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Left and right ventricular trabecular patterns
Consequence of ventricular septation and valve development

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SUMMARY Study of serial sections of human embryos ranging from 3·6 to 25 mm crown rump length shows that the ventricular septum develops from three sources. The primary septum develops between the inlet and outlet which are the two first discernible segments of the ventricular portion of the primary heart tube. Two other septa develop within the inlet and within the outlet, respectively. Before and during septation all ventricular trabeculations are identical. In later stages, the atrioventricular valves and their tension apparatus develop from the inner myocardial layer of the left and right ventricular inlet parts. The outlet trabeculations do not take part in this process. These observations are suggested to explain the typical trabecular patterns of the apices of the mature left and right ventricles, which develop from the inlet and from the outlet, respectively.

Congenital malformations of the ventricular portion of the heart might be explained by comparing them with the normal anatomy. A problem arises, however, when structures known from the normal heart cannot be recognised, or when pathology cannot, without difficulties, be translated into normality. An example of this problem has been given with respect to malformations of the crista supraventricularis.[1]

Normal embryonic development should be a much more reliable source of understanding of normal and pathological anatomy. But published reports on the normal development of the ventricles, the ventricular septum, and the atrioventricular connections are not uniform,[2–11] and much misunderstanding is caused by different terminologies.[12]

The investigations of one of us[13] have led to a concept of ventricular septation which has been shown to be applicable to congenital malformations.[14 15] Some questions, however, remain unanswered. In the present paper, we try to clarify our views on the boundaries between different parts of the ventricles and on the site of formation of the atrioventricular valves.

Materials and methods

We re-examined 78 human embryos (Department of Anatomy and Embryology, University of Leiden and Department of Histology and Embryology, University of Vienna), all sectioned serially and stained with routine histological methods. Their crown rump lengths ranged from 3·6 to 25 mm. Where necessary, we made graphic reconstructions[16] of the heart or of part of the heart.

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GROWTH OF VENTRICULAR CAVITIES

In the youngest embryo available, the looping process has already taken place. Distinction can be made between five serially connected segments (Fig. 1 and 2a). The systemic veins of the embryo drain into the sinus venosus which itself connects with the atrium. The next portion of the heart tube will eventually give rise to the left and right ventricles, but at this stage it consists only of two serially connected segments. The first of these is conveniently called the inlet, the next segment being named the outlet. The constricted portion of the heart tube between atrium and inlet is the atrioventricular canal. More downstream, the heart tube bends dorsally to form the final segment, the truncus arteriosus, which is supported by the outlet. The inlet and outlet cavities, that is the ventricular portion of the heart, are the main subject of this study (Fig. 2b).

Inlet and outlet communicate by a somewhat constricted portion of the heart. This communication, which is called the primary foramen, is surrounded by the primary fold. The primary fold corresponds with the external primary groove. In the inner curvature of the heart, that is superiorly and posteriorly, the

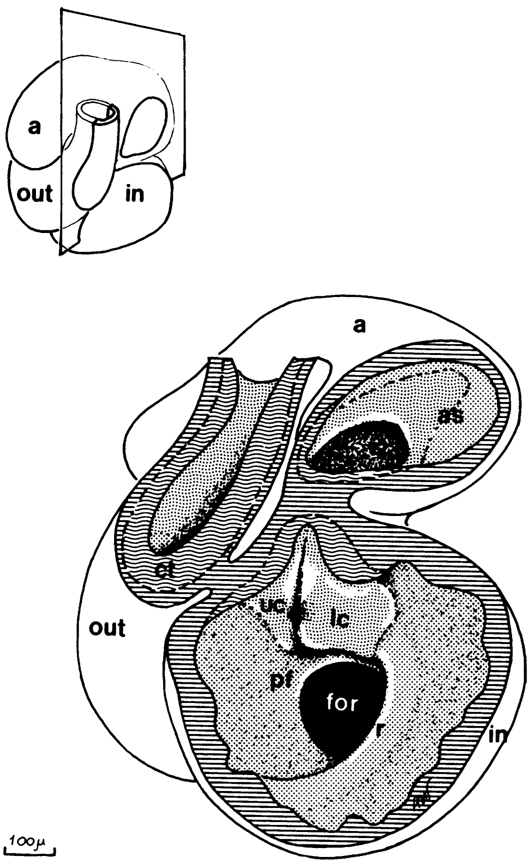

Fig. 1 *Graphic reconstruction of the heart of a human embryo of 3·6 mm crown rump length. The model has been sectioned in the oblique sagittal plane (see inset, which shows the anterior view) and is shown from the left. The atrium (a), in which a partial septum (as) is already present, connects with the inlet (in) by way of the atrioventricular canal. This canal is guarded by the upper (uc) and lower (lc) atrioventricular cushions and lies to the left of the primary fold (pf). The posterior wall of the inlet shows a ridge (r) which consists of loose trabeculations (see Fig. 3a) and hides part of the primary foramen (for) from view. The primary foramen connects the inlet with the outlet (out). The distal outlet is covered internally by endocardial cushion tissue (ct). The truncus arteriosus has been removed.*

primary groove coincides with the right portion of the constriction formed by the atrioventricular canal (Fig. 2b).

The atrioventricular canal and the distal part of the outlet are filled by endocardial cushion tissue, or rather by masses of cardiac jelly as they are better termed at this young stage (Fig. 1). These parts do not show trabeculations. The walls of the inlet and the proximal outlet are about equally thick and they do show trabeculations, which are not different in either cavity (Fig. 3a). The only difference is that the inlet trabeculations are more numerous, particularly on the posterior wall. Here they constitute a ridge just to the left of the primary fold. This mass of trabeculations can be distinguished from the primary fold, because the latter is smooth and more compact (Fig. 1 and 3a).

During further development up to 10 mm crown rump length, both the inlet and the outlet expand and, consequently, the primary fold between them enlarges. In particular, the anterior and apical parts of these cavities grow out and therefore also the anterior and apical part of the primary fold becomes larger. It forms a partial septum between inlet and outlet and is called the primary septum (Fig. 2c).

At the same time, the mass of trabeculations on the posterior inlet wall becomes more compact to form a second septum, the inlet septum. The anterior part of the inlet septum fuses with the posterior part of the primary septum, on the left side of the latter (Fig. 3b). The basic anatomy of the definitive left and right ventricles can be recognised (Fig. 2d). Formation of the inlet septum has caused partitioning of the inlet and the right hand portion of the inlet has been allotted to the right ventricle. There is no fundamental difference in the trabecular patterns of the right ventricular inlet and outlet portions (Fig. 3c), nor can such difference be noted between the apex of the outlet (which belongs to the right ventricle) and the apex of the inlet (which belongs to the left ventricle) (Fig. 3d). An important difference, however, from the normal adult heart is the fact that the right ventricular inlet portion is still very small. Similarly, the initial contribution of the outlet to the left ventricle does not seem to be very extensive. In the left ventricle, the primary fold (that is the boundary between inlet and outlet) borders directly upon the future aortic orifice, as in the right ventricle the primary fold is very close to the future tricuspid orifice.

The (small) outlet to the aorta is furthermore bordered by the outlet septum. This is a third septal component which develops in the downstream portion of the outlet (Fig. 2e). It is constituted by two endocardial ridges which eventually fuse to assign the left-hand part of the outlet to the left ventricle. Completion of septation by fusion of all three septa is not effected before the 16 mm stage. Until that time, an interventricular communication remains.

Between 11 and 25 mm crown rump length, development is characterised by expansion of the inlet. This causes an important change in the anatomy of the right ventricle, which, until this stage, had only a very small inlet portion. The expansion of the inlet coincides with the process which leads to formation of the atrioventricular valves. In the left ventricle, valve formation causes widening of the outflow tract, at the expense of its inlet portion, which is described below.

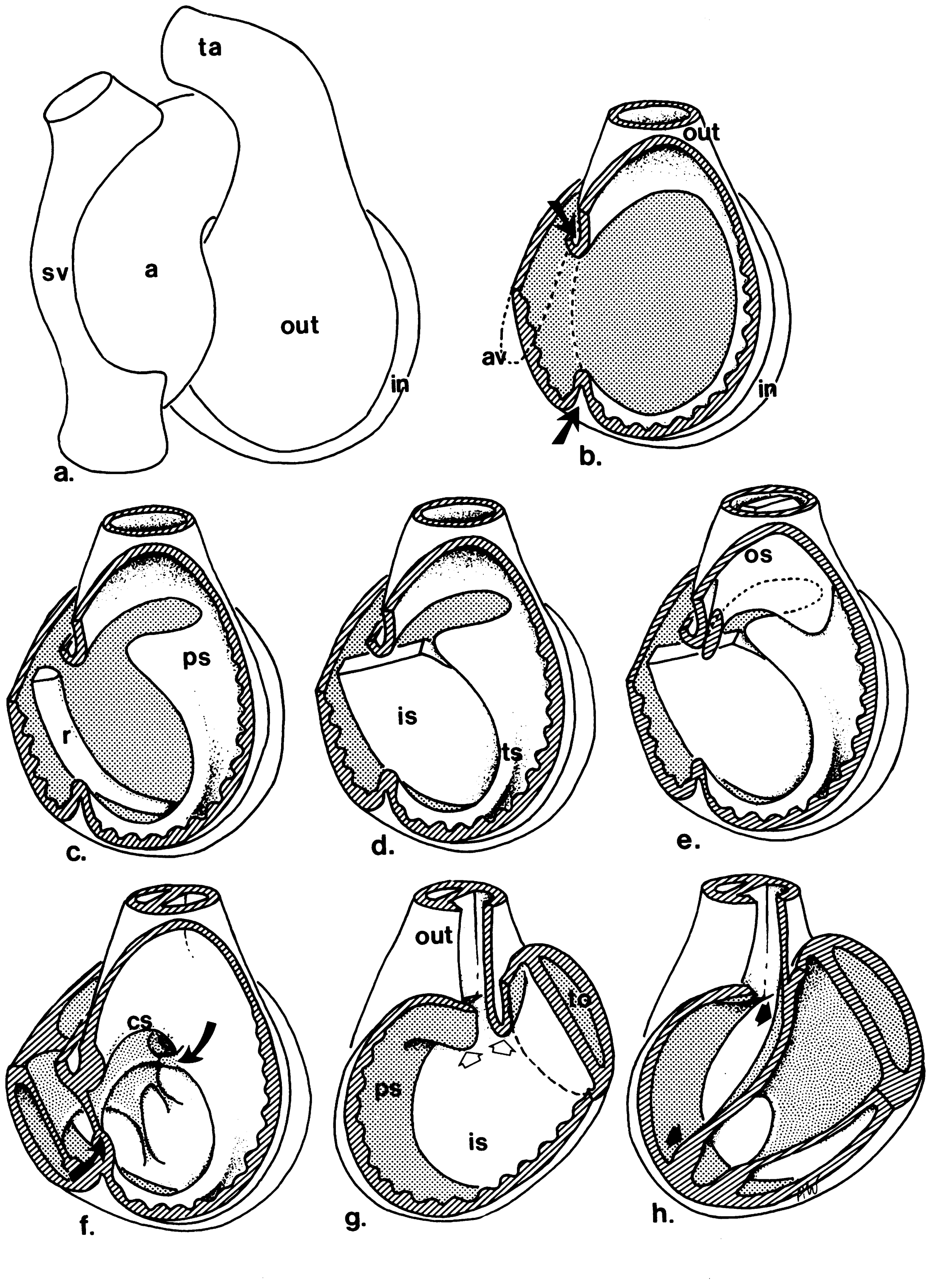
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Fig. 2 *Diagrams to show the processes of septation and valve formation. (a) The heart after looping, viewed from the right. sv, sinus venosus; a, atrium; in, inlet; out, outlet; ta, truncus arteriosus. (b) The same view, after removal of the truncus arteriosus and of the atrium and sinus venosus, leaving only the inlet (in) and outlet (out). An additional incision, made to show the interior of both cavities, cuts through the primary fold (arrows) which forms the junction between inlet and outlet. Posteriorly (upper arrow), the primary groove coincides with the atrioventricular groove (av). (c) Expansion of inlet and outlet has lead to enlargement of the anterior and apical part of the primary fold, to form the primary septum (ps). Note that this enlargement is relative and is not caused by active ingrowth of the fold. In the inlet, a posterior ridge (r) becomes visible, which will grow out to form the inlet septum (see Fig. 3a). (d) As (c), after completion of the inlet septum (is) which has fused with the primary septum. The posterior edge of the primary septum remains recognisable as the trabecula septomarginalis (ts). (e) Final stage of septation, in which the endocardial ridges in the distal outlet have fused to form the outlet septum (os), still leaving a small interventricular communication between the three septal components. After formation of the outlet septum, part of the primary fold (interrupted line) belongs to the left ventricle. (f) Right ventricular view after completion of septation, showing formation of the tricuspid valve. Undermining of the trabeculated myocardial layer of the inlet part of the right ventricle, that is the right part of the primitive inlet, involves the inlet aspect of the primary gold (arrows). Note that the crista supraventricularis (cs) originates from coalescence of primary fold and outlet septum (compare Fig. 2e). (g) Left ventricular view after completion of septation but before valve development. Both the inlet and the outlet (out) parts of the left ventricle have been opened and, therefore, the incision passes through the left ventricular part of the primary fold (arrows). Note that the fold (right hand arrow) is directly anterior to the mitral orifice, which has been widely opened (interrupted line). Anteriorly, the primary fold (left hand arrow) is continuous with the primary septum (ps). is, inlet septum; to, tricuspid orifice (compare Fig. 3d.) (h) The same as (g), now showing development of the mitral valve by undermining of the trabeculated myocardial layer of the inlet part of the left ventricle, that is the left part of the primitive inlet. In this process, the primary fold (arrows) forms the aortic leaflet of the mitral valve. The undermining causes apical displacement of the fold and relative enlargement of the left ventricular outlet part (compare Fig. 3f and g). Note that in this diagram the boundaries of the septal components are still indicated for the sake of comparability. In reality, after valve formation, these boundaries are no longer visible.*

FORMATION OF ATRIOVENTRICULAR VALVES

It is important to note that valve formation takes place on the basis of the septated heart. We agree with Van Gils[17] that the atrioventricular endocardial cushions do not make a substantial contribution to the valves or their tension apparatus. Instead, these structures are the result of invagination of the atrioventricular sulcus and undermining of ventricular myocardium. The details of this developmental process will be reported elsewhere.

The present study mainly relates to the topographical aspects of valve development. Since the primary fold belongs to the walls of the inlet, the undermining process extends into this fold as well. Beyond the primary fold, that is in the outlet, no such undermining takes place.

Between 11 and 25 mm crown rump length, a gradual coarsening of the trabeculations is seen in both ventricles. In the right ventricle, a difference can be noted between the apex (that is outlet) and the inlet portion. The inlet trabeculations are coalescing to form the papillary muscles and chordae tendineae (which in these stages are muscular), whereas the trabecular pattern at the outlet side of the primary fold remains relatively undisturbed (Fig. 3e). In the 25 mm stage, the right ventricle gives a clear picture of its future normal anatomy. It has an inlet portion which is filled with coarse muscular structures, representing the tricuspid valve and its tension apparatus, and an apex in which the trabeculations have remained relatively close to the wall (Fig. 2f).

Development in the left ventricle is different. In the 11 mm stage, the part of the outlet allotted to this ventricle is small, and the primary fold which encloses the outflow tract towards the aorta shows broad attachment to the (anterior) primary septum (Fig. 3d). In subsequent stages, almost the entire left ventricle (that is its inlet component) shows coarsening of the trabeculations, showing formation of the papillary muscles and their chords. The undermining process is much more extensive than in the right ventricle. Most of the primary fold is loosened from the septum and these disengaged trabeculations end up being attached only to the apical part of the ventricular wall, where they come very close to the trabeculae which are loosened from the ventricular free wall (Fig. 3f and g). The left side of the ventricular septum is stripped of its original trabeculations (Fig. 2g and h).

Evidently, the original architecture of the right ventricle is not changed very much after septation. Only its inlet part has to expand, and this process coincides with valve formation. Initially, the right part of the myocardial primary fold forms the junction between inlet and outlet parts of the right ventricle. By undermining of the inlet aspect of the fold this junction is transformed but not displaced. After full development, the trabecula septomarginalis, the parietal part of the crista supraventricularis, and the anterior leaflet of the tricuspid valve, with its tension apparatus, together constitute the original junction between inlet and outlet parts of the right ventricle (Fig. 2f).

In the left ventricle, the left part of the primary fold is very close to the aorta in stages directly after septation (Fig. 2g). Undermining of the inlet myocardium also involves the inlet aspect of the primary septum and, therefore, the primary fold is completely disengaged from the septum. This means that the tension apparatus of the aortic leaflet of the mitral valve is

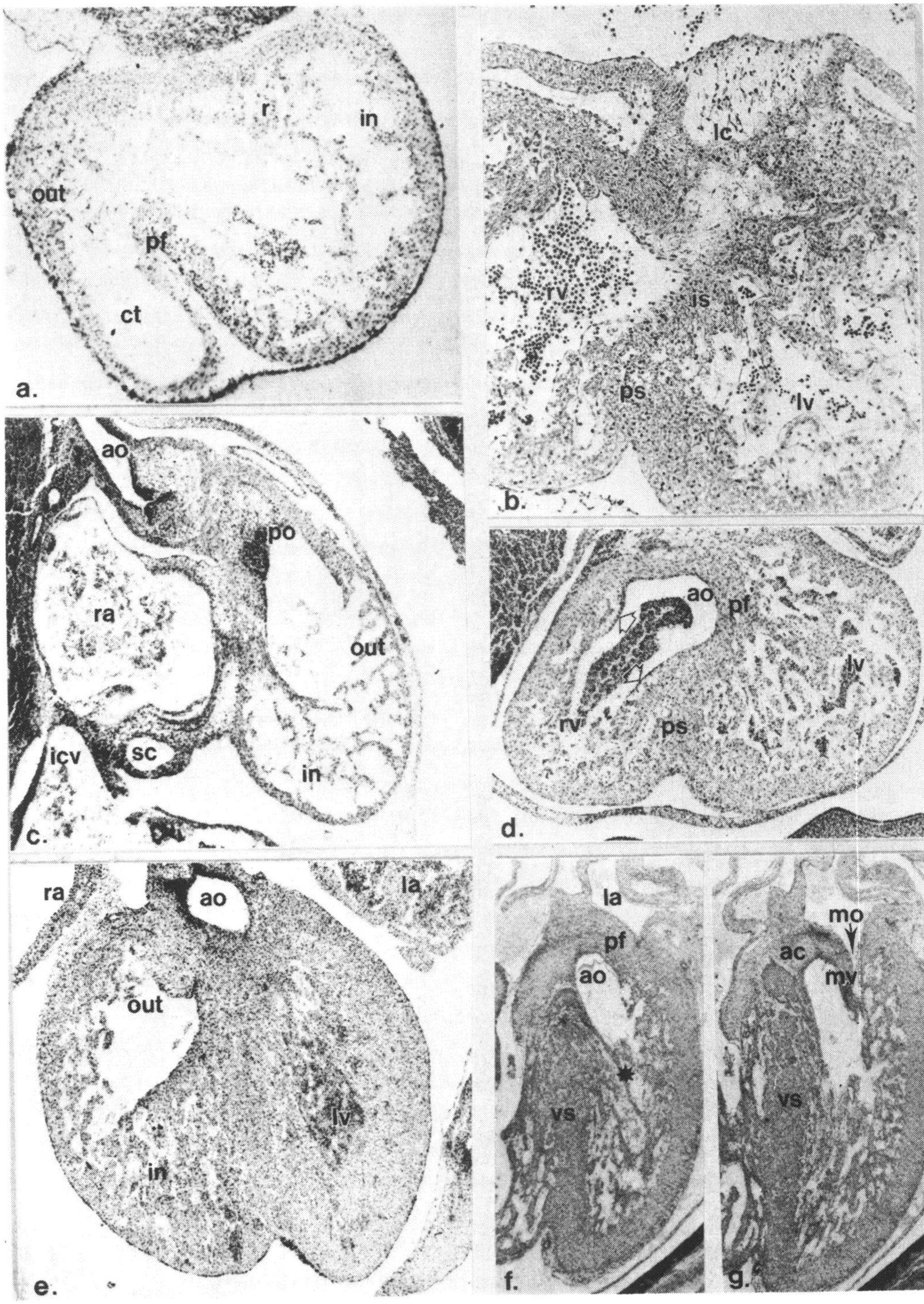
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Fig. 3 Sections of human embryonic hearts to show development of trabeculations and atrioventricular valves. (a) Transverse section (3·6 mm crown rump length) to show that trabeculations in the inlet (in) do not differ from those in the outlet (out). Posteriorly, the inlet trabeculations constitute a ridge (r). The distal part of the outlet contains endocardial cushion tissue (ct). pf, primary fold. (b) Transverse section (6 mm crown rump length) to show that the posterior inlet trabeculations have formed the inlet septum (is), which has fused with the primary septum (ps) anteriorly. lv, left ventricle; rv, right ventricle; lc, lower atrioventricular endocardial cushion. (c) Sagittal section (11 mm crown rump length) of the right ventricle, to show that the trabeculations in its outlet part (out) do not differ from those in its inlet part (in). icv, inferior caval vein; sc, coronary sinus; ra, right atrium; po, pulmonary orifice; ao, aortic orifice. Note that the distal outlet, that is just below the pulmonary orifice, does not show trabeculations. (d) Transverse section (11 mm crown rump length) to show that the trabeculations in the apices of the left ventricle (lv) and the right ventricle (rv) are not different. The outlet septum is not yet completed, but is precursors, the endocardial ridges, are visible (arrows). Note that the left ventricular part of the primary fold (pf) encircles the outlet to the aorta (ao) at its left side. This part of the fold is continuous with the primary septum (ps) (compare Fig. 2g.) (e) Transverse section (21 mm crown rump length) to show that the trabeculations in the inlet part of the right ventricle (in) are more coarse than those in its outlet part (out), as a consequence of valve formation. The right ventricular inlet trabeculations do not differ from those in the left ventricular inlet part (lv), in which the mitral valve is formed. ra, right atrium; la, left atrium; ao, aortic orifice. (f) Transverse section (25 mm crown rump length) to show how the left ventricular part of the primary fold (pf) which encircles the outlet towards the aorta (ao) is loosened (asterisk) from the ventricular septum (vs). la, left atrium. (g) More posterior section of the same heart as shown in (f). The aortic leaflet of the mitral valve (mv) is completely detached from the ventricular septum (vs) at this level. Note that at this level the atrioventricular endocardial cushion (ac) is incorporated in the valve leaflet. mo, mitral orifice.

displaced apically, and this process leads to a relative widening of the outlet of the left ventricle. Here, the original boundaries between inlet and outlet are displaced functionally. Anatomically, the boundaries between the different septal components are no longer visible (Fig. 2h).

Discussion

Understanding the development of the ventricles and the atrioventricular valves will benefit from using simple and descriptive terms. For this reason we have followed Anderson and Becker[10] who have divided the ventricular portion of the heart tube into inlet and outlet segments. The anatomy of the mature left and right ventricles favours the concept of a third component within the ventricular portion of the heart,[9 10] but such a "trabecular component" is not a separate embryonic entity. Trabeculations belong either to the inlet or to the outlet. Therefore, our main distinction remains that between inlet and outlet. If, in the mature heart, we use the term "ventricular apex" and not "trabecular zone", as Anderson and Becker[10] do, it is because we want to avoid the impression that we consider these zones as derived from a distinct embryonic segment. This is not contrary to the notion that the ventricular septum develops from three different components: one within the inlet, another within the outlet, and a third one being interposed between inlet and outlet.

The outlet can be divided into proximal and distal portions: the first portion shows trabeculations in our youngest specimen, the second portion is smooth walled and lined by endocardial cushion tissue. But no such subdivision is seen in the inlet. This cavity shows trabeculations all over its inner surface and, as such, it differs from the smooth walled atrioventricular canal which is lined by endocardial cushion tissue. Because the inlet septum develops within the trabeculated inlet, the right part of this inlet is allotted to the future right ventricle. Development of the (endocardial) outlet septum assigns the left part of the smooth walled distal outlet to the future left ventricle. Thus, we distinguish between "inlet" and "outlet" as such (being primary cardiac segments) and "inlet portion" and "outlet portion" of the left and right ventricles (representing parts of the primary segments after septation).

After septation, distinction remains possible between inlet and outlet because they are separated by the primary fold. The primary septum has developed from the anterior and apical part of this fold, and separates the apices of the future left and right ventricles. Further distinction is not possible, because inlet and outlet show the same trabecular patterns. Here, our observations differ from those reported by Van Praagh *et al.*[18] It should be noted that our present observations on the trabeculations do allow a subdivision of the outlet as was suggested by DeVries and Saunders.[6] The outlet part allotted to the future left ventricle has no trabeculations.

Since the trabecular patterns of inlet and outlet are identical before and directly after septation, the different trabecular patterns of the apices of normal left and right ventricles[18 19] remain to be explained. We believe that these trabecular patterns develop late. Development of the atrioventricular valves and their tension apparatus implies consolidation of the inner, trabeculated, layer of myocardium of the left and right parts of the inlet. In the outlet, however, this layer is not changed in this respect and, therefore, after valve formation the trabecular patterns of inlet and outlet may be expected to be different.

In the normal heart, the right ventricular apex stems from the outlet and the left ventricular apex originates from the inlet—hence the typical right and left ventricular trabecular patterns.

Hearts with complete double inlet "left" ventricle, with tricuspid atresia (absence of the morphologically right atrioventricular orifice), and with two chambered right ventricle all have small additional ventricular chambers with typical "right ventricular" trabeculations. These additional chambers share the feature that no valvular tension apparatus has developed within them. We believe that this is the explanation for their typical trabecular patterns. In these malformations, the trabeculated outlet has been abnormally separated from the inlet.[14]

In conclusion, valve formation plays a major role in the establishment of ventricular trabecular patterns. On the other hand, abnormalities of the septation process may lead to abnormal valve formation, as we have suggested in the case of straddling atrioventricular valves.[20 21]

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