Morphogenesis of univentricular hearts

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Two main theories exist for the explanation of univentricular hearts. One states that the bulboventricular septum becomes realigned to form the interventricular septum, and that univentricular hearts are a consequence of failure of this realignment. The other states that bulboventricular and interventricular septa are different structures, and that the univentricular heart results from failure of formation of the posterior interventricular septum. Four hearts are described in which both the posterior septum and an anterior bulboventricular septum are present. In each heart, therefore, the right ventricular sinus is separated both from the left ventricular sinus and from a discrete outlet chamber which supports the pulmonary artery. It is argued that these findings militate strongly against theories proposing reorientation of the bulboventricular septum to form the definitive interventricular septum. They support strongly the concept that the definitive right ventricle is formed in part from the bulbus and in part from the primitive ventricle. On the basis of these findings, it is suggested that the distinctive feature of the univentricular heart is absence of the posterior septum. Such hearts can properly be termed 'primitive ventricle'. It is also suggested that hearts with atretic or straddling valves should be included within this category.

For some considerable time, hearts with one effective ventricular chamber have been the topic of controversy and confusion. In recent years much of this disagreement has centred upon differences in opinion regarding the correct usage of the terms 'single' and 'common' ventricle, as applied to these hearts (Lev, Paul, and Miller, 1962; Van Praagh, Ongley, and Swan, 1964; Somerville, Becu, and Ross, 1974). Other points of contention are more fundamental and relate to differing theories regarding the embryogenesis of both the normal right ventricle and the univentricular heart. Keith (1906, 1909) pointed out that the primitive bulbus formed only part of the definitive right ventricle, and that the bulbus could persist as a discrete cardiac chamber. The concept that the primitive ventricle formed the sinuses of both right and left ventricles subsequently received support from the embryological investigations of Pernkopf and Wirtinger (1933). Both Harley (1958) and Lev *et al.* (1969) subsequently suggested that the main chamber in univentricular hearts was composed of both right and left ventricular sinuses. In contrast,

the studies of Streeter (1942, 1945, 1948) had indicated that the trabeculated pouch of the right ventricle was a derivative of the primitive bulbus. From this finding, others assumed that the primitive bulbus formed the entirety of the definitive right ventricle, and that the embryonic primitive ventricle formed only the definitive left ventricle (de Vries and Saunders, 1962). Since the primitive ventricle originally received blood from both right and left atria, de la Cruz and Miller (1968), therefore, argued that 'single ventricle with outlet chamber' resulted from failure of migration of the right atrioventricular canal from the primitive ventricle to the bulbus. Since they believed the primitive ventricle formed only the left ventricle, they suggested that these hearts should be termed 'double inlet left ventricle'. Van Praagh *et al.* (1964) had previously argued in similar fashion, but had concluded that the right ventricular sinus was absent in 'single ventricle with outlet chamber'. The keystone of this controversy is, therefore, the fate of the original septum between the primitive bulbus and the primitive ventricle (Fig. 1). If this septum is considered as possessing right and left parts, which can be termed ridges, applying the

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FIG. 1 Diagrammatic representations to illustrate the form of the primitive heart tube following bulboventricular looping. (A) View of a frontal section through the loop. The primitive atrium communicates only with the primitive ventricle. The junction between the two, the atrioventricular canal, is becoming septated by the endocardial cushions to form the right and left atrioventricular orifices (RAVO, LAVO) which perforate will open into the primitive ventricle. The primitive ventricle opens to the primitive bulbus through the bulboventricular foramen. This foramen is bounded inferiorly by the bulboventricular septum, superiorly by the inner curvature of the heart tube (conoventricular flange), and to right and left by the bulboventricular (BV) ridges. The bulbus supports the truncus, which leads to the aortic sac. (B) Section through the loop at level B-B. (C) Relation at this stage between the bulboventricular foramen and the atrioventricular orifices. The cross-hatching will remain constant throughout the succeeding figures.

theory of Streeter (1942) to development it can be seen that active migration of the right atrioventricular canal would convert the right bulboventricular ridge into the posterior interventricular septum (Fig. 2A). In contrast, application of the concept of Pernkopf and Wirtinger (1933) reveals that regression of this ridge would be required during development, with subsequent growth of a new posterior septum to divide the primitive ventricle (Fig. 2B).

If it could be shown that a heart existed in which a posterior septum divided the right and left

ventricular sinuses, while in the same heart an anterior septum divided the ventricular inflow portions from an outlet chamber, this finding would constitute strong evidence in favour of the concept for development of 'single ventricle with outlet chamber' espoused by Harley (1958) and Lev *et al.* (1969). It would militate against the arguments of Van Praagh *et al.* (1964) and de la Cruz and Miller (1968) (Fig. 3). We have recently examined four such hearts. The findings are described here and it is suggested that they form the basis for a classification of the univentricular heart.

← FIG. 2 Diagrams illustrating the different theories regarding the mode of development of the definitive right ventricle. The primitive state is shown in the upper figure (B—bulbus; PV—primitive ventricle; LBVR, RBVR—left and right bulboventricular ridges; RAVO, LAVO—right and left atrioventricular orifices). Series A illustrates the theory espoused by de la Cruz and Miller (1968). They suggested that the right bulboventricular ridge becomes reorientated after migration of the right AV orifice. The RBVR becomes the posterior interventricular septum. The definitive right ventricle is consequently formed entirely from the bulbus, while the primitive ventricle forms only the definitive left ventricle. The relations of the AV orifices to the BV foramen following this process are illustrated in Fig. 2A2. In contrast, Lev et al. (1969) suggested that the primitive ventricle contributed to both ventricular sinuses. This mechanism is illustrated in Fig. 2B. Expansion of the atrioventricular canal and regression of the right BV ridge enables both bulbus and primitive ventricle to contribute to the definitive right ventricle. A new septum is formed in the primitive ventricle dividing the chamber into the definitive right and left ventricular sinuses. The anticipated relations of the AV orifices to the BV foramen after this mode of development are illustrated in Fig. 2B2. When applied to the anomaly of the univentricular heart, Theory A would result in this anomaly following failure of migration of the right AV orifice from the primitive ventricle to the bulbus. If this theory were correct, the univentricular heart would indeed be a 'double inlet left ventricle'. However, Theory B would account for this anomaly as a consequence of failure of septation of the primitive ventricle and persistence of the right bulboventricular ridge. If this theory were correct, it would be inappropriate to label this anomaly 'double inlet left ventricle'; 'double inlet primitive ventricle' would be the correct term.

Description of specimens

Case 1

This heart was from the cardiopathological collection of Grimsby General Hospital. Only the heart was available for examination. The arch and apex were both to the left in the presence of atrial situs solitus. The pulmonary artery was anterior and to the left of the aorta, the great arteries being of similar size. The coronary arteries were normally arranged with right dominance, but a large right marginal artery was seen (Fig. 4A). The right atrium received the superior and inferior caval veins and the coronary sinus. There was a large ostium primum defect between right and left atria, with an additional small patent foramen ovale. The left atrium received the four pulmonary veins. At first sight it appeared that a common atrioventricular valve was present. However, on closer examination (Fig. 4B) it was seen that the lower edge of the atrial septum straddled the left ventricle which received a normal mitral valve. The interventricular septum was deviated to the right as a consequence of gross hypoplasia of the right ventricular inflow portion. On opening this small chamber (Fig. 4C) it was found to contain a separate but hypoplastic tricuspid valve. The aorta arose from the large left ventricle and fibrous continuity was present between the aortic and mitral valves. The pulmonary artery arose from a discrete anterior outlet chamber. This chamber (Fig. 4D) possessed a smooth upper

portion and a trabeculated apical portion. It communicated with the hypoplastic right ventricular inflow segment through a slit-like apical defect, and also with the left ventricle through a small sub-aortic defect. The diagnosis was: (1) Solitus concordant-normal connexions; (2) ostium primum atrial septal defect; (3) hypoplasia of right ventricular sinus and tricuspid valve; (4) origin of pulmonary artery from discrete outlet chamber.

Cases 2 and 3

Case 2 was also from the cardiopathological collection of Grimsby General Hospital. Case 3 was from the collection of the Royal Liverpool Children's Hospital. The hearts were similar in appearance and can be best described by reference to Case 3. The heart alone was available for examination. The atria were in solitus position and the arch and apex were to the left. The pulmonary artery was anterior and to the left of the aorta, and was slightly smaller than the aorta (Fig. 5A). The coronary artery distribution was normal, with right dominance. The right atrium received the superior and inferior venae cavae and the coronary sinus. The atrial septum was closed. The left atrium received the four pulmonary veins. Both atria communicated through separate atrioventricular valves with a partially septated ventricular cavity (Fig. 6A). The left atrioventricular valve was tethered by two pairs of multiple papillary muscles joined together at the ventricular apex (Fig. 5C). This part of the

FIG. 3 This diagram illustrates the relations between the two theories of development described in Fig. 2 (upper panels) and a theoretical heart. If Theory B were correct, it would be anticipated that a heart would exist in which the bulboventricular septum persisted to separate the right ventricular outflow tract (bulbus) from the sinus (primitive ventricle). At the same time, the right ventricular sinus could be separated from the left ventricular sinus, both derived from the primitive ventricle, by the posterior interventricular septum, itself derived from the primitive ventricle. Such a heart is shown in diagrammatic form in the lower panel (TV—tricuspid valve; MV—mitral valve; AO—aorta; PA—pulmonary artery; IVR—interventricular ridge; other abbreviations as before). The diagram illustrates that it is difficult to account for this heart by application of the theory which assumes reorientation of the right BV ridge to form the posterior interventricular septum. →

main ventricular cavity was coarsely trabeculated (Fig. 5C, D). The right atrioventricular valve was tethered posteriorly by multiple small papillary muscles and anteriorly was tied down by short chordae to an anterior septum. A larger anterior papillary muscle arose from the posterior aspect of this septum (Fig. 6B). Posteriorly the ventricular cavity was partially divided by a ridge-like septum which swept down to form a shallow apical septum (Fig. 6A). Anteriorly it swept up to fuse with the anterior septum (Fig. 6B). This posterior septum was coarsely trabeculated on both sides (Fig. 5C, 6B) and was overridden by the aortic valve which was in continuity with both the right and left atrioventricular valves (Fig. 5D, 6A). A further defect was present beneath the tied-down anterior cusp of the right atrioventricular valve (Fig. 5D, 6C). This

defect passed into a discrete anterior outlet chamber which gave rise to the pulmonary artery. This outlet chamber had a trabeculated apical segment and a smooth upper segment (Fig. 5B). The posterior wall of the smooth segment was in part derived from the conus septum between aorta and pulmonary artery. Some of the chordae tethering the anterior cusp of the right atrioventricular valve were arising from the outlet chamber aspect of the anterior septum (Fig. 5B). The diagnosis in both cases was: (1) solitus-primitive ventricle-normal connexion; (2) partial septation of primitive ventricle; (3) pulmonary artery from discrete outlet chamber.

Case 4

This heart was present in the anatomical museum

FIG. 4 Photographs of Case 1. (A) Anterior view of the heart. The aorta and pulmonary artery (AO, PA) are normally connected and related. The outlet chamber (OC) is delimited by the anterior descending coronary artery (ADA). (RA—right atrium; MCA—marginal branch of right coronary artery.) (B) Atrioventricular junction opened from behind through a cut in the left ventricle. The deviated posterior septum is seen (PS) with the mitral valve (MV) attached to its crest. The aortic outflow tract (AOT) is seen beneath the anterior cusp of this valve. The pointer indicates the hypoplastic right ventricular sinus which receives the tricuspid orifice (TO). An ostium primum defect is present and the lower edge of the septum primum (SP) straddles the left ventricle. The left atrium (LA) is seen beneath this through the primum defect. (CS—coronary sinus; PFO—patient foramen ovale.) (C) Hypoplastic right ventricular sinus (RVS) opened from behind. The hypoplastic tricuspid valve (TV) is tethered into this cavity. (D) The outlet chamber which supports the pulmonary artery has smooth infundibular (Inf) and apical trabeculated (T) portions. It is separated from the ventricular inflow portions by a well-formed anterior septum (AS). →

of St. Bartholomew's Hospital Medical School, London, and was brought to our attention by Professor O. J. Lewis. The atria were arranged in situs solitus and the arch and apex were to the left. The pulmonary artery was anterior and to the left of the aorta, and was about two-thirds of the size of the aorta. There was dominance of the right coronary artery, and a prominent right marginal

branch was observed (Fig. 7A). The venous drainage was normal, and the atrial septum was closed. The right atrium drained to a coarsely trabeculated ventricular sinus which was septated both from the left ventricle and from the right ventricular outflow portion (Fig. 7B-D). The valve in the right ventricular sinus was typical of a tricuspid valve, having multiple posterior papillary muscles, a large anterior

FIG. 5 Photographs of Case 3. (A) Anterior view of the heart. The great arteries (Ao, PA) are normally connected and related. The pulmonary artery arises from an anterior outlet chamber (OC). (B) Opened outlet chamber, which has a smooth upper infundibular portion (Inf) and an apical trabeculated segment (T). Note that the tricuspid valve is visible above the anterior septum (AS) through the outlet foramen (OF). (C) Left ventricular inflow tract. The mitral valve (MV) enters a coarsely trabeculated sinus (LVS) and communicates with the right ventricular sinus through an interventricular foramen (IVF). The aorta (AoV—aortic valve) overrides this foramen. (D) Anterior aspect of both ventricular inflow tracts, opened through a sagittal cut in the main ventricular chamber. The posterior part of the chambers is reflected to the top right part of the figure, and a posterior septum (PS) is seen separating the mitral and tricuspid valves (MV, TV), both being in continuity with the aortic valve (AoV). The anterior wall of the chamber is separated into right and left sides (RVS, LVS) by the shallow posterior septum (PS). The probe is placed in the outlet foramen beneath the tricuspid valve.

FIG. 6 Further photographs of Case 3. (A) Posterior wall of the main ventricular chamber, opened as described for Fig. 5D. The atrioventricular valves (TV, MV) are both in continuity with the aortic valve (AoV). The right and left ventricular sinuses (RVS, LVS) are separated by the posterior septum (PS), which approximates posteriorly to the ridge (PR) seen in primitive ventricular hearts. (B) View of the right ventricular sinus opened through its parietal wall. The right atrium (RA) communicates with this sinus (RVS) through the tricuspid valve. The septal (SC) and anterior (AC) cusps are seen, and the interventricular foramen (IVF) is visible. The outlet foramen is beneath the anterior cusp (To OF). (APM—anterior papillary muscle.) (C) Further view of the anterior parts of the ventricular inflow tracts opened through the sagittal incision described above. The probe is placed through the outflow foramen. Note that the anterior septum (AS) is separate from the posterior septum (PS).

FIG. 7 Drawings of Case 4. The heart was in a 'pot' in the anatomical museum of St. Bartholomew's Medical School, and could not be adequately photographed. (A) Anterior aspect of the heart, with the pulmonary artery (PA) arising from a discrete outlet chamber which is delimited by the anterior descending (LAD) and marginal coronary arteries ('delimiting artery'). (B) Detail of the outlet chamber with two outlet foramina. (C) Right ventricular inflow portion (VSD—ventricular septal defect; TSM—trabecula septomarginalis; OF—outlet foramen). (D) The left side of the heart.

papillary muscle, and a conal papillary muscle (Fig. 7C). The posterior septum was well formed and trabeculated on its right aspect. The left aspect was smooth, and a typical morphologically left ventricular sinus received a valve with morphological characteristics of the mitral valve (Fig. 7D). The aorta overrode a large defect between the right and left ventricular sinuses, and there was fibrous continuity between the aortic and mitral valves. The septum separating the right ventricular sinus from the outlet chamber was overlaid on its posterior aspect by a large trabecula septomarginalis which gave rise to conal and anterior papillary muscles (Fig. 7C). Defects were present between right ventricular sinus and outlet chamber both above and beneath the trabecula (Fig. 7C). The outlet chamber was a well-formed structure and possessed a smooth upper portion and a large apical segment which received both defects from the right ventricular inflow tract (Fig. 7B). The prominent marginal artery marked the position of the right part of the septum between inflow and outflow chambers (Fig. 7A).

The diagnosis was: (1) Solitus-concordant-normal connexions; (2) Fallot's tetralogy; (3) origin of pulmonary artery from discrete outlet chamber.

Discussion

The hearts described here have in common the feature that in each heart the anterior great artery (pulmonary artery) arose from a discrete outlet chamber. It is significant that this outlet chamber observed is directly comparable to the outlet chamber seen in 'single ventricle with outlet chamber' when this outlet chamber *also supports the pulmonary artery*. This situation in 'single ventricle' is frequently referred to as the 'Holmes' heart (Holmes, 1824; Rosenquist, Olney, and Roe, 1963; Marin-Garcia *et al.*, 1974; Somerville *et al.*, 1975). It is further significant that such outlet chambers are also directly comparable with the so-called 'right ventricle' seen in tricuspid atresia with normally connected great arteries (Edwards *et al.*, 1965; Gasul, Arcilla, and Lev, 1966).

The hearts described also have in common the fact that though the outlet chamber is separated from the right ventricular sinus by a well-formed anterior septum, the right ventricular septum is separated from the left ventricular sinus by a posterior septum of varying dimensions and proportions. In two of the hearts (Cases 2 and 3), this posterior septum is comparable with the 'posterior ridge' seen in 'single ventricle with outlet chamber' (Lev *et al.*, 1969; Anderson *et al.*, 1974). In one heart (Case 1), the septum is well formed but is

deviated as a consequence of hypoplasia of the right ventricular sinus. In the remaining heart (Case 4) the posterior septum is directly comparable to the normal interventricular septum, and indeed the relations between this septum and the aorta are as seen in Fallot's tetralogy. In each case, therefore, it is as though the right ventricle were divided into two portions, and 'two-chambered right ventricle' would be an alternative designation for each of the hearts. In this respect, Case 4 is very similar to some of the hearts recently reported within this designation by Rowland, Rosenthal, and Castaneda (1975).

The important feature of these hearts is that in each case discrete and different septa divide the inlet portions of the heart from each other and from an outlet chamber. This is of major significance in relation to hearts in which an outlet chamber is separated from a main ventricular chamber by an anterior septum, but in which the main chamber is unseptated and receives both atrioventricular valves ('single ventricle with outlet chamber'). De la Cruz and Miller (1968) have argued that in these hearts the anterior septum is the malaligned posterior septum. It is supposedly in anterior position as a consequence of failure of migration of the right atrioventricular canal to the bulbus. They quote as further evidence in support of this concept the fact that hearts are found in which the right valve straddles the anterior septum, arguing that these hearts are intermediate specimens in the process of migration of right atrioventricular orifice from left ventricle to bulbus. It is clear that the hearts presently described constitute important evidence against this hypothesis. Since both anterior and posterior septa are present in the same specimens, the one could not possibly be formed by realignment of the other as is implied by the concept of de la Cruz and Miller (1968).

It can be argued from our data that the anterior septum between the outlet chamber and right ventricular sinus is the original bulboventricular septum, while the posterior septum is the septum derived from growth within the primitive ventricle. This presumes that the right ventricle is developed after regression of the original right bulboventricular septum. However, it could equally be argued that the anterior septum is a 'false' septum, derived from the extensions of the conus septum together with the trabecula septomarginalis, as suggested by Lev (Gasul *et al.*, 1966; Lev *et al.*, 1969). Alternatively the 'septum' could be derived from anomalous insertion of the trabecula septomarginalis (or moderator band) as suggested by Rowland *et al.* (1975). Whatever the origin of the septum, there is no doubt in our minds that the septa seen in the hearts described here are directly

Absence of Interventricular Septum gives **PRIMITIVE VENTRICLE**

FIG. 8 Diagrams illustrating the concept of classification of univentricular hearts as 'primitive ventricle'. Primitive ventricle can be defined as absence of the posterior interventricular septum. Presence or absence of the right bulboventricular ridge (RBVR) then enables primitive ventricles to be classified as either 'primitive ventricle with outlet chamber' or 'primitive ventricle without outlet chamber'.

comparable with the septa seen in 'single ventricle with outlet chamber'. We suggest that if this septum is 'false' in one category, it is also 'false' in the other. Further evidence is pertinent to this problem. Van Praagh *et al.* (1964) had suggested that conducting tissue studies would solve the problem concerning the nature of the septum. Our own studies indicated that the septum in 'single ventricle with outlet chamber' carried both the atrioventricular bundle and bundle-branches (Anderson *et al.*, 1974). This finding was confirmed by Bharati and Lev (1975). However, these histological results still did not indicate whether the septum was in its anterior position as a consequence of failure of migration of the right atrioventricular orifice or persistence of the right bulboventricular ridge. We now believe that the present findings indicate that the anterior septum is indeed a persistent right bulboventricular ridge, and our gross studies in Cases 2 and 3 suggest that the anterior septum carries conducting tissue. We await histological confirmation of this fact. We, therefore, submit that the evidence presented indicates that, as suggested by Keith (1906) and endorsed by Lev *et al.* (1969), the definitive right ventricular sinus is a derivative of the primitive ventricle while the outlet portion can

persist as a discrete chamber derived from the primitive bulbus.

Although the premise of de la Cruz and Miller (1968) assumes that the primitive ventricle contributes only to the definitive left ventricle, these workers agree that the embryonic primitive ventricle initially receives the atrioventricular canal in its entirety. Lev *et al.* (1969) pointed out that whichever theory of development was adopted, it would always be correct to speak of the chamber receiving the atrioventricular valves in univentricular hearts as the *primitive ventricle*. We suggest that this can be extended to provide the basis of an alternative classification for the univentricular heart which totally avoids the use of the contentious terms 'single', 'common' or 'double inlet left' ventricle.

Primitive ventricle can properly be defined in anomalous conditions as absence of the posterior interventricular septum (Fig. 8). It can then be subdivided, depending upon presence or absence of the anterior bulboventricular septum, into *primitive ventricle with outlet chamber* and *primitive ventricle without outlet chamber* (Fig. 8).

This concept can be taken further. We indicated above that the outlet chambers in the hearts we have

described are directly comparable with the so-called right ventricle seen in tricuspid atresia. At present it is usual to exclude hearts with atresia of an atrioventricular orifice from the category of the univentricular heart (Van Praagh *et al.*, 1964; Gasul *et al.*, 1966). No scientific reason is given for this exclusion. We believe that the similarity in chamber morphology makes the exclusion unwarranted. Furthermore, we contend that the similarities are related to the fact that tricuspid atresia is morphogenetically linked to primitive ventricle. It has previously been argued by others that primitive ventricle itself results from lack of migration of the atrioventricular canal across the bulboventricular septum. We have argued that this is not the case, since our evidence indicates that primitive ventricle is a consequence of failure of development of the posterior septum. This process would demand normal *expansion* of the atrioventricular canal in order to form right and left atrioventricular orifices. It can be shown that

absence of the posterior septum coupled with *failure of expansion* of the atrioventricular canal, and eccentric fusion of the endocardial cushions and the septum primum would result in formation of hearts with atresia of the right atrioventricular orifice (Fig. 9). Thus, since the posterior septum would be absent, tricuspid atresia could justifiably be considered as a variant of primitive ventricle. Furthermore, it could be expected to exist with or without an outlet chamber. Extending this argument, it follows that straddling right atrioventricular valve cannot be explained on the basis of incomplete migration of the valve to the bulbus. Further evidence in favour of this conclusion comes from the study of Dor and Corone (1973). In their experimental study of the chick heart, they showed that actual *migration* of the atrioventricular canal did not occur. However, their investigation did not rule out the possibility of *expansion* of the canal during development. On our theory, straddling valves can be easily accounted for, since the septum

FIG. 9 Diagrams illustrating the similarity in morphogenesis between primitive ventricle with two atrioventricular valves and tricuspid atresia. Both can be considered as absence of the posterior interventricular septum and persistence of the bulboventricular septum. Tricuspid atresia results from failure of expansion of the atrioventricular canal together with eccentric fusion of the endocardial cushions. In contrast, primitive ventricle with two valves demands normal expansion of the atrioventricular canal. (B—bulbus; V—primitive ventricle; Ao—aorta; PA—pulmonary artery; TA—tricuspid atresia; PR—posterior ridge.)

FIG. 10 Diagrams illustrating the concept of straddling atrioventricular valves. (A) Frontal section through the primitive heart tube (A—primitive atrium; PV—primitive ventricle; B—bulbus; T—truncus). (B) Cross-section at the level of the line. The right and left bulboventricular ridges (RBVR, LBVR) separate bulbus from primitive ventricle. The primitive ventricle itself is divided into the right ventricular sinus (RVS) and left ventricular sinus (LVS) by the interventricular ridge (IVR). (C) Should the bulbus persist as an outlet chamber (OC) with primitive ventricle (PV), then the right atrioventricular valve can straddle the bulboventricular septum. The left atrioventricular valve may also straddle the bulboventricular septum in primitive ventricle with outlet chamber. (D) The mitral valve may also straddle the interventricular septum when right and left ventricles are normally separated (Inf—infundibulum). Reprinted from Shinebourne, Macartney, and Anderson (1976).

straddled in the case of the right valve would be the bulboventricular septum rather than the interventricular septum (Fig. 10). Thus if the anterior papillary muscle arose from the bulbus rather than from the primitive ventricle, in a situation in which the anterior septum was not completely resorbed, then primitive ventricle with outlet chamber and straddling right atrioventricular valve would be formed, as described by Liberthson *et al.* (1971). (Fig. 10).

We, therefore, propose that the univentricular heart is defined as a heart in which the posterior interventricular septum is absent. Such hearts can exist with or without an outlet chamber, with atresia of an atrioventricular orifice, or with a straddling atrioventricular valve. It also follows that the hearts can exist with all possible combinations of atrial chamber morphology and with all possible ventriculo-arterial connexions (Fig. 11). We have thus far studied approximately 200 hearts

FIG. 11 Diagram illustrating the possible variations which may be expected in the anomaly of primitive ventricle, defined as absence of the posterior interventricular septum. The scheme is based upon the premises that (a) primitive ventricle can exist with or without an outlet chamber; (b) with any disposition of atrial chambers; (c) with varying malformations of the atrioventricular valves (AVV); (d) with any possible ventriculo-arterial connexion.

in these categories and the results are in complete agreement with the hypothesis presently advanced. These findings will be published in the near future (R. H. Anderson, A. E. Becker and J. L. Wilkinson, unpublished observations).

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References

- Anderson, R. H., Arnold, R., Thapar, M. K., Jones, R. S., and Hamilton, D. I. (1974). Cardiac specialized tissue in hearts with an apparently single ventricular chamber (double inlet left ventricle). *American Journal of Cardiology*, **33**, 95.
- Bharati, S., and Lev, M. (1975). The course of the conduction system in single ventricle with inverted (L-) loop and inverted (L-) transposition. *Circulation*, **51**, 723.
- De La Cruz, M. V., and Miller, B. L. (1968). Double-inlet left ventricle: two pathological specimens with comments on the embryology and on its relation to single ventricle. *Circulation*, **37**, 249.
- De Vries, P. A., and Saunders, J. B. C. M. (1962). Development of the ventricles and spiral outflow tract in the human heart. *Carnegie Institution of Washington, Contributions to Embryology*, **37**, 89.
- Dor, X., and Corone, P. (1973). Le rôle du conus dans la morphogenèse cardiaque. Essai d'étude sur l'embryon de poulet. *Coeur*, **4**, 207.
- Edwards, J. E., Carey, L. S., Neufeld, H. N., and Lester, R. G. (1965). *Congenital Heart Disease*, p. 358, W. B. Saunders, Philadelphia.
- Gasul, B. M., Arcilla, R. A., and Lev, M. (1966). *Heart Disease in Children*, p. 289. J. B. Lippincott, Philadelphia.
- Harley, H. R. S. (1958). The embryology of cor triloculare biatriatum with bulbar (rudimentary) cavity. *Guy's Hospital Reports*, **107**, 116.

- Holmes, A. F. (1824). A case of malformation of the heart. *Transactions of the Medical and Chirurgical Society of Edinburgh*, Vol. I, p. 252; republished by Abbot, M. E. (1901). *Montreal Medical Journal*, **30**, 522.
- Keith, A. (1906). Malformations of the bulbus cordis. An unrecognized division of the human heart. Quatercentenary Publication, p. 55–76. University of Aberdeen.
- Keith, A. (1909). Malformations of the Heart. *Lancet*, **2**, 359, 433, and 519.
- Lev, M. (1953). *Autopsy Diagnosis of Congenitally Malformed Hearts*, p. 154. Charles C Thomas, Springfield, Illinois.
- Lev, M., Liberthson, R. R., Kirkpatrick, J. R., Eckner, F. A. O., and Arcilla, R. A. (1969). Single (primitive) ventricle. *Circulation*, **39**, 577.
- Lev, M., Paul, M. H., and Miller, R. A. (1962). A classification of congenital heart disease based on the pathologic complex. *American Journal of Cardiology*, **10**, 733.
- Liberthson, R. R., Paul, M. H., Muster, A. J., Arcilla, R. A., Eckner, F. A. O., and Lev, M. (1971). Straddling and displaced atrioventricular orifices and valves with primitive ventricles. *Circulation*, **43**, 213.
- Marin-Garcia, J., Tandon, R., Moller, J. H., and Edwards, J. E. (1974). Common (single) ventricle with normally related great vessels. *Circulation*, **49**, 565.
- Pernkopf, E., and Wirtinger, W. (1933). Die Transposition der Herzostien—ein Versuch der Erklärung dieser Erscheinung: Die Phonomie der Herznetzwicklung. *Zeitschrift für Anatomie und Entwicklungsgeschichte*, **100**, 563.
- Rosenquist, G., Olney, M., and Roe, B. B. (1963). The Holmes heart—a variant of Cor Triloculare Biatritum: report of a case in a child. *Circulation*, **27**, 1143.
- Rowland, T. W., Rosenthal, A., and Castaneda, A. R. (1975). Double-chamber right ventricle: experience with 17 cases. *American Heart Journal*, **89**, 455.
- Shinebourne, E. A., Macartney, F. J., and Anderson, R. H. (1976). Sequential chamber localization. The logical approach to diagnosis in congenital heart disease. *British Heart Journal*, **38**, 327.
- Somerville, J., Becu, L., and Ross, D. (1974). Common ventricle with acquired subaortic obstruction. *American Journal of Cardiology*, **34**, 206.
- Somerville, J., Ross, D. N., Yacoub, M., and Radley-Smith, R. (1975). Primitive ventricle with acquired subpulmonary stenosis. *European Journal of Cardiology*, **3**, 193.
- Streeter, G. L. (1942, 1945, 1948). Developmental Horizons in Human Embryos. *Carnegie Institution of Washington Contributions to Embryology*, **30**, 211; **31**, 27; **32**, 133.
- Van Praagh, R., Ongley, P. A., and Swan, H. J. C. (1964). Anatomic types of single or common ventricle in man. *American Journal of Cardiology*, **13**, 367.

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