What are double-outlet left atrium and double-outlet right atrium?

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Briefly, these are rare *ventriculo-atrial malalignment defects*.

You may be wondering, 'What does THAT mean?' If so, a little anatomic and embryologic knowledge greatly facilitates understanding.

Let's assume that visceroatrial situs solitus is present, i.e., that the locations of the viscera and atria are normal. The morphologically (anatomically) right atrium (RA) lies to the right of the morphologically (anatomically) left atrium (LA).

Let's also assume that D-loop ventricles are present, i.e., that the interrelationship between the ventricles is normal. The morphologically right ventricle (RV) is located to the right of the morphologically left ventricle (LV).

It is also important to know that the atria and the ventricles do not connect with each other muscle-to-muscle, because of the interposition of the atrioventricular (AV) canal or junction. This is why the ventricles can be aligned with the atria in almost any conceivable way – because the ventricles do not connect directly with the atria. If the RV were connected directly with the RA, and if the LV were connected directly with LA, then the many ventriculo-atrial malalignments that occur in congenital heart disease – e.g., atrioventricular discordance – would probably be developmentally impossible.

The three main cardiac segments are the atria, the ventricles, and the great arteries. The main segments are like the "bricks."

The two connecting cardiac segments are the AV canal or junction, and the conus arteriosus or infundibulum. The connecting segments are like "mortar" that connect, and separate the main segments (the "bricks"). The AV canal or junction normally also electrically insulates the ventricles from the atria, except at the AV bundle of His.

Because the three main cardiac segment {atria, ventricles, great arteries} do not connect directly with each other, due to the interposition of the two connecting cardiac segments, this is why so many possible alignments can occur between adjacent segments.

Thus, the distinction between cardiac segmental *alignments* and cardiac segmental *connections* is fundamental:

1. The three main cardiac segments can be aligned in many different ways because they normally do not connect with each other tissue-to-tissue.
2. The connecting cardiac segments normally connect and separate the main cardiac segments.
3. Thus, the main cardiac segments *are connected* in many different ways in congenital heart disease. Please note the passive voice of the verb *are connected*. The main cardiac segments do not *connect* in many different ways in congenital heart disease. The active voice of the verb *connect* is wrong embryologically and anatomically.

The fact that the three main cardiac segments do not connect directly, because of the two intervening connecting cardiac segments, helps to explain why so much of the complexity of congenital heart disease is possible. Double-outlet left atrium (DOLA) and double-outlet right atrium (DORA) are rare cases in point.

It also helps to know that the atria are relatively fixed in position by the great veins (the inferior vena cava and the superior vena cava), the diaphragm, the pulmonary veins, and the lungs.

In contrast, the bulboventricular heart tube is a "professional contortionist" that undergoes a great deal of movement during normal cardiac morphogenesis.
Highlights:

1. The mesoderm develops from the ectoderm on the 15th day of life in the normal human embryo.
2. The cardiogenic crescent of precardiac mesoderm is formed by the 18th day of age following fertilization. The intra-embryonic celom – the precursor of the body cavities also appears on day 18.
3. The cardiogenic crescent becomes a straight heart tube by 20 days of embryonic age.
4. By 21 days of age, normal D-loop formation of the heart tube begins, and the heart starts to beat at the end of the third week of life.
5. In the fourth week of embryonic life (days 22 to 28), D-loop formation normally is completed; the LV and

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the RV begin to be developed – the LV somewhat ahead of the RV; the circulation begins; and cardiovascular septation is initiated.

6. In the fifth week of life (days 29 to 35), the LV, RV, and ventricular septum continue to develop; the aorta passes through the interventricular foramen and comes into continuity with the developing mitral valve and the LV; the aorta and the pulmonary artery are separated by the aorticopulmonary septum; the mitral and tricuspid valves are separated; the right ventricle enlarges; *the ventricular septum moves leftward, beginning to become aligned with the atrial septum*; *the tricuspid valve now opens into the RV, made possible by the leftward movement of the ventricles and the ventricular septum*; the ostium primum normally is closed by the endocardial cushions of the AV canal, thereby separating the atria; and the ventricles and the ventricular apex continue to move leftward. Thus the ventricular apex has moved horizontally from right to left: From dextrocardia following D-loop formation, through mesocardia, to normal levocardia.

This leftward movement of the ventricles results in concordant AV alignments: RA to RV and LA to LV. Hence, the 5th week of embryonic life is when the primitive *in-series circulation*, i.e., RA to LA to LV to RV to great arteries is converted to the definitive *in-parallel pulmonary and systemic circulations,* i.e., RA to RV to pulmonary artery (PA), and LA to LV to aorta (Ao). The fifth week is also when cardiovascular septation is nearly completed.

In the sixth and seventh weeks of embryonic life (days 36 to 49), the conal (infundibular) septum normally is closed, and the membranous interventricular septum also normally closes. Although normal closure of the membranous septum usually occurs between 38 and 45 days of embryonic age, this final event in cardiovascular septation can be delayed until after birth, when it is known as *spontaneous closure* of a ventricular septal defect, *spontaneous* meaning interventionally or surgically unassisted closure.

So, what are DOLA and DORA? They are really defects in ventricular development. As in the paper concerning DOLA in this issue of the Annals,[1] the ventricles and ventricular septum have moved too far to the left relative to the atria and the atrial septum. Consequently, the ventricular septum is malaligned to the left of the atrial septum. Consequently, the LA opens into both the LV and the RV. And the RA opens into nothing because the RV lies to the left of the RA.

Thus, *the excessively left shifted ventricles and ventricular septum* resulted in both DOLA (LA to LV, and LA to RV) and in right atrial outlet atresia (RA opening into neither ventricle). In DOLA, the problem is ventriculoatrial malalignment with excessive left-shift of the ventricles.

DORA is the opposite, as is also well documented in this issue of the Annals.[2] *There was subnormal leftward movement of the ventricles and ventricular septum relative to the atria and the atrial septum.* Consequently, the ventricular septum lay anteroinferiorly relative to the RA, and the atrial septum lay well to the left of the ventricular septum. Hence, the RA opened into both the RV and the LV. The LA also opened into the LV; and there was no mention of mitral stenosis secondary to the rightward ventricular malalignment relative to the atria, which can occur.

When multiple orifices are present in an AV valve, and when all orifices of that valve drain into one and the same ventricle, this we call multiple orifice AV valve,[3] for example *double-orifice mitral valve,*[4] and *double-orifice tricuspid valve*.

But when multiple orifices are present in an AV valve, and when these orifices drain into two different ventricles, this we call double-outlet atrium, for example, *double-outlet right atrium,*[5] and *double-outlet left atrium*.

Where the AV orifice drains is important clinically and surgically, as these two papers reported in this issue of the Annals indicate. Hence, the distinction between *multiple orifice AV valve*[3,4] (all orifices opening into the same ventricle) and *multiple outlet atrium*[5] (orifices opening into two different ventricles) is clinically and surgically important.

Although ventriculo-arterial malalignment is widely understood to be important concerning the conotruncal malformations such as transposition of the great arteries and double-outlet right ventricle etc, *the importance of ventriculo-atrial malalignment*[6] seems to be far less widely understood concerning anomalies involving the atria and the AV valves. In order to understand the conotruncal malformations, it is necessary to know that, with the exception of truncus arteriosus, the great arteries *per se* are normally formed and that the malformation involves the subsemilunar conal free walls.[7,8]

Similarly, in order to understand DOLA and DORA, it is necessary to know that the atria and the AV valves are essentially normally formed, and that the malformation lies primarily at the level of the ventricles, resulting in these ventriculo-atrial malalignments.

To summarize, DOLA and DORA are ventriculo-atrial malalignments caused by *excessive* leftward morphogenetic movement of the ventricles and ventricular septum relative to the atria and the atrial septum (DOLA with RA outlet atresia), or caused by *subnormal* leftward morphogenetic movement of the ventricles and ventricular septum relative to the atria and the atrial septum (DORA).

Given that the conoventricular part of the human heart is a "professional contortionist" compared with the largely fixed atria and atrial septum, it is remarkable that these types of ventriculo-atrial malalignment are as rare as they are.

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