Andreas Vesalius, the Predecessor of Neurosurgery: How his Progressive Scientific Achievements Affected his Professional Life and Destiny

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Andreas Vesalius, the father of modern anatomy and a predecessor of neuroscience, was a distinguished medical scholar and Renaissance figure of the 16th Century Scientific Revolution. He challenged traditional anatomy by applying empirical methods of cadaveric dissection to the study of the human body. His revolutionary book, De Humani Corporis Fabrica, established anatomy as a scientific discipline that challenged conventional medical knowledge, but often caused controversy. Charles V, the Holy Roman Emperor and King of Spain to whom De Humani was dedicated, appointed Vesalius to his court. While in Spain, Vesalius’ work antagonized the academic establishment, current medical knowledge, and ecclesiastical authority. Consequently, his methods were unacceptable to the academic and religious status quo, therefore, we believe that his professional life—as well as his tragic death—was affected by the political state of affairs that dominated 16th Century Europe. Ultimately, he went on a pilgrimage to the Holy Land that jeopardized his life. While returning home, his ship was driven ashore on the Greek island of Zakynthos (Zante) where he became ill and suddenly died in 1564 at the age of 49. Vesalius’ ideas helped free medicine from the limitations of the 16th Century and advanced scientific knowledge. His influence is still felt more than 500 years later. In this article, we acknowledge Vesalius’ neuroanatomic contributions and we discuss the historical facts and political circumstances that influenced his scientific career and personal life, emphasizing the conditions of his pilgrimage to the Holy Land that led to his untimely death.

INTRODUCTION

“There are two ways of spreading light; to be the candle or the mirror that reflects it.”

—Edith Wharton, Vesalius in Zante. (1564)

Andreas Vesalius (1514–1564) is considered a founder of modern medicine and a distinguished medical scholar and Renaissance figure of the 16th Century (Figure 1). He challenged and changed the understanding of human anatomy by embracing empirical scientific methods via cadaveric dissections. His key scientific effort De Humani Corporis Fabrica is not only an innovative study of anatomy, but also a high-quality aesthetic and artistic work. The novelty and precision of his pioneering findings and his inventive methods to propagate these findings throughout the scientific community were indispensable, making Vesalius a central and unique figure in the history of medicine. He dared to challenge the status quo regarding research, teaching, and spreading scientific knowledge and in confronting dogmas of his contemporary academic world.

Many consider Vesalius also as a predecessor of neuroscience because his numerous achievements included major breakthroughs in the understanding of the accurate morphology and functioning of the nervous system, which laid the groundwork for modern neurosurgery as a separate scientific discipline. His influence on medical knowledge in general—as well as on neurologic surgery in particular—is still relevant today, more than 500 years later.

Despite his significant contributions, Vesalius was harshly opposed by his critics, which won him both fervent supporters and fanatical foes. He substituted traditional reliance on medical authority with observation and illustration, encouraging his students not to rely on undisputed preexisting knowledge. He exposed and confronted anatomic inconsistencies presented in Galen of Pergamon’s work and in the work of other eminent medical scholars from antiquity. By doing this, he challenged the academic establishment and its entire body of medical knowledge. His critics believed his work...
Andreas Vesalius was born on December 31, 1514 in Brussels, in what was then the Habsburg Netherlands—a geopolitical entity consisting of the present-day Netherlands, Belgium, Luxembourg, and northern France. He was the son of a wealthy family of physicians and pharmacists. Both his parental ancestors served the emperor of the Holy Roman Empire.5-7 Vesalius began his studies in 1529 at the University of Louvain, Belgium, where he learned classical languages, rhetoric, philosophy and logic like most of his wealthy contemporaries.7 The university flourished in the 16th Century because of the presence of famous scholars and professors, such as Erasmus of Rotterdam (1466–1536), the great Dutch humanist,8 who advocated an evangelical piety and questioned many of the medieval superstitions that had crept into church philosophy. Afterward, Vesalius went to France in 1533 to study medicine at the University of Paris to complete his medical degree.5 While there, he was a student of the famous French anatomist Jacques Dubois (a.k.a. Jacobus Sylvius) (1478–1555), who was very committed to Galen’s ideas and considered them infallible.7,9-11 This position made the study of anatomy frustrating for Vesalius, motivating him to go to Paris cemeteries at night in search of cadavers of his own to dissect.5,7 Besides, the war between France and the Hapsburg Empire, of which Vesalius was a subject, hard-pressed him to leave Paris as a persona non grata.9 Finally, Vesalius went to the University of Padua, Italy in 1537 to complete his doctorate, which was a flourishing environment of medical humanism at the time.4,12-14 The University was founded in 1222, and was one of the oldest and most prominent academic settings in early modern Europe.12 After completing his doctorate, he was immediately appointed a Professorship of Surgery at the age of 23 because of his excellent performance during his studies.15-17 While holding this post, he transformed anatomic classes entirely, improving them by performing cadaveric dissection, which was a rare practice in the major medical universities of Medieval Europe.7,14,18 In addition, he encouraged direct communication with his
students to avoid being a strict and inaccessible authority figure. As a consequence, he became more scientifically critical and promoted direct observation, abandoning the traditional medical curriculum established from the ideas of Galen of Pergamon (AD 129–circa 216). Galen was one of the most prominent Greek physicians during the Roman Empire, and established animal dissection-based theories of human anatomy that dominated Western medicine for more than 1300 years.

Although Galen’s accomplishments in antiquity advanced medicine, he introduced some incorrect theories and errors. Many renowned scholars fiercely defended Galen’s ideas in opposition to Vesalius’ methods. It appeared that this antagonism may be one of the reasons why Vesalius left Padua in 1543 to be the personal physician to Emperor Charles V (1500–1558). Vesalius also served Charles’ son and successor to the throne, King Philip II (1527–1598) for over 2 decades. Apparently, Vesalius did not enjoy life in the Court. He sought to be released from royal service and left Spain in 1564 to return to Padua, Italy to resume the teaching of anatomy following Garbrelle Fallus (1527–1582) who died from tuberculosis. Fallus was another prominent anatomist, who held Vesalius’ previous Chairmanship of Anatomy.

On his way back to Padua, he suddenly decided to take a pilgrimage to Jerusalem and the Holy Land, possibly stopped on the Greek island of Zakynthos (Zante) when returning to Venice. He fell ill and died there immediately after landing on October 15, 1564 at the age of just 49.

Vesalius’ masterwork De Humani Corporis Fabrica was published in Basel, Switzerland in 1543, dedicated to the Emperor Charles V, and established anatomy as a distinctive evidence-based scientific discipline. It is one of the greatest contributions to medical knowledge and science up to that time. It is one of the most influential manuscripts on human anatomy and one of the remaining leading biological sources in the history of Western science. The work was comprised of 7 volumes encompassing all organic systems of the human body, which were meticulously illustrated with woodcut engravings. The third volume covered the vasculature and circulation and included a comprehensive explanation of the arteries and veins, including cerebral arteries and veins. The fourth volume of De Humani Corporis Fabrica was dedicated entirely to nerves, whereas the seventh volume focused on the brain itself and is considered the true foundation of neuroscience. Almost certainly, Vesalius’ work was a fundamental inspiration for anatomist William Harvey’s masterpiece of blood

**VESALIUS AS A PHYSICIAN**

After successfully completing De Humani Corporis Fabrica, Vesalius went into medical practice, which was family tradition for 4 generations. He accepted the position of the royal physician at the Spanish Court in 1544, leaving his academic post in Padua. Over the next 20 years, he treated battle and tournament injuries as a military surgeon, as well as conducting postmortem examinations and administering medications to royalty. Vesalius emphasized the importance of understanding correct anatomic body structure during his practice, insisting that surgery had to be based on anatomy. In 1559, Vesalius was asked to give advice concerning medical treatment of King Henri II of France (1519–1559) who was fatally injured during a jousting tournament by a penetrating brain injury from a splintered wooden lance fragment (Figure 2). Together with Ambroise Paré (circa 1510–1590), the most celebrated surgeon of the century, Vesalius eventually proposed trephination that was never carried out. Vesalius also treated the brain injury of Crown-Prince Don Carlos of Asturias (1545–1568) in 1562 when he fell down stairs and fractured his skull.

Compared with other established medical disciplines, anatomy and surgery were considered lower disciplines. As a result, Vesalius’ more conservative and traditional colleagues did not appreciate his modern methods, which they criticized and vigorously opposed.

**DE HUMANI CORPORIS FABRICA**

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circulation *De Motu Cordis*, which appeared more than 80 years later in 1628.\(^{22}\) It was also influential to the work of Thomas Willis (1621–1675), another great anatomist of 17th Century, and a father of modern neuroscience.\(^{20,21}\)

An abridged version of Vesalius’ work called *De Humani Corporis Fabrica Librorum Epitome* was printed in 1543,\(^{30}\) and was intended to be a concise and descriptive handbook for students and surgeons. The book was dedicated to King Philip II of Spain. The fifth chapter was concerned with the brain and nervous system.\(^{17,24,26}\)

The drawings in the Vesalius’ *Fabrica* are some of the most famous medical figures in the history of science because of their previously unseen quality and precision. However, the identity of the illustrators who produced the roughly 300 amazingly accurate images remained unknown.\(^{9,23}\)

Some researchers have speculated that Vesalius’ drawings were associated with the studio of a famous late-Renaissance Venetian master painter Titian (1488/1490–1576).\(^{5,9,13,18,30,37,40}\) The illustrations attracted immediate and enormous interest, particularly among medical professionals and among the renowned artists of that time.\(^{37}\)

The famous Renaissance artist Michelangelo Buonarrotti (1475–1564) allegedly planned a collaboration with anatomist Realdo Colombo (1516–1559)—Vesalius’ colleague at the University of Padua—to create a rival book of anatomical drawings to compete with *Fabrica*’s images.\(^{16}\) However, this collaboration never materialized, possibly due to Michelangelo’s advanced age.

Likewise, Leonardo da Vinci (1452–1519) created numerous anatomic drawings, including those depicting the spinal lordosis for the first time, but he was unable to complete his objective of producing a systematic description of human anatomy because those drawings remained unknown to a wider audience.\(^{72}\)

**NEUROANATOMIC OBSERVATIONS**

Vesalius was also the most innovative neuroanatomist.\(^{39}\) His contributions to the field of modern neuroscience were highly valued, although not acknowledged enough.

The seventh volume of the *Fabrica* and the fifth chapter of the *Epitome*, were concentrated on the anatomy of the brain, and included descriptions of the dura, skull, and cerebral vessels, as well as cranial, spinal, and peripheral nerves (Figures 3-5).\(^{15,17,30,40}\) These illustrations were the first in anatomic history with pictorial accuracy.\(^{27}\)

Vesalius also ridiculed and rejected Galen’s ventricular theory of cognition in which mental functions were thought to be contained within the cerebral ventricles.

Vesalius’ findings added more accuracy to the ventricular structures, which were meticulously drawn and labeled in detail. However, his drawings of the cerebral hemispheres were short of key distinguishing cortical features and did not reveal the gyral-sulcal pattern, as it is recognized today.\(^{31}\)

Although Vesalius did not consider the spinal column with its double curvature as a single arch, he provided a functional-anatomic idea of the lower thoraco-lumbar spine, which remained relevant to a certain extent.\(^{42}\)

The olfactory tract and bulb—mistakenly not classified as a nerve—were nevertheless correctly described at the base of the brain and facing the anterior cranial fossa.\(^{20}\) In the second edition of *Fabrica*, the report on the effect of section of the recurrent nerve with consequent laryngeal paralysis was included.\(^{30,39,43}\)

**POLITICAL CIRCUMSTANCES IN EUROPE IN 16TH CENTURY**

Historians consider the 16th Century when the ascent of the West over the rest of the world first began. This epoch of colonialism and trade established mercantilism as the principal economic theory of the day, which further modernized Europe and expanded its influence worldwide. However, it also simultaneously caused numerous power struggles within Europe itself.

During the reign of Philip II of Spain, who was a harsh enforcer of Catholicism, the Spanish empire reached the height of its power, having conquered and colonized lands on every known continent.

Meanwhile, in the Vatican, Pope Leo X (1475–1521) was the leading Church authority and a patron of arts and learning. However, he did not take growing demands for church reform seriously,
Other great scientific breakthroughs developed at this time that went against the status quo. Nicolaus Copernicus (1473–1543)—another Padua University alumnus—proposed the theory of heliocentric universe. His book De Revolutionibus Orbium Coelestium published just before his death in 1543 was a major landmark in the history of science and appeared the same year as Vesalius’ Fabrica. Both books received similar critiques of the revolutionary concepts presented in each. A contemporary of Copernicus, Pope Paul III (1468–1549) to whom Copernicus dedicated his book became the first Pope to confront Protestantism, but his efforts created more problems than solutions. One of the most momentous artistic works of his reign was The Last Judgment fresco by Michelangelo, which decorates the altar wall of the Vatican’s Sistine Chapel and was completed in 1541, 2 years before Fabrica was published. The painting also generated controversy because of its realistic portrayal of the nude human body.

At the same time, the Ottoman Empire continued to expand and the Ottoman Sultan Suleiman the Magnificent (1494–1566) proclaimed himself Caliph. He initiated key legislative improvements in society, education, science, art, taxation, and criminal law, and supported religious tolerance as well. Therefore, conflict with the West was unavoidable. This was also a time of frequent pilgrimages to the Holy Land. Medieval pilgrims of the Crusades who visited holy sites experienced the perils of war and faced a variety of other difficulties. Unlike those who traveled to the Holy Land to reclaim it for Christendom, the subsequent pilgrims of the Renaissance were mostly motivated by religious piety and/or the need to apologize personal sins. They were not warriors and soldiers, but mainly the nobility or wealthy seeking some kind of atonement.

Nonetheless, the age of the Renaissance brought abundant intellectual change to all of society by modernizing society and encouraging critical thinking. The medieval world retreated slowly but steadily, which enabled the eventual rise of a novel and progressively more rational philosophy founded in the arts, literature, science, and medicine to some extent. Universal human values, as well as body morphology, took center stage and were observed and researched thoroughly for aesthetic, anatomic, and functional features.

The introduction of the printing press by Johannes Gutenberg (1400–1468) in 1439 in Mainz, Germany, entirely transformed book publishing, and the dissemination of information to broader audiences. Books, which were once scarce and few and were cautiously cared for in rare libraries, quickly became abundant and widely available. However, the Church and most European governments during the 16th Century attempted to control printing, which permitted widespread and quick transmission of information and ideas.

The broad-based combination of the scientific approach, innovative teaching, and publishing made achievable during the Renaissance was found mostly throughout the university environment of the Italian city-states, including the city of Padua, part of Venetian Republic. The Italian city-states managed to keep strict Church control and imperial power at bay, creating an optimal foundation for social and economic progress, and for major intellectual and artistic changes.

Besides all conflicts and controversies of the 16th Century, which threatened the very existence of prominent scientists, including Vesalius himself, it was still a time of multifocal improvement of every aspect of life, particularly for art and science. According to Francis Bacon (1561–1626), the English philosopher and advocate of the scientific method, the aim of modern science—after being removed from previous metaphysical assumptions—should be focused on empirical observation, real experience, and experimentation. Apart from being idealistic, and despite numerous obstacles to progress, it would be Vesalius’ legacy as well.

MEDICINE IN 16TH CENTURY EUROPE

During the Middle Ages, the Church controlled all aspects of life, including the practice of medicine. At the turn of the 15th to 16th Century, Galen’s ideas and concepts still dominated medicine and were thought to be infallible. Diseases were believed to be initiated by body disturbances, mirroring an inner harmonious imbalance. Prevalent
general methods for restoring physical balance included bleeding, cupping, and purging, administered by barber-surgeons who were often illiterate medical practitioners with no formal education.\textsuperscript{2,22} Bleeding was a dangerous procedure because of the lack of anatomic knowledge and the increased risk of infection. Nevertheless, it was used randomly for all kinds of ailments. To execute bleeding, leeches were commonly used.

Before Vesalius’ time, anatomy and surgery were underdeveloped compared with other medical disciplines. Surgery was still nascent, consisting of wound management and crude limb amputations performed by barber-surgeons.\textsuperscript{22} Human body dissections were not common in Europe, apart from some Italian city-state republics and largest Spanish cities.\textsuperscript{46,49} Subsequently, medicine of that time mainly remained stagnant.

The first formal anatomists of antiquity were Herophilus (335–280 BC) and Erasistratus (304–250 BC).\textsuperscript{16,28} Both of whom had emerged in Hellenist Alexandria approximately 300 BC.\textsuperscript{4,49} Both men established the use of cadaveric dissections for anatomic medical study.\textsuperscript{50} It is generally accepted that human anatomic dissections were nonexistent during the Middle Ages. However, they reemerged in medieval Italy at the beginning of the 14th Century.\textsuperscript{49-51} The University of Bologna was the earliest place of this revival.\textsuperscript{7} Mondino de Luzzi (1270–1326) introduced human cadaveric dissection in Bologna in 1315,\textsuperscript{9,20,49} and published the first practical manual of anatomy, the Anathomia in 1316.\textsuperscript{20} It became the primary medieval neuroanatomic text as well, describing meninges and cerebral ventricles responsible for fantasy, memory, and cognition.\textsuperscript{47,51} However, Mondino’s central philosophy was to confirm Galenic writings rather than differ from them.\textsuperscript{47,51}

Nevertheless, dissections remained a limited practice until the Renaissance when such a procedure became less restricted. Dissections were then routinely introduced into many medical universities as an important tool for developing academic medical knowledge.\textsuperscript{43-49} Throughout the 16th Century, the practice of anatomic dissection was also consolidated in Spain.\textsuperscript{46}

Prior to Vesalius’ work, Guido da Vigevano (1280–1349), Mondino’s successor who wrote the first anatomic atlas,\textsuperscript{49,51} and Berengario de Carpi (1460–1530), both the
anatomists from the University of Bologna, began to modernize the discipline. Bernegario made a number of entirely novel anatomic observations, and he was the first one not overwhelmed by earlier authorities. He also contributed considerably to brain anatomy, providing detailed description of the meninges and cranial nerves, as well the ventricular system, including choroid plexuses, intraventricular foramen, infundibulum, and pituitary stalk and gland.

Both Leonardo Da Vinci and Michelangelo produced detailed anatomic drawings based on cadaveric human dissections, but they remained unknown to the academic world. All of that had created the basis and inspiration for Vesalius’ milestone work.

Consequently, this new understanding of human anatomy allowed surgery to emerge as a more prosperous field and affirmed the importance of surgeons like Ambroise Paré, Vesalius’ contemporary and a strong supporter who is considered the “father of modern surgery.”

THE PILGRIMAGE AND PREMATURE DEATH

The prevailing Christian doctrine during the Middle Ages and beyond emphasized the soul but not the body in which it was contained. Therefore, we suppose that Vesalius antagonized religious and political authorities by his methods, his revolutionary ideas, and the content of his scientific works.

There are a few theories of Vesalius’ final days that attempt to explain the reasons for his sudden departure to the Holy Land. Vesalius’ prominent biographer advocated that he used the pilgrimage as a prerequisite to leave the Spanish Court and to reclaim his professorship at Padua University. Another theory suggested that Vesalius was accused of having performed dissection on a Spanish aristocrat when the heart was still beating, and was ordered to take a pilgrimage as penance for this sinful act. A different source stated that Vesalius had been severely ill and decided to take a pilgrimage out of gratefulness for his recovery. Modern scholars suggest that Vesalius did not leave the Court for his pilgrimage to Jerusalem under pressure, but that he left on his own with the full support of the King Philip II who provided him with introduction letters to Spanish embassies abroad.

It is surprising that the reasons for his pilgrimage are so contradicting, bearing in mind how renowned and famous Vesalius was. Nonetheless, we hypothesized that he took the mandatory pilgrimage to Jerusalem to endorse his obedience to political and ecclesial authorities. Considering the society’s prevailing conservatism, and political background of the events precipitating the journey, this seems the most plausible explanation to us, although some respectful Vesalius’ biographers stated otherwise.

During his stay in Jerusalem, it appeared that Vesalius was more concerned with local botany than the pious doings of a pilgrim. After a few months stay in the Holy Land, Vesalius apparently embarked on an inadequate ill-equipped vessel with the limited storage of food and water supplies on his return voyage. Possibly, his alleged personal parsimony was blamable for choosing such a humble ship offering bad traveling conditions. Finally, his ship was stopped on the Greek island of Zakynthos (Zante) in the Ionian Sea (a possession of the Venetian Republic), where the completely exhausted and sickened Vesalius was put ashore alone (Figure 6). He died shortly thereafter, probably from a contagious disease or fatigue because of the ship’s poor settings. The most plausible explanation of his death seems to be illness, possibly exacerbated by general weakness.

CONCLUSIONS

This historical vignette discusses conditions and events associated with the life and final pilgrimage leading to the tragic death of Andreas Vesalius, who introduced a revolutionary concept of anatomic teaching based on human cadaveric dissection, observation, and illustrations. His ideas and methods helped to advance medicine well beyond the limits of the 16th Century. He first understood the importance of learning through one’s own experience and how this understanding could aid in the acquisition of new knowledge. At the same time, he created an anatomic textbook, a masterpiece that is considered the most important biological manuscript in the history of Western science. His impact on modern neuroscience was exquisite as well. However, his life and destiny were burdened by political circumstances and the social conservatism of that time, which supposedly contributed to his tragic death.

REFERENCES
