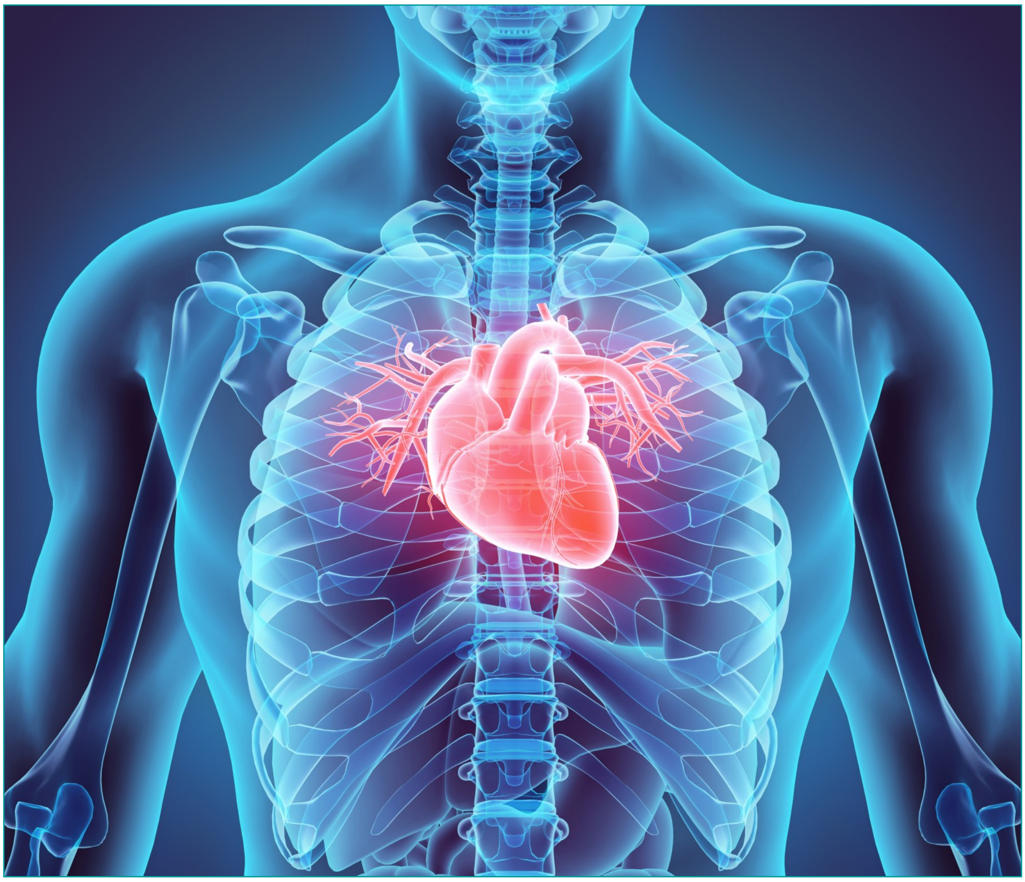
‘Many a person only finds his heart, when he has lost his head’

Friedrich Nietzsche (1833)

‘When you see a good man, think how you can stick to him;
if you see a bad man, examine your own heart. ’

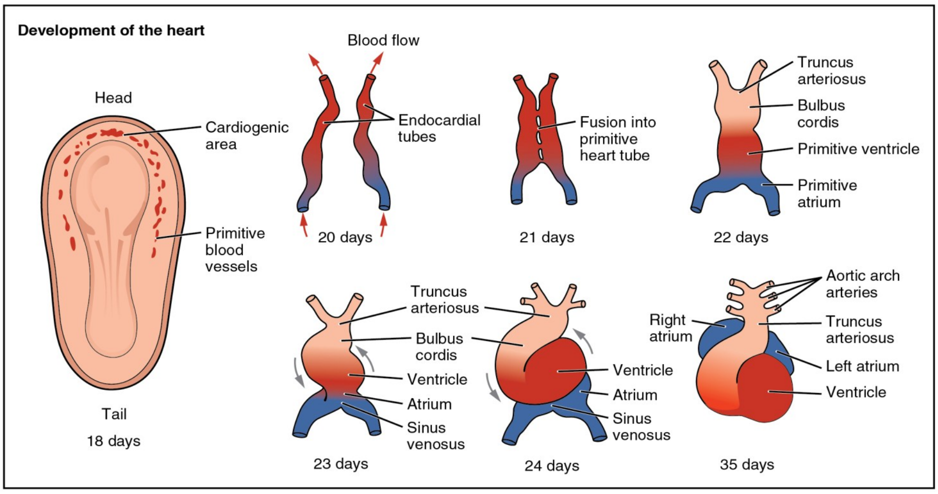
Confucius (500 v. Chr.)

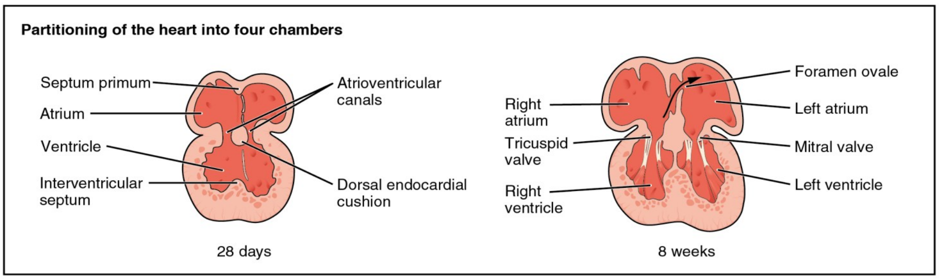


19. COR

19.6. BRIEF EMBRYOLOGY COR

Heart development (also known as cardiogenesis) is the prenatal development of the heart. This begins with the formation of two endocardial tubes that merge to form the tubular heart, also known as the primitive heart tube. The heart is the first functional organ in vertebrate embryos and in humans it beats spontaneously around week 5 of embryonic development.





Development of the heart:

Development of the human heart during the first eight weeks (top), and the formation of the heart chambers (bottom).

In this image, the blue and red colours represent the inflow and outflow of blood (not venous and arterial blood).

Initially, all venous blood flows from the tail / atria to the ventricles / head, a very different pattern than that of an adult.

Source: Betts JG (2013) Anatomy & physiology. page 787–846. ISBN 978-1938168130. 2013.

19.6.1. Global development

The tubular heart differentiates rapidly into the truncus arteriosus, bulbus cordis, primitive Ventricle, primitive Atrium and sinus venosus. The truncus arteriosus splits into the ascending Aorta and the lung trunk. The bulbus cordis is part of the Ventricles. The sinus venosus is connected to the fetal circulation.

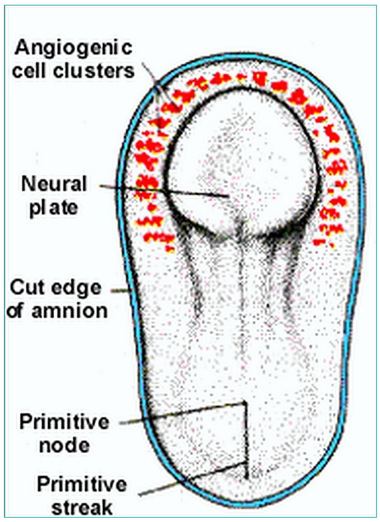
The heart tube lengthens on the right side, loops and becomes the first visual sign of the left-right asymmetry of the body.

Early development

The circulatory system can be understood as a system of paracrine communication over a longer path with a certain direction, which is given by a channeling system.

The 'engine' behind this form of metabolism is a concentration gradient, that is the beginning of diffusion & osmosis. Metabolic activity leads to changes in osmolarity in and around cells and tissues.

If we consider this on a larger scale, we can conclude that the metabolic activity of cell clusters gives rise to a certain fluid flow. It can be considered a precursor of the later circulation system.



The embryo shows higher cranial metabolic activity and the fluid flow progressively gains more direction and structure. The beginning of the canalization is formed by angiogenetic material, the so-called blood islets. These form endothelial channels. The first canalizations can be seen in the suture stem and a little later also in the embryo.

In summary, the development is as follows:

Angioblasts form in the mesoderm and which form blood islets and a transformation takes place:

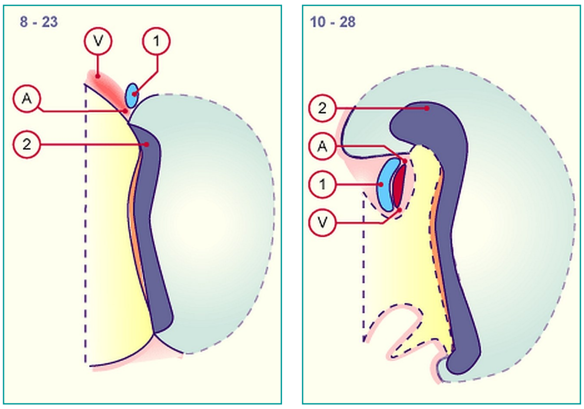
- • centrally located cells form primitive blood cells.
- • peripheral cells form the endothelial lining.

More and more aAgioblasts are forming around the blood islands.

The hollow blood islets fuse with each other, creating endothelial channels that increasingly grow into the surrounding tissue.

Mesenchymal tissue around the endothelial channels form muscle tissue and (supporting) connective tissue:

- • complexity is increasing.
- • transition from more fluid to more structure.
- • the structure strengthens the function (which was already there) which provides more structure: larger and larger blood vessels are forming.



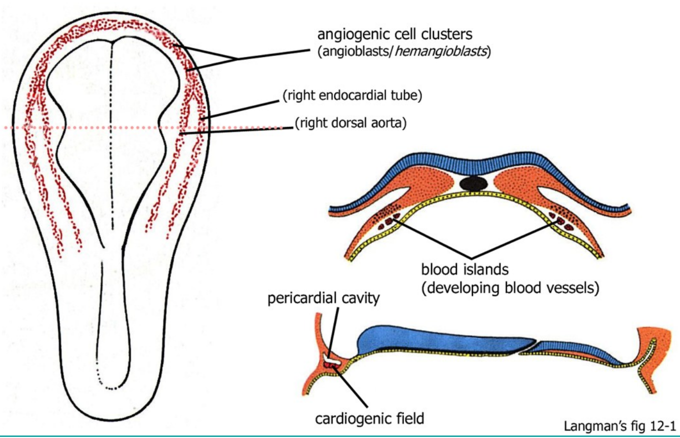
1 = pericardial cavity.
2 = cranial end embryo.
A = arteria part (outflow).
V = venous part (inflow).

When the neural plate is closed and the cerebral vesicles are formed, the central nervous system begins to grow so rapidly in the cranial direction that it bends over the cardiogenic zone, which until then was rostral to the neural plate.

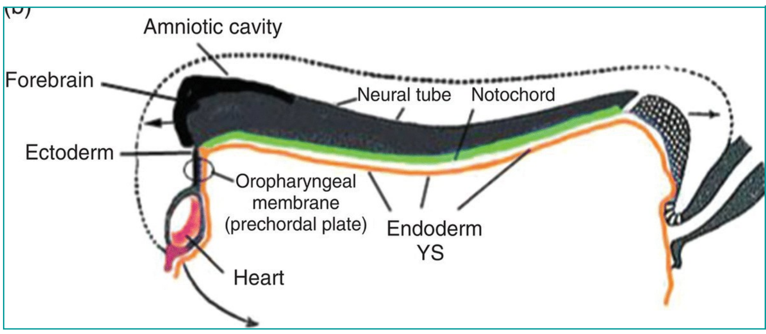
The result of the growth of the neural tube is called the head-folding of the embryo. It leads to the heart first being in the cervical region and finally ending up in the Thorax.

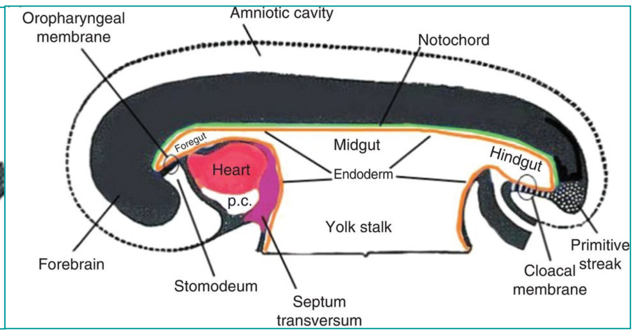
In this way, the primitive heart is absorbed into the embryo, as it were; it lies between the heart cavity and the primordial intestine, after which it grows, as it were, in the heart cavity.

The cardiogenic field is established in the mesoderm just after gastrulation (~18-19 days) and develops into a fully functional, multi-chambered heart by the 8th week

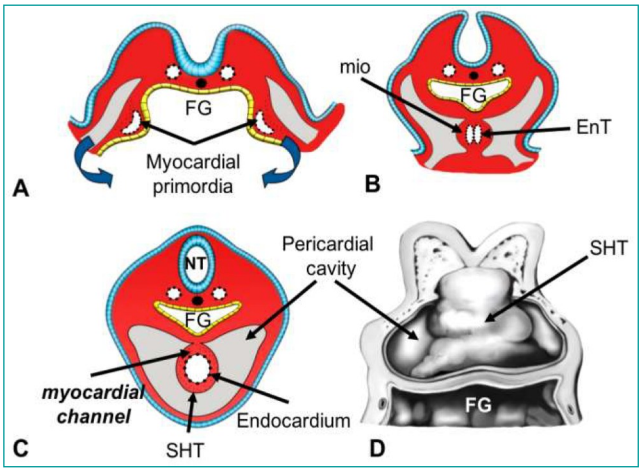


The heart tube is continued on its cranial side by two aortic arches. The bottom of the heart, the sinus venosus, is located in the Septum transversum. This is how the heart is fixed.





The delimitation phase describes the phase in which the embryo moves around a cranio-caudal axis and acquires a more 3-dimensional character. Endothelial ducts also appear, which are called endocardial tubes at the level of the future heart. Due to the delimitation phase, the heart tubes move towards each other, touch each other and fuse.



The surrounding mesenchyme densifies into an epimyocardial-mantle or cardiac gelatin. This mantle contains a lot of hyaluronic acid that provides a separation with the Endothelium. From the epimyocardial-mantle the Myocardium and the Epicardium develop.

Ultimately, the wall of the heart consists of three layers:

- • Endocardium; the endothelial inner lining.
- • Myocardium; the heart muscle tissue.
- • Epicardium or lamina visceralis of the Pericardium covering the outside of the tube.

Further development

On the 18th-19th day, the first development of the heart appears at the level of the cardiogenic zone as a thickening of the splanchopleura. Cells condense into cell strands with a lumen. This is how the primitive heart tube is created bilaterally.

Due to the cephalocaudal and transverse rotation, both fuse into a central endocardial tube, which moves to caudally. The adjacent mesoderm condenses into a myo-epicardial-mantle. The Endocardium arises from the endocardial tube, while myo-epicardial-mantle provides the Myocardium.

In the meantime, the heart tube grows in length and dilations occur:

- • sinus venosus.
- • primitive Atrium.
- • primitive Ventricle.
- • bulbus cordis.

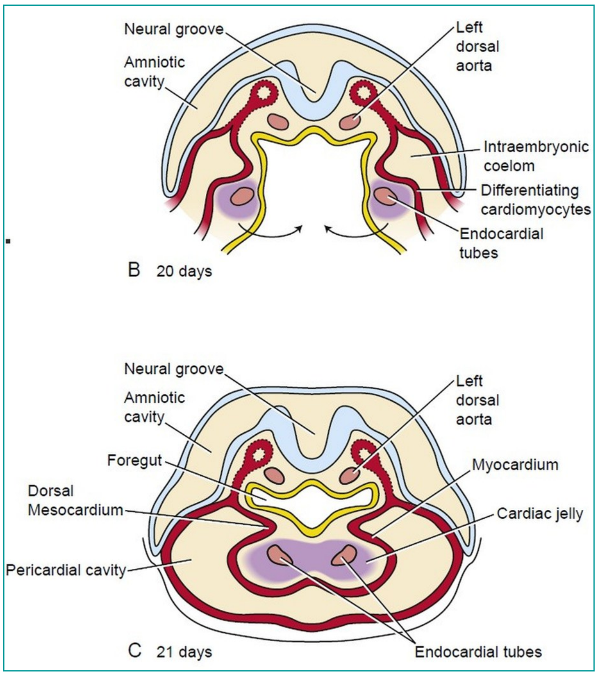
The primitive Atrium later forms the two atria. The primitive Ventricle forms the left Ventricle. From the inferior part of the bulbus cordis the right Ventricle develops, while from the superior part the truncus arteriosus develops.

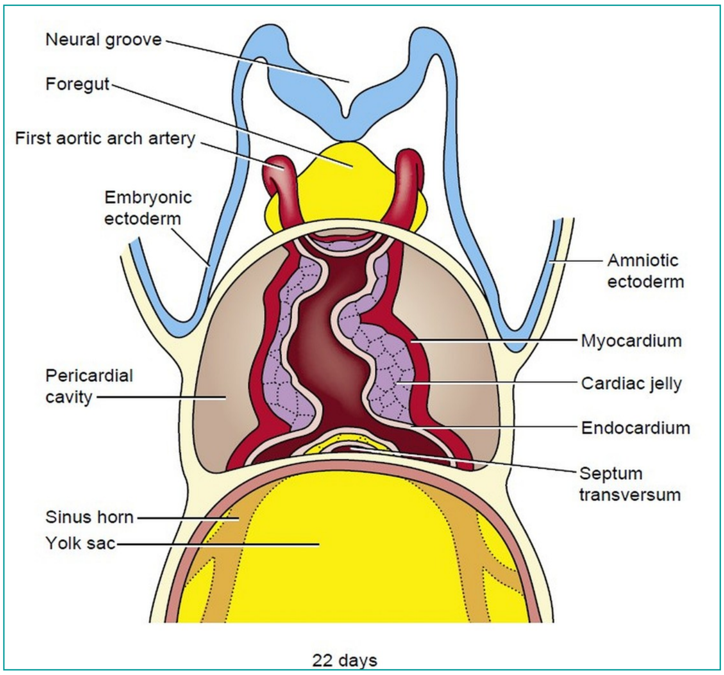
The bulbus cordis and the Ventricle grow faster than the other parts, creating a U-shaped curvature (bulbo-vertricular loop). Later it becomes S-shaped. This movement positions the Atrium and sinus backwards-upwards. At this stage, the sinus venosus has moved into a left and right sinus horn. The Ventricle makes a translation to the left and the bulbus moves to the inferior, anterior and right.

All this is surrounded by the pericardial cavity. Originally, it is attached to a dorsal Mesocard, which later disappears. The pericardial cavity is separated from both pleural cavities by the formation of the pleuro-pericardial membranes.

In addition, the primitive venous and arterial systems develop. Inside the heart, various cavities develop, with septa and valve system, Myocardium and the complete cardiac conduction system.

The first heart action is detectable after 21 days. In the 5th week, the heart rate is about 100 / min, increasing towards the 8th week to 160-180 / min. At birth, the average heart rate is around 120 / min.





Formation of the heart at day 20 & 21. *With two Aorta's and the developing Cardiomyocytes.*
The primitive intestines closes.

Formation of the heart on day 22. *The Entoderm forms as a blood layer and the Myocardium originates from Splanchno-mesoderm. There is an extracellular jelly between the two layers.*

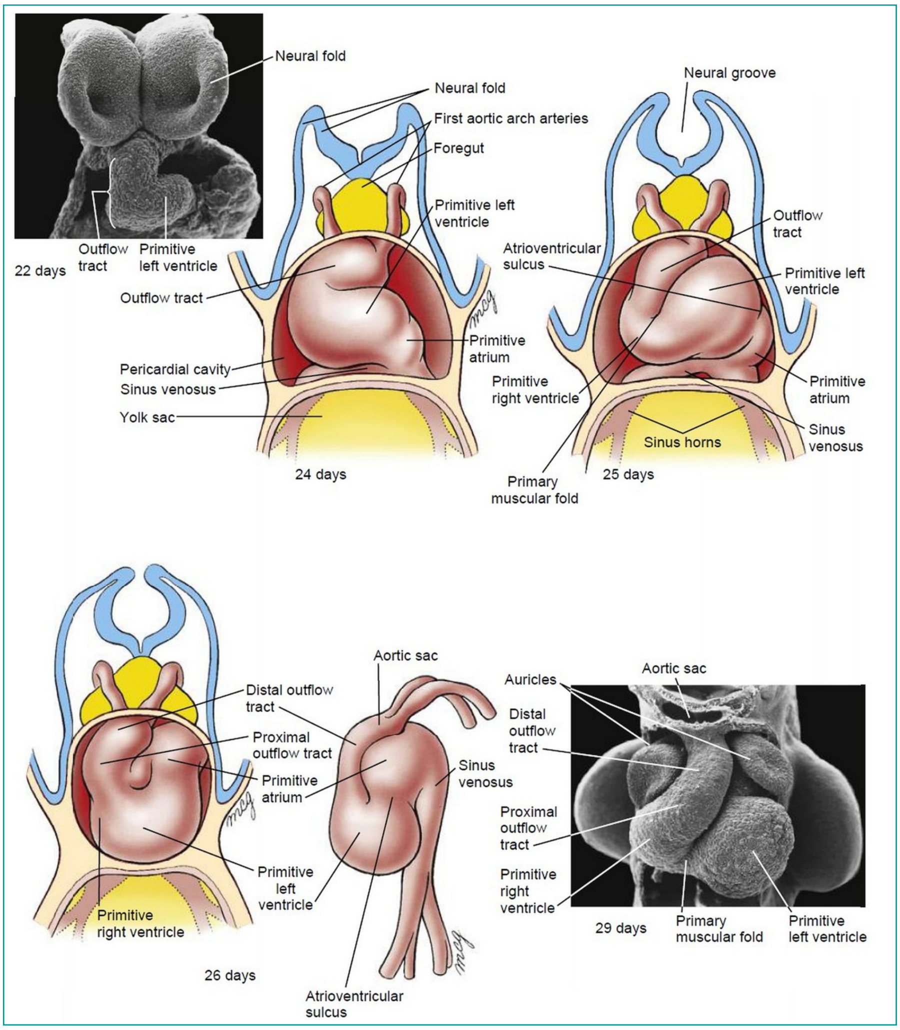
Development of the heart tube

The heart tube lengthens and undergoes a looping.

This makes it in line with the Outflow Segment.

As a result, the primitive left Ventricle turns to the left and the primitive Atrium to dorsal and cranial.

The Myocardium at the atrial end forms the right Ventricle.



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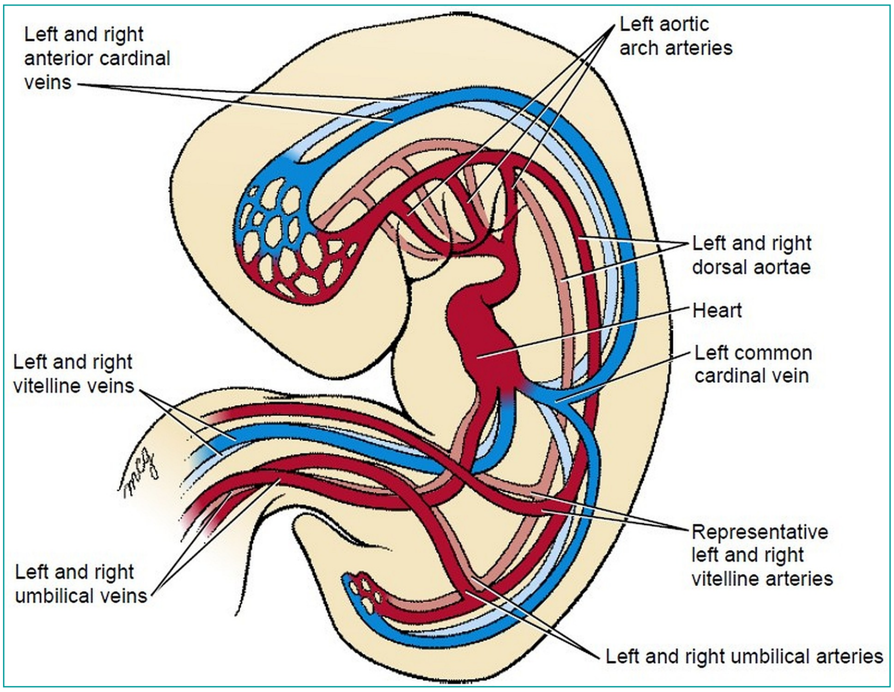
- Villavicencio-Guzmán, L.; Sánchez-Gómez, C.; Jaime-Cruz, R.; Ramírez-Fuentes, T.C.; Patiño-Morales, C.C.; Salazar-García, M. Human Heart Morphogenesis: A New Vision Based on In Vivo Labeling and Cell Tracking. Life 2023.
- Langman, J. Inleiding tot de embryologie, Bohn, Scheltema en Holkema, Utrecht / Antwerpen, 1982.



Schematic representation of the embryonic vascular system in the middle of the fourth week.

The heart has started beating and circulating blood.

The Outflow Segment is now connected to three pairs of aortic-arche-arteries and the paired dorsal Aortae that circulate blood to the head and trunk.

Three pairs of veins – Vv. Umbilicalis, Vv. Vitilinae and Vv. Cardinalis – supply blood to the Inflow-Segment of the heart.

Blood vessels heart:

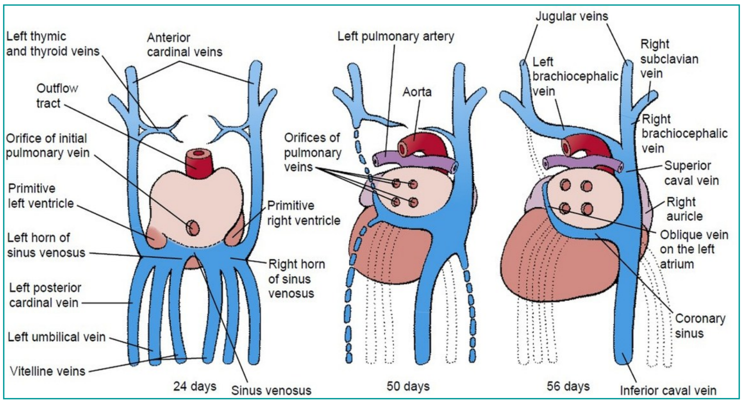
Rearrangement of the Inflow-Segment of the heart between weeks four and eight, so that all systemic blood flows into the future right Atrium.

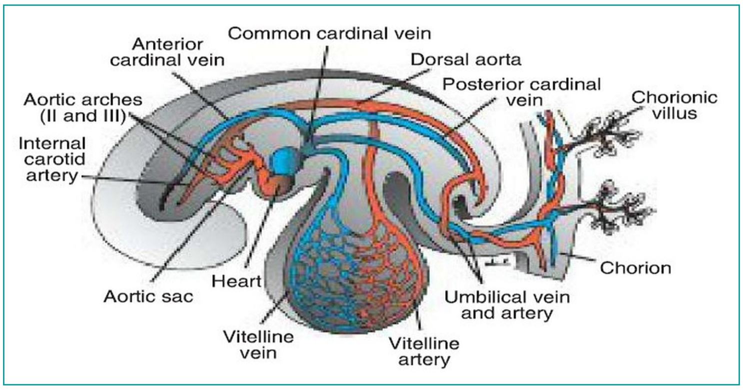
The left sinus horn is reduced and pulled to the right side.

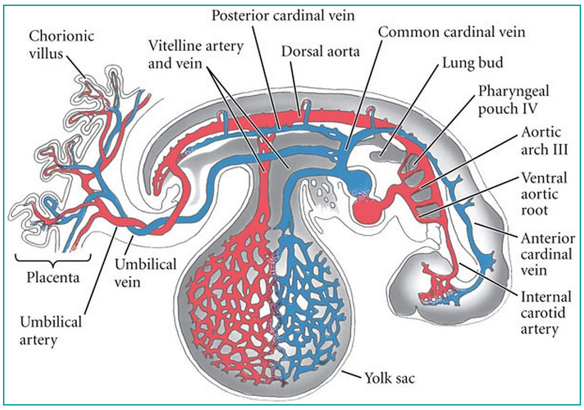
It loses its connection to the left V. Cardinalis Anterior and becomes the coronary sinus, draining blood only from the heart wall.

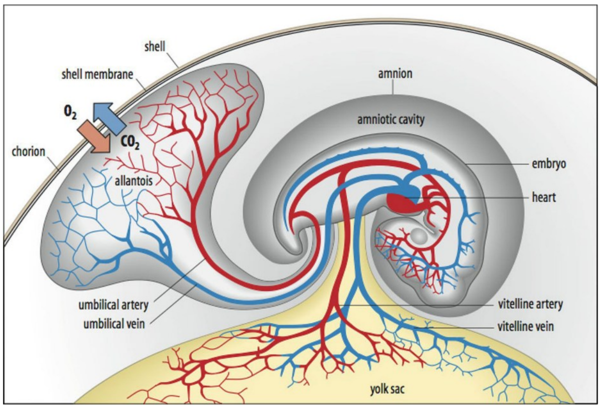
The left V. Cardinalis Anterior is connected to the right V. Cardinalis Anterior by an anastomosis of thymus and thyroid veins, which form the left V. brachio -cephalis.

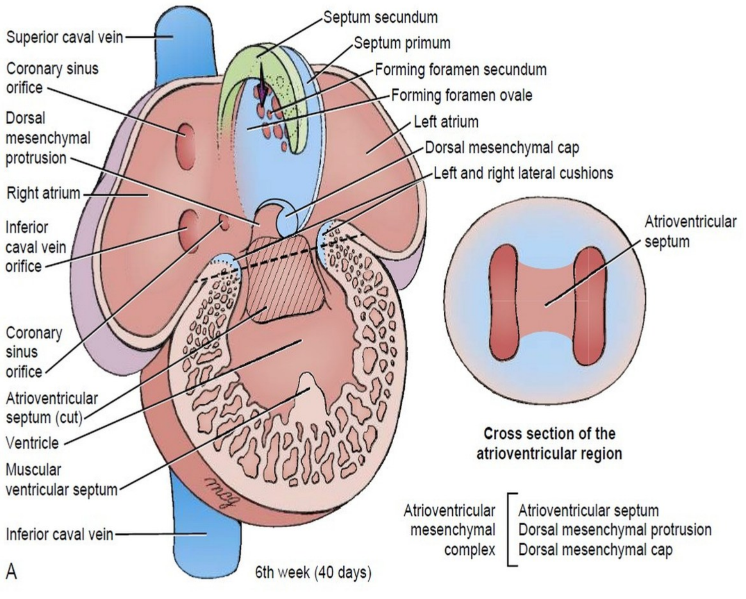
A remnant of the right V. Vitellina becomes the terminal segment of the V. Cava Inferior.











Septation (formation of the septum)

Further septation of the Atria.

During the 6th week, the thick septum secundum grows out of the roof of the right Atrium, and the septum primum, dorsal mesenchymal cap, and dorsal mesenchymal protrusion fuse with the atrioventricular cushion to fill the foramen primum.

However, before the foramen primum is obliterated, the foramen secundum is formed by the fusion of small fractures in the septum primum. Dotted line represents the level of the cross-section through the atrioventricular canal region.

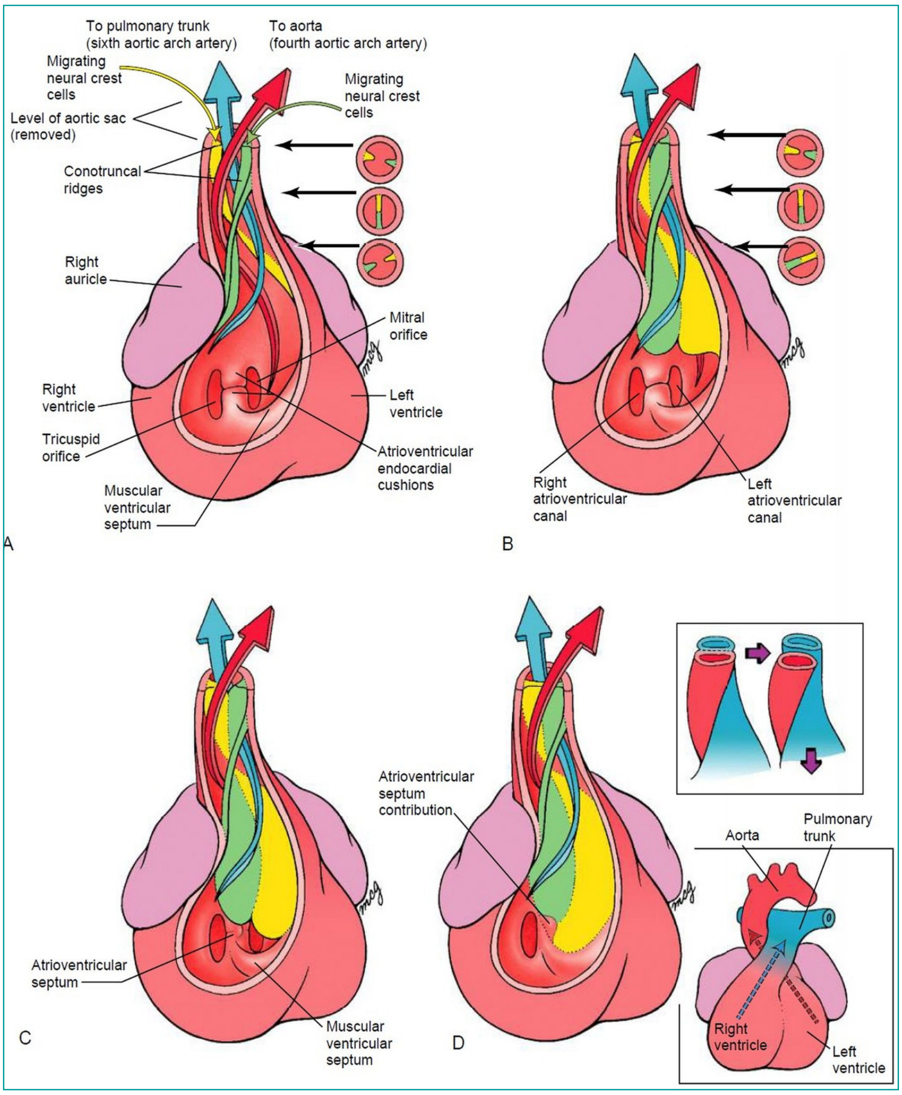
Septation of the Cardiac Outflow and completion of ventricular separation.

The cranio-lateral wall of the right ventricle has been removed to represent the inside of the right ventricular chamber and the probable outflow channels of both ventricles.

A, B, From the 5th week, the right and left conotruncal ridges grow out of the walls of the common Outflow Segment.

Endocardial and neural crest cells fuse with each other in a cranial to caudal direction to form the conotruncal septum, which separates the aortic and pulmonary outflow channels.

C, D, By the 9th week, the caudal end of the conotruncal septum has reached the level of the muscular part of the Ventricular septum and the atrioventricular septum. Here it merges with these others to complete the Ventricular Septum.



Sources:

- Larsen, W.J., PhD, Human Embryology, Page 293, Figures 12.17, 12.28, Churchill Livingstone, New York, 1993.
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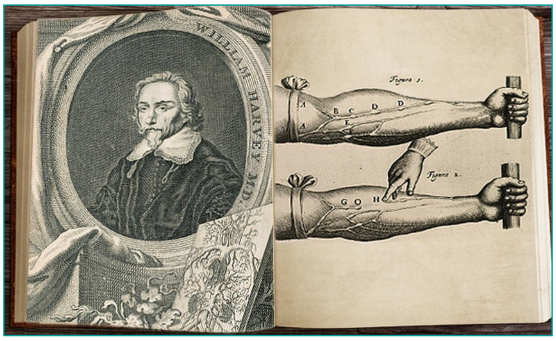
19.6.2. A Different View of the Heart

Inca-stone heart.

The anatomy and function of the heart have been a subject of curiosity, exploration, and discovery for many centuries. The form and function of the heart and circulatory system were undoubtedly a subject of curiosity and wonder in the minds of men, even in distant prehistoric times, long before the written records of history began to pile up.

It was the Greek physician and philosopher Galenus, who put forward some of the earliest recorded theories about blood circulation in the second century AD.



Other thinkers followed with more descriptions and theories, such as Erasistratus, Ibn al-Nafis, William Harvey, Jean Baptiste de Senac, Andreas Vesalius, Jules Cloquet, Thomas Bartholin, Robert Koch, and at least twenty others. In this line of collaborators, it was the English physician William Harvey (1578-1657) who first accurately described how blood circulates from the heart. Galen and Erasistratus came close to Harvey's accuracy in their earlier descriptions.

19.6.2.1. History of Knowledge of the Heart

Ca. 1500 BC

Papyrus image of the weighing the heart.

For the Egyptians, the heart is the central organ in which conscience resides. Everything is stored there: the light, pure and the bad, heavy deeds, determine the weight of the human heart. After death, the heart is placed on one of the scales of a scale.

The counterweight is the feather of truth that is placed on the second scale of the balance by the goddess Ma'at. If this is as light as a feather, the deceased can go directly to Osiris, who gives access to the realm of the dead. The burdened heart can count on a heavier transition.

The ancient Egyptians discovered the connection between the heart and blood vessels. The ancient Egyptians thought that inside the body must be a system of canals, just like the irrigation canals along the Nile. These channels would ensure the transport of blood and nutrition through the body.

The ancient Egyptians were convinced that the heart grew larger and larger until the age of fifty. Then the heart would shrink at the same rate. That is why a person never lived beyond a hundred years of age. The ancient Egyptians got their wrong idea by looking at the heart of mummies: after death, the heart dries out and becomes smaller.

400 BC

The Greek Alcmaeon *was one of the first to cut open dead people to study their construction. For example, he discovered that there are two types of blood vessels that look different: the arteries and the veins. Alcmaeon's contemporaries had already discovered that the heart is a muscle.*

Alcmaeon determined that after death the arteries are empty. Based on this discovery, he thought that the blood flow through the arteries also stops during sleep, but of course that is not the case. After death, the blood supply from the heart to the arteries comes to a standstill, but during sleep it continues. The scientific name of arteries is based on Alcmaeon's mistaken idea: arteries. Aèr means air.

Texts from about 425 BC, attributed to **Hippocrates***, describe the heart as a pump.* **Aristotle** *adopts this view and also sees the heart as the source of spiritual life, which is the inner fire from which warmth and light are present in man. According to Aristotle, the brain was of secondary importance: 'they didn't even have a blood supply and were cold and insensitive. The brain served to secrete mucus as cooling for the heart.'*

The Greek philosopher **Plato** *describes the heart as a kind of alarm-centre, because it reacts strongly to internal and external stimuli.*

Galenus, *the founder of Western medicine, whose ideas remain unchanged for 1,400 years, also sees the heart as a source of heat, but he shifts the place of the soul from the heart to the brain. He sees in man three pneumas that should be balanced in the body: the spirit of life, the spirit of the soul and the natural spirit.*

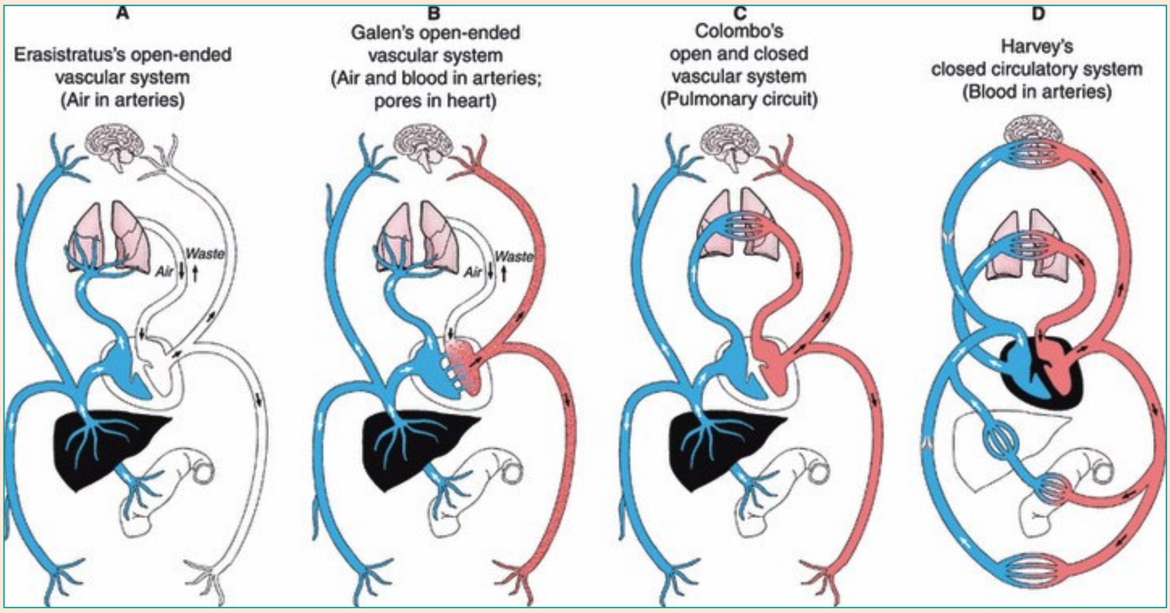
Galenus did not yet know of the existence of the circulatory system. He thought that the blood in the blood vessels moved back and forth, just like the sea at low and high tide.

1. *Blood from the liver, which is formed from intestinal juices, flows to the veins.*
2. *In the hollow veins, the blood moves back and forth.*
3. *The blood enters the lungs through the right hemisphere of the heart. There it is purified of grime and cooled down by the inhaled air.*
4. *Air (Pneuma) flows from the lungs into the left hemisphere of the heart.*
5. *The blood flows from the right ventricle to the left ventricle. This ensures cleaning of the blood.*
6. *In the brain, the so-called spiritus animalis arises from the spirit of life, which is responsible for human actions.*
7. *The mixture of air and blood creates the other spirit of life (spiritis vitalis), which flows to the Aorta.*

5th century

In classical antiquity, it was thought that the body contains four fluids: blood, phlegm, yellow and black bile. According to Greek doctors, the balance between those fluids would be disturbed in the event of illness. Bloodletting caused the excess blood to flow away, restoring the balance. In reality, the patient suffered from blood loss and did not get better.

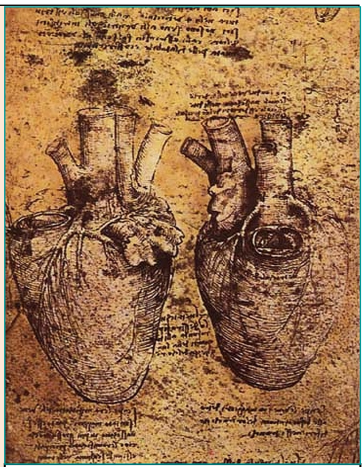
Bloodletting was used until the nineteenth century. There were various methods for this, such as the head-schnapper. The round box contains a spring with a knife attached to it. When operated, the spring shoots out with the blade and cuts a wound into the patient's skin.



15th century

*In the fifteenth century, **Leonardo da Vinci** (1452 – 1519) faithfully draws the heart by doing anatomical research. He describes the heart as a hollow muscle fed by an artery. He observes 4 cavities, two above and two below, and examines the swirls of blood through these cavities.*

His studies and drawings remained hidden for a long time, but still prove their value in the development of artificial valves in which blood vortex plays an important role.



Anatomisc drawing of the heart by Leonardo da Vinci.

Quaderni d'Ánatomia IV.

*In the sixteenth century, **Andreas Vesalius** (114 – 1564) first describes the entire structure of the heart with blood circulation, a term he introduced.*

He renounces Galen's theories and lays the foundation for our current anatomical science. From this time on, all mysticism about the heart as a carrier of warmth, light and conscience is thrown overboard.

*When, later, in the seventeenth century, the British physician **William Harvey** (1578 – 1657) really rids the heart of all its inner workings, it is only a small step for Descartes to separate body and mind.*

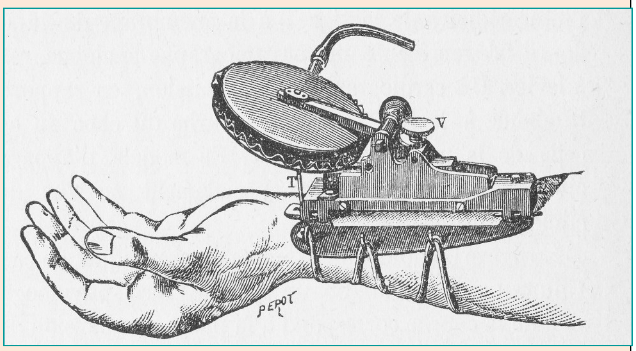
From that time on, people only look at the physical functioning of the heart, an engine that is controlled by the brain and can only be known by dissecting and describing.

19th century

*The French physician **René Théophile Hyacinthe Laënnec** (1781-1826) did not think it was cool to have to put his ear against an often unwashed chest of his patients to hear the heartbeat. At first he used a rolled-up newspaper for this, later he developed the stethoscope. He listened to the heart to diagnose heart disease.*

The first stethoscopes were no more than wooden tubes. Around 1850 they were replaced by double stethoscopes, with two earplugs. They are still used today.

*In the mid-nineteenth century, people were looking for an objective way to express the pulse in numbers, instead of feeling the pulse. The French physician and physiologist **Etienne-Jules Marey** (1830-1904) developed a pulse meter or sphygmograph (sphygmos = pulse rate) for this purpose.*

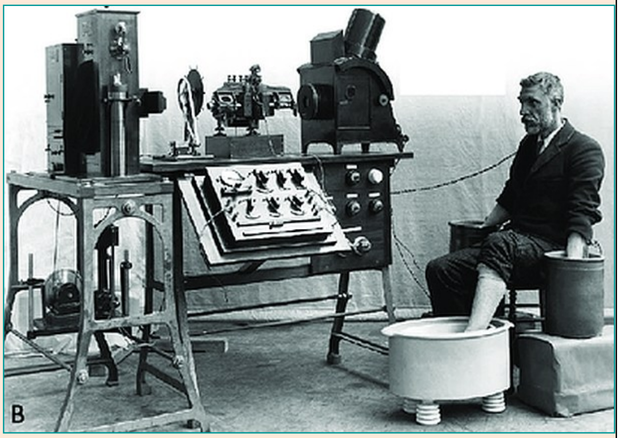


The device was tied around the wrist, resting on the pulse artery. A writer, who moves in the rhythm of the pulse, scratches a thin line on a glass plate that is covered with soot. That line is a representation of the pulse.

*The Dutch physician **Theodor Wilhelm Engelmann** (1843-1909) recorded how the contraction of the heart muscle is controlled by the heart itself, without the intervention of the brain. He also described the factors that influence the speed of the heartbeat.*

*The Italian physician **Scipione Riva-Rocci** (1863-1937) was the first to develop a blood pressure monitor with a cuff to measure blood pressure in patients. He used a mercury manometer, which is now banned because of the toxicity of mercury. The expression of blood pressure in millimeters of mercury pressure comes from this method and is still used today.*

*The Leiden physiologist **Willem Einthoven** (1860-1927) developed the string galvanometer for measuring heart activity. Heart films were made with his device. Electrodes on the patient's skin measure the natural electrical current that runs through the heart step by step.*



The electrodes then set a very thin string in motion. A bright lamp, which illuminates the string, casts shadows on an unexposed film. After development, the movement of the string can be seen on the film as a black zigzag line: the electrocardiogram or heart film. In 1924, Einthoven received the Nobel Prize for his invention of the string galvanometer.

*In **1967**, the first heart transplant took place.*

***1967**: The first heart bypass surgery, by Favoloro (Argentina) and Effler (USA).*

***1969**: The first implantation of an artificial heart in humans, American phys. Denton A. Cooley.*

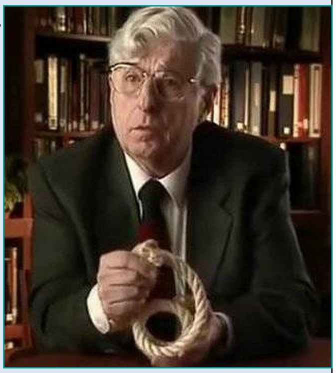
***1980-1990**: New drugs (ACE inhibitors) help patients with impaired heart pumping function. They dilate the blood vessels, making it less difficult for the heart to pump the blood. Aspirin is used as a means to prevent blood clotting. New drugs (statins) that lower cholesterol levels are becoming popular.*

***1990-2000**: Scientific studies show the link between exercise and the risk of cardiovascular disease. Development of new anticoagulants, they are used by patients with an increased risk of myocardial infarction. Research into the use of an external defibrillator (from 1962, Lown) by the police and fire brigade may be able to further improve the initial treatment of patients with cardiac arrest.*

- ***Misconception: the heart grows and shrinks (1,500 BC):** The ancient Egyptians were convinced that the heart grew larger and larger until the age of fifty. Then the heart would shrink at the same rate. That is why a person never lived beyond a hundred years of age.*
- ***Misunderstanding: during sleep, the blood disappears from the vessels (500 BC):** Alcmaeon established that after death the arteries are empty. Based on this discovery, he thought that the blood flow through the arteries also stops during sleep.*
- ***Misunderstanding: bloodletting makes the sick better (400 BC):** In classical antiquity, it was thought that the body contains four fluids: blood, phlegm, yellow and black bile. According to Greek doctors, the balance between those fluids would be disturbed in the event of illness. Bloodletting caused the excess blood to flow away, restoring the balance.*
- ***Misunderstanding: the pulse is caused by the blood vessels themselves (350 BC):** Hippocrates did not establish a connection between the heart and the blood vessels. Therefore, he thought that the heartbeat we feel in the wrist artery is caused by the blood vessel itself.*
- ***Misunderstanding: the heart as an oven (200 AD):** The Greek physician Galenus thought that the heart housed a source of heat. The heart was no longer the seat of the soul; according to Galenus, it was in the brain. Galenus thought that the inner fire of the heart was responsible for the heartbeat.*

Intermezzo: The Helical Heart.

The ventricular anatomy of the heart, the spatial arrangement of the fibers, and the layers of the muscular system were not fully understood until much later. This structural mystery about the heart has long been called the "Gordian knot" of cardiac anatomy. It has indeed been an elusive thing and difficult to understand.



*In 1954, **Francisco Torrent-Guasp** published his first work on the subject of the heart in Salamanca, entitled 'The Cardiac Cycle'. After performing dissections on hundreds of animal hearts, as well as some human cadaver hearts, Torrent-Guasp, in 1972, literally unravelled the until now unknown anatomy of the heart's coiled ventricular muscles.*

He revealed that the muscle of the right and left ventricles is actually a single band of tissue coiled on itself and arranged in the configuration of a double spiral spiral. This single band of the heart muscle is now known as the spiral ventricular myocardial band, or the HVMB (Helical Ventricular Myocardial Band).

This discovery, which he made in 1972, was completely new at the time, and it opened doors to a deeper understanding as a few more decades passed. As is often the case with great discoveries and contributions, its significance was met with the usual resistance, skepticism, and doubt in academic circles.

Dr. Torrent-Guasp's heart muscle dissections were always performed through a blunt tissue dissection technique that used only his fingers, rather than using a scalpel or scissors to cut through the tissue planes of the heart. Dissections with surgical instruments may not reveal the natural architecture of tissue planes. Every surgeon knows this fact from years of direct experience.

By means of this 'finger technique', he did not accidentally or unconsciously cut and disturb the natural integrity of the HVMB. Instead, he was able to gently unravel and uncoil the single muscular ligament that makes up both the right and left ventricles, as well as the Septum Interventricularis that separates them. The HVMB is an uninterrupted muscle band that descends from the opening of the A. Pulmonalis, twists and turns at the top of the heart, and then rises back up to the Aorta.

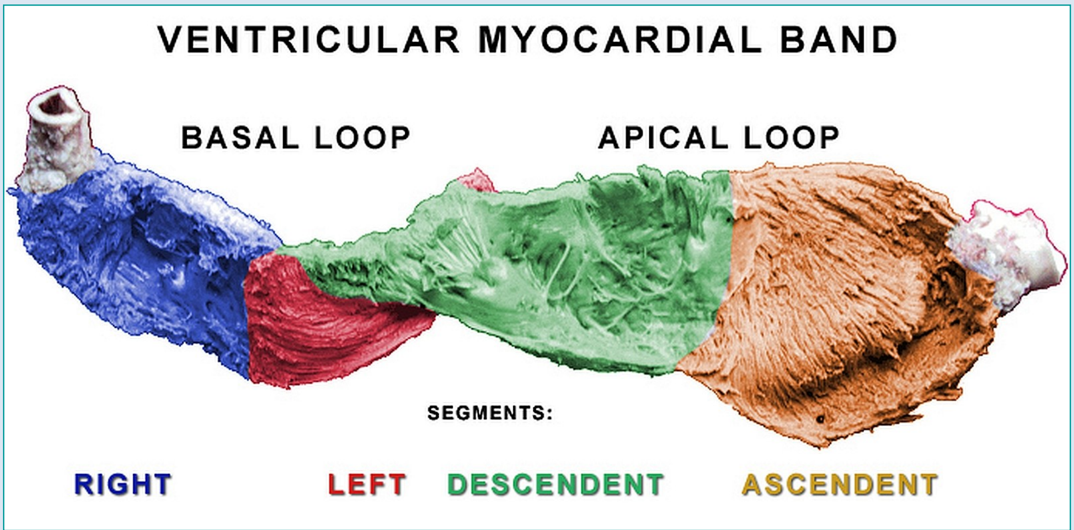
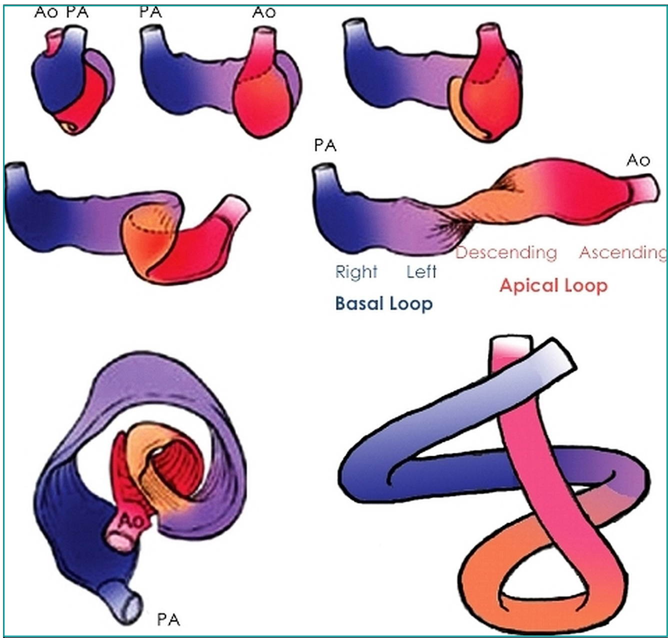


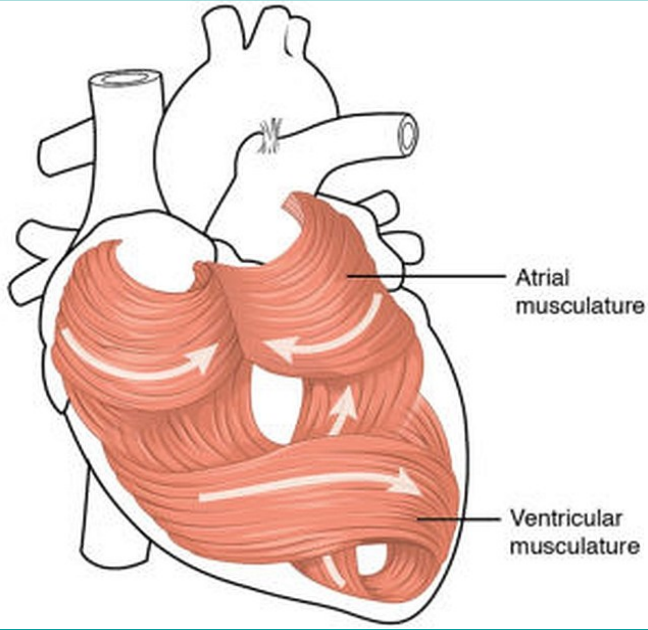
Image of the unravelled HVMB that is coloured with 4 segments.
The blue and red segments correspond to the right myocardial ventricle, and the green and brown segments correspond to the larger and stronger left ventricular myocardium.
At the point where the red segment meets the green segment, the twisting of tissue that forms the apex of the heart takes place.



The unrolling of the HVMB when it is dissected.

The tipping point is also shown in the expanded view from cranial towards caudal in the image below left.

PA = A. Pulmonalis; AO = Aorta.



The wriggling Myocardium visualized as the muscle image of the heart that we know. The atrial musculature is added on top of the HVMB. Interconnections of collagen and muscle fibres of the right and left ventricles are not shown.

The Gordian knot of anatomy in the architectural arrangement of ventricular muscle mass, may have finally been understood. The description of Francisco Torrent-Guasp's model of the spiral heart, includes 2 simple loops, which start at the A. Pulmonalis and end in the Aorta. A non-curled ventricular band is shown, achieved by blunt dissection extending between the origo of the right Ventricle, at the radix of the A. Pulmonalis, to the end at the radix of the Aorta, in the left Ventricle.

These components include a helical horizontal basal loop that surrounds and changes direction between the right and left ventricular cavities to cause a second spiral, produced by almost vertically oriented fibres, which gives rise to the helical configuration of the ventricular myocardial band.

These anatomical structures are activated sequentially, as in a peristaltic wave, starting at the right ventricle (just below the A. Pulmonalis) and evolving towards the Aorta. They produce a sequence of narrowing, caused by the contraction of the basal loop, shortening (mainly related to the contraction of the descending segment), elongation (produced by the contraction of the ascendant segment) and widening, due to different factors acting during ventricular myocardial relaxation.

These sequences control the ventricular events responsible for the release (Systole) and the suction (Diastole). These mechanical interactions of structure and function are defined in relation to the chronological location of the successive cardiac 'blood takes' in the Aorta, Left Ventricle and Left Atrium.

Source:

- Torrent-Guasp F, Buckberg GD, Clemente C, Cox JL, Coghlan HC, Gharib M. The structure and function of the helical heart and its buttress wrapping. I. The normal macroscopic structure of the heart. Semin Thorac Cardiovascular Surgery. PMID: 11807730. 2001.