Studying circulation on cadavers that lacked it: Vascular medicine’s evolution from dead bodies to living cells

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Curiosity may have killed the cat but did it not also lead the greatest anatomists of all time to dissect the cat itself afterwards? The body and its secret, sacred mysteries have always fascinated those who occupied themselves with anatomy and physiology and back in time hands-on on the cadaver was the only, yet of tremendous difficulty, way of exploring how the species grew and functioned.

ANCIENT TIMES—EGYPT, INDIA AND GREECE

Back in time in ancient Egypt embalmers held the responsibility of preparing the body for the afterlife and thus, for religious reasons, they emptied [1] the body from internal organs giving rise not only to anatomical studies and surgical procedures but also to the modern embalming techniques.

In ancient Greece’ Hippocrates (460–370 BC) (Figure 1) was the first to correlate the carotid artery disease to transient ischemic attack (TIA) and stroke and invented the term ‘apoplexia’ which means to knock down to describe it [2], connecting higher neurological function to blood supply to the brain via the carotid. The significance of the carotid artery and its link to brain activity is underlined by the name itself: Karos in ancient Greek meaning ‘to stupefy’ [3]. Soon after Hippocrates, Herophilus of Chalcedon (335–280 BC) and Erasistratus of Ceos (304–250 BC) were the pioneers [4, 5] in systematic dissection and vivisection. Especially, Herophilus contributed

Figure 1: Hippocrates from Kos, is considered as the father of modern medicine. He was the first who organized the existing medical knowledge and transformed ancient medicine to developing science.

Source: https://hippocratesmedicine.wordpress.com/2014/01/12/ιπποκράτης-ο-πατέρας-της-ιατρικής/
immensely to understand the arterial and surprisingly the venous blood flow of the brain [6]. Galen of Pergamon (130–210 AD) (Figure 2) on the other hand, was prohibited to contact cadaver research so he turned in animals [7] to fill his knowledge, leading to the belief that the brain was the center of the mental activity, not the heart [8]. Galen also tried to explain circulation but failed to do so because he assumed the intraventricular septum had pores [9]. That belief perpetuated by many anatomists after him.

It has been stated [10] that many surgeons of Roman times and early Byzantium years worked on vascular surgery with Antyllous (2nd century AD) and Oribasius from Pergamum (325–403 AD) being the prominent two. Incredibly enough it seems that not only they gave a definition of aneurysms but Antyllous also described two techniques for aortic aneurysm repair.

In India, the ancient Sanskrit text of Sushruta Samhita [11] underlined the significance of knowledge of the anatomy to young physicians; due to dissections being prohibited the bodies were first soften by steam to make it possible to remove the tissues off without the use of a knife. It is now believed that ancient Indian physicians have been only a few steps away from understanding blood flow [12].

**MEDIEVAL TIMES—ARABS AND EUROPEANS**

The knowledge that massage of the carotid artery (or of what it is known today as the carotid gland) will result in a state of loss of consciousness is saved and transferred by Muslim scholars [13] during the early medieval times. Known for his work Hali Abbas (died 982–994 AD) provided a first anatomical description of the carotid arteries and predicted the existence of the capillaries well before William Harvey discovered it [14]. One of the first to question Galen’s work, Ibn Al-Nafis (1213–1288 AD) set the basis for the discovery of pulmonary circulation [15]. The prohibition of dissection of human corpses in Europe and the Arabic world possibly meant a big step back in studying anatomy. However, in 1315 the first public dissection takes place by Mondino de Luzzi [16] (1270–1326 AD) allegedly aiming to prove the works of Galen, changing the future of medicine for the years to come.

**RENAISSANCE—SCIENCES’ MODERN SPRING**

Da Vinci’s (1452–1519 AD) outstanding works are not only to be found in the fields of art; it is well known that he dissected human remains with astonishing precision even though he lacked the modern knowledge on how to fixate the corpse [17]. He also described [18] atherosclerosis. Vesalius (1514–1564 AD) indisputably raised emphasis on the significance of dissection of human cadavers in studying anatomy; not only did he correct mistakes made by Galen [19] that previous anatomists refuse to admit but also he engaged himself actively in dissections leading to a surgical revolution [20]. In his work, he has named the great vessels mapping their position on the human body and he has even come to the conclusion that the thought-to-be perforated intraventricular septum was in fact not perforated [19].

It was in 1628 when William Harvey (1578–1657 AD) (Figure 3) published his work explaining the flow of the blood inside the vessels, the role of the valves and the capillary, work completed by his student Malpighi soon afterwards using a microscope [21]. This was a huge leap for vascular medicine as the two thought-to-be unrelated vascular systems of the human body are now recognized to utilize the same function.

**ON THE LYMPHATICS—A FORGOTTEN SYSTEM**

Hippocrates described the axillary lymph nodes while Galen the mesenteric lymph nodes and Paul of Aegina tonsils [22]. In 1622, Gaspare Aselli (1581–1626 AD) vivisected a well fed living dog and noticed several white cords [23] raising interest on the lymphatics. However, it was not until Eustachi (died 1574 AD) discovered the thoracic duct and the notorious dispute of Bartholin (1616–1680 AD) and Olaus Rudbeck (1630–1702 AD) in the seventieth century [22] that field of lymphatics really
evolved. Soon afterwards Hunters brothers discovered (mid 1700 AD) the function of the lymphatic system while William Hewson [24] (1739–1774 AD) did a great work in its comparative anatomy between different species and Cruikshank (1786) published his illustrations on the topic [22]. It was yet another great medical discovery that was meant to change the history of science.

FROM 19TH CENTURY TO MODERN MEDICINE

Valentine Mott [25] (1765–1865) and Rudolph Matas [26] (1860–1957) linked their names with the birth and blossom of vascular surgery in the 19th century, with the latter successfully treating an aortic aneurysm in 1923. Their work on the field gathered the academic knowledge of their times and actually used it in the operation theater and on living patients. Their courageous application of theory in practice eventually led to new discoveries. During the 20th century six Laureates associated with circulation and vascular surgery were nominated for Nobel Prize [27]. In 1912 to Alexis Carrel for his surgical advances, in 1920 to Steenberg Krogh for work regarding the capillaries, in 1924 to Einthoven for the electrocardiogram, in 1938 to Heymans on his work on sinus and the aorta, in 1956 to Cournand, Forssmann and Richards for heart cauterization and in 1998 to Furchgott, Ignarro and Murad for their work on signaling and circulation. Another major breakthrough in cardiovascular medicine happened in 1990 when Juan C. Parodi performed the first endovascular abdominal aortic aneurysm [28] repair opening a new road for Vascular Medicine.

EYES ON THE FUTURE

Modern medicine does not count on the scalpel as much as in the past. Focus nowadays is on vascular biology. The detailed structure of the endothelium and its metabolism, angiogenesis and angiogenic factors, understanding endothelium cell signaling are only few of the new research aspects this field has to present [29]. Genetics lead to the discovery of the Nox gene family and the role they play in oxidative stress of the epithelium [30] while in the meantime epigenetics [31] provided new possible targets for preventing vascular damage. Another study [32] linked miRNA to atherosclerosis. The CANTOS [33] trial gave promising results regarding the role inflammation plays in atherosclerosis and even proposed new therapeutic approaches using antibodies. It seems that a new era is in front of us making “molecular bypass” [34] sounding less of a vascular surgeon’s nightmare and more of a verisimilar scenario of the future.

CONCLUSION

Modern medicine owes its deep understanding of the circulatory system to pioneers of their time who solved the puzzle of the human body piece by piece. The study of the remains offered a great deal of information on the structure and physiology of human nature and thus should be considered a cornerstone in the history of exploring and teaching medicine. However, as science evolves biology seems to take the leading role not only explaining the nature of cardiovascular disease but discovering new ways to treat. Until then, the scalpel seems to remain an arrow in the medical quiver.

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