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Embryology of the Ventricular Septum

Separate Origin of Its Components

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Summary. The formation of the ventricular septum was studied in human embryos ranging from 3.6 to 25 mm CR-length.

Before septation, two distinct chambers are present which will contribute to the adult ventricles. They are called the bulbus and the ventricle. The circular constriction between these chambers is the bulboventricular fold.

The anterior portion of the ventricular septum develops from this bulboventricular fold. Posteriorly, it fuses with a second septum, which is of purely ventricular origin. This is the inlet septum. Another portion of the bulboventricular fold persists as the trabecula septomarginalis. The trabecula septomarginalis divides the normal right ventricle into an inlet portion, stemming from the embryonic ventricle, and an outlet portion which derives from the bulbus.

Key words: Ventricular septum – Cardiac embryology – Bulbus – Ventricle.

Introduction

For several reasons, septation of the ventricular part of the heart was restudied in human embryos.

Observations on congenitally malformed hearts suggest that the ventricular septum is not a single structure (Goor et al. 1970a; Wenink 1978; Wenink et al. 1979). Goor et al. (1970b) have also derived this multiplicity from normal cardiogenesis, and Bersch (1971; Kreinsen and Bersch 1972) based a classification of ventricular septal defects upon his meticulous studies of late septation stages. However, the literature is not consistent as to the primary site of origin of the muscular ventricular septum. This structure has been reported to be first recognizable in relation to the anterior bulboventricular groove (Waterston

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1921), or alternatively, to the inferior atrioventricular endocardial cushion (Frazer 1940).

The question of the role of the bulbus in the formation of the definitive right ventricle (Waterston 1921; Frazer 1940; DeVries and Saunders 1962; Goerttler 1963; Van Mierop 1979; Dor and Corone 1979) was a second reason for this study. Conclusive evidence on the formation of the ventricular septum might settle this question.

Obviously, such evidence would contribute to the problem of nomenclature. Two questions are pertinent. First, are there two separate chambers of the heart tube, both of which contribute to the ventricular mass, and both of which are recognizable before there is any evidence of a ventricular septum? Second, can these chambers still be distinguished in the presence of the definitive ventricular septum? A positive answer to both questions means enough factual evidence to dispose of the terms primitive left and right ventricle (Van Mierop 1979) or inlet and outlet portion of the heart tube (Anderson et al. 1979). Noncommittal terms are only helpful to a certain extent.

The present study is descriptive, and provides a basis for the understanding of congenital malformations. It tries to reconcile pediatric cardiology and embryology.

Materials and Methods

From the collections of the Department of Histology and Embryology, University of Vienna, and the Department of Anatomy and Embryology, University of Leiden, 78 human embryos were studied. They ranged from 3.6 to 25 mm crown-rump-length. All embryos had been serially sectioned at thicknesses of 7 to 10 µm, and stained with routine histological methods.

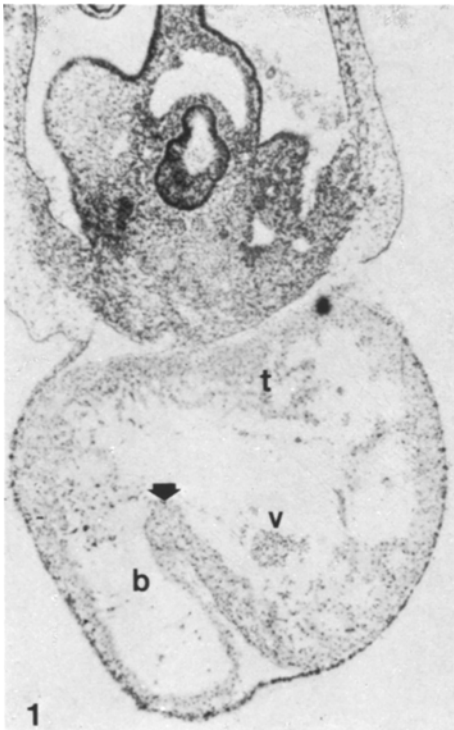
In individual cases, reconstructions were made by a graphical technique (Tinkelenberg 1979). Although the general build up of the individual hearts was noted, the study was concentrated upon the ventricular mass of the heart and its relation with the atrioventricular canal.

Results

In the youngest specimen, measuring 3.6 mm CR-length, the atrioventricular canal opened into a distinct, left-sided chamber, which is called the ventricle. The atrioventricular canal was largely filled up by two endocardial masses, to be called the upper and lower atrioventricular cushions, the latter being more posterior.

The ventricle emptied into an adjacent chamber, to be called the bulbus, which was to the right. From the outside, the ventricle and the bulbus were separated by a distinct groove, the bulboventricular groove. This groove, encircling the heart in a nearly sagittal plane, corresponded with an elevation of the inner heart wall and created a distinct bulboventricular orifice. Posteriorly, this elevation, the bulboventricular fold, was directly to the right of the atrioventricular canal.

Cranially, the heart tube bent in a posterior direction to bridge the atrium and to reach the mediastinum. The portion of the heart tube distal to this bend is called the truncus arteriosus. No other distinction could be made between



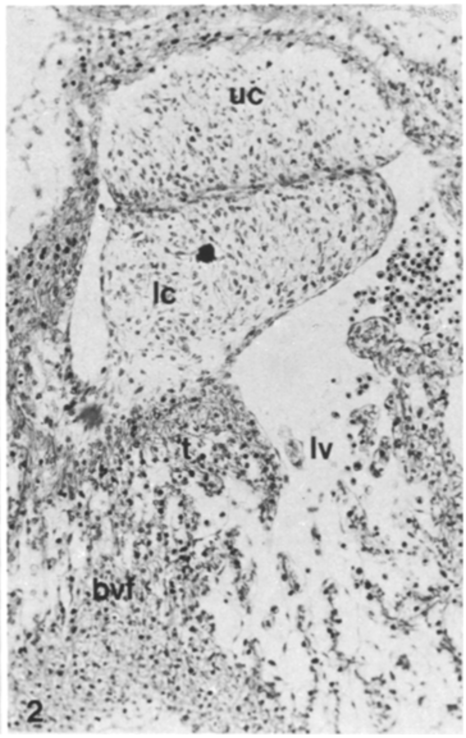


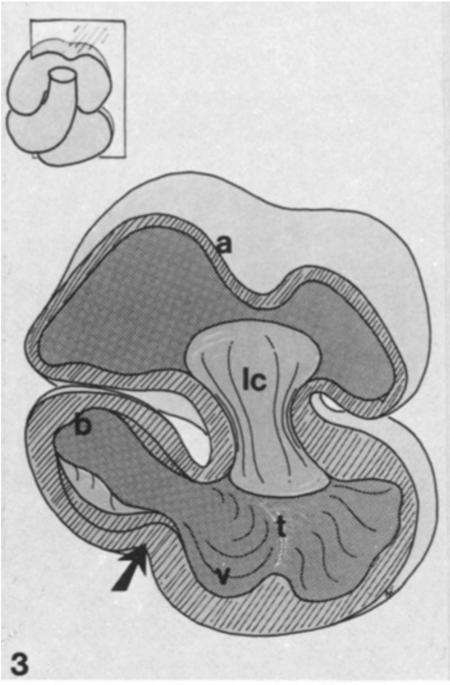
Fig. 1. Transverse section of the heart of a human embryo of 3.6 mm CR-length. Between the bulbus (*b*) and the ventricle (*v*) a distinct bulboventricular fold (*arrow*) is present. The posterior ventricular wall is invested with a conspicuous mass of trabeculations (*t*). (×66)

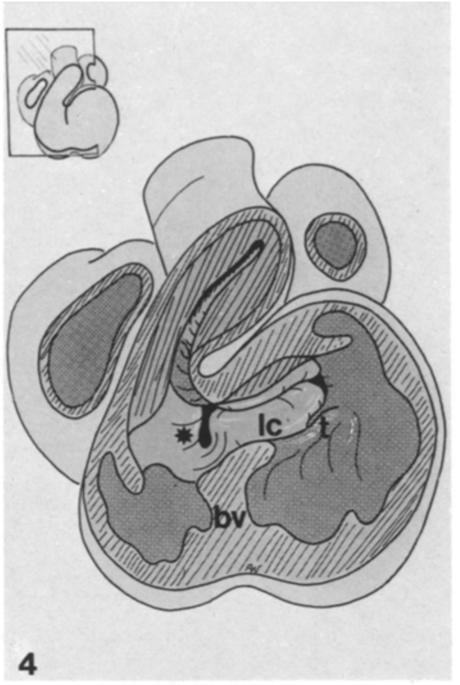
Fig. 2. Transverse section of the heart of a human embryo of 7.5 mm CR-length. The ventricular septal anlage consists of two components. Anteriorly, the bulboventricular fold (*bvf*) is seen. The posterior component consists of many trabeculations (*t*) which are topographically related with the lower atrioventricular endocardial cushion (*lc*). *uc:* upper atrioventricular cushion, *lv:* future left ventricular cavity. (×135)

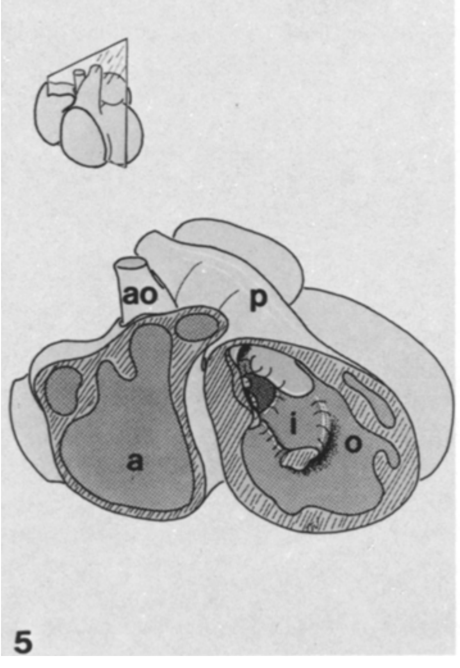
the bulbus and the truncus arteriosus than their individual directions of blood flow.

Between the bulbus and the ventricle, a difference was noted regarding the build up of the myocardial wall. Generally, the inner surface of the myocardium was rather smooth, but the ventricle showed small trabeculations, particularly on its posterior wall (Fig. 1). Reconstruction showed that these trabeculations together formed an elevation on the posterior ventricular wall, just below the lower atrioventricular cushion (Fig. 3). It was only a slight elevation and because it consisted of individual trabeculations, it differed from the bulboventricular fold, which was more solid.

In older embryos, both the bulbus and the ventricle had expanded relative to the atrium. The bulboventricular fold had become more conspicuous, particularly at the anterior side where a true bulboventricular septum became recognizable (Fig. 2). Although the inner trabeculations of bulbar as well as ventricular







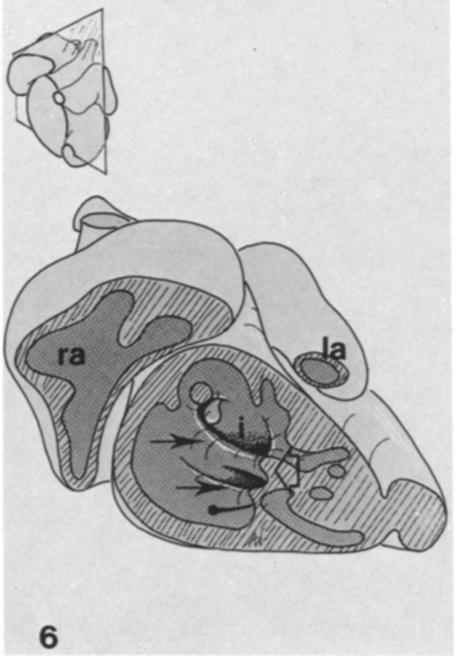


Fig. 3. Reconstruction of the heart of a human embryo of 3.6 mm CR-length. The anterior part has been sectioned away (*inset*), the posterior portion is shown from a frontal view. The bulbus (*b*) is to the right of the ventricle (*v*). The ostium between atrium (*a*) and ventricle is partly filled by the lower atrioventricular cushion (*lc*). The posterior ventricular ridge (*t*) is to the left of the bulboventricular fold (*arrow*)

Fig. 4. Reconstruction of the heart of a human embryo of 7.5 mm CR-length. The anterior portion has been sectioned away (*inset*), the posterior portion is shown from a frontal view. The trabeculations (*t*) on the posterior ventricular wall connect with the bulboventricular fold (*bv*). The more lateral portion of this fold (*asterisk*) is to the right of the right AV-orifice, which is shown in black. *lc:* lower atrioventricular cushion

myocardium had become more profuse, they had become still more distinct on the posterior ventricular wall. They constituted a ridge, which was to the left of the bulboventricular fold, posteriorly. But more anteriorly, they formed one structure with the bulboventricular fold (Fig. 4).

In summary, the ventricle was separated from the bulbus by a septum, which was particularly well developed anteriorly, whereas the posterior ventricular wall was invested with a ridge, that continued into the anterior bulboventricular fold. The posterior portion of this fold did not seem to have increased proportionately.

These changes had important haemodynamic consequences. Whereas in the 3.6 mm embryo (Fig. 3) the entire atrioventricular canal emptied into the ventricle, the situation had changed in a 7.5 mm specimen (Fig. 4). Here, the right portion of the atrioventricular canal was more committed to the bulbus. It is important to note that no change of spatial relationships appeared to be the cause of this difference. The right portion of the atrioventricular canal was already close to the bulbus in the youngest embryo. Only a relative lack of growth of the posterior portion of the bulboventricular fold and the appearance of the posterior ventricular ridge, lead to the different situation in the 7.5 mm embryo.

In a way, the future right ventricle could be recognized in the 7.5 mm embryo. But a proper inlet portion was still missing, there being only a small "porch" between the right portion of the atrioventricular canal and the bulbus. This situation had not changed much in an 11 mm embryo (Fig. 5), but growth of a distinct inlet portion (and by that of an inlet septum) had only just started in a 15 mm specimen and was obvious in the heart of a 25 mm embryo (Fig. 6). In this latter embryo, undermining of the myocardium (leading to formation of the atrioventricular valves and tension apparatus) was in progress. The myocardium had been liberated from the inlet septum and from the rim of the bulboventricular fold, but not from more apical portions of bulbar myocardium, that is, beyond the trabecula septomarginalis. Because of the mentioned similarity to the adult right ventricle, that part of the bulboventricular fold that separated inlet and outlet portions was already called the trabecula septomarginalis in these developmental stages.

Fig. 5. Reconstruction of the heart of a human embryo of 11 mm CR-length. A right hand portion has been sectioned away (*inset*), the opened heart being shown from a right lateral view. The inlet portion (*i*) of the right ventricle is small relative to the outlet portion (*o*). *p* pulmonary trunc, *ao* ascending aorta, *a* right atrium

Fig. 6. Reconstruction of the heart of a human embryo of 25 mm CR-length. A right hand portion has been sectioned away (*inset*) and the opened heart is shown from a right lateral view. The inlet septum (*i*) has grown and myocardium has been liberated (*arrows*) to provide for the tricuspid valvular apparatus. The trabecula septomarginalis (*asterisk*) has been sectioned. *ra* right atrium, *la* left auricle

Discussion

This study shows that two separate components together form the muscular ventricular septum. This observation substantiates the earlier hypothesis, which was based on congenitally malformed hearts (Wenink et al. 1979). It is further shown that two distinct chambers are recognizable in pre-septation stages, and that these chambers remain distinguishable after formation of the septum. These chambers are partly separated, and remain so, by the bulboventricular fold. In this context, the bulboventricular fold refers to the circular structure, surrounding the bulboventricular orifice.

The anterior portion of the fold gives rise to part of the septum, while its laterally continuing portion remains as the trabecula septomarginalis. The inlet portion of the septum develops as a condensation of myocardium in the embryonic ventricle.

The relationships of the anterior portion of the septum and the trabecula septomarginalis are clearly shown in the microdissections by Asami (1969), although his nomenclature differs from the one used here. The present results suggest the presence of only two embryonic cavities that contribute to the adult left and right ventricles and, after Davis (1927), they are termed ventricle and bulbus respectively. No further distinction is made between a proampulla and a metampulla (Goerttler 1963; Bersch and Doerr 1976). The use of these terms is not fully consistent since Dor and Corone (1979) seem to have assimilated the term of metampulla with that of bulbus.

Many congenital malformations may be interpreted in the terms found suitable for normal embryology. The central muscular ventricular septal defect (Wenink et al. 1979) results from lack of coaptation of the inlet and bulboventricular septa. Univentricular hearts with an outlet chamber have an incomplete bulboventricular septum and accentuation of what normally becomes the trabecula septomarginalis (Wenink 1978). These hearts are comparable with cases of two chambered right ventricle (Anderson et al. 1976), in which accentuation of the trabecula septomarginalis is added to grossly normal septation. In hearts with an atrioventricular defect, the inlet septum has not fully developed (Wenink et al. 1978).

Much data from the literature on normal embryology fit with the present results. While Frazer (1940) first noted the ventricular septal anlage to be related to the lower atrioventricular endocardial cushion, Waterston (1921) related such an anlage to a pronounced anterior groove. Alternatively, Goor et al. (1970b) distinguished two separate septal components, but they did not distinguish them in the present topographical way.

In a recent paper by Meredith et al. (1979) the ventricular septum is described as a spiral, of which the posterior portion ends at the lower ventricular cushion. The basal portion of this spiral is formed by several structures (Doerr 1952) which in the adult heart have to be situated in the region of the crista supraventricularis (Bersch and Doerr 1976). The other end of the spiral is the inlet septum as described in this study. Proper septation is only possible if normal morphogenesis brings all components of this spiral into approximately the same plane (Doerr 1955; Goerttler 1963).

This study shows that the normal right ventricle is derived from the embryonic bulbus and the embryonic ventricle. The outlet portion of the right ventricle is derived from the bulbus. The inlet portion of the right ventricle derives from the embryonic ventricle and is separated from the adult left ventricle by the inlet septum.

It is interesting to note that definite statements about the origin of the right ventricle have been attributed (Van Praagh et al. 1979) to previous authors (Davis 1927; Streeter 1951). However, Davis (1927) only described pre-septation stages and distinguished between a ventricle and a bulbus, whereas Streeter (1951) started his investigations on hearts that showed early septation and deliberately did not use the terms bulbus and ventricle. For the younger stages he referred to Davis (1927).

The present results show that the inlet septum, once it has been formed, has only small dimensions. Consequently, the inlet portion of the right ventricle starts as a small "porch", which may account for Van Mierop's (1979) statement that most of the right ventricle stems from the bulbus.

Apart from the topography, there is an additional difference between the two components of the ventricular septum. The anterior, bulboventricular part develops as a fold between two separate cavities. The posterior part, the inlet septum, develops by coalescence of myocardial trabeculae on the posterior wall of the embryonic ventricle. The inlet septum is modelled from originally loosely built myocardium. It is probably this modelling process that has been described as "splitting off" of the posterior septum (Van Mierop 1979) and as "migration" of this septum (Dor and Corone 1979). The present material does not indicate any migration in a convincing way.

The modelling process by which the inlet septum develops must be closely linked to the process by which the atrioventricular valves develop. These valves and their tension apparatus develop largely by undermining of ventricular myocardium (Van Mierop 1977; Van Gils 1978, 1979). From the present study it appears that this undermining process is largely restricted to the inlet septum and the neighbouring myocardium. No tension apparatus arises within the bulbus.

Although Goerttler (1955) has stated that the myocardial septal structures are less dependent on the bloodstream than the endocardial structures, hemodynamic influences have been suggested to take part in the formation of the posterior part of the septum (Meredith et al. 1979). They undoubtedly play a role in valve formation. Oppenheimer-Dekker (1977) studied chorionic vascular development and thus produced evidence for an increase in blood flow in human embryos of 10 to 20 mm CR-length. It appears now that the inlet septum has small dimensions before this developmental period (the sixth embryonic week), and begins to grow during it. It is therefore reasonable to suppose that the inlet septum enlarges as a result of haemodynamic influences.

In conclusion, it is shown that the normal muscular ventricular septum has two major components, which develop differently and which may also behave differently in abnormal hearts. A third component, not described in this study, develops from the bulbar septum and in adult hearts is known as the infundibular septum. To give the septation in this area full credit, one

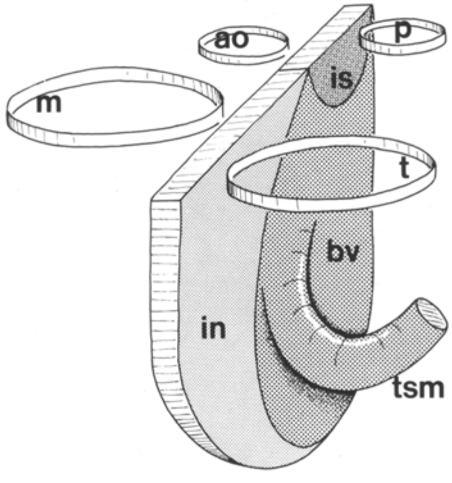


Fig. 7. Right posterior view of the ventricular septum, to show diagrammatically its separate components. *in* inlet septum, derived from the posterior wall of the embryonic ventricle. *bv* bulboventricular septum, derived from the embryonic bulboventricular fold. *is* infundibular septum, derived from the embryonic bulbar septum. *tsm* trabecula septomarginalis. *m* mitral anulus. *t* tricuspid anulus. *ao* aortic anulus. *p* pulmonic anulus

has to go into the final stages of closure of the interventricular foramen, which is not the purpose here. It is, however, a critical phase in cardiac development which has been extensively described as such (Doerr 1952; Bersch 1971; Bersch and Doerr 1976). In Fig. 7, the present results are summarised and here the infundibular septum is shown as well.

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