

Letter to the Editor

Evolution of the theory of circulation[☆]

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Abstract

The first known descriptions regarding the basic aspects of circulation was probably in 500 B.C., by the Greek thinker Alcmaeon of Croton who observed arteries and veins to be dissimilar in animal dissection, and this was followed by the description of the human heart as a three chambered organ by Aristotle in 350 B.C. Herophilus of Chalcedon, a Greek anatomist, confirmed the findings of dissimilarity between arteries and veins in human cadaver dissections in 300 B.C., and determines that arteries were thicker than veins and contained blood. The advancement by far in the learning of human circulation was made possible first by significant contribution of Galen followed by observations of Ibn al-Nafis, Servetus, Colombo, Cesalpino, Vesalius and Fabricius. In 17th century William Harvey, an English physician, made important advancements into the understanding of this important area of medicine, advancements that continued with the observations of Malpighi.

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1. Early descriptions

The first known descriptions regarding the basic aspects of circulation was probably in 500 B.C., by the Greek thinker Alcmaeon of Croton who observed arteries and veins to be dissimilar in animal dissection, and this was followed by the description of the human heart as a three chambered organ by Aristotle in 350 B.C. Herophilus of Chalcedon, a Greek anatomist, confirmed the findings of dissimilarity between arteries and veins in human cadaver dissections in 300 B.C., and determines that arteries were thicker than veins and contained blood.

Claudius Galenus of Pergamum, more popularly known as Galen, in second century made one of the earliest significant contributions to the knowledge of human circulation. He was thought to be one of the greatest physicians of his time. By dissecting and experimenting on animals, he proved not only that arteries contained blood and not air, but also that the systems of arteries and

veins were completely distinct. He studied particularly the movements of the heart, the action of the valves, and the pulsatile forces in the arteries. According to Galen there were two kinds of blood. The one, contained in the venous system, was dark and thick serving the general nutrition of the body. This system originated in the liver. From the liver extended the venae cavae, one to supply the head and arms, the other the lower extremities, and extending from the right heart was a branch, corresponding to the pulmonary artery, the arterial vein which distributed blood to the lungs. This was the closed venous system. The second was the arterial system, which carried brighter, warmer blood, characterized by the presence of an abundance of the vital spirits. The two closed and separate systems communicated with each other only through certain pores or perforations in the septum separating the ventricles. However, Galen recognized that the arteries anastomose with the veins peripherally and they mutually receive from each other blood and spirits through certain invisible and extremely small vessels. He was among the first to recognize the heart as a 'pump'. Despite remarkable discoveries, he failed to complete the 'circuit' of circulation, which involved the transit of blood from the right to the left ventricle through the lungs.

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In mid-1200s, an Egyptian physician Ibn al-Nafis discovered and described the flow of blood to and from the lungs. This discovery of pulmonary circulation, centuries before any European reached the same conclusion, presaged the eventual decline of many medical beliefs held to be true since ancient Greece.

2. Sixteenth century progress

Michael Servetus (1511–1553), a Spanish physician, thoroughly studied Galen's writings. He, unaware of Ibn al-Nafis' findings, suggested that blood flowed from one side of the heart to the other via the lungs instead of through the wall between the ventricles, which refutes Galen's theory. He also pointed out that the pulmonary artery carrying blood from the right heart to the lung was too huge to carry blood to nourish only the lung and that its size indicated that it carried all the blood of the body to the lungs, so that the lungs could alter the blood itself. His second confirmatory observation was that the arteries in the lung emptied into its veins, which in turn emptied into the left ventricle. Contrary to Galen's theory, he declared absence of pores in the septum separating right and left ventricles. He was burned at the stake as a heretic, nine months after his manuscript had appeared in print [1].

Realdo Colombo (1510–1559), the celebrated Paduan anatomist and a contemporary of Servetus, made three important observations. His scientific work was made possible by his dissection of living animals. First, he not only revealed the presence of valves in the four vessels entering and leaving the right and left ventricles, but also discovered that these vessels permitted the flow of blood in one direction only; from the right ventricle to the lungs, back again to the left ventricle, and from there to the aorta. Second, he correctly described the contraction phase of the heart ventricles (the systole) and the relaxation phase (the diastole). Finally, an important observation of his was that the pulmonary veins leaving the lungs to empty into the left ventricle carried only blood and no air [2].

Cesalpino (1524–1603), a Pisan botanist and anatomist, made two major new observations. The first being a temporary closure of a vein in the arm or leg was followed by distension of the vein below the closure. His second observation was that the vena cava, as it emptied into the right auricle, had a diameter wider than when it left the liver, but he reached a mistaken conclusion that the vena cava carried blood from, and not to the heart [3].

The Belgian anatomist Andreas Vesalius (1514–1564), the founder of modern anatomy, also criticized Galen in the second edition of his book detailing human anatomy, *De Fabrica*. In 1539, he first described the veins that drew blood from the side of the body and opened the way to the study of the venous valves. Fabricius, an anatomist from Padua, published his work 'On The Valves In Veins' in 1603,

featuring the first drawings of vein valves [4], leading ultimately to the discovery of the circulation of blood by William Harvey.

3. William Harvey's discovery

William Harvey (1578–1657) is credited with the discovery of circulation [5]. He portrayed the anatomy of the auricles, ventricles and blood vessels, in addition the valves of the blood vessels entering and leaving the heart chambers. He noted the semilunar valves of the pulmonary artery and pointed out the manner of their opening and closing. He indicated that the pulmonary artery must carry blood to the lungs from the right ventricle. Harvey emphasized that the heart's only function was to pump blood and clearly differentiated the contractions of the auricles from those of the ventricles, noting that the auricles contracted before the ventricles. This last observation was truly novel. This discovery was achieved by dissection and observation of slow beating hearts of cold-blooded animals, such as fish, and also the warm-blooded animals during their process of dying, at which time their heart's contractions became slower and slower. Harvey went further to describe the dynamics of the pulmonary circulation. He proposed in a subtle manner that there might be a motion, as it was, in a circle. The blood forced by the action of the left ventricle into the arteries, was distributed to the body at large, and it then passed through the veins and along the vena cava, and so round to the left ventricle. Which motion he called *circular*. His subsequent investigations of the flow of blood in peripheral veins and arteries added further substance to his concept of the circulation of blood. He pointed out that when a vein was ligated, the segment below the ligature always swelled; the segment above the ligature always collapsed. Even more telling, when he ligated an artery, the veins connected to this artery always collapsed, only to open and fill with blood as soon as the ligature was removed. He proceeded to point out that the valves of all the body's veins were so constructed that they allowed the flow of blood in one direction only. Harvey summarized as follows.

Since all things, both argument and ocular demonstration, show that the blood passes through the lungs and heart by the action of the auricles and ventricles, and is sent for distribution to all the parts of the body, where it makes its way into the veins and pores of the flesh, and then flows by the veins from the circumference on every side to the center, from the lesser to the greater veins, and is by them finally discharged into the vena cava and right auricle of the heart, and this in such a quantity or in such a flux and reflux thither by the arteries, hither by the veins, as cannot possibly be supplied by the ingesta, and in much greater than can be required for mere purposes of nutrition; it is absolutely necessary to conclude that the

blood is in a state of ceaseless motion; that this the act or function which the heart performs by means of its pulse; and that is the sole and only end of the motion and contraction of the heart.

This summarizing sentence is perhaps the most significant medical declaration ever published. With his observations Harvey had made a remarkable contribution to medicine.

4. The progress continued

The story of circulation continued with the discovery of the microscope by a Dutch naturalist Anton van Leeuwenhoek (1632–1723). With the advent of microscope an Italian anatomist Marcello Malpighi (1628–1694) detected

the tiny capillaries through which blood in the arteries flowed to reach the veins [6]. Harvey's circle was completed with this finding and also laid the foundation for advances of this vital area of medicine.

References

- [1] Servetus M. *Christianismi Restitutis*. Vienna: Balthasar Amoulet; 1553.
- [2] Colombo R. *De re Anatomica*, Libri XV. Venice: Nicolai Beullacuae; 1559.
- [3] Cesalpino A. *Peripateticarum Questionum*, Libri Quinque. Venice: Apud Luntas; 1571.
- [4] Fabrici G. *De Verarum Osticulis*. Padua: Lorenzo Pasquati; 1603.
- [5] Harvey W. *Exercitationes de generatione animalium*. London: O. Pulleyn; 1651.
- [6] Malpighi M. *Opera Omnia*. London: R. Scot; 1686.