Complexities of Heart Development: The Weird Stuff

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Disclosures

• No financial relationships to disclose
Our understanding of heart development in particular has lagged behind that of other more tidily developing organs that have the leisure of putting themselves together before they have to do anything. Perhaps it is for these reasons that the molecular age has come to heart development a bit slower and more painstakingly than to other systems.


Image courtesy of David Sedmera.
So how do we get from this 2 layer embryo

http://www.med.unc.edu/embryo_images
To a 4 chambered heart?
Early Development

From *Heart Development*, 1999
Determination of Sidedness

- Very early process, before visible break in R-L symmetry of the embryo
- Cells of Hensen’s node have cilia that beat in a unidirectional fashion creating a signalling cascade to differentiate right side from the left
Early Development

From *Heart Development*, 1999
Ventral view

Dorsal view

http://www.med.unc.edu/embryo_images
Forebrain

Cardiac crescent

Saggital View

Forebrain

Cardiac crescent

http://www.med.unc.edu/embryo_images
The Cardiac Crescent and the Tube Heart

From *Heart Development*, 1999
The Tube Heart

From *Heart Development*, 1999
Segmental Contraction

From *Heart Development*, 1999
Looping and Septation

From Heart Development, 1999
Ballooning Model

Christoffels et al
Dev Biol 223:266-278
The Endocardial Cushions

From *Heart Development*, 1999
Atrioventricular Cushions

- Form AV (mitral and tricuspid) valves
- Form the portion of the atrial septum adjacent to the AV valves
- Form the inlet portion of the ventricular septum
- Begin as swellings of cardiac jelly (extracellular matrix) that then become populated by cells
AV Junction Cushions

- Anterior (Superior)
- Posterior (Inferior)
- Lateral (2)
- Anterior and Posterior fuse in the midline to form separate mitral and tricuspid orifices

http://www.med.unc.edu/embryo_images
• Common atrium
• AV Junction connects atrium to only left ventricle

http://www.med.unc.edu/embryo_images
Inner Curvature Remodelling

- Right AV junction must expand rightwards to allow direct flow of blood from right atrium to right ventricle
- Aorta must become “wedged” into left ventricular outflow tract
Atrial Septal Development

http://www.med.unc.edu/embryo_images
**Ventricular Septum**

- 1 = Inlet septum from AV cushions
- 4 = Conal septum from OFT cushions
- 2+3 = Muscular septum
Outflow Tract Development

- Contributions from neural crest and anterior heart field
- Outflow tract cushions contribute to the semilunar (aortic and pulmonary) valves and outflow tract septum (conal septum)
- Aorticopulmonary septum separates the aorta and PA above the valves
Outflow Tract Development

From *Heart Development*, 1999
The Aortic Arch Arteries

Kirby et al
From Dr. R. Anderson
Double Lumen Aortic Arch
Edwards’ Pluripotential Arch
Systemic Venous Development

Arey, Developmental Anatomy
Systemic Venous Development

Arey, Developmental Anatomy
Systemic venous development

A: PuV, LSCV, LA, LSH
B: RSCV, RA, oblique vein
C: LA, RA, SCV, CS, RV, LV, ICV

Wessels and Sedmera, Physiol Genomics 2003
Coronary arteries

Perez Pomares 2003

Wessels and Perez Pomares, 2004
Anomalous RCA Origin
Anomalous RCA Origin
<table>
<thead>
<tr>
<th>Human Gestational Age (approximate days)</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Precardiac mesoderm</td>
</tr>
<tr>
<td>17</td>
<td>Cardiac crescent</td>
</tr>
<tr>
<td>19</td>
<td>Tube heart</td>
</tr>
<tr>
<td>22</td>
<td>Heart beat</td>
</tr>
<tr>
<td>22-27</td>
<td>Looping</td>
</tr>
<tr>
<td>32-33</td>
<td>Atrial septation</td>
</tr>
<tr>
<td>32-37</td>
<td>Vent and OFT septation</td>
</tr>
<tr>
<td>22-37</td>
<td>Aortic arch</td>
</tr>
<tr>
<td>37-</td>
<td>Coronary arteries</td>
</tr>
<tr>
<td>33-47</td>
<td>Conduction system</td>
</tr>
</tbody>
</table>
Minimum Requirements for a Heart

- Venous vessel to bring blood to heart
- 1 atrium
- 1 AV valve
- 1 ventricle
- 1 arterial vessel
- Without a placenta – some way to get blood to lungs and body (PDA/collaterals/etc)
- Myocardial function
Developmental Arrest/Abnormality During Development

- CAVC
- DORV
- TOF, TOF/PA
- Conoventricular VSDs
- TGA
- Truncus

- Interrupted Aortic Arch Type B
- Vascular Rings
- TAPVC
- Heterotaxy **
Developmental Arrest/Abnormality AFTER Development

- HLHS/ Critical AS
- Pulmonary Atresia with Intact Ventricular Septum
- Coarctation/Interrupted Aortic Arch Type A
Heterotaxy

- “Heteros” and “Taxis” from Greek meaning “other arrangement”
- Wide spectrum of malpositions of visceral organs and cardiac malformations
- Also known as “Atrial Isomerism”, Ivemark syndrome
- Asplenia=Right atrial isomerism
- Polysplenia=Left atrial isomerism
Visceral Situs

Situs Solitus

Situs Inversus

“Situs Ambiguus”
Bronchial Anatomy

- Right main bronchus is eparterial
- Left main bronchus is hyparterial
- Bilateral eparterial bronchi (B) in 81% of asplenia
- Bilateral hyparterial bronchi (C) in 72% of polysplenia
Anomalous PV Drainage

- Malposition of septum primum may cause normally connected pulm veins to drain abnormally
- Blue = normal
- Yellow = PAPVD
- Red = TAPVD
- Seen with polysplenia
Anomalous PV Connection
From S. Van Praagh
- CAVC
- DORV
- TAPVC
Anatomically Single Ventrices

- “Complex Cyanotic Congenital Heart Defects”
- Controversial definitions of “ventricle”
- Van Praagh: “the essence of a ventricle is the inflow or trabecular portion”
Definitions- Boston

- “Single ventricle is present when both AV valves or a common AV valve open entirely or predominately in to one ventricular chamber” RSVP, Herz 4: 113-150, 1979
- EXCLUDES mitral and tricuspid atresia and straddling and overriding AV valves
- Single LV = DILV with outflow chamber
- Single RV = DI/DORV
Definitions - London

- “Single Ventricle”
- “Double Inlet Ventricle”
- “both atriums connected to one chamber within the ventricular mass”
- “Univentricular atrioventricular connections”
Univentricular AV Connections

Double Inlet

Single Inlet

Common Inlet
How many ventricles do we have?

- 2??? 3????
- LV is a single whole structure
- RV is a two-part structure
  - Inflow or trabecular portion
  - Infundibulum or conus
- Single RV does not have any recognizable LV structures
- Single LV does have an outflow chamber (infundibulum)
Double Inlet Left Ventricle

- Two separate AV valves enter into large LV
- LV gives rise to one great artery
- Small “outflow chamber” gives rise to other great artery
- Most commonly PA is from large LV, Aorta is from small outflow chamber – worry about aortic obstruction
Bulboventricular Foramen

- In the setting of DILV or Tricuspid Atresia
- Not a “VSD” because there is not a real true ventricular septum
- Important to consider size – have to get 1 cardiac output across hole to outflow valve
- Natural history – BVF tends to get smaller with time
- Matitiau et al (JACC 1992; 19: 142-8) developed a formula to predict potential for obstruction at the BVF. A BVF of < 2 cm²/m² was predictive of late obstruction.
Holmes Heart

- DILV with normally related great arteries
- Dates from 1822 or 1823, originally published in 1823
- Maude Abbot found the heart in 1900 and William Osler encouraged her to re-publish the case (1901)
- Re-published by Van Praagh in 1996
- Still in existence at McGill in Montreal
Double inlet-double outlet RV
Not congenital, but definitely weird
After TOF repair
• “RVOT Aneurysm” - thin walled, paradoxical motion with ventricular systole, is the “hood of the conduit”

• “RVOT Pseudoaneurysm” – leak along suture line, most typically along the hood of the conduit, does not have a true wall, is held together by adhesions
Resources

• http://www.med.unc.edu/embryo_images/
  – UNC embryology review website with animations of development of heart and other organs

• International Society for Nomenclature of Pediatric and Congenital Heart Disease
  – IPCCC.NET
International Society for Nomenclature of Paediatric and Congenital Heart Disease

International Paediatric and Congenital Cardiac Code

The International Society for Nomenclature of Paediatric and Congenital Heart Disease (ISNCPCHD) was constituted in January of 2005 with the overall mission of unifying paediatric cardiac disease under a single terminology. Since its inception over a decade ago, the society has worked to cross link multiple coding systems as well as to create definitions that may be utilized across the globe.

The society has evolved into three working groups:

- The International Working Group for Mapping and Coding of Nomenclatures for Paediatric and Congenital Heart Disease, also known as the Nomenclature Working Group (NWG).
- The International Working Group for Defining the Nomenclatures for Paediatric and Congenital Heart Disease, also known as the
Thanks!

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