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HYPOTHESIS OF DEVELOPMENT OF PULMONARY VEIN IN HUMAN

Anatomy

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ABSTRACT

Introduction: Hypothesis of different theories of development of the pulmonary vein

Methods: Study of various theories regarding the development of pulmonary vein available in current data is done. On the basis of these studies we have developed new theory (TheoryNo.3).

Results: Human embryos between 24-34 days showed that common pulmonary vein develops as outgrowth from superior wall of left auricle on medial side and unites with angioblastic plexus of developing lung bud. No evidence was found that vein connects directly with sinus venosus in early stages and later shifts in position as atrial septum grows. Initially the early cardiac development is complicated because it is associated with other processes of development such as embryonic folding of coelomic-cavity and vascular development. Due to this it is necessary to integrate experimental and morphological analyses. Observational controversies are frequent rather than result from differences in interpretation. In development of pulmonary vein and systemic venous sinus (sinus venosus), a 3D study in the chicken embryo of the developing venous pole shows that pulmonary vein separates from a greater vascular plexus within splanchanic mesoderm. The development of systemic venous sinus at junction between somatic and splanchnic mesoderm. Pulmonary vein in human heart originates from systemic venous sinus appears as new structure draining to left atrium. In addition, we examined sequence of incorporation of the initially solitary pulmonary vein to the stage at which four venous orifices opened to left atrium.

Discussion: According to Theory No-1&2, a development of single embryonic pulmonary vein as an outgrowth of posterior left atrial wall just to left of septum primum.

KEYWORDS

Pulmonary Veins, Splanchanic Plexus, Common Cardinal Venous System, Umbilicovitelline Venous System, Solitary Vein

INTRODUCTION:

Early cardiac development is associated with formation of venous systems in embryo. Initially bilateral paired vitelline veins located between the endoderm of yolk sac and splanchnic mesoderm is only embryonic vasculature. In embryonic midline these vitelline veins fuse to form a ventral vessel.[3] This primary heart tube is formed as walls of this vessel differentiate into myocardium.[4] Subsequent with growth of the embryo proper there is development of cardinal and umbilical venous systems occur. The species relying on lungs for the oxygenation of blood, there also formation of a pulmonary vein or veins. During the development of these vessels and their connection to heart myocardium grows and there changes its shape by combination of proliferation[5], addition and muscularization of the precursor cells.[6]

Development of the Cardiac Venous Pole:

The embryo can be represented as a trilaminar disc made up of endoderm, mesoderm and ectoderm after Gastrulation. The mesoderm gives rise to tube and its venous tributaries. With formation of coelomic cavity lateral plate mesoderm separates into splanchnic and somatic layers which line the endoderm and the ectoderm respectively. In lateral edges of the splanchnic mesoderm gradually form lumen to form the vitelline veins. Vitelline veins basically are bilateral gutters in the splanchnic epithelia that both contain an endothelial tube. These developed endothelial tubes present in extra-embryonic mesoderm covering the yolk sac. Immediately the embryo folds these paired vitelline veins progressively fuse in embryonic midline. And their walls facing future pericardial cavity[8] and than rhymically following fusion start to contract[9] thus formed structure so-called primary heart tube.[10] Now the walls of these vitelline veins do not proliferate and then gradually progressive addition of rapidly dividing cells from splanchnic mesoderm form heart tube.[7] The vitelline veins continue to fuse subsequent for formation of heart tube and becoming the portal vein. Accompany with umbilical veins, the portal vein contributes to the hepatic vascular bed.[11] Mentioned above the primary myocardial heart tube forms by fusion of two epithelial gutters, initially it is unclosed dorsally where dorsal mesocardium connecting the heart to splanchnic mesoderm that overlies the embryonic pharynx. The only site through which vessels or additional tissue can dorsally enter the heart is this Mesocardium.

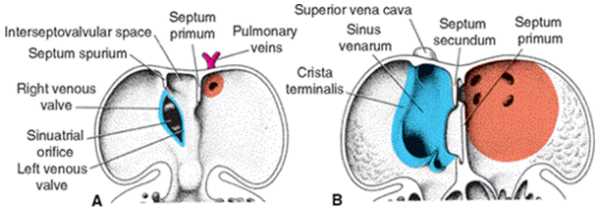
Abnormal Pulmonary Venous Connections:

It is well known in the congenitally malformed heart that pulmonary venous return is via systemic venous channels instead directly to the morphologically left atrium. The sites of such abnormal connections are diverse and are generally divided into, 1) direct right atrial connections 2) connections via derivatives of right-sided common cardinal systems, mainly superior caval and azygos veins 3) connections via derivatives of the left common cardinal system specifically the coronary sinus and 4) connections through umbilico-vitelline system via portal vein and venous duct.[1] Although these above-described phenotypes might differ the initial separation of the splanchnic plexus. Drainage through right common cardinal system indicates failure of the separation of normal pulmonary vein and communication of splanchnic plexus with right common cardinal vein. Drainage through left common cardinal system also follows a similar principle. Drainage into umbilico-vitelline system indicates failure to separate the normal pulmonary vein from cranial aspect of the splanchnic plexus with continuing drainage into the developing hepatic circulation. Relation between pulmonary vein and systemic venous sinus regarding relation between pulmonary vein and sinus venosus is long-standing clinical manifestations of anomalous pulmonary venous return. Normally drainage of pulmonary vein into the left atrium is caused by cranial separation of pulmonary vein from splanchnic plexus and formation of atrium septum from right pulmonary ridge.

THEORY No. 1:

A single embryonic pulmonary vein develops initially as an outgrowth of posterior left atrial wall which is just left of septum primum. Pulmonary vein then gain connection with veins of the developing lung buds. Further during development the pulmonary vein and its branches are incorporated into left atrium and forms large smooth walled part of adult left atrium. One vein initially enters the left atrium and ultimately four pulmonary veins enters as branches are incorporated into expanding left atrial wall.[12]

FIGURE – 1



THEORY No. 2:

Normally, primitive foregut gives rise to lung buds and share common vascular (splanchnic) plexus which drains initially into common cardinal and umbilico-vitelline venous systems. As the formation of the lungs (during 27-29 days of gestation) a portion of the splanchnic plexus differentiates into primitive pulmonary vascular bed.1 Simultaneously primitive left atrium forms primordial evagination (future common pulmonary vein) from the dorsal wall of atrium in the sino-atrial region that grows into and joins the pulmonary portion of the splanchnic plexus. Once the connection is established the primitive pulmonary venous system separates from the umbilico-vitelline veins and cardinal vein. Part of common pulmonary vein are subsequently incorporated into the wall of left atrium and become two left and two right pulmonary veins each of which enters the left atrium via a separate orifice. Failure of the left atrium to link to pulmonary venous plexus, results in the retention of connections to the primitive umbilicovitelline and cardinal drainage systems.The anatomical variants of TAPVC are dependent upon which the connections are retained.The cardinal venous system provides connections to the right atrium, innominate vein, superior vena cava or azygous vein and Umbilicovitelline system provides connections to portal or hepatic vein or inferior vena cava.

The pulmonary veins are distance of about 4mm to common pulmonary vein is visible as an evagination of dorsal wall of the atrium. The bud subsequently grows out into dorsal mesocardium in direction of primitive foregut which gives rise to the lung buds for future lungs. As the atrial cavity continues to develop, the stem of the pulmonary vein is continuously incorporated into the left atrial wall. The incorporation of the pulmonary veins continues into atrial cavity until 2 left and 2 right branches of the pulmonary stem enter atrial cavity.

Gradually a single common pulmonary vein opens into the primitive left atrium but afterwards expands parts of the vein are gradually absorbed into wall of left atrium. The proximal parts of the branches of the pulmonary vein are also absorbed progressively, so the 4 pulmonary veins all open independently into the left atrium. Only the left auricle (which derived from the primitive atrium) has trabeculated and rough appearance. The pulmonary vein that develops by separation from a greater venous plexus which is located within splanchnic mesoderm. The systemic venous tributaries develop laterally on the junction between the somatic and splanchnic mesoderm by muscularization of mesenchyme that surrounds the common cardinal veins.

DISCUSSION:

Early during formation of the lungs, the blood coming from the lung buds drains to splanchnic plexus which connects to the both paired common cardinal and umbilicovitelline veins. Later the right common cardinal system changes into the right sinus venosus which in turn becomes right superior vena cava and azygos vein. The left common cardinal vein changes into left sinus venosus which in turn, becomes left superior vena cava and coronary sinus. The umbilicovitelline system forms the inferior vena cava, ductus venosus and portal vein. At 25-27 days gestation, the developing pulmonary venous plexus keeps connections to right superior vena cava, left superior vena cava and portal system. Direct communication to the left atrium does not exist. Then at 27-29 days gestation, the primitive pulmonary vein appears as an endothelial outgrowth from either posterior superior left atrial wall or from central part of the sinus venosus proximal to the primitive lung venous plexus. At 30 days of gestation connection between the primitive pulmonary vein and pulmonary venous plexus occurs. The common pulmonary vein enlarges and incorporates into the left atrium, and then normally the pulmonary venous part of the splanchnic plexus gradually loses its connection with umbilicovitelline veins and cardinal.[13] The splanchnic plexus gives rise to primitive pulmonary veins. The pulmonary venous plexus shares venous drainage with splanchnic plexus, which is connected with the umbilical and cardinal venous plexus.[14]Systemic venous sinus (sinus venosus) develops at the junction between the somatic and splanchnic mesoderm. On other hand the pulmonary vein is separated from a greater splanchnic venous plexus that extends from the heart to liver.[15] Successive analyses suggested that common cardinal veins, which lie at basis of future sinus horns originate from somatic mesoderm by same methods, the pulmonary vein derive from the splanchic mesoderm that overlies foregut.[16] Instead of this proof relating to the fate and lineage of these cells, and convincing observations of direct drainage of the pulmonary vein into the left atrium in human,[17,18] mouse[19] and chicken[20] , some researchers argue that the pulmonary vein originates from the sinus venosus.[21] Drainage through the right common cardinal system represents failure of the separation of the normal pulmonary vein, and communication of the splanchnic plexus with the right common cardinal vein. Drainage through left common cardinal system follows a similar pattern. Drainage into the umbilicovitelline system indicates failure to separate the normal pulmonary vein from the cranial aspect of the splanchnic plexus, with continuing drainage into the developing hepatic circulation.

Evolutionary considerations of pulmonary venous development

In embryo the development of the pulmonary vein from a splanchnic plexus may also allow for some facts on evolutionary origins of the pulmonary circulation. Primitive animals follow the earliest embryonic stages of higher vertebrates by the presence of an massive vascular plexus that surrounds a tubular endodermal gut.[22] This endodermal gut does not contain specialized organs and both oxygen and nutrients that pass via the gut are taken up by this venous plexus to be distributed throughout body by the peristaltic pumping of a embryonic unsepted heart. As ventilation through lungs awake the heart gradually became septed and the circulatory system changed into a parallel arrangement of systemic and pulmonary blood flow. Necessarily the pulmonary vein separated from the venous returns of other endodermal organs such as the stomach and intestines. Evolution of incomplete septa as still seen in lungfish and amphibians presently[23] that generate left and right sided atrial, ventricular and outflow compartments which increased the efficiency of separation of the circulatory systems. In birds and mammal these flows have become completely separated by formation of complete atrial and ventricular septa. During development of embryo, however our circulatory system follows the evolution of our ancestors starting with a simple straight cardiac tube that gradually separates into four-chambered mammalian heart that receiving blood from two parallel circulations namely pulmonary and systemic. The pulmonary circuit carries deoxygenated blood away from your heart through pulmonary arteries and returns oxygenated blood to heart through pulmonary veins.

THEORY No. 3:

1 Blood from the yolk sac to sinus venosus carried by Omphalo-mesenteric veins. Cardinal veins drain the body of the embryo proper and Umbilical veins carry oxygenated blood from chorionic villi to the embryo.

2 The right SVC develops from right cardinal venous system whereas the left cardinal venous system mostly disappears and may potentially develop into left SVC (in <1% of individuals). The umbilicovitelline veins develop into the vessels like IVC, portal venous system and ductus venosus.

3 In the embryo division of the foregut forms the primordia of the lungs, larynx and tracheobronchial tree. So during early stage of development lungs are surrounded by the vascular plexus of the foregut. During this stage lungs is not directly connected with the heart. There are numerous connections with splanchnic plexus i.e, umbilicovitelline and cardinal venous systems.[24]

4 In early stage of embryo at around 27-29 days of gestation the lung buds are surrounded by the vascular plexus of the foregut (splanchnic).A small evagination arises in the left atrium (posterior wall) to the left of the developing septum secundum. It forms the common pulmonary vein.[25](Fig.2)

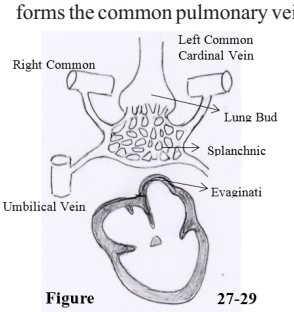
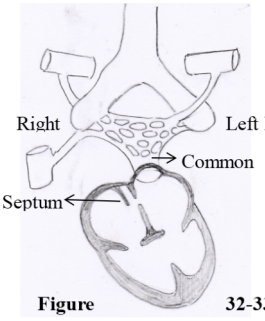


Figure 27-29

5 By the end of the 1st month at 32-33 days of gestation common pulmonary vein makes connection between the pulmonary venous plexus and the sino-atrial portion of the heart.Connection between pulmonary venous plexus and splanchnic venous plexus are still patent at this stage.[25] (Fig.3)

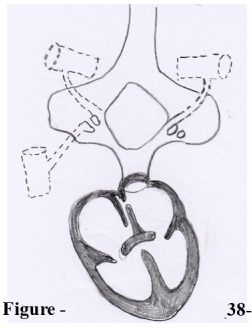


Common pulmonary vein established connection between

Connection between pulmonary venous plexus and splanchnic

Figure 32-33

6 Connection between splanchnic venous plexus and pulmonary venous plexus involutes. Common pulmonary vein incorporates into left atrium so that individual pulmonary veins connect separately and directly to the left atrium at gestational age of 38-40 days.[25] (Fig.4)



The connection between pulmonary venous plexus and splanchnic venous plexus involutes.

Common pulmonary vein incorporates into the left atrium so that individual pulmonary vein connect separately and directly to the left atrium

Figure - 38-40

7 The pulmonary vein canalised as a solitary vessel within the mediastinal tissues so as to connect intra-parenchymal pulmonary venous networks to the heart using the growing dorsal mesocardium as its portal of cardiac entry. The opening of the solitary vein became committed to the left atrium by growth of the vestibular spine.

The walls of the initially solitary vein in humans become included by a morphologically asymmetric process so that four pulmonary veins eventually drain independently into the left atrium. Failure of this incorporation on the left side in atrium may provide the substrate for congenital division of the left atrium.[18]

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