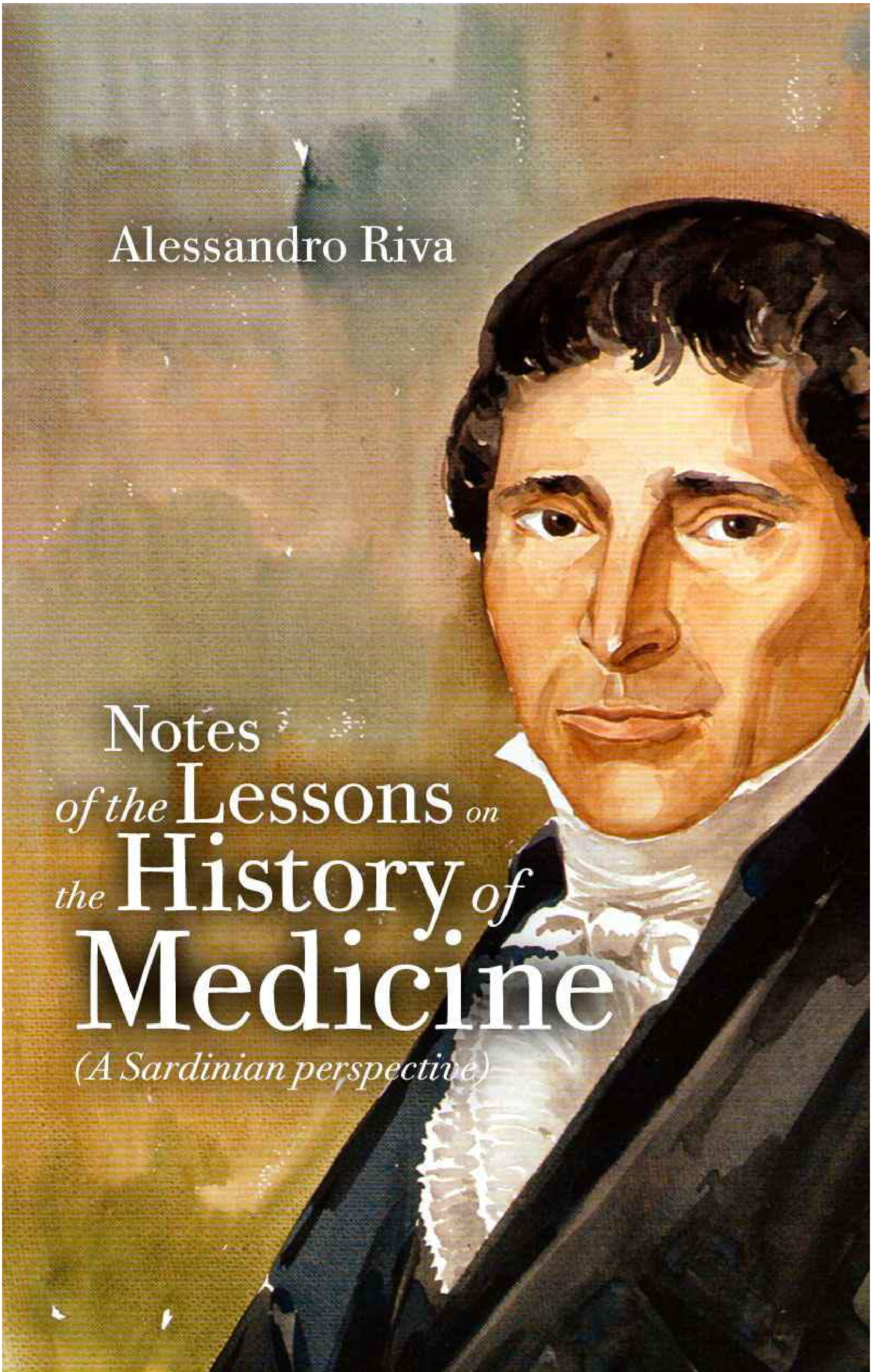
Alessandro Riva
Notes of the Lessons on the History of Medicine
(A Sardinian perspective)

Alessandro Riva

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(A Sardinian perspective)

Colophon

Notes from the lessons on History of Medicine, taught to the students of the schools of medicine and nursing of the University of Cagliari, by Alessandro Riva, Professor Emeritus of Human Anatomy and of History of Medicine, Founder and Director (1991-2016) of the Museum of Clemente Susini's Anatomical Waxes.
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Owing to the extent of the subject and of the limited time allowed by the present curricular regulations, the outline of History of Medicine resulting from these notes is, necessarily, incomplete and based on personal choices. For a more comprehensive study, readers may refer to the bibliographical references reported at the end.

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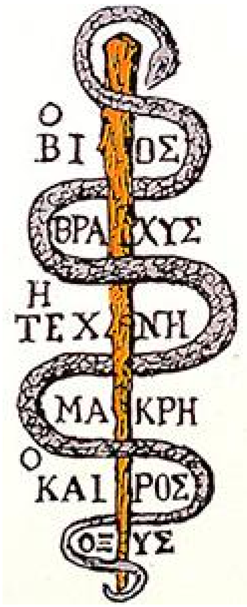
To the memory of Professor Robert (Robin) A. Stockwell (1933 - 2014):
Scientist, Man of Culture, lifelong Friend.

Chapter 1

The Medicine of Ancient Greece



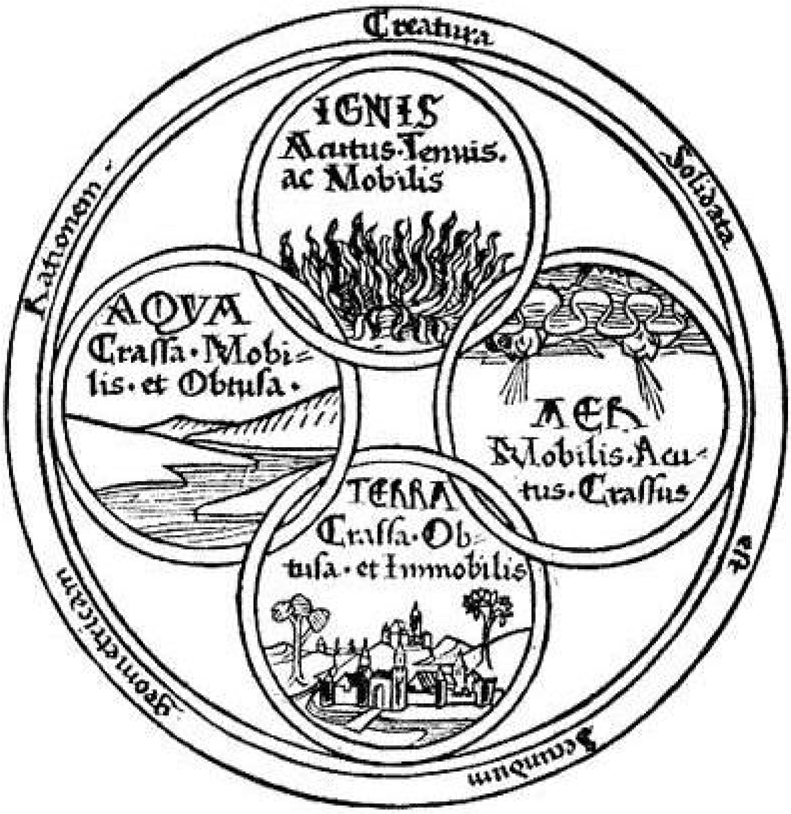
The symbol of medicine

In its early phases, western medicine (we are not concerned here with Oriental medicine) was a theurgic medicine, in which the disease was considered to be divine castigation, a concept which is found in a great many Greek texts such as the Iliad, and is still connaturalised by man today.

The symbol adopted for medicine was the serpent, thought of as a sacred creature because it was erroneously believed to be immune from illness and disease. However, according to another version the symbol is not the representation of the serpent, but the extirpation of the worm *Dracunculus medinensis* known as the worm of Medine. Moreover, the serpent had an important practical function in ancient medicine: every temple had a type of underground passage with serpents. In fact, the temple was not only a place of devotion, but also the site where the ill and sick were brought. The purpose of the serpent pit was to frighten the patient, who probably received potions to help him, or her, in order to induce a state of shock and make the God appear in front of them who would thus heal them.

With the passage of time, medicine moved further and further away from religion until the rational medicine of Hippocrates arrived, signalling the boundary between rationality and magic. The first schools to develop were in Greece and in Magna Grecia, that is to say, in Sicily and Calabria in Italy. Among these, the most important was the Pythagorean school.

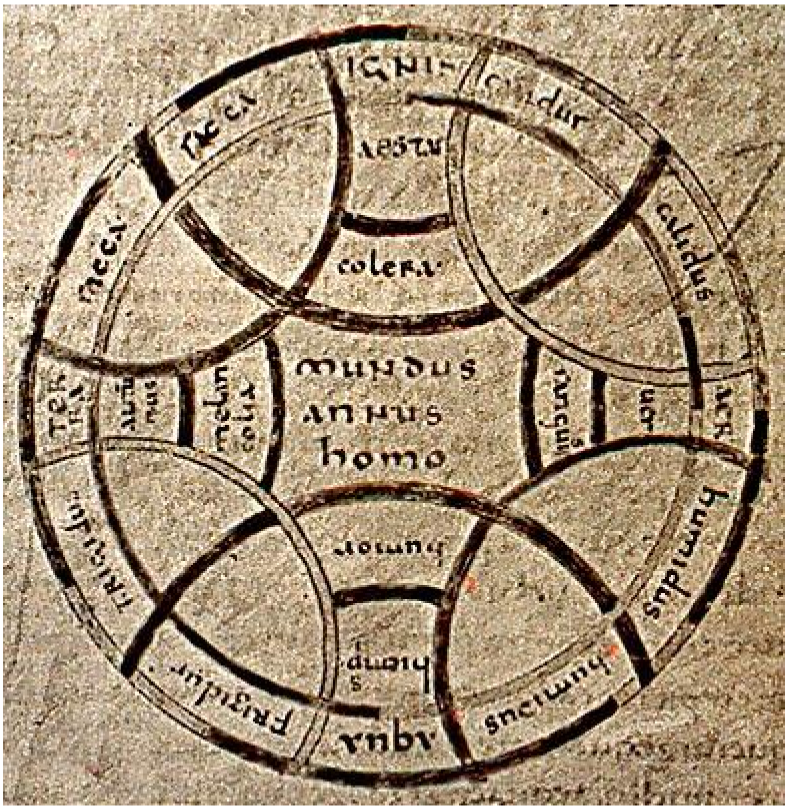
The great mathematician **Pythagoras (VI century B.C.)** originally from the island of Samos, moved to Crotone when the tyrant Policrates took power in his island. He brought his theory of numbers to natural science, as yet not definable as medicine: according to Pythagoreans, some numbers had precise meanings and, among these, the most important were 4 and 7. Seven always had a significant meaning. For example, in the Bible the number of infinity is indicated by 70 times 7. Among other things, 7 multiplied by 4 is 28, that is to say, the duration of lunar month ad of menstrual period; seven multiplied by 40 is 280, that is to say, the duration of gravidity in days. Furthermore, the magic seven meant that it was better for a baby to be born in the seventh month rather than the eighth. The period of quarantine, too, the forty days that served to avoid contagion from diseases, is derived from the concept of the number 40 being sacred.



The four elements

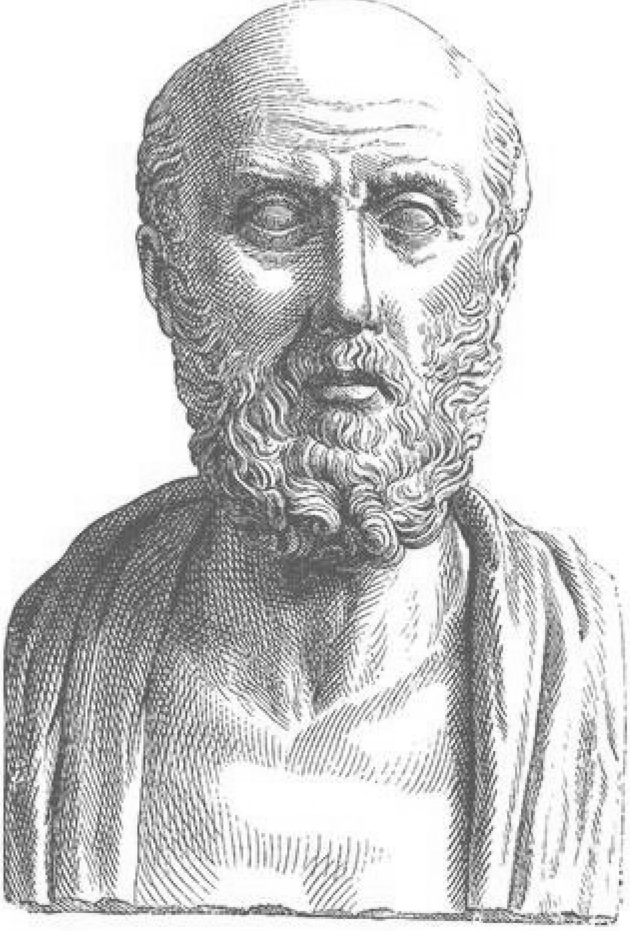
Taletes (VII-VI centuries B.C.) elaborated an important system according to which the universe was composed of the fundamental elements: air, water, earth, to which **Heraclytus (VI-V centuries B.C.)** added fire. In this period great relevance was also given to the qualities of dryness and humidity, hot and cold, sweet and bitter, etc. **Alcmaeon of Crotone (VII-VI centuries** B.C.), was the first to have the idea that man might be a microcosm constituted of four individual elements. According to him, a person's state of health derives from the equilibrium of these elements, which he called isonomy or democracy, whereas disease derived from monarchy, or rather from the prevalence of one element over and above the others. Alcmaeon also was the first to identify the brain as the most important organ in the body. Until then, very little importance had been given to the brain: in Greek times the body was sacred and so dissection was not practised, but even during animals sacrifices, brain was seen only as a cold and gelatinous mass of little interest. Alcmaeon, instead, asserted that it was the very organ that controlled the whole organism. He also may have deduced, a fact that was then denied by others, that the nerves might serve to conduct motor and sensitive nervous impulses, but this idea made no headway in science at that time.

The real and true rational medicine is attributed to **Hippocrates (460-370 B.C.)**, so he is known as the father of medicine. Hippocrates was born on the island of Kos, in the Dodecanese, where he developed the rational school with which a great many of the ideas attributed to Hippocrates are associated. He lived in the 50 years of Periclean peace, a period in which philosophy flourished, and travelled extensively in the Mediterranean area. We know that his journeys took him, *inter alia*, to mainland Greece, Sicily, Alexandria, Cyrene, and Cyprus. Fundamentally, the basis of rational medicine is a negation of divine intervention in the disease. Even the famous sacred illness, epilepsy, was attributed to a dysfunction of the organism. Hippocrates also made humours correspond with the seasons: the first season, that of blood and air corresponded to spring; the summer was fire, bile and liver; autumn was earth, black bile and spleen, while winter was the season of water, of phlegm (mucus) and of the brain. In addition, a parallel was drawn between the four seasons of life, infancy and early youth, then mature youth, followed by virile advanced years, and, ultimately, senility.



The theory of humors

Referring back to what Alcmaeon of Crotone had said, Hippocrates maintained that disease was caused by a disequilibrium, no longer speaking of democracy or monarchy so as not to offend the tyrants, and that where there was equilibrium between the humours there was health. Cures lay in removing the humour that was in excess. His theory also explained the various temperaments: a coleric subject had too much bile, a phlegmatic one too much mucus, and so on. The most important element at the centre of Hippocrates' conception was not the disease, which he explained in a holistic manner, but man. Compared to the rival Cnidus's school, which focused on a reductionist conception of disease much as occurs today, Hippocrates' conception made his school's fortune; his school prevailed as it concentrated on the man, while that of Cnidus concentrated on the disease and, because it did not have the necessary evidence to carry out its ideas, it ceased to exist, whereas that of Hippocrates remained active.



Portrait of Hippocrates

Underlying Hippocrates' conceptions was a profound and practical philosophy based notably on common sense. The fundamental principles were simply to leave things to nature, that is to say, to the healing powers of nature, and to observe the illness very carefully, intervening as little as possible, and paying attention to nutrition and to the wholesomeness and healthiness of the air. In order to eliminate the disequilibrium, the excess material (the so-called *materia peccans*) had to be removed. Means available to dispose of *materia peccans* were 'head purges' (= purges of the head which consisted of inducing sneezing with drugs such as pepper), and enema (clyster), or otherwise by blood-letting. The latter was not much used by Hippocrates' followers, but in the Roman Epoch, and especially in the Middle Ages, it became a very common procedure with grave consequences for patients who, in some cases were bled to death. It must be noted, however, that, Hippocrates recommended that physicians employ all medical treatments with the maximum of frugality.

Hippocrates texts, or those believed to be such, were taught in the universities until 1700. These texts were composed of a series of aphorisms, amongst which is the famous "Life is brief, art is long, opportunity is fleeting, experience is fallacious, judgment is difficult"; these form the basis of his philosophy and lead to careful, repetitious thought before a medical intervention. Hippocrates thus created a holistic medicine based on the man or microcosm, preaching the use of the available therapies with the maximum of conservation. Remedies were few because at that time pharmacology did not exist and the first hint of herbal medicine did not arrive until about a century later, from one of Aristotle's students called Theophrastus. Hippocrates is also remembered because he expressed the first concepts of medical ethics, which still apply today, and in fact are contained in the Hippocratic oath, effectively encoding the person of the doctor.

The Hippocratic Oath. Original Version

I SWEAR by Apollo the physician, Aesculapius, and Health, and All-heal, and all the gods and goddesses, that, according to my ability and judgment, I will keep this Oath and this stipulation.

TO RECHON him who taught me this Art equally dear to me as my parents, to share my substance with him, and relieve his necessities if required; to look up his offspring in the same footing as my own brothers, and to teach them this art, if they shall wish to learn it, without fee or stipulation; and that by precept, lecture, and every other mode of instruction, I will impart a knowledge of the Art to my own sons, and those of my teachers, and to disciples bound by a stipulation and oath according the law of medicine, but to none others.

I WILL FOLLOW that system of regimen which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to any one if asked, nor suggest any such counsel; and in like manner I will not give a woman a pessary to produce abortion.

WITH PURITY AND WITH HOLINESS I will pass my life and practice my Art. I will not cut persons laboring under the stone, but will leave this to be done by men who are practitioners of this work. Into whatever houses I enter, I will go into them for the benefit of the sick, and will abstain from every voluntary act of mischief and corruption; and, further from the seduction of females or males, of freemen and slaves.*

WHATEVER, IN CONNECTION with my professional practice or not, in connection with it, I see or hear, in the life of men, which ought not to be spoken of abroad, I will not divulge, as reckoning that all such should be kept secret. WHILE I CONTINUE to keep this Oath unviolated, may it be granted to me to enjoy life and the practice of the art, respected by all men, in all times! But should I trespass and violate this Oath, may the reverse be my lot. (This is a jeremiad against surgery because surgery had disastrous results at that time. In fact, there was no incentive at all to study anatomy because it was believed that disease was caused by the disequilibrium of the humours and so organs had no importance at all. Therefore, surgery was empirical, an incision was made without knowing what was being cut, and there were no concepts of asepsis or of anaesthesia. Owing to this prohibition, for about two millennia surgery was considered to be a secondary skill of no practical use: in fact it was not thought of as a science until the end of the 18th century. Surgeons and physicians wore different clothing: the physicians, were graduates and wore magistri gowns, whereas surgeons could not wear a gown, for they were not formally educated and did not know Latin, which was the language of teaching in the medieval and more modern eras (in the surgery of the 16th, 17th and 18th centuries doctors in the long toga down to their feet were distinguished from surgeons with uncovered legs). While this corollary was at first justified, it brought about as the practice of surgery by people deprived of any theoretical knowledge at all.)

The Hippocratic Oath. Modern Version

I SWEAR in the presence of the Almighty and before my family, my teachers and my peers that according to my ability and judgment I will keep this Oath and Stipulation.

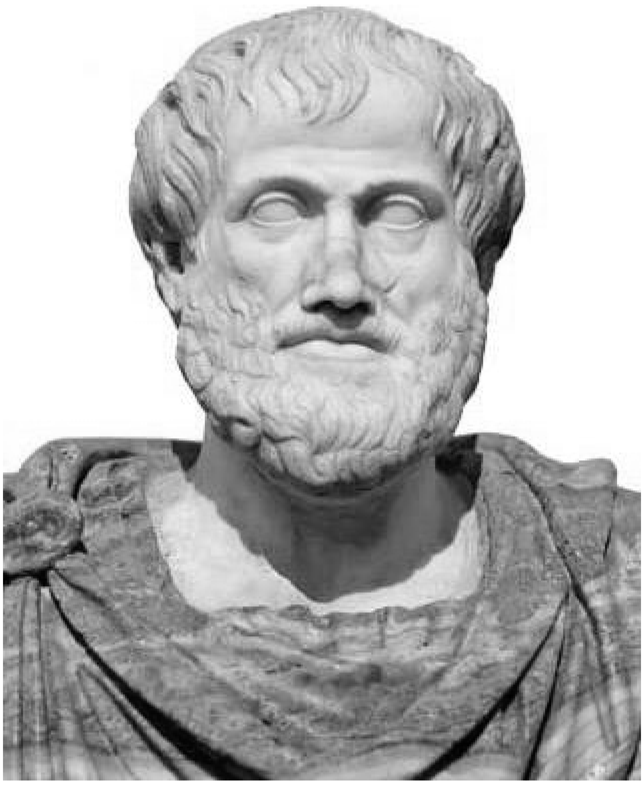
TO RECKON all who have taught me this art equally dear to me as my parents and in the same spirit and dedication to impart a knowledge of the art of medicine to others. I will continue with diligence to keep abreast of advances in medicine. I will treat without *exception all who seek my ministrations, so long as the treatment of others is not compromised thereby, and I will seek the counsel of particularly skilled physicians where indicated for the benefit of my patient.*

I WILL FOLLOW that method of treatment which according to my ability and judgment, I consider for the benefit of my patient and abstain from whatever is harmful or mischievous. I will neither prescribe nor administer a lethal dose of medicine to any patient even if asked nor counsel any such thing nor perform the utmost respect for every human life from fertilization to natural death and reject abortion that deliberately takes a unique human life.

WITH PURITY, HOLINESS AND BENEFICENCE I will pass my life and practice my art. Except for the prudent correction of an imminent danger, I will neither treat any patient nor carry out any research on any human being without the valid informed consent of the subject or the appropriate legal protector thereof, understanding that research must have as its purpose the furtherance of the health of that individual. Into whatever patient setting I enter, I will go for the benefit of the sick and will abstain from every voluntary act of mischief or corruption and further from the seduction of any patient.

WHATEVER IN CONNECTION with my professional practice or not in connection with it I may see or hear in the lives of my patients which ought not be spoken abroad, I will not divulge, reckoning that all such should be kept secret. WHILE I CONTINUE to keep this Oath unviolated may it be granted to me to enjoy life and the practice of the art and science of medicine with the blessing of the Almighty and respected by my peers and society, but should I trespass and violate this Oath, may the reverse by my lot.

Even if the body was taboo in Greece, the enormous development of figurative arts, above all of sculpture, presupposed some anatomical knowledge, which in turn indicates that dissection was practised in Greece. Certainly, it is known that dissection of human body was little practised after the Hippocratics and actually found most favour in the Alexandrian school.



Aristotle

The greatest scientist and biologist of the ancient world was **Aristotle (384/3 B.C.-322/1 B.C.)**, who contributed enormously, not only to medicine *per se*, but also to the natural sciences, for he was the first to classify animals (and his pupil Theophrastus was the first to classify plants). Unfortunately, certain steps taken by Aristotle, perhaps because they were interpreted badly, brought about an error which had grave consequences on the evolution of science. It seems that he sustained the notion that certain “inferior” animals such as insects (whose name derived from the evident segmentation of the body into its components) came into the world spontaneously from decomposing material regenerating and so their growth could not be limited or restrained. This concept began to be attacked only at the end of the 17th century. Aristotle elaborated a physiological system centred on the heart, in which according to him, there burned a life-giving vital flame maintained by a spirit named pneuma or spiritus vitalis (vital spirit) that produced heat. He felt that the lungs and the brain had a primary function of cooling. The heart was the most important organ because when the heart stopped, the body died. Furthermore, in his studies of embryology, Aristotle noted that the heart began to beat in the initial phases of the organism’s development: primum oriens, ultimum moriens (The first to be born, the last to die).

In his theory, heat was the most important thing and gave life. He sustained that man, having a great deal of heat, managed to use all his body’s resources and to produce sperm. On the other hand, women did not have enough heat so a part of the body’s blood was eliminated during menstruation. With its heat, sperm acted on menstruation, producing the embryo. According to Aristotle, his theory was validated by the heat derived from the sperm in the puerperium period causing women to produce milk: in most cases, menstruation itself was not fully present because this blood, being in abundance, was transformed into milk thanks to the heat. Aristotle also taught Alexander the Great, who brought Hellenic culture to its maximum fruition, expanding throughout the Mediterranean. But the great expansion later led to collapse.

Chapter 2

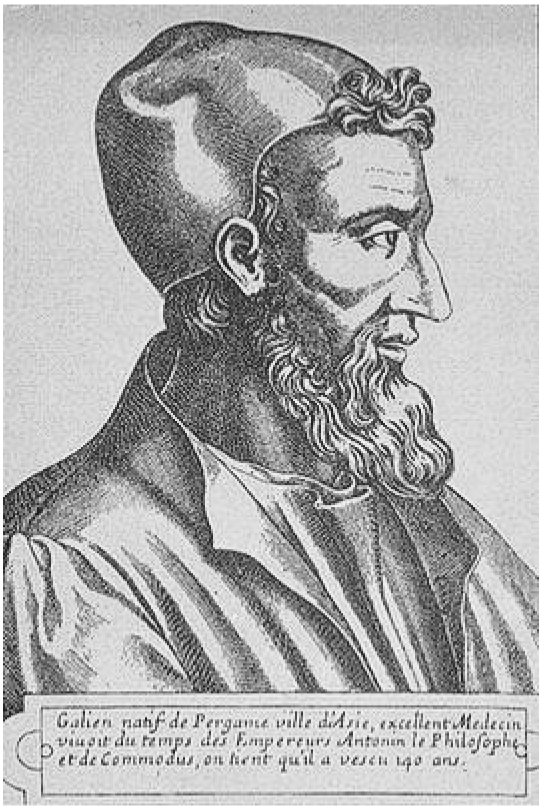
Hellenistic-Roman Medicine
Arab Medicine
Medieval Times

Alexander the Great conquered all of the Mediterranean but, as often happens, such great expansion ultimately brought about the collapse of Alexander's empire. He left power in the hands of various generals, and so his Empire was divided into numerous kingdoms. Among the most important kingdoms was that of Pergamon and, above all, that of the Ptolemies in Egypt. Here the Greek culture fused with the Egyptian.
During the Ptolemies' empire, a cultural movement of vast proportions developed at Alexandria in Egypt. The largest and most famous library in ancient times was built, which contained the sum of the epoch's knowledge, and which, unfortunately, suffered several misfortunes in the following centuries. It was set on fire by Caesar and by other Roman emperors, and was definitively destroyed around 640 by an Arab Caliph. This library was a true and real university in which scientists trained in the Aristotelean school. However, they dissected not only animals, but also humans. Egypt was a land which, for millennia, had practised funerary, so dissection had been performed as a preparation for mummification. Therefore, the technique of postmortem examination acquired importance, not only in terms of dissection, but as also occurred in the Renaissance, as a fundamental part of a doctor's professional activities.
Very important was the empirical school, widespread in Alexandria, according to which a doctor's work consisted of three fundamental activities: anamnesis (case history), autopsy (visiting the ill, in the sense of inspecting the patient), and diagnosis. Thus, the school had very interesting principles which bring to mind those of today, but all the same it failed because there was no concrete possibility of either making an accurate diagnosis or consequently, due to their lack of knowledge, providing an *ad hoc* therapy for the illness.
At the same time as the empirical school trained doctors, the dogmatic school which was a continuation of the Hippocratic school and the methodical school, which had a great success, were flourishing in Alexandria.
Two outstanding scientists working outside the above-mentioned schools also lived in Alexandria, namely **Herophilus (330 B.C.)** (1) and **Erasistratus (304 B.C.-250 B.C.)**. The latter was a great scientist, above all because he was the first to recognize that the arteries are vessels, opposing Aristotle's belief that arteries did not transport blood but *pneuma* (2). Moreover, he placed great emphasis on the study of the pulse, on the concept of body temperature etc., contributions which were lost in the course of the following centuries.
As already mentioned, the most important school in Alexandria was the methodical school. This did not no rest on the philosophy of the four elements, but on the rival philosophy, the atomistic theory of **Democritos (V-IV centuries B.C.)**. The Hippocratic conception was finalistic, analogous to that of Aristotle, whereas the theory of Democritos was based on the case. According to this school the pores had great importance: so, according to whether the pores were open or closed, the patient had a condition of looseness or tension respectively. It was necessary to do everything to keep the pores in their normal open mode, and attention had to be paid to how one washed, and to the water's temperature This concept, reported by Galen, became the cause of extremely poor hygiene in Medieval times because it was interpreted wrongly and taken to mean that water was condemned for causing the pores to close.
In Ancient Greek and then, in Roman times, there were great developments in hygiene. The

body's physiological needs were no longer carried out in the external environment or in communal open places (streets, clearings...) but in appropriate buildings, public lavatories equipped with a water supply and a sewage system. Rome had an efficient sewage system in addition to an extremely functional water supply system. This was not only for the rich, but included everyone; in the *insulae* (tenanted houses in ancient Rome), there was a fountain, with running water brought to every house by aqueducts. These aqueducts were constructed using lead pipes, a very malleable material, and were blamed for the fall of the Roman Empire because of the disease caused by lead compounds in the water resulting in lead poisoning, also known as saturnism. In fact, it seems that it was not so much polluted water that caused this illness, but wine. Indeed, water came from mountainous areas and was rich in calcium compounds which were deposited with the passage of time on the inside of the lead pipes and so formed a protective layer keeping the water from the lead which thus could no longer enter into the running water. On the other hand, wine was rich in soluble lead compounds because these were used to control the wine's fermentation in the same way as disulphide is today. Moreover, wine was commonly added to drinking water to prevent pollution.

Medicine was practiced in a family environment in Rome (the family doctor was the *pater familias* who had absolute power over the family) and although medicine was not based on any true real theory, it was, however, a rationalized empirical science. The herbalist was very important even if, he too, worked in an empirical manner (3).

Medicine arrived in Rome with the conquest of Greece. To be a doctor in Rome was considered disdainful, something that only a foreigner would do. Since, after its conquest by the Romans, Greece was poverty-stricken after numerous wars had wasted it, there were a great many medics who sold themselves as slaves so as to be able to go to Rome and exercise their profession. Many of these became famous and bought their freedom, becoming freedmen. The sect that enjoyed the best fortune was the Metodic (4), with **Asclepìades (129-40 B.C.)** and his student Temison influencing the Roman medical culture very strongly. Furthermore, there were very important writers of treatises in Rome, among whom was the founder of herbal medicine, **Dioscorides Pedanius (First Century A.D.)** who published a book entitled *De materia medica*, which remained the basis of pharmacology until the early 1800s. **Soranus of Ephesus (I/II century A.D.)**, a Greek doctor, published a gynaecological treatise, and above all **Aulus Cornelius Celsus (14 B.C.-37 A.D.)** with his treatise *De Medicina*, also were important. The latter textbook was a kind of medical encyclopaedia that discussed arguments of surgery and of medicine from a scholarly point of view rather than that of an expert in the subject, simply compiling a great list of common practices in Rome. This enables us to gain an idea of the development of surgery at that time, above all in particular fields such as dentistry (5).



Portrait of Galen

However, the most characteristic element of Roman sanitation was hygiene. The Romans washed a great deal, to which the use and the number of thermal baths existing at that time bears witness. Leaving an extremely important mark on western culture, the most important doctor in Roman times was **Galen (129-216 A.D.)** from Pergamon (6). He was the son of the kings' architect who thus came from a wealthy family and after his apprenticeship at Alexandria went to Rome where he was doctor to the gladiators, acquiring anatomical experience, even though he followed Greek concepts, and he dissected animals above all else. The most studied animal was the pig ("the animal most similar to man" said Galen) and the monkey (7). Galen's instinct lead him to realize the fundamental importance of the organs and their effective role. For example, he understood that the urinary bladder did not produce urine but that this came from the ureter (he demonstrated this by joining the ureters together) and for the first time described the recurrent nerve and its role in phonation. He was very important as a practicing physician: basing his treatment on medicinal plants, he introduced several pharmaceutical drugs. For example, use of willow bark for fevers, laudanum (an opium tincture) as anaesthetics. However, together with these useful drugs, he used some completely useless potions, amongst which were theriac (8), a broth containing the strangest of things: goat dung, pieces of mummy, adder's heads. The only good thing about this brew was the fact that it was boiled for long time sterilising the material contained in it. It was used until the end of the 18th century, generally being produced once a year under the responsibility of the magistrate in the various cities, and then sold in the pharmacies. Notwithstanding his numerous intuitions, possibly because the most accepted theory of the time was the Hippocratic, Galen embraced the theory of the humours. Furthermore, he emphasized the therapeutic aspect of the *materia peccans*. Among the *materia peccans* was pus, which was called "*bonum et laudabile*" by Galen because it was an expression of *materia peccans* that had to be eliminated: he understood that pus is a substance that does require elimination. However, unfortunately and above all by Galen's followers, this theory was exploited very narrowly: in fact, Galen's writings were used to advocate the formation of pus in order to promote healing of wounds. This concept continued to be considered valid until the end of the 16th century.

The preparation of "theriac" in Middle Ages

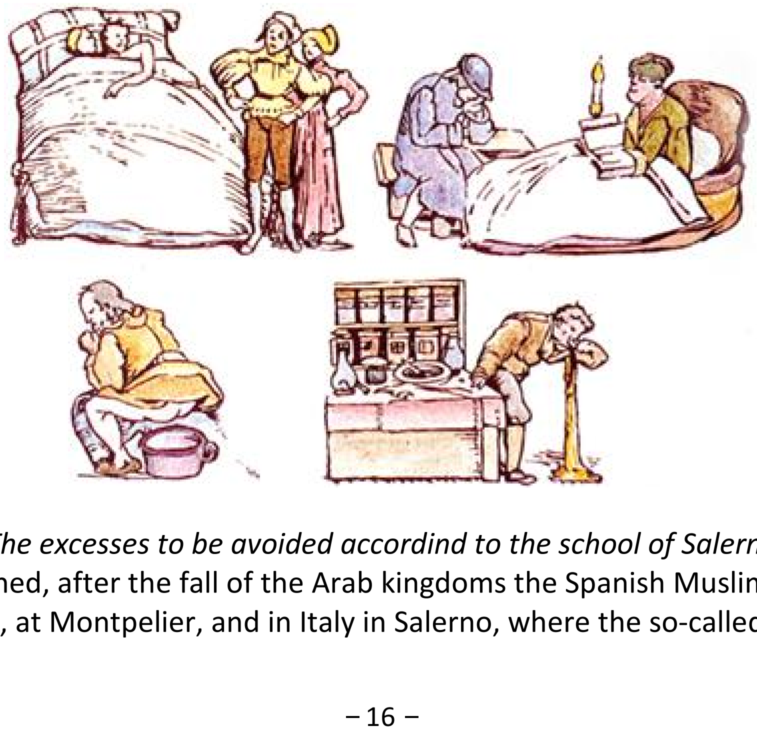
Furthermore, Galen emphasized other therapeutic methods, such as blood-letting. He also introduced the methodist concept of the pores, but this was distorted into an invitation not to wash oneself because water could obstruct the pores.

Galen elaborated a philosophical theory in order to understand how our body functioned and how blood circulated. On the basis of many of Aristotle's assertions (he was the first to consider digestion as a method of processing ingested food in the stomach), Galen maintained that the nutritious substances were then brought to the liver (the principal organ for blood distribution) via the mesenteric veins (the chyliferous vessels had not been discovered at that time). This material became blood in the liver and was enriched in *spiritus naturalis* (natural spirit). Most of this blood went from the liver, through the veins, to all parts of the body where it was consumed as a nutriment. On the other hand, some blood went through the vena cava to the heart in which burnt the living *spiritus vitalis* (vital spirit, see Aristotle in lesson 1), which in turn enriched the blood. In particular, the blood reached the heart on its right-hand side and from here reached the left-hand side of the heart through the pores of the septum. From here through the arteries, as they were considered to be vessels, the blood above all reached the brain. However, before reaching the brain the blood passed through a special vascular network (the *rete mirabile*) situated in the neck (9). The blood reaching the encephalon, was enriched by another spirit, the *spiritus animalis* (animal spirit), and through the nerves, which were considered to be the third system of vessels, it reached the body's organs where it gave life. This theory did not hypothesize that blood circulates, only that it moves: in Galeno's opinion it moved according to the sea's tides. Naturally, this theory could be easily refuted. In reality, if this concepts were true, there would have to be an enormous quantity of blood. If the blood consumed itself as it reached the body's parts, it is logical that the body would continuously consume a notable quantity of it. Slitting the throat of an animal would be enough to demolish this theory, as Harvey did 1500 years later. Furthermore, according to Galen's theory the blood was filtered in the brain, so that its impurities could be discharged through the cribriform plate (a lamina of the ethmoidal bone so-called because it is akin to a sieve - *cribrum* in Latin) giving

rise to tears, saliva, mucus and sweat.
Although was a fascinating theory, it had no experimental basis, but, because it fitted well with Christian doctrine, it then became almost a dogma and was still considered to be valid in the 16th century at the times of the great Vesal. In addition to that of the blood, among the Galenic conceits thus rendered untouchable was its anatomy mainly founded on animal studies.
As evidence of Galen's unassailable position is the fact that, notwithstanding all the evidence presented by any skeleton seen by any physician, for more than a millennium anatomists went on to assert that the humerus is curved and that any straight ones were nothing else than tricks played by nature. After Galen there was a multitude of medics who worked in the Western empire, but also in the Eastern empire with a consequent diffusion of knowledge from the West to the East.
In the wake of the great importance placed on hygiene the first true and real hospitals were built in Roman times. As reported by **Vitruvius (I century B.C.)**, they had facilities such as waste disposal, a water supply system, sewerage, and free circulation of air as evidenced by the numerous windows with which these hospitals were provided.
In parallel with the transfer of power to Byzantium, there was a transfer of the medical culture and hygiene too. Baths and hospitals were numerous, and social medicine made its appearance. There were famous doctors such as Paul of Egina in the city of Byzantium, but these did nothing else but repeat what Galen had said. In Byzantium, a dispute arose between Bishop Cyril and Bishop Nestorius. The latter lost and was expelled from Constantinople. So he sought refuge in the Middle East in areas found in present day Iraq and in Egypt. Nestorius carried all his classical cultural baggage with him including that of being a doctor, originating a medical concept very similar to that found in Ancient Rome.
Great importance was given to hygiene: very advanced hospitals were built in Baghdad, other Iraqi cities, and in Cairo along the lines of those constructed by the Romans. In this Arab era no importance was assigned to anatomy, but the concept of holistic medicine continued. So the notion of washing oneself frequently (10) remained firmly established. In Arab medicine, religion also was very influential. One of the Koran's concepts was that the human body should not be cut because, along with the blood, the soul also would leave the body. This meant that surgery could not be practised. Moreover, this belief, disallowed dissection for 24 hours after death for fear of damaging the soul. In order to prevent this happening, the Arabs invented cauterization (which is still used today in order to block the vessels temporarily during a surgical operation) (11). At that time eschar had to be followed by suppuration in order to create pus, bonum et laudabile, fully respecting the therapy of the time, even it often led to the patient's death.
Furthermore, to their credit, the Arabs handed down the writings of the Ancient Greeks, that had reached them through the Nestorians or as gifts from various Western princes, by scrupulously translating them into Arabic whilst leaving the parallel Greek test. Great Physicians were **Rhazes (864-925)** and **Avicenna (980-1037)**. Around the half of 1200 the Syrian **Ibn-Al-Nafis (1213-1288)**described the pulmonary circulation. It is unlikely, however, that his discovery did influence western medicine since it surfaced only in 1924.
The Arab (Moorish) civilization (12) reached its zenith in Islamic Spain. At Cordoba in particular there were great physicians as **Maimonides**, **Giuannizzius**, **Albucasis**, and **Averroes (1126-1198)**. After the fall of the Moors the Arab empire collapsed and their knowledge came back to Europe, particularly to Montpellier and Salerno.

Albucasis

Although in the east the Arab developed an extremely advanced society based on the ancient inheritance of the classic, and sustained by the nascent Islamic conception that translated and commented on the ancient texts, in the West it was a period of obscurantism and return to *theurgic* medicine. The saints were believed to be *adjuvant* and their relics were thought to have miraculous powers. Wars were even fought over these relics (13). The concept of the Cult of Saints was particularly widespread in this period. The most famous among the adjuvant saints were Saints Cosmas and Damian (14): they were the patrons of the Medici family as well as of doctors, and were called *anargiri* (unmercenary) because they did not ask for fee. A posthumous "miracle" was attributed to them: they attached a leg taken from a black man's cadaver to the sacristan of their church, who had a gangrenous leg. There were protecting saints for every organ and against all diseases: St. Lucy was protector of the eyes, St. Apollonia of the teeth, St. Blaise for the throat, St. Fiacre protected against haemorrhoids, St. Anthony against leprosy, and St. Roch against plague, St. Anne parturition and St. Agatha against diseases of breast.



The excesses to be avoided accordind to the school of Salerno

As already mentioned, after the fall of the Arab kingdoms the Spanish Muslim scientists settled above all in France, at Montpelier, and in Italy in Salerno, where the so-called Salerno school

flourished and which, according to legend, was founded by a Greek, by a Latin and by a Hebrew and by an Arab a little before the year 1000. A plethora of Greek and Arab manuscripts were to be found in this school. As a result, there was a return to Greek and classical culture and Hippocratic medicine. In this epoch great importance was placed on moderation in diet and in wine. In addition, advice was given on what needed doing and what, on the other hand, should be avoided. For example, overdoing amorous activities was to be avoided, reading by candlelight should also be avoided, as should forcing oneself during defecation, and not overindulging in wine was essential. The principles of hygiene returned, of washing one's hands frequently, of wholesome healthy fresh air. Great importance was given to the concept of temperament, four of which were identified: the jovial temperament, the loving or amorous temperament, the choleric and the phlegmatic.
So, above all, great importance was given to what one ate in relation to the temperament. For example, if a person was very choleric, it meant he had a great deal of bile and too much fire. It was necessary to tone down and dampen such a temperament by making the person eat fish from marshes, which is cold, or otherwise the coot (which was considered to be a fish).
Emphasis was place on examining the ill and on examining the urine. There was a degree of development in surgery, but not in the condition of the surgeon, who was still considered to be a sort of servant (as underlined by his raiment) and not a doctor.

The four temperaments

The first universities were founded in this period. At first, there were the *Studia*, which were institutes sponsored by the lay civil community, whereas the university ("*Universitas studiorum*"), was, at first, a spontaneous phenomenon, originated where itinerant students chose a valid teacher by offering him a salary. In this case power lay in the hands of students who could change teacher when they wished if they were not satisfied. The emperor, Frederick Barbarossa, was the first to finance these students, giving them financial support if they remained and settled in his cities. Then, the Church entered into the situation and the University could only become such through the issuing of a Papal Bull. The first university in the western world given a Papal Bull was the University of Bologna (1088). The first Universities

were based on the liberal sciences of the trivium (rhetoric, dialectics and grammar) and of the quadrivium (mathematics, geometry, astronomy (15) and music (16)).
(1) One recalls Herophilus's torcular.
(2) This was due to the fact that when an incision was made into an animal, the veins were full of blood while the arteries were not.
(3) One recalls the first attempt to classify the various vegetables with particular attention being paid to their medicinal properties, made by Theofrastos, a student of Aristotle.
(4) This is the sect which went back to the atomistic theory, to that of pores.
(5) Dental surgery is of Etruscan origin: actually remnants of dental prosthetics and of dental implants were found in their tombs.
(6) People from Pergamon used dried sheep skins as a support for writing and by binding them together invented the books which were employed as substitutes for the much more costly Egyptian papyrus.
(7) The first of these was quite diffuse in Europe and is still present in Gibraltar nowadays where there is a colony of monkeys on the Rock.
(8) It is believed that is was introduced by Mithridates, king of Ponto.
(9) This system was described by Aristotle following his studies on animals, which mainly concerned animals with long necks, such as horses in whose neck exists a vascular system which acts to keep the blood warm in the long passage towards the encephalon.
(10) On the occasion of the first exchanges between eastern and western, the former complained about the fact that the westerners smelt, and not just a little! Indeed, in the 17th century the King of France only washed once a year!
(11) An eschar forms in these which blocks the blood flow.
(12) An exquisite product of the Moorish civilization is conserved in Cagliari in the National Art Gallery: It is a jug taking the form of a bird made of bronze which was offered to the guest so that he or she could wash their hands before the meal (a ewer).
(13) Among other things the remains of one of the saints and one of the church doctors were conserved for a good 500 years in Cagliari: St. Augustine of African origin, who had been Bishop of Hippo, in Numidia. When the Barbary pirates invaded Roman Africa, the African Bishops of Hippo brought the remains of St. Augustine to a safe place, namely Cagliari, where they remained for about 500 years until the Lombard king Liutprandus acquired the remains and those of St. *Lussorius*, *Camerinus* and *Cesellus*, who were the latter's grooms, from the judge of Cagliari in order to demonstrate that he was a truly Catholic king. St. Augustine and the other saints were buried in Pavia. On the other hand, the head of St. *Lussorius* ended up in Pisa, in the Church of the Cavalieri. A silver bust of him was also commissioned to the famous Donatello. Demonstrating the strength of the cult of the saints, the tenure of the President of the Italian Republic (formerly of the King of Italy) was dedicated to St. Rossore (the Pisan equivalent of St. *Lussorius*).
(14) Until recently, the church of St. Saturnin at Cagliari was dedicated to Saints Cosmas and Damian since the two saints were painted in a picture inside the church. Today this church has been rededicated to its original saint.
(15) In reality it is astrology.
(16) It was considered to be an exact science in that it was composed of the exact succession of the seven notes.

Chapter 3

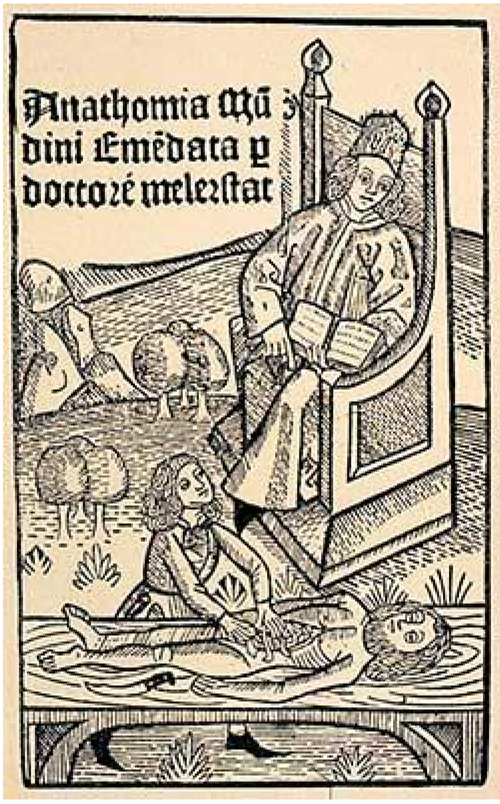
Medicine in the 13-16th centuries
Universities, Hospitals
Anatomical Revolution

Medicine made a late entrance into the universities becoming a teaching subject only in the late 13th century. It was thanks to the work of **Taddeo degli Alderotti (1223-1303)** that medicine was fully accepted at Bologna. Other universities followed. The second in Italy was Padua (students from Bologna moved to Padua), then came Naples, Siena, Rome, Pisa, Pavia, Turin and so on. Other universities were established in Europe: Paris, Montpellier, Oxford, Cambridge, Salamanca, Coimbra, Heidelberg, Prague, and Vienna. In Sardinia the University of Sassari was founded in 1616, and that of Cagliari in 1620. An evidence of the Spanish origin of the Cagliari University is the light blue stole worn by the Professors of Medicine on their academic dress. By a matter of fact, light blue, the colour of the ancient *Universitas Artistarum* to which Medicine belonged, it is still used in the Hispanic world.
The first hospitals grew out of hospices for needy people more than from places for cures. Only in female wards could animals (chickens) be kept. The hygienic conditions were quite basic, for example, the bed sheets were never changed, (the picture shows two patients in the same bed and monks preparing coffins in the same room).

Interior of a hospital in Middle Ages

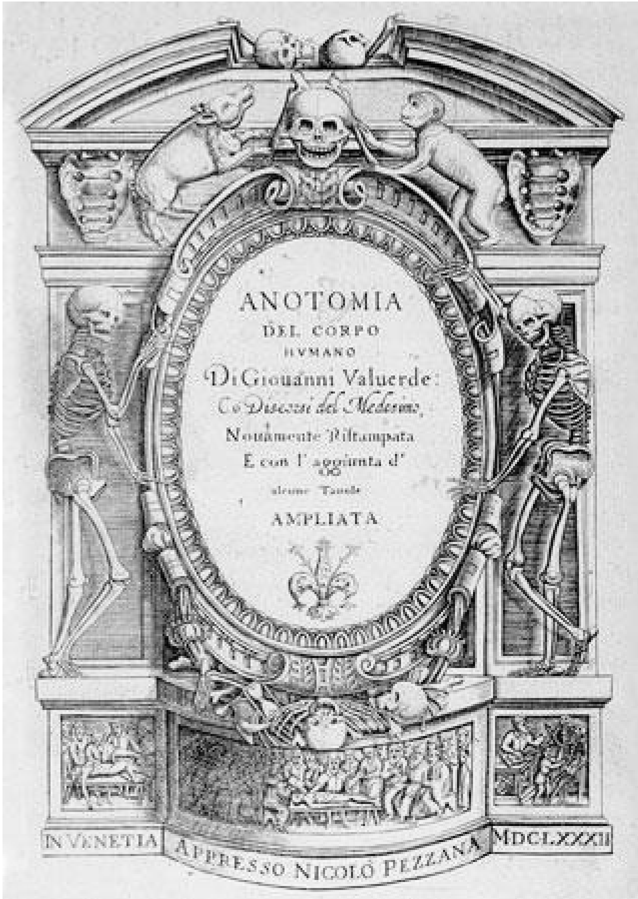
The door of Medieval hospitals were positioned toward the Vatican so that the healing Holy Spirit was more likely to enter the hospital (this continued until recent times, and is the case in the old Hospital of San Giovanni di Dio in Cagliari). They were built with a chapel that could be seen from all of the hospital's wards. The first hospital in mainland Italy was that of Santo Spirito (Holy Spirit) in Rome, the second was that of St. Maria Novella in Florence which was built from funds donated by **Folco Portinari**, the father of Beatrice, the woman loved by **Dante Alighieri**.
The medical profession began to perform dissections again in the 13th century. However, there was a period in which this ceased from about 1299 when **Pope Boniface VIII** (who sold Sardinia to Catalonia) issued a Papal Bull entitled "De sepolturis"which forbade manipulation of corpses and the reduction of them to bones. This had two principal aims: 1) stop the dismemberment of cadavers to produce relics; 2) stop the commerce that had developed in bones from soldiers killed in the Holy land.

The Bull was not meant to impede dissection but in practice did stop it. A few years later, dissection once again began thanks to later Popes who understood the mistake which had been made and who issued Bulls allowing dissection in specific periods of the year (above all dissection of women in Lent as they, at the time, were thought by some zealots to be bereft of their soul, and only later on men). As seen from illustrations, the Professor who wore a long robe that almost concealed his shoes (in order to show his cultural status), was sitting reading a textbook by Galen whereas the surgeon, who was the one who performed the dissection, wore a short gown (the legs could be seen which showed his inferior rank). We know that the findings of the surgeon were by no means taken as real. For instance, because, the humerus demonstrated by the surgeon was straight, and therefore not the same as that described by Galen (who did describe a curved humerus from a pig), the professor stated that it was one of nature’s jokes to make the bones seems straight when in reality they were curved. Galen’s assertions were a dogma which could not be criticised, because he, and not nature, was the true authority.
The surgeons did not have access to anatomical knowledge because they did not know Latin, and could not read the textbooks; this was the reason why anatomy became a type of philosophical exercise. The first official dissection was performed at the University of Bologna by **Mondino de’ Liucci** (1270- 1326), a pupil of Taddeo degli Alderotti. Although dissection was indirect, being a sort of comment on Galen’s texts, Mondino was the most important precursor of modern human anatomy. There were other human anatomists, such as **Guido da Vigevano** who suspended the corpses so as to be able to dissect them.



Mondino de Liuzzi during an anathomical demonstration

In order to understand how long the practice of dissecting animals continued, the title page of one of the few books on anatomy in Italian (dated 1632 and translated from the textbook written in Spanish by **Juan de Valverde**, and which can be found at Central Biomedical Library of Cagliari University) shows a cranium flanked by a pig and a short-tailed monkey: the animals on which Galen’s anatomy was mainly based.

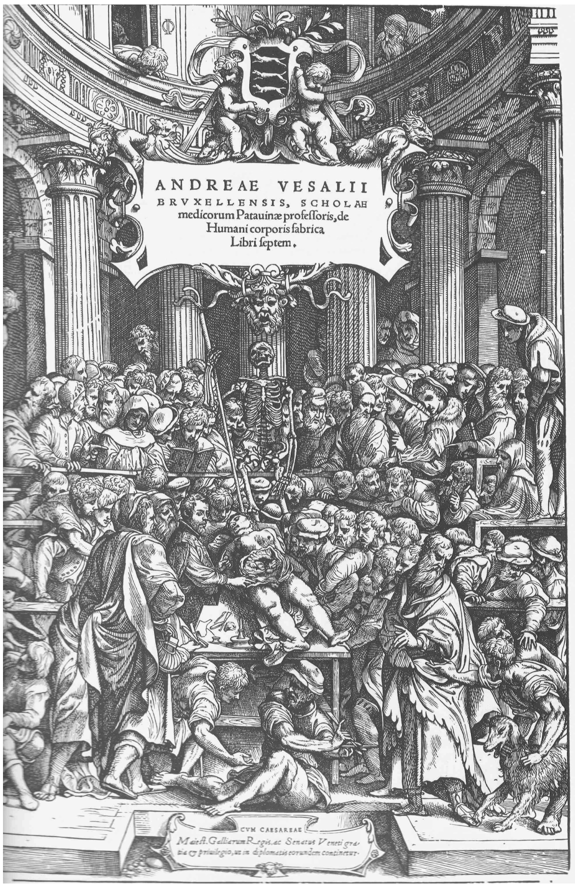


Title page of the Italian edition of the "Anatomia" by Juan Valverde

In fact, those who truly practised human anatomy were the artists. Some of the artists gave up their salaries in order to avail themselves of corpses from the bishops (Leonardo, Michelangelo, and many others). Above all, **Leonardo da Vinci (1452-1519)** was the finest of anatomists. He made numerous discoveries that were faithfully reproduced in the manuscripts which remained more or less secret until they were sold to the English Royal family, and so today are referred to as the Windsor manuscripts. However, this did not influence anatomy at all. In truth, Leonardo wanted to make an atlas by working together with the anatomist **Marco Antonio della Torre**, but the latter died very young. Furthermore, also **Michelangelo Buonarroti (1475-1564)** wanted to make an atlas of anatomy together with **Realdo Colombo**, but this came to nothing as well. In addition to the anatomical studies by artists, there were also those who discussed the whole of Hippocratic-Galen theory: **Paracelsus (1493-1541)** medical philosopher and a Protestant. He is considered to be the founder of iatrochemistry but in reality he was an alchemist since he placed great emphasis on the chemical elements. The elements that he considered to be the basis of the universe were salt, sulphur, and mercury (all things considered, something of the conception of 4 elements was present). He practised alchemy, saying that the basis of disease was a chemical alteration. He was the first to use ether, and he noted that it had anaesthetic qualities (this practice declined and was rediscovered in America 300 years later). He also used laudanum to alleviate pain and other chemicals such as antimony. His physiology remained, above all, confused, even if it certainly contrasted with Galen's physiology.

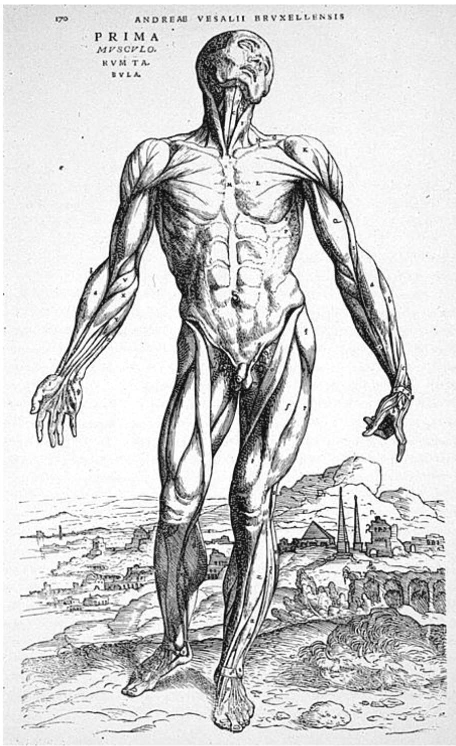
Paracelsus

The Catholic religion did not deter dissections, because the body is only a vessel which contains the soul. In fact *"pulvis es et in pulverem reverteris"* (you are dust, and to dust you will revert). There were great anatomists who began practising anatomy by themselves, without the intervention of a servant surgeon: for example **Berengario da Carpi (1460-1530)**, and **Giambattista Canani (1515-1579)**.



Frontispiece of Vesalius's Fabrica

But the great development of anatomy took place thanks to **Andreas Vesalius** (1514-1564) (son of Emperor Charles V's pharmacist). After having attended famous universities such as Louvain and Paris, and after having received a classical Galenic education, he became professor of anatomy at Padua while he was still very young. In 1543 he published his monumental work "*De Humani Corporis Fabrica*" in which he describes the human body viewed in dissections performed by himself and illustrated by magnificent woodcuts. Dissection became autopsy in the Hellenistic sense, something which was physically seen by the eyes of the operator himself (note the proud affirmation of the Renaissance man who said: I report only the things which I have seen myself). The frontispiece shows the anatomist (Vesalius himself) operating directly on the corpse of a woman. This picture was the work of the painter who served Vesalius in drawing the illustrations in the book, namely, Jan Stephen van Calcar, a student of Titian.



A Table from Vesalius's Fabrica

Calcar's plates are very precise portrayals of the dissected parts of the human body: both by themselves and with imagined landscape. The plates were in black and white because colour printing was not in use at the time. Vesalius corrected Galen on 250 points. However, he did not attack the Galenic conception of blood flow even if he demolished it by demonstrating that pores did not exist in the heart, and nor existed a *rete mirabile*, but that was all he had to say on the subject. In the same year Nicholas Copernicus' book "*De Revolutionibus Orbium Celestium*" was published, the book which refuted the geocentric theory of the earth.

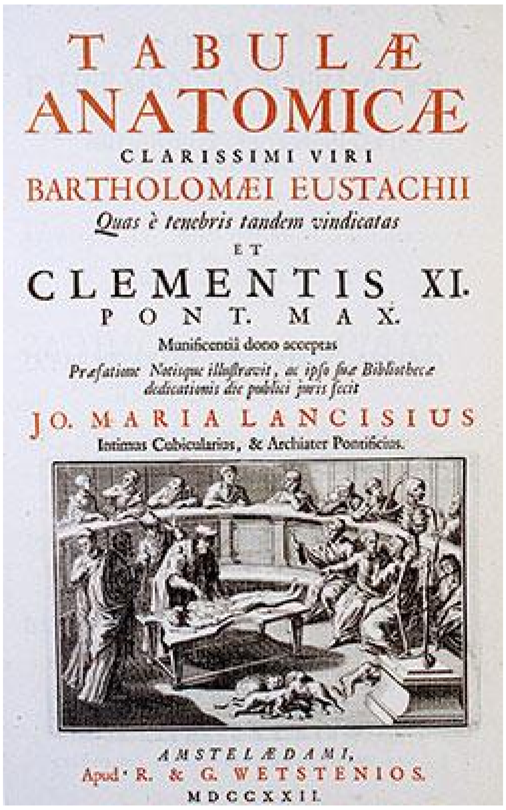
1543 is a year to remember in the history of man, because two of the most important scientific myths of the era were refuted: the *anthropocentric* conception and the *geocentric* concept.

The Paduan School became the most important. The students there were separated according to their nationality and Latin was the official language. From the beginning in Padua the degree was not conferred by the Bishop (as in all other universities), but, rather, it was conferred by the Mayor. This fact was significant because for several years after the Reformation, whereas in the case of the other Catholic universities, Protestants no longer attended because they had to swear allegiance to the Catholic faith, in Padua they did come, at least until the Republic of Venice managed to politically oppose the influence of the papacy. The religious intolerance caused by the Reformation was one of the reasons for the decline of the Italian universities.

In certain respects, the story of Vesalius is obscure. Shortly after the publication of this book (he was 29 years old) he stopped teaching. According to him this was caused by the criticism of the Galenists (which were ferocious), but, in fact, it seems there may have been another motive: the offer from Emperor Charles V to become his physician. Vesalius accepted, but after a while thought of returning to Padua because the Venetian Senate called him back. Unfortunately, he had an accident: he performed a dissection on a man who resulted not to be dead (his protector, Charles V had died and his successor, Philip II, was not very fond of him). An inquisition followed, and Vesalius was prosecuted, but managed to obtain a pardon by promising to make a pilgrimage to Palestine. So he went there planning to return to Padua, but he died of plague, when the ship moored at the island of Zante. He was buried there, but his grave was lost. He was the genius who shattered the Galenic dogma, and founded on direct observation.

Vesalius and his successors in the teaching of Anatomy at Padua's University

In Padua after Vesalio there were: **Realdo Colombo (1510-1559)**, **Gabriele Fallopia (1523-1562)**, and **Fabricius (Girolamo Fabrici di Acquapendente 1533-1619)**. **Casserius (Giulio Casserio 1552-1616)** is also worthy of mention because he was an uneducated servant to Fabricius who studied Latin and Greek and became a professor. He was the founder of comparative anatomy (he made, *inter alia*, a very important contribution to the study of larynx and the organs of senses). He edited the *Tabulae*, the masterpiece of Baroque Anatomy.

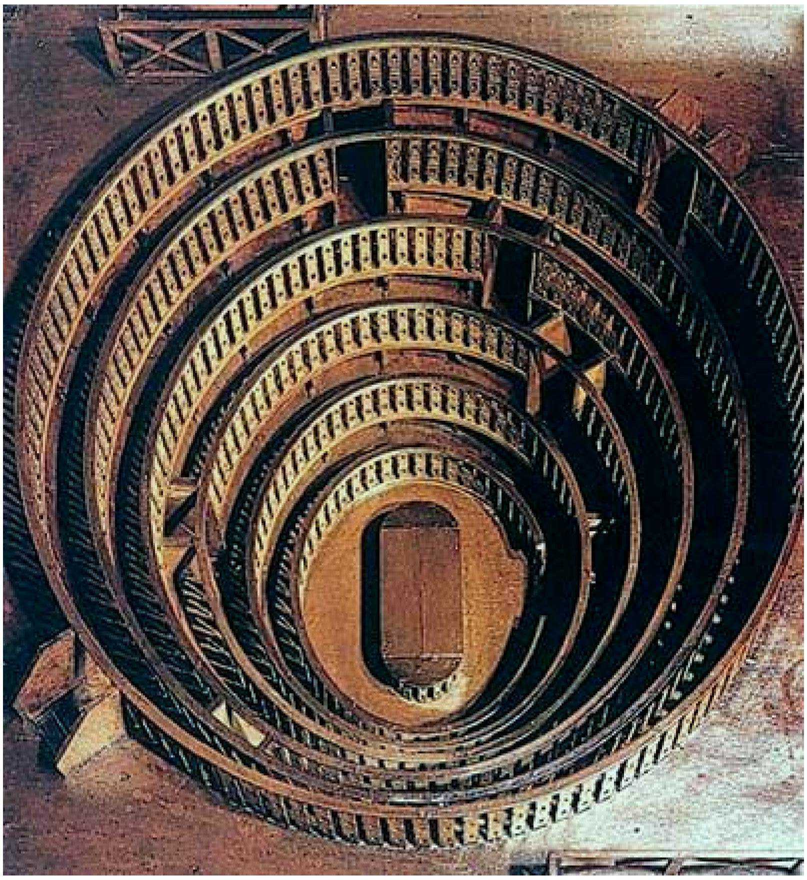


TABULÆ
ANATOMICÆ
CLARISSIMI VIRI
BARTHOLOMÆI EUSTACHII
Quas è tenebris tandem vindicatas
ET
CLEMENTIS XI.
PONT. MAX.
Munificentiâ dono acceptas
Præfatione Notisque illustravit, ac ipso suæ Bibliothecæ dedicationis die publici juris fecit
JO. MARIA LANCISIUS
Intimus Cubicularius, & Archiater Pontificius.

AMSTELÆDAMI,
Apud R. & G. WETSTENIOS.
MDCCXXII.

Frontispiece of anatomical tables of Bartolomeo Eustachio

Bartolomeo Eustachi (1500/1510-1574) from Rome, produced a series of anatomical tables almost surpassing those of Vesalius, at least from a scientific point of view. The tables, engraved in copper, were forgotten until the beginning of the 18th century when **Giovanni Maria Lancisi (1654-1720)** discovered and published them. Despite the delay in publication, they managed to influence science: it contained details that Vesalius had omitted. During his life he published the *Opuscola Anatomica* and was the first to describe the anatomy of teeth, the adrenal glands, the auditory (Eustachian) tube and, in the horse, the thoracic duct.



Wooden model of the Anatomy Theatre of Gerolamo Fabrici from Acquapendente

Fabricius was a surgeon and anatomist at Padua from 1565 to 1616. He published numerous surgical treatises and was the teacher of William Harvey, the discoverer of blood's circulation. Fabricius gave great contribution to the anatomy of sense organs and embryology, and was the discoverer, in fowl, of the lymphatic organ which now bears his name (Bursa of Fabricius). He built the world's first stable anatomical theatre in Padua. The theatre was circular, the students stood, and the dissection table was in the centre so that all had a precise view of the corpse lying on it. Beneath the table there was an aperture communicating with a canal, which served to take away waste and bring the corpse into the theatre. From then public anatomical dissections, became social events. Fabricius also merits another distinction: the idea of producing an atlas in colours was his. He entrusted this job to skilled painters of his time, and, at his death, willed more than 200 plates to the Marciana library of Venice, where they remained unknown until 1910, when **Giuseppe Sterzi (1876-1919)** who has been Professor of Anatomy in the University of Cagliari, discovered them. The tables, which were well known by his contemporaries, illustrate several important anatomical discoveries that were later ascribed to other anatomists.

The Anatomy Lesson by Rembrandt in the Hague

The most celebrated painting of an anatomical dissection ever to exist is that of Rembrandt, preserved in the museum at The Hague. Artistically it is one of the best paintings in the world: **Nicolas Tulp (1593-1674)**, who had studied at Padua, is seen showing a dissection to his colleagues. However, from an anatomical point of view, it is a disaster. This demonstrates how anatomy became a kind of still life. The first Italian anatomies are representations of butchery. Among the most famous painters of the subject there was Bartolomeo Passarotti of the Bolognese school who was author (50 years before Rembrandt) of an anatomy showing the dissection of a corpse in the presence of the most famous Italian artists.

In Medieval times Surgery was mostly carried out by the monks. Following the Bull (1215) that reinstated the pronouncement issued from Council of Tours (1163), the monks had to give up surgery, so it was carried out by ordinary unlearned people. In Umbria, near Norcia and Preci, the abbey of St. *Eutitius* was an important centre of surgical culture. When they had to stop doing surgery, the monks instructed the peasants who lived there. Among other things, Norcia was already well-known for its ancient tradition of castrating animals (so there were already people who had some practical surgical experience). The people of Norcia and the people of nearby Preci and Cerreto became very skilled craftsmen and handed down the secrets of surgery from father to son. The people of Preci became famous above all for curing the eyes (the Scacchis, who were for years the eye doctors of the French Royal family, became very wealthy and famous). The people of Norcia carried out very advanced plastic surgery, operated on cataracts, and on hemorrhoids and even performed extraction of calculus (stones). They also castrated male children to have unbroken voices for religious choirs, because women were not allowed to sing in churches in the Middle and part of Modern Ages.

Minor surgery (dental extractions, healing wounds, etc.) was carried out by licensed barbers: their sign today still is the pole with the red (for the blood) and white (for the bandages) spiral stripes.

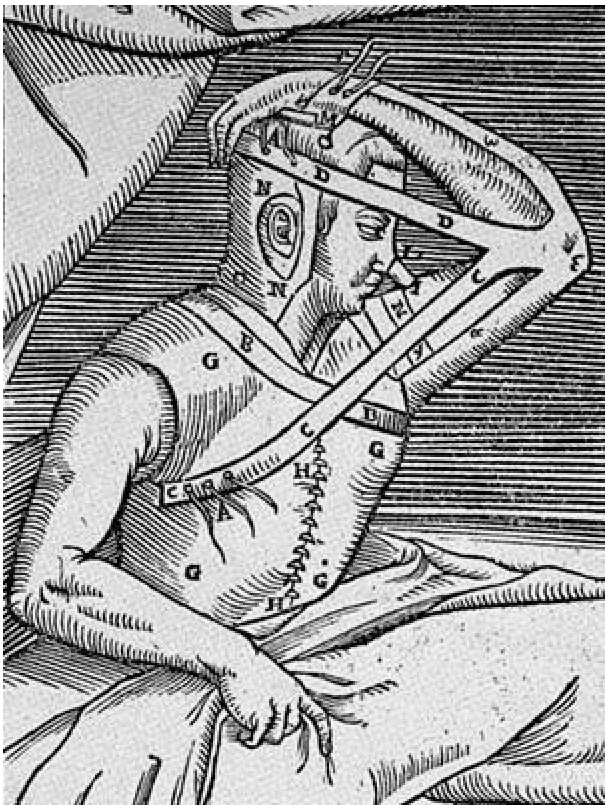
Ambroise Paré

Of the development of anatomy the few doctors who practised it did take advantage, but this remained the privilege of an elite. There were famous surgeons (this happened especially in France) who studied anatomy. **Ambroise Paré (1510-1590)** created the confraternity of the saints Cosmas and Damian, distanced from that of the barbers (they were not as yet true doctors because they did not know Latin, as officially recognised). They operated in France from 1550 onwards. Parè, who became the surgeon of the king, is also remembered because he gave instructions not to use boiling oil on amputations. In one of his treatises he recounts that while he followed a campaign in Piedmont, and had no more boiling oil to put on an amputated leg (it was believed that the boiling oil served to extract the *materia peccans*), a man from Norcia (Norcino), on the basis of what had been published by **Bartolomeo Maggi (1477-1552)**, advised him to use rose oil (which contains phenol, a mild disinfectant) and to his great surprise noted that the patients treated with rose oil did better than those treated with boiling oil. He placed great importance on anatomy and dissection as a basis for surgery. He was also the one who re-introduced in obstetrics the technique of delivering a breech baby, a practice forgotten since the times of Soranus of Ephesus (I/II century A. D.).

Chapter 4

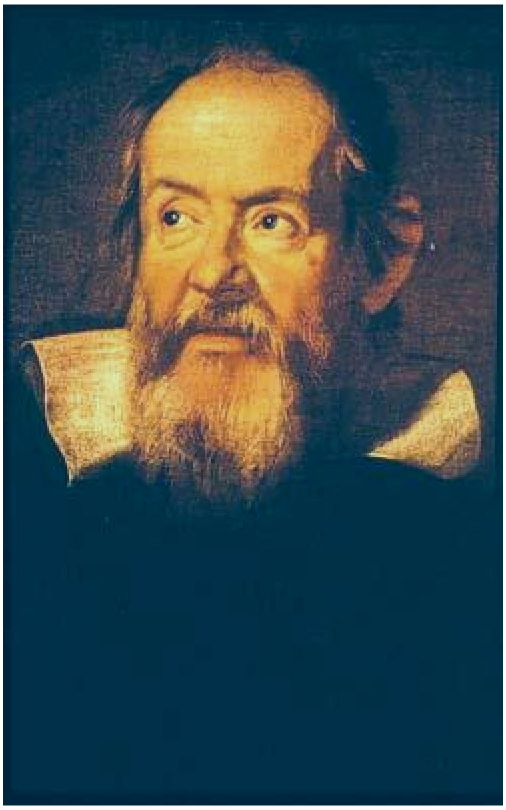
The 17th century. Scientific Revolution.
Circulation of the Blood.
The Doctrine of Contagion.
Witch Hunting

Fabrizio Hildanus (1545-1599) asserted that pus must not enter the wound, and that before operating, a ligature must be applied to the vessels. **Gaspare Tagliacozzo (1545-1599)** learnt the method of nose reconstruction from the “Norcini” who operated in southern Italy. Nasal reconstruction was important given that nose was destroyed by many diseases such as tuberculosis and syphilis, as well as because of the very frequent mutilations caused by firearms.



Reconstruction of the nose according to Gasparre Tagliacozzo

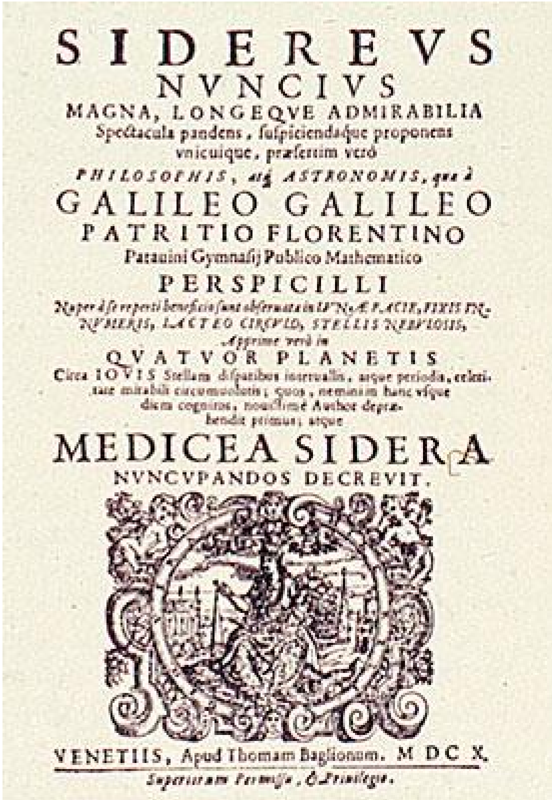
Tagliacozzo’s method was to take a skin graft from the arm and use it to reconstruct the nose. He became famous throughout Europe. However, one year after his death Tagliacozzo’s corpse was exhumed from the consecrated cemetery and reburied some time later when the Church decided that his reconstructive work did not violate a prerogative of God. After his death, his work was continued in the south of Italy by a pupil: **Giovanni Battista Cortesi (1553-1633)**, but reconstructive surgery was not performed any more after Cortesi’s death. The memory of Tagliacozzo’s work survived thanks his treatise on plastic surgery (*De curtorum chirurgia per insitionem*). Plastic surgery was rediscovered only in the 19th century at the time when the Indian system of plastic surgery was in use, which was simpler, but also much more disfiguring. This consisted of taking a piece of skin from the forehead and placing it on the nose.



Galileo Galilei

The end of the 16th century and the 17th century were characterized by the scientific revolution largely brought about by **Galileo Galilei (1564-1642)**. He was the son of a famous Pisan musician and his father wanted to make of him a physician, but he, instead, became interested in mathematics. He was the first to introduce mathematics into scientific experiments. Galileo embraced Democritus’ theories in opposition to those of Aristotle who had believed that everything that occurred in nature has a purpose. Democritus maintained that the universe and its organisms are formed by atoms in a continuous and casual movement. Democritus’ philosophy was therefore based on observation, and not on finalism as was that of Aristotle: on how, not on why.

In the *Sidereus Nuncius* Galileo asserted that he had managed to demonstrate the theory of Copernicus experimentally. In fact, using the telescope he discovered the three satellites of Jupiter and demonstrated that the sun was at the centre of the universe, not the earth, thereby proving that the theory of Ptolemy was false. Upon producing this evidence, Galileo had great problems with the Inquisition. When he left Padua, where he taught at the university, he made the mistake of going to Florence, a city that was very close to the Pope unlike Venice which still enjoyed a certain degree of autonomy because of its political strength and its distance from Rome. So, despite his friendship with the ruling Medici family, he was persecuted by the Inquisition.


SIDEREVS
NVNCIVS
MAGNA, LONGEQVE ADMIRABILIA
Spectacula pandens, suspiciendaque proponens
vnicuique, præsertim verò
PHILOSOPHIS, atq; ASTRONOMIS, quæ à
GALILEO GALILEO
PATRITIO FLORENTINO
Patauini Gymnasij Publico Mathematico
PERSPICILLI
Nuper à se reperti beneficio sunt obseruata in LVNÆ FACIE, FIXIS IN-
NVMERIS, LACTEO CIRCVLO, STELLIS NEBVLOSIS,
Apprime verò in
QVATVOR PLANETIS
Circa IOVIS Stellam disparibus interuallis, atque periodis, celeri-
tate mirabili circumuolutis; quos, nemini in hanc vsque
diem cognitos, nouissimè Author depræ-
hendit primus; atque
MEDICEA SIDERA
NVNCVPANDOS DECREVIT.
VENETIIS, Apud Thomam Baglionum. M DC X.
Superiorum Permissu, & Priuilegio.

Title page of the Sidereus Nuncius by Galileo Galilei

Galileo also had the insight of not only using the telescope to see the planets, but also to use lenses to investigate the small things of this world, and advised his students to do so. It was one of his pupils, **Francesco Stelluti (1577-1652)**, who named the instrument a microscope and published (1630) the first pictures of insects as seen under the microscope. There is a tradition without any historical basis that a Dutchman Zacharius Jansen discovered the microscope. In fact, the only certain thing is that he made lenses. The use of the microscope to observe invisible things can be attributed only to Galileo. In one of his letters dated 1624 he exhorts his students to use the microscope.

His most important contribution to science was certainly the use of mathematics, necessary to quantify experiments.

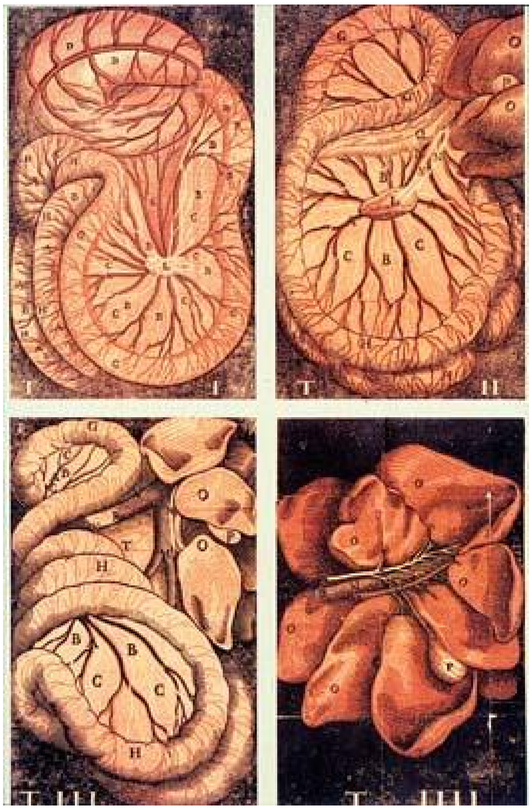
Because Galileo was a physicist, he elaborated a theory according to which the body was a machine and the organs were smaller or minute machines, moreover, he had to research the elementary machine.

Galileo's microscopes had great problems because they refracted and reflected the light so much that many illusory images were seen: this brought strong criticism of the microscope.

Marco Aurelio Severino (1580-1656) was born in Tarsia, Calabria, and lived in Naples where he was Professor of Anatomy and Medicine. He fully embraced Galileo's philosophy and by the microscope he described the uterus of the beetle (which it does not possess, naturally). All the same he demonstrated that the insects have organs which are found in the higher orders of animals. He also felt the microscope had to be used to see invisible things and that anatomy must not be considered as the "art of dissection" but must serve to uncover and research into atoms (*Anatomia dissutrix non dissectrix*).

Severino was also a great surgeon and the author (1632) of the first illustrated textbook on surgical pathology. In Naples there was an epidemic of diphtheria and he performed laryngectomy thereby saving many lives. During the plague he did not flee the city, as many other doctors did, but remained to care for sick persons; unfortunately, he succumbed to and died of plague. The studies of insects using the microscope proved that things that seemed to be absolutely simple were, in fact, very complicated.

Some of the students of the school of Galileo used clever devices in order to disclose hidden structures, thereby creating the so called “artificial” anatomy. For example, in Sicily, **Giovanbattista Odierna (1597-1660)** by boiling the eye of a fly proved that it was made of a myriad of crystalline lenses which allowed the insect to have 360° vision. Besides the microscope, the *micoscopius naturae* (the microscope of nature) could be used. In fact, Auberius (Claude Aubery), a student of **Giovanni Alfonso Borelli (1608-1679)**, who himself was a Galileo’s pupil, to show how the testicle is made, studied the much bigger testis of pig, the animal which had previously struck Galen because its organs were similar to those of man. Auberius discovered the seminoferous tubules, the efferent canals and the epididymis, which were then compared to those of man. Borelli, who wrote “*De Motu Animalium*” and is considered the founder of iatromechanics, also demonstrated, with the use of the Galileo-Sanctorius thermometer that the mammalian heart was not hotter than other organs, dispelling the notion of innate heat of the left ventricle, which was introduced by Aristotle and shared by Harvey.
The fact that science was based on experiment and that significance could be given to findings only after having been observed and measured, brought consequences that were at times at the limit of the possible. For example, the great **Sanctorius Sanctorius (1561-1636)**, who hailed from Istria and was acquainted with Galileo, spent a large part of his life in a balance in which he weighed himself when he ate and after he defecated, measuring what was left after he had eaten: he thus gained an intuition about metabolism. He also understood that perspiration served to eliminate heat. He was also the first to measure the pulse and to use a thermometer to measure body temperature.



Aselli’s tables of the chyliferous vessels, the first ones printed in colour

Gaspare Aselli (1581-1626) was a doctor in Milan and also a professor at the University of Pavia (at the time there was no University at Milan) who discovered the chyliferous vessels. While carrying out an experiment on a small dog in which he wanted to show how diaphragmatic excursions happened and also how they could be stopped with the resection of the phrenic nerve, he saw in opened abdomen, under the diaphragm, an extremely white network in the mesh of the mesentery and thought that he had made a great discovery, that is to say, had

discovered the fourth type of vessels besides veins, arteries, and nerves then regarded as a kind of vessels. When he tried to repeat the discovery at the University of Pavia he used a very large dog, but after having opened it in front of everyone he could not see anything. So Aselli, after a moment of uncomfortable reflection, thought that the difference between the two dogs was that one had eaten while the second dog, which was a stray, had fasted. So he decided to repeat the experiment with a third dog, which he opened after having made it eat. Finally, this time he could see the network of chyliferous veins and was able to demonstrate their existence to his colleagues.
Following his death, his friends published an atlas which contained the first prints in colour. A great error made by Aselli was that he confused a lymph node with an organ that was called the pancreas of Aselli. The lymphatic system was illustrated only some decades later. **Jean Pequet (1622-1674)** discovered the chyle cystern, and, then, lymphatic circulation was described, with some mistakes, by **Giovanni Guglielmo Riva (1627-1677)**, and, correctly, by the Danish **Thomas Bartholin (1616-1680)**. It should be remembered that Bartolomeo Eustachi had already described the thoracic duct of the horse in 1564.

Harwey and his king

William Harvey (1578-1657) studied at Padua where he was a pupil of both Fabricius and Casserius. He was interested in the circulation of the blood. He started by measuring the quantity of blood in the body of an animal (he took an animal and cut a vein in order to extract all the blood) and saw that its quantity was limited. This fact contrasted with the concept of Galen according to which blood was produced continuously in order for it to be absorbed by the peripheral structures.

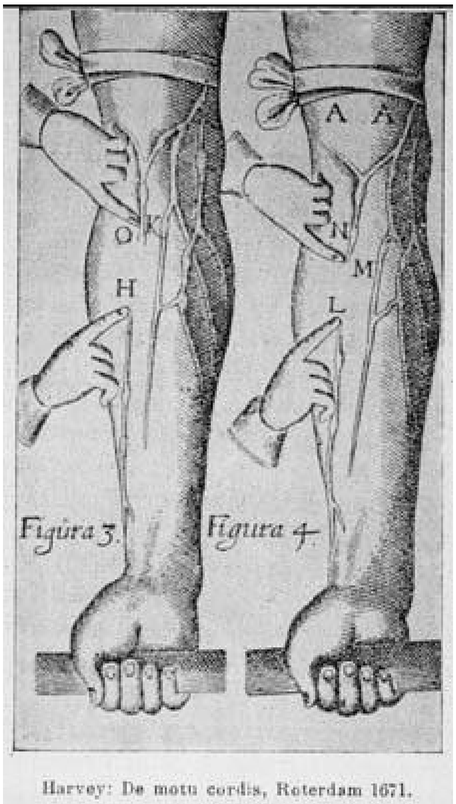


Illustration from Harvey's De Motu Cordis

1628: this is the historical date in which Harvey published his tract entitled *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*. Harvey, using the same plate as Fabricius ab Aquapendente, demonstrated that the blood in the veins did not have centrifugal flow, as reported by Galen, according to whom blood went from the liver to the periphery. Fabricius had interpreted those swellings (due to the venous valves, that can be seen when a vein is compressed) as small gates that served to slow down the flow from the centre to the periphery. Harvey demonstrated the exact opposite: in fact when he placed a loop around a vein he observed that it became turgid and then, by compressing another segment between two fingers, he noticed that the blood did not go from the centre to the periphery, but from the periphery towards the centre. Therefore, Harvey understood the mechanism of venous circulation, and postulated that the heart is a pump which makes the blood circulate from the arteries to the veins. He could not, however, demonstrate the nexus between the arteries and the veins because he was not able to see the capillaries with the naked eye. The capillaries were later discovered using the microscope by Malpighi in cold blooded animals, and by **William Cowper (1666-1709)** and by Spallanzani in the warm blooded ones.
The new theory had several supporters, but also many critics, whereas the concept of circulation was associated with a political idea on the circulation of power. Although Harvey was initially much criticized, the theory was later accepted, resulting in the liver being declassified as the principal organ, its function being reduced to bile secretion. Furthermore, a famous anatomist: Thomas Bartholin (who was also Stensen's teacher) published the *Exequiae* (exequies) on the liver.

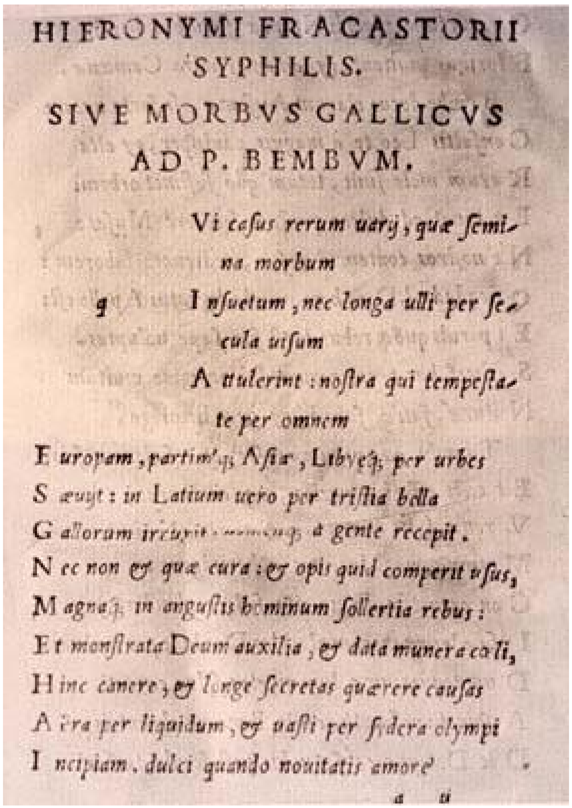
The Problem of Contagion

German engraving of the 18th century depicting a physicial during the plague

During the course of the plagues the doctors dressed in a particular way: they wore a bird's beak on the nose containing a perfumed sponge because they believed that smells (miasmas) were the cause of infectious diseases (clearly a false theory).
Notwithstanding the fact that there had been plague in the 14th and in 17th century, and that there were a great many endemic illness such as leprosy and tuberculosis, the concept of contagion through living organisms (live contagion) did not develop.
It was not understood how the diseases were transmitted: the most accredited idea was that smells (miasmas) carried the contagion, but they did not really understand how and why this occurred. There was no concept of hygiene, the patients were placed on dirty beds with sheets which were recycled and never washed. This lead to the spread of the diseases, especially in the most populous areas. Sardinia is a typical example of how diseases such as plague took root in the city, but seldom in the villages.
The vehicle causing plague is the flea. In fact, it is the rat on which the flea lives which falls ill with the plague, and then the flea transmits the plague to human beings, after which, the plague becomes a pulmonary disease meaning that the contagion goes directly from man to man. The plague came from the Orient, having been brought to Messina by a Genoese ship which had escaped from Kaffa (Crimea) a city that was being besieged by Mongols. The latter had thrown corpses of the plague's dead victims into the city, so some sailors fell ill and brought the disease to Messina from where it spread throughout Italy, and then throughout all Europe.
The later disappearance of plague was favoured by the fact that around the end of 17th century there was an invasion of brown rats which supplanted the black rat, which is much more receptive to the plague, and also because wooden floors in which the rats could live stopped being built (above all this happened in places with hot climates). Another hypothesis maintained that this was due to the appearance of a less virulent germ, which caused the immunisation of rats.
Almost contemporaneously with the publication of the work of Andreas Vesalius, there was a Veronese physician: **Hieronymus Fracastoro (1478/9-1553)**, who named an endemic disease

which had already developed: syphilis. Syphilis broke out for the first time in an epidemic fashion during the 1496 siege of Naples by Carlo VIII, king of France. Until Italy was a leading nation, syphilis was called ‘French disease’, but when Italy declined, the French appellation: ‘Neapolitan illness’ prevailed.

First page of Gerolamo Fracastoro’s poeme on syphilis



HIERONYMI FRACASTORII
SYPHILIS.
SIVE MORBVS GALLICVS
AD P. BEMBVM.

Vi casus rerum varij, quæ semina morbum
Insuetum, nec longa ulli per secula visum
Attulerint: nostra qui tempestate per omnem
Europam, partimq; Asiæ, Libyæq; per urbes
Sævijt: in Latium vero per tristia bella
Gallorum irrupit [illegible] a gente recepit.
Nec non & quæ cura: & opis quid comperit usus,
Magnaq; in angustis hominum sollertia rebus:
Et monstrata Deum auxilia, & data munera cœli,
Hinc canere, & longe secretas quærere causas
Aëra per liquidum, & vasti per sidera olympi
Incipiam. dulci quando novitatis amore

First page of Gerolamo Fracastoro’s poeme on syphilis

Syphilis may have been caused by the recrudescence of an illness which had altered its physiognomy and that was endemic in the Arab world to the east. Another theory was that it was carried from America by Christopher Columbus’s sailors. At any rate, it was understood from the beginning that syphilis is spread by sexual contact. In fact, it was said that the disease had developed from the union of a prostitute with a leper.

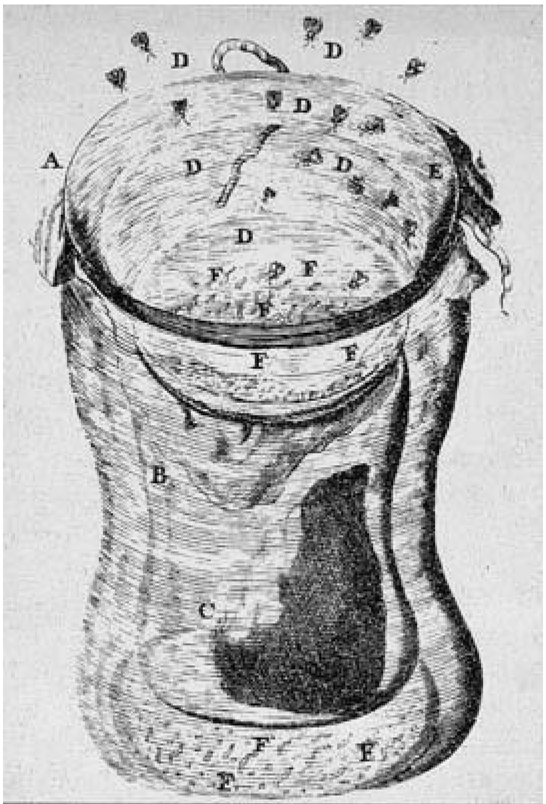
Fracastoro named the disease “syphilis” in a famous little poem dedicated to Pietro Bembo. In it he also spoke of the *legno santo* (holy wood) which was one of the principal therapies at the time: it was believed that this particular resin, guiacum, which caused profuse sweating and drooling, cured syphilis because, according to Hippocratic principles, it eliminated the *materia peccans*. The excess of phlegm, at the origin of the disease, had to be removed by using pharmaceutical drugs which caused sweating and drooling, such as the guiacum, and also mercury. Syphilis was a disease which made the fortune of many physicians because in 30% of the cases it apparently healed itself. When a person recovered, the doctor maintained that it was because of the effectiveness of his cure, although of course this was not really the case. To fight syphilis, mercury was administered, which, being toxic for the sweat and salivary glands, caused a very potent secretion. At that time the treatment proposed to avoid sweating and drooling was to place an incandescent iron bar on the patient’s head since it was believed, as we have seen, that saliva and sweat came from the brain. Mercury also made teeth turn black, forcing noble women to file their teeth in order to hide the fact that they were undergoing the mercury therapy against syphilis.

Fracastoro maintained, but was not believed, that invisible living organisms existed which

spread contagion. These he called ‘*seminaria*’ which can best be translated as ‘seeds’ and can be thought of as being akin to bacteria or virus. These ‘*seminaria*’ could be transmitted not only by direct contact but also through clothes, sheets, and objects.
Another endemic illness frequent at that time was leprosy. Leprosy in Sardinia took root especially in villages because it is an illness whose incubation is very slow. Leprosy is quite similar to tuberculosis and the two micro-organisms are rivals for, where there is leprosy, there is no tuberculosis and vice versa. Till a few years ago, there were many leprosy hotbeds in Sardinia. To contract leprosy, prolonged contagion is necessary for the infection to take root, therefore it is unlikely that a person who travels a lot would contract it. Leprosy was an illness to be feared, having rather particular social implications. In fact, when it was discovered that someone had leprosy (at the end of Medieval times and the beginning of modern times) a funeral was arranged and the poor fellow lost all his rights. However, since lepers were kept in isolation at the community’s expense, poverty-stricken people declared themselves to be lepers in order to survive through receiving this form of social security.
The infamous practice of **witch hunting** started between the end of the XIV century in the Christian world, both among Catholics and Protestants. The criteria useful to detect witchcraft and to persecute witches as heretics, were detailed in the notorious: *Malleus Maleficarum* a textbook authored in the XV century by two fanatic German Dominican monks: **Jakob Sprenger** and **Heirich Institor Kramer**, which had, for the time, an enormous circulation (34 editions with more than 30000 copies). Witch hunting took place particularly between the end of 1400 and the first half of 1600. The alleged witches belonged to common people and were usually widows or single women, midwifes, herbalists, sorceresses or prostitutes. Many “witches” were subjected to horrible torments and burned alive. Their “confessions”, wrung by torture, were used as evidence to indict other unfortunate women. As a rule the practice, with some exceptions, was limited to the female sex. The last trials for witchcraft where the “witches” were sentenced and burned alive, took place in Protestant Switzerland in 1782, and in Catholic Poland in 1793.

Chapter 5

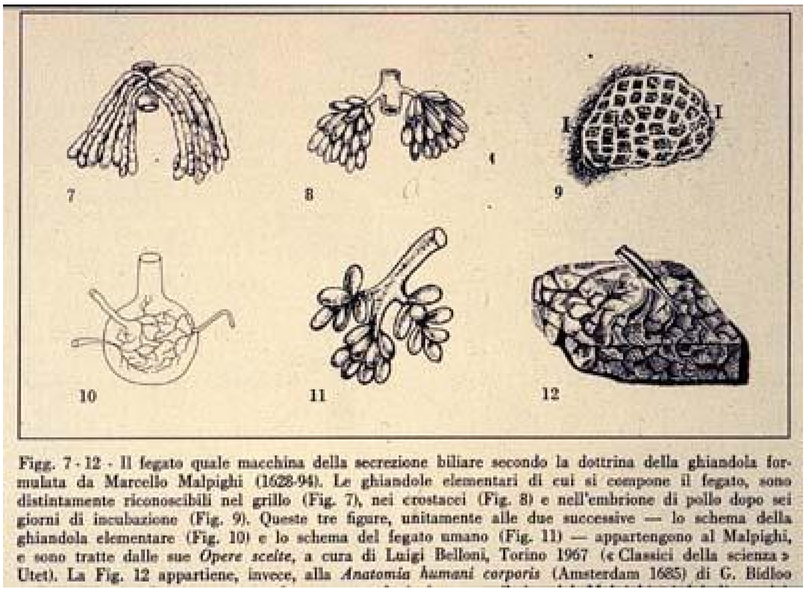
The end of the 17th century, the beginning of the 18th century.
Spontaneous generation.
Acarus as the cause of scabies.
Microscopic anatomy.
Anatomical waxworks



Redi's experiment on insects generation

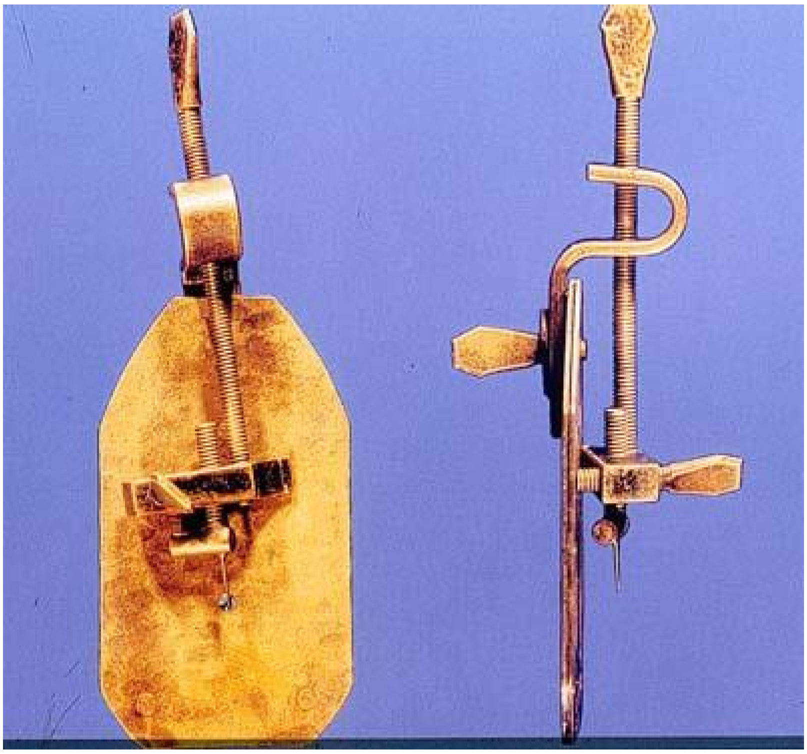
Towards the end of the 17th century (1668) there were important discoveries by **Francesco Redi (1626-1698)**, a student of Galileo. He took a large vase and put a piece of meat inside it, and then covered the vase with a piece of gauze. He noted that grubs formed only when the eggs, gathered from the gauze, were inseminated on the meat. He thus demonstrated that, through the eggs, insects originated from other insects and that, consequently, spontaneous generation was not a valid concept.
Redi also founded parasitology, and performed experiments on how to exterminate worms. He introduced several drugs that have been used against worms since then.
Another illness suffered by our ancestors was scabies, which was caused by a type of mite (*acarus* = atom of flesh). This was considered to be a particle of *materia peccans* because it was thought that the scabies was caused by an excess of black humour (*melaina colè*), so the treatment would try to remove this humour. **Cosimo Bonomo (1666-1696)** was a student of Redi and doctor to the galere (which were ships to which the jailed were sent to be punished by rowing, and amongst other things these prisoners were particularly subject to scabies). Bonomo looked for a way to eradicate scabies and found that bathing in antiseptic for a certain period of time was sufficient to kill the larvae deriving from the hatching of the egg inside the skin, and

therefore to eliminate the disease. Thanks to the help of **Giacinto Cestoni (1637-1718)** he isolated the mite and described how it appeared under the microscope. He explained all to Redi and it was published in 1687. Much later, in 1834 a Corsican student called Simone Renucci who sat in a lesson on scabies taught by the famous Prof. Alibert at the San Luigi of Paris Hospital, told the professor that in Corsica scabies sufferers were washed in disinfectant. The professor was surprised at this, since the treatment discovered by Bonomo had remained within Tuscany, Corsica and Sardinia, without being passed on to the rest of Europe.



The glands according to Malpighi

In that period, **Marcello Malpighi (1628-1694)** a student of Galileo sustained that all the organs were formed by minute machines, namely the glands. This is both true and false. Indeed, it is true that a glandular structure can be recognized in the liver, in the kidneys, and in the lungs, but this is not the case in the brain or in other organs. Malpighi also made other important discoveries: the layers in the epidermis, the renal *glomerulus*, the corpuscles of the spleen, the red corpuscles, but his genius stemmed from being able to distinguish between what was false and what was true since microscopes at that time produced truly fallacious images. In addition, he discovered the capillaries in the lungs of a frog (a cold-blooded animal) thus completing Harvey's schema.



Leeuwenhoek's microscope

Anthony Leeuwenhoek (1632-1723) was a textile salesman and was so passionate about microscopes to make one with his own hands. A skilled observer, he was not a learned person and his descriptions, written in Dutch and illustrated by his drawings, were with no theoretical interpretations. They were translated into Latin and sent to the Royal Society in London. Leeuwenhoek reported that in the plaque of his teeth, in organic fluids and in his faeces, there were very small organisms which, as seen from his drawings, were protozoa or bacteria. He did not relate them, however, to infectious diseases. By Leeuwenhoek's microscope, the medical student Johan Ham discovered the spermatozoon, a finding soon confirmed by Leeuwenhoek. This Dutch amateur described many other things, which, being too much ahead of his time, were fully appreciated and verified only decades later. Leeuwenhoek's discoveries were partly confirmed, on behalf of the Royal Society, by **Robert Hooke (1635-1703)** who built a new compound microscope. In 1665 Hooke published the atlas: "Micrographia" illustrated by his beautiful drawings. In it he described, inter alia, the minute "cells" of cork.
Returning to Malpighi, the concept of glands was given impetus by the Danish student, **Niels Stensen (1638-1686)** who had discovered by accident, the *ductus parotideus*, which at first he considered to be a vessel, while dissecting a lamb's head in Amsterdam in the house of his Professor of Anatomy. The latter whose name was Blasius, managed to hear about this discovery and published it, much to Stensen's annoyance. Thus, after having moved to Leiden, Stensen carried out dissections of other animals and, besides stating that what he had seen was an excretory duct, he realized that saliva was derived from blood, that is to say, produced by the gland and carried by the duct to the mouth. The same argument applied to the lachrymal and sweat glands: these too derived their secretions from blood. Stensen made other discoveries, for example he was the first to have the courage to say that the heart was simply a muscle and did not contain the soul, and the first to call the uterine tubes oviducts. Furthermore, he established the homology between the ovaries of mammals and that of birds and provided a mathematical model of muscle contraction. In Florence he also was engaged in the study of the anatomy of the earth and he made important discoveries in this field too. He was first to discover the principles of sedimentology, maintaining that the oldest strata are the deepest, and

he doubted whether the Earth was only 4000 years old. He formulated a law (Stensen's rule) which distinguishes between a quartz crystal and a diamond crystal: a crystal grows *non mutatis angulis* (with equal angles), and so crystals can be recognized from their angles. After this, Stensen became a priest and so abandoned science in keeping with his vows. He was sent as a missionary to Lutheran areas and died in a condition of extreme poverty, having given everything he had to the poor. The Grand Duke of Florence, Cosimo III, directed Stensen's body to be brought to Florence and buried first in the crypt, then moved to a chapel dedicated to him in the church of San Lorenzo, the basilica of the Medici family. In 1988 Stensen was beatified by Pope John Paul II and made Saint patron of scientists.

Bernardino Ramazzini, the founder of Occupational Medicine

Among the important figures from the end of the 17th century there was **Bernardino Ramazzini (1633-1714)**. Ramazzini had a worker who came to his house to clean the lavatories and who went blind after some time. Ramazzini was curious and so made some inquiries, ascertaining that many other lavatory cleaners had gone blind. The same argument applied to chimney sweeps: many contracted cancer. So Ramazzini understood that a great many jobs influence health and as a result published the textbook on occupational medicine ("*De Morbis Artificum*") in which he described a great many illnesses connected to employment situations.
Doctors at the time began to realize that, in fact, the therapy itself might be disastrous for the patient. **Thomas Sydenham (1624-1689)** and **Hermann Boerhaave (1668-1738)** returned to Hippocratic ideas, that is to say, to extreme caution in treating the patient. They also said it was necessary to have hospitals not only as places of cure, but for teaching medical students as well. So the first University clinic was founded in Leiden, in Holland, where Boerhaave worked, at the university which had been presented to the people of Leiden more than a century earlier by the Prince of Holland as a prize for having fought bravely against the Spanish in the War of Independence.
As for the state of surgery at the start of the 18th century, surgeons had to operate quickly for the longer the operation lasted, the greater was the risk of infection. The patient was held down

firmly by servants and in general, before the operation, was interviewed by a confessor. The larger part of surgeons did not know any anatomy, and were considered to be uneducated people. **Giovanni Alessandro Brambilla (1728-1800)** promoted the development of surgery in Central Europe in his role as an enlisted surgeon in the Austrian army. He was very intelligent; the commandant of his regiment took him under his wing so that Brambilla was able to become a personal surgeon to Joseph II, firstborn and heir of Maria Theresa, Empress of Austria. Brambilla used his influence on Joseph II so that Latin was taught to surgeons in order for them to study scientific texts, and so be placed on an equal footing with doctors. First, they were taught Latin, and then how the human body is constructed. Thanks to him a great academy (the Josephinum) was founded in Vienna in which Latin and science (in particular, human anatomy which had become very important following Morgagni's teaching) were taught to surgeons. Splendid wax anatomical models were brought from Florence (these are still to be found at the Josephinum), with the aim of using them to instruct the students of surgery. In conclusion, he managed to elevate surgeons to equal status with physicians. In fact, a symbol of this is present in medical schools of the Universities of the Austrian Empire: two ladies, both wearing the long robe distinctive of scholars, shaking hands in order to represent, on equal footing, the new alliance between medicine and surgery. Under the picture there is the sentence:" *In Unione Salus"* (in union for health).

Felice Fontana

Abbott Felice Fontana (1730-1805) was a great scientist and a valued adviser of the Grand Duke of Florence, Peter Leopold, cadet brother to Joseph II. He had the idea of making anatomical wax moulds in order to instruct the surgeons. His was an useful idea for two reasons: 1) Colour printing was, at the time, technically inadequate and exceedingly expensive 2) because the surgeons did not know Latin, they could not read anatomical and medical textbooks, generally written in that language 3) since there were no freezing facilities,nor chemical fixatives, it was very difficult to keep cadavers for teaching. So at the La Specola Museum in Florence, with the help of several anatomists, Fontana equipped a workshop in which moulds of parts of the human body were initially made of plaster then turned into wax by skilled artisans.

Francesco Antonio Boi

Carlo Felice of Savoy (1759-1824), Viceroy of Sardinia, sent the anatomist and native of Olzai (central Sardinia), **Francesco Antonio Boi (1767-1855)** from Cagliari to Florence in order to obtain wax anatomical models to be exhibited in his museum. These models were personally made by the great Clemente Susini based on dissections performed by Boi, and are true masterpieces that can still be admired in the Wax Museum in Cagliari.
Other scientists at the beginning of the Eighteenth century were **Domenico Cotugno (1736-1822)** who discovered cerebrospinal fluid, described sciatica, and reported the presence of albumin in the urine of people suffering from kidney disease; **Luigi Galvani (1737-1798)**, an anatomist from Bologna discovered animal electricity, even though according to some, credit should also be given to his wife, who whilst she was preparing some frogs, touched the animals' legs with a bronze teaspoon and noted that they contracted. Following this, Galvani carried out experiments and was the first to speak of animal electricity. However, Volta demonstrated that it was not animal electricity, but just a physical phenomenon.

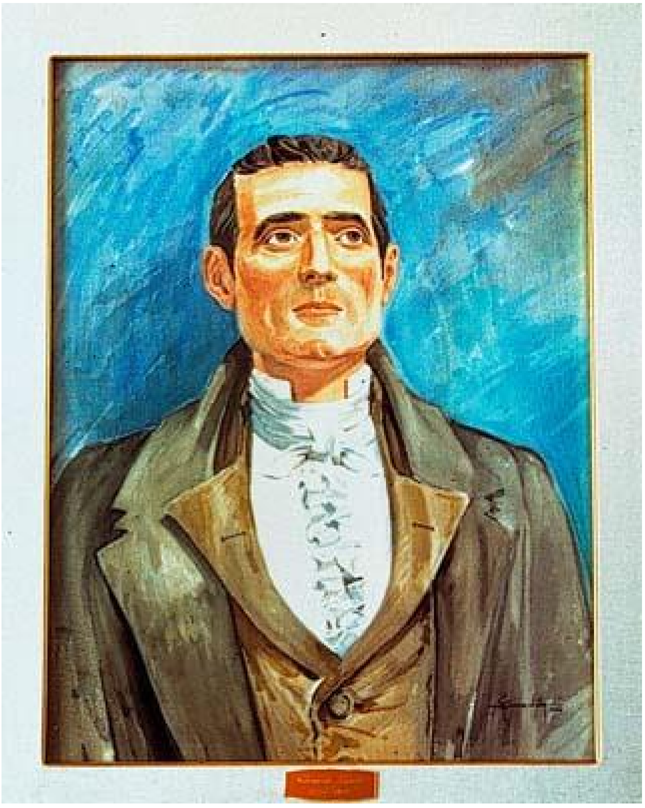
Antonio Scarpa

Another important anatomist and surgeon was **Antonio Scarpa (1752-1832)**, who worked in Modena and above all in Pavia, where Brambilla requested his presence. He made important contributions to the anatomy of the eye, to the ear (endolymph and secondary timpanum), to the surgical treatment of hernia and of aneurisms. Together with **Felix Vick D'Azyr (1746-1794)**, he discovered the olfactory nerves, he also described the nasopalatine and the cardiac nerves. He made great contributions to the definition of topographical anatomy, especially of that in the lower limbs and is considered to be the founder of modern Surgical Anatomy along with John Hunter.

Chapter 6

The 18th century
Clinical anatomy and the pathology of organs
Spallanzani. Jenner

The anatomical wax models were a visual means of teaching and spreading anatomy. Anatomy was still the preserve of educated doctors who knew Latin and who thus had access to textbooks. It was not the arena of surgeons who were lower ranked in status, being barbers in the vast majority of cases, people who had not had a classical education and who had no access to University and to scientific works.



Clemente Susini

The anatomical wax models were produced on a large-scale in Florence, and then exported throughout Europe. Of the organ to be reproduced (for example, the heart) a plaster mould was made that, before it hardened, was split in two by using a string, was reassembled, and then filled with wax. After this, the wax was coloured, and lastly, the sculptor's hand defined all the details.

As we have already seen, the wax models which are now in Cagliari were personally made by **Clemente Susini (1754-1814)** in cooperation with Francesco Antonio Boi, and the wax mixture also contained precious substances, such as splinters of gold and ground pearls in order to make the wax luminous. Moreover, the wax works suffered more from the cold than from the heat because the wax mixture was made of diverse substances with varying degrees of dilation, and when the temperature falls below zero, the smallest vibration was enough to shatter and ruin them. Because in Cagliari never falls below freezing, the waxworks kept there have the status of

never having to be restored in contrast to those of the great collections in Florence and in Vienna (the waxworks in Vienna are in part copies of those in Florence, having been made in Florence and brought to Vienna by Giovanni Alessandro Brambilla). As a matter of fact, all anatomical waxes produced in the La Specola Museum, apart from those of Cagliari which are all signed by Susini, were known as “Waxes of Fontana” till the fifties of the last century. The first study that reports in its title Susini as the author of the Florentine waxes was the one by **Luigi Castaldi (1890-1945)**, Anatomist of the University of Cagliari, written during the thirties and posthumously published in 1947.
As seen before, **Giovanni Alessandro Brambilla** was the first in central Europe to place surgery on a par with medicine. In other countries this had come about in a more physiological manner, that is to say, the surgeons had become so good that they had become as good as doctors. This occurred in England as **John Hunter (1728-1793)**, a great surgeon, lived there. Hunter carried out an experiment on himself: since it was maintained that it was not possible for a patient to suffer at the same time from two illnesses, in order to establish whether or not gonorrhea and syphilis were two separate diseases or not, he inoculated his glans penis with pus from a subject suffering from gonorrhea in order to see if gonorrhea or syphilis appeared. He fell ill with syphilis because the subject had both the diseases and Hunter was fortunate because he apparently recovered from it. This experiment was publicized throughout the world and created confusion, because it was seen as evidence that gonorrhea and syphilis were the same disease.
Luigi Rolando (1773-1831), when he was Professor of Anatomy in Sassari (north Sardinia) wrote in 1809 the essay “The real structure of the brain of man and animals”. He followed the fashionable theory of animal electricity, and by touching the cortex of a pig on one side in front of the central sulcus of the brain (*rolandic sulcus*), provoked muscular contraction. Rolando also compared the cerebellum to a battery and stated that it was involved in control of motion.

Giovan Battista Morgagni

However, the true founder of modern clinical medicine was **Giovanni Battista Morgagni (1682-1771)**. He derived his medicine from the school of Galileo because he was a student of **Antonio**

Valsalva (1666-1723), who in turn was a student of Malpighi, Malpighi of Borelli, and these two had been students of Galileo. Morgagni applied the concept of iatrophysics but used the eye instead of the microscope: according to the principles of his school he tried to discover how organs functioned by regarding them as machines. Morgagni referred to previous publications, the most accurate of which came from the 15th century: a book entitled *"De abditis morborum causis"* (the hidden causes of diseases) written by **Antonio Benivieni (1443-1502)** who in Florence carried out several autopsies and correlated them with the cause of death. Another treatise published in the late 17th century was the *"Sepulcretum"* by **Theofile Bonet (1620-1689)**, which included anatomical reports of many cases. However, all these reports lacked the correlation between clinical history and anatomic-pathological findings. With Morgagni there was a return to the ancient Alexandrian tripod consisting of clinical history, the autopsy, and then the clinical diagnosis. Morgagni collected 700 autopsies, correlated them with the patient's clinical history, and demonstrated that for the great majority of the diseases the organ had a peculiar pathology. At that time, there was no means of carrying out live autopsies (autopsy as meant by the Alexandrian concept, that is to say, an examination of the patient with the doctor's own eyes), so autopsy was really dissection, but the concept here was that of correlating the clinical history with the disease. Morgagni was a well known anatomist, being called 'his anatomical majesty' throughout Europe because he had published notes on anatomy entitled *"Adversaria Anatomica"* which became very famous for the notably precise descriptions of details that had been overlooked by previous researches.
His major work a real milestone in the birth of modern medicine, was published in 5 volumes in 1761 and was dedicated to the most important medical academies of the time. It was published in Latin and entitled *"De Sedibus et causis morborum per anatomen indagatis*" (On the Sites and Causes of Diseases Studied Through Anatomy). It must be noted that some of the 700 clinical cases reported in the book belonged to Malpighi and to his teacher Valsalva, an anatomist who had made many important discoveries, especially about the ear.


JO. BAPTISTÆ
MORGAGNI
P. P. P. P.
DE SEDIBUS, ET CAUSIS
MORBORUM
PER ANATOMEN INDAGATIS
LIBRI QUINQUE.
DISSECTIONES, ET ANIMADVERSIONES, NUNC PRIMUM EDITAS COMPLECTUNTUR PROPEMODUM INNUMERAS, MEDICIS, CHIRURGIS, ANATOMICIS PROFUTURAS.
Multiplex præfixus eſt Index rerum, & nominum accuratiſſimus.
TOMUS PRIMUS
DUOS PRIORES CONTINENS LIBROS.
VENETIIS,
MDCCLXI.
EX TYPOGRAPHIA REMONDINIANA.
SUPERIORUM PERMISSU, AC PRIVILEGIO.
Il « De Sedibus » di G. B. Morgagni.

Title page of "De Sedibus" by Giovannni Battista Morgagni

This momentous textbook attracted so much interest throughout the world at that time that the first edition was sold out within two years. There followed many other editions and they were translated into all the other European languages. One of the last editions was in Italian, both because Italian doctors were familiar with Latin (until the French Revolution the language of science was Latin), and because in Italy the 'morgagnesque verb' had difficulty taking root. On the other hand, Morgagni's principles were applied and were the basis on which clinical medicine developed in Northern Europe. However in Italy, he influenced Domenico Cotugno and had Antonio Scarpa as one of his pupils.
In the same period in which Morgagni published his tract, a small tract appeared in 1761 in Vienna, *"De Inventu Novo"* in which the son of a cooper called **Leopold Auenbrugger (1722-1809)** described percussion as a means by which the alterations of the thoracic organs could be observed in living patients. This book remained unknown until the beginning of the 19th century when Napoleon's doctor **Jean Nicolas Corvisart (1755-1821)** revived clinical percussion. Auenbrugger was still living and, 30 to 40 years after his book's publication, shared in its success. Among the most well- known Morgagni's precursors there was **Giovanni Tommaso Porcell (1525-1590)**, born in Cagliari (Sardinia), but naturalized as Spanish. Supporter of Fracastoro's ideas, taught in both the Universities of Salamanca and Saragossa. He is regarded as the founder of Spanish Morbid Anatomy for having described, in his book dated 1564, the postmortem findings of bubonic plague.
Important problems in the 18th century were those of respiration and of combustion. It had been hypothesised by **Georg Ernst Stahl (1660-1734)** the existence of a substance called phlogiston that, when consumed, produced fire. However, this concept did not explain several experiments which were carried out by the Oxford school. For example, on placing an animal under a bell with a burning candle, it was observed that as the candle burned the animal showed signs of asphyxia until it died. What connection existed with phlogiston was not understood. It was said that the air had become "fixed air". An Englishman, **Joseph Priestley (1733-1804)**, was the first to suggest that a gas must be consumed.
The person who demonstrated that this gas is oxygen was **Antoine Laurent Lavoisier (1743-1794)**, the great scientist and founder of modern chemistry. Lavoisier was guillotined for being an aristocrat. History records that just before being guillotined he was reading a science book!

Lazzaro Spallanzani

Immediately after the discovery of oxygen, the abbot **Lazzaro Spallanzani (1729-1799)**, one of the greatest scientists who ever lived, worked out the relationship between the consumption of oxygen and tissue respiration. Spallanzani was a great experimenter and showed that during flight, bats navigate using ultrasounds; in order to demonstrate the action of gastric juices, he inserted a sponge with some meat inside it into his stomach. The sponge with the meat was removed some hours later so that the effect of gastric juices could be verified. Spallanzani above all is famous in the field of reproduction. By putting a type of waxed underpants on a male toad, he was the first to demonstrate that without contact between the liquid semen and the egg, fecundation was not possible. Later on, he performed the first successful artificial insemination in a bitch. He also discovered white blood cells and demonstrated the existence of capillaries, the *"capillamenta"*, in warm-blooded animals (in the chick), confirming the observations previously (1702) made by **William Cowper** in the mesentery of cats and dogs. Among Spallanzani's most important discoveries (for which **Pasteur** revered him) was that of refuting the thesis of spontaneous generation of protozoa. The problem of spontaneous generation was an interest of **Redi** who demonstrated that insects are derived from other insects. There had been some precursors, for example, among the Italians, **Antonio Vallisneri (1661-1730)** a Paduan doctor, who thought that there were "Semi" (seeds) in the air, similar to those described by Fracastoro; **Carlo Francesco Cogrossi (1682-1769)** maintained that bovine plague was transmitted by a living microorganism, responsible for contagion. However, both these theories were disproved.

Edward Jenner's inoculating his son with cowpox

An Irishman, **John T. Needham (1713-1781)**, stated that the *infusoria* (which could be seen under the microscope because they were protozoa) were derived from the fluid in the flask, and therefore not from other protozoa. Although his conclusions were supported by the greatest naturalist of the time, **Georges Buffon (1707-1788)**, Spallanzani refuted them, because if the flask also had been sterilised by heat (he was the first to carry out the procedure, which was also applied later by Pasteur), the protozoa did not grow. He demonstrated therefore, that protozoa arise from pre-existing protozoan. This was the first demonstration that very small beings are derived from other very small beings.

At the end of the 18th century there was a great empirical discovery. An English surgeon **Edward Jenner (1749-1823)**, a student of John Hunter, noticed that milkmaids who had previously suffered from cowpox, always recovered when they fell ill with smallpox. Smallpox was the most terrible and feared of diseases at that time. The plague had nearly disappeared because of the change in the rats and thanks to improved hygiene and, although there existed serious diseases such as tuberculosis and syphilis, the most deadly one was smallpox which affected children.

There had already been previous attempts, going back to the late 17 century, to eradicate the disease with variolation. The latter consisted of the inoculation in a healthy subject of a small amount of pus taken from a patient who was close to recovering. Unfortunately, this procedure was often lethal and many babies died. Smallpox inoculation was promoted by Lady Montagu, the wife of the British ambassador in Constantinople, because she saw it being practised there as it had been in the Orient for many centuries. This procedure was then introduced into Italy by Greek doctors, who worked in Venice. These Greek doctors had a great champion in Pope Benedict XIV (Pope Lambertini) who tried to introduce smallpox inoculation into the Papal State.

Jenner's discovery resolved the problem of smallpox. Jenner carried out his first inoculation on his gardener son and later on his own child: he took a small amount of pus from a cow's pustule, then injected his son and could see that the pustule of the vaccination (which was not

called vaccination, but a graft) meant the child was protected from smallpox. The vaccination created great interest, even though it was violently opposed by certain parties, above all by clerics who felt it was an insult to the Creator since it was a mixture between the bestial, that is, the animal, and man. Therefore, in the rest of Europe vaccination only took place on a large-scale because the French Revolution occurred. It became a flagship of the left, of the Jacobins. The Jacobins vaccinated, but the reactionaries did not.
In Italy, a Milanese, **Luigi Sacco (1769-1836)** spread vaccination in the Cisalpine Republic causing the death rate from smallpox to fall dramatically.

Pietro Leo, professor of Anatomy and Medicine in the University of Cagliari

It was **Pietro Leo (1766-1805)** who introduced the vaccination to Sardinia. He was a Professor of Anatomy and had learnt how to vaccinate in Paris during the French Revolution. Other early apostles of vaccinations in Sardinia were **Francesco Antonio Boi** and **Sebastiano Perra (1772-1826)** who wrote a book (1808) on vaccination. At first, however, vaccination spread rather slowly in Sardinia, but was later helped by the work of another professor of anatomy, **Giovanni Falconi (1817-1900)**.
In 1794 **Philippe Pinel (1743-1825)** in Paris, possibly anticipated by the Italian **Vincenzio Chiarugi (1759-1820)** and by other European physicians, set the lunatics free from chains stating that they were sick people and not delinquents.
At this point the discussion about live contagion re-emerges. Among Spallanzani's students was **Giuseppe Baronio (1759-1811)** who, based on what he had learned from Spallanzani, was the first to perform skin grafts in animals, a precursor to cutaneous grafts and plastic surgery in humans. He was also the first to demonstrate the important principle that an autograft from the same animal would take, whereas an allograft from another animal was rejected.
Agostino Bassi (1773-1856) was the son of a wealthy farmer and a lawyer who also had a passion for biology. His father did not want him to take up biology, but wanted him to care after the family's property, to become a civil servant and to join the Imperial administration. All the same, he constantly followed Abbott Spallanzani's lessons until the latter died. One-day the

silkworms he kept were infected by a terrible disease, muscardine, that killed the silkworms reducing them to pieces of chalk. Bassi patiently began studying this phenomenon in order to understand whether or not a living organism had been responsible for this phenomenon, and he discovered that a fungus, which was later called *Botritis* or *Beauveria bassiana*, had caused the death of these silkworms. He also found a disinfectant that used to prevent this fungus and to clean the rows in which the silkworms were kept.
His tract entitled *"Del Mal del Segno, Calcinaccio o Moscardino"* was translated into French and spread throughout Europe. Immediately afterwards the fungal aetiologies of certain illnesses were discovered, such as tinea (ringworm) in the hair. **Louis Pasteur (1822-1895)**was greatly influenced by his work (in Pasteur's office there were the portraits of both Spallanzani and of Bassi).
At that time the microscope could recognize only fungus and protozoans, for bacteria were too small to be seen. It was only in the 1820s that an astronomer who made telescopes **Gian Battista Amici (1786-1863)**, invented the reflecting prism. (After this, the microscope was perfected by the English and Germans above all). This meant that microscope resolution was greatly improved.
In his book Bassi wrote: "I would be very happy if in the future my discoveries serve to open up study and find cures for the fatal diseases which affect mankind, including cholera". In the spirit of this book, the Italian anatomist **Filippo Pacini (1812-1883)** discovered in 1854 the choleric vibrio in the faeces of cholera sufferers, but this discovery was so ahead of its times that it was ignored. However, in 1965, the International Committee on Nomenclature adopted the name *Vibrio cholera pacini*, Pacini 1854, formally aknowledging his priority.

Robert Koch

In 1884 **Robert Koch (1843-1910)** also discovered the choleric vibrio but then emerged that it had already been clearly described by Pacini. There was a long argument that was eventually resolved by giving the credit to Pacini. However, from a practical point of view, this was of little value since his precocious discovery had not spread to the wider scientific community.

Eventually, a method for identifying illnesses was found. There was a return to the old school of Cnidos so that the illness, not the person, became the focus of medicine. In this period the means of disease diagnosis came about: although the method which Morgagni had found was the scalpel on the body of a dead person, Auenbrugger had already shown that it was possible to carry out the “autopsy” by using percussion. Later, at the beginning of the 19th century, a Frenchman, **Renè Laennec,** invented the stethoscope. **Claude Bernard (1813-1878)**, a pupil of **François Magendie (1783-1855)**, is regarded as the founder of the modern physiology based on animal experimentation. Just because of vivisection, which he continued to practice until the end of his life, he was abandoned by both his wife and daughter. To Bernard we owe fundamental discoveries on the organs function and on the nervous visceral system; his are the concepts of milieu interieur (later called omestasis) and that of the liver glycogenic function. Other great physiologists of the time were: **Johannes Peter Müller (1801-1855)**, **Emil Du Bois-Reymond (1831-1889)**, **Hermann von Helmholtz (1821-1894)**, **Carl Ludwig (1816-1894)** and **Carlo Matteucci (1811-1868)**.

Chapter 7

First part of the 19th century
Semeiotics,
Sanitary assistance,
Cell Pathology, and Microbiology

René Théophyle Hyacinte Laennec (1781-1826), was a student of **Corvisart** (Napoleon's doctor), and had the idea of making a tube which he called stethoscope. This was the precursor of the modern phonendoscope which allows the respiration and the heartbeat etc. to be heard.

Fig. 26 - Stetoscopio originale in legno usato da René-Théophile Laennec (1820). (Wellcome Museum of the History of Medicine - London).

Woodden stethoscope used by René Théophile Laennec

The importance of the stethoscope's contribution arose from the fact that it was not possible to listen with the ear on a patient's chest, especially if was a woman, and particularly if she belonged to the upper class. It was actually unthinkable that a man could place his ear in contact with a woman's chest and the instrument served above all to avoid this. The physician was only allowed to inspect the urine and check the radial pulse at the wrist. Thus medicine took another major step forward in semeiotics: after inspection, auscultation (of the heartbeats and lungs) and percussion were now possible. The "autopsy" now took place on the living, in whom the illness was taken to be as a morbid entity, leaving man out of the consideration. This is the reductionist principle upon which modern medicine is based.
By the start of 18th century all durations of semeiotic processes were known: observation, palpation, percussion and auscultation. Laennec, who later died of phthisis (consumption), made many important contributions to the definition of aneurisms and of pulmonary diseases, such as pneumonia and tuberculosis which he rightly recognised as a single disease, while, before him, its various forms and localisations were regarded as separate entities.

Manuel Garcia, inventor of the laryngoscope

Manuel Garcia (1805-1906) was a tenor who invented the laryngoscope in order to inspect the status of his vocal chords. In this period the oesophagoscope was invented. A doctor saw a sword swallower which gave him the idea of a light on the end a tube in order to see the oesophagus. It was illuminated from above by the flame of a candle, which was reflected in a small mirror which in turn allowed the inside of the oesophagus to be seen through a hollow tube. **Herman Ludwig Helmotz (1821-1894)**, who gave outstanding contribution to the understanding of ear and eye physiology, invented in 1851 the ophthalmoscope, the instrument that allows the examination of the *fundus oculi*.

Apart from sepsis (septic poisoning) caused by operating with bare hands, among the most important problems of surgery was the fact that anaesthesia did not exist. Several people discovered it in America, including **Horace Wells (1815-1848)** and **William Green Morton (1819-1868)**. In America recreational use was made of ether during holidays and people, under the influence of the ether, noticed that they no longer felt pain. This was immediately used during dental extraction. Following this, there was an endless dispute about who had discovered it first, and although a prize was put up, it was never collected.

Besides ether, nitrous oxide and chloroform came into use. Anaesthesia with chloroform was administered to Queen Victoria by **John Snow (1813-1858)** during her delivery of Prince Leopold.

In this period (1859) came the appearance of the first sanitary institutions, the very first of these being the Red Cross. It was founded because of an episode during the course of the Battle of Solferino. There was a rich Swiss financier, **Henry Dunant (1828-1910)**, who had mining interests in Algeria. In order to obtain a concession he had to confer directly in person with Emperor Napoleon III who was at the battleground, so Dunant went to Solferino. Although he was not able to speak with the Emperor, he was so struck by the way in which the wounded were left on the battleground that he experienced a kind of epiphany. He abandoned all of his other activities in order to dedicate himself to this problem and, through great sacrifice (he became impoverished), he managed to persuade the governments to inaugurate this neutral association, which was called the Red Cross in honour of Switzerland - the flag of the Red Cross is the inversion of the Swiss flag. There was a worldwide Congress in which the neutrality of this organization was sanctified, therefore meaning that the wounded could be evacuated from the battlefield and treated. After the Red Cross, the Red Crescent was founded for Islamic countries. It was a great step forward for humanity.

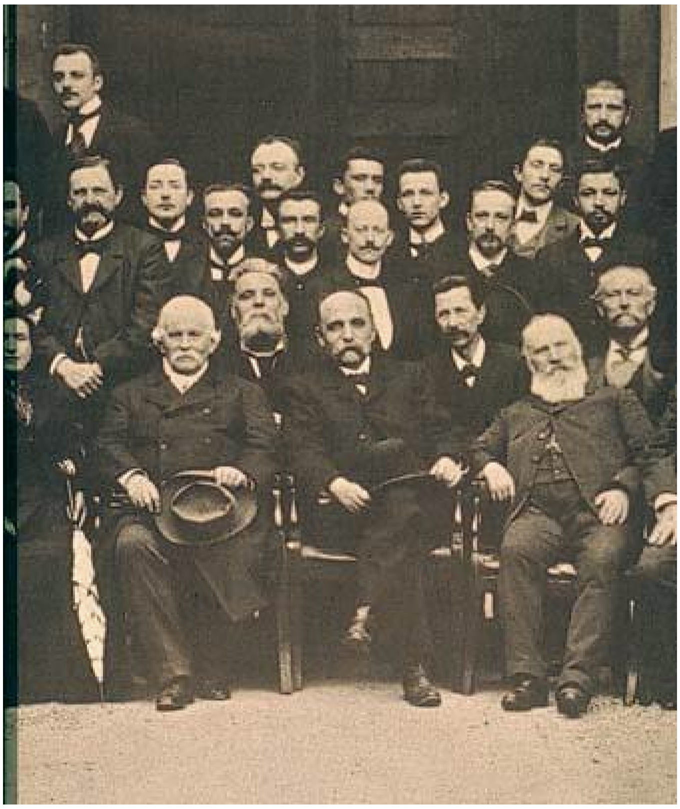
Florence Nightingale

Equally important was the work of **Florence Nightingale (1820-1910)**. Before her, the idea of a paramedical body had not been conceived, and people working in hospitals were persons of very low culture (servants, ex-prostitutes, and the incarcerated who were obliged to work in hospitals). It must also be said that this state affairs was peculiar to Protestant countries for, in Catholic nations, sanitary assistance was under the care of religious orders. This changed during the British expedition to the Crimea (1856), when Florence Nightingale, a lady belonging to the English upper class, insisted that a body of nurses be formed to follow the English army. She did this all practically at her own expense and the corps of nurses proved to be exceptionally important in assisting the patients. A terrible epidemic of cholera broke out, and these women excelled in curing the patients through, for example, putting hygiene measures into practice. On returning to Britain, they were highly praised and honoured. As a result, Nightingale created the first school for specialized nurses at St Thomas's Hospital.

In the early 19th century sanitary police measures became efficient: quarantine and exchange of goods were regulated in a more serious manner.

In France in 1800, before Laennec, **Marie Francois Xavier Bichat (1771-1802)** criticised the microscope in that this instrument was absolutely useless, as indeed it had been up to that point. He said it was necessary to return to ancient times, that is to say, to using artificial methods, such as boiling (as Malpighi had done) in order to discover the body's fundamental components, which according to him were the tissues. On boiling the tongue he managed to peel it and noted the papillae under the epithelium and that it was possible to decompose the organ into layers: the tissues. Because he said that lesions were to be found, not in organs, but

in the tissues, he went to a finer level than Morgagni had. It is a curious fact that Bichat, who negated the use of the microscope, coined the term histology. Later on (1838) **Mathias Jacob Schleiden (1804-1881)**, demonstrated that vegetable organisms are formed of cells, and the same (1839) was confirmed for animals by **Theodor Schwann (1810-1882)**.
In 1858 **Rudolph Virchow (1821-1902)** noted that the lesions of the diseases could be found in cells stating that cells derived from other cells. He published his famous treatise "The cellular pathology". He was the founder of histopathology, which today still is the basis of diagnosis; he was the first to coin the terms and to describe: leukaemia, leukocytosis, neuroglia, thrombosis, embolism, and amyloid, and described the infestation by *Trichinella* in humans. Being also an anthropologist he demonstrated that races do not exist in humans, thus negating the existence of a distinctive German race; for which, Hitler never forgave him. He was a left-wing politician, and applied himself to improving the hygiene conditions of miners and promoted the construction of the sewer system of Berlin. All the same, he also made some mistakes: for many years he refused to believe in the doctrine of contagion through germs formulated by Pasteur and Koch.
Other important discoveries were the theory of evolution by **Charles Darwin (1809-1882)** and the laws of genetics discovered about 1870 by **Gregor Mendel (1822-1884)**. The latter laws were initially ignored, and then rediscovered 30 years later by **Hugo de Vries (1848-1935)**.
Another consequence of the cell theory was the use of colorants to demonstrate the lesions which Virchow had managed to demonstrate in part because he, at first, only had carmine available to him. A short time later other colorants were introduced such as haematoxylin-eosine and they were added to tissue preparation techniques: microtome, paraffin embedding, etc.
However, there were great problems in regard to the nervous system that was almost impossible to study with the methods then in use. In fact, only the nucleus, as well as part of cytoplasm, but not the cellular processes were demonstrated, rendering impossible to obtain an idea of the whole nervous cell, later called neuron.

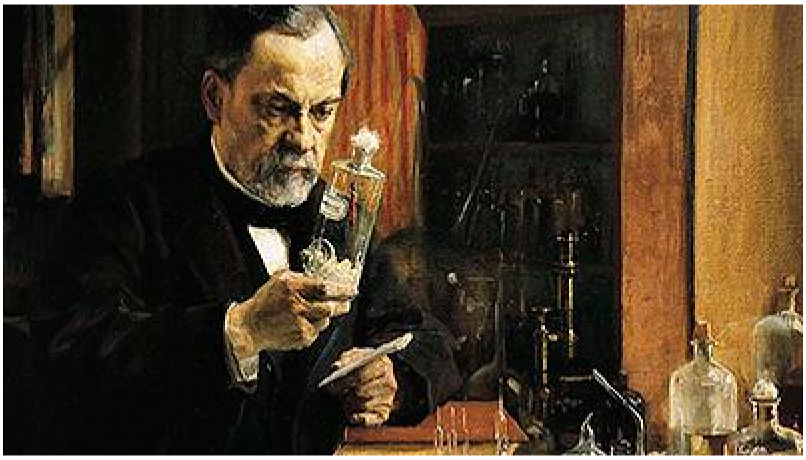


Camillo Golgi sitting in the center of a group of anatomists. Anatomical Congress. Pavia (1900)

The method for studying the nervous system was perfected by **Camillo Golgi (1843-1926)**, a pupil of **Giulio Bizzozzero (1846-1901)** the discoverer of blood platelets. Thanks to this method it was possible to see the cellular processes (Golgi's method used silver and was called the black reaction). An emulator of Golgi, **Santiago Ramon y Cajal (1852-1934)** put together several ideas and arrived at the concept of neurons as independent cellular entities. Formulated by **Wilhelm His senior (1831-1904)** and then by **Robert Scott Sherrington (1857-1952)**, the concept of axons (neurites) as cellulifugal (in term of direction of the nerve impulse) processes and that of dendrites as cellulipetal ones, allowed Cajal to describe the first nervous pathway in the retina. Preparations stained with silver and observed under the microscope seemed to show that nervous processes were connected by a network of processes. Thus, Golgi maintained that the neurons were not separate entities but connected in a network of processes. By contrast, Cajal extrapolated the concept of the cell as an independent unit to neurons, and it was he who made formidable contributions to neuroanatomy. Cajal was from Spain, a country which, at that time and in the previous decades, was marginal to international science, Golgi, instead, came from Pavia, a city which had been under Austrian rule until 1860. This meant that all scientific contributions made in the University of Pavia till when the city and Lombardy were part of the Austrian Empire, were translated into German and diffused throughout central Europe. At the end of the Austrian rule, Lombardy, once again, became a provincial country and so Golgi's discoveries were little recognized abroad. On the other hand, Cajal spread his discoveries by going to congresses, and by speaking and writing in French and German. In 1906 he and Golgi were jointly awarded the Nobel prize. Golgi made also notable contributions to cytology (Golgi apparatus) and to the study of the pathology of malaria. He deduced the connection between the appearance of the fever and the discharge of the parasite from the red blood corpuscles and stated that this was the right time for administering quinine. He also discovered that *plasmodia* took refuge in liver and spleen, causing enlargement of these organs.

Little progress was made on contagious diseases; the infant mortality rate of women in labour in hospitals with doctors and students was high, but was lower for women giving birth at home or in hospital departments maintained by midwives. The assistant professor at a clinic in Vienna, **Ignac Fulop Semmelweiss (1818-1865)**, was struck by this phenomenon and thought that the doctors and the students of medicine were the ones responsible because they palpated the intimate areas of women without gloves, passing disease from one to another. Above all, hygiene was generally poor in hospitals where the sheets were only changed once a month. Semmelweiss (1847) insisted that doctors and students washed their hands with calcium chloride between visits. He was a difficult character and felt so psychologically persecuted that he had to be committed to a lunatic asylum. Later on, when hospital hygiene became widespread, he was given credit for being prophetic.

At the beginning of the second half of the 19th century the idea of contagion was still unknown: surgery was carried out with bare hands, ignoring hygiene, but thanks to **Louis Pasteur (1822-1895)** this ended.



Portrait of Louis Pasteur

He was a chemist employed by the French government to study the mechanisms of wine and beer fermentation, and realized that fermentation took place because of the action of microorganisms called *saccharomycetes*. He developed a method of conserving foodstuffs with moderate heat: pasteurization, which still is used today. He was entrusted with checking the truthfulness of spontaneous generation and to investigate upon certain diseases of silkworms, such as pebrine, which he demonstrated to be caused by a protozoa and bacteria. Basing his judgment on the ideas of Spallanzani and Bassi, he concluded that bacteria existed, which were germs responsible for diseases. Unfortunately, at forty-six years of age, he suffered from a stroke but this did not impede him in making his important discoveries. Moreover, he found a way to attenuate the germs through suitable treatments and he developed a series of extremely important vaccines (his own term coined in honour of Jenner) such as the vaccine to immunize animals against anthrax as well as the vaccine against rabies. The whole world was enthusiastic about this last discovery when Pasteur vaccinated the shepherd boy Meister with success, as well as several Russian peasants sent to him by the Czar. Pasteur was also the man who first coined the term "microbiology" from "microbe" introduced in 1878 by **Charles Emmanuel Sedillot (1804-1883)**.

Another great microbiologist was **Robert Koch (1843-1910)**, Nobel prize winner in 1905. A country physician, became interested in bacteria when his wife gave him a microscope for his twenty-eighth birthday. He isolated the bacillum anthracis, developed a methods for producing pure cultures and introduced agar. He proposed the four criteria (Koch's postulates) to ascertain that a germ really is responsible for a particular disease. In 1882 he discovered the bacillus responsible for tuberculosis and thought that he had discovered a therapy based on tuberculin on the basis of his experiments on guinea pigs. However, it was a grave error because this substance is only of value in diagnosis, having no therapeutic value at all on humans. Then in 1883 he discovered the vibrion responsible for cholera as described twenty years beforehand by **Filippo Pacini**, inspired by **Agostino Bassi**.


Joseph Lister

Pasteur's article on the theory that germs are responsible for infection reached the hands of an English chemist who in turn persuaded **Joseph Lister (1827-1912)** a surgeon operating in Edinburgh to look at it. Inspired by the fact that phenol had been used to cleanse the drains of an English town, Lister atomised this substance during the entire process of a surgical operation, and obtained drastic reductions in deaths caused by sepsis (septic poisoning). This process became known as antisepsis. Later, it was understood that the preventive sterilisation (asepsis) introduced by a the German surgeon **Ernest von Bergmann (1836-1907)**, was more practical and efficient than antisepsis. Use of rubber gloves in surgery was introduced by American surgeon **William Halsted (1852-1922)**. In 1884 **Ilya Metchnikoff (1845-1916)** discovered phagocytosis and elaborated the theory of cellular immunity. Emil von Behring and Shibasaburo Kitasato, in the early nineties, produced the antitoxins active against diphtheria and tetanus. The so called germ theory of contagion based on the discoveries by **Pasteur**, **Koch**, **Emil von Behring (1854-1917)**, **Shibasaburo Kitasato (1852-1931)**, **Almroth Edward Wright (1861-1941)** and many others, had a momentous influence, especially in the Western world, on the everyday life and even on economy. It is due to the fear of contagion that women abandoned the multiple petticoats and the long garments of Victorian era, and that men shaved their faces. The development of the modern industry of sanitary equipment for houses, of chemical disinfectants, and that of disposables such as toilet paper, sanitary napkins, paper cups etc., also was a consequence of it.

Chapter 8

19-20th Centuries.
Specialisations. Malaria.
Women in biomedical sciences and in clinical, social and care medicine.
Chemotherapy. Antibiotics.
The latest discoveries.
Giuseppe Brotzu and cephalosporin

By the end of the 19th century surgery had taken gigantic steps forward, and in fact, there was now an anatomical underpinning, and anaesthesia had come into being, along with the concept of sepsis, but one important component was still lacking: monitoring the condition of the patient during surgery. In fact, when the surgeon operated on a patient under anaesthesia it was not known whether the latter was about to die or not.

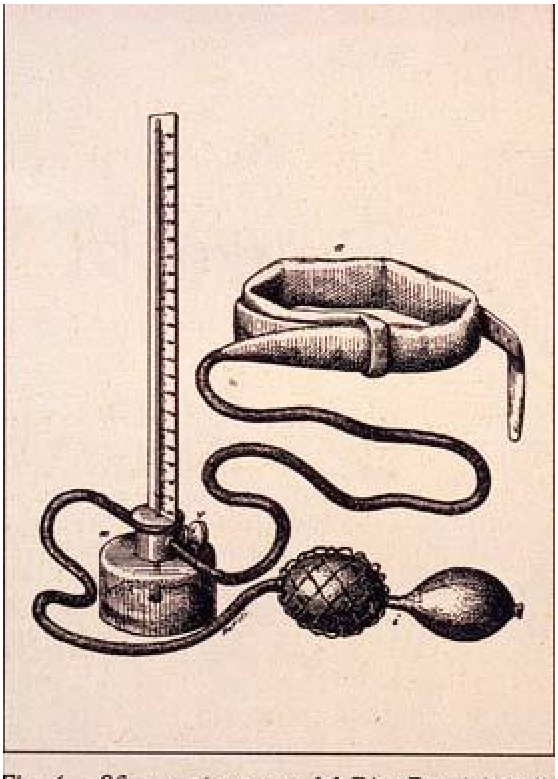


Fig. 6. - Sfigmomanometro del Riva-Rocci (1896).
Riva-Rocci's sphygmomanometer

Scipione Riva-Rocci (1863-1937), a student of **Carlo Forlanini (1847-1918)**, was the person who invented in 1896 the equipment to monitor the patient. He used simple objects (an ink-pot, mercury, a bicycle tubular tire) to construct a piece of equipment that, because of its small size and handiness, could be used in the operating theatre or by the duty doctor. In fact, instruments to measure blood pressure had already been invented, but they were very cumbersome and difficult to use. The sphygmomanometer was then perfected by the auscultation with the phonendoscope of the cardiac tones discovered by the Russian **Nicolaj Sergievich Korotkov (1874-1920)**. This allowed to measure minimum arterial pressure as well. Riva-Rocci's sphygmomanometer interested **Harvey Cushing (1869-1939)**, a famous American neurosurgeon, who came to Italy specifically to meet him and to see the instrument of which he

personally made a drawing. Cushing took the sphygmomanometer back to America with him and, from there, its use spread throughout the world.
In that period (late 19th century) humanity was afflicted by various infective diseases among which were Yellow Fever and Malaria. It is worthy of note that in Sardinia the population was more resistant to Malaria because there was a high percentage of hereditary microcytemic carriers whose erythrocytes were resistant to P*lasmodium* infection. On the other hand, colonisers coming from the mainland were not protected and were decimated by Malaria so few groups managed to establish themselves in Sardinia; among them the inhabitants of the island of Carloforte, the Greeks, and the inhabitants of the Padus Basin, all originating from areas of endemic Malaria among which hereditary microcytemia was widespread.

Giovan Battista Grassi, discoverer of the malaria cycle in humans

A student of Pasteur, **Alphonse Laveran (1845-1922)**, discovered the aetiological agent of Malaria to which he gave the name *"oscillatorium malariae"* (it was later named "Plasmodium" by the two Italian malariologists **Ettore Marchiafava (1847-1935)**, and **Angelo Celli (1857-1914)**. **Walter Reed (1851-1902)** discovered the role played by a mosquito (*Aedes Aegypti*) in the transmission of Yellow Fever, while the Englishman, **Ronald Ross (1857-1932)** demonstrated the malaria cycle in birds. In fact, it was **Giovanni Battista Grassi (1854-1925)**, who made the most important contribution to understanding the biological cycle of the parasite in man as he identified the mosquito of the Anopheles genus. However, for political reasons the Nobel Prize was given to Ross.
In Sardinia malaria was eradicated only in 1950 by the **Rockefeller Foundation**, which employed 30,000 men (mostly Sardinians) for 4 years, to launch out a massive campaign of land drainage and reclamation using the insecticide DDT. The operation's headquarters were situated in Cagliari at the Riva Villasanta school in Piazza Garibaldi. (See memorial plate)
Among the epoch's other illnesses were:
- **Pellagra**: although the existence of vitamins had not yet been discovered, the beginnings of an understanding of the fundamental cause of this disease, first described by **Francesco Frapolli** in

1771 and widespread in the plains of Lombardy-Veneto, had developed. It was in some way connected with the mono-diet based on maize. This disease, which brought grave complications to the nervous system, was eradicated when a varied diet containing the necessary vitamins was introduced.
- "**Miner's anaemia**": this illness afflicted many workers employed in great public construction projects at the end of the 19th century (for example, the Gottardo and Simplon Tunnels). It is a disease caused by the hematophagous parasite *Ancylostoma duodenal*e (discovered by **Angelo Dubini, 1813-1902)** which lives in hot humid environments and entered into the miner's bodies through the skin of their bare feet. This disease also was widespread in the south of the USA where it became known as "Hookworm disease".
In 1895 the German physicist **Wilhelm Konrad Roentgen (1845-1913)** accidentally discovered that the rays from a cathode ray tube could pass through the bones of the skeleton and leave an impression on a photographic plate or on a fluorescent screen. Thus radiology was born (the first radiography taken by him was of his wife's hand and went around the world).

Wilhelm Roentgen's first x-ray

Obviously the unrestrained use of X-rays without any protection, affected the doctors who thus used it badly since they were unaware that it would cause lesions (many radiologists died of radiodermatitis or from tumours). Great progress in radiography was then made by the American physiologist **Walter Cannon (1871-1945)** who introduced the use of methods of contrast which allowed otherwise invisible organs to be seen. Canon, also, defined the functions of the sympathetic versus those of the parasympathetic one by the famous sentences: "**Fight and Flight**" for the first, "**Rest and Digest**" for the second, respectively. Then, gradually, new techniques were perfected such as ecography (which uses ultra-sound - ultrasonography) after which followed CT (computerised tomography) and Nuclear Magnetic Resonance Imaging (MRI).
Another great discovery at the start of the 20th century, important to both medicine and surgery, was the discovery of the blood groups by the Austrian doctor **Karl Landsteiner (1868-1943)**. Finally it was understood why the blood of different subjects was incompatible. In 1940,

in cooperation with the American **Alexander Wiener**, he discovered the Rh factor as well.
In 1901 **Willem Einthoven (1860-1927)**, built the first machine to make electrocardiograms, furher improved in later years.
Great discoveries also were made in the field of bacteriology at the beginning of the 20th century. The diphtheria bacillus was identified and several vaccines were developed. In 1905 the German **Fritz Richard Schaudinn (1871-1906)** identified *Treponema pallidum*, the aetiological agent of syphilis which was widespread until then, making this an epoch-making discovery.
Some years later in 1910 an excellent bacteriologist, **Paul Ehrlich (1854-1915)**, for the first time perfected a synthetic pharmaceutical drug (chemotherapy) capable of attacking a germ: in this case the spirochete Treponema pallidum. He noticed that certain colorants bonded with the bacteria from which he got the idea of finding a substance which would bind to the bacteria and kill it. In cooperation with the Japanese **Sahachiro Hata (1873-1938)** he tried 605 compounds before finding one based on arsenic which was effective. He called it Salvarsan, 606. Being toxic, it was substituted by the less toxic Neosalvarsan.
In the meantime women had entered the scientific and medical scene:

Marie Curie

- the physicist **Marie Curie (1867-1934)** won two Nobel prizes, one for physics and one for chemistry, for her discoveries with radiation which were immediately applied to curing tumours.
- the biochemist **Gerty Theresa Cori (1896-1957)** studied the cycle of the pentose phosphate.
- the pediatric cardiologist **Helen Taussig (1898- 1986)** studied cardiac malformations and explained the surgical treatment for children affected by blue disease (tetralogy of Fallot). In the 1950s the American government gave her the job of discovering the causes of phocomelia which affected a large number of children. Taussig discovered that thalidomide, a sleeping pill which the mothers had used during their pregnancy, was responsible. In January 1953, **Rosalind Franklin (1920-1958)** an English crystallographer, was the first to demonstrate the double helix structure of the DNA molecule, paving the way to Watson and Crick discovery. She also gave fundamental contribution to the knowledge of viruses' molecular configuration.

-**Lillian Wald (1867-1940)** gave up her medical studies to give assistance to foreign immigrants living in New York most destitute areas, by creating the Henry Street Settlement, otherwise known as the Visiting Nurse Society (VNS) of New York. That later became a public service extended to all the nation. She devoted herself to assuring sanitary and social assistance to poor people with no racial nor religious prejudices.

Lillian Wald

She fought for the vote to women and supported Margareth Sanger program of birth control. In 1910 thanks under her request, the Columbia University of New York established the first Chair of Nursing and the first Faculty of Nursing. Before then nursing being taught in the hospitals
First women to be awarded a degree:
Elena Cornaro Piscopio, Philosophy, Padua 1678
Laura Bassi, Physics, Bologna 1732 who was also the first female professor in a scientific discipline: Experimental Physics, Bologna, 1776
First women M.D. in the world:
Margareth Ann Buckley, (*alias* James Miranda Stuart Barry), Edinburgh 1812, who disguised herself as **James Barry (1792?-1865)**, and made a distinguished career in the British medical military corp. Her female identity was discovered only after her death, at the autopsy that revealed even the signs of a pregnancy.
Elizabeth Backwell, New York 1849
First women M.D. in Italy:
Ernestina Paper, Florence 1877 (originally from Odessa). First year in Zurich.
Maria Valleda Farnè, Turin 1878
Anna Kuliscioff, Naples 1887
Maria Montessori, Rome 1894
First women M.D in Sardinia:
Paola Satta*, Cagliari 1902
Adelasia Cocco in Floris, Sassari 1913
Caterina Lombardi, Cagliari 1925, paediatrician.
In the light of new discoveries, at the beginning of the 20th century a great many sciences flourished including vitaminology and above all endocrinology, whose founder was **Charles E. Brown Sequard (1817-1894)**. The most important discoveries in this field were made in the 1920s by **Charles H. Best (1899-1978)**, **Frederick G. Banting (1891-1941)** and **John J. Mac Leod**

(1876-1935) in Toronto (the two latter physicians were awarded the Nobel prize for this work in 1923). They discovered that diabetes, a widespread disease and fatal at that time, could be cured with insulin, a hormone produced by the pancreas, and from which it could be extracted. Some years late, in 1935, **Gerhard Domagk (1895-1964)**, a student of Ehrlich, by starting with a derivative of aniline discovered prontosil-rubrum, precursor of a class of chemotherapeutic drugs: the sulphamides. In a time when infectious diseases decimated the population to such an extent that life expectancy was about 60 years, the sulphamides become very important. Moreover, they were immediately produced everywhere on a large scale because they were based on aniline, a molecule that was under international patent since many years. Some time later, a group of scientists at the Pasteur Institute in Paris, among whom were **Federico Nitti (1905-1947)** and **Daniel Bovet (1907-1992)**, discovered the reason why the sulphamides were effective *in vivo* and not *in vitro* (in culture): in order to be effective it was necessary for one part of the molecule to be removed when the drug entered the organism. Daniel Bovet, who later became professor of Pharmacology at the University of Sassari, was awarded the Nobel prize in 1957 for his work on antihistamines.

Alexander Fleming, discoverer of penicillin

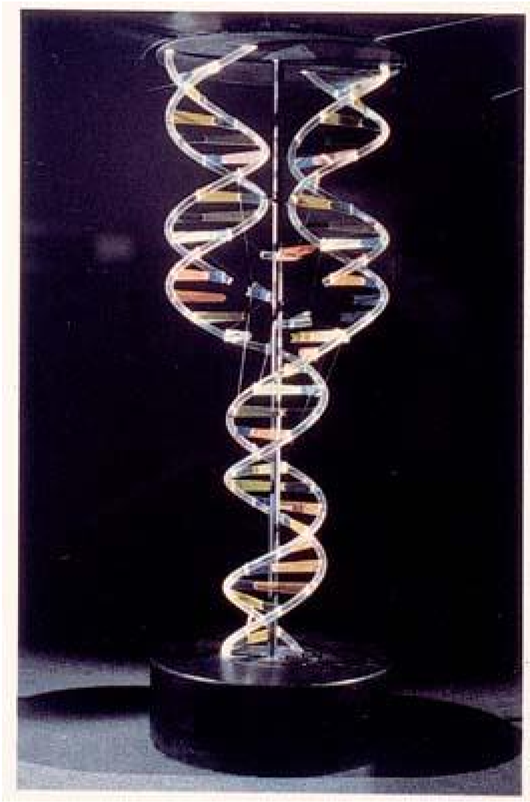
Meanwhile, the first antibiotic penicillin was discovered in 1928. The British bacteriologist **Alexander Fleming (1881-1955)** discovered that on a Petri dish he had left near a window, areas of inhibition had formed in which germs had not grown. He deduced that there must have been something blocking the growth of the micro-organisms, so he asked a colleague to analyse the culture and a fungus was found. However, he was mistaken in his initial analysis for instead of *"Penicillum notatum"* (which inhibited the growth of bacteria) he identified another, ineffective, *Penicillum*. Fleming noticed the error, and published the work on *Penicillum notatum* which, however, was then only used to clean bacteriological cultures rather than as a pharmaceutical drug. In the Second World War it became necessary to find a drug to fight at least some of the numerous infections, so under the auspices of both the British and the American governments the Jewish chemist of German origin **Boris Chain (1906-1979)**, and the Australian doctor **Howard Florey (1898-1968)**, worked together to make penicillin a pharmaceutical drug. They were employed for an enormously important purpose and they began to produce penicillin in Britain and in America on a large scale as soon as possible (1941). However, it became an Allied monopoly, so to obtain it in Italy, at that time, "gold" had to be paid on the black market. After penicillin, another antibiotic was discovered by **Selman Abraham Wacksman (1888-1973)** in 1944: streptomycin. This drug was effective against tubercular *mycobacteria* and even though it is toxic to an extent, it is still used today.

These were years in which great medical progress was made.
Margaret Sanger (1879-1966) was born in a time when contraceptives were criminalized in almost all the world. One of eleven children born to a working class Irish Catholic family in Corning, New York, at 19 years Margaret saw her 50 years old mother die of tuberculosis, following eleven childbirths and seven miscarriages. Trained as a nurse in New York, Margaret Sanger devoted her life to legalizing birth control and making it universally available for women. In 1914 she coined the term "birth control" and soon began to provide women with information and contraceptives. After having been repeatedly arrested and indicted, in 1921 she founded the American Birth Control League and spent her next three decades campaigning to make available a safe and effective birth control.

Margaret Sanger

By the 1950s, however, although she had won many legal victories, Sanger was far from happy with the limited birth control options available to women. By a matter of facts, since the 1842 invention of the diaphragm in Europe and the introduction of the first full-length rubber condom in 1869, there had been no new advances in contraceptive methods. Since 1912 she had been dreaming of a "magic pill" for contraception that could provide women with cheap, safe, effective and female-controlled contraception. Her search ended in 1951 when she met **Gregory Goodwin Pincus (1903-1967)**, a medical expert in human reproduction who had been expelled from the University of Harward for having published a book on the *in vitro* fertilization of rabbit eggs, who was willing to take on the project and was searching for funds. Soon after, she found a sponsor in her rich friend **Katharine McCormick (1875-1967)** one of the first female ever graduated in technology. In the synthesis of hormones Pincus was aided by research chemists **Russell Marker (1902-1995)** and **Carl Djerassi (1923-2015)**; the clinical experimentation was carried in Puerto Rico by a catholic physician, **John Rock (1890-1984)**. Their collaboration would lead in 1960 to the first oral contraceptive (Enovid). In Italy birth control was approved only in 1971.
George Papanicolau (1883-1962) perfected a method for colouring and collecting vaginal strips (the Pap-test); so thanks to him prevention of tumours in the uterine cervix made "huge steps forward".
1949: The discovery of Sickle Cell Anaemia (the first molecular disease) caused by a mutation causing the substitution of an amino acid in the Hb protein beta chains (**Linus Pauling 1901-**

1994).



Watson and Crick's model of the double helix

1953: The discovery of the double helix model of DNA (**James Dewey Watson, 1928-2004**, and **Francis Harry C. Crick, 1916-1953**).
Another important discovery was that of neurotransmitters identified by **Julius Axerold (1912-2014)**, **Ulf Svante von Euler (1905-1983)**, **Bernard Katz (1911-2003)**, **Henry Hallet Dale (1873-1981)**, **Otto Loewi (1873-1981)**. Significant contributions on the understanding of neurotransmitters function and pharmacology have been produced at the University of Cagliari by **Gian Luigi Gessa (1932-)** and his School. In 1983 **Françoise Barré Sinoussi (1943-)** and **Luc Montagner (1932-)** discovered the virus AIDS HIV.
In the 1960s anticancer preventive medicine was developed following identification of carcinogenic agents such as tobacco smoke, dioxin, and so on.
In addition, transplanting organs (see tables) became a possibility. The pioneer of this type of operation (in the early 20th century) was a French scientist who settled in America, **Alexis Carrel (1873-1944)** who managed to keep human cells alive on a plate and then attempted transplants on animals.
1967: The first heart transplant was carried out in South Africa by **Christian Barnard (1922-2001)**. Unfortunately Barnard's attempts failed because Cyclosporin was not available (it was introduced in 1978 thanks to **Jean Borel**) so these patients only survived for a short period after the transplant. Cyclosporin is a drug which induces immuno-suppression thus impeding the likelihood of the new organ being rejected (that is, the new organ being attacked by the recipient's immune system).
The first heart transplant to take place in Italy was carried out by **Vincenzo Gallucci (1935-1991)** in 1985 in Padova, and the second by **Mario Viganò** in the same month of the same year in Pavia. Mario Viganò also carried out both the first heart-lung transplant and the first permanent artificial heart implant in Italy. The first liver transplant was carried out in Colorado in 1967 and by **Raffaello Cortesini** in Italy in 1982. In Sardinia transplants of Bone marrow, Heart, Kidney and Liver are currently performed both in Cagliari and in Sassari.

Dame Cicely Saunders the Doctor who invented Palliative Care and the Hospice

Cicely Saunders was born in London on June 22, 1918, the eldest of three children, to a wealthy family who moved to southern England. After high school she was admitted to St Anne College in London where she enrolled in the faculty of political science, philosophy and economics. In 1939, at the outbreak of the world war she left the university, to which returned later, to attend as a volunteer the Nursing School of St Thomas's and other large London hospitals. She soon distinguished herself for her dedication to patients and, in particular, for those in terminal state, often left to die alone, without adequate analgesic therapy and psychological support. Despite the hard work and the consequent aggravation of her scoliosis, she took the nursing diploma and, shortly thereafter, that of social worker to be close to the most serious patients. These titles allowed her, in 1947, to become part of the structure of St. Thomas's Hospital specialized in the treatment of cancer patients and in other institutions for terminally ill patients. Her affective participation in the desperate situation of the patients led her to a spiritual crisis and the consequent conversion to the Evangelical Church. Since she was convinced that to achieve an improvement in the conditions of the patients, her action would have had much greater weight if she had been a doctor, in 1951, at the age of 33, she enrolled in medicine. She obtained her degree in 1957, despite her heavy welfare commitments. Cecily then attended the school of clinical pharmacology at St Mary's Hospital to investigate, with research, the effects of opioids on "total" (physical and moral) pain of the dying. Her results, in line with her long care experience, had a wide resonance not only in the scientific environment, but in public opinion as well. Cicely showed, in fact, that treatment with opioids, administered orally at moderate doses and at regular intervals, was much more effective and not addictive, as was the case with the old protocol of administration at the request of the patient. Another important effect on the patient's condition were affective-psychological and environmental support. Based on these assumptions, Saunders managed, in 1967, to open the St. Christopher Hospice in London, an institution that hosted (and still hosts), free of charge, in addition to terminally ill cancer or other diseases, chronic bedridden patients, alone and without hope of recovery. Palliative care had to be personalized and provided, even with the help of volunteers, including family members of the same hospitalized, by doctors and nurses with proved humanity and dedication to the sick. By the oral administration of analgesic drugs at appropriate dosages and at predetermined intervals, patients remained autonomous and conscious, with reduced perception of physical pain. In addition, the human warmth of the health care personnel and of the volunteers, the comfort of the environment, the psychological support, made the terminal stages of the incurable disease much more bearable.

Thanks to Saunders' managerial and propaganda skills, the surprising results obtained at St Christopher led to the diffusion, first in the United States and then in the entire world, of Hospices operating according to her criteria. Cicely refused to propose a hierarchical control structure, but he wanted the Hospices to be free and autonomous structures, based on the principles set out above. In Italy they are managed directly by the Regional Healthcare Service or by voluntary associations and consortia affiliated with the Service itself. By statute, the Hospice is a place of welcome and hospitalization aimed at offering the best Palliative Care to sick people when home care cannot be implemented. It also provides temporary hospitalizations for relief to families engaged in assistance.

Cicely, after receiving prestigious awards and recognitions, among which the title of Dame (the equivalent of Sir) died, at 87 years old, of cancer, precisely in the same St Christopher where, in 1995, her beloved husband also had passed away.

Transplants in the world

1902	Alexis Carrel	develops a technique to join blood vessels, indispensable in organ transplantation
1943	Willem J Kolf	constructs the first artificial kidney
1944	Peter Medawar	demonstrates that rejection is a immune-related phenomenon
1954	Joseph Murray	first kidney transplant in identical twins
1958	Georges Mathé	first bone marrow transplantation
1960	Renè Kuss	first kidney transplant
1966	William D. Keyy Richard Lillehei	first pancreas transplant
1967	Christian Barnard	first heart transplant
1967	Thomas Starzl	first liver transplant
1968	Frits Derom	first lung transplantation
1978	Roy Calne	first clinical use of cyclosporin, discovered by Jean Borel
1981	Norman Shumway Bruce Reitz	first heart-lung transplant
1982	William C. DeVries	first artificial heart transplant
1986	Joel Cooper	first lungs transplantation
1991 1997	RV Rajotte et al. A.Secchi et al.	Islet transplantion with insulin independence
1998	Jean Michel Dubernard	first hand transplant
2005	Bernard Duvauchelle e Jean Michel Dubernard (Amiens-Lyon)	face transplantion
2010	Joan Pere Barret e Coll.	total face transplantation
the list refers to successful organ allotransplantations and associated accessory techniques in humans		

Transplants in Italy

1976	Piero Confortini, Edmondo Malan e Girolamo Sirchia - Ospedale Maggiore Milano	promote the Nord Italian Trasnsplant (NITp) program, in order to coordinate transplant activity (then limited to Kidney) in the North of Italy
1976	Alberto Marmont, Genova	bone marrow
1981	Egidio Tosatti, Genova	pancreas
1982	Raffaello Cortesini, Roma	liver
1985	Vincenzo Gallucci, Padova	heart
1987	Mario Viganò, Pavia	artificial heart
1991	Mario Viganò, Pavia	heart-lung
1991	Costante Ricci, Roma	lung
1997	Antonio Secchi et al.	inslet tranplantation with insulin independence
2000	Marco Lanzetta, Monza	hand
2005	Luciano De Carlis e Vincenzo Sansalone, Ospedale Niguarda Milano	liver-pancreas
2009	Mario Viganò, Andrea D’Armini, Giulio	first heart –lung transplant supported by ECMO

	Orlandoni, Pasquale Totaro, Roberto Veronesi, Bruno Lusona, Maddalena Gerletti, Pavia	(extra corporeal membrane oxygenation) on a patient sent from another hospital

Note: The list concerning transplants both in the world and in Italy is incomplete and arbitrary owing to the difficulty of collecting and verifying the relevant data.

Rita Levi Montalcini

Furthermore, it is thanks to the Italian scientist **Rita Levi Montalcini (1909-2012)** that the Nerve Growth Factor was discovered. NGF is important in the prevention of certain diseases such as Alzheimer. It was a discovery that was to win her the Nobel Prize for medicine in 1986 together with **Stanley Cohen (1922-)**.

However, it must not be forgotten that notwithstanding the great progress made, some infectious diseases still were widespread, one of which was poliomyelitis caused by the polio virus (it is sufficient to remember that a whole wing of the pediatric hospital of Cagliari was given over to polio victims).

Poliomyelitis was a devastating disease as it destroyed the medullar alpha motoneurons causing flaccid paralysis, atrophy of the muscular tissue which was replaced with connective tissue, and problems in bone formation. This disease was eradicated thanks to a vaccine developed (with dead germs) in America by **Jonas Edward Salk (1914- 1995)** in 1955, ten years after polio victim President Roosevelt had passed away. The vaccine was immediately used on a large scale, but, unfortunately, there were serious complications because some germ cell types were not killed and, once injected, caused the very disease, poliomyelitis, that they were supposed to prevent. Later **Albert Bruce Sabin (1906-1993)**, introduced the oral vaccination (which was introduced in Italy at the beginning of the 1970s). This vaccine is prepared as a live attenuated strain that embeds itself in the intestinal mucosa where it replicates and having lost most of its neurotropism, does not usually produce complications in the nervous system. After a period

when both types of vaccine were used, the one still employed is that of Salk.
Oncology and cancer therapy At first the only therapy was the surgical removal of the tumour. In the last decades of the XIX century the American surgeon **William Steward Halsted (1852-1922**) introduced the radical removal of the diseased organ, of adjacent tissues and of lymph nodes and this practice, particularly in the case of mammary gland, was continued to the mid-1970s

Early attempts to treat tumours by x ray-therapy were performed at the beginning of 1900 by the irradiation of the lymph nodes and of the spleen in the course of certain malignant blood diseases. Unfortunately, in the early times the excessive usage of Radium, due to a complete ignorance of its dangerous side effects, caused serious lesions. With time the development of new techniques and of nuclear medicine radiation procedures became progressively more efficacious on malignant cells and less dangerous for the normal ones

Cancer chemotherapy, viz the use of drugs (called radio mimetic) capable of selectively killing tumour cell, originated from a war event kept strictly secret by U.S. military intelligence. On December 2 1943, following the conquest of South Italy, an American ship at anchor in the harbor of Bari was hit by a German air raid and sunk with all its secret load of 70 tons of mustard gas (yperite). American sailors and Italians resident around the harbour, were badly intoxicated and several hundredths of men and women subsequently died. As autopsy of the victims demonstrated that the gas, alike radiations, had selectively destroyed white blood cells precursors of their bone marrow, the American pharmacologists **Louis Goodman (1906-2000)** and **Alfred Gilman (1908-1984)** had the idea of using yperite derivatives to treat patients with malignant lymphomas. Although early attempts gave only temporary results with serious side effects, cancer chemotherapy was progressively improved, becoming more efficacious and less toxic.

A great improvement in the prognosis of tumours, and particularly on those of the mammary gland, happened in **1972-75** at the Istituto Tumori of Milan thanks to **Gianni Bonadonna (1934-2015)** and **Umberto Veronesi (1925-2016)** who demonstrated (by the so called protocol of Milan) that the association of conservative surgery with chemo- and radiotherapy had highly beneficial effects.

In recent years the discoveries on immunology (monoclonal antibodies), molecular biology, genetics (oncogenes and tumour suppressor genes) and nuclear medicine lead to new and substantial successes in several kinds of neoplasms.

Beside the resounding successes due to organ transplantation, the grafting of various tissues and cells and the availability of artificial prosthesis, outstanding therapeutic results, prompted by progress in basic sciences, are obtained by the constant development of drugs active on the most widespread diseases.

Recent achievements which have greatly reduced the frequency and invasiveness of open surgery are obtained by interventional radiology which encompasses all mini- invasive procedures guided by imaging techniques such as angiography, fluoroscopy, CAT, MRI, echography, robotics, etc. The imaging techniques combined with the use of catheters allow the insertion, transcutaneously or by venous or arterial routes, of devices such as the pacemaker and the defibrillator that can regulate or stimulate cardiac activity. Likewise, other stimulators are inserted into some cerebral areas or peripherally, in order to control motor syndromes or the perception of pain. Moreover, the use of catheters under visual control is employed for the removal of emboli, thrombus and aneurysms of the peripheral and / or cerebral circulation.

Endoscopy, thanks to catheterization through natural orifices has found important applications in disciplines such as urology, gynecology, otorhinolaryngology. Finally, important results have been achieved in the understanding of the physiological phenomena that occur in sleep and in the influence that sleep disorders have on the genesis of diseases such as depression,

Alzheimer's disease, learning deficit, cardiovascular diseases, cancer etc.
Finally, we must signalize the spectacular results recently obtained by medical genetics. Following the definition of the entire human genome, carried out by a team led by **Renato Dulbecco (1914-2012)**, scientists have devised techniques, such as the CRISPR/Cas **(Francisco Mojica (1963-)**, **Jennifer Doudna (1964-)**, **Emmanuelle Charpentier (1968-)**, **Feng Zhang (1982-)** and others) that promise to edit or substitute, even in man, altered genes, as already done in plants and animals. (see in Bibliography the books by Meldolesi A, 1917 and of Doudna J and Sernberg S, 2017). https://en.wikipedia.org/wiki/CRISPR

The Discovery of Cephalosporin *

The Professor of Hygiene of the University of Cagliari, Giuseppe Brotzu (1895-1976), wondered why typhoid fever was less virulent in his city than elsewhere. He had formulated various hypotheses, all in vain. One day, while he was passing through the neighbourhood of the bay of “Su Siccu” he saw some young people bathing in the sea, just in the waters where Cagliari sewer system debouches without contracting the disease.

Su Siccu, near the harbor of Cagliari, the site where cephalosporin was discovered

So he took a sample of the water to test its effect on a culture of Salmonella typhi. Since it was wartime and there was no meat to make the broth for the culture medium, Brotzu used the placentas obtained from the maternity ward, that he then boiled in order to obtain the medium. With the help of his assistant **Antonio Spanedda (1907-1998)**, he isolated from this water a fungus that in 1948 he identified as *cephalosporium acremonium*; it produced an effective substance against Gram-negative bacteria- (the typhoid is in fact caused by *Salmonella typhi*, which like all the *enterobacteriaceae* is Gram- negative) however, the fungal extract he had prepared was a raw compound which could not be produced on a larges scale. When Brotzu asked for funding from the Italian Committee for research it was not given to him for political reasons since he had previously adhered to Fascism, as did almost all Italian university professors. Moreover, Brotzu dedicated himself less to research because he got more involved in politics, first becoming Mayor of Cagliari and then President of the Region of Sardinia.

Giuseppe Brotzu

Memorial plaque placed by the Municipality of Cagliari on the gate of the Institute of Hygiene, in 2001 twenty-fifth anniversary of his death, on the initiative of Alessandro Riva

* The notes on the discovery of cefalosporin are taken from the book by Paracchini R: "Il signore delle cefalosporine". Demos, Cagliari. 1992. Information of the first female M.D. in Sardinia come from the article by Enrico Fanni: Paola Satta la prima donna medico sarda. Bollettino Ordine dei Medici della Provincia di Cagliari, 6: 14-15, 2008

Final comment

During fascist times, Brotzu had already been involved in the fight against malaria. After the war he was a consultant to the **Rockefeller Foundation** which, thanks to land reclamation and the massive use of DDT, succeeded in eradicating malaria (1950) by eliminating its carrier. Notwithstanding his great merits (for having discovered the cephalosporium he was proposed for the Nobel Prize) he is not usually mentioned in Italian texts, whereas, in contrast, he is

named in pharmacological textbooks throughout the world.
Not finding financiers in Italy Brotzu asked for help **Dr. Blyth Brooke**, an English health officer with whom he had collaborated during the anti-malarial campaign in Sardinia. Brooke questioned the Medical Research Council in London who advised him to send a culture of the mold and a copy of Brotzu's paper to **Howard Florey**, the discoverer of Penicillin. Florey entrusted the study of the therapeutic potential of cephalosporium to the biochemist **Abraham Edward (1913-1999).** The latter together with **Guy GF Newton** isolated the first cephalosporin in 1949. The drug was then marketed with an enormous profit by the pharmaceutical companies Glaxo and Lilly. Brotzu did not ask for any economic recognition: even the modest sum of 25,000 pounds that was awarded to him by the Research Council as a share of its royalties, it was totally donated by him to the University of Cagliari.
The drug was then sold throughout the world by the pharmaceutical companies Glaxo and Lilly making an enormous profit for them.
During these lessons the way in which the concept of “Medicine” has changed through the centuries has been seen. Initially holistic conceptualizations predominated that placed man at the centre of everything (because it was no possible to define the diseases and their causes). Successively, especially from Morgagni onwards, medicine passed to a reductionist conceptualization (from the study of the organ, to the tissue, to the cell, to the molecule). This has brought about an increased specialization that while positive, has placed the disease at its centre rather than humankind. It is necessary to consider the organism itself, the human in his or her entirety as a microcosm composed of body and psyche.

Appendix

The Nobel Prize for Medicine

1901	EMIL ADOLF VON BEHRING (Germany) Research on serum therapy and treatment of diphtheria
1902	RONALD ROSS (GB) Studies on malaria
1903	NIELS RYBERG FINSEN (Denmark) Treatment of diseases with light radiation (phototherapy)
1904	IVAN PETROVIC PAVLOV (Russia) Studies of the physiology of digestion
1905	R0BERT KOCH (Germany) Research on tuberculosis
1906	CAMILLO GOLGI (Italy) and SANTIAGO RAMON Y CAJAL (Spain) Research on the nervous system
1907	CHARLES LOUIS ALPHONSE LAVERAN (France) Research on protozoa
1908	ILJA IL'JICH MECHNIKOV (Russia-France) and PAUL EHRLICH (Germany) Studies on immunity
1909	EMIL THEODOR KOCHER (Switzerland) Research on thyroid disease
1910	ALBRECHT KOSSEL (Germany) Studies of cellular chemistry
1911	ALLVAR GULLSTRAND (Sweden) Research on dioptric media eye
1912	ALEXIS CARREL (France-USA) Transplantation studies and sutures of blood vessels
1913	CHARLES ROBERT RICHET (France) Researches on anaphylaxis
1914	ROBERT BARANY (Austria) Studies on the apparatus vestibular
1919	JULES BORDET (Belgium) Studies on immunity
1920	SCHACK AUGUST STEENBERGER KROGH (Denmark) Studies on the capillaries
1921	unassigned
1922	ARCHIBALD VIVIAN HILL (GB) OTTO FRIZ MEYERHOF (Germany) Studies on the physiology of muscles
1923	FREDERICK GRANT BANTING and JOHN JAMES RICHARD MACLEOD (Canada) Discovery of insulin
1924	WILLEM EINTHOVEN (Netherlands) Mechanisms electrocardiogram
1925	unassigned
1926	JOHANNES ANDREAS GRIB FIBIGER (Denmark) Studies on carcinomas
1927	JULIUS WAGNER VON JAUREGG (Austria)

	Studies on malariotherapy in paralytic dementia
1928	CHARLES JULES HENRI NICOLLE (France-Tunisia) Studies on thyphus
1929	FREDERICK GOWLAND HOPKINS (GB) Studies on nutritional factors CHRISTIAAN EIJKMAN (Netherlands) Studies on beriberi
1930	KARL LANDSTEINER (Austria-USA) Studies on blood groups
1931	OTTO HEINRICH VON WARBURG (Germany) Studies on enzymes
1932	EDGAR DOUGLAS ADRIAN and CHARLES SCOTT SHERRINGTON (GB) Studies on the physiology of the neuron
1933	THOMAS HUNT MORGAN (USA) Studies on chromosomes
1934	GEORGE RICHARD MINOT, WILLIAM PARRY MURPHY and GEORGE HOYT WIPPLE (USA) Treatment of anemia
1935	HANS SPEMANN (Germany) Studies on embryonic development
1936	HENRY HALLET DALE (GB) and OTTO LOEWI (Austria) Chemical transmission of nerve impulses
1937	ALBERT SZENT-GYORGYI VON NAGYRAPOLT (Hungary) Studies on vitamin C
1938	CORNEILLE JEAN-FRANCOIS HEYMANS (Belgium) Studies on the mechanisms of breathing
1939	GERHARD DOMAGK (Germany) Studies of the antibacterial effects of sulfonamides
1943	HENRIK CARL PETER DAM (Denmark) EDWARD ADELBERT Doisy (USA) Discovery of vitamin K
1944	HERBERT SPENSER GASSER and JOSEPH ERLANGER (USA) Studies on nerve fibers
1945	ERNST BORIS CHAIN, ALEXANDER FLEMING and HOWARD WALTER FLOREY (GB) Discovery of Penicillin
1946	HERMANN JOSEPH MULLER (USA) Studies on the effect of radiation mutations
1947	BERNARDO ALBERTO HOUSSAY (Argentina) Research on the role of the pituitary gland in sugar metabolism CARL FERDINAND CORI and GERTY THERESA RADNITZ CORI (USA) Studies on glycogen metabolism
1948	PAUL HERMANN MUELLER (Switzerland) Effectiveness of DDT
1949	WALTER RUDOLF HESS (Switzerland) Studies on diencephalon ANTONIO CAETANO DE ABREU FREIRE EGAS MONIZ (Portugal) Application of leucotomy
1950	EDWARD CALVIN KENDALL (USA), PHILIP SHOWALTER HENCH (USA) and TADEUS REICHSTEIN (Switzerland) Studies on the adrenal hormones

1951	MAX THEILER (USA-South Africa) Studies on yellow fever
1952	SELMAN ABRAHAM WAKSMAN (USA) Discovery of streptomycin
1953	FRITZ ALBERT LIPMANN (USA) Discovery of Coenzyme-A HANS ADOLF KREBS (GB) Studies on the citric acid cycle
1954	JOHN FRANKLIN ENDERS, FREDERICK CHAPMAN ROBBINS and THOMAS HUCKLE WELLER (USA) Studies on the polio virus
1955	AXEL HUGO THEODOR THEORELL (Sweden) Studies on enzymes oxidants
1956	ANDRÉ FREDERIC COURNAND (USA), WERNER FORSSMANN (Germany) and DICKINSON W. RICHARDS JR. (USA) Studies on disease circulatory and cardiac catheterization
1957	DANIEL BOVET (Switzerland-Italy) Studies on antagonists of acetylcholine, adrenalin and histamine
1958	GEORGE WELLS BEADLE and EDWARD LAWRIE TATUM (USA) The study of genes as regulators of chemical events JOSHUA LEDERBERG (USA) Studies on the genetic material of bacteria
1959	ARTHUR KORNBERG and SEVERO OCHOA (USA) Studies of RNA and DNA
1960	FRANK MACFARLANE BURNET (Australia) and C. PETER BRIAN MEDAWAR (GB) Studies on acquired immunological tolerance
1961	GEORG VON BEKESY (USA) Studies on the cochlea
1962	FRANCIS HARRY COMPTON CRICK (GB), JAMES DEWEY WATSON (USA) and MAURICE HUGH FREDERICK WILKINS (GB) Studies of the structure of nucleic acids and genetic information
1963	JOHN CAREW ECCLES (Australia), ALAN LLOYD HODGKIN Studies on nerve impulse and synaptic transmission
1964	KONRAD EMIL BLOCH (Germany-USA) and FEODOR LYNEN (Germany) Studies on the metabolism of cholesterol and fatty acids
1965	FRANCOIS JACOB, ANDRÉ MICHAEL LWOFF and JACQUES MONOD (France) Discoveries on the genetic control of the synthesis of enzymes and viruses
1966	PEYTON ROUS (USA) Discovery of oncogenic viruses CHARLES BRENTON HUGGINS (USA) Research on the hormonal treatment of prostate cancer
1967	ARTHUR RAGNAR GRANIT (Finlandia-Sweden), HALDAN KEFFER HARTLINE and GEORGE WALD (USA) Studies on the physiology of visual processes
1968	ROBERT W. HOLLEY, HAR GOBIND and MARSHALL WARREN NIRENBERG (USA) Studies on the genetic code and function in protein synthesis
1969	MAX DELBRUECK (USA), ALFRED D. HERSHEY (USA) and SALVADOR E. LURIA (Italy-USA) Studies on the virus genetics and on the mechanisms of replication
1970	JULIUS AXELROD (USA), ULF SVANTE VON EULER (Sweden)e BERNARD KATZ (GB)

	Studies of chemical mediators in nerve endings
1971	EARL WILBUR SUTHERLAND JR. (USA) Studies on the mechanism of action of hormones
1972	GERALD MAURICE EDELMAN (USA) and RODNEY ROBERT PORTER (GB) Studies on the chemical structure of antibodies
1973	KARL VON FRISCH (Germany), KONRAD LORENZ (Austria) and NIKOLAS TINBERGEN (GB) Behavioral studies
1974	ALBERT CLAUDE (Belgium), CHRISTIAN DE DUVE (Belgium)and GEORGE E. PALADE (USA) Research on cell structure and cell physiology
1975	DAVID BALTIMORE (USA), RENATO DULBECCO (Usa-GB) and HOWARD MARTIN TEMIN (USA) Research on the relationship between tumor viruses and the genetic material cell
1976	BARUCH SAMUEL BLUMBERG and DANIEL CARLETON GAJDUSEK (USA) For their discoveries concerning new mechanisms for the origin and dissemination of infectious diseases
1977	ROSALYN YALOW, ROGER GUILLEMIN and ANDREW SCHALLY (USA) Studies on radioimmunoassay of protein hormones in the brain
1978	WERNER ARBER (Switzerland), DANIEL NATIAANS and HAMILTON 0. SMITH (USA) Discovery of restriction enzymes and their use in the field of genetics
1979	GODFREY N. HOUNSFIELD (GB) and ALLAN MACLEOD CORMACK (USA) Studies of computed tomography
1980	BARUI BENACERRAF (Venezuela-USA), JEAN DAUSSET (France) Research on the cellular structures of regulating immunological reactions
1981	ROGER W. SPERRY (USA) Studies on the functional specialization of the cerebral hemispheres DAVID H. HUBEL (USA) and TORSTEN N. WIESEL (Sweden -USA) Research on the visual system
1982	SUNE K. BERGSTROM (Sweden), BENGT I. SAMUELSSON (Sweden) and JOHN R. VANE (GB) Research on prostaglandins
1983	BARBARA MCCLINTOCK (USA) Discovery of mobile genetic elements
1984	NIELS K. JERNE (Denmark-Switzerland), GEORGES J.F. KOHLER (Germany-Switzerland) and CESAR MILSTEIN (Argentina-GB) The immune system, and techniques for the production of monoclonal antibodies
1985	MICHAEL STUART BROWN and JOSEPH L. GOLDSTEIN (USA) Research on cholesterol metabolism
1986	STANLEY COHEN (USA) and RITA LEVI MONTALCINI (Italy-USA) Discoveries of growth factors
1987	SUSUMU TONEGAWA (Japan-USA) Discovery of the principles of genetic diversity antibody
1988	JAMES W. BLACK (GB), GERTRUDE B. ELION and GEORGE H. HITCHINGS (USA) Studies on the principles of pharmacological treatment
1989	MICHAEL J. BISHOP and HAROLD ELIOT VARMUS (USA) Studies on retrovirus oncogenes
1990	JOSEPH E. MURRAY and DONNALL THOMAS (USA) Research on transplants
1991	ERWIN NEHER and BERT SAKMANN (Germany) Studies on intracellular ion fluxes
1992	EDMOND FISCHER and EDWIN KREBS (USA)

	Discoveries in the field of protein and oxidative phosphorylation
1993	RICHARD J. ROBERTS (GB) C PHILLIP A. SHARP (USA) Studies on the discontinuous construction of genes
1994	ALFRED GILMAN and MARTIN RODBELL (USA) Discovery in the field of the study of proteins and on their role as cell signal transductions
1995	CRISTIANE NEUSSLEIN-VOLHARD (Germany); ERIC WIESCHAUS and EDWARD LEWIS (USA) Discoveries in the genetic control of embryonic development
1996	PETER DOHERTY (Australia) and ROLF ZINKERNAGEL (Switzerland) Studies on the immune system and the ability of virus recognition by T-lymphocytes
1997	STANLEY B. PRUSINER (USA) Discovery of prions, a new biological principle of infection
1998	ROBERT F. FURCHGOTT, LOUIS J. IGNARRO and FERID MURAD (USA) Discoveries on the action of NO on the cardiovascular system
1999	GÜNTER BLOBEL (USA) Discovery that proteins have intrinsic signals that govern their transport and localization in the cell
2000	ARVID CARLSSON (Sweden), PAUL GRENGARD, ERIC R. KANDEL (USA) Signal transduction in the nervous system
2001	LELAND H. HARTWELL (USA), R. TIMOTHY HUNT, PAUL M. NURSE (GB) Cell cycle regulation
2002	SYDNEY BRENNER (GB), H. ROBERT HORVITZ (USA), JOHN E. SULSTON (GB) Genetic regulation of organ development and programmed cell death
2003	PAUL C. LAUTERBUR (USA), Sir PETER MANSFIELD (GB) For discoveries concerning magnetic resonance imaging
2004	RICHARD AXEL (USA), LINDA B. BUCK (USA) For discoveries on odorant receptors and organization of the olfactory system
2005	J. MARSHALL (Australia), J. ROBIN WARREN (Australia) For the discovery of the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease
2006	ANDREW Z. FIRE (USA), CRAIG C. MELLO (USA) For studies on RNA interference
2007	MARIO R. CAPECCHI (USA), SIR MARTIN J. EVANS (GB), OLIVER SMITHIES (USA) For discoveries on stem cells and recombinant DNA
2008	HARALD ZUR HAUSEN (Germany) For studies on the human papilloma virus as the cause of cervical cancer FRANÇOISE BARRÉ-SINOUSSI (France), LUC MONTAGNIER (France) For discoveries on the virus acquired immune deficiency (AIDS)
2009	Elizabeth H. Blackburn, Carol W. Greider (USA) and Jack W. Szostak (Canada) For discoveries on telomerase and processes of cellular aging
2010	Robert Geoffrey Edwards (GB) For IVF
2011	Bruce Beutler (USA) Jules Hoffmann (Luxembourg) For the discovery of the activation of innate immunity Ralph M. Steinman (Canada) For studies on dendritic cell and acquired immunity
2012	John Gurdon (GB) and Shinya Yamanaka (Japan) For discoveries on stem cells
2013	James E. Rothman (USA), Randy W. Skekman (USA) and Thomas C. Südhof (Germany)

	For the discovery of the regulatory mechanisms of intracellular vesicle trafficking
2014	John O'Keefe (GB-USA), Mary-Brit Molser and Edward Moser (Norway) For their discoveries of the cells that constitute the positioning system of the brain
2015	Youyou Tu (China) For the discovery of a new treatment for malaria William C. Campbell (Eire/USA) and Satoshi Omura (Japan) For new therapies against infection by parasitic worms
2016	Yoshinori Ohsumi (Japan) For the discovery on the mechanism of cellular recycling
2017	Joffrey C. Hall. Michael Rosbash, Michael W. Young (USA) For their discoveries on molecular mechanisms controlling the circadian rhythm
2018	Jim Allison (USA) and Tasuku Honio (Japan) for their discovery of cancer therapy by inhibition of negative immune regulation

2019 WILLIAM G. KAELIN JR (USA), SIR PETER J. RATCLIFFE (GB) AND GREGG L. SEMENZA (USA)
For their discoveries of how cells sense and adapt to oxygen availability

(Taken from "History of Medicine" - Bruno Zanobio and Giuseppe Armocida. Masson 1997; amended and updated)

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