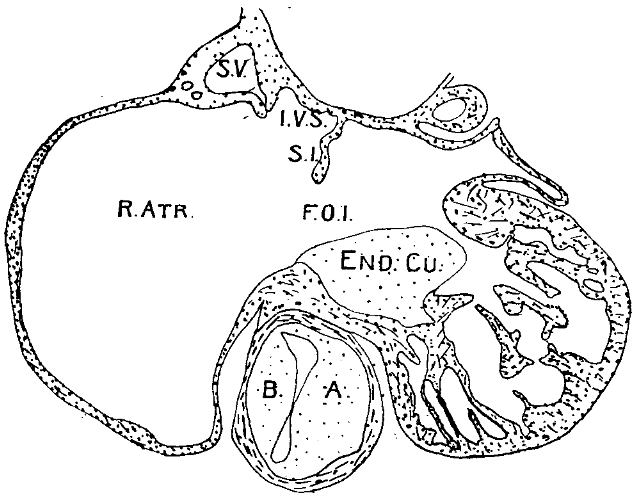
The right venous valve—the more prominent of the two—measures 8 mm. in length, and in structure consists of a more loosely reticular tissue than the adjacent heart wall, and vacuoles or spaces are present within it. The two venous valves united orally to the orifice form a long, narrow "tensor valvulæ," prolonged on to the roof of the atrium (Plate-fig. 3).

Atrium.—The shape of this chamber is considerably altered, and it forms a large crescentic cavity, enclosing in its bay the tubular portion of the bulbus cordis. The dorsal convex wall of the crescent is indented centrally by the dorsal body wall.

Near the middle line there is an almost complete septum primum atriorum uniting the dorsal and ventral walls. It does not reach the ventral portion of the floor of the atrium, and there is present the foramen ovale primum, measuring in the model some 20 mm. in vertical height (text-fig. 3).

In the upper part of the septum primum there is a small orifice with ragged edges—the foramen ovale secundum.

The septum primum terminates caudally and ventrally in the cushion tissue of the atrio-ventricular canal. The right portion of the atrium is much larger than the left, and forms a very large chamber lying to the right of the septum primum.



TEXT-FIG. 3.—Transverse section (slide 11) of heart of 6-mm. embryo.

Between the septum primum and the sinu-atrial orifice is a distinct recess, the intersepto-valvular space.

TABLE II.

Dimensions of Heart of S1. × 100.

Vertical height	170	mm.
Atrium, transverse width	150	,,
,, vertical height	150	,,
Sinu-atrial orifice, height	25	,,
Distance between right and left venous ostia	40	,,
Ventricle, left, vertical height	115	,,
,, ,, transverse width	50	,,
,, ,, thickness of wall	12 to 18	,,
,, right, transverse width	60	,,
,, ,, thickness of wall	7 to 12	,,
Interventricular foramen { dorso-ventrally	21	,,
Interventricular foramen { vertically	30	,,
Distance of interventricular foramen from interventricular cleft	45	,,

Atrial Canal.—The exit from atrium to ventricle is now divided into two minute channels by the union with one another of the endocardial cushions of the atrial canal.

The interval between these orifices, or venous ostia, represents the single atrial canal of the former specimen, which has moved to the right and lies almost ventral to the sinu-atrial inlet into the atrium.

The atrial septum, prolonged forward, would lie nearer to the right than to the left orifice. The fused endocardial cushions form a mass, extending into the floor of the atrium to the base of the septum primum.

The left orifice opens into the left ventricle, and the right into the bulbus cordis; and the right margin of the right atrio-ventricular opening is limited by one of the two bulbar cushions (Plate-fig. 3).

Ventricular and Bulbus Portions.—This portion shows a partial division into right and left ventricles by a thick, rounded muscular partition which projects into the interior from the ventricle wall, and is represented on the surface by a groove on the ventral aspect and a notch upon the caudal margin of this portion of the heart. Of the two chambers, the left ventricle forms a spherical, thick-walled chamber, with reticulated muscle tissue in its interior, receiving the left atrio-ventricular orifice in its dorsal cephalic wall. The interventricular foramen forms the sole outlet for this chamber, and by it the blood can pass to the distal portion of the bulbus cordis (Plate-fig. 3).

The wall of the right ventricle is of less thickness, and is not so fully reticulated. The ventricle is flask-shaped, and the lower portion, dilated and capacious, leads into a narrow tubular portion, where the lumen shows incomplete division into two channels. Within the lower portion are found the terminations of the two chief bulbar cushions, one on the interventricular septum, the other forming a prominence on the right of the right atrio-ventricular orifice.

Within the tubular portion are found the distal portions of the bulbar cushions.

The spiral course and the general shape and arrangement of these cushions may be gathered from the reconstruction figured in Plate-fig. 4.

The ultimate derivatives of these two portions of this chamber are very different, and the nature of the two portions is discussed later.

For the present, the names of conical portion and tubular portion may be given to distinguish the two parts from one another.

Heart of Embryo B1 (8 mm. in Length). Plate-figs. 5, 6, and 7.

External Form.—The heart in this embryo and that in embryo M1 (9 mm.) resemble one another very closely indeed.

The large ventricular portion shows clear indication upon its surface of the internal division into right and left chambers by the interventricular furrow and the notched caudal border.

The interventricular furrow continues in a caudal direction the left margin of the tubular "bulbus cordis" portion.

The right ventricle and its tubular continuation have the same flask shape noted in S1.

Internal Structure.—Sinus venosus.—The right horn of the sinus venosus forms a chamber lying near the dorsal right corner of the atrium, and marked off from it externally by a vertical groove extending between the right margins of the venæ cavæ superior and inferior. The superior vena cava (right duct of Cuvier) opens into it high up on the dorsal wall, while the vena cava inferior and the transverse portion of the sinus venosus open into its floor; between the latter two orifices is a small ridge.

Sinu-atrial Junction.—The venous valves are much larger than in the former specimen, the right one particularly so, and it projects so far into the atrium as almost entirely to cut off the portion on its right from that on its left side. Along the floor of the atrium it extends as far as to the cushions of the atrial canal (text-fig. 4, and Plate-fig. 6).

The left venous valve is shorter, but it also is prolonged for some distance along the floor of the atrium. Orally it blends with the right valve and forms a large "tensor valvulæ."

The orifice between the two valves is a vertical slit. The right venous valve shows again a recognisable difference in structure from the remainder of the heart wall, and is loose in texture.

Atrium.—A wide bay on the outer surface of the roof of the atrium corresponds to the upper attachment of the septum primum.

Table III.

Dimensions of Model of the Heart of B1. × 100.

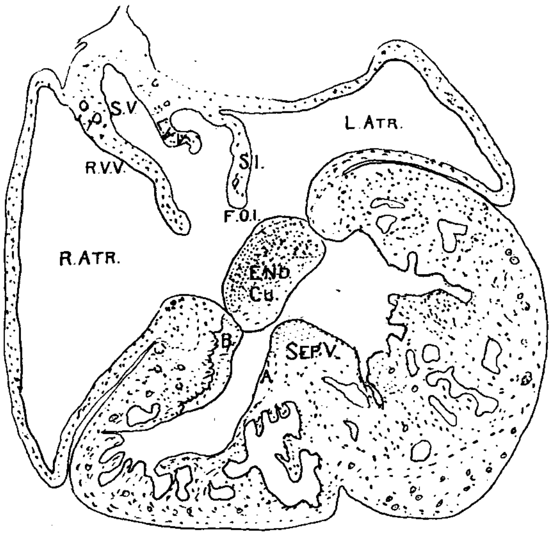
Vertical height	130	mm.
Atrium, transverse width { right	100	,,
Atrium, transverse width { left	90	,,
,, vertical height	140	,,
Sinu-atrial orifice, vertical height	50	,,
Right venous valve, depth	65	,,
Left ,, ,,	20	,,
F. ovale primum still present, diameter	10	,,
,, secundum, vertically	25	,,
Distance between right and left venous orifices	42	,,
Ventricle, left, vertical height	105	,,
,, ,, transverse width	90	,,
,, ,, thickness of wall	40–60	,,
,, right, transverse width	90	,,
,, ,, vertical height (conical portion)	65	,,
,, ,, thickness of wall	25	,,
Interventricular foramen, diameter	35	,,
,, ,, vertically	similar.	
Distance of interventricular foramen from interventricular cleft	75	mm.

Right and left venous valves united caudally and orally.

On a transverse section the atria are crescentic in shape, and they are very capácious—many times more so than the ventricles. It is probable that the atrium has been fixed in diastole and the ventricle in systole.

The septum primum is not complete, for there is a small foramen ovale primum close to the region of the atrial canal. The septum is S-shaped in section, and shaped so as to direct the inflowing blood from the vena cava inferior towards the foramen ovale secundum, an orifice of some size in the upper part of the septum, with irregular margins.

Atrio-ventricular Openings.—These orifices resemble closely the orifices seen in S1. They are very small indeed, and lie on either side of the fused mass of the



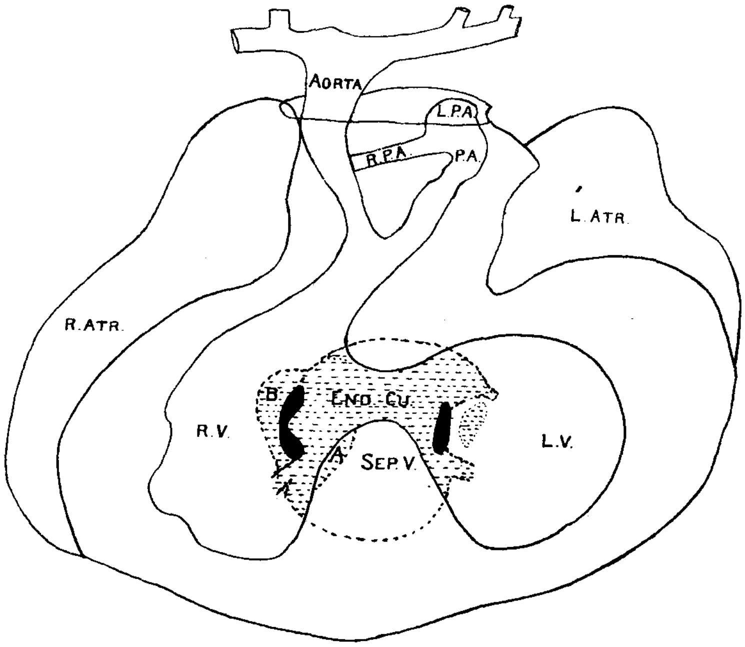
TEXT-FIG. 4.—Transverse section (slide 10, section 20) of heart of 8-mm. embryo.

endocardial cushions. The extent and arrangement of these cushions are shown diagrammatically in text-fig. 5.

The upper cushion is of loose texture, and the nuclei are widely separated from one another, but there are small areas where they are closely packed together.

The margins of the cushion stain more deeply and are marked off distinctly from adjacent muscular tissue. The upper endocardial cushion begins high up in the ventricle and on the ventral surface of the septum primum of the atria. At this level it lies embedded in the muscle substance of the ventricles. Traced downwards, it passes to the free margin of the interventricular septum and projects on each side into the lumen of the right and left ventricles. Its right margin extends to blend with the lateral bulbar cushion above the level of the right atrio-ventricular orifice, and to the left it joins the trabecular musculature of the left side of the ventricle above the left atrio-ventricular orifice. On the left of the left atrio-ventricular orifice there is a small patch of cushion tissue. Slightly caudally this upper endocardial cushion diminishes in size, and the right and left atrio-ventricular orifices appear on each side of it. At this level a transverse area of closely packed, deeply staining nuclei runs across the mass of cushion tissue, but probably this area may indicate the line or junction of the upper and lower cushions. This area can be traced from the dorsal surface of the cushion, where it begins in the floor of the atrium, onwards to the apex of the interventricular septum, and hence corresponds to the region of the atrio-ventricular node and bundle.

At the external atrio-ventricular groove on the surface of the heart there is a very distinct region of loose connective tissue, intervening partially between the atrial and the ventricular musculature.



TEXT-FIG. 5.—Linear frontal reconstruction of heart of 8-mm. embryo B1. × 50.

The lower endocardial cushion, between the right and left atrio-ventricular orifices, lies against the base of the septum primum, and is continued below the septum primum in the floor of the atrium to reach the margin of the orifice of the vena cava inferior, and is prolonged also towards the wall of the coronary sinus.

On the ventricular side it passes on to the interventricular septum below the interventricular opening. To the right it blends with bulbar cushion B below the right atrio-ventricular orifice, and to the left it merges into the trabecular musculature of the left ventricle (text-fig. 5).

The right ventricle is triangular in shape and is smaller than the left, but has a larger cavity and thinner walls.

The muscle wall is irregularly reticulated.

The cavity is narrow, and passes gradually into the cavity of the distal portion.

The displacement of the atrio-ventricular orifice towards the right, so that its right extremity opens into the bulbus, has produced a corresponding alteration in the muscle coats, and the atrial muscle wall at the right side is now directly continued into the muscle tissue of the bulbus wall, from which it was primarily separated by the whole width of the base of the ventricle.

Septum.—The interventricular septum springs from the floor and ventral wall of the ventricle, and extends on the dorsal wall as high up as to the endocardial cushions.

The interventricular foramen is an almost circular opening lying between the apex of the muscular interventricular septum on the one side and the fused endocardial cushions on the other (Plate-fig. 7). The opening leads from the cavity of the left ventricle into that of the right at the junction of the conical and cylindrical portions.

The arrangement of the tissues around the venous ostia is particularly instructive, for it shows these openings before any definite valve apparatus has been formed.

The transverse width of the atrial canal measures rather less than 90 mm., while the atrium and the ventricle are more than twice this diameter. The canal is very short, forming an annular narrow constriction, and there the muscle walls of the atrium and ventricle are directly continuous with one another.

The connective tissue of the annulus fibrosus is considerably thicker than on other parts of the heart, and on section it forms a large oval mass.

The inner part of the wall of the left ventricle, beside the left venous ostium, forms a loose network, and is becoming undermined in the fashion described by HIS.

At the right ostium a more definite lateral valve cusp is formed. Here the mass of cushion tissue formed by the downward prolongation of the bulbar cushion B forms a large oval swelling in the inner surface of the wall. This cushion extends nearly to the lowest part of the ventricle, and there it lies on a band of muscle tissue which has become undermined and passes to the right surface of the ventricular septum, like the "moderator band" of the adult heart.

There are no indications of medial cusps at either the right or the left orifice. The interventricular septum passes downwards with smooth walls from the medial border of each ostium.

Nor are there any definite indications of the formation of papillary muscles, with the exception of the strand already referred to in the right ventricle.

The arrangements and attachments of the endocardial cushions, which form the medial boundaries of the venous ostia, are shown in the linear reconstruction (text-fig. 5).

Right Ventricle.—The figure of the external form at this stage (Plate-fig. 5, compared with Plate-fig. 2) shows the nature of the considerable changes which have taken place.

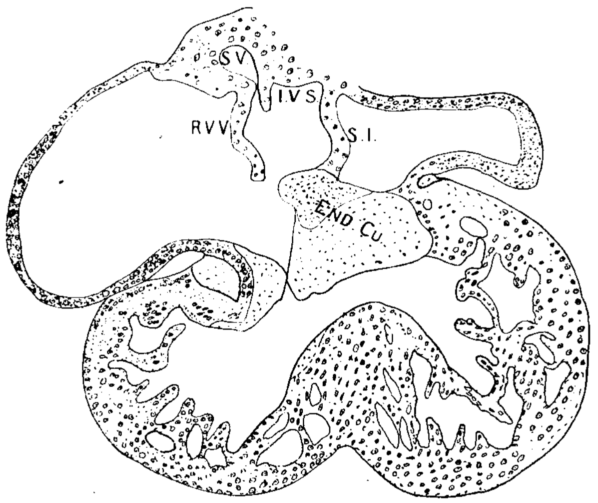
(1) The conical basal portion or right ventricle proper has increased in its relative size.

(2) The upper cylindrical portion is now oblique in direction, and slopes from right to left and towards the dorsum as it ascends.

(3) The termination of the heart tube, *i.e.* the junction with the truncus arteriosus, can be clearly determined by the structure of the wall.

The lumen of the truncus is divided into two separate channels, aorta and pulmonary artery, and each of them is continuous with a portion of the incompletely divided lumen of the cylindrical portion of the bulbus cordis.

The increasing obliquity of the region has led to a lengthening of the convex



TEXT-FIG. 6.—Transverse section (slide 10, section 10) of heart of embryo M1.

portion. The bulbar cushions are distinct, though only two can be made out (see also embryo M1).

EMBRYO 9 MM. IN LENGTH (M1).

Reconstruction at 100 *Diameters.*—The heart of this embryo resembles closely the former specimen (B1) both in size and in shape. The external form is almost identical with that of B1 (Plate-fig. 5). There are the same wing-like expansion of the atria, the surface division between right and left ventricles, and the modified flask-like character of the right ventricle passing orally into a tubular portion.

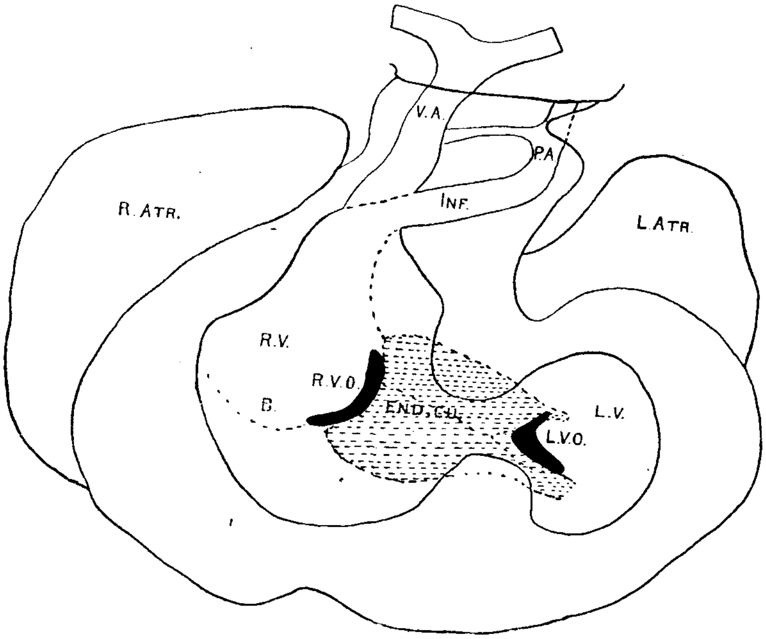
Internal Structure.—The relationship of sinus venosus to atrium resembles so closely that in B1 that it requires no further description. The disposition of the venous valves and septum primum is practically identical with the former specimen (text-figs. 4 and 6).

Sections in this specimen stained with picro-indigo-carmine indicate very clearly the extent and connections of the muscle coat.

Atrio-ventricular Junction (text-fig. 6).—The upper endocardial cushion, as before, lies against the septum primum dorsally, while ventrally its upper part forms the dorsal wall of the ventricle.

Within this cushion are shown very clearly strands of closely packed, deeply staining nuclei, which traverse the loose general tissue of the cushion and extend from beneath the lumen of the atrium downwards and forwards towards the ventricle. This upper cushion blends on the right with the bulbar cushion B, both above and below the atrio-ventricular orifice. To the left it blends with the trabecular tissue in the wall of the ventricle, ventrally with the interventricular septum, and on the surface of this septum there is seen exactly the same arrangement of the bulbar cushion A as was seen in B1.

The lower cushion makes its appearance first to the left of the right atrio-ventricular orifice, where it forms a round tubercle, and the line of junction of the



TEXT-FIG. 7.—Linear frontal reconstruction of heart of embryo M1. × 50.

upper and lower cushions runs obliquely from right to left and caudally. There is a similar extension of this lower cushion across the floor of the atrium to the dorsal wall, and also similar strand-like arrangements of nuclei within its substance. This cushion forms the right margin of the right atrio-ventricular orifice, and below that orifice its left extremity is attached to the trabecular musculature of the ventricles. It descends for some little distance on the left side of the interventricular septum.

The extent and connections of these cushions are shown in the frontal reconstruction, text-fig. 7.

The interior of the cylindrical portion of the right ventricle is shown in Plate-fig. 8.

In the proximal portion the lumen is undivided, and the prominent bulbar cushion A projects into it. More distally the lumen is divided into two, and the bulbar cushion is prolonged into each as a projection on the interior.

The whole extent of the cushion tissue is uniform, and there is no indication whatsoever of "distal" as contrasted with "proximal" bulbar cushions.

EMBRYO B2 (13 MM. IN LENGTH).

In this heart the condition of the upper part of the bulbus cordis resembles, on the whole, the condition found in B1 and M1. The pulmonary artery and the aorta are separated from one another in the upper part of their extent; proximally the stems of these two vessels unite and are continued as a single stem into the upper part of the right ventricle. The bulbar cushions A and B are prolonged downwards on to the lateral ventricle wall and to the septum respectively.

Atrio-ventricular Junction.—The right bulbar cushion (B) joins with the right margin of the upper endocardial cushion above the right atrio-ventricular orifice. This orifice is of some size, and its lower boundary is formed by a tubercle of the lower endocardial cushion. The upper endocardial cushion extends to the base of the septum primum atriorum and passes across to the left side, forming the upper boundary of the left atrio-ventricular orifice. The lower endocardial cushion is prolonged to the apex of the interventricular septum, below the level of the interventricular foramen, and forms a large mass extending from the dorsal wall of the atrium across the floor to the interventricular septum. From its left extremity a tubercle projects into the cavity of the left ventricle and forms the right margin of the left atrio-ventricular orifice.

A small accessory left endocardial cushion forms the left boundary of that opening.

The muscle wall of the ventricles shows a complex network of trabeculæ, and a cortical layer which is considerably thicker in the left than in the right ventricle.

In this specimen the endocardial cushions are very distinct, as the nuclei alone are stained, while the muscle wall is of a pinkish colour.

The atrio-ventricular valve apparatus is rudimentary, but the stage of development is only slightly more advanced than in B1.

In other details the heart in this specimen resembles closely the heart in S4; and as the latter shows more perfect histological detail, a fuller account need not be given of B2.

HEART OF EMBRYO S4 (12·5 MM. IN LENGTH).

The heart of this embryo was modelled at a magnification of 100 diameters, from sections 10μ in thickness.

External Form.—The figure (Plate-fig. 9) shows the external form from the front. The atria, greatly expanded, enclose the upper segment of the bulbus cordis in a deep groove, and this portion of the bulbus lies almost horizontally.

The ventricular portion resembles generally that of the earlier specimens. The left ventricle, somewhat spherical in shape, is separated from the right ventricle by a deep interventricular sulcus and by a notch on the caudal margin.

The proximal conical portion of the right ventricle is continued uninterruptedly into a distal tubular portion, on which an almost vertical furrow, lying on the right side, forms an external constriction corresponding to an internal division of the lumen. The portion behind the constriction contains the ascending aorta, and that in front the infundibulum leading to the pulmonary artery.

TABLE IV.

Dimensions of Heart of S4. × 100.

Vertical height	200 mm.	
Transverse width, left ventricle	125 ,,	
,, ,, right ,,	125 ,,	
Dorso-ventral width, atria (middle)	112 ,,	
Left ventricle	205 ,,	
Right ,,	155 ,,	
,, venous ostium	45 ,,	× 15.
Thickness of wall, compact	25 ,,	
Interventricular opening	20 ,,	× 15 mm.
Distance from apex	120 ,,	

Internal Structure.—The incorporation of the sinus into the atrium has advanced, and the position and attachments of the venous valves and of the atrial septum are of great interest (text-figs. 8, 9, and 10).

The venous valves stretch from the dorsal to the ventral wall of the atrium both orally and caudally, and they enclose between them a central narrow slit-like chamber which receives blood from the venæ cavæ and the coronary sinus. On each side is the widely dilated atrium proper. The central chamber communicates with each of these by a small somewhat oval opening, and they in turn lead into the ventricle on each side. This central chamber may be termed the sinu-atrial chamber. The venous valves meet and blend with one another in both the roof and floor of the chamber. The vena cava superior opens by a narrow orifice through the upper part of its dorsal wall, and the vena cava inferior and the coronary sinus open in the floor separately, the latter far forward.

The right venous ostium lies on the right side of the base of the right venous valve.

Closely blended with the left venous valve is the septum primum atriorum.

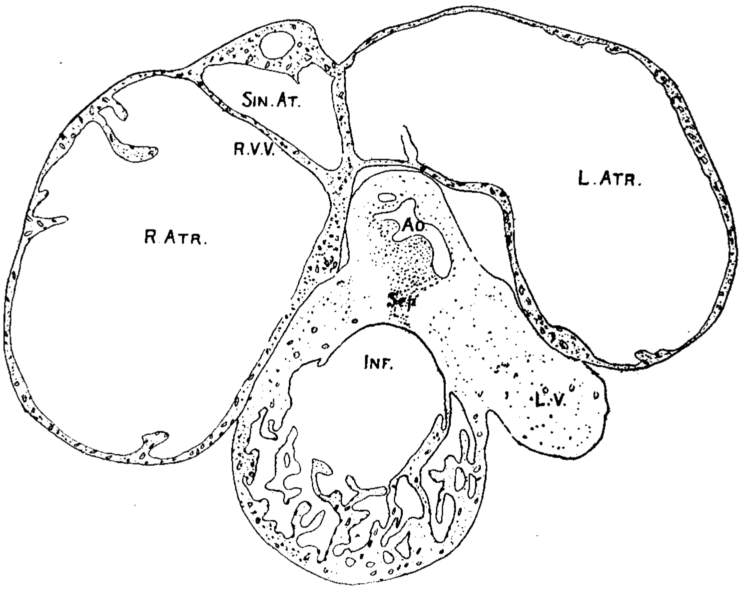
From the left side of the septum primum the wall of the left atrium slopes sharply to the left ostium.

The septum primum forms a complete ring round the interior of the circumference of the atrium, but the foramen ovale secundum is so large that nowhere is the septum of any considerable height. The septum and the venous valves are shown in Plate-fig. 10 viewed from the left side. It is deepest in the ventral inferior portion and very shallow indeed on the dorsal wall, and at its dorsal and inferior attachments it is largely blended with the left venous valve.

The single large pulmonary vein opens into the left atrium immediately to the left side of the septum primum.

Atrio-ventricular Junction.—The ostia from the right and left divisions of the atrium into the corresponding ventricles are large, and around these orifices there is a definite though rudimentary arrangement of valves. The right ostium is a long vertical slit, 50 mm. long and 12–15 mm. in width; while the left is slightly smaller but is wider, measuring some 30 mm. by 20 mm. The right ostium is bounded on the right by a large flap formed by an infolding of the tissues into the interior of the ventricle.

Similarly in the left ventricle there is an early "mitral" valve, the lateral cusp formed by an infolding from the left side, while the medial (aortic) cusp is derived from the cushion tissue between the left and right atrio-ventricular orifices.



TEXT-FIG. 8.—Transverse section (slide 38, section 7) of heart of embryo S4.

The cusps of the valves are attached by a network of muscle tissue to the ventricular wall. Some bands are specially distinct. In the right ventricle one sweeps from the lateral cusp already described on to the interventricular septum, and it is clearly derived from the similar band seen in B1.

There is an advance in the condition in B1, but the differences are not so great as to prevent the recognition of corresponding structures.

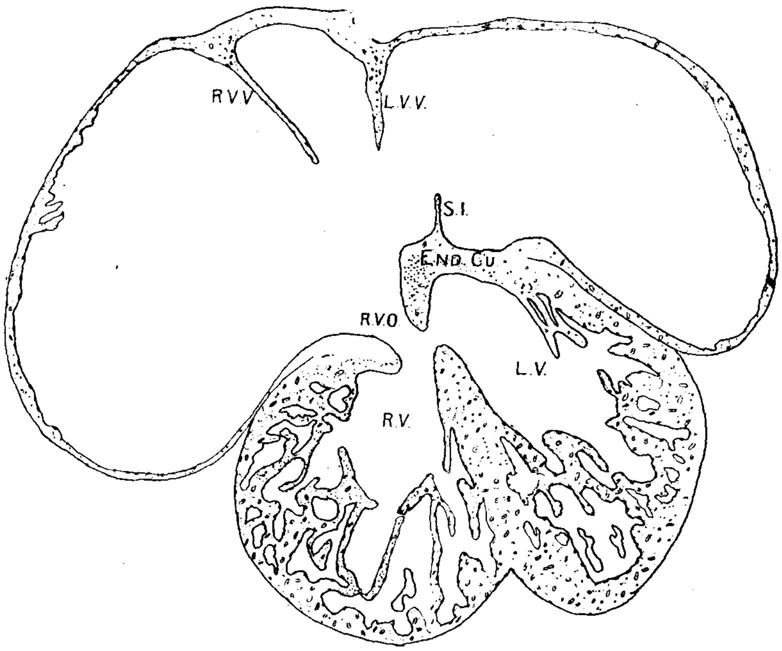
The transverse width of the muscular wall of the atrial canal is, in this specimen, 180 mm.

At the right venous ostium, the atrio-ventricular junction is infolded into the interior of the ventricle so as to form a large curved flap, undermined and concave on the ventricular aspect, extending from the caudal border of the ostium along its right side to its cephalic border and on to the interventricular septum. In the caudal portion this flap forms a cusp of some thickness and is attached to the interventricular septum (text-figs. 9 and 10).

More orally, its margin is free, and above it sweeps above the level of the interventricular foramen and is connected to the bulbar septum, as described later.

The muscle wall of the ventricle is trabecular, and many of the strands are undermined. The anterior papillary muscle is foreshadowed as a thick strand of muscle incompletely separated from the wall of the ventricle, united at one end to the ventricular surface of the cusp, and at the other attached to the lateral wall of the ventricle. Its base is connected to the septum by a short, stout band of muscle.

The "tricuspid" valve at this stage possesses but a single cusp, representing the anterior and posterior cusps of the adult heart. Its most oral part gives rise to the tendinous cord attaching the anterior cusp to the bulbar septum.

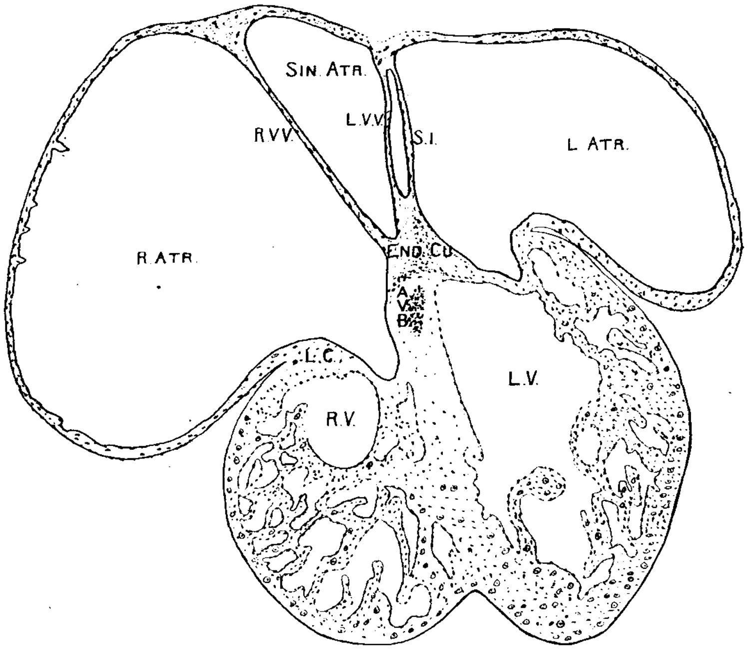


TEXT-FIG. 9.—Transverse section (slide 40, section 7) of heart of embryo S4.

On the left side the structures are simpler both in the valve cusps and the papillary muscles. Medial and lateral cusps are present—the medial a thick rounded projection from the central endocardial cushions attached to a prominent muscle bundle in the floor of the ventricle, and orally prolonged on to the lateral wall. The lateral cusp overhangs into the cavity from the atrio-ventricular junction, and it extends to both the anterior and posterior papillary muscles.

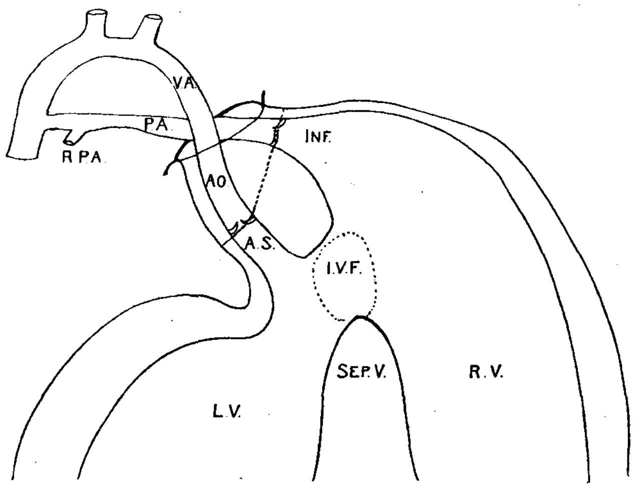
Right Ventricle.—The tubular portion lies even more horizontally than that in the former specimen, and it is flattened from side to side. The proximal end has widened out and extends towards the right ventricle. A short partial spiral groove, distinct on the right side, marks off a more dorsal and vertical portion from the ventral oblique portion.

The accompanying figure (text-fig. 11) shows the extent of the septum dividing the lumen into two portions, the position of the pulmonary and aortic valves, and the position of the interventricular foramen. The extent of the muscular coat is



TEXT-FIG. 10.—Transverse section (slide 41, section 14) of heart of embryo S4.

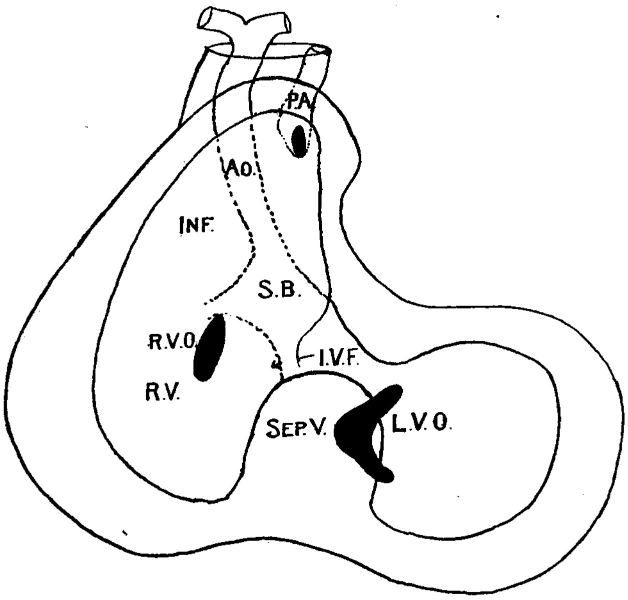
indicated, and the pulmonary and aortic valves are seen to lie at the distal extremity of the heart tube. These valves, and especially the pulmonary valve, are plump and well developed.



TEXT-FIG. 11.—Linear reconstruction (lateral) of portion of heart of embryo S4.

As has been stated, there is an interventricular foramen of some size. Its position and exact boundaries are of considerable interest. It lies close to the basal portion of the ventricles, and it is between the two venous ostia. It is bounded dorsally by the cushiŏn tissue between the ostia, and ventrally by the concave free margin of the interventricular septum (text-figs. 11 and 12).

The boundaries are rendered more complex by the approximation and extensions of the bulbar septum. The proximal edge of this septum is concave, and the ventral right end is continued on to the ventral and upper part of the interventricular septum; while the other end, dorsal and to the right, joins with the tissue between the venous ostia and is continued on to the interventricular septum. From its right margin a prolongation of this septum of the bulb extends towards the right side above the right venous ostium, and joins the flap which sweeps on to the interventricular septum. The interventricular opening is, in this specimen, unobscured by valve cusps on the septal wall, and its boundaries are shown with remarkable clearness in the model.



TEXT-FIG. 12.—Linear reconstruction of heart of embryo S4.

Tubular Portion.—There is a complete separation of the aorta from the infundibulum of the right ventricle.

There is a considerable change, however, in the general position and diameter of the infundibulum of the right ventricle from the condition found in the earlier stages. Comparison of the linear reconstructions of these specimens shows the changes.

The lumen within the tubular portion of the bulbus cordis has expanded and now forms a chamber continuous with the cavity of the lower part of the right ventricle.

EMBRYO (16 MM. IN LENGTH), PROF. PETER THOMPSON'S SPECIMEN.
Plate-figs. 11 and 12.

In this specimen, and in all the later ones, a definite advance in the development of the heart is marked by the closure of the interventricular orifice. It was pointed out that in the earlier specimens the sole outlet for the blood from the left ventricle was the interventricular foramen. With the closure of that foramen the left ventricle is brought into direct continuity with the aortic channel in the cylindrical portion of the right ventricle.

External Form (model at 50 diameters magnification).—The heart is relatively small in comparison with that of the 12·5 mm. specimen, and measures only 110 mm. vertically, 95 mm. transversely, and 130 mm. dorso-ventrally in the model. The atria are small and in systole. The left ventricle exceeds in vertical depth the right ventricle. The external form of the ventricular portion is similar to that part of S4, and there are similarly distinct interventricular furrow and notch.

Interior of the Heart.—Sinus Venosus and Atrium.—The sinus is now largely merged into the atrium. The vena cava superior has a long oblique course through the dorsal wall. The orifice of the vena cava inferior is directly caudal to it.

The right venous valve shows an arrangement similar to that in S4, and forms a long vertical and almost complete partition extending across the atrium from the right of the venæ cavæ to the left side of the right venous ostium.

The inferior attachments of the right and left venous valves are completely separated from one another (Plate-fig. 12).

Sinu-atrial Chamber.—This chamber is distinct, but is modified in its shape from that of S4, partly by the condition of systole. Into it there open the vena cava superior dorsally and the vena cava inferior and coronary sinus caudally, well separated from one another. The lateral boundaries are the venous valves. The left venous valve forms a ring-like fold, attached around its circumference to the wall of the atrium. The caudal attachment is blended with the septum primum, and orally the attachment of these two folds to the wall forms a stout mass.

For the rest, the septum primum also forms a ring-like projection into the atrium, with a large central orifice, the foramen ovale secundum, towards which the lower part of the septum is inclined. The interval between this deflected portion and the left venous valve constitutes the remains of the intersepto-valvular space.

Ventricles.—The ventricles were apparently fixed in systole, and their cavities are extremely small, hence the specimen is not a favourable one for determining the arrangement of the atrio-ventricular valves.

The position of the interventricular orifice is found to be occupied by a fibrous septum continuous orally with the septum separating the aorta from the right ventricle.

The wall of the right ventricle is not so thick as that of the left ventricle.

Within the upper part of the muscular interventricular septum there is a rounded mass of deeply-staining nuclei embedded in loose connective tissue which is a definite rudiment of the atrio-ventricular bundle, but its connection with other portions could not be traced.

The heart in the following embryo (S3), of approximately a similar stage of development, affords a clearer picture of the condition of the chambers at this stage.

Heart of 20-mm. Embryo (S3).

Model of the Heart magnified 50 *diameters* (Plate-fig. 13).

Dimensions.—1.	Vertical (of ventricles)		150 mm.
2.	Transverse width	right ventricle	50 ,,
		left ,,	60 ,,
3.	Dorso-ventral, whole heart		165 ,,

The heart was modelled within the pericardium and the body wall, and the external appearances reproduce accurately the shape of the heart within the embryo.

In external form the heart resembles the former specimen, but is somewhat flattened in an oblique direction. The impression on the under aspect of the right ventricle is caused by the projection of the right lobe of the liver against the floor of the pericardium.

The heart appears to have been fixed in systole, and the cavities are small, particularly those of the ventricles.

The atria form vertically elongated narrow channels enclosing the dorsal half of the upper portion of the heart.

The right and left ventricles are separated by an oblique furrow, and the upper part of the right ventricle forms a bulging prominence whose upper margin lies horizontally.

The aorta occupies very much the same position as in the adult heart.

Interior of the Heart (Plate-fig. 13).—The incorporation of the sinus and atrium is far advanced, and the venous valves and the septum primum are so prominent that in cross-section the three-chambered appearance of the atrium is very striking. At each side lie the expanded lateral portions of the atria, and between them lies the sinu-atrial chamber.

The vena cava superior opens by an oblique channel through the dorsal wall, and then turns forwards; and the vena cava inferior and the coronary sinus open separately on the floor.

The right venous valve again forms a large vertical septum stretching dorso-ventrally across the right atrium, perforated only by a small orifice which allows blood to escape from the sinu-atrial chamber into the right atrium proper and so to the right ventricle. The condition of the left venous valve is not easily determined in this specimen, for only a small portion of it is at all distinct. It forms a small flap on the left side of the orifice of the vena cava superior. That orifice is a narrow one, and the small flap blends with the right venous valve both oral and caudal to the opening.

The septum primum is separate and distinct. Its lower part forms an S-shaped fold, the bay of the S leading to the foramen ovale II, and directing the blood stream from the vena cava inferior directly to it.

The septum is more complete than in the former specimen, and the orifice of the foramen ovale II is only a small hole in a nearly complete partition, and it lies close to the oral border.

The arrangement of these structures is further modified by the size and shape of the atria, which are of great vertical height.

The wide bay which existed in the earlier specimens in the roof of the atrium, and which indicated the line of the division, is now replaced by a deep, narrow cleft, at the bottom of which the septum primum is attached. The apparent infolding of the wall of the atrium constitutes an early stage of the formation of the septum secundum, but it is produced not by a downgrowth of a septum but by the upgrowth of the atria.

A large pulmonary vein opens immediately to the left of the septum primum; and further to the left side there is an elevation of the floor of the left atrium, apparently marking off the quadrilateral sinus of the left atrium from the appendix (auricle).

Atrio-ventricular Junction.—The atrio-ventricular junction shows now an almost complete separation of the muscle wall of the atrium from that of the ventricle. Connective tissue from the atrio-ventricular orifice passes deeply into the interior of the substance of the flaps forming the lateral boundaries of the atrio-ventricular orifices: so that the tissue on the atrial surface of the valve cusps is continuous with the atrial musculature, while that on the ventricular surface is continuous with the trabecular musculature of the ventricles.

Rudimentary or embryonic muscle tissue is recognisable on the atrial surface of these valve cusps. The rudimentary medial or septal cusp of the tricuspid valve is present as a rounded projection on the right surface of the interventricular septum, consisting mostly of endocardial cushion tissue.

The interventricular septum is now complete, but where it joins the region of the endocardial cushions its texture is very loose, while in the centre of this loose tissue is a very distinct rounded rudiment of the atrio-ventricular bundle.

The medial (anterior or aortic) cusp of the mitral valve (not shown in the figure) is very distinct and projects from the left side of the atrio-ventricular septum, with which its ventricular surface is continuous; but this flap throughout is less muscular in texture than the opposite cusp.

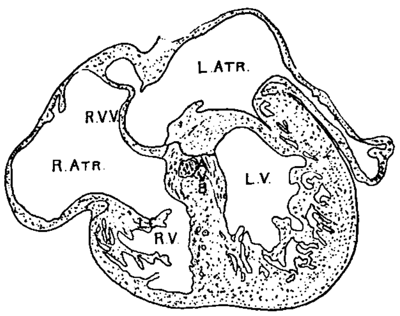
The pulmonary artery and the aorta are completely separated from each other, and the semilunar valves of each of them are well formed. The semilunar valves of the aorta lie immediately above the level of the interventricular septum; while the pulmonary valves, on the other hand, lie 50 mm. orally at the termination of the tubular part of the bulbus cordis.

The condition of the whole of the right ventricle is very similar to the condition found in S4. There is, for example, the same narrowing of the lumen of the most distal portion near the root of the semilunar valves; proximal to this a more dilated but still tubular part; and, finally, the lower part of the cavity of the ventricle with the valve cusps, papillary muscles, and trabeculæ of the ventricular cavity proper.

Heart of 22-mm. Embryo (B3).

Both ventricles present a rounded outline; the wall of the left ventricle is almost twice as thick as that of the right; both show extensive trabeculæ; the cusps of the aortic valve are well formed and plump; and the interventricular septum is completely formed, though extremely thin in the membranous part.

The right atrio-ventricular orifice, widely open, possesses right and left cusps, both of which, especially the right, are undermined by trabecular musculature, and their apices are continued by stout muscle bundles to the ventricular wall. A wedge or cone of rudimentary connective tissue penetrates for a short distance into this



Text-fig. 13.—Transverse section (slide 26, section 23) of heart of embryo B3. ×20.

marginal cusp, and on the atrial surface of the cusp an oval area of cushion tissue is present. The septal cusp shows a condition similar to those seen in S3.

Left Atrio-ventricular Orifice.—Shows very clearly the origin of the anterior cusp of the mitral valve from the endocardial cushion tissue of the atrio-ventricular junction, and as yet shows no muscular tissue in its substance; while the posterior or marginal cusp is distinctly muscular in structure.

Atrio-ventricular Bundle.—Rudiments of this are very clearly seen within the loose endocardial tissue of the atrio-ventricular junction (text-fig. 13).

The condition of the atria is, on the whole, similar to that shown in S3.

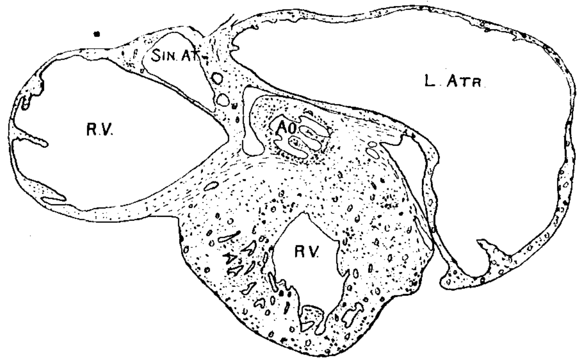
30-mm. Embryo, Prof. Bryce's Specimens. Plate-figs. 14 and 15.

The anterior view of the model of this heart, reconstructed 50 diameters, is shown in Plate-fig. 14.

External Form.—The external form of the heart shows it to have advanced considerably towards the adult form, and the internal structure of the ventricle is practically the same as is found in the adult, the right and left ventricles being completely separated. The atria, however, communicate freely with one another.

The right ventricle considerably exceeds in the anterior view the left ventricle, and its upper part, widely dilated, leads to the pulmonary stem, which lies horizontally.

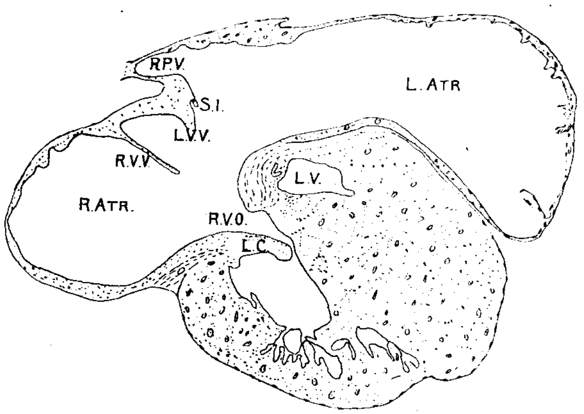
The atria are of relatively enormous size, enclosing the ventricular portion on each side, are of irregular outline, and are apparently in diastole; while the small size of the cavity of the ventricles and their thick walls point to the condition of systole



TEXT-FIG. 14.—Transverse section (slide B13) of heart of 30-mm. embryo (BRYCE).

of the ventricles. The wall of the left ventricle is very considerably thicker than that of the right ventricle.

Internal Structure.—The Interior of the Right Atrium.—The auricular portion of this cavity—large, wide, and with trabeculæ of muscle tissue upon its wall—forms by



TEXT-FIG. 15.—Transverse section (slide B17) of same heart as fig. 14.

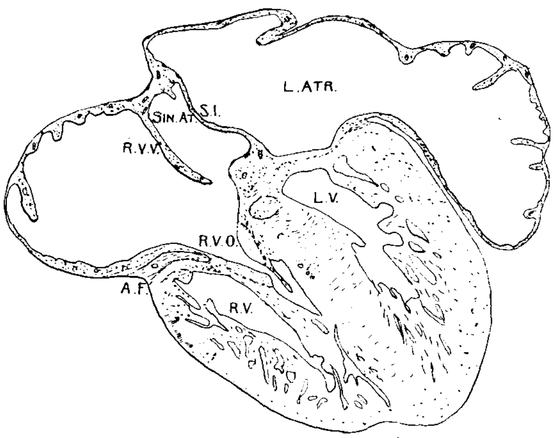
far the greater part of this cavity. The right venous valve forms a large, almost vertical partition, stretching from the dorsal wall along the floor to the anterior wall and shutting off a small cavity on its left side from the large cavity on the right; there being only a small, rounded orifice between the anterior concave margin of the central part of this valve on the one hand, and the anterior wall of the atrium on the other hand (text-figs. 14, 15, and 16).

The anterior attachment of the base of the right venous valve is split into two thin laminæ for a distance of 25 mm., and between these two limbs is the rounded orifice of the coronary sinus.

To the left of the right venous valve the vena cava inferior opens into the floor of the atrium, while the opening of the vena cava superior is directed vertically downwards and about 75 mm. orally. The arrangement of the left venous valve and of the septum primum shows considerable modification towards the adult form.

The left venous valve forms a small sickle-shaped ridge, 30 mm. in maximum height, projecting from the atrial wall especially dorsally and orally. It extends forwards on the roof of the atrium, and its anterior end merges into the right venous valve.

The intersepto-valvular space has very largely disappeared, and the left surface



TEXT-FIG. 16.—Transverse section (slide B17) of the same heart as figs. 14 and 15.

of the left venous valve is in contact partly with the right surface of the septum primum. The arrangement of these parts is shown in Plate-fig. 15.

Two pulmonary veins, a right and a left, separated by a considerable interval, open into the left atrium. On the left side of the left vein is an enormous dilatation forming the cavity of the auricular portion. The ventricular orifice from the left atrium lies ventrally to the openings of the pulmonary veins. The opening into the right ventricle lies to the right of the right venous valve (text-fig. 16).

Right Ventricle.—The cavity of the right ventricle is narrow but much elongated, and rudimentary valves are present around the right atrio-ventricular orifice in the form of a large muscular flap passing from the right margin of the atrio-ventricular junction towards the interventricular septum, while on the opposite side of the orifice there is a similar thinner cusp resting on the interventricular septum. The minute structure of the right cusp shows that it consists near its base of (1) a layer of muscle tissue continuous with the muscle tissue of the ventricle; (2) a layer of embryonic connective tissue passing in a wedge-shaped manner from the atrio-ventricular ring into the interior of the cusp; (3) a layer of rudimentary muscle tissue continuous with the atrial wall.

The first and third layers merge into one another, and beyond that level the valve cusp consists of a single rather thick layer of muscle tissue, and it is covered on its atrial surface by an oval mass of endocardial cushion tissue.

There are no chordæ tendineæ, but the muscle tissue of the flap is attached by a number of muscle strands to the trabecular tissue of the ventricle. The septal cusp shows a somewhat similar arrangement, its ventricular surface being formed of muscle tissue covered by a large mass of endocardial cushion tissue, but the auricular wall does not form any part of the substance of this valve cusp.

The cavity of the right ventricle is continued upwards in a spiral fashion to become continuous with the pulmonary artery; the trabecular arrangement of fibres being distinct on the ventral wall, while the dorsal wall is largely composed, not of muscle tissue, but of fibrous tissue derived from the septum separating it from the aortic stem. The muscle wall is continued to the base of the semilunar cusps of the pulmonary valve and ceases abruptly, the wall of the pulmonary artery and of the ascending aorta consisting quite definitely of fibrous tissue only. Proximal to the semilunar cusps for a distance of less than an inch there is the same narrowing of the lumen noticed in earlier specimens; the stem of the pulmonary artery to its bifurcation now measures 45 to 50 mm. The wall of this part is undulating, showing two constrictions, as was seen in earlier specimens.

The cavity of the left ventricle is very small; medial and lateral cusps can be recognised at the atrio-ventricular orifice, and the aorta takes origin from a definite infundibulum corresponding in extent to the pars membranacea septi (text-figs. 15 and 16).

The aortic valves lie again immediately above the upper margin of the membranous part.

The wall of the right ventricle is in the model 30 mm. in thickness, while that of the left is 45 mm.

Embryo 28·6 mm. in Length (E1). (Text-figs. 17 and 18.)

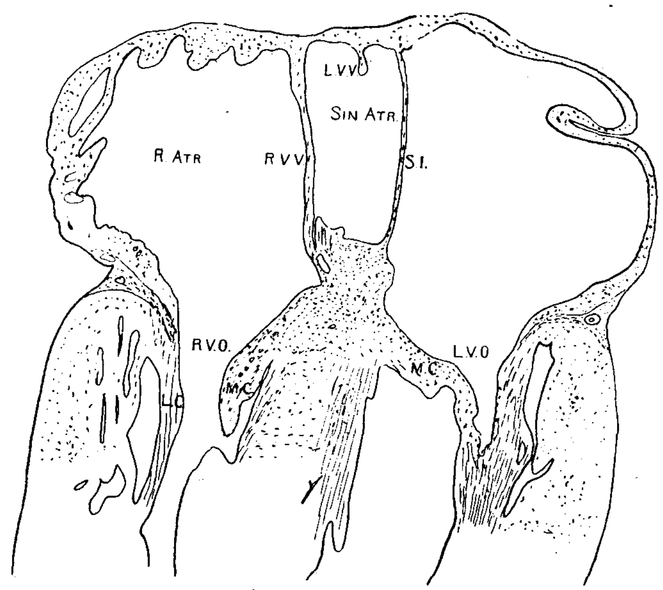
The sections and the model of this singularly perfect specimen constitute a good picture of the heart at the close of the period of development specially studied, a stage when all the principal developmental changes of intrauterine life have been completed.

In general shape the heart externally resembles that in the 30-mm. embryo.

Internal Structure.—The atrial portion is partly divided into three portions—a central and two lateral, of which the central smaller chamber communicates with those on either side, while they in turn open into the corresponding ventricles.

The right venous valve, as in the former specimen, forms a large vertical septum. In structure, especially at its basal attached margin, it differs from the atrial wall—the tissue is not striated, the cells are larger, and vacuoles are present. Along its left margin is a continuous line of large, very darkly staining cells similar to those seen in the endocardial lining of some portions of the ventricles, and which probably afterwards form Purkinje cells.

The ventral attachments of both the right and left venous valves run into a mass of indefinite cushion tissue at the central portion of the atrio-ventricular junction, and especially into a mass of deeply-staining cells lying immediately to the left of the orifice of the coronary sinus, in the position of the atrio-ventricular node of the adult heart. This mass in turn is connected with a mass of similar cells lying in the interior of loose vacuolated tissue in the apex of the interventricular septum, similar to the structure seen in earlier specimens already described. This structure is



TEXT-FIG. 17.—Transverse section (slide 64, section 9) of heart of 28·5-mm. embryo.

identical with that described by MALL as the rudiment of the atrio-ventricular bundle in the embryonic heart.

The structure described above constitutes a continuous medium of communication between the nodal tissue, or rather pre-nodal tissue, which from an early stage is recognisable at the base of the right venous valve, and the definite atrio-ventricular node lying near the coronary sinus.

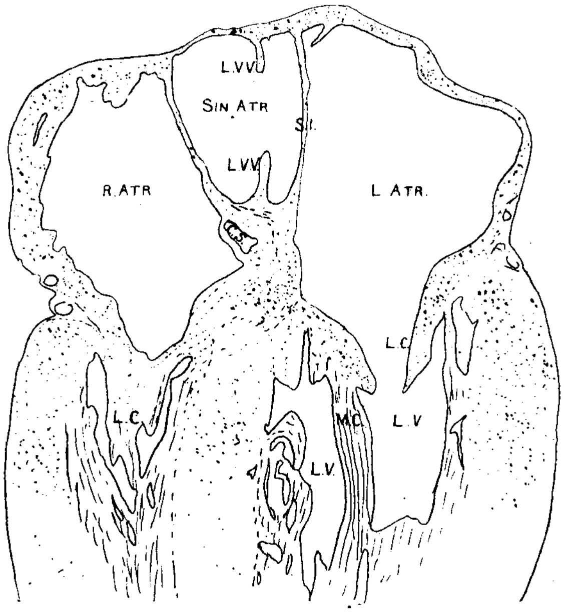
The lower part of the septum primum forms a partition of considerable height, and it forms the lower left boundary of the sinu-atrial chamber. Its lower attachment is separate and distinct from that of the left venous valve, but the two structures gradually approach one another orally.

The foramen ovale secundum is placed so far ventrally that its ventral boundary is the level of the wall of the atrium. Dorsally, however, the foramen does not extend to the dorsal wall of the atrium, but here the remains of the septum primum form a slight ridge, which merges into the left venous valve.

The dorsal attachments of the left venous valve and of the septum primum are fused, and at their origin from the wall of the atrium there is an infolding of the atrial wall, consisting of two layers of muscle tissue in apposition, separated only by a small amount of connective tissue. This slight invagination is the rudiment of the septum secundum.

The embryo was specially examined to determine the presence of any conducting tissue between atrial and ventricular muscle in other regions.

At the circumference of the atrial canal, at the junction of atrium and ventricle, an apparent infolding of the wall takes place, involving both the atrium and the ventricle; and as a result a wedge-shaped mass of connective tissue is formed, its base



TEXT-FIG. 18.—Transverse section (slide 65, section 9) of heart of same embryo as fig. 17. × 25.

at the free surface and its apex passing into the interior of the lateral valve flaps of the venous ostia.

These lateral valve cusps are formed of embryonic heart muscle, and there is also present in each of them a mass of cushion tissue lying on the atrial surface of the cusps.

This infolding was traceable around the lateral margins of the atrial canal; and as the muscle tissue present in the cusps is later transformed into connective tissue, there cannot be any continuity between the atrial and ventricular muscle at these levels. Orally and caudally there is not the same infolding, but in these regions also there appeared to be a complete break between the muscle wall of the atria and that of the ventricle and bulbus.

The Atrio-ventricular Valves.—The valve apparatus of the right and left sides forms a clear illustration of the formation of these structures.

On the right side there is a single large lateral cusp attached to the septal wall and to the anterior and posterior walls of the ventricle. This cusp contains a portion of bulbar cushion B, and also the extension to the right of the septum of the bulb, and this cusp forms an investment for the right and for the oral margin of the right ostium.

On the opposite side—namely, on the septal aspect—there is as yet no cusp, but a large oval prominence is present on the septal wall, which probably becomes undermined later and forms the medial cusp. The moderator band of the adult heart is formed from a portion of the septal wall on which lay bulbar cushion A, which is gradually undermined.

At the left ostium two cusps are present, forming practically the adult arrangement—the medial cusp derived from the endocardial cushions of the atrial canal, and the lateral from the infolding of the atrio-ventricular junction.

These cusps are large, and there is already fully developed the apparatus connected with them of papillary muscles.

The medial cusp extends from the oral to the caudal margin of the orifice, and its apex is widely separated from the septum.

Comparison of this specimen with S4 shows the changes which have occurred in the structures found in the earlier specimen. As in the former, the right venous ostium has a valve of one cusp, viz. a large right or lateral cusp, representing the two cusps, lateral and anterior, of the adult heart. The most oral attachment of this cusp is effected by muscular cords which pass to the infundibulum of the pulmonary artery, and are attached to the region of the former septum of the bulb.

There is no proper septal cusp, but its position is indicated by prominent rounded elevation.

On the left side the cusps of the mitral valve are attached, the medial cusp to a large anterior papillary muscle, to which the marginal cusp also is attached, and also to a small anterior papillary muscle.

The interventricular foramen is barely closed.

There is a large "vestibule" in the left ventricle, below the root of the aorta.

Discussion.

The series of specimens is sufficiently comprehensive to afford an almost complete account of the successive stages in the development of the heart from the stage at which the heart tube is formed.

The transition from the 3-mm. to the 6-mm. stage is perhaps rather less completely illustrated than the others, but the gap is adequately filled by specimens described in the literature of the subject, among which I would refer particularly to the 4·5-mm. embryo described by Ingalls, as well as by specimens figured by Tandler from the Vienna collection.

The developmental changes which occur in the heart subsequent to the earliest stage described here may conveniently be discussed in the following groups :—

1. Changes in the external form of the heart.
2. Changes affecting the sinu-atrial junction.
3. The division of the atrium.
4. The atrial canal and the bulbus cordis.
5. Changes in the primitive bulbus cordis.
6. The atrio-ventricular junction, the formation of the atrio-ventricular valves and of the conducting mechanism.

1. *Developmental Changes in the External Form of the Heart.*

The changes in the external form of the heart indicate successive changes in the size and position of the various segments of the primitive heart tube.

Atrium.—The atrium is from the first placed dorsally, and extends across the whole transverse width of the heart. Its cephalic surface is rounded and only slightly indented centrally by the truncus arteriosus. The atrium is everywhere separated by a deep groove from the ventricle and from the bulbus cordis. Throughout it retains this dorsal position. Wing-like expansions grow out on either side, curving round and partly enclosing the bulbus and, later, the pulmonary artery and the aorta.

After the formation of the septum primum, the atria increase greatly in their relative vertical depth, but the region of the attachment of the primitive septum grows less rapidly, and hence an infolding of the wall is produced in that region.

Ventricle.—The ventricular portion of the heart consists at first of a V-shaped loop, with right and left limbs, separated from one another, except at the apex, by an oblique groove, the bulbo-ventricular groove.' These limbs at a still earlier stage lie—the one cephalic, the other caudal—in position, and the intervening groove is horizontal; but a gradual rotation occurs, so that the groove becomes oblique and eventually vertical in position. The bulbo-ventricular groove extends nearly to the opposite margin of the heart, and its termination lies opposite to a slight notch upon that border.

The left limb of the ventricle is at first triangular in outline, but later becomes more spherical in shape and forms the left ventricle. The right portion becomes flask-shaped, the caudal portion being spherical and the oral tubular in form.

The right and left ventricles are from the first clearly demarcated from one another by the groove upon the ventral surface and by the notch upon the caudal margin of the connecting piece. The notch may persist and be present even in the adult heart.

The right ventricle, at first placed with its long axis vertical, becomes slightly oblique from right to left orally, and the distal portion slopes more and more obliquely in the dorsal direction. The deep cleft between the oral portion of the two ventricles becomes shallower, especially dorsally, and the dorsal half of the tubular portion of the right ventricle becomes directly continuous with the left ventricle.

The ventral surface of the right ventricle shows a groove at the junction of the two parts forming it, but this groove gradually becomes shallower and disappears by the 12·5-mm. stage.

The proximal portion of the right ventricle retains a triangular form; the distal tubular portion becomes more and more oblique. The groove on the surface of the conus arteriosus which marks the septum dividing that vessel into the pulmonary artery and the aorta, becomes deeper and is prolonged spirally on to the bulbus cordis, marking off a dorsal from a ventral portion. The dorsal portion becomes reduced in length, and its root passes to the left side and joins the base of the left ventricle. The ventral portion, at first tubular, dilates to a marked extent and forms the infundibulum of the adult right ventricle.

Dorsally the sinus venosus and the atrium become largely incorporate at the 9-mm. stage. The transverse portion of the sinus venosus become applied to the dorsal surface of the heart and lies obliquely on the dorsal surface of the atrium.

The dorsal wall of the atrium expands with the formation of the pulmonary veins, and the sinus venosus (transverse portion) is displaced and comes to lie in the atrio-ventricular groove, or circular sulcus of the adult heart.

The adult arrangement of four pulmonary veins has been reached in the 28·6-mm. embryo.

2. *Developmental Changes affecting the Junction of the Sinus Venosus and Atrium.*

The portion of the sinus venosus which participates in these changes is the right horn, and to a lesser degree the transverse portion.

The changes which occur in this part of the heart are known to consist largely in the incorporation of the right horn into the atrium, so that these two portions come to form in the adult a single chamber in which only slight demarcation can be determined of the sinus portion from the atrium proper.

Stated briefly, the changes involved in this incorporation are as follows:—

At the junction of the sinus and atrium there is externally a slight groove, a narrow smaller chamber joining on to one of larger size. The groove becomes invaginated at each side, producing in the interior two loose flaps of tissue—the right and left venous valves, the right one being formed before the left. Whether these valves are formed merely by a passive invagination or by active ingrowth cannot be determined. In histological structure, however, the right venous valve, and to a less degree the left one, differ from the wall of the sinus or atrium; the cells are larger and less fibrillated, and numerous vacuoles are present.

The sinus opening into the atrium resembles the "valvula coli" of human anatomy in being merely a slit on the summit of a prominent ridge, and the ridge is prolonged on the wall of the atrium, especially orally, forming the septum spurium, better termed the "tensor valvulæ."

The right venous valve grows rapidly forwards, and the slit-like sinu-atrial orifice enlarges orally and caudally, reaching to the floor of the atrium. The right valve extends forwards on the floor as far as to the atrio-ventricular cushions. It extends orally along the roof of the atrium and forms an almost complete partition, shutting off the portion of the atrium lying to its right side from the portion on the left. The prolongation of this venous valve extends to the left side of the atrio-ventricular orifice.

The wall of the atrium to the right of this partial septum is smooth internally, but at 12·5 mm. muscle bands are present, and these increase in number and in size and constitute the musculi pectinati of the atrium. Up to a late stage of development these bands do not spring from the venous valve, but arise some short distance from it. They run obliquely down to the region of the atrio-ventricular junction.

The further development of the portion of the atrium lying to the right of the right venous valve need not be more fully described. Its size varies in different specimens, depending largely upon whether the atrium is in systole or diastole at the time of fixation.

The views of the external surface of the various hearts show how, on both the right and left sides of the heart, the marginal portions of the atrium expand and form two wing-like processes lying on either side of the cylindrical bulbus cordis. In the adult heart they form the auricles or appendices of the atria.

The most important and most complex developmental changes occur in the portion of the atrium lying to the left side of the right venous valve.

The extension forwards of the right—and later of the left—venous valves into the cavity of the atrium and the septum primum atriorum mark off clearly a chamber to which it seems advisable to give a special name, since it can be recognised through all the later stages of development, and in the adult heart forms the "sinus venarum." To this chamber of the embryonic heart I propose to give the name of the sinu-atrial chamber. Its limits are: on the right, the right venous valve; on the left, the left venous valve and the septum primum; the roof formed by the wall of the atrium between the upper diverging limbs, and the floor formed by the area between the lower attachments of the venous valves. In the adult heart this chamber includes the whole of the posterior part of the right atrium from the vena cava superior to the vena cava inferior, its right margin formed by the crista terminalis, and its continuation the valve of the vena cava inferior, the left wall formed by the fossa ovalis and the limbus above it as far as to the roof of the atrium. The left wall is a composite wall, formed, as will be shown, by the septum primum in the floor of the fossa ovalis, by left venous valves merged into it, and by a partial fusion of the adjacent walls of the two atria. The lower attachment of the right venous valve to the floor of the atrium becomes modified after the 20-mm. stage.

At the stage of the 8-mm. embryo the vena cava inferior and the coronary sinus open into the sinus venosus dorsal to the atrium. The widening of the sinu-atrial orifice caudally allows the opening of both of these vessels to move forwards so that their orifices come to lie in the floor of the sinu-atrial chamber near the atrio-ventricular opening.

This attachment extends as far as to the atrio-ventricular junction, and thence on the ventral wall of the atrium, and divides into two limbs. This splitting is connected with a change in the position of the opening of the coronary sinus, which moves forwards in the floor of the sinu-atrial chamber and comes to open between the two limbs. Its orifice therefore is separated from that of the vena cava inferior by the left limb of the attached margin. This limb forms the valve of the coronary sinus, while the right limb forms the valve of the vena cava inferior.

The vena cava superior does not move forwards to the same extent, nor do the venous valves diverge so much from one another orally. For a time, at about the 20-mm. stage, the orifice of the vena cava superior appears to be guarded by a definite valve, formed by the right venous valve and a portion of the left venous valve. This condition is well illustrated in the figure of the 20-mm. embryo. The left venous valve later is displaced to the left, and the narrow orifice becomes a wide one.

There can be little doubt that the terminal parts of the venæ cavæ superior and inferior are formed from portions of the sinus venosus, for the orifices of these vessels widen out and merge very gradually into the atrium.

Left Venous Valve.—In the 6-mm. embryo the left venous valve forms a small flap united to the right valve at its upper and lower ends.

In the 8-mm. specimen the two valves are more widely separated. Subsequently their union caudally is divided and each valve is attached separately to the floor of the atrium.

The left venous valve is at first separated from the septum primum of the atrium by an interval which forms a small bay in the posterior part of the atrium, the inter-septo-valvular space. This interval gradually disappears, and the left venous valve and septum primum come into contact with one another. In the 12·5-mm. specimen these two folds are united caudally for a short distance and form a single vertical fold. Above the level of this union the left valve is continued along the roof of the atrium, and forms there a ridge which extends as far forwards as to the atrio-ventricular junction. In the 16-mm. embryo the left valve is attached caudally to the septum primum, but orally passes to the roof of the atrium and on to the ventral wall, forming a complete ring separating the sinu-atrial chamber from the inter-septo-valvular space. In the 20-mm. embryo a portion of the left venous valve forms a small flap limiting on the left the opening of the vena cava superior into the sinu-atrial chamber. Caudally it is fused with the base of the septum primum, which now forms the left margin of the orifice of the vena cava inferior (Plate-fig. 15).

In the embryo of 30-mm. length the left venous valve is merged at its root with the septum primum, but at a higher level it projects as a crescentic ridge along the roof of the atrium, and extends to the ventral wall.

3. *The Formation of the Atrial Septum.*

The specimens show the origin of the septum primum as usually described and the formation of the foramina ovalia primum and secundum.

The septum primum is fairly completely formed, even at the 6-mm. stage, and it forms an almost vertical septum, joining the dorsal and ventral walls of the atrium to one another near their middle. The septum appears to form orally and grows downwards to the floor of the atrium, and it unites with the dorsal portion of the floor of the atrium at an early stage. It is, however, for some time incomplete caudally and ventrally, where it fails to reach the floor of the atrium, leaving a channel between the two halves (foramen ovale primum). This orifice is shown in the 6- and 8-mm. embryos, but has closed at 12·5 mm. The lower margin of the foramen ovale primum is formed by the cushion tissue of the endocardial cushions of that atrial canal, and its closure is probably due largely to the increase in size of those structures and their extension dorsally.

I have, however, found a specimen of the heart of a fully-developed human embryo in which the foramen ovale primum had not become closed, but persisted with a foramen ovale secundum (Plate-fig. 16).

The foramen ovale secundum is formed, even at the 6-mm. stage, as an irregular orifice with ragged edges in the upper part of the septum primum. It gradually increases in size, and at 8 mm. it is large, and only a small portion of the septum primum is found inferiorly to it. It is, in many specimens, placed in the hollow of a bay in the septum by which the current from the vena cava inferior is conducted to the foramen.

In structure the septum primum seems for a long time to be fibrous instead of muscular.

It is convenient here to describe the exact conditions of the fold known as the septum secundum atrium.

RETZER states in regard to it that in the pig "the septum secundum in BORN'S sense does not exist. Search for it was made in vain in the embryonic hearts of man, monkey, and rabbit.

"The conus arteriosus is the fixed point physically, and the growing atria, in their efforts to expand and form auricles, grow around the fixed point and cause a bulging inwards of the wall. It is, therefore, a passive formation, and never attains such a size that one is justified in calling it a septum. The septum primum of BORN remains the ultimate septum."

In the same paper RETZER describes and figures the attachment to the floor of the atrium of the right venous valve as it occurs in my own specimens, and his figure I can corroborate.

The formation of the septum atriorum as illustrated in the models is as follows:—

The Oral Surface of the Roof of the Atrium.—In the 6-mm. embryo there is a central slight indentation of the roof of the atrium at the point where the septum primum and left venous valve are present. This surface indentation is more distinct in the 8-mm. embryo, in which there is a wide dorso-ventral groove of considerable depth, and on each side of it the roof of the atrium forms a large cupola.

In the later stages these lateral cupolæ increase greatly in size, and form narrow, long vertical chambers, quite separate from one another.

At a still later stage the two adjacent walls of the two dilated portions meet and become slightly attached to one another. Thus the appearance is produced of a narrow communication between the right and left atria situated caudally, bounded cephalad and dorsally by an area of atrial wall of considerable extent.

This area consists of a narrow margin—the edge of the "limbus fossæ ovalis," formed by the fused left venous valve and the remains of the upper portion of the septum primum, and of an area where the walls of the two atria are in coaptation.

In this region there is no true blending of the atrial walls, for even in the adult heart the walls of the right and left chambers can be separated from one another without the division of any muscle tissue as far as practically to the margin of the limbus fossæ ovalis.

To show this it is only necessary to incise the epicardium on the dorsal wall of the atria along a vertical line between the right pulmonary veins on the one hand, and a line joining the left borders of the venæ cavæ inferior and superior on the other. The walls of the right and left atria can then be separated from one another by merely dividing a little loose connective tissue, and the separation can be carried as far as practically to the margin of the limbus fossæ ovalis. The whole of the dorsal and oral portion of the so-called septum secundum atriorum is therefore merely the result of the coaptation of adjacent portions of the walls of the two atria, and is not a true septum comparable to the septum primum.

To this extent I can confirm the view expressed by Retzer, in so far as he states that the septum secundum is not a true septum comparable to the septum primum.

The sections of the more advanced embryonic hearts show the infolding of the wall quite clearly.

4. *The Atrial Canal and the Bulbus Cordis.*

Born has pointed out the importance of the change which occurs in the position of the opening of the atrial canal into the ventricle. At first that canal lies on the left side of the heart, but it gradually moves to the right, and at the same time the orifice elongates in the same direction and becomes a horizontal slit. This alteration in position is due probably as much to a growth change in the atrium and in the ventricle, extending them to the left side, as to an actual transition in the position of the canal; but there is also an actual extension of the orifice. At the same time the loose reticular tissue lying beneath the endocardium (seen in embryo 2W1) becomes arranged into two definite masses which form the upper and lower cushions of the atrial canal. The extension of the orifice to the right side passes beyond the bulbo-ventricular septum and beyond the limits of the original ventricle, so that the right portion of the opening leads from the atrium into the chamber termed the bulbus cordis. The endocardial cushions of the atrial canal also extend in the same direction, and their right margins come into contact with the bulbar cushion lying on the right and dorsal aspect of this portion of the bulbus.

This is a morphological fact of considerable importance, since it justifies the statement that the right atrium comes to open into the bulbus cordis. This fact is clearly shown in some of BORN'S figures, but its morphological significance has not been pointed out. The upper portion of the bulbo-ventricular furrow remains as an infolding of the wall, marking the separation between ventricle and bulbus cordis. The contact of the bulbar cushion with the cushions of the atrial canal is well seen in the 6-mm. as well as in the 8- and 9-mm. specimens.

It is convenient at this stage to turn to the bulbus cordis and to consider the part which it plays in the formation of the adult heart and its homologies.

Considerable uncertainty exists as to the exact relationship of the bulbus cordis and ventricular portions respectively of the early embryonic heart to the chambers and vessels of the adult heart.

Since the time of HIS it has been recognised that the ventricular portion of the early embryonic heart is in the form of a V, the two limbs being separated by a deep groove.

In an early specimen described by HIS, similar to the youngest specimen of my series, such an arrangement exists. HIS gave to the left or descending limb the name of "conus venosus," and to the right or ascending limb the name of "conus arteriosus." Such a terminology has obvious drawbacks, such as the fact that the name of conus arteriosus is used in adult human anatomy for a definite structure, not the same as the structure so named in the embryonic heart.

Considerable light is thrown upon the significance of these portions of the heart by the study of the hearts in embryo as well as in adult fishes and reptiles.

BOAS, working on the heart in the Anamnia, recognised "a clearly separated independent portion of the heart, which should be added as a third chamber to the auricle and ventricle," and termed it in Anamnia the conus arteriosus.

KOLLIKER and BORN termed a similar portion of the heart in embryo Amniota the bulbus aortæ, or bulbus arteriosus.

LANGER, working on embryo fishes and reptiles and later on birds and mammals, identified a chamber in the heart possessing similar characters, and gave to it the name of bulbus cordis, a term which has been generally recognised and adopted. Thus BORN at a later date substitutes the term bulbus cordis for the portion termed by HIS the conus arteriosus; and TANDLER, in describing the development of the human heart at an early stage, terms the descending limb of the V-shaped loop the ventricular limb and the ascending the bulbus limb.

The distinctive features of the bulbus cordis chamber in embryo hearts can be clearly laid down.

(1) Its wall is composed of a muscular tissue similar to that of the myocardium of the ventricle.

(2) It contains in its interior thickenings of subendocardial tissue, which form the "bulbar cushions."

(3) In position it lies between the ventricle and the truncus arteriosus.

GREIL has followed the changes which occur in the bulbus cordis in the developing heart of Lacerta, and in the crocodile; and he has shown that in Lacerta it forms in its caudal portion a definite chamber in the ventricular part of the heart, from which arise the pulmonary artery and the left systemic aorta.

It has also been recognised that in the mammalian heart, including man, the bulbus cordis forms at least a portion of the right ventricle (KEITH, etc.); and BORN derives from its upper part a portion at least of the pulmonary artery, as well as of the right ventricle.

By some writers it is assumed that the bulbo-ventricular is synonymous with the interventricular furrow of the heart.

Thus MALL (*Amer. Journ. of Anat.*, vol. xiii, p. 252), describing the heart of an embryo 3·5 mm. in length, states: "The lower connecting piece unites the left ventricle with the bulb, which later on gives rise to the right ventricle." And again, in reference to the heart of an embryo 4¼ mm. in length, he states: "The trabecular system has extended into the bulbus—that is, into the right ventricle."

In examining a series of embryos such as the present one, one is very much struck by the definite characters shown throughout all the early stages of development by the "bulbus cordis."

Its wall is composed of muscle tissue similar to that of the left ventricle, and this muscle tissue ceases abruptly at the line of junction of the bulbus with the truncus arteriosus. The interior shows at the earliest stages the loose subendocardial reticulum, which is later replaced by definite masses, the bulbar cushions, and it lies between the left ventricle and the truncus arteriosus.

The principal features to be discussed are: (1) alteration in the direction of the bulbo-ventricular groove; (2) the extent of the bulbar cushions; and (3) the relation of the bulbar cushions to the right ventricle and to the definite muscular interventricular septum.

Relation of the Conus Arteriosus to the Chambers in the Adult Heart.

From the condition shown in THOMPSON'S model (2), in which the bulbo-ventricular groove lies horizontally, through the specimen 2W1 and onwards to the stage of the 5·2-mm. embryo figured by TANDLER, the bulbo-ventricular groove is seen to rotate gradually from a horizontal to an oblique, and finally to an almost vertical position. In the last specimen mentioned the groove forms a practically vertical furrow on the ventral surface of the heart, extending from the left side of the base of the truncus arteriosus to the caudal margin of the ventricle, where a notch is found on this border of the heart. Such a notch is present at earlier stages also, and is present even in the model prepared by THOMPSON, though not shown in the figures.

BORN'S models of this region of the heart in the rabbit are not at all conclusive. In two hearts closely resembling one another, he shows in the younger a bulbo-ventricular cleft running obliquely on the heart wall; and in a slightly older specimen a similar furrow is present, from which a depression extends across to the right side, and the latter is taken to be the bulbo-ventricular furrow, while the former is termed the interventricular furrow.

He states repeatedly, however, that there was no clear indication of the division of the bulbus from the ventricle.

Of my own specimens, the heart of the embryo of 6-mm. length follows closely upon the TANDLER specimen from a 5·2-mm. embryo, so far as the external form is concerned. In it the figure shows a vertical furrow extending on the anterior surface of the heart to the caudal border. It corresponds internally to the interventricular septum, and the appearances suggest that it is no more than a deepened bulbo-ventricular furrow.

It must further be noted that in the lower part of the interventricular septum (septum ventriculorum inferius) there is to be found the termination of one of the proximal bulbar cushions. This fact seems to afford strong support for the view that this portion of the interventricular septum is derived from the bulbo-ventricular ridge; for were the interventricular septum formed to the left side of the bulbo-ventricular septum, and within the cavity of the primitive ventricle, it is difficult to see how the bulbar cushion could be prolonged on to it.

From the 6-mm. stage onwards through the 7- and 8-mm. and on to the 12-mm. specimens, the evidence from the study of the position of the bulbar cushions and the muscle wall goes to show that the bulbo-ventricular groove is the same as the interventricular groove of later stages.

The right atrio-ventricular orifice is enclosed on its right side by one of the bulbar cushions, and the septal wall of the ventricle supports the other proximal bulbar cushion.

It is true that neither of these cushions reaches to the very apex of the right ventricle, but that fact is not sufficient in itself to justify the division of the right ventricle into two parts of separate developmental origin. The appearances strongly suggest that the mammalian right ventricle is formed entirely from a primitive chamber homologous with the bulbus cordis of fishes and reptiles. If the mammalian right ventricle is derived solely from the bulbus cordis, and if the mammalian muscular interventricular septum be the bulbo-ventricular septum, then the muscular interventricular septum of the reptilian heart is not represented as such in the heart of mammals, and the anterior and posterior ventricles of the reptile are not homologous with the right and left ventricles of the human heart.

GREIL has pointed out also that in Varanidæ there is no question of the division of the ventricle into a right and a left ventricle, for both of the atrio-ventricular openings belong to the dorsal chamber (the ventricles being dorsal and ventral, and not left and right). It must, however, be pointed out that the anterior ventricle of the reptilian heart, consisting as it does of bulbar and ventricular portions, separated partially from one another by a muscular ridge, gives rise not only to the pulmonary artery but also to the left systemic aorta, and hence it is not entirely comparable with the right ventricle of the mammalian heart.

It can, moreover, be shown that in the development of the heart of man the bulbus is divisible into two portions—an upper cephalic and a lower caudal; and that these two parts give rise to different parts of the adult right ventricle—the upper to the infundibulum, and the lower to the expanded portion of the ventricle.

5. *Developmental Changes in the Bulbus Cordis.*

If we assume, on the grounds previously stated, that the chamber in embryo S1 which forms the right portion of the ventricle is the bulbus cordis, this specimen affords a convenient starting-point from which to trace the subsequent changes in this part of the heart tube.

In this specimen, as in other specimens of similar age described by other writers, that portion of the heart is flask-shaped, and is divisible into a caudal spherical and an oral cylindrical portion. In the latter the lumen is almost completely divided into two channels by the projection into the interior of the bulbar cushions, while in the former the bulbar cushions are widely separated from one another and diverge on opposite sides of the ventricular cavity.

Distal Portion.—Plate-fig. 4 shows a reconstruction of a portion of the distal part of the bulbus, with one of the two large cushions found in it. This cushion begins above at the separation of the root of the combined sixth aortic arches from the truncus arteriosus, and extends uninterruptedly downwards in a clockwise spiral. On the opposite wall, which has been removed, there was another cushion of similar extent.

The upper portion of these cushions corresponds precisely to the "distal bulbar swellings" 1 and 3 respectively figured by TANDLER in the heart of an embryo

6·5 mm. in length. In my specimen, however, there is no separation such as he describes between proximal and distal cushions. Between the cushions 1 and 3 of TANDLER there lie two additional cushions, namely, the distal bulbar cushions 2 and 4. Successive sections of the bulbus in my specimen show that these swellings are extremely small and indefinite, and, were it not for the fact that four such cushions are readily recognisable in the developing hearts of lower forms, it is extremely doubtful whether they would be described as occurring at all in the human heart.

In short, it is extremely doubtful whether there are distal bulbar cushions as distinct from the large proximal cushions in the human embryo at all.

The cushions described above pass as far distally as to the root of the aortico-pulmonic septum.

The figures from reconstructions of this portion of the heart in embryos from 6 to 12·5 mm. show the successive transitions which occur.

Thus in the 6-mm. embryo the distal portion of the bulbus cordis forms a cylindrical tube, lying within the pericardium and obliquely crossing the upper part of the atrium (Plate-fig. 2).

The muscle coat does not extend as far as to the pericardium, and beyond the muscle-coated part is the truncus arteriosus. At the junction of bulbus and truncus the right and left sixth arterial arches arise dorsally very close to one another.

Within the bulbus there are two distinct and large endocardial cushions, which almost meet with one another, so as to divide the lumen into two channels. These channels form the exit from the heart for the blood from both the left and the right ventricles, and at this stage the whole of the blood from the left ventricle must pass through the narrow interventricular foramen.

In the next specimen (B1) the portion of the bulbus is more oblique in position and lies more horizontally on the roof of the atrium, and its muscle coat ceases at a greater distance from the pericardial wall.

Within the terminal portion the lumen of the bulbus is divided into two channels—one, ventral and to the left, is continuous with the orifice of the fused sixth arterial arches; and the other, dorsal and to the right, is continued into the truncus arteriosus.

Proximal to this region, within the bulbus, are two large, plump spirally arranged cushions, one of which passes to the interventricular septum, and the other to the right margin of the atrio-ventricular opening.

In the succeeding specimen (M1) the condition is very similar, and does not require special description. The figure shows that the large cushions are continued along the walls of the two separated vessels in the terminal part of the bulbus, and, in addition, some small intermediate swellings of a similar character have appeared there (bulbar cushions 2 and 4) (Plate-fig. 8).

There is at this stage no definite formation of either aortic or pulmonary valves.

In the next specimen modelled (12·5 mm.) a considerable change has occurred.

The muscle coat of the bulbus can be traced quite definitely to a point where it abruptly becomes continuous with the fibrous coat of the truncus arteriosus, and at that level are found the commencing pulmonary and aortic valves.

The terminal part of the bulbus has now become more horizontal, and there is a marked inequality in the length of the ventral and dorsal walls: the ventral wall has increased in length, while the dorsal wall has remained stationary or has even shortened.

Hence the valves (pulmonary) of the more ventral vessel lie some distance above the heart, while the aortic valves are near to it.

Within the bulbus the division of the lumen into two vessels now extends along practically its whole length, and there are two distinct channels, both of which, however, communicate with the right ventricle below.

Perhaps the more striking change—it certainly directed my own attention specially to this region—is the dilatation of the channel leading to the pulmonary artery.

Up to the 12·5-mm. stage the lumen was narrow and inconspicuous. Now it is large and dilated, and the orifice into the pulmonary artery is placed upon the dorsal wall, not at the termination (text-figs. 11 and 12).

The ventral wall is lined with a reticulated formation of muscle continuous with that of the ventricle. Thus the "infundibulum" of the right ventral is formed.

The so-called congenital stenosis of the pulmonary artery is due to failure in the dilatation of this part of the right ventricle.

The development of this region of the heart may be summarised:—

1. The pulmonary artery of the adult is developed from a portion of the truncus arteriosus, the lumen of the truncus arteriosus being divided into:

(*a*) The pulmonary artery, from which arise the sixth pair of arches, very close together.

(*b*) The ascending aorta.

2. The pulmonary and the aortic valves are formed at the distal extremity of the bulbus cordis. The infundibulum of the right ventricle is formed from a portion of the bulbus cordis, and is at first merely a narrow channel, but becomes distended.

3. The increasing obliquity and the consequent relative elongation of the ventral wall causes the pulmonary valves to lie some distance above the right ventricle, while the aortic valves lie near the base of the left ventricle.

The septum of the bulbus is continued downwards in a spiral and oblique direction to join the upper margin of the septum of the ventricle, in such a way that the dorsally placed vessel (the aorta) is in continuity with the left ventricle, while the infundibulum communicates with the right ventricle only.

6. *The Atrio-ventricular Junction, the Formation of the Atrio-ventricular Valves and of the Conducting Mechanism.*

The atrial canal is at first a short channel lying on the left side of the heart, but it moves to the right and comes to lie centrally, and it is no longer visible from the surface but is concealed by the overlapping atria and ventricles.

The upper and lower cushions of the canal fuse with one another centrally, and the lateral margins of the channel remain as the venous ostia. All these changes are exactly as are shown in BORN'S models and figures.

The orifices are at first destitute of valves, but soon rudiments of valves appear on both sides, right and left; the first to appear being a large laterally placed cusp formed by the infolding of the atrio-ventricular junction into the interior, and by its undermining on the ventricular side.

This cusp represents, on the right side, the lateral and anterior cusps of the tricuspid valve, and on the left side the lateral cusp of the mitral valve.

This cusp formation, by infolding, has an important bearing upon the loss of continuity between the muscle walls of the atrium and the ventricles.

The structure of the infolded cusp is a centrally placed wedge-shaped mass of connective tissue derived from the external surface of the atrio-ventricular junction, with a layer of muscle tissue continuous with the atrial muscle coat on the atrial surface, and of ventricular muscle substance on the ventricular aspect. On the atrial surface there may, in addition, be small masses of cushion tissue.

At the margin of the cusp the two layers of muscle tissue are continuous with one another. As the tissue of the cusp becomes altered into fibrous tissue this continuity is destroyed.

The right lateral cusp is of large size, and it is attached to the ventricular wall by muscle bands of considerable size. Orally it gains an attachment to the infundibulum, close to the region of the septum which divided this channel from the aorta, and this attachment as a rule remains fibrous and can be readily identified in the adult heart.

At each orifice later a second cusp is formed, the medial cusp being in each case derived from the central mass of tissue representing the fused cushions of the atrial canal, and from the adjacent muscle tissue of the septum of the ventricles.

The endocardial cushions of the atrial canal form a central mass of considerable size, connected dorsally with the atrium, and especially with the atrial septum, and ventrally with the ventricle muscle tissue.

The cushion mass extends widely on either side, and on the right side a prolongation of the upper cushion extends above the right venous ostium and joins with the bulbar cushion B.

On the left side, the upper and lower cushions send prolongations to the ventricle muscle wall above and below the left venous ostium.

Development of Nodal Tissue and Connecting Tissue (Atrio-ventricular Bundle).

Nodal tissue possessing the adult characteristics cannot be definitely recognised in the developing heart at the stages described, probably because its histological features are not sufficiently differentiated.

The right venous valve from an early stage, however, shows histological characters which distinguish it from adjacent portions of the heart wall, such as a loose texture and vacuoles, and this may precede the formation of the sinu-atrial muscle of Keith and Hoch.

Neither does the atrio-ventricular bundle present in the young embryonic heart the features which allow it to be recognised in the adult.

The most that can be said, from the specimens examined, is that from an early stage a structure can be identified which has special histological characters, and which lies in the position afterwards occupied by a part of the atrio-ventricular bundle.

This structure is recognisable in the 16-mm. embryo, and is very distinct in the 20-mm. embryo as well as in later specimens.

It consists of a rounded mass of cells whose nuclei stain rather darkly and are more closely packed together, surrounded by a ring of very loose tissue.

This structure is most clearly seen in the upper part of the muscular interventricular septum, close to the apex, and it appears to run into and to be connected with the cushion tissue of the atrio-ventricular canal. The peripheral connections of this structure with the walls of the ventricles cannot be discovered, except that on the right side it appears to pass towards the origin of the "moderator band."

This band is in part covered by the continuation of the bulbar cushion to the ventricular septum, and it is interesting to find that the path in the adult heart of the principal limb of the atrio-ventricular bundle lies in tissue immediately underlying a layer derived from cushion tissue.

The histological characters of this mass have been fully described and figured by Mall, and his figures represent accurately the condition found in my specimens from 20 mm. onwards.

Towards the atria I have not been able to trace definitely any connections of this bundle, beyond the fact that it runs into or below the cushion tissue of the atrio-ventricular canal and joins with the right and left venous valves.

It may here be pointed out that the process of development of the heart as described here shows a short-circuiting of part of the blood stream. In the early stages the blood passes from atrium to ventricle, and thence to bulbus cordis.

The alteration in the position of the atrial canal allows part of the blood stream to pass from the right division of the atrium into the bulbus cordis and so to the truncus arteriosus, without passing through the primitive ventricle at all.

At the stage when the right and left ventricles become completely closed off from one another, this short-circuiting of part of the blood stream necessitates an alteration in the original peristaltic wave, so that the left and right ventricles may beat simultaneously, and it is when this separation has been affected that in my specimens there is the first indication of the presence of the atrio-ventricular bundle.

Towards the expenses of preparing the models a grant was received from the Royal Society of London, and the expenses connected with the illustrations have been largely defrayed by a grant from the Carnegie Trust for the Scottish Universities.

To these two bodies I wish to express my thanks for this assistance.

LITERATURE.

The literature of the development of the heart is an extensive one, and need not be referred to in detail here, as adequate summaries are found in the KEIBEL-MALL *Textbook of Embryology* and in TANDLER'S *Das Herz*, as well as in HOCHSTETTER'S comprehensive bibliography in HERTWIG'S *Handbuch der vergleichenden und experimentellen Entwickelungslehre.*

The works to which reference has been specially made, in addition to those above mentioned, are the following :—

(1) WATERSTON, *Journ. of Anat. and Phys.*, vol. xlix.
(2) THOMPSON, P., *Brit. Med. Journ.*, 1909.
(3) TANDLER, *Anatomie des Herzen*; and KEIBEL-MALL, *Manual of Human Embryology*, vol. ii.
(4) MALL, *Amer. Journ. of Anat.*, vol. xiii.
(5) KEITH, *Journ. of Anat. and Phys.*, vol. xli.

LIST OF PLATE ILLUSTRATIONS.

PLATE I.

Fig. 1. Ventral view of wax-plate model of heart of 3-mm. embryo (2W1).
Fig. 2. Ventral view of model of heart of 6-mm. embryo (S1).
Fig. 3. Interior of the above model.
Fig. 4. Dorsal wall of distal portion of the bulbus cordis in the same model.
Fig. 5. Ventral view of model of heart of 8-mm. embryo (B1).
Fig. 6. View from the right of the interior of the right atrium and ventricle of the same model.
Fig. 8. Interior of a model of the distal portion of the bulbus cordis of embryo M1 (9 mm.) to show the endocardial cushion B, the root of the pulmonary artery and of the aorta.
Fig. 9. Ventral aspect of model of the heart of 12·5-mm. embryo (S4).

PLATE II.

Fig. 7. Caudal half of the same model divided horizontally.
Fig. 10. View from the left of the same model after removal of the lateral wall of the left atrium.
Fig. 11. Ventral aspect of model of 16-mm. embryo.

Fig. 12. The same model from the right side after removal of the lateral wall of the right atrium and ventricle, and of the right venous valve.

Fig. 13. Caudal portion of model of heart of 20-mm. embryo, divided horizontally.

Fig. 14. Ventral aspect of model of 30-mm. embryo.

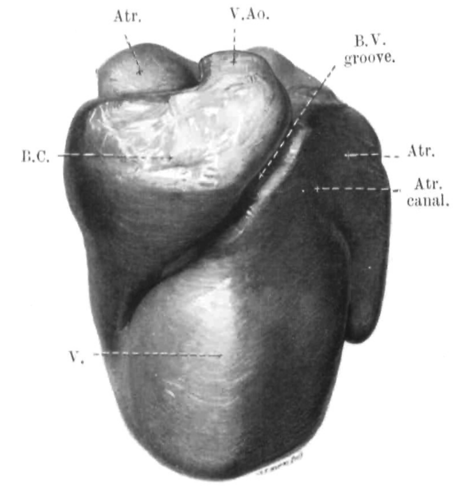
Fig. 15. Same model viewed from the right after removal of the lateral wall of the atrium and of the right venous valve.

Fig. 16. Interior of the left atrium of heart of a fully developed child, with foramen ovale I persisting in addition to foramen ovale II.

The lettering in the figures is as follows:—

A. = Bulbar cushion A.
Ao. = Aorta.
A.S. = Aortic sinus.
Atr. = Atrium.
A.-V.V. = Atrio-ventricular valve.
A.-V.B. = Atrio-ventricular bundle.
A.F. = Annulus fibrosus.
B.Cu. = Bulbar cushion.
B. = Bulbar cushion B.
B.C. = Bulbus cordis.
B.V. = Bulbo-ventricular.
C.S. = Coronary sinus.
E.T. = Endothelial tube.
End. Cu. = Endocardial cushions of the atrial canal.
F.O. I and F.O. II = Foramen ovale primum and secundum.
Inf. = Infundibulum of right ventricle.
I.V.C. = Inferior vena cava.
I.-V.S. = Intersepto-valvular space.
I.V.F. = Interventricular foramen.
L.A. = Left atrium.
R.A. = Right atrium.
L.C. = Lateral cusp of atrio-ventricular valve.
M.C. = Medial cusp of atrio-ventricular valve.
L.V. = Left ventricle.
L.A.-V.O. R.A.-V.O. = Left and right atrio-ventricular openings.
L.V.O. = Left venous ostium.
R.V.O. = Right venous ostium.
L.V.V. and R.V.V. = Left and right venous valves.
O. = Opening of sinu-atrial chamber into the right atrium.
P.A. = Pulmonary artery.
P.V. = Pulmonary vein.
R.V. = Right ventricle.
R.P.V. = Right pulmonary vein.
S. I = Septum primum atriorum.
S.-A.O. = Sinu-atrial orifice.
S.B. = Septum of the bulbus cordis.
S.V. = Sinus venosus.
S.V.C. = Superior vena cava.
Sin. At. = Sinu-atrial chamber.
T.A. = Truncus arteriosus.
T.V. = Tensor valvulæ.
V.Ao. = Ventral aorta.
V.C.S. = Vena cava superior.

Professor D. Waterston on "The Development of the Heart in Man."—Plate I.



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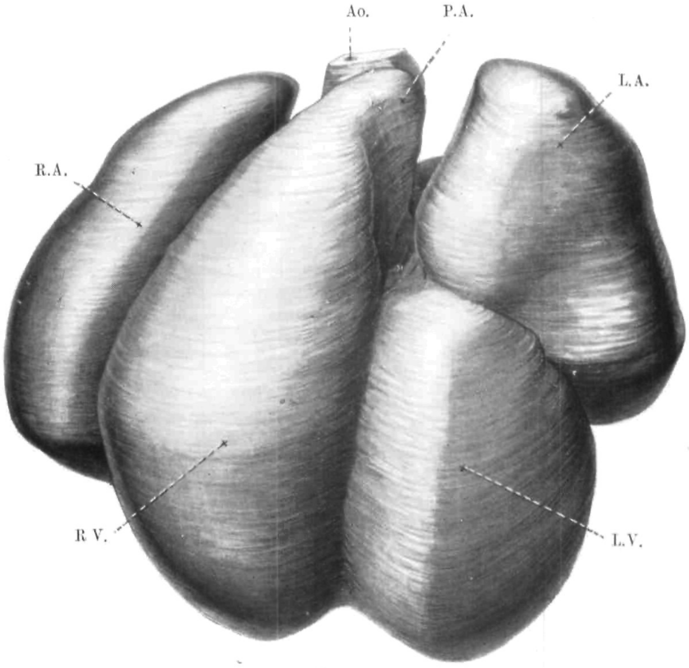

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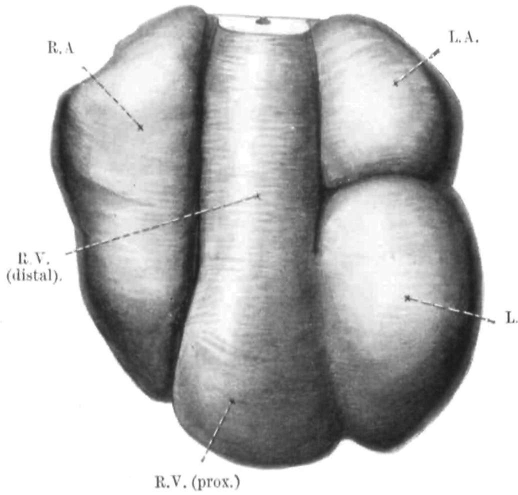

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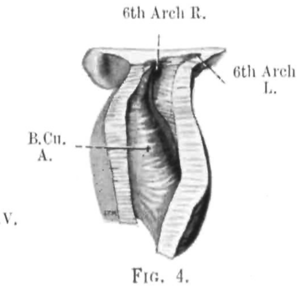

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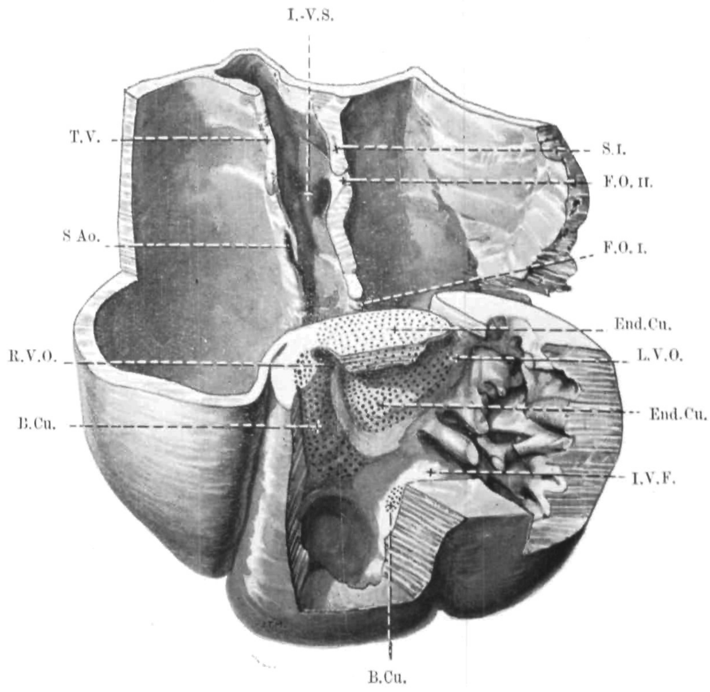

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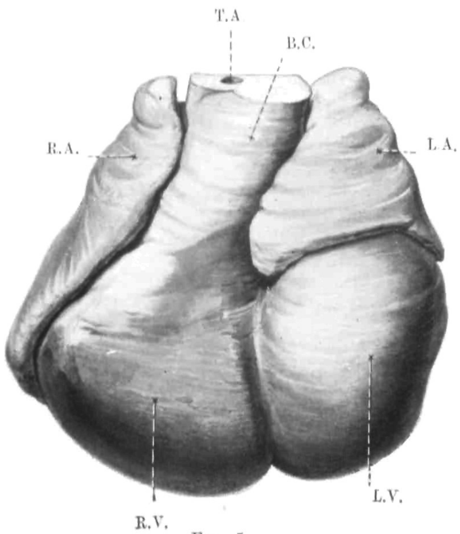

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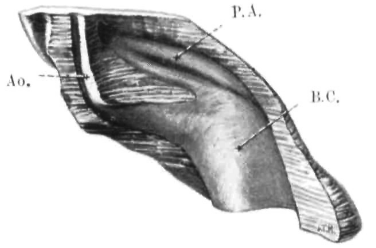

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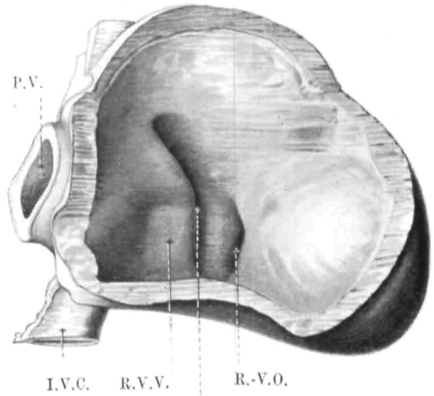
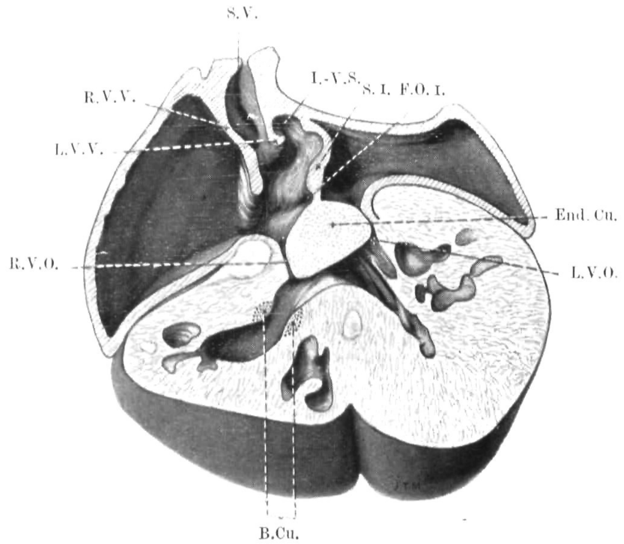


Fig. 6.

Professor D. Waterston on "The Development of the Heart in Man."—Plate II.



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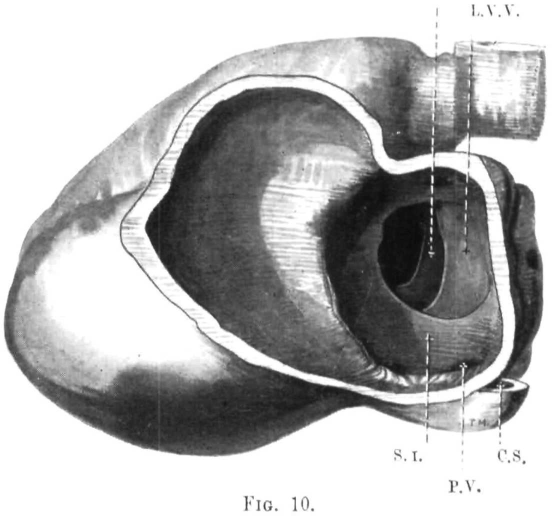

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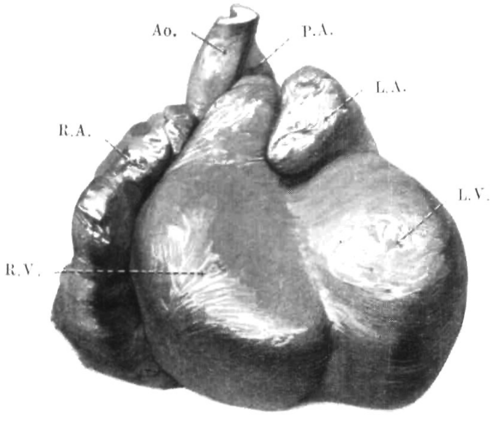

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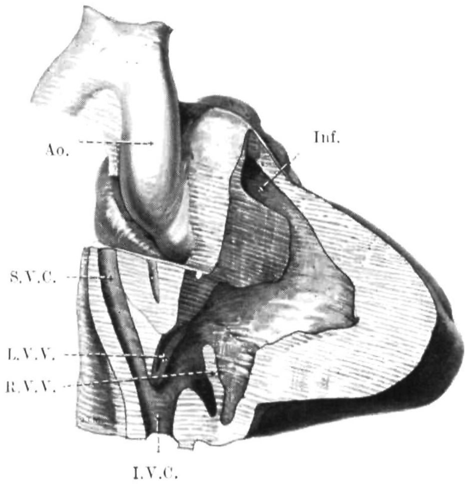

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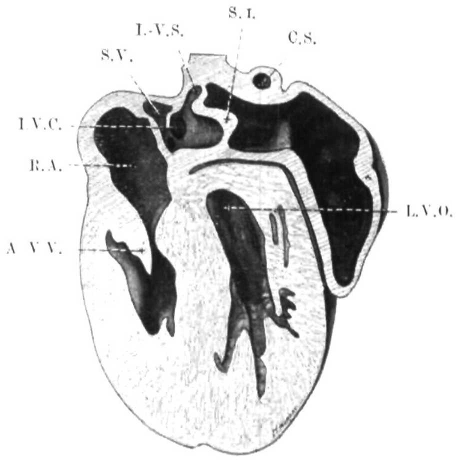

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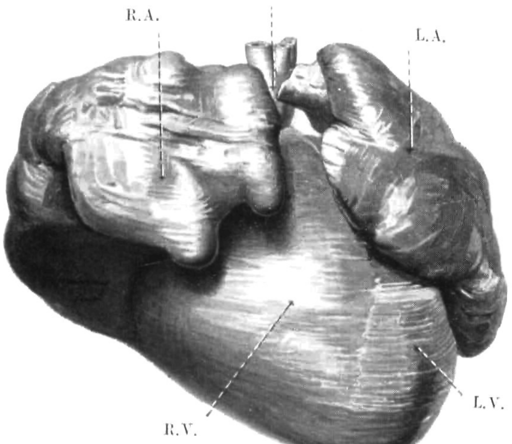

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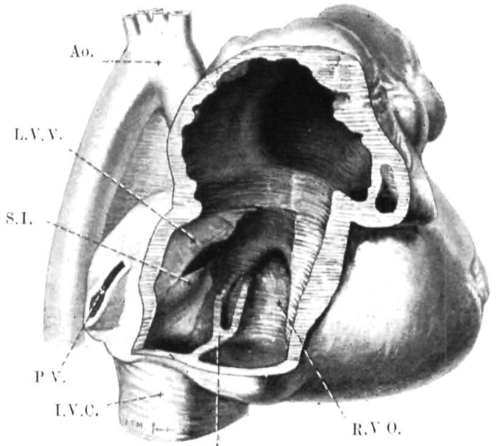

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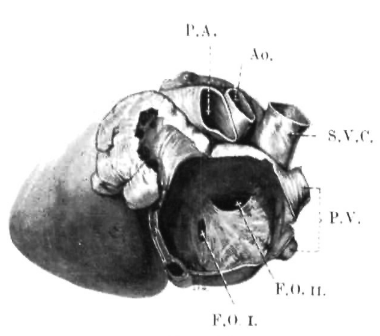

Fig. 16.