The discovery of circulation and the origin of modern medicine during the Italian Renaissance

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It is significant that I am delivering this lecture at the University of Bologna, the oldest in the world, since this University is the "alma mater" of my own University, that of Padua. Following a dispute between the monks of Santo Stefano and the Councillors of Bologna, a group of students and professors migrated from the University of Bologna and founded the University of Padua in 1222. Saint Anthony of Padua, whose eighth centenary since birth is celebrated this year, was a lecturer in Theology at the University of Bologna from 1223 to 1225, and most probably was involved in this migration. The last part of his life was spent preaching in the province of Padua, where he died on June 13, 1231. The huge number of University personnel present at his funeral gave testimony to his very close bonds of friendship with many University teachers and scholars. These scholars strongly supported a petition for his canonization, which was granted in a very short time, exactly in 1232, only one year after his death, thanks to Anthony's extraordinary power to perform miracles. Among the several miracles, which allowed him to attain sanctity, I bring to your attention the particular one linked to Science and Medicine, namely the miracle of the usurer. A very rich, miserly merchant died in old age, and Anthony was called to bless the body. Anthony came, but denied Christian burial saying, "This man was heartless in life and his heart is now with the treasure he left." The jeweled coffer was then opened, and to the great astonishment of the onlookers, a heart was found inside. "Scientific" proof was necessary to verify the miracle, and an autopsy on the miser's body disclosed the absence of any heart within the chest (Figure 1). This miracle inspired many painters. Four centuries later, in 1618, Damini painted the scene depicting Fabricius ab Acquapendente, Professor of Anatomy and Surgery at the University of Padua, as he performed the postmortem.

Scholarship and Sanctity were closely linked throughout the following period of Renaissance. Many saints were scholars at the lay University of Padua before following a philanthropic or ecclesiastical calling. Many of them should be considered the Nobel Laureates of that time, in terms of inspiration and theological background.

All historians agree that Modern Science was born during the Italian Renaissance in the 15th-16th centuries. The Renaissance was a great revival of the liberal arts, science and religion based on humanism, namely the rediscovery of man, nature, and natural philosophy as formulated in antiquity. A new concept of erudition was advanced according to which not only mathematics and logic, but also poetry, philology and liberal arts were considered superior to metaphysics and theology.

The major events determining the onset of the Renaissance were the Fall of the Byzantine Empire in 1453, the invention of the printing press in 1452, and the discoveries of the New Worlds from 1487 to 1502. Thirst for discovery was one of the essential components of the civilization of the Renaissance fervor, and the Portuguese became the messengers and eyes and ears of Europe in the world.

After the Fall of Constantinople in 1453, Greek culture was once again scattered all over Modern Europe, and the invention of the printing press accelerated the circulation and exchange of ideas. In 1468, Cardinal Bessarione donated 482 Greek and 264 Latin codes to the Venetian Doge, thus transferring classical Greek erudition to Italian culture. At that time he wrote, "In the absence of books, the same tomb holding the body would cancel also the memory of man." Erasmus of Rotterdam also came to Italy "to know Greek" in 1506.
One of the fundamental achievements of the Renaissance was the elevation of painting, sculpture and architecture to the status of liberal arts. The sculptures of incomparable Renaissance masters, such as Michelangelo’s body of Jesus Christ in the Pietà (1498-99) at Rome, display an understanding of structure that cannot be explained without accepting the sculptor’s deep knowledge of the human body. In the biography of Antonio Pollaiolo, published in 1568, Giorgio Vasari reported that the artist had flayed many bodies to see the anatomy beneath. The sculptor Lorenzo Ghiberti, in his First Commentary of 1450, stated that “It is necessary to have seen dissection in order that the sculptor wishing to compose a ‘statua virile’ knows how many bones are in the human body and in a like manner knows muscles and all the tendons and their connections.” It was indeed a magic moment, during which science and art were not yet differentiated, and had not seen themselves as opposed.

It is generally believed that the dissection of cadavers was performed secretly, because it was forbidden by the authorities. This is untrue. In 1482, the University of Tübingen presented the following petition to Pope Sixtus IV: “Permission to take the bodies of legally executed criminals from the place of execution, and to dissect them according to medical rules and practice without any special license from the Holy See.” The request was granted “provided the dissected bodies be given burial.” The Venetian Moderators of Padua University wrote the following letter to the Podestà (Mayor) of Padua on December 15, 1556: “Since Anatomy is very useful to students of Medicine, and the present time is very appropriate, I beg your Magnificence to give some subject, sentenced to death, to the most excellent Fallopius (Professor of Anatomy) who will perform a dissection to the great expectation and satisfaction of those scholars…”

Leonardo da Vinci (1452-1519), the greatest artist-anatomist who ever lived, conducted the most important scientific studies of the human body in the history of art. He was an exceptional individual, an artist and a scientist at one and the same time. Leonardo’s anatomical drawings reveal that he was a gifted observer of the human body in all its parts. He not only studied living men and women, but also dead ones, which he dissected with painstaking care in order to draw each vessel, muscle and organ with extreme precision. Although he never worked as a professional anatomist, he collaborated in dissecting human cadavers with Marcantonio.
della Torre, a young professor of Anatomy at the University of Pavia, from 1510 to 1511, when the plague struck that city. Leonardo had performed more than ten dissections by 1509, and more than thirty before he died. He truly combined the ability of an artist and an anatomist in a supreme manner.8

Leonardo’s study of the heart dates to approximately 1511-1513, and was performed in Florence. He followed the Galenic theory of blood being generated in the liver (Figure 2), and the concept of flux and reflux through the veins: “The blood is thinner when it is more beaten, and this percussion is made by the flux and reflux of the blood generated from the two intrinsic ventricles of the heart to the extrinsic ventricles called auricles.... which are dilated and receive into themselves blood driven from the intrinsic ventricles and then they contract returning the blood to those extrinsic ventricles.” And again, “All veins and arteries arise from the heart, and the reason is that the biggest veins and arteries are found at their conjunction with the heart... veins arise in the gibbosity of the liver because they have their ramification in the gibbosity...”

If Florence was the Center of Artistic Renaissance, where Platonism and Idealism prevailed, Padua was the Center of the Scientific Renaissance. And it was not fortuitous that architecture, the liberal art most close to science, developed under the influence of the Venetian Republic as a sort of rediscovery of the Grecian style, combined with the study of classic monuments. Andrea di Pietro della Gondola (1508–1580), known as Palladio from the Goddess Pallade, who was born in Padua and lived in Vicenza, exemplified the Humanist, and was a scholar of classical Greek art. For Palladio, the dignity of a discipline derived not only from the nobility of the subject, such as theology from God, but also from the rigor of methods and the certainty of achievements. In chapters XII-XIII of the second book of his treatise “I quattro libri dell’architettura”9 he describes the ideal residences of the “homo universalis” (humanist) “...The town residences suit the gentleman for their magnificence and comfort as he must live there during the time needed to attend to his public and private affairs. But no less benefit and pleasure will he get from his country mansions, where he will spend the rest of the time looking after and improving his land and possessions, and where he will strive with his art and ingenuity to increase the wealth of the agriculture... where, given that exercise on foot and horse-riding is usually taken there, the body will more easily preserve its health and vigor, and where finally the spirit, tired by the troubles of the life of the town, will find restoration and consolation amidst the quietude of the countryside, and will pleasantly attend to the study of the Arts and the contemplation of Nature...” (Figure 3). This surely is exhortation to return to reality and “dignitas

Figure 3. Villa Foscari “La Malcontenta” by Andrea Palladio, completed around 1560, mirrored in the Brenta River.

Figure 4. The upper colonnade around the courtyard Palace called “Il Bo” by Andrea Moroni (1545), the finest example of Renaissance architecture in Padua.
By general consent, the University of Padua is credited with having given rise to Modern Medicine. Butterfield in 1958 wrote: “William Harvey... was for a few years at the University of Padua, where his most important predecessors worked: Vesalius, Columbus, Fabricius. It is impossible to ignore that this chapter on the history of the heart is the pride of this University... Also Copernicus and Galileo were at this University during the most productive periods of their lives;... If the honor to have been the site of scientific revolution might belong to a single place, such honor should be credited to Padua, the Queen of Science.”

Several circumstances favored the origin of Modern Science at Padua University. Its northern geographic position was strategic in favoring cultural and commercial exchanges with other European countries, and the use of Latin as an international language further facilitated communication. Of utmost importance were the civil and religious freedom and tolerance, guaranteed by the Republic of Venice (Figure 5), of which Padua had been the University since 1405. The motto of the University of Padua “Universa Universis Patavina Libertas” well underlines the importance of freedom and an open mind in international relations. The professors enjoyed unlimited liberty in their teaching, and the University of Padua was considered “Magistra totius Europae.” Incredibly enough, at that time the University of Padua graduated as many scientists as saints. Although it was nominally a Catholic University, a profession of faith was not required from the students as was the case in other confessional Universities, like Bologna, Pisa and Rome. This allowed the attendance and graduation of Protestant and Jewish foreign scholars, who formed the vast majority of the student body. With few exceptions, the English graduates of Padua were later to be found among the elite of England’s medical profession. The value and fame of the teachers were worldwide, and the Venetian Ambassadors scattered throughout the world were continuously on the lookout to single out and import the best foreign minds, offering them the position of Professor. “Only men of demonstrated excellence in their profession are given charge over the education of the young” was the proclamation of the Venetian Senate, thus guaranteeing the best in the Faculties of their University. Moreover, to prevent nepotism, neither Venetian patricians nor citizens of Padua were allowed to hold a chair of Ordinary Professor, and, with a few exceptions, not even the position of Extraordinary Professor. From the Venetian viewpoint, it appears that the University had become more important than the town in which it was located or, as expressed by Bernardo Navagero, one of the Venetian overseers known as “Riformatori dello Studio di Padova,” “without the University, Padua would not be Padua.”

Why this town gave rise to the so-called “scientific revolution” despite its being, among the European Universities, the one in which Aristotelian philosophy had a long-standing, and sound tradition is one of the paradoxes concerning the University of Padua. The biologist more than the metaphysician who was Aristotle attracted the Padovan philosophers. Aristotelism in Padua was not in any way anti-humanistic, and declared the autonomy and total separation of physics (=science)
from metaphysics (=philosophy), according to the teaching of Averroës. In this respect, Pietro d’Abano (1250-1318) and Caietanus Thienaeus (1367-1465) (Figure 6) [See Editor’s Note], the latter an Ordinary Professor of Philosophy in the University of Artists (=Medicine and Philosophy), were the outstanding representatives of this philosophical School.

Experience by observation and induction (=empiricism) was considered to be at the basis of scientific logic. These two prerequisites facilitated the onset of a method which proved essential for the renewal of anatomical studies by coupling objectivism with rationalism.16

The sequence of books published by the famous anatomists well depicts the history of discoveries that account for the development of modern medicine in Padua (Table). The titles of the volumes are significant for understanding the progression of knowledge, from anatomy (De Humani Corporis Fabrica, by Vesalius in 1543) to physiology (Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus, by Harvey in 1628) to pathology (De Sedibus et Causis Morborum per Anatomam Indagatis, by Morgagni in 1761). The word anatomy appears in the title of both the anatomo-pathological and physiological textbooks, because the dissection of cadavers was essential to achieve such goals. The lesson in Anatomy was purely “ex cathedra” prior to Alessandro Benedetti (1455-1525), the first Professor to use a mobile anatomical theatre for autopsy. While the autopsy was performed, an Extraordinary Professor of Medicine would read the book Anathomia by Mondino dei Luzzi, a Professor of Anatomy at the University of Bologna (1270-1326). An Ordinary Professor would concomitantly point to the viscera within the cadaver to demonstrate the truth of the statements, and nothing else could be done until such evidence was reached (Figure 7). The dissection itself was carried out by the Surgeons, who were nothing but technicians.17 With time, the doctors lost the skill of dissecting as well as the knowledge of visceral anatomy.

It was with Andreas Vesalius (1514-1564) that these three positions (lector, ostensor and sector) were combined into a single one. The learning of anatomy was then "per oculos, non per aures" (by observation, not by hearing).18 Vesalius exemplified this spirit of inquiry into nature, to which the vast body of modern scientific knowledge owes its origin. Vesalius did not shy from handling the knife himself in order personally to con-

Table. University of Padua and the origin of modern medicine: milestone publications.

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<thead>
<tr>
<th>Date</th>
<th>Publication</th>
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<tbody>
<tr>
<td>1493</td>
<td>Historia corporis humana</td>
<td>Alessandro Benedetti (1455-1525)</td>
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<tr>
<td>1543</td>
<td>De humani corporis fabrica</td>
<td>Andreas Vesalius (1514-1564)</td>
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<td>1559</td>
<td>De re anatomica</td>
<td>Realdus Colombus (1516-1559)</td>
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<td>1605</td>
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<td>Hieronymus F. ab Acquapendente (1533-1619)</td>
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<td>1628</td>
<td>Exercitatio anatomica de motu cordis et sanguinis</td>
<td>William Harvey (1578-1657)</td>
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<td>1761</td>
<td>De sedibus et causis morborum per anatomen indagatis</td>
<td>Giovanni Battista Morgagni (1682-1771)</td>
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Figure 7. Lesson of anatomy "ex cathedra" (from Fasciculus Medicinae, Venetis, 1494).
duct the postmortem (Figure 8).

Anatomy was considered the foundation of all medicine, and the anatomical studies of the XVIth century represented the wonderful dawning of Modern Medical Science, which culminated with the publication of De Humani Corporis Fabrica (On The Building of the Human Body) by Vesalius in 1543. This year was the turning point in the history of science during the Renaissance. With the posthumous publication of “De Revolutionibus Orbium Coelestium” by Nicolaus Copernicus (On Revolutions of Celestial Bodies), the sun replaced the earth as the center of the Universe. And it is not incidental that, with the studies of Vesalius, the heart started to replace the liver as the center of the network of vessels: heliocentrism and cardiocentrism vs geocentrism and hepatocentrism.

But Vesalius was still far from the correct concept of the circulation and pulmonary function. He still believed in the existence of pores in the ventricular septum, and flux and reflux of the blood through the veins. In his book Tabulae Sex, published in 1540, in the drawing of heart, veins and arteries, you see that the left atrium is still considered the cavity where “Arteria venalis in sinistrum sinum aerem ex pulmonibus deferens” ("Pulmonary vein carries air from the lungs to the left atrium") (Figure 9).

The illustrations of De Humani Corporis Fabrica are unique, and represent the perfect union between art and science. They are the result of a collaboration between a communicative anatomist (Andreas Vesalius) and a receptive illustrator (Stefan Van Calcar from the workshop of Titian in Venice). In a very humanistic sense, the anatomy lesson represented the irreplaceable rite of the discovery of the values of nature and life in the most complex work of the Creation, The Human Body. It is impressive to recognize the likeness that exists between the Venus de Milo at the Louvre and the portrayal of a female nude by Vesalius (Figure 10).

Finally, in 1543, there occurred another extraordinary event that changed the course of the history of Medicine. The Professor of Practical Medicine, Giovanni Battista Da Monte (1478-1551), started teaching students at the bedside, as reported in a record of a visit to the Hospital of St. Francis in Padua (April 1543, 17th visit, patient affected by syphilis).12,21

Da Monte, who was then the first Professor of Clinical Medicine in the history of Medicine, stated:
"When you approach a patient, you must do the following, namely first look at his face, then talk with him, take his pulse and observe anything you believe necessary to understand the disease. "The need for practice in addition to lectures, both in anatomy and the clinical setting, was very much appreciated by students: "Few or none of us have come here only for the sake of lectures, and all of us have come to learn practice. We do not lack for lectures in our own country or elsewhere, and we also have books at home which we can just as well read there as here. It is the study of practice that has led us to cross so many mountains, and at such great expense." Thus, in 1578 the Venetian Senate decreed: "Two of the professors of practice will visit the hospital at established times, there to hold forth about the diseases presented by the occasion, for the utility of the students." To implement the onset of Clinical Medicine, in 1545 the Venetian Senate granted that Professor Francesco Bonafede (1474-1558) set up the Ortus Botanicus, the first garden of medicinal herbs in the world.

Fine anatomical dissections were the prerequisite for the next findings regarding the circulation of blood. Realdus Colombus (1516-1559), who succeeded Vesalius, experimented in living dogs and found that the pulmonary veins carried blood, not air, thus discovering lung function and circulation (Figure 11): "I believe... the function of the pulmonary vein is to carry blood mixed with air from the lungs to the left ventricle of the heart and this is unquestionable. In fact, if you observe cadavers as well as living animals, you will always find the pulmonary vein full of blood, which is not possible if this..."
Figure 12. The famous anatomical Theatre of Fabricius ab Acquapendente (1595) at "Il Bo," where venous valves were discovered through dissection of cadavers.

vein had to carry only air and fumes." And again: "I am sure that this new function of the lung, which no anatomist has ever imagined, will appear unbelievable to the skeptics and followers of Aristotelian theories; but you, unprejudiced reader, make the experiment on animals. You will find the pulmonary vein full of blood as I described, and not full of air or fumes."

It was the discovery of valves within the veins, reported in De Venarum Ostiolis (1603) by Hieronymus Fabricius ab Acquapendente (1533-1619), that prompted William Harvey (1578-1657), his pupil, to conceive of the circulation of blood. Fabricius, Professor of Anatomy and Surgery, is known worldwide for the building of the Anatomical Theatre, the first Scientific Laboratory of Medicine, in 1595. This year marks the 400th Anniversary of this event. It is a magnificent work of art which epitomizes the golden century of anatomy (Figure 12). "In this place, so different from others, in this secret and almost sacred place, those who had the right to enter, whether students or professors, became different. In no other place, in no other lesson than the anatomical one... such an awareness of, and pride in scientific values could be present."

By applying the Galilean experimental method, according to which Science is based on observation and measure,16 Harvey (Figure 13) conjectured that the presence of venous valves would hinder reflux of blood,
so that movement of the blood would be centripetal, not centrifugal in the venous network (Figure 14). Moreover, he estimated the volume of blood passing through the heart at a given time, and surmised that the liver would be unable to produce such an amount of blood in such a short period of time. Thus, blood volume could be kept constant only in a closed circulatory system. In chapter IV of his book, Harvey discussed the motion of the heart and auricles in animals, issuing the first clear statement on the origin and conduction of the heart beat: “The movement seems to start in the auricles and to spread to the ventricles.” This is unanimously reported as the birth of physiology in the History of Medicine.

The term “circulation,” however, had previously been coined by Andreas Cesalpinus (1524-1603), a keen friar working at the University of Pisa. In his books “Peripateticarum questionem” (1571) and “De Plantis” (1583) he wrote that “Through veins the blood goes to the heart, and through arteries it is distributed to the whole body...” and moreover, “The blood crosses from arteries to veins through communicating vessels, called anastomoses, and then goes to the heart.” The nature of these anastomoses (capillaries) was eventually discovered by Marcello Malpighi (1628-1694), an anatomist in Bologna, who in De Pulmonibus (1678) described the following: “I saw the blood flowing into the arteries like a flood, and I expected that it would spread over an empty space and then be collected from the mouth of a vessel... My thought changed when I observed the dry lung of a frog... With the help of a lens, I didn’t see scattered points, but vessels joined together like rings... Thus, it was clear that the blood flowed in sinuous vessels and did not spread over spaces, but was always contained within tubules.”

The final step in the revolution of Medical Science occurred in the field of pathology, and was achieved thanks to the contribution of Giovanni Battista Morgagni (1682-1771), who in the Encyclopedia Americana is reported as follows (Figure 15) “…His greatest work published in 1761 ... established Pathological Anatomy as Science and changed the course of medical diagnosis.” He perceived that “it is impossible to pursue the nature and cause of any disease without dissection of the respective cadavers.” His method was based upon a comparison between clinical symptoms and signs and pathologic findings (clinicopathologic correlations), and on the epicrisis (=final critics). Thanks to this method, anatomical empiricism turned into Medical Science. This method is well exemplified by the first clinical and pathologic description of a congenital cardiac malformation, namely pulmonary stenosis, in the De Sedibus et Causis Morborum per Anatomen Indagatis, 1761: “A girl, who was sick since birth, complained of dyspnea and asthenia. At the age of sixteen she died. The heart was small... the right ventricle had a shape similar to the left ventricle... The right atrium was double the size of the left atrium... The foramen ovale was patent... The semilunar pulmonary valves were cartilagineous... and fused leaving only a lentil-like orifice... I believe that the lesion was present since birth... Livid skin was explained by blood stagnation with dilation of the right chambers and veins, as well as by patency of the foramen ovale, the valve of which was pushed from right to left... Poor perfusion of the brain and the entire body, as well a small amount of blood crossing the lungs accounted for the asthenia and dyspnea...”

Research, diagnosis and education were an inseparable trinity in the minds of these Masters of Science. Morgagni, a pupil of Valsalva at the University of Bologna, was appointed as Professor of Theoretical Medicine at the University of Padua in 1711. At the age of only 29 years, in his inaugural lecture, he addressed the problem of teaching and education in the Faculty of Medicine: “Finally, I became convinced that treating patients is not sufficient for the distinguished doctor we intend to form, but his experience must also serve posterity; thus he must present what he has learned through his skill in a clear and simple manner.” This message still embodies all the significance of being a Professor of Medicine today, at the eve of the third millennium.
Galileo Galilei (Figure 16), who introduced the experimental method, was Professor of Mathematics at the Universitas Artistarum (Faculty of Medicine and Philosophy) of Padua from 1592 to 1610 ("eighteen years, the best of my life"),27,28 exactly when Fabricius ab Acquapendente was Professor of Anatomy and Surgery. Thus, he taught William Harvey. With the discovery of Jupiter's planets, published in Sidereus Nuncius in 1610, Galileo further embraced the heliocentric Copernican theory, which was banned and persecuted by the Holy Office of the Roman Church because it opposed the Bible. Galileo left the tolerant Republic of Venice in 1610 to move to the clerical Florence, thus losing his "Patavina Libertas." He became a case-symbol of the conflict between faith and science, namely between the need for freedom in research and the obligation to obey the doctrinal authority of the Church. In his letter to Cristina Lorena in 1615, he quotes Cardinal Baronio, a very famous historian of the Roman Church and pupil of St. Filippo Neri, as having said that "the aim of the Holy Spirit is to teach how to go to heaven, not how heaven is going."28 In that same year, Cardinal Bellarmino, a Jesuit who graduated from the tolerant University of Padua and was later canonized, wrote to Father A. Foscarini recommending "... to act with caution in explaining the Holy Scriptures which appear contrary, and say instead that we do not understand rather than calling false that which is demonstrated."29 Despite these authoritative statements, the intolerant position within the Holy Office prevailed and, in 1633, Galileo was sentenced to recant his theories.

The split between Science and Faith continued for centuries. In 1992, the 400th Anniversary of Galileo's appointment at the University of Padua, Pope John Paul II acknowledged the error, and in a letter29 to the Rector of the University of Padua closed the controversy by saying "... The common vocation of both scientists and theologians is to contribute to the best knowledge of the Truth."

References

Press, Cambridge, 1979, pp 335-370

[Editors’ note: Caietanus Thienaeus is the latin equivalent of Gaetano Thiene. There were two Gaetano Thiene during Italian Renaissance, both forebears of the Mannheimer Lecturer. The first (1367-1465) was Ordinary Professor of Philosophy. The second (1480-1547) graduated in jurisprudence in 1505 and was himself canonized; his portrait is to be found in a mural in the new part of the Bo of the University of Padua.]