Double-Inlet Left Ventricle

Two Pathological Specimens with Comments on the Embryology and on Its Relation to Single Ventricle

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SUMMARY

Two pathological specimens are presented in which the morphological left ventricle contains the right atrioventricular ostium, completely or in its major portion and, totally, the left atrioventricular ostium. It is suggested from a consideration of these cases and of the pathological material available in the literature that this constitutes an entity that can be usefully separated from the heterogeneous group of single ventricle with which it has previously been classified. The entity is called double-inlet left ventricle and is defined as existing when two separate atrioventricular ostia open in a morphological left ventricle.

An ontogenetic explanation is presented based on the study of normal human embryos. These cases resemble the heart of the embryo during the horizons XIII to XVI of Streeter. It is suggested that there has been a partial arrest in the widening of the atrioventricular canal and the changing relation of the atria with the ventricles at these stages.

It is noted that both atria open into the morphological left ventricle whether situated to the left or to the right. This is an expected finding, since the left ventricle is derived from the primitive ventricle and the primitive ventricle is always connected with both atria during the early stages of embryological development.

Other malformations include transposition of the great arteries in both cases and ventricular inversion in one.

Two pathological specimens are presented in which the morphological left ventricle contains the right atrioventricular ostium, completely or in its major portion and, totally, the left atrioventricular ostium. This condition, called double-inlet left ventricle, is presented as further documentation of the premise that many, if not most, of the congenital entities of the heart and great vessels represent the persistence of normal developmental stages. These two hearts, described in detail to allow comparison with subsequent case material, are key anatomicopathological cases in illustrating the principle of arrested development as it concerns the A-V (atrioventricular) canal. Embryologically, this would represent a very early arrest in the development of the A-V canal, between horizons XIII and XVI of Streeter.*

It is postulated that widening of the A-V canal exerts a major influence, by bringing an atrial chamber to make contact with the bulbus cordis, on the normal development of the morphological right ventricle. An arrest in this process of expansion of the A-V canal would result in the atria remaining with the morphological left ventricle, which is derived from the primitive ventricle and in underdevelopment of the right ventricle.

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*See references.
Figure 1

Anatomical specimen of a case of double-inlet left ventricle, type A. A. External view of the heart, showing the aorta (Ao) anterior and parallel to the pulmonary artery (PA), the charac-
DOUBLE-INLET LEFT VENTRICLE

With this concept of the embryo-anatomicopathology of these cases, it is suggested that double-inlet left ventricle be extracted from the heterogeneous group of single ventricle, common ventricle, and cor triloculare biatriatum with which it has previously been classified. "Double-inlet left ventricle" would appear to be a simple and connotative term for the entity.

The associated malformations in these cases, including straight truncoconal septum in both, and inversion of the bulboventricular loop in one, and less rare, have been discussed previously.1-3

Description of Specimens

Case 1

Specimen 1067 was a 5-year-old boy at time of death. The heart is in a visceroatrial situs solitus individual, and the apex is to the left (fig. 1A). The atrium, which has the anatomical features of a right atrium, is situated on the right and is dilated. The left atrium* is situated on the left and is small. The ventricles are normally situated, that is, the right ventricle, containing parietal and septal bands of the crista supraventricularis, the anterior papillary muscle, and the papillary muscles of the free wall of the type seen in the right ventricle, is situated to the right (fig. 1B). The right ventricle is hypertrophied but small. The left ventricle is to the left and posteriorly and is hypertrophied and dilated (fig. 1C).

The aorta arises from the right ventricle in front of the crista supraventricularis (fig. 1B). Its course is parallel and anterior with relation to the pulmonary artery, which has a discretely diminished caliber, being of smaller diameter than the aorta (fig. 1A). The pulmonary artery also arises from the right ventricle, but it is behind the crista supraventricularis and overrides slightly the interventricular septum. There is valvular as well as subvalvular pulmonary stenosis, and the pulmonary valve is bivalvar. The branches of the pulmonary artery are normal. The ductus arteriosus is closed.

There is a large ventricular septal defect in the basal portion of the septum, extending from the posterior part of the crista supraventricularis to the posterior wall of the ventricles and occupying one fourth of the septum measured from its apex to the base. The foramen ovale is probe patent; the remainder of the atrial septum is intact.

The left atrium opens by means of a mitral orifice into the left ventricle (fig. 1C). The ring of the mitral valve is of discretely reduced diameter. The right atrium opens through a tricuspid orifice almost totally into the left ventricle, a small portion opening into the right ventricle (fig. 1C). Consequently, the tricuspid valve overrides the ventricular septum. The mitral and tricuspid orifices are completely separated (fig. 1D). The aortic leaflet of the mitral valve is intact, there being no suggestion of a cleft.

The anterior leaflet of the tricuspid valve is small and inserts in the right ventricle, partly into the anterior papillary muscle and partly into the papillary muscles of the free wall. A very small portion of the septal leaflet of the tricuspid valve inserts into the posterior group of papillary muscles of the left ventricle, the major portion inserting into the anterior papillary muscle of the right ventricle. The posterior leaflet is divided into two portions of equal size. The portion adjacent to the anterior leaflet inserts into the free wall of the right ventricle, partly into papillary muscles and partly directly by means of chordae tendineae. The portion adjacent to the septal leaflet inserts into the posterior group of papillary muscles of the left ventricle. Hence, the insertion of the tricuspid valve leaflets is predominantly in the right ventricle although the ostium is almost entirely in the left ventricle.

The parts of both leaflets of the mitral valve that are contiguous to the external commissure...
Figure 2
Anatomical specimen of a case of double-inlet left ventricle, type B. 
A. Right lateral view of the heart. The aorta (Ao) is anterior and parallel to the pulmonary artery (PA), the character-
insert into the anterior group of papillary muscles of the left ventricle. At the internal commissure the two leaflets unite to insert also in the left ventricle, but directly into the septum by means of chordae tendineae. Diagnoses were transposition of the great arteries in situs solitus; pulmonary stenosis, valvular and subvalvular; double-outlet right ventricle; overriding of the pulmonary artery; ventricular septal defect; double-inlet left ventricle; overriding of the tricuspid valve; mitral valve-ring stenosis, slight; probe-patent foramen ovale.

Case 2
Specimen 2948 was a 2½-year-old boy at time of death. The heart is in a viscerocardial situs solitus with the apex to the left (fig. 2A). The right atrium is situated on the right and is slightly dilated. The left atrium is situated on the left and is dilated and hypertrophied. There is inversion of the ventricles. The left ventricle (whose septum is smooth in its upper two thirds and trabeculated only in its lower third and which contains two groups of papillary muscles) is located on the right and is markedly dilated and hypertrophied (fig. 2C). The infundibulum of the right ventricle, containing the parietal band of the crista supraventricularis and a small area of the interventricular septum, is situated to the left and superiority, and presents a small chamber but normal thickness of the free wall (fig. 2B).

The aorta is of normal caliber and arises from the right ventricle in front of the crista supraventricularis (fig. 2B). Its course is parallel, to the left and anterior with relation to the pulmonary artery, which is also of normal caliber, being slightly larger than the aorta (fig. 2A). The pulmonary artery arises from the left ventricle. Neither the pulmonary artery nor the aorta is stenosed; the valvular and infundibular portions of both are normal.

There is a small ventricular septal defect (9 by 7 mm as compared to the aortic orifice of 17-mm diameter) in the basal portion of the septum behind the aorta by means of which the left ventricle communicates with the infundibulum of the right ventricle. The foramen ovale is probe patent, the remainder of the atrial septum being intact. The branches of the pulmonary artery are normal. The ductus arteriosus is closed.

The left atrium opens by means of a mitral orifice into the left ventricle (fig. 2C). The ring of this orifice is of moderately reduced diameter, producing mitral stenosis. The valve leaflets are normal but both insert into the posterior group of papillary muscles of the left ventricle.

The right atrium also opens entirely into the left ventricle (fig. 2C), and does so through an atrioventricular orifice, which is completely separate (fig. 2D) but similarly is bicuspid. The anterior leaflet inserts into the anterior group of papillary muscles and the posterior leaflet inserts into the posterior group of papillary muscles of the left ventricle. Diagnoses were ventricular inversion with transposition of the great arteries in situs solitus (corrected transposition in situs solitus); ventricular septal defect; double-inlet left ventricle; mitral valve-ring stenosis; probe-patent foramen ovale.

Discussion
Double-inlet left ventricle exists when two separate A-V ostia open in a morphological left ventricle. This definition excludes cases in which there is atresia of either the mitral or tricuspid valve, or in which there is a common A-V valve, as occurs in various forms of endocardial cushion defects. Accessory mitral valve, or double mitral orifice, is also excluded, as this is not “two separate A-V ostia” opening in the left ventricle, but merely a developmental rent in a leaflet of the mitral valve. Similarly, cor triatriatum, or congenital stenosis of the common pulmonary vein, should cause no difficulty, as it consists of a musculofibrous partition across the chamber of the left atrium and is easily distinguished from an A-V ostium. Furthermore, that the ostia open in a morphological left ventricle should make it evident that the left ventricle is identifiable by usual internal anatomical characteristics, that the interven-

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*istic relationship of transposition of the great vessels. B. Left lateral view of the heart, showing the morphological right ventricle situated to the left and opened. Observe the aorta (Ao) emerging in front of the crista supraventricularis (CS). C. Right lateral view of the heart, showing the opened morphological left ventricle situated to the right. The arrow (1) that crosses the mitral orifice (M) indicates that this opens into the left ventricle, and the arrow (2) that crosses the tricuspid orifice indicates that it also opens exclusively within the left ventricle. D. The opened atria, seen from above, showing that the tricuspid (T) and the mitral (M) orifices are completely separated and that there is no splitting of the leaflets.*
tricular septum is present, and that the right ventricle, although expected to be small and frequently represented only by the infundibular portion, can also be identified.

It should be stated that the partition between the infundibulum and the larger ventricular chamber in these cases is considered to be the interventricular septum, which is abnormally situated owing to the lack of development of the sinus region of the right ventricle. The morphological features of the septum, especially well illustrated by case 2 (fig. 2C), support other findings that have recently been reviewed by Van Praagh and associates, who arrived at the same conclusion. The authors also agree with the aforementioned that this malformation is not related to the single ventricle of lower animals (for example, the frog), but is an abnormality of ontogenetic development rather than a phylogenetic regression.

Furthermore, the definition of double-inlet left ventricle, it should be noted, concerns itself with the inflow portion of the heart and does not specify the state of the great vessels; nor does it dictate the presence or absence of septal defects although a ventricular septal defect would be expected for reasons explained below.

Both cases presented above have double-inlet left ventricles. The left ventricle contains the left A-V ostium completely in both, whereas it contains the right A-V ostium completely in one, and, partially, though in its major portion, in the other. The differences in the two types of double-inlet left ventricle represented can be summarized as follows. In case 1 the tricuspid valve overrides slightly the interventricular septum (figs. 1C and 3d), and the right ventricle although small is complete, having easily identified landmarks of both the sinus region* and the outflow tract. However, in case 2 both A-V ostia open entirely in the left ventricle, with no overriding, and the right ventricle is represented only by the infundibulum.†

The importance of the differences in these two types of double-inlet left ventricle is that a correlation emerges suggesting an embryological mechanism. The findings imply that as an atrial chamber makes increasing functional contact with the morphological right ventricle, development of the ventricle advances further toward normality. When the right atrium made partial contact with the right ventricle, the ventricle, although small, developed all its components. Thus case 1 occupies a key position in suggesting a spectrum of possibilities between normality and the situation in which there is no atrial contact with the right ventricle, which is represented only by the infundibulum (case 2). The embryological explanation of the observed relationship is presented below.

Relation of Double-Inlet Left Ventricle to Single Ventricle

Double-inlet left ventricle has been included by other authors in the heterogeneous group of single ventricle, common ventricle, and cor triloculare biaatriatum. Although we suggest that double-inlet left ventricle constitutes an entity that is best removed from this group, it is only in these classifications

*The sinus region of the right ventricle includes all of the inflow tract—that portion posteroinferior to the muscular ring made up of the parietal and septal bands of the crista supraventricularis, the moderator band, and the anterior papillary muscle. It is also limited by the A-V valve. Additional identification features are the trabeculated character of the septum and the type of papillary muscles, several single muscles rather than two groups as seen in the left ventricle. It is probable that the sinus region also includes that portion of the outflow tract from the muscular ring described above up to the inferior border of the infundibulum, a suggestion supported by the frequency of a single ventricle with an infundibular chamber.

†The infundibulum is only the cephalic portion of the outflow tract of the right ventricle. Its walls are the parietal portion of the crista supraventricularis, the interventricular septum, and the free wall of the right ventricle. The superior limit is the floor of the sigmoid valve, and the inferior limit is an imaginary plane at the level of the inferior border of the parietal portion of the crista supraventricularis perpendicular to the interventricular septum and the free wall of the right ventricle.
that we can search for similar cases and incidence of occurrence at this juncture. However, in so doing we can also consider further the relationship of double-inlet left ventricle to the group.

Van Praagh and collaborators, noting the deficiencies in grouping such dissimilar cases, have offered a subclassification of single ventricle according to the sinus portions, types A-D, and the outflow portions, I-IV. Of 47 cases in Van Praagh's type-A single ventricle, described as absence of the right ventricular sinus and containing cases with a common A-V valve as well as cases with separate A-V ostia, 33 appear to fit the definition of double-inlet left ventricle. Two cases are shown (their figs. 10 and 12) with overriding tricuspid valve similar to our case 1, and other cases are shown that are similar to our case 2 with both A-V ostia completely in the left ventricle. However, the number of cases pertaining to each group does not emerge. From the facts that a single ventricle with a rudimentary outlet chamber has been the most common type of single ventricle reported and that there has been little mention of an overriding tricuspid valve, it seems that double-inlet left ventricle with both ostia completely in the left ventricle may be more common. The only other cases that appear to be double-inlet left ventricle with overriding tricuspid valve we have encountered in the literature are the three cases reported by Keith and associates as "overriding tricuspid valve in complete transposition of the great vessels" with no further details given.

Fontana and Edwards in analyzing pathological specimens of patients with congenital heart disease found an incidence of cor triloculare biaatriatum of 2.1% in selected studies, and 3.4% in their own material. Although in this series cases with a common A-V valve were excluded, an unspecified number had atresia of one or the other of the A-V ostia. In a recent series Elliot and associates reported 11 of a group of 26 cases of common cardiac ventricle with transposition of the great vessels, that were apparently cases of double-inlet ventricle.

In summary, we consider single ventricle, common ventricle, and cor triloculare biaatri-
Figure 4

Frontal view drawings of molding of the cavities of normal human hearts in different stages

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Figure 5

Frontal views of moldings of the cavities of a normal heart from a human embryo at horizon XVII. Note the complete division of the atrioventricular canal and the establishment of communication from each of the atria to its respective ventricle. (From Streeter, G. L.: Contrib Embryol 32: 133, 1948.)

Normal Embryology Relevant to This Condition

In the young human embryos studied by Davis, he was able to identify, by the sulci that separated them, the following cardiac cavities: bulbus aorticus, bulbus cordis, primitive ventricle, and atria. Also, he described an endocardial plate made up of endothelial trabeculae extending toward the myocardium in the bulbus cordis and another in the primitive ventricle. Streeter continued the work of Davis, studying older embryos and discovered that the endocardial plate of the bulbus cordis forms the trabecular portion of the right ventricle, and that the endocardial...
plate of the primitive ventricle gives origin to the left ventricle.

Kramer,\textsuperscript{13} in studying the partitioning of the truncus conus, found that the narrow cephalic portion of the bulbus cordis (conus) gives origin to the infundibulum of the right ventricle and the cephalic portion of the outflow tract of the left ventricle. In this stage of development, however, the bulbus aorticus has been transformed into the truncus and the sulci that had separated the bulbus aorticus from the bulbus cordis in the younger embryos have disappeared. For this reason there is no anatomical separation between the truncus (bulbus aorticus) and conus (part of the bulbus cordis), and Kramer\textsuperscript{13} fixed as an arbitrary level that where the aortic and pulmonary valves are later formed.

In summary, the bulbus cordis gives origin to all of the right ventricle, the sinus region as well as the outflow tract. The primitive ventricle gives origin to all of the left ventricle except the cephalic portion of the outflow tract, which is derived from the conus (bulbus cordis) and acquired by the left ventricle when the conoventricular flange disappears.

The atria at the time of formation of the primitive heart tube are caudal and connect with the primitive ventricle. On completion of the formation of the bulboventricular loop (horizon XIII)\textsuperscript{11} both atria are still connected with the left ventricle, which has developed from the primitive ventricle (fig. 4B). At this stage, however, the atria already occupy a dorsal cephalic position as in the adult heart. Widening of the atroventricular canal begins in horizon XIII, but both atria continue to be connected to the left ventricle through horizon XV,\textsuperscript{12} the stage in which partitioning of the truncus conus (connected with the right ventricle) begins (fig. 4C). It is in horizon XVI\textsuperscript{12} that the development of the atroventricular ostia begins and that the right atrium first makes connection, through further widening of the canal, with the right ventricle, the left atrium remaining with the left ventricle (fig. 4D). The separation of the single atroventricular canal is due to the development of two endocardial cushions, the dorsal and the ventral. The separation of the atroventricular canal is complete with the right atrium connecting only with the right ventricle and the left atrium connecting only with the left ventricle in horizon XVII\textsuperscript{12} (fig. 5).

From the beginning of the circulation of the blood through horizon XV\textsuperscript{12} the route of the blood through the heart is from the two atria to the left ventricle (primitive ventricle), and from there through the right ventricle and the truncus conus. It is important to note that in all of the stages in which the right atrium is still connected with the left ventricle, the right ventricle, in spite of giving rise to the truncus conus, remains small. This lack of development may suggest that the

\begin{figure}[h]
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\includegraphics[width=0.5\textwidth]{figure6.png}
\caption{Photomicrograph of the frontal view of the normal heart of a chick embryo of 5 days' development. Observe the two atria communicating fundamentally with the left ventricle. LA, left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle; T, truncus.}
\end{figure}
left ventricle provides the motive force, and the right ventricle is, relatively, an outflow tube at this stage. When the right atrium makes connection with the right ventricle the latter develops and expands rapidly.

Studies of the chick embryo heart show that both atria are initially in contact with the left (primitive) ventricle (fig. 6) and only later does the right atrium make contact with the right ventricle. Direct observation of the functioning chick embryo heart lends dynamic support to the suggestion that the left ventricle is the propelling force until the right atrium makes contact with the bulbus cordis.

**Anatomicoembryological Correlation**

The two cases of double-inlet left ventricle presented here have both atria communicating with the left ventricle, which is a characteristic of the embryo up to horizon XVI. The difference is that in these cases the A-V canal continued to develop, producing two separate complete A-V ostia, whereas in the embryo this normally occurs only as the right atrium makes improved and exclusive connection with the right ventricle, horizons XVI and XVII.

Case 1 strongly resembles the embryo of horizon XVI, in which the right atrium is just beginning to make contact with the right ventricle (fig. 4D). The tricuspid orifice overrides the interventricular septum with its major portion still emptying into the left ventricle. Both the sinus region and the outflow tract of the right ventricle are present but poorly developed. There is a large basal medial ventricular septal defect due to the lack of alignment of the endocardial cushions of the A-V canal, which are displaced to the left, with the muscular portion of the septum which grows up from below. The lateral position of the truncus conus, which causes both great vessels to stay with the right ventricle, that is, a double-outlet right ventricle, demonstrates an arrest in development of the outflow area at approximately the same time as the arrest of the A-V canal expansion. In addition, the lateral position prevents alignment of the truncoconal ridges with the muscular portion of the septum, so that this contribution to the formation of the septum is also lacking.

Case 2 has maintained approximately the condition seen in the embryo in horizon XIII, although the right ventricle is even less developed (fig. 4B). There has been nearly complete failure of development of the endocardial plate of the bulbus cordis, and the only part of the right ventricle to develop well was the infundibulum, which is derived from the conus portion of the bulbus cordis. The sinus region, or trabecular zone, of the right ventricle is absent. Both atria thus open entirely into the left ventricle, but with the characteristic that the A-V canal is divided into two A-V ostia. This division normally occurs in the embryo only when the A-V canal widens to bring the right atrium to connect with the right ventricle, beginning in horizon XVI. It is interesting to note that the development of the trabecular pouch of the left ventricle, which is derived from the endocardial plate of the primitive ventricle, produces, even in the absence of development of the sinus region of the right ventricle, a left surface of the interventricular septum with all of the normal elements, smooth in its upper portion and trabeculated in its lower portion. A small ventricular septal defect connects the left ventricle with the infundibulum of the right ventricle.

Both cases are in viscerocarial situs solitus and, in both, the heart is normally situated with the apex to the left. Both have transposition of the great arteries, which depends on the development of a straight truncoconal septum, causing the aorta to lie anterior and parallel to the pulmonary artery (fig. 3D and E). Case 1 has a degree of lateral position, causing the truncus conus to arise from the morphological right ventricle, and, due to the transposition, it is the pulmonary artery that overrides the interventricular septum. Furthermore, case 1 has unequal partition of the truncus conus at the expense of the pulmonary artery, causing
valvular and subvalvular pulmonary stenosis. In case 2 the truncus conus arrived at the midline normally and the partitioning was equal; hence, the aorta arises from the infundibulum of the right ventricle (due to the transposition), and the pulmonary artery entirely from the left ventricle. Both cases have stenosis of the mitral orifice, which may be due to unequal partition of the A-V canal or to failure of the left portion of the canal to widen.

The atria are connected with the ventricle that is morphologically the left ventricle in both cases, although one case has the ventricles normally situated and the other has ventricular inversion. The morphological left ventricle is derived from the primitive ventricle and is therefore the ventricle which is more apt to be connected with the atria because this condition is found in some stages of the normal development of the heart. This is true regardless of whether the left ventricle is situated to the right or to the left relative to the right ventricle, since this depends only on the rightward or leftward torsion of the bulboventricular loop (fig. 3A, B, and C).

References
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