BRIEF HISTORY OF ANATOMY
(with emphasis on cardiovascular anatomy)

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The development of anatomy as science extends from the first examinations of victims of sacrifices to the sophisticated analyzes currently done by modern scientists. It is characterized, over time, by the continuous development of the understanding of the structure of the body and the function of the organs. Human Anatomy has a prestigious history and is considered the most prominent of the biological sciences until the 19th century and early 20th century. Methods of study improved dramatically, allowing study from examination through dissection of bodies to the use of technologically complex.

Anatomy is one of the foundations of medical education and is taught since at least the end of middle age. The format and amount of information prepared to young doctors have evolved and changed in association with the demands of the medical profession. What is trained today differs significantly from the past, but the methods used to teach have not changed much. For example, the famous public dissections that occurred at the end of middle age and early renaissance can now be considered the 'anatomical demonstrations' used in practical classes.

Ancient anatomy

Charak born in 300 BCE[1] and was a significant contributor to the ancient Indian art and science of *Ayurveda*[2]. *Charak* studied the anatomy of the human body. He described the number of bones as being 360, including the teeth and mistakenly believed that the heart had only one cavity connected to the rest of the body through thirteen channels. From these channels, there would be numerous others of varying sizes that would supply the various tissues. He also said that obstruction in one of these channels would lead to disease and deformity of the body.

Egypt

There are reports of the anatomical study of the human body since the year 1600 BCE, date of the surgical papyrus of Edwin Smith. This treatise shows that the ancient Egyptians recognized the heart and its vessels, the liver, the spleen, the kidneys, the hypothalamus, the uterus, and the bladder. They also knew that the blood vessels were from the heart. Other vessels were described, some containing air, others containing mucus. Two vessels

[1] Common Era is the period that measures the time from the first year in the Gregorian calendar. It is an alternate term for Anno Domini, Latin for "in the year of (Our) Lord", also translated as the Christian Era. All these names of eras are chronologically equivalent, that is, the number of any given year is the same regardless of which of these names of ages is used. When using the term 'Common Era', background years are described as 'Before the Common Era' (BCE). When using the terms anno Domini or Christian Era, antecedent years are described as before Christ or before the Christian Era. None of the designations uses a zero year and the two designations are numerically equivalent; then '2012 EC' corresponds to 'AD 2012' and '399 BCE' corresponds to '399 BC'.

[2] Ayurveda is the name given to medical knowledge developed in India about 7,000 years ago, which makes it one of humanity's oldest medical systems. Ayurveda means, in Sanskrit, Science (veda) of life (ayur).

connected to the right atrium were said to hold 'the breath of life,' while two vessels connected to the left atrium were said to contain 'the breath of death.' Egyptian iconography illustrates the story of the 'weighing of the heart' (Fig. 1), as a necessary test before the dead being raised by Osiris.

The Ebers papyrus (1550 BCE) deals with the 'heart' theme and regards the organ as the center of the blood supply, with vessels attached to each limb of the body. The Egyptians knew little of the function of the kidneys and made the heart the meeting point of numerous vessels that carry the body fluids - blood, tears, urine, and sperm.

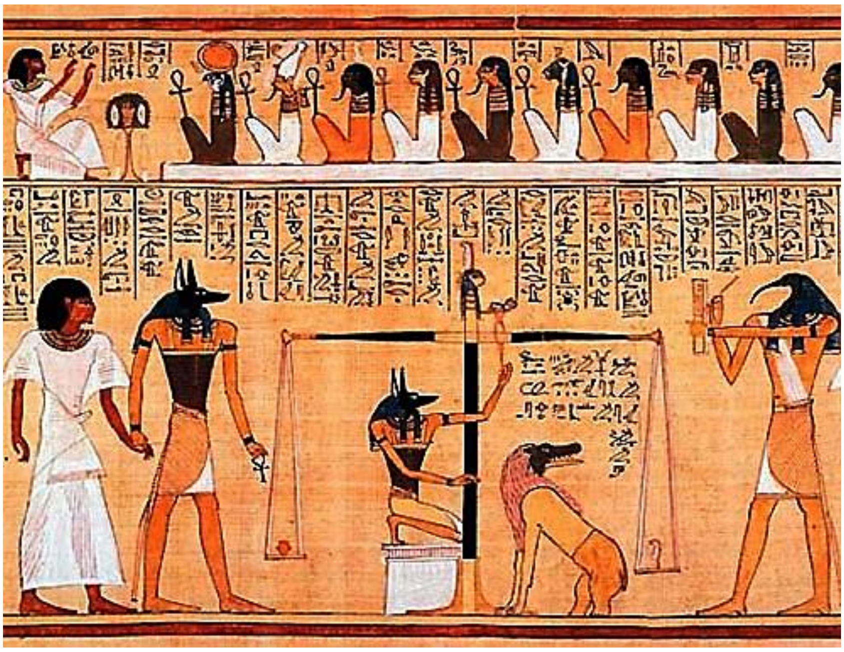

Fig. 1 Weighing the heart at the resurrection ceremony

Greece

The earliest scientific medical work that has survived to this day is due to Hippocrates (460-377 BCE), who had a basic knowledge of skeletal and muscular structure, and the beginning of the understanding of the function of some organs, such as the kidneys. Hippocrates was the first to recognize the tricuspid heart valve, which he documented in the treatise on the heart (in the Hippocratic Body).

Diogenes (of Apollonia) was a pre-Socratic philosopher who lived in the 5th century BCE and made the first systematic description of the architecture of blood vessels in man. In the 4th century BCE, *Aristotle* (Fig. 2) and several of his contemporaries produced a system of knowledge based on the dissection of animals.

Praxagoras is recognized as being the first to identify the differences between arteries and veins. The first use of cadavers for anatomical research occurred in the 4th century BCE with *Herophilus* and *Erasistratus*. They could dissect still living individuals (vivisections), in the case criminals of Alexandria under the auspices of the Ptolemy dynasty. *Herophilus* in particular synthesized anatomical knowledge more closely to current expertise than any other until that time. The Greek *Theophrastus* (? - 287 BCE), a disciple of *Aristotle*, also carried out dissections in humans. He coined the term 'anatomy' (Greek, 'anna temnein'), which became generalized, encompassing the whole field of biology that studies the form and structure of living beings, existing or extinct.

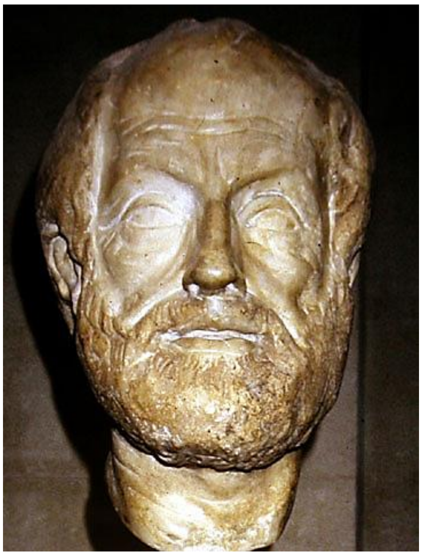

Fig. 2 - Aristotle (Louvre Museum)

Fig. 3 - Galen

Galen

Aelius Galenus or *Claudius Galenus* (Pergamon, 129, now Bergama in Turkey - probably Sicily, 200) was a prominent Greek physician (educated in Alexandria), surgeon and philosopher. *Galen* contributed much to the understanding of numerous scientific disciplines, including anatomy, physiology, pathology, pharmacology, neurology, and philosophy. Galen's anatomy and medicine were influenced by the 'humorism' theory practiced by many Greek physicians, including *Hippocrates*.

Galen's theories dominated and influenced Western medical science for almost 'two millennia.' His anatomical analyzes, based on the dissection of animals (apes, pigs, and dogs), remained incontestable until 1543 when detailed descriptions and drawings of dissections of the human body were published in *De Humani Corporis Fabrica* (by *Andreas Vesalius*). Galen's theory for the functioning of the circulatory system still lasted until 1628, when *William Harvey* published the *Anatomical Exercitatio of Motu Cordis et Sanguinis in Animalibus* and established that the blood circulated, and the heart propelled him like a bomb.

Galen elucidated the anatomy of the trachea and was the first to demonstrate that the larynx generates the voice. *Galen* probably understood the importance of artificial ventilation because one of his experiments used to inflate the lungs of a dead animal. One of his most significant contributions to medicine was work on the circulatory system. He was the first to recognize that there are differences between venous (dark) and arterial (bright) blood. With his anatomical experiments on animals, he better understood the circulatory, nervous, respiratory and other structures. However, his work still contained many inaccuracies. *Galen* believed that the circulatory system consisted of two unidirectional blood distribution systems, rather than a single unified circulation system.

His understanding was that venous blood would be generated in the liver (from where it would be distributed to the body and then consumed). *Galen* also postulated that the arterial blood would be produced in the heart (from where it would be distributed to the body and then consumed). The liver and heart, then, would be responsible for regenerating the blood, completing the cycle. *Galen* believed in the existence of a group of blood vessels called the rete mirabile, near the dorsal part of the brain.

Unfortunately, Galen's original work was lost in time. We are aware of a fraction of his work thanks to the compilations made by Arab medicine, which were recovered in the Renaissance in Europe.

Middle Ages

After the decline of the Roman Empire, the study of anatomy stagnated in Christian Europe as it flourished in the Islamic world. The physician Persian *Avicenna* (980-1037) absorbed the anatomical teachings of *Galen* by expanding them in his "Principle of Medicine" (1020)[3].

The physician *Ibn Zuhr* (1091-1161) was the first Arab to perform dissections in man, as well as necropsies to study the cause of death. He recognized that scabies was caused by a parasite, a finding that was contrary to the 'mood theory' that came from the Greeks. Removal of the parasite from the patient's body produced healing and did not involve any purging of humor, bleeds, or any other traditional treatment associated with the four humors. In the 12th century, the private physician of the great politician and conqueror Saladin, *Ibn Jumay*, also performed dissections in the human body and urged his peers to do the same to understand medicine better. Another Arab physician, *Abd-el-Latif*, during the famine in Egypt in 1200 observed and examined many bodies, which led him to disagree with the teachings of *Galen* on the formation of bones, especially the jaw and the sacrum.

Ibn al-Nafis

The Arab physician *Ibn al-Nafis* (1213-1288) was prominent in dissections of human bodies and performing necropsy. In 1242 he described, for the first time, the pulmonary circulation and the coronary circulation, and was therefore considered the 'father of the circulation theory.' *Ibn al-Nafis* also issued the first concept of metabolism and developed new systems of anatomy that replaced the doctrine of the four humors of *Avicenna* and *Galen*. He described the pulse, bones, muscles, intestines, sensory organs, bile ducts, esophagus, stomach, and anatomy of almost every part of the human body.

[3] This was the most important treatise on anatomy in the Islamic world until the appearance of Ibn al-Nafis in the 13th century, whose book dominated medical education in medieval Europe until the 16th century.

Early modern anatomy

The 'Principle of Medicine' (from *Avicenna*, which incorporated the teachings of *Galen*) was translated into Latin. With this, it remained the most important text of anatomy in medical education in Europe until the 16th century. The first significant development in anatomical knowledge in Christian Europe since the fall of Rome occurred in Bologna between the 14th and 16th centuries. There several anatomists dissected corpses and contributed with more precise descriptions of organs, identifying their functions.

The first significant challenge of Galen's doctrine in Europe occurred in the 16th century. Thanks to the advent of the Gutenberg press[4] there was in Europe a collective effort to circulate the works of *Galen* and *Avicenna*. *Andreas Vesalius* (1514-1564) published a treatise on anatomy in 1543, *De humani corporis fabrica libri septem*[5], which was a challenge to *Galen*. *Vesalius* went from Leuven to Padua, where he can dissect bodies of criminals condemned to death (hangings) without fear of being persecuted. His drawings are detailed descriptions of the human anatomy that evidence the differences about the reports made by *Galen* (in animals). Many other anatomists who came after *Vesalius* also challenged 'galenic knowledge,' but it still reigned for another century.

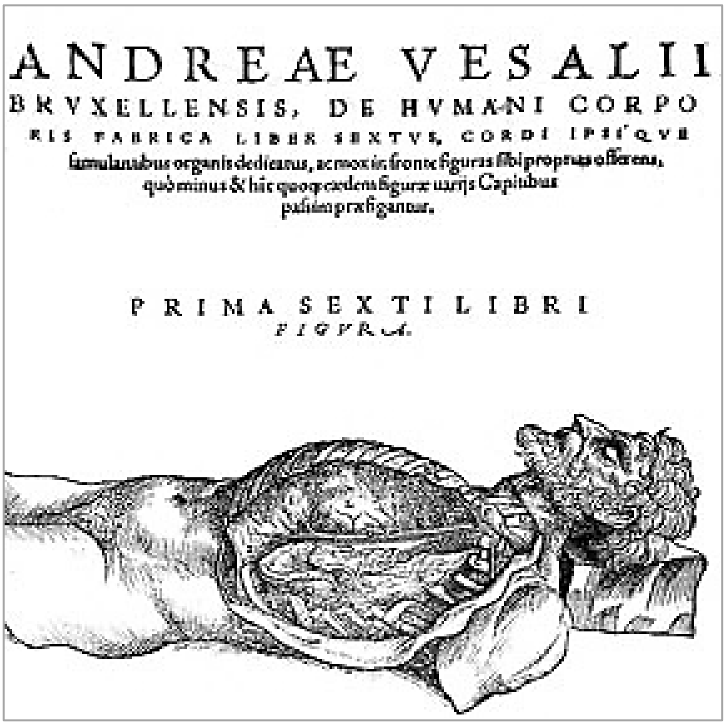

Fig. 4 – Illustration of the work of Vesalius (1543) with realistic drawing of a dissection.

[4] *Johannes Gensfleisch zur Laden zum Gutenberg* (Mainz, 1398-1468) German inventor and graphic designer who introduced the modern form of book printing. His invention of the mobile mechanical type for printing began the Revolution of the Press and is widely considered the most important event of the modern period. He played a key role in the development of the Renaissance, the Reformation and the Scientific Revolution, and laid the material foundation for the modern knowledge-based economy and the spread of mass learning.

[5] This book, along with Nicolaus Copernicus's "On the Revolutions of the Celestial Bodies" and Isaac Newton's "Principia Matematica" compose the list of the three books that most revolutionized human knowledge.

The foundation of the School of Medicine of the University of Bologna was a long process that began in 1063, with the first Professorial Professors appearing around the year 1170. The statute of the city of Bologna for the teaching of medicine dates from 1378. Many prominent personalities have contributed their activities through the centuries to the celebration of the University of Bologna. Between the end of the 13th century and the beginning of the 14th century, *Mondino Dei Liuzzi* (1270-1326) reestablished the Alexandrian school tradition of vivisection practice and published his observations in an anatomy book that was used until the late 16th century (in fact, can be considered the first book of experimental research in anatomy). In Bologna, *Alessandro Achillini* (1463-1512) studied the bile duct and the gallbladder; *Berengarario da Carpi* (1466-1530) was a famous surgeon for his description of the vermiform appendix, the thymus, the function of the heart valves (he also talked about fracture treatment and already used mercury in the treatment of syphilis); *Giulio Cesare Aranzio* (1530-1589) became interested in embryology ('the duct of Arancio') and blood vessels (bodies of Arancio); *Costanzo Varolio* (1543-1575) studied the encephalon ('bridge of Vario').

Miguel Servet (1511-1553) was a Spanish theologian, physician, cartographer, and humanist, the first European to describe the function of pulmonary circulation. He participated in the Protestant Reformation and, finally, created 'non-Trinitarian Christology' (which ignored the Holy Trinity), which was condemned by both Catholics and Protestants. He was arrested in Geneva and burned on a stake as a heretic by order of the Protestant governor of Geneva under the direction of John Calvin[6]. *Servet* studied medicine in Paris, graduating degree in 1536. Among his professors were Sylvius, Fernel, and Guinter (who spoke of him to *Vesalius* as 'his most skilled assistant in dissections'). Despite Servet's contribution to the knowledge of pulmonary circulation, his work was not recognized in his time mainly because his descriptions were made in a treatise on theology, *Christianismi Restitutio*, and not in a medical book. Many copies of this treatise were quickly burned after publication in 1553 because of persecution by religious authorities. Only three copies were spared, but they remained hidden for many years.

The most prominent 'son' of Bologna was *Marcello Malpighi* (1628-1694), 'father of microscopic anatomy' and a defender of the use of experimental methods. *Malpighi* graduated as a Doctor of Medicine at the University of Bologna in 1653. He married Francesca Massari, the younger sister of his anatomy professor, in 1654. *Malpighi* used the microscope to study the capillaries of the pulmonary alveoli (Fig 5), corpuscles of the kidney, the spleen corpuscles, and the epidermis follicles. His pupil, *Antonio Maria Valsalva*, investigated the vagus nerve and created the 'Valsalva maneuver.'

A succession of anatomists refined anatomical knowledge and lent their names to numerous anatomical structures. The 16th and 17th centuries witnessed remarkable advances in the understanding of the circulatory system, the function of the heart valves and venous valves. Blood flow was described, and the hepatic veins and lymphatic vessels were identified as separate portions of the circulatory system.

[6] John Calvin (1509-1564), French Christian theologian (Calvinism), was never ordained a priest. After his departure from the Catholic Church, he was the voice of the Protestant movement. He was persecuted in France and fled to Geneva in 1536, where he died.

17th and 18th Centuries

The study of anatomy flourished in the 17th and 18th centuries with the advent of the press, which facilitated the dissemination and exchange of ideas. Because the study of anatomy was heavily based on observation and drawings (the anatomists' popularity was related to their ability and talent in the drawing).

William Harvey (1578-1657) was an English physician who studied at the University of Padova, a disciple of *Fabrizio d'Acquapendente* (1533-1619) (who built the Anatomical Theater in Padua, where he taught for 50 years; the exact description of the venous valves). *Harvey* received his medical degree in 1602 and maintained a long friendship with *D'Acquapendente* for a lifetime. It was Harvey's interest in D'Acquapendente's work, 'De Venarum Ostiolis,' which led him to study the circulation of blood.

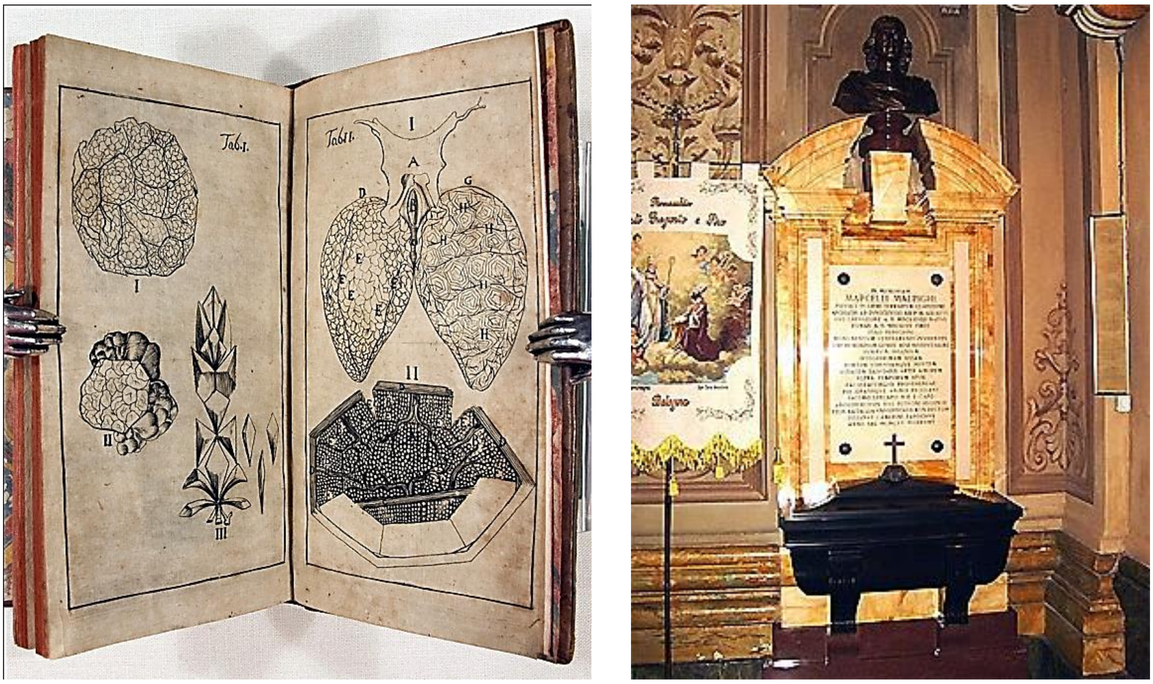

Fig. 5 – Illustration from the Malpighi book describing the 'pulmonary capillaries' (left) and the place where Malpighi is buried in Bologna (right).

Harvey was not the first anatomist to postulate that blood circulation was through the arteries and veins, but he was the first to demonstrate this fact convincingly. He also did experiments on the function of the heart by pumping blood. Harvey's mathematical reasoning led him to calculate the volume of blood in the body, which counteracted the Galenian theory that the blood was made in the liver.

In *De Motu Cordis* (Fig. 6A) *Harvey* adapted the diagram used by his master *D'Acquapendente* in *De Venarum Ostiolis*. There are distended veins in the forearm and the position of the venous valves. When the vein is pressed centrally (milked), and its extremity is closed (compressed), the vein only fills with blood when pressure is relaxed. Blood cannot be forced into the 'wrong' direction (Fig. 6B).

Many famous artists studied anatomy, dissected bodies and published their drawings for money, from *Michelangelo* and *Da Vinci* to *Rembrandt*. *Leonardo Da Vinci* (1452-1519) learned anatomy with *Andrea del Verrocchio* (1435-1488). As an artist, he quickly became master of topographical anatomy, designed many studies of muscles, tendons and other anatomical parts, always seeking perfection. Being a successful artist, he was allowed to dissect human bodies at the Hospital of Santa Maria Nuova in Florence and then in hospitals in Milan and Rome.

Fig. 6 – Illustration from Harvey's book on blood circulation. **A** - Frontispiece of the book (Thesis), **B** - direction of blood flow in the veins of the forearm.

Leonardo Da Vinci (1452-1519) did many studies on the skeleton and muscles. We can say that these studies are a harbinger of the modern science of biomechanics. He also designed the heart and vascular system, sexual organs, and other internal organs and made the first scientific drawing of copulation (Fig. 7) and the development of the fetus in the uterus. He also designed the effects of aging and emotion on the human face, as well as the 'three-dimensional anatomy' of body segments (Fig. 8). From 1510 to 1511 *Da Vinci* collaborated with *Marcantonio della Torre* (1481-1511), and together they prepared an anatomy work where *Da Vinci* drew more than 200 boards (which was only published in 1680, 161 years after Da Vinci's death, under the title of Treaty of Painting).

Many European cities such as Amsterdam, London, Copenhagen, Padua, and Paris had Anatomical Academies held by the local government. Thus, Nicolaes Tulp[7], mayor of Amsterdam, can perform numerous dissections and public demonstrations (Fig. 9). At that time, students traveled through Europe where bodies were available (hanged, for example) to perform dissections (no way to keep bodies in study conditions long after death and their dissection should be done quickly).

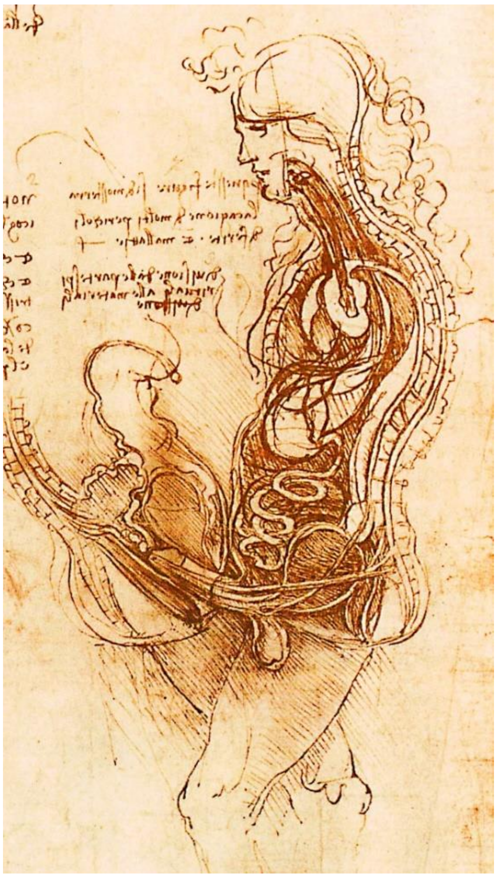

Fig. 7 – Drawing by Leonardo Da Vinci illustrating copulation.

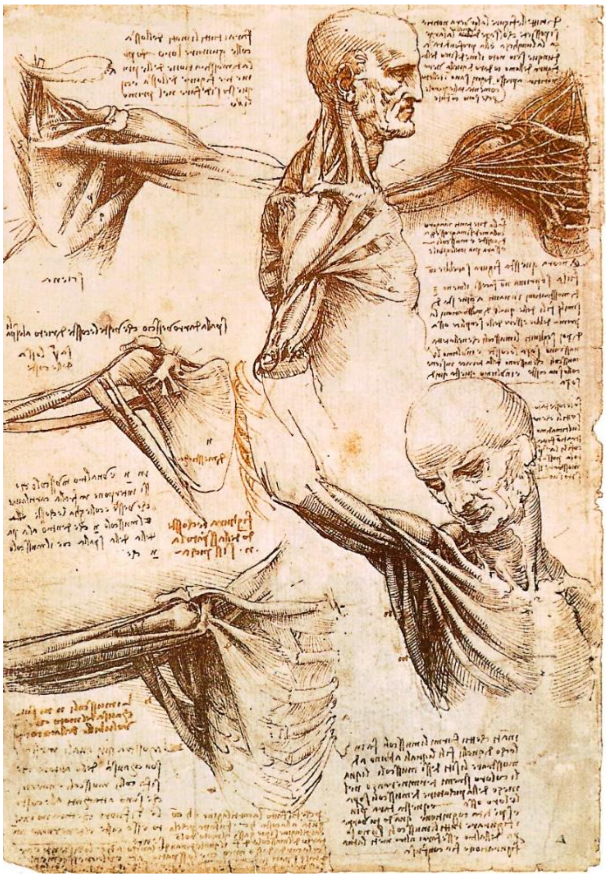

Fig. 8 – *Leonardo Da Vinci drew different levels of dissection of a body (possibly that of a 100-year-old elder whom he met still alive, dead on the same day).*

Europeans interested in anatomy traveled to Italy, which was the high center of the anatomy of the time. Only in Italy was it possible to dissect a woman's body, for example. *Renaldus Columbus* (1516-1559) and *Gabriele Falloppio* (1523-1562) were disciples of *Vesalius*. *Columbus* was his successor in Padua and later a professor in Rome. *Columbus* accurately described the bones, the shape of the heart cavities, the pulmonary artery, the aorta, and their leaflets, and traced the course of blood from the right side to the left side of the heart. Also, it made a good report of the encephalon and its vessels and the ventricle of the larynx. The name of *Columbus* is also associated with the description of the clitoris (which he considered *Amor Veneris*, *Vel Dulcedo Appelletur*, that is, "must be called love or sweetness of Venus"). *Columbus* was not the first to designate the clitoris

[7] Dr. Tulp's "Anatomy Lesson" (Fig. 9) is an oil painting on canvas by Rembrandt, painted in 1632. It is one of his most famous and revolutionary works. The work portrays an anatomy class of Dr. Nicolaes Tulp. The body that appears in the picture is of a marginal who had been condemned to death by robbery the day before the lesson. Anatomy lessons really existed and took place in amphitheaters, given by anatomist doctors.

but was one of the first to propose its role in female sexual pleasure. Fallopio described the uterine tubes ('Fallopian tubes').

Fig. 9 – Anatomy Lesson of Dr Tulp (Rembrandt).

19th century

During the 19th century, the anatomists finalized and systematized the human descriptive anatomy that they inherited from the anatomists of the preceding centuries. The increase in anatomy research has increased the demand for corpses, which led to the mistrust that some used obscure means to obtain them (including committing a crime[8]). Discipline has also progressed and has increasingly established connections with the histology and biology of development, not only in man but also in other animals. The Société Anatomique de Paris is one of the oldest medical societies still in operation, founded by *Dupuytren* and *Lænnec* in 1803, under the aegis of Emperor *Napoleon Bonaparte* (currently works at UFR Biomédicale des Saints-Pères (Fig. 10).

Why does the heart pulse? The issue is known as myogenic theory versus neurogenic theory dominated cardiac research in the 19th century. *Marie Francois Xavier-Bichat* and *Nysten* reported experiments with beheaded individuals (in Paris, 1800-1802) in whom they caused the heart to resume pulsating using electric shock (during the French Revolution it should not have been a problem to obtain bodies of beheaded[9]).

[8] Two Irishmen William Hare and William Burke of Edinburgh in the mid-19th century committed a series of murders in order to sell the victims' bodies for dissection in anatomy classes.

[9] Individual rights were suspended and daily, with popular applause, carried out publicly and en masse. The Jacobin leader Robespierre, sanctioning the summary executions, had announced that France needed no judges, but more guillotines. The result was the death sentence of 35,000 to 40,000 people.

Fig. 10 – UFR Biomédicale des Saints-Pères (Université Rene Descartes, Paris V), where the Société Anatomique de Paris still operates today.

Jan Evangelista Purkinje (1787-1869) discovered in 1839 fibers in the subendocardium of the ventricles ('Purkinje fibers' of the conduction system of the heart). *Walter Gaskell* in 1886 described specialized muscle fibers connecting the atria and ventricles, which when sectioned cause blockage. It also identified the area of onset of cardiac excitation in the region derived from the venous sinus. *Wilhelm His, Jr* (1863-1934) examined a series of histological sections of the heart of human embryos and showed that there is connective tissue surrounding a beam from the right atrium to the ventricles, the bundle of His. *Sunao Tawara* (1873-1952) followed the 'bundle of His' (atrioventricular, AV) to its connection with the ‘compact’ portion of the AV node at the base of the interatrial septum. *Tawara* concluded that the 'AV connection system' originates from the AV node, penetrates the septum (like the His bundle) and divides into right and left branches ending in the 'Purkinje fibers.' *Arthur Keith* (1866-1955) and *Martin Flack* (1882-1931) found, in 1907, a peculiar structure at the sinoatrial junction that recalled the structure of the AV node; they considered that the heart rhythm started there and called it the sinoatrial node region. In 2006 and 2007 was celebrated the 100th anniversary of the anatomical discoveries of the cardiac conduction system.

A unique opportunity for in vivo experiments occurred in 1882. Catharina Serafin (Prussia), a 46-year-old woman, had a chest tumor that was excised along with the left wall of the left hemithorax, exposing the heart, which could be seen covered by a thin layer of skin. *Hugo Von Ziemssen* stimulated the heart of Mrs. Serafin using electric current, which altered the frequency of heartbeats. Years later, *Einthoven's* electrocardiogram showed a better understanding of the electrical phenomenon that occurs in the contraction of the heart.

Modern Anatomy

The anatomical research in the last 100 years has benefited from technological innovations and the growing understanding of related sciences such as 'evolution' and 'molecular biology.' Endocrinology explained the purpose of the glands that the anatomists could not tell. Sophisticated medical devices allow us to study anatomy in living people. Today, progress in anatomy is mainly in the study of ontogenetic and phylogenetic development and the study of the function of specific structures, using techniques such as immunohistochemistry / confocal microscopy by laser scanning, neuronal tracers or others.

Increased knowledge of cardiac anatomy and congenital heart disease led to the first surgery to treat congenital heart disease in November 1944 at Johns Hopkins Hospital (in 1938 the persistence of ductus arteriosus had been corrected, but now for the first time, there was a specific procedure to correct a congenital heart defect). The operation was called the Blalock-Taussig shunt and opened the door for new methods to be attempted in this area.

Anatomy is already thoroughly documented in man, but the nonhuman anatomy is still full of possibilities. Modern anatomists are still interested in performing experiments on animals since they allow us to understand the primary organization of organs and the principles of functioning of structures with the use of advanced techniques of microscopy, physiology, cellular and molecular biology.

There are still mysteries in the human body that need clarification. The current challenge of cardiovascular morphology is to characterize the exact role of stem cells[10]. Stem cell research has been a field of increasing activity since the works of *Ernest McCulloch* and *James Till* in the 1960s at the University of Toronto. There are two different types of stem cells in mammals: embryonic stem cells, isolated from the inner cell mass of the blastocyst and stem cells found in adult tissues. Possible mechanisms of stem cell activation in heart cell therapy include the generation of cardiomyocytes, stimulation and growth of new blood vessels (angiogenesis), secretion of growth factors, and possibly some other mechanism still unknown.

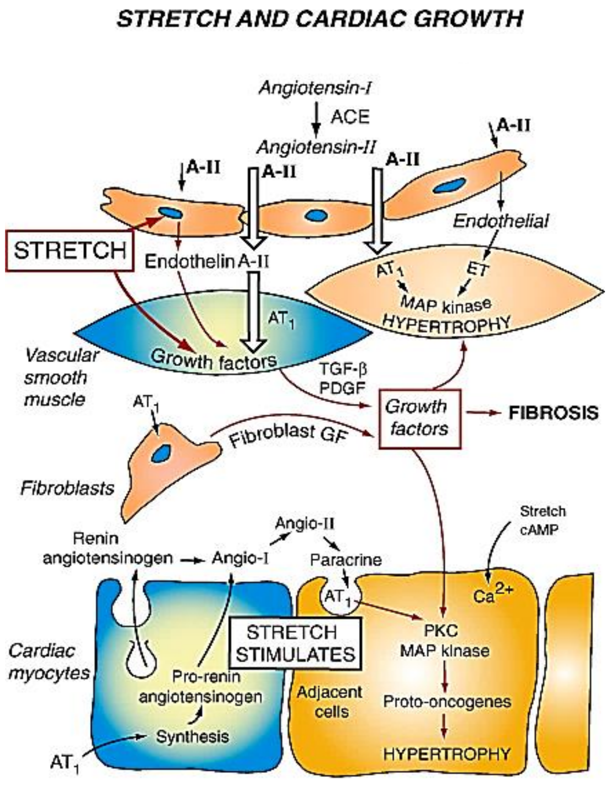

Fig. 11 – Diagram illustrating the innumerable possible ways of stimulating the cardiomyocyte that lead to cardiac hypertrophy (Opie & Gersh, 2008).

[10] Stem cells are cells found in every multicellular organism. They are characterized by the ability to renew by mitotic division and differentiate into a wide range of specialized cell types.

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Timeline of anatomical knowledge