Absence of a Primary Division of the Pulmonary Trunk

An Ontogenetic Theory

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The two main varieties of this syndrome differ from one another in that, usually, "absence of the right pulmonary artery" occurs in otherwise normal hearts, while "absence of the left pulmonary branch" is accompanied by additional cardiovascular abnormalities, often of the Fallot type. A recent clinical observation of typical examples of the two varieties prompted a search of the literature for an embryologic explanation. It was noted that none of the proposed theories could satisfactorily be applied to all variants of the syndrome. The pertinent normal embryology was then reviewed for a developmental stage and locus in which a single derangement would subsequently cause either "absence of the left pulmonary artery" and tetralogy of Fallot, or "absence of the right pulmonary artery" and otherwise normal cardiac architecture.

Normal Human Development

The pulmonary arterial system develops from three different Anlagen: the main pulmonary artery (or pulmonary trunk) derives from the septation of the truncus arteriosus; its right and left branches originate from the sixth paired aortic arch; and the intrapulmonary arteries develop from the primitive vessels of the lung bud. The pulmonary trunk and its two primary divisions thus belong to the aortic-arch system.

In the 6-mm. embryo the aortic sac, which subsequently elongates to become the truncus arteriosus, gives off three paired arches, which extend laterally to join the dorsal aorta on each side (fig. 1): these are the third, fourth, and sixth. The first two arches have already disappeared. The fifth pair is not shown in figure 1. According to Tandler¹ this arch is the last to develop and has a very transient existence.

The sixth paired arch is a complex structure (fig. 2) consisting of a "proximal segment," originating from the aortic sac, of a "primitive pulmonary artery," which enters the hilum of the primitive lung, and of a "distal segment," which departs from the dor-

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Figure 1

Aortic arch system of a 6-mm. embryo (modified from Congdon¹). The third paired arch becomes the common carotid artery when the shaded portion of the dorsal aortae is absorbed. R.I.C. and L.I.C., right and left internal carotid arteries; R. and L. 3, 4, and 6, right and left third, fourth, and sixth aortic arches; R. and L.P.P.A., right and left primitive pulmonary arteries; R. and L.D.A., right and left dorsal aortae; U.C.A., unpaired caudal aorta.
ABSENCE OF PRIMARY DIVISION OF PULMONARY TRUNK

The primitie pulmonary artery divides the sixth arch into two segments: one proximal and one distal to the aortic sac.

Soon after the completion of the sixth paired arch, the segment of the dorsal aortae comprised between the third and fourth arches is reabsorbed (shaded area in fig. 1). This allows the former third arch to acquire a cephalad orientation and to become the carotid artery. At this stage the aortic arch system can be schematically represented as in figure 3. It will be noted from the diagram that this developmental phase is still marked by symmetry. It must be emphasized, however, that future transformations toward a left-sided predominance are greatly influenced by the interplay of two forces: one mechanical (pull of the heart and realignment of vessels) and one hemodynamic (preferential flow pathway and increasing blood volume).

The division of the truncus arteriosus (T.A.) and of the conus (C) results from the appearance of two ridges (1 and 2) which grow toward one another until they meet to form a septum. This extends throughout the truncoconus in a clockwise spiral of 180°, thus separating the ascending aorta (A.A.) from the pulmonary trunk (P.T.) and the left ventricular outflow tract from the right. The semilunar valves (S. Vs.) form at the level of the truncocoanal junction. For the sake of clarity, in this diagram the conus is drawn cephalad to the ventricular cavity (V.C.), although it is actually bent ventrally over the latter.

Schematic representation of the truncus arteriosus (T.A.), the paired fourth and sixth arches, and the right and left dorsal aortae, which join to form the unpaired caudal aorta. The common carotid arteries (R. and L.C.C.A.) derive from the third paired arch. The subclavian arteries (R. and L.S.A.) are migrating cephalad along the dorsal aortae.

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Blood from the pulmonary trunk flows preferentially into the left dorsal aorta through the distal segment of the left sixth arch (ductus arteriosus). The right dorsal aorta then atrophies as does the distal segment (D) of the right sixth arch (R, 6), while the proximal segment (P) of this arch persists as the initial portion of the definitive right pulmonary artery. The subclavian and the vertebral arteries (R. and L.V.A.) are still migrating cephalad.

clockwise spiral of 180° from the cephalic end of the truncus, between the fourth and sixth arches, to the base of the conus. Growing toward one another, they meet to form the truncus conus (fig. 4), which thus separates the ascending aorta from the pulmonary trunk and the two ventricular outflow tracts (derivatives of the conus). Moreover, by falling into alignment with the muscular portion of the ventricular septum, with which it fuses, it completes the separation of the two ventricles.

Cephalad, the newly formed pulmonary trunk is posterior to the aorta, and incorporates the right and left sixth arches, which have emerged from the posterior aspect of the truncus arteriosus.

While the truncal septation is still in progress, the mouth of the right sixth arch shifts through the dorsal wall of the pulmonary trunk until it reaches the mouth of the left, so that the two arches acquire a common origin. Simultaneously, the proximal segment of the left sixth arch is absorbed into the wall of the pulmonary trunk, causing the distal segment (ductus arteriosus) to align with the latter. Thus, the pulmonary trunk connects up with the left dorsal aorta by a shorter and more direct route than with the right dorsal aorta. Pulmonary blood will then preferentially flow into the left dorsal aorta, while the right dorsal aorta, owing to the decreased flow, involutes. Likewise, the distal segment of the right sixth arch, which no longer channels blood into the involuting right aorta, since it is being stretched by the pulmonary trunk, involutes and disappears (fig. 5).

The pulmonary arterial system has now formed and assumed the characteristic asymmetry of the "adult" plan. The left pulmonary branch (which derives solely from the primitive pulmonary artery) turns caudad as soon as it takes off from the pulmonary trunk, while the right branch (composed of the proximal portion of the right sixth arch and of the primitive pulmonary vessel) follows a horizontal course behind the aorta before curving down to the right hilum.

While these processes have been taking place in the aortic arch system, the right and left subclavian arteries have migrated cephalad along the dorsal aortae on each side to their definitive positions. As a result of the resorption of the right dorsal aorta, the right fourth arch becomes the innominate artery, while the left fourth arch persists as the definitive arch of the aorta (fig. 6).

Unequal Partitioning of the Truncus Conus
De la Cruz and da Rocha noted that if
the truncoconal ridges do not arise diametrically opposite one another, a variety of cardiovascular anomalies may result. They classify this group of anomalies under the heading "unequal partitioning of the truncus and conus." This is caused by the shifting (dorsal or ventral) of either the right or the left ridge, with the result that one great artery is larger than the other. The eccentric position of the ridges may be localized either at the cephalic end of the truncus or at the base of the conus, or may extend uniformly throughout the truncus and conus.

If it is limited to the truncus, and the ridges shift back to their normal positions at the level of the conus, the truncoconal septum will still fall into line with the muscular ventricular septum and the two will fuse. No intracardiac defects will ensue.

If, on the other hand, the conus is unevenly partitioned, the outflow tract of either ventricle will be stenosed. Furthermore, the truncoconal and the muscular ventricular septa will fail to align and a high ventricular defect will result. The larger sized artery will override the ventricular defect.

Malformations of the Fallot type result from uneven partitioning of the truncoconus at the expense of the pulmonary trunk.

**Review of Earlier Theories**

Several theories have been advanced to explain the absence of a primary division of the pulmonary trunk.

Ambrus \(^6\) postulated involution of the sixth arch and persistence of the fifth to form a bridge between the fourth (innominate artery) and the primitive pulmonary artery. This theory is unsatisfactory because it presupposes two unrelated embryologic errors: the involution of the sixth arch and the unlikely persistence of the fifth—a structure which in man has, at most, a very transient life.

McKim and Wiglesworth \(^7\) emphasized that an inverse relationship often exists between the side of the aortic arch and the side of the absent pulmonary division. They suggested that the proximal portion of the sixth arch was reabsorbed, while the distal portion (ductus arteriosus) persisted so as to connect the primitive pulmonary artery with the descending aorta or the innominate artery. Emanuel and Pattinson \(^8\) agreed with this view and remarked that the association of absent left primary division with defects of the Fallot type was too frequent to "be accounted for by chance."

Anderson, Char, and Adams \(^9\) enlarged upon the concept of abnormal resorption of the proximal segment of the sixth arch and emphasized the importance of hemodynamics in determining the asymmetrical normal development of the fourth and sixth arches. They further suggested naming the syndrome "proximal interruption of a pulmonary arch."

Pool, Vogel, and Blount \(^10\) recently suggest-
ed that the proximal portion of the sixth arch fails to develop. The “affected” lung would then receive its blood supply either from the bronchial arteries or from the ductus arteriosus (distal portion of the sixth arch) connecting the systemic circulation with the primitive pulmonary artery. These authors use Schneiderman’s theory (vide infra) to explain cases of “absent” right pulmonary artery in which the blood supply to the “affected” lung is provided by an artery arising from the ascending aorta.

What is dissatisfying about these theories is that after having shifted the problem from “absence” of a pulmonary artery to “faulty resorption (or interruption) of the proximal portion of the sixth arch” one is still left without an explanation as to why resorption (or interruption) occurred in the first place.

Schneiderman’s theory differs from the others in that it does not invoke a “resorption” process. This author explains the “absence” of the right pulmonary artery on the grounds of failure of the right sixth arch to migrate dorsally and to the left about the truncus. When the truncus divides, the right sixth arch thus remains incorporated in the ascending aorta.

Apart from the fact that this theory cannot be applied to cases of “absent” left pulmonary artery, it presumes that at some developmental stage the truncal take-off of the right sixth arch is ventral to the plane of truncal division. The observations of Bremer and Congdon do not support this view.

All the above theories fail to explain the frequent combination of absent left primary division and malformations of the Fallot type, or why the aortic arch is often located on the side opposite that of the absent division.

**Proposed Ontogenetic Theory**

The diagrams in figures 4 and 7A illustrate the close proximity between the truncal ridges and the origins of the pulmonary arches. If one ridge should arise from a more dorsal position than is normal, the sixth arch on that side would be incorporated in the anterior vessel resulting from the division of the truncus (aorta). Only one lateral pul-

monary artery would then arise from the posterior vessel (pulmonary trunk). The absence of a primary division of the pulmonary trunk is thus due to defective septation of the truncus and not to a developmental error of the sixth arch.

As figure 7A shows, the truncal ridges arise from two diametrically opposite regions on a plane oblique to the sagittal, the left ridge being more ventral than the right. Therefore, the degree of shifting required for the left ridge to arise dorsally to the origin of the left sixth arch (fig. 7C) is greater than that required for the opposite ridge to bypass the right sixth arch (fig. 7B).

![Figure 8](http://circ.ahajournals.org/lookup/doi/10.1161/01.CIR.29.1.128)

**Figure 8**

Absent right division of the pulmonary trunk. A. The systemic right pulmonary artery originates from the ascending aorta through the proximal segment (P) of the right sixth arch. B. The right pulmonary artery takes off from the innominate artery (I.A.) through the distal segment (D) of the right sixth arch.

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This considerable degree of dorsal shift on the part of the left ridge leads to uneven septation of the entire truncoconus at the expense of the pulmonary trunk (tetralogy of Fallot).

Several rare and complex examples of the syndrome have been reported, all of which can be explained by the proposed theory. In the following paragraphs only the two most common variants are discussed in detail.

**Normal Heart, Left Aortic Arch, and Absent Right Division**

According to the theory just outlined, this anomaly results from dorsal shifting of the right truncal ridge: the right sixth arch is then incorporated into the newly formed ascending aorta (fig. 7B). The pulmonary trunk gives rise solely to the left pulmonary artery. If the dorsorotation of the right ridge affects only the most cephalad portion of the truncus, no additional cardiovascular anomalies will occur. Essentially normal hemodynamics still result in a predominance of the left dorsal aorta and, consequently, in a left-sided aortic arch.

The destiny of the right sixth arch is dependent on hemodynamic and mechanical factors. With the resorption of the right dorsal aorta, the right fourth arch (innominate artery) acquires cephalad orientation (fig. 8). The right sixth arch is then pulled in three different directions: cephalad from the innominate, caudally from the right lung, and medially from the ascending aorta. Depending on the direction of the resulting force, the primitive pulmonary artery aligns either with the proximal or with the distal segment of the arch. In the first case (fig. 8A) the distal segment, under unfavorable mechanical and hemodynamic influences, would atrophy and the right pulmonary artery would then depart from the ascending aorta. In the second event the anomalous right pulmonary artery would arise from the innominate (fig. 8B).

**Fallot, Right Aortic Arch, and Absent Left Division**

This complicated anatomic picture results from dorsorotation of the left truncoconal ridge (fig. 7C). The incorporation of the left sixth arch into the ascending aorta requires a degree of dorsorotation so pronounced as to cause hypoplasia of the pulmonary trunk and of the right ventricular outflow tract. The truncoconal and the muscular ventricular septa lying on different planes cannot fuse and a ventricular defect, overridden by a large aorta, ensues.

Cephalad, the abnormally cloven ascending aorta is slanted to the right and thus imparts to the blood column a rightward swing (fig. 9). Blood then flows preferentially into the right fourth arch and the right dorsal aorta. The left dorsal aorta, receiving less of this blood and none from the pulmonary trunk, involutes. Consequently, the fourth arch on the left becomes the innominate artery and on the right persists as the definitive aortic arch. The aberrant left pulmonary artery will arise either from the ascending aorta (fig. 10A) or from the left innominate (fig. 10B), depending on whether the primitive pulmonary vessel aligns with the proximal or the distal segment of the sixth arch.

**Aberrant (Systemic) Pulmonary Artery**

The present theory postulates the existence of both lateral pulmonary arteries, but while one originates normally from the pulmonary trunk, the other is aberrant in that it arises...
Absent left division of the pulmonary trunk and right-sided aortic arch. A. The systemic left pulmonary artery originates from the ascending aorta through the proximal segment (P) of the sixth arch. B. The left pulmonary artery arises from the left innominate artery (I.A.) through the distal segment (D) of the sixth arch.

from a systemic vessel. The term “absence of a pulmonary artery” is thus inappropriate, and it would perhaps be preferable to describe the syndrome morphologically as “absence of a primary division of the pulmonary trunk.”

Although some of the more recent reports have included a description of the aberrant vessel, in many cases this has neither been visualized by angiocardiography nor demonstrated at autopsy.

Wagenvoort et al. have noted that the initial portion of the “systemic” pulmonary artery contains ductal tissue with an inherent tendency to obliterate postnatally by a process of endothelial proliferation. Depending on the extent of this process, which apparently does not always occur, the terminal portion of the vessel (primitive pulmonary artery) is under less hemodynamic stimulus or none at all, and thus either remains hypoplastic or atrophies. This might be the reason why angiography so often fails to visualize the aberrant pulmonary artery which, at times, cannot be recognized at the autopsy either. This might also explain the very large collateral circulation to the “affected” lung in cases in which the aberrant pulmonary artery is hypoplastic or atrophic. Ellis and associates demonstrated in rats that ligation of one pulmonary artery causes a striking enlargement of the bronchial arteries on the same side, and Liebow et al. have shown that the establishment of a pulmonary collateral circulation occurs more rapidly the younger the subject is at the time the pulmonary arterial flow is impaired.

As has been discussed in detail, the “systemic” pulmonary artery may originate either from the ascending aorta or from the innominate. The actual site of origin depends on the interplay of forces responsible for aligning the primitive pulmonary artery either with the proximal or with the distal portion of the sixth arch.

**Summary**

An ontogenetic theory is proposed to explain the absence of a primary division of the pulmonary trunk on the basis of an error in the septation of the truncus arteriosus, and the two common varieties of the syndrome are discussed in detail. It is suggested that:

Both lateral pulmonary arteries are present in this syndrome, but one of them arises anomalously from the systemic circulation.

The aberrant origin of one lateral pulmonary artery derives from the dorsal shifting of one of the two ridges responsible for the septation of the truncus arteriosus. The sixth arch on the side of the dorsorotated truncal ridge then becomes incorporated into the newly formed ascending aorta.

The combination of tetralogy of Fallot, right aortic arch, and absent left primary pulmonary division results from a single primordial error: a dorsorotation of the left ridge extending throughout the truncus conus.

The initial portion of the aberrant
emic) pulmonary artery may obliterate post-natally, thus impairing maturation of the terminal portion. This would explain the frequent failure to demonstrate the artery by angiography and, occasionally, at dissection.

References

William Withering

In 1783 Withering's health broke down completely and undoubted evidence of tuberculous infection of the lungs manifested itself. He was compelled to give up practice for several months and take a complete rest and, though he made a good recovery, in the following year he was again compelled to stop work.

Withering spent some of the time during this period in preparing for the Royal Society the paper "Experiments and Observations on the Terra Ponderosa," in which he described the natural barium carbonate named Witherite in his honor by the German geologist Werner, in 1790.

The most important task, however, was the preparation of his book on digitalis. This appeared in 1785 under the title "An Account of the Foxglove."—Louis H. Roddis, M.D. William Withering: The Introduction of Digitalis Into Medical Practice. New York, Paul B. Hoeber, Inc., 1936, p. 60.
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