Prevailing Theories in Cardiovascular Physiology during Ancient and Classical Times

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Currently accepted theories of human physiology have been proposed only in the last two centuries, with understanding of many molecular processes proposed within the last 50 years. However, theories of human physiology have been debated for thousands of years. This paper focuses on the theories of physiology discussed in ancient and classical times, with a focus on the structure and function of the heart and its vessels. The experiments and subsequent conclusions of physicians and philosophers of antiquity have led to some interesting interpretations. Notably, anatomical studies remain remarkably similar to today's understanding, whereas ideas of function and physiology are drastically different.

INTRODUCTION

Human physiology is the study of function in living human organ systems. In the past century, knowledge in this field has been enriched by studies in a plethora of other disciplines, including cell biology, chemistry, physics, genetics, epigenetics, population studies, and even sociological studies. Incredibly, this fund of knowledge is only a recent achievement in the history of human thought. This paper explores the prevailing theories of human physiology during antiquity more than 2,000 years ago, much of it only sparingly in agreement with modern theories. Because the topic of human physiology is vast, the paper will limit its focus primarily to cardiovascular theories in ancient and classical times.

ANCIENT EGYPT

Our knowledge of ancient Egyptian medicine is limited to the preservation of a handful of papyrus scrolls more than 3,000 years old. Through these scrolls we learn that magic and science were part of a single, inseparable concept called *heka* (Veiga, 2009). Like today's physicians, the magician-physicians of ancient Egypt prescribed mixtures of plant and animal products that could have had active ingredients also found in today's medicines (Lefebvre, 1963). In most cases, however, these magician-physicians would invoke spells, recite incantations, or perform exorcisms to cure illnesses; any pharmaceutical prescription was simply an adjunct to the larger healing ritual. Although such practices are illogical and incomprehensible to modern sensibilities, Veiga (2009) suggests that for a predominantly illiterate ancient Egyptian population, the ability to decipher hieroglyphics to perform rituals could seem especially magical and therefore therapeutic. In that case, medical practice in ancient Egypt might have been benefiting from a strong placebo effect.

Despite their penchant for the occult, ancient Egyptian magician-physicians were also familiar with many modern medical topics. Their remedies for conditions such as dislocations and compound fractures remain remarkably similar to treatment today: sutures, brick supports for stabilizing head and neck injuries, wooden splints, and a recipe for creating adhesive plaster (Lefebvre, 1963). Internal diseases familiar to any modern healthcare provider are also described: headache, constipation, dysentery, amenorrhea, cystitis, and even a hematuria that was most likely due to schistosomiasis in the Nile River (Bryan, Smith, & Joachim, 1974). Egyptian medicine was apparently so complex that the magician-physicians were known to be specialists managing single types of disease: there were dentists, ophthalmologists, and even proctologists (literally translated as "herdsmen of the anus") (Nuun, 2002). But above all, these and all other internal diseases were believed to be supernatural afflictions. It therefore followed that an illness of supernatural origin should have a supernatural remedy.

Not surprisingly, ancient Egyptians' understanding of cardiovascular physiology differs drastically from currently accepted principles of physiology. Anatomically, 46 vessels were said to originate from the heart and extend to all the limbs. Through these vessels, the heart controlled all physiological processes of the body (Lefebvre, 1963). For example, certain vessels from the nostrils would carry air directly to the heart; the air would then pass from the heart to the lungs before dispersing throughout the body (Lefebvre, 1963). Other vessels were specialized to carry other bodily fluids such as sperm, urine, fecal material, tears, mucus, and blood. Diseases arose when the bodily fluids existed in abnormally disproportionate amounts in the heart.

Because the heart was also said to be the body's central organ for emotions and consciousness (Lefebvre, 1963; Veiga, 2009), feelings such as sadness and anger were similarly the result of the heart closing itself off from its vessels (Bryan et al., 1974). Despite hieroglyphic language suggesting that the Egyptians attributed arterial pulses to the heartbeat, they seemed to regard the heart as a simple well instead of as a pump (Bryan et al., 1974; Lefebvre, 1963). This anatomical and physiological disconnect might have been due to the mummification tradition, in which the heart was not removed from the body; in the afterlife the heart could then be judged and weighed against the feather of Maat for possible sins against the gods (Veiga, 2009). The ancient Egyptians would therefore have had little opportu-

nity to study cardiac anatomy and infer the heart's possible physiological function.

ANCIENT GREECE

Pre-Hippocratic ancient Greek medicine did not significantly differ from that of neighboring civilizations, including ancient Egypt and Mesopotamia, with respect to superstition and supernatural influence (Longrigg, 1993). Diseases in ancient Greece were thought to be manifestations of a god's anger, and could be cured only by appeasing that god with prayers and sacrifices. The Homeric tales are replete with references to epidemics attributed to the wrath of the gods, and even battle-inflicted wounds represented a spiteful god withdrawing his divine protection in displeasure (Longrigg, 1993). The Greek pantheon also included Asclepius, the god of healing and medicine, whose ritual purifications could cure afflicted believers. The cultural impact of Asclepius remains evident today: his name is invoked in the oft-recited Hippocratic oath, and his serpent-entwined staff, the rod of Asclepius, is still the symbol of medicine and healthcare.

Hippocrates of Cos (ca. 460–377 BCE) was the first physician-philosopher to produce a body of medical theories and observations almost entirely devoid of supernatural, superstitious, and religious references. Today, he is regarded as the father of Western medicine, but he was also heir to a long and vibrant tradition of philosophical thought. The roots of his thinking date back to the sixth century BCE, when a group of thinkers now known as the Ionian philosophers attempted to explain their natural world—from lightning to earthquakes to air—without the trappings of the supernatural (Longrigg, 1993). Hippocrates himself believed that supernatural explanations of disease came from a lack of understanding of natural processes:

> I am about to discuss the disease called "sacred" [epilepsy]. It is not, in my opinion, any more divine or more sacred than other diseases, but has a natural cause, and its supposed divine origin is due to men's inexperience, and to their wonder at its peculiar character. Now while men continue to believe in its divine origin because they are at a loss to understand it, they really disprove its divinity by the facile method of healing which they adopt, consisting as it does of purifications and incantations. (Hippocrates, 1998)

Hippocrates implied that understanding the nature and origin of disease was not just a matter of philosophical or religious debate. Supernatural etiologies were not merely erroneous, but also prevented effective treatment of diseases such as epilepsy.

Hippocrates, like some of his contemporaries—philosophers such as Democritus of Abdera and Anaxagoras of Clazomenae—believed that the human body was a balanced microcosm of the universe that consisted of fire, water, air, and earth. These four elements were endowed with four opposing qualities: the hot, the cold, the dry, and

the moist (a principle first espoused by an elder philosopher named Alcmaeon of Croton) (Rothschuh, 1973). Good health required a balanced blend of these elements and qualities. Over time, the Hippocratic physicians developed these principles into the concept of the four bodily humors: the warm and moist blood, the moist and cold phlegm, the cold and dry black bile, and the dry and warm yellow bile (Rothschuh, 1973). (Notably, the concept of different bodily fluids can be traced back to the ancient Egyptians.) Maintaining a healthy mixture of humors required an internal fire located in the left ventricle of the heart, with combustion possible only by breathing air (*pneuma*) and receiving nourishment (Rothschuh, 1973).

Over time, the followers of Hippocrates recognized that the heart contained two ventricles and two atria. A Hippocratic writer even recognized that the atria contracted separately from the ventricles: "one might observe the heart tossing about as a whole, but the ears independently inflating and collapsing" (Katz & Katz, 1962). "Ears" refers what we now call the atria. Hippocratic use of the word "ears" to name the atria persisted to the mid-20th century. Medical texts published in the 1950s termed the left and right atria the left and right auricles, which is an Anglicization of the Latin word for ear: *auricula*. Today, the right and left auricles refer to the right and left atrial appendages. The cardiac valves are similarly described with anatomic precision:

> There is a pair of [veins] at the entrance to which there have been constructed three membranes for each, rounded at the extremity at least, to the extent of a half-circle, and when they come together it is marvelous that they close the outlets, and the end of the veins. . . . If someone . . . removes the heart of a dead man and takes up one of these membranes and bends another up against it, water will not go through into the heart, nor even the breath when forced in. (Katz & Katz, 1962)

The anatomy and function of the cardiac valves were correctly deduced, but no apparent connection was made to their role in ensuring the unidirectional circulation of blood. The Hippocratic writers did not appear to recognize the phenomenon of blood circulation, nor did they believe that the left ventricle was filled with blood. Instead, the bloodless left ventricle was the location of the body's innate internal fire, and the heartbeat was a function of this internal fire. Blood flow was simply the internal motion of a body humor that moved in healthy balance with the other body humors. The movement of blood was postulated to be part of a vague process of all organ development involving blood coagulation (Rothschuh, 1973).

A century later, Aristotle (384–322 BCE) revived the ancient Egyptian belief that the heart and blood vessels were part of a connected system of which the heart was the epicenter. Like the ancient Egyptians, Aristotle believed that the heart was the central organ of the body and the seat of the soul. (Hippocrates believed that the brain was the central

organ of the body.) The heart was the location of the vital internal fire, the site of the body's blood production, and the origin of the body's vascular system. These processes interacted to produce the body's pulse, cardiac contraction, and respiratory movements (Rothschuh, 1973). Newly produced blood in the left ventricle created an expanding heat that caused the chest wall to expand. Inspired air traveled from the lungs to the left ventricle via the pulmonary veins to cool down the blood, resulting in the expiratory movement of the chest (Rothschuh, 1973). When the innate heat expanded again, a pulse-wave pushed blood through all the blood vessels. The blood eventually was converted to organs and tissues, and other fluids of the body were all somehow derived from blood (Rothschuh, 1973). Aristotle's physiology therefore marked an important shift away from the theory of balanced body humors to a physiology based on directionally flowing blood.

Aristotle definitively localized blood to the blood vessels within the body, but some of his intellectual successors wondered if these biological vessels could possibly contain substances other than blood. These hypotheses may have come from Aristotle. He apparently killed animals with chloroform (Huxley, 1879), which left a conspicuous anatomical artifact: dissections prepared in this manner engorged the right atrium with so much blood that it appeared to be continuous with the vena cava (Huxley, 1879). (Aristotle therefore recognized only three heart chambers: the right ventricle, the left atrium, and the left ventricle.) In contrast to the right side of the heart, the left side of the heart and the arteries could have appeared relatively empty (Fulton & Wilson, 1966). If the thickened muscular walls of the arteries did not collapse when empty, in dissection they could appear to be hollow tubes inside the body. This observation left the possibility that the arteries carried only air. The Latin word *arteria* originally referred to the trachea and associated bronchioles.

Herophilus of Chalcedon (ca. 335–280 BCE) was one of the physicians of antiquity who believed that the arteries carried only air. He remains the first and only physician in antiquity to study human cadavers, and he dissected at least 600 of them in his career (Rothschuh, 1973). In these dissections he distinguished arteries as those vessels that were six times as thick as the vessels he called veins (Fulton & Wilson, 1966). Using this thickness criterion, Herophilus concluded that the arterial system was located primarily on the left side of the body, and the venous system was located primarily on the right. Most interesting to him were the pulmonary artery and the pulmonary vein. The pulmonary vein connected to the left side of the heart (an "artery" in Herophilus's system), but it was as thin as a vein. Herophilus therefore called it a "vein-like artery," *arteria venalis* (Fulton & Wilson, 1966). Similarly, the connection of the thick-walled pulmonary artery to the right side of the heart prompted Herophilus to call it an "artery-like vein," *vena arterialis* (Fulton & Wilson, 1966). Both terms would persist through the 17th century CE. Herophilus additionally noticed that the arteries, but not the veins, exhibited a

pulsing nature (Fulton & Wilson, 1966), and that the rate of this pulsing was directly related to the respiration rate (Beaujeu, 1963). He therefore concluded that the arteries must contain only air. This conclusion, however erroneous, represented an attention to physiological and anatomical detail not previously witnessed in antiquity.

Erasistratus of Julis (ca. 310–250 BCE), a younger contemporary of Herophilus, agreed that the veins contained only blood, and the arteries held only air. Unlike Aristotle, he believed that blood was created from digested food in the liver, and then moved to the right ventricle by means of the vena cava (Rothschuh, 1973). Inspired air resided in the lungs and moved into the left ventricle by means of the pulmonary vein (the "vein-like artery"). The heart contracted and expelled both air and blood to the entire body via their respective arterial and venous systems, and the heart valves worked to prevent reflux back into the heart (Beaujeu, 1963)—a hypothesis from antiquity that bears some resemblance to the current cardiovascular understanding of unidirectional circulation. Thus, Erasistratus's ideas largely reflect a synthesis of Aristotle's and Herophilus's theories.

Pneuma, not blood, was the primary substance in Erasistratus's physiology. The lungs apparently consumed all blood that entered the pulmonary artery (the "artery-like vein"), and somehow transformed air into a substance called *pneuma* by the time it reached the left ventricle. The *pneuma* was then pumped through the bloodless arterial system, where it could transform again into *pneuma psychikon* in the brain to enable nerves to feel sensation and muscles to contract (Beaujeu, 1963; Rothschuh, 1973). The *pneuma* could alternatively transform into *pneuma zotikon*, which controlled the body's vegetative functions, including moving blood for nourishment of the organs and tissues (Beaujeu, 1963; Rothschuh, 1973).

Like that of Aristotle before him, Erasistratus's physiology advocated active movement of some bodily substance— first as blood in the venous system and then as *pneuma* in the arterial system—but more firmly reconciled his ideas to objective observations.

One argument against the *pneuma* hypothesis was the observation that blood spurted from a cut artery until the animal died, suggesting that arteries did carry blood. Erasistratus therefore postulated that there should be a connection, too small to be seen with the naked eye, between veins and arteries. He called these connections *synanastomoses* (Fulton & Wilson, 1966). Under normal conditions, blood naturally remained in the veins. However, when an artery was cut in a live animal, all the *pneuma* in the artery instantly escaped through the opening and created a vacuum. Because nature abhors a vacuum (a concept called *horror vacui* and advanced by the philosopher Strato of Lampsacos) (Rothschuh, 1973), blood subsequently rushed from the veins through the *synanastomoses* into the arteries and out of the body (Fulton & Wilson, 1966). Without

the technology to refute this hypothesis, the teachings of Erasistratus stood unchallenged for more than 450 years.

ANCIENT ROME

The next great advance in physiology occurred during Roman times under the physician and philosopher Galen of Pergamon (ca. 130–201 CE). Galen was a learned man who was a product of his times. He advocated the Hippocratic theory of humors, and he supported the long-standing idea of the *pneuma* (Rothschuh, 1973). He even agreed with the basic premise of a right-sided venous system and a left-sided arterial system, in which the liver created blood that would ultimately mix with air to form *pneuma*. However, he also conducted numerous animal dissections and experiments that revolutionized the Romans' understanding of human physiology.

Galen's most celebrated achievement in cardiovascular physiology, in direct opposition to the ideas of Erasistratus, demonstrated that blood actually resided within the arteries. He isolated a single dog's artery from all other tissues and tied that artery in two places. By cutting into the artery between the two tied knots, Galen demonstrated that blood existed at all times within the artery (Beaujeu, 1963). He similarly demonstrated the presence of blood in the left ventricle during a vivisection experiment on an animal, in which he punctured the animal's left ventricle (Rothschuh, 1973). While conceding that it was not possible for an internal fire to reside in a blood-filled left ventricle, Galen still maintained that some sort of innate heat emanated from the heart. Proof of this innate cardiac heat lay in the observation that if a limb were bandaged tightly enough, it would lose its pulse as it became cold and pale. When the bandage was released, the pulse would be restored and heat would return to the arm (Fulton & Wilson, 1966). The distribution of this innate heat throughout the body continued to be a major role of the arterial pulse in Galen's physiology.

In order to reconcile his findings with the long-held belief that bodily distribution of *pneuma* is required for life, Galen proposed that the arteries mixed both *pneuma* and blood within their lumen. He thought that the mechanism in which this mixing occurred also lay in the rhythmic dilation and contraction of the heart and arteries. By dilating and enlarging their lumen, the arteries created a vacuum in which venous blood could be pulled into the arteries and in which *pneuma* could be suctioned into the arteries by passing through minute pores in the skin (Fulton & Wilson, 1966). Reciprocal contraction of the arteries would reverse the movement of blood and *pneuma*. This palpable pulse originated from the heart, which Galen demonstrated by tying an isolated artery and showing that no pulse-wave existed distal to the tied knot. Galen then attached a tube to the artery and demonstrated that the pulse-wave was propagated through the tube (Beaujeu, 1963). These ideas represent the first cohesive hypothesis in which heart contractions and arterial pulses were intimately related, and the movement of bodily fluids was driven by contractile instead of thermodynamic forces.

Galen, however, was not convinced that the presence of arterial blood could be explained by suction pull from venous blood via arterial dilation alone, and therefore borrowed Erasistratus's idea of *synanastomoses*. Like Erasistratus, he envisioned that blood flow began in the liver, where all blood was produced with the help of a hepatic innate heat (Rothschuh, 1973). Some of the blood flowed directly from the liver to other organs via the venous system, while the rest of the blood flowed to the right ventricle via the vena cava. At the level of the right ventricle, most of the blood flowed through *synanastomoses* located in the interventricular septum and into the left ventricle, where it would mix with *pneuma* and the cardiac innate heat (Rothschuh, 1973). Blood not traveling through the interventricular septum would pass through the pulmonary artery to nourish the lungs. Galen conceded that collapse of the lung during expiration might push some blood from the lungs into the pulmonary vein via pulmonary *synanastomoses*, but the amount of blood that traveled this route was minuscule compared to the amount traveling through the interventricular septum (Fulton & Wilson, 1966). Galen was therefore tantalizingly close to deducing pulmonary circulation, and from that intellectual standpoint the possibility of unidirectional circulation. That discovery would not occur for another fifteen centuries.

CONCLUSION

The unidirectional circulation of blood from the heart through pulmonary and systemic vasculatures and back to the heart would not be advocated until 1628 CE, when William Harvey published his treatise *Exercitatio Anatomica de Motu Cordis et Sanguinis* (*On the Motion of the Heart and Blood*). This discovery set the stage for a radical reconceptualizing of all organs and their functions, particularly the nature of the heart and the liver, and the origin of internal heat. From this seminal discovery, the field of cardiology and vascular medicine has since witnessed astounding achievements beyond what any physician of antiquity could possibly have imagined: cardiac electrophysiology, interventional cardiology, and even epigenetic associations with cardiac disease. But in reviewing what our ancient predecessors believed and how they came to their conclusions, we should remember that any and all future intellectual breakthroughs will depend on the same skill set that the physicians in antiquity possessed: deductive reasoning, free of preconceived assumptions, that is applied to objective, reproducible observations.

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