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Galen and the beginnings of Western physiology

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West JB. Galen and the beginnings of Western physiology. *Am J Physiol Lung Cell Mol Physiol* 307: L121–L128, 2014. First published May 30, 2014; doi:10.1152/ajplung.00123.2014.—Galen (129–c. 216 AD) was a key figure in the early development of Western physiology. His teachings incorporated much of the ancient Greek traditions including the work of Hippocrates and Aristotle. Galen himself was a well-educated Greco-Roman physician and physiologist who at one time was a physician to the gladiators in Pergamon. Later he moved to Rome, where he was associated with the Roman emperors Marcus Aurelius and Lucius Verus. The Galenical school was responsible for voluminous writings, many of which are still extant. One emphasis was on the humors of the body, which were believed to be important in disease. Another was the cardiopulmonary system, including the belief that part of the blood from the right ventricle could enter the left through the interventricular septum. An extraordinary feature of these teachings is that they dominated thinking for some 1,300 years and became accepted as dogma by both the State and Church. One of the first anatomists to challenge the Galenical teachings was Andreas Vesalius, who produced a magnificent atlas of human anatomy in 1543. At about the same time Michael Servetus described the pulmonary transit of blood, but he was burned at the stake for heresy. Finally, with William Harvey and others in the first part of the 17th century, the beginnings of modern physiology emerged with an emphasis on hypotheses and experimental data. Nevertheless, vestiges of Galen's teaching survived into the 19th century.

ancient Greeks; body humors; cardiopulmonary system; Vesalius; Harvey

CLAUDIUS GALENUS (129-c. 216 AD) (Fig. 1), who is universally known as Galen of Pergamon, was a famous Greco-Roman physician and physiologist. He is an appropriate subject for this essay on the beginnings of Western physiology for several reasons. First, he and his school had an extraordinary influence on medical science including physiology for about 1,300 years. It is not easy to think of a comparable situation in any other area of science where one school dominated thinking for so long. In fact, some medical students were still studying Galen's writings in the 19th century and some of the practices that he advocated, for example bloodletting, were still being used at that time.

Another reason for choosing Galen as an introduction to Western physiology is that he was heavily influenced by the teaching of the ancient Greeks. He therefore allows us an opportunity to summarize this important body of work. Admittedly many of these mainly theoretical musings of over two millennia ago do not resonate with present-day physiologists, but some of the influences of this group can still be seen.

Finally, the writings of Galen and his school were extremely voluminous and much of the material still survives. For example, Karl Gottlob Kühn collected no less than 22 volumes (11). Other large collections of Galen's writings also exist. Therefore there is a wealth of information about the man, his school, and his teachings.

The main purpose of this essay, as with the others in the series, is to introduce medical and graduate students to his work and show how his teachings lasted up to the Renaissance. Then with the advent of Vesalius, Harvey, Boyle, and many of their contemporaries, a sea change in attitudes occurred, and the beginnings of modern physiology are clearly seen. For graduate and medical students who would like an introduction to Galen, the short books by Singer (18, 19) are recommended. More recent extensive studies have been carried out by Nutton (12). An article by Boylan (2) has a useful list of primary and secondary sources.

Brief Biography

Galen was born in Pergamon (modern day Bergama, Turkey), which at the time was a very lively intellectual center. The city boasted a fine library that had been greatly expanded by King Eumenes II, and it was only bettered by the famous library in Alexandria. Galen's father was a well-educated and affluent man who had high hopes that his son would continue in his own philosophical traditions. However, a remarkable event narrated by Galen was that when he was about 16, he had a dream in which the god Asclepius urged his father to have his son study medicine. His father agreed and Galen was initially a student in Pergamon, which was a famous medical center and attracted many sick people who could afford to get the best treatment. Three years later his father died, leaving him wealthy, and he was able to travel widely and visit the most important medical centers including the outstanding medical school in Alexandria.

At the age of 28 Galen returned to Pergamon, where he became a physician to the gladiators. This institution was run by the High Priest of Asia who was enormously influential. Galen spent four years treating the gladiators for their wounds and also emphasizing their training, fitness, and hygiene. It is said that during this period there were only five deaths among the gladiators while he was in charge, which was an enormous improvement over the previous period when many gladiators died of their wounds. There is an interesting recent article on head injuries of gladiators whose bodies were exhumed from a cemetery in Ephesus, Turkey (9). A feature was the large number of extensive fractures of the skull despite the fact that most gladiators are believed to have worn helmets. Perhaps the blows were delivered after the victims had received other serious injuries to put them out of their misery.

When he was 33 Galen went to Rome, then the center of the civilized Western world. However, he recounted that he fell out with some of the prominent physicians there and, fearing that he might be harmed, he moved away from the city. A few years later he was recalled by the Roman emperors Marcus Aurelius and Lucius Verus, who ruled together, to serve in the army. A

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Fig. 1. Galen of Pergamon (Claude Galien in French). Lithograph by Pierre Roche Vigneron, Paris ca. 1865.

great plague broke out in Rome at that time and large numbers of patients developed severe skin lesions and many died. It is now thought that the disease was smallpox. Galen remained in Rome for the rest of his life and there has been much discussion on when he died. However, many historians now believe that his death occurred in about 216 when his age was 87. This was an exceptionally long life in those times.

Physiology in Ancient Greece

As indicated above, Galen and his school were much influenced by earlier Greek thinking. Students of today often find it difficult to see the relevance of many of these developing ideas and there is some reluctance to grapple with them. However, many vestiges of early Greek thinking remained in the work of the Galenical school, for example, the notion of how four humors determine the medical status of an individual, and it is interesting to review how such concepts developed.

Historians often chose to start the beginnings of early Greek physiology with the work of Anaximenes (ca. 570 BC). He argued that "pneuma" (πνεύμα, Greek for breath or spirit) was essential for life. This is hardly surprising because death is often signaled by a cessation of respiration. However, Anaximenes expanded the idea of pneuma, which was seen as an all-pervading property that was essential for life everywhere. For example, he stated "As our soul, being air, sustains us, so pneuma and air pervade the whole world" (19).

About a hundred years later, Empedocles (490–430 BC) wrote about the movement of blood, and he developed the idea that this ebbed and flowed from the heart in a reciprocating manner. A related notion was "innate heat," which was seen as a life-giving principle and was distributed by the blood throughout the body. Empedocles was also one of the first philosophers to suggest that all things are made up of four essential elements: earth, air, fire, and water. This notion evolved into the philosophy of the four humors that persisted in different forms right up to the European Renaissance. Earth, air, fire, and water represented the concepts of solidity, volatility, energy, and liquidity. This idea was taken up a hundred years later by Aristotle (384–322 BC) and was still part of physiological dogma 2,000 years later.

Hippocrates (c. 460–360 BC) was one of the giants of the ancient Greek period. His school produced an enormous volume of work known as the Hippocratic Corpus that was studied extensively until the European Renaissance. The emphasis here was on the practice of medicine rather than its physiological principles. For example, this was the origin of the Hippocratic Oath, which sets out ethical principles for physicians and is still often used in one form or another for graduating medical students.

Many clinical signs that are still taught to medical students can be found in the Hippocratic Corpus. For example, there is a description of the succussion splash, that is the sound that can be heard if a patient with air and fluid in the pleural cavity or an abdominal viscus such as the stomach is moved from side to side. Another sign included in the Corpus is the pleural friction rub. This is the sound heard through a stethoscope, or the ear applied directly to the chest, when there is disease of the pleural membranes, and they move over each other during breathing with a rasping sound like sandpaper. Hippocrates also described some of the clinical features of pulmonary tuberculosis, which was rife at the time. For example, he stated that the disease was associated with fever and coughing up of blood and that it was usually fatal (8).

The Hippocratic Corpus also continued the belief, earlier enunciated by Empedocles, that the heart is the origin of innate heat and that the primary purpose of respiration is to cool this fiery process. Plato (428–348 BC) expanded on these views in his book *Timaeus*, where he stated "As the heart might be easily raised to too high a temperature by hurtful irritation, the genii placed the lungs in its neighbourhood, which adhere to it and fill the cavity of the thorax, in order that their air vessels might moderate the great heat of that organ, and reduce the vessels to an exact obedience" (quoted and translated in Ref. 20).

Aristotle was not only the most eminent biologist of Greek antiquity but many would say that he deserved this accolade up to the time of the European Renaissance. He was a pupil of Plato and incidentally also tutored Alexander the Great (356–323 BC). Aristotle had an inexhaustible curiosity and his writings on various animals give pleasure even today. One of his great strengths was in the classification of animals. It is said that he described 540 different species. Aristotle's colorful text *De Partibus Animalium* (*On the Parts of Animals*) (1) still makes enjoyable reading. For example, here is his description of the elephant trunk: "Just then as divers are sometimes provided with instruments for respiration, through which they can draw air from above the water, and thus may remain for a long time under the sea, so also have elephants been furnished by nature with their lengthened nostril; and, whenever they have to traverse the water, they lift this up above the surface and breathing [sic] through it" (1). It could be argued that

Aristotle's contributions to systematizing biology were not equaled until the time of Carl Linnaeus (1707–1778). Aristotle's three great books on biology were *History of Animals*, *Parts of Animals*, and *The Generation of Animals*. His contributions include a diagram of the "ladder of nature" (scala naturae) shown in Fig. 2.

However, although Aristotle had such remarkable insights into the diversity of nature, his footing in physiology was not always secure. For example, although it had previously been concluded by others that the brain was the seat of intelligence, Aristotle made a backward step and elevated the heart to this status. As we saw, Empedocles had initiated this idea many years before. Also strangely, Aristotle believed that the arteries normally contained air. This error resulted from the fact that in preparing some animals for dissection by strangulation, the arteries were left virtually empty. Another interesting feature of Aristotle's beliefs was that living creatures were fundamentally different from inanimate objects because there was a special principle essential for life. This notion, known as vitalism, has recurred many times in the history of physiology, and it could be argued that it survived until Claude Bernard (1813–1878) finally put it to rest. Having said that, even the great British physiologist J. S. Haldane (1860–1936) believed that the lung secreted oxygen and his arguments supporting this were associated with a nod toward vitalism (5).

Erasistratus (c. 304–250 BC) was one of the last Greek physiologists, some would say the greatest, prior to Galen. He is credited with promulgating the pneumatic theory of respiration. This recognized the critical importance of inspired air but was curious in that it taught that air from the lungs passed by way of the pulmonary circulation to the left ventricle where it was endowed with "vital spirit." This was distributed by air-filled arteries to the various tissues. Some of the vital spirit found its way to the brain where it was changed to "animal spirit" and then distributed via the hollow nerves to the muscles. Venous blood was believed to contain products of food, and this was modified by the liver and delivered to the right heart. As we shall see, a variant of this scheme was adopted by the Galenical school and dominated cardiorespiratory physiology for some 1,300 years.

Physiology of the Galenical School

The teachings of the Galenical school were based on those of the ancient Greeks especially Hippocrates, for whom Galen had enormous admiration, but also Aristotle, Plato, and Erasistratus. Two major areas of teaching stand out. The first was the dominating effects of the four humors emanating from the four bodily fluids: blood, yellow bile, black bile, and phlegm. This tradition closely followed the work of Hippocrates. Health was seen as a situation where the humors were equally balanced. An imbalance resulted in a particular type of temperament or disease. For example, an overemphasis of blood led to a sanguine personality, too much black bile made the subject melancholic, an excess of yellow bile resulted in a choleric temperament, and too much phlegm caused the subject to become phlegmatic. We can easily see how the present use of these terms reflects the supposed pathological basis. People with a sanguine temperament were happy, optimistic, extraverted, and generally good company. We could wish we were all like that. People with a superabundance of yellow bile had excessive energy and were likely to have short tempers. By contrast, an excess of black bile resulted in melancholy, a subdued temperament, and perhaps a bipolar personality with periods of depression. Finally the phlegmatic personality was on a more even keel but perhaps with a tendency to occasional depression. On the other hand these people were affectionate.

We shall see later that this theory of the four humors had an enormous influence on medicine up to the Renaissance. For example, the popularity of bloodletting was in part due to the belief that if one of the humors was dominating the patient, removal of some blood could reduce its influence. Even today we frequently characterize people based on their temperament and this is not so different from invoking one of the humors.

The second major area of teaching that influenced medical thinking right through to the Renaissance was Galen's scheme for the cardiopulmonary system. This is shown in Fig. 3 and clearly derives from the work of Erasistratus. In this concept food that was absorbed by the gut underwent "concoction" and then was transported by the blood to the liver, where it was imbued with "natural spirit." The blood then entered the right

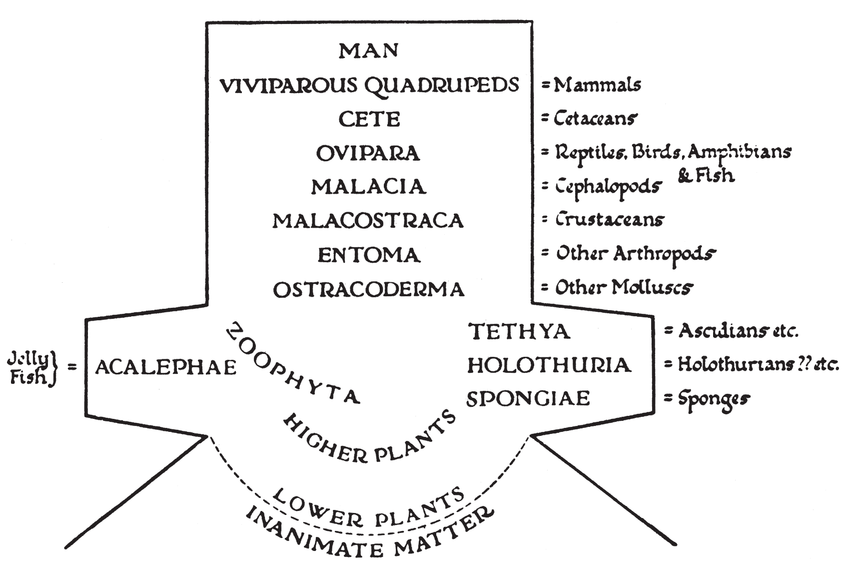

Fig. 2. The Ladder of Nature (scala naturae) of Aristotle demonstrating the great breadth of his interests in the whole animal kingdom, plants, and inanimate materials. From Ref. 18 by permission.

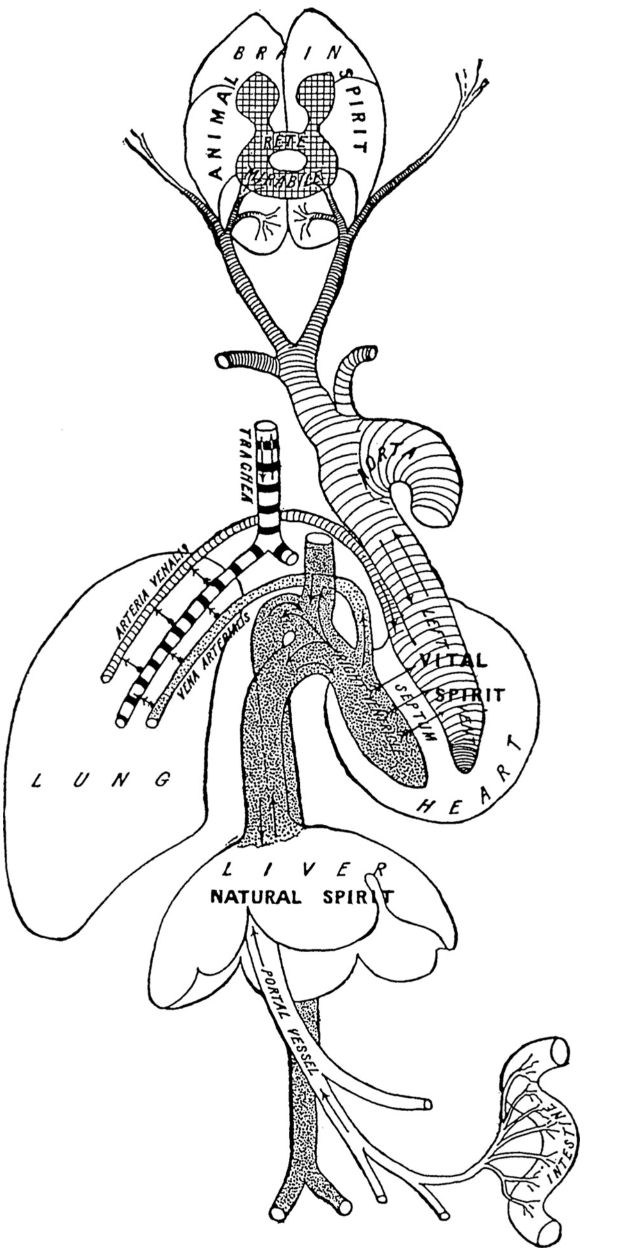

Fig. 3. Galen's cardiopulmonary system, which held sway for 1,300 years. During inspiration, pneuma entered the lung through the trachea and reached the left ventricle via the pulmonary vein. Blood was formed in the liver, where it was imbued with natural spirit, and entered the right ventricle. Most then entered the lung but a portion passed through minute channels in the interventricular septum to the left ventricle. Here vital spirit was added and this was distributed through arteries to the rest of the body. The blood that reached the brain was charged with animal spirit that was distributed through the hollow nerves. From Ref. 18 by permission.

ventricle of the heart and most of it flowed through the pulmonary artery to nourish the lungs. However, some passed through "invisible pores" in the interventricular septum to the left ventricle where the blood was mixed with pneuma from the inspired air and thus endowed with vital spirit. This air reached the left ventricle from the lungs via the pulmonary vein. "Fuliginous (sooty) wastes" traveled back from the heart to the lungs along the same blood vessel. From the left ventricle the blood with its vital spirit was distributed throughout the body in the arteries. Blood that arrived in the brain formed animal spirit and was distributed to the various organs of the body through the hollow nerves. As we have seen, much of this scheme was originally suggested by Erasistratus. Also there are clear parallels with modern views on pulmonary gas exchange. For example, the addition of pneuma to the blood to provide vital spirit has similarities with the process of oxygenation, and the removal of fuliginous wastes via the lung reminds us of the elimination of carbon dioxide, which is a product of metabolism.

Galen's scheme may seem strange to us today but it included some basic physiological principles having to do with the movement of substances through tubes. Admittedly some features of the scheme were difficult to understand. For example, his notion that air entered the left ventricle from the lung via the pulmonary vein, but in addition, "fuliginous wastes" traveled back from the ventricle to the lungs along the same route puzzled Harvey 1,400 years later (3). He could not understand how a tube could carry flow in both directions simultaneously. Having said this, the great Harvey was confused about some aspects of the pulmonary circulation. For example, he wondered why the lung needed such an enormous blood flow, stating "it is altogether incongruous to suppose that the lungs need for their nourishment so large a supply of blood" (7).

In addition to his teachings on the importance of the four humors, and his elaborate scheme for cardiopulmonary function, Galen made many other contributions to physiology especially in the area of respiration. As has already been pointed out, Galen was the physician to the gladiators in Pergamon and as such he must have seen many serious injuries. One of the most interesting observations he made had to do with the effects of dislocations of the neck. He recognized that some of the injured men died immediately but others who were paralyzed below the neck were able to continue to breathe because the diaphragm was still active. Remarkably Galen was able to make sense of these observations using experiments on pigs. He found that when the spinal cord was cut halfway through affecting only one side, the muscles below this were paralyzed. Furthermore he was able to demonstrate that if the spinal cord was completely cut at the level of the third cervical vertebra, the animal stopped breathing. However, when the spinal cord was severed between the seventh and eighth cervical vertebrae, he showed that the animal continued to breathe with the diaphragm. Related to these studies, he reported that the diaphragm was controlled by the phrenic nerve that had its origin from cervical levels three, four, and five. A good source for these observations of Galen can be found in Fulton (4).

The Galenical school made other contributions to the physiology of respiration. The diaphragm was seen as not only a partition between the thorax and the abdomen, but it was also recognized to be an important muscle of respiration. It was also stated that the abdominal muscles were used for forced expiration and also for the production of voice (15). Galen described the larynx in some detail and remarkably reported that cutting the recurrent laryngeal nerve prevented squealing in pigs. He also understood how the lung expands when he stated "When the whole thorax expands in inspiration. . . [this] causes the entire lung to expand to fill the space left vacant." He reported that on inspiration the airways increase both their caliber and length, and he recognized the importance of the upper airways in modifying the inspired air. He wrote that one of the functions of the nose and nasopharynx was to warm the inspired gas and filter out dust particles. He went on to say that the walls of the airways were lined with sticky substances that retain the dust that fell on them.

In addition to these very perceptive insights on physiology, the Galenical school made important advances in anatomy. Here they were at a disadvantage because dissection of human cadavers had been forbidden in Rome since about 150 BC. As a result Galen turned to the Barbary macaque ape, *Macaca inuus*, which resembles humans in many respects but of course is not identical. Other studies were carried out on pigs. The anatomical work was reported in 16 books. For description of bones, Galen had access to human skeletons, and the long bones and spine were described in some detail. Pioneering work was done on the anatomy of muscles although necessarily most of this was on animals. Galen's description of the cranial nerves was the basis of teaching until the Renaissance. He stated that there were seven pairs of cranial nerves including the optic, oculomotor, trigeminal, facial, glossopharyngeal, and hypoglossal nerves. In his work on the anatomy of arteries he corrected the error made by Erasistratus that the arteries contain air, showing by applying ligatures proximally and distally that they only contain blood.

Galen was a skilled surgeon and operated on many human patients. Some of the procedures that he initiated were not used again for many centuries. Remarkably, he attempted to cure blindness caused by cataract by removing the opaque lens using a needle.

Galen's Legacy

In the years following Galen's death in 216 there was a dramatic decline in science in Western Europe. In 391 the great library in Alexandria where Galen had studied was destroyed by Christian fanatics. Shortly after, in 410, Rome was conquered by the barbarians, and theologians such as St. Augustine of Hippo emphasized preparing for the afterlife rather than survival in the dismal conditions that prevailed at the time. In central Europe the centers of learning were mainly limited to the monasteries, and while theology was studied, science withered.

It was very fortunate, however, that much of the knowledge accumulated in Greek antiquity and expounded at great length by the Galenical school was picked up by the Islamic civilization. In fact, the period from the eighth to the fifteenth century is sometimes described as the Islamic Golden Age. At that time the Islamic empire was enormous, extending from the Iberian peninsula in the west to the Indus Valley in the east. In addition it covered the area from the southern part of Arabia to the Caspian Sea in the north. Eminent scholarly institutions existed with some of the most important being Baghdad, Damascus, and Cairo. Whether the term Islamic science is accurate has been discussed by some scholars who prefer the term Arab science since many of the writings were in Arabic, which was the common language of the movement. On the other hand, although most of the scientists were Arab, some of them including the most distinguished, Avicenna, were in fact Persian. It has also been pointed out that although the majority of the scholars were Muslims, some were not.

Some of the institutions that developed had similarities with modern research universities in that they consisted of groups of academicians whose role was teaching. Often these institutions were associated with large hospitals or libraries such as that in Alexandria. Some historians claim that the University of al-Karaouine in Fes, Morocco is the oldest university in the world, having been founded in 859. Another eminent institution was the al-Azhar University in Cairo, which began in the 10th century and offered academic degrees. One of the most notable scholars was Avicenna (c. 980–1037), who was born in Persia in what is now Uzbekistan. He wrote very influential textbooks including "The Canon of Medicine" and "The Book of Healing" and made contributions in many areas including pharmacology, physiology, and infectious diseases.

An important figure from the point of view of Galen's teachings was Ibn al-Nafis (1213–1288), who was born in Damascus but spent much of his adult life in Cairo. He published a notable book titled "Commentary on Anatomy in Avicenna's Canon" that included one of the first challenges to Galen's scheme of the cardiopulmonary system shown in Fig. 3. Ibn al-Nafis stated very vigorously that blood could not pass through the interventricular septum because there are no invisible pores. The statement is important because it shows that although the academics of the Islamic Golden Age are mainly praised for their work in preserving the advances of the Greco-Roman schools, they also challenged some of Galen's writings.

It is not easy at first to understand how Galen's writings developed such an enormous influence that lasted for 1,300 years until the end of the sixteenth century. But it is a fact that the prodigious written output of the school became the official canon not only of medicine but of the Church itself. Remarkably, his scientific edifice was seen as consistent with Christian dogma and indeed Galen's authority became so great that people who challenged his doctrine could be branded heretical by both Church and State. His books were copied and recopied by innumerable scribes before the dawn of printing and many manuscripts are still extant. The fact that Galen's views were adopted as official canon of the Church is often not widely appreciated but it helps to explain why the Church reacted so violently to his critics such as Vesalius and Servetus when the European Renaissance began.

Andreas Vesalius and the Rebirth of Anatomy and Physiology

One of the first big challenges to Galen's teachings came from Andreas Vesalius (1514–1564), who published a splendid atlas of human anatomy in 1543 titled *De humani corporis fabrica* (On the fabric of the human body). This immediately challenged many of Galen's conclusions and resulted in a sea change in thinking about human anatomy. Vesalius founded anatomy as a modern science by reestablishing the experimental method. This inspired people to throw off the encumbrances of theological dogma and start thinking again for themselves.

Vesalius was born in Brussels, Belgium and received his early training in Louvain. He then moved to Paris, where he carried out dissections, and when he was only 22 he began to have doubts about some features of the Galenical texts. These attitudes worried his director, Joannes Guinterius, who was an ardent Galenist, and other people as well. At the age of 23 Vesalius moved to the University of Padua, where one of his responsibilities was to conduct dissections for both the students and also the public. The university had a famous steeply raked lecture room for anatomy demonstrations that was built in 1594 and that remarkably still exists.

At the age of 28 Vesalius published his masterpiece *De humani corporis fabrica*, a magnificent production of nearly 700 pages. Many reproductions of the famous woodcuts exist. An accessible series is on the Web at https://tinyurl.com/k43mh3n. Another useful source is Saunders and O'Malley (16). Figure 4 shows one of the most famous plates. Note that the artist has decorated the rather stark illustration of anatomy with part of the Italian countryside. The genius of this book was that for the first time the structure of the human body was systematically described and accurately depicted in detailed images. It is interesting that the book was published in the same year as Nicolaus Copernicus's *De revolutionibus orbium coelestium* (On the revolutions of the celestial spheres), which removed the earth from the center of the universe and thus helped to overturn the medieval teachings on cosmology.

Vesalius's masterpiece *De humani corporis fabrica* consists of seven books, the first being on bones and joints. An interesting tidbit is that a skeleton prepared by him is still extant. Vesalius was passing through Basel, where his book had been printed several years before, and he presented the skeleton to the University where it remains to this day and is probably the oldest anatomical preparation in existence. The seven books of *De humani corporis fabrica* deal with the skeleton, muscles, vascular system, nervous system, abdominal viscera, heart and lungs, and brain, respectively. A number of differences from the structures described by the Galenical school are noted. Of particular interest to us are Vesalius' comments on the interventricular septum of the heart. Recall that, in the Galenical scheme shown in Fig. 3, part of the blood from the right ventricle was thought to enter the left through pores in the septum. However, in the second edition of *De humani*, Vesalius wrote "Not long ago I would not have dared to turn aside even a nail's breadth from the opinion of Galen the prince of physicians. . . But the septum of the heart is as thick, dense, and compact as the rest of the heart. I do not, therefore, know . . . in what way even the smallest particle can be transferred from the right to the left ventricle through the substance of the septum. . ." (17).

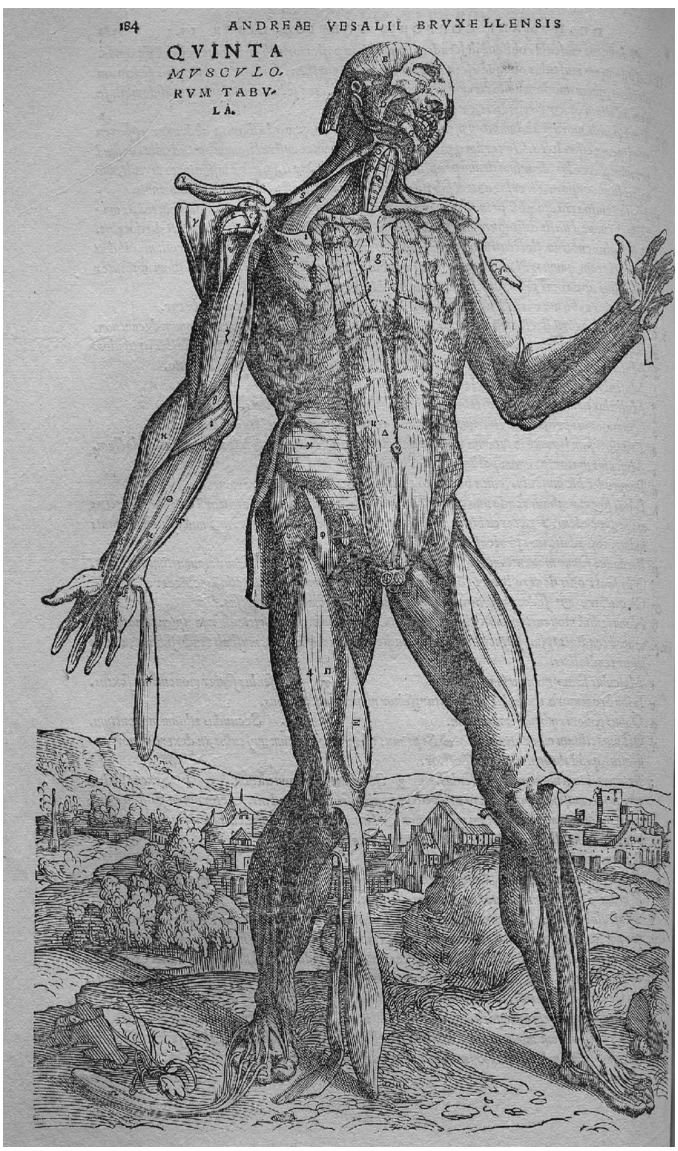

Fig. 4. Typical woodcut from *De humani corporis fabrica* by Vesalius. From Ref. 21.

Vesalius was subjected to a number of attacks because his great book challenged the accepted views of Galen and the Church. At one stage the Emperor Charles V set up an inquiry to determine the religious errors in his work, and although Vesalius was not found guilty at that time, some attacks continued. Many people were unwilling to accept the new anatomy and clung to the teachings of Galen. A remarkable rebuke came from Jacobus Sylvius (1478–1555) with whom Vesalius had worked in Paris and who was an ardent Galenist. Sylvius stated in writing that the anatomy of the human body must have changed since Galen described it!

Michael Servetus and His Assertion of the Pulmonary Transit of Blood

Interestingly, Vesalius did not remark on the possibility of the movement of the blood from the right to the left side of the heart through the lungs, although Galen recognized this, as did Ibn al-Nafis. However, a famous early statement of the pulmonary transit was made by Michael Servetus (1511–1553), who was a physician, physiologist, and theologian (Fig. 5). He was born in Villeneuve in northern Spain and studied law in Toulouse in southern France at the university there. Later he traveled to Paris to study medicine where his teachers included the anatomist Jacobus Sylvius, known for aqueduct of Sylvius in the brain, and Jean Fernel, who apparently was the first person to introduce the term "physiology" into medicine.

Servetus has the distinction of being the first European to state categorically that blood could not pass through the interventricular septum and, in keeping with this, that it moved from the pulmonary artery to the pulmonary vein. This was the first assertion of the pulmonary transit. Curiously, the statement was made in a theological context in his book *Christianismi Restitutio* (The Restoration of Christianity). Servetus was concerned with how the God-given spirit could be spread throughout the human body. He argued that it did this by entering the blood in the lungs and was thus delivered to the left ventricle and from here to the rest of the body. He wrote about the pulmonary blood flow as follows "However, this communication [from the right to the left ventricle] is made not

Fig. 5. Michael Servetus (1511–1553). He was the first European to describe the pulmonary transit and was burned at the stake for heresy as indicated in the upper part of the image. From an engraving by Christian Friedrich Fritzsch (1719–1774).

through the middle wall of the heart, as is commonly believed, but by a very ingenious arrangement the refined blood is urged forward from the right ventricle of the heart over a long course through the lungs; it is treated by the lungs, becomes reddish-yellow and is poured from the pulmonary artery into the pulmonary vein" (13). As we have seen, Ibn al-Nafis made a similar statement 200 years earlier but it was probably not known to Servetus.

The writings of Servetus were very confrontational in many ways and he was accused of heresy by both the Church of Rome and the Protestant Calvinists. The main theological issue was that he believed that the manifestation of God in Jesus occurred at the moment of conception and was not eternal. He therefore referred to Christ as "the Son of the eternal God" rather than "the eternal Son of God." For this heresy he was condemned to be burned at the stake. The great physician William Osler (14) described the terrible event as follows. In the procession to the place of execution Servetus was exhorted by the pastor accompanying him to change his statement about Christ. After being bound to the stake he cried out "Jesus, thou son of the eternal God, have mercy upon me" but the fire was lit and he perished. Strange, is it not, that could he have cried, "Jesu, thou eternal Son of God" even at this last moment he would have been spared. Such were the monstrous attitudes of those times.

This ghastly episode in the chronicle of man's inhumanity to man reminds us of one more that took place about one hundred years later. Galileo Galilei (1564–1642), having observed the moons circling Jupiter, promoted the heliocentric view of the world first suggested by Copernicus in the same year as the publication of *De humani corporis fabrica*. As a result, the Holy Office of the Inquisition ordered Galileo to stand trial. He was found vehemently suspected of heresy; he was shown the instruments of torture; he was required to abjure, curse, and detest his views; he was forbidden to publish anymore; and he remained under house arrest for the rest of his life. Little had changed in the hundred years.

William Harvey and the Beginnings of Modern Physiology

William Harvey (1578–1657) is a convenient figure with which to announce the emergence of modern physiology. The publication of *Exercitatio anatomica de motu cordis et sanguinis in animalibus* (An anatomical exercise on the motion of the heart and blood in living beings) in 1628 describing the circulation of the blood was a turning point in the history of physiology (Fig. 6). The book was an example of the vigorous use of scientific method and the result was an abrupt acceleration of knowledge. During the ensuing 50 years a host of new advances in physiology were made and men such as Torricelli, Pascal, Boyle, Hooke, Malpighi, Lower, and Mayow all made


EXERCITATIO
ANATOMICA DE
MOTV CORDIS ET SAN-
GVINIS IN ANIMALI-
BVS,
GVILIELMI HARVEI ANGLI,
Medici Regii, & Professoris Anatomiæ in Col-
legio Medicorum Londinensi.

FRANCOFVRTI,
Sumptibus GVILIELMI FITZERI.
ANNO M. DC. XXVIII.

Fig. 6. Title page of William Harvey's book *Exercitatio anatomica de motu cordis et sanguinis in animalibus*. From Ref. 6.

important contributions. The attitudes toward hypothesis, experimental data, and other evidence were very different from the situation one hundred years before.

Having said this, it should not be thought that physiologists of the 17th century necessarily made a clean break with the past. For example, John Aubrey (1626–1697) was a well-known writer, and his selection of biographies known as *Brief Lives* contained colorful accounts of many 17th-century luminaries. He met Harvey on several occasions in Oxford and elsewhere and in 1651 when Aubrey was contemplating a trip to Italy he wrote the following. "He [Harvey] was very communicative and willing to instruct any that were modest and respectful to him. And to my journey gave me, that is dictated to me, what company to keep, what bookes to read, how to manage my studies; in short, he bid me goe to the fountain head and read Aristotle, Cicero, Avicen [Avicenna], and did call the neoteriques shitt-breeches" (10). Neoteriques referred to people with the latest ideas.

Finally it should be noted that although there was a great renaissance in physiology in the 17th century, vestiges of Galenism lasted well into the 18th and even 19th centuries. Bloodletting continued to be prescribed although increasingly leeches were used rather than venesection. Indeed there are images of bloodletting by venesection as late as 1860. Even today venesection is occasionally used for diseases such as hemochromatosis and polycythemia although of course the reason is not because of the humoral theory.

In conclusion, Galen was a key figure in the early history of Western physiology. The voluminous writings of his school were based on the advances of the classical Greeks including Hippocrates and Aristotle. An extraordinary feature of the Galenical school was that its influence on medicine and physiology lasted some 1,300 years right up to the European Renaissance. One of the first challenges to the teachings of the school came from Andreas Vesalius, who produced a magnificent book on human anatomy. Finally in the early 17th century William Harvey used modern scientific methods including hypotheses and reliance on experimental findings. This resulted in an enormous acceleration of new knowledge in the mid-17th century. However, vestiges of Galen's teachings could still be seen in the 19th century. It is not easy to find another example of a school whose teachings had such a long-lived influence as that of Galen.

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