

## At the origins of modern medicine

Giorgio Zanchin, Padova University Medical School, Italy

All of the historians agree on the extraordinary role played by the Republic of Venice as forerunner of public health legislation, by the University of Padova on the development of medical knowledge.

In Venice, the experience made during the epidemics of the XIV century contributed to the affirmation of the contagion hypothesis. This theory maintained that the cause of the plague, identified with the so called "miasma", corrupting the air and decomposing the bodies, could attach from an individual to another, or even adhere itself to clothing or to objects, thereafter passing to whoever touched them.

Accordingly, systematic measures of isolation, such as sanitary cordons, quarantine and disinfection were taken.

In 1423, the Senate ruled out to assign the monastery of Saint Mary of Nazareth to the isolation of people affected by the plague. Called the "old" *lazaret*, it was the first institution to be established for this purpose.

The place of origin of a traveller or of a ship was classified as *infected* ("in which the plague reigns"), *suspected* ("which borders with the infected one"), *suspended* ("which borders with the suspected") and *free* ("bearing no suspect of contagious disease").

In this last case, according to the habitual formula, the location was decreed as *healthy (thanks to God) and free from any doubt of contagious illness*: a "fede di sanità" that is a specific written license bearing this statement, was released in such a condition by the local sanitary officers.

Otherwise, only when the prescribed period of the quarantine was terminated without evidence of the plague the "*libera prattica*" (that is free entrance) was granted.

Even today in the "new" *lazaret* are still visible the "graffiti" done mostly during the sixteen century by people kept in isolation for such a long time.

The measures of prevention against the importation of the contagion included the disinfection of objects. The treatments varied according to the quality and value of the merchandise, but from a sanitary standpoint two large groups of merchandise were distinguished: "susceptible" and "not susceptible". Under the name of "susceptible" goods were encompassed those items that were considered to be able to transmit the contagion: these included materials that by their nature seemed to retain more easily the "contagious miasma" such as wool and clothes. To the contrary, "not susceptible" were those incapable of such a transmission.

Disinfection of the goods took place with the "*sborro*", that is the exposure to air and sun; or with heating, immersion in sea water, spraying with vinegar, ["perfuming" that is with] fumigation [which aimed at neutralizing the miasma substituting it with the "fumes" of aromatic woods, as we see from the brown appearance of the "fumigated" letter.]

The sanitary preoccupations of the Republic were particularly directed upon people and goods originating from the territories of the Ottoman Empire, and pesthouses were built in the Venetian possessions in the oriental Mediterranean sea to control the busy traffic with the Turkish domains, from where periodic bouts of epidemics originated.

About this context, we studied an important document, preserved in the State Archive of Venice. It is a detailed report [by the "Avvocato fiscale" (Public Attorney) Lorenzo Alugara] on the successful containment of the plague which reached the lagoon on an Ottoman ship in 1793.

The way we found it is rather curious.

Since the year 1521, the Venetian Doge used to have coined every year a special silver medal, called "*osella*", commemorating the most relevant events of the Serenissima Repubblica.

Being interested on the impact of the plague on the Venetian traditions, our research brought us to identify, among the 275 *osellas* coined until the end of the Venetian State, five occasions in which the coins were referring to the plague.

This rather unknown iconography appears indeed as a relevant document of the popular faith, since in most instances a religious symbolism is prominent. However, the picture of the last osella “of the plague series”, coined in 1793 under the Doge Manin and commemorating an episode of successful prevention of epidemics in Venice, makes reference not only to the Virgin protection, but also to factual measures of isolation: in the forefront we see the Virgin, encircled by the inscription “*Nec nuper defeci*” (Even in this distress I did not abandon you). In the background, the little church identifying the island of Poveglia, the last lazaret of Venice, is well recognizable, as well as a ship put in quarantine.

We were able to identify in the State Archives the detailed official report of this event.

On a “Tartanella”, a little commercial ship, with Ottoman flag and a crew of thirty people, a case of bubonic plague developed [with “*petacchie nere, antraci, buboni*”]. Strict preventative measures were immediately taken [“to stop the infection in the same place” in the Poveglia’s canal, that for this purpose was get rid of any other ship.] The crew, put ashore, was divided in affected and in suspected groups, which were held in separate locations. An internal ward of soldiers was established on the island; around it an external circle of armed ships was distributed. [As a whole, internal and external wards were formed by one hundred forty individuals, plus nine ships and two boats. Everything -food, water, garments- that was necessary for the well-being of the crew was brought ashore and continuous fires were kept alive to purify the air from the contagious miasma.]

At the end, twenty members of the Ottoman crew survived and the plague was successfully contained within the land. The feelings of gratitude for the Republic are well documented by a letter wrote to the Venice health officers by the captain and the surviving crew in their safe way home.

The examination of this primary source put in evidence relevant aspects of the Venetian fight against the plague. Indeed, the Serenissima [since the establishment in its lagoon of the first lazaret since 1423,] played for all the span of its history the role of pioneer and model for the measures adopted to prevent the diffusion of epidemics and the protection of public health.

Let’s now to consider the role of the Padova University on the development of modern medicine. The decline of the Roman empire and the establishment of a dichotomy between the terrestrial and the celestial world and between the body and the soul, started a downfall in the interest for the observation of nature.

Gradually, after the year one thousand, different factors contributed to a new attention focused upon the physical world: a relevant cultural event was the rediscovery in the Western world of numerous classical book. In particular, the knowledge of the so called “physical” writings of Aristotle originated a renewed interest in nature in opposition to theological themes. In those years, the Aristotelian interpretation given by the Moem Averroes (1126-1198) with the proposition of the double truth, allowed the believer to overcome the apparent contradiction between the revealed word and scientific knowledge.

As an expression of these renewed interest, throughout the course of the thirteen hundreds the dissection of the human body began to be performed in the North East of Italy, namely in Bologna and in Padova. Here we find Pietro d’ Abano, father of the Paduan Medical School, an iconic character supporting the averroism, who made the first local dissection for forensic reasons.

For all that concerns anatomical and physiological knowledge, strictly prevailing was the influence of Galen (131-201 p.c), whose teaching was transmitted in an acritical manner, emblematically represented by the modality in which were carried out the lessons in anatomy: the professor merely commented ex cathedra upon the text of Galen without assuming any direct role in the dissection. This latter was performed by the dissector whose role was purely manual and who was aided by a third individual, the ostensor, who pointed out in an orderly fashion the various organs.

With Venetian expansion of 1405, Padova became the site of the state university of the Saint Mark’s Republic. In Padova, studies had assumed a philosophical direction that emphasized the empiristic content of the biological works of Aristotle and favored, as a result, the observation of nature, an essential aspect of the revival of the anatomical investigations.

At least from the mid fourteenth-century examination of the cadaver for academic interest was codified in the statutes of the Paduan school, which established the obligation to proceed yearly with the anatomical dissection of at least two human bodies.

In this background was situated the activity of the pre-Vesalian anatomists in Padova, and in particular the teaching of Benedetti (ca. 1455-1525), who at the end of fourteenth century advocated the necessity of dissection, of the direct observation of the human body, in the formation of the physician: on a practical level, he realized the construction of a dismountable anatomical theatre, aimed to an improved instruction based precisely upon objectivity.

This was the cultural climate that surrounded Andreas Vesalius upon his arrival in Padova. It was during the five fruitful years spent (1537-1543) as a professor of surgery and anatomy at the same University of Padova where he graduated in medicine that *De humani corporis fabrica* was realized. Published in 1543, this work, considered the fundament of modern medical thought, is the result of the fruitful interaction between the personality of its author and the stimulating environment of the University of Padova, which Vesalius himself defined as "*the most illustrious in all the world*".

As we can see in the frontispiece, Vesalius worked unaccompanied at the dissecting table. The three individuals (lector, dissector and ostensor) taking part in the traditional demonstration of Galenic anatomy disappeared. The original character of Vesalius's teaching arose from the fusion of *homo sapiens* and *homo faber* into a single investigator.

In this revolutionary book, the dissected cadavers are illustrated according to the ideals of Renaissance beauty, with regard to the principles set forth by the Venetian school of Titian.

Vesalius's fostering of the use of anatomical illustration is pivotal since, for the first time in the history of medicine, iconography is not a mere ornament but an intrinsic and highly informative part of the contents that integrates the written morphological description with an immediate visual image.

Doubtless, the illustrations of the brain are extraordinarily realistic, possessing a naturalism that was previously unknown, as we can clearly see by comparing a selection of them with the representation of this organ given by Berengario da Carpi only 20 years before. Vesalius' images reveal for the first time a whole series of detailed anatomical structures, such as the venous sinuses and the meninges; the corpus callosum, the lateral ventricles and the choroid plexuses; the division between gray and white matter. Moreover, the base of the brain finds here its first representation, along with the origin of cranial nerves.

The way had been paved. After Vesalius, Columbus followed, who first described the small circulation; and later Fallopius, who gave outstanding contributions to the knowledge of cranial nerves and of the female reproductive system.

It is the golden era of the Paduan School of Medicine: attended by many foreign students who here converge from all of the European countries.

In those years Padova was the center of the medical Renaissance like Florence was the center of the artistic Renaissance.

In the same year when Vesalius' *De humani corporis fabrica* is published, da Monte introduces the method of clinical instruction at the bedside at the Hospital of San Francesco Grande. The critical attitude of the anatomist is transferred to the physician teaching at the bedside of the sick. Two years later, Girolamo Fracastoro in his *De contagione et contagiosis morbis* firstly explains the contagion by the presence of *Seminaria morbi*, foreseeing the microbial theories established only three centuries later.

In this century, Padova reaches an indisputable supremacy, documented by such events as the institution of two scientific vanguard structures, the first university botanical garden, and the first permanent anatomical theatre.

Established in 1545, the Botanical Garden allows the "*Ostensio simplicium*", that is the demonstration of the real plants, developed from the "*Lectura simplicium*", that is the mere literary description of the subject. Erected in 1594 by Fabrici D'Acquapendente, the Anatomical Theater is the material expression of the Paduan anatomical tradition at its apex. It became the model of the demonstrative teaching of anatomy in the various European universities, so that similar structures were to be erected by pupils going back from Padova to Leiden, Copenhagen, Basel, Uppsala.

Among the other great accomplishments of its promoter, Fabrici, we remember his embryological studies, the description of the venous valves and the collection of colored anatomical paintings which he left in his testament to the Venetian State. For this anatomical atlas, Fabrici is recognized as the first to sense the importance of colored illustrations for anatomical preparations, as it has been said:

*With a pictorial sensibility such as to give the realistic impression not only of the form, not only of the color of an organ, but also to say, of the physical state, of dry and soft, of rough and viscid, and even of the alteration made by manipulation.*

This idea sums up the most relevant scientific contribution of Fabrici, quoting the anonymous verse which parallels that one referring to the poet Virgil: "Acquapendente was my birthplace, I rest in Padova. My fame is entrusted to the theatre, to the anatomic tables, to the studies on the fetus and on the valves of the veins".

Fabrici was also the teacher of William Harvey, the discoverer of blood circulation. Attracted to Padova by the reputation of its University, the young Harvey got here his degree in medicine in 1602. After returning to England, in 1628 Harvey published his outstanding contribution, that is recognized as directly connected with his education in Padova, since there he learned of the existence of the valves of the veins from Fabrici and of the quantitative method from Galilei.

A second flourishing season of the Paduan Medical School occurred in the XVIII century, when Giovanni Battista Morgagni marked a turning point in medicine by the adoption of the anatomic-clinical approach to pathology, introducing a new paradigm for the classification and the understanding of diseases.

Morgagni (1682-1771) graduated in Bologna. Drawn by the cultural environment and freedom of thought of the Venetian Republic, [he came to Venice. In 1711 he was offered the Second Chair of Theoretical Medicine in Padova, and he held later the Chair of Anatomy in Padova for the rest of his life, for sixty years. Only at the age of 79 did Morgagni publish his most important work *De sedibus et causis morborum per anatomen indagatis*. Printed in 1761, this pivotal book, introducing the anatomo-clinical method laid down the fundament of contemporary medicine.

*De sedibus* is a collection of seventy letters, grouped into five books (respectively on diseases of the head, chest, abdomen, surgical treatment, and a supplement on the above topics). This work reports the results of about 700 dissections, which summarise the experience developed in more than half a century of research. Each case contains a description of the most significant symptoms, the result of the autopsy and, finally, the epicrisis of relation between clinical and autoptic findings.

While Hippocratic and Galenic medicine considered the disease as the disturbed balance of the four humors, Morgagni shifts focus from humors to organs, thus replacing *humoral medicine* with *solidistic medicine*. The disease must be investigated detecting the link between symptoms presented during life and lesions found in the cadaver: *Negabimus ullius morbi naturam et causas sine respondentibus cadaverum dissectionibus ... esse proponendam*, he says: that is "We state that it is not possible to put forward any hypothesis on the nature and the causes of a disease without the support of the dissection of cadavers" (*Nova institutionum medicarum idea*, 1712).

Hence, the modern nosography begins: a disease is now considered as an entity defined by a specific set of clinical signs and organic lesions.

Morgagni's innovative paradigm, the *anatomo-clinical method*, was also a remarkable stimulus to development of semiotics, focusing on the site of a disease through the addition to clinical examination of percussion and auscultation techniques.

When faced with a patient, the physician now seeks to detect in vivo the anatomical changes that, found in the cadavers of subjects who had presented similar conditions, had proven to be the cause of the disease: a mindset inconceivable within the framework of the humoral theory that believed in the involvement of the fluids of the whole body.

We performed a detailed original research on *De sedibus*, with reference to a specific topic, headache. The first step in diagnosis is the recognition of the benign nature of headache (*primary*) vs an underlying, potentially dangerous, cause (*secondary*). In *De sedibus* references to *primary headaches* are limited; instead, *secondary headaches* are prevailing throughout, as we can see when we consider the quotations on the pain of the head we identified in the first, second, third, fourth and fifth book.

All together, in *De sedibus*, among the 50 headache cases considered, only 8 are *primary*, being the remaining *secondary*. Clearly, this conflicts with epidemiological data, which report a 10:1 *primary* vs *secondary* ratio in the population.

A possible explanation could be found if we consider that in the *anatomo-clinical method* the finding of a underlying structural lesion is instrumental to put forward a pathogenetic hypothesis, as we see from the material causes identified in the pathogenesis of different *secondary headaches*, such as, possibly, for obstructive hydrocephalus, subarachnoid haemorrhage, purulent meningitis, cranial malformation. Instead, *primary headaches* (migraine, tension-type, cluster headache), with no organic cause, are scarcely treated in the *De sedibus*, probably because Morgagni is looking for a link between headache symptoms [, which he is very accurate to collect,] and anatomical changes, not detectable in these primary forms. Our investigation demonstrates that the headache chapter is coherently framed within the theory of solidistic medicine, the Morgagni's heritage, which continues to permeate modern clinical practice. The *anatomo-clinical paradigm* inaugurated a method that generates considerable results even today, when we make a diagnosis by exploiting the highly sophisticated devices, especially in the field of radiology, that enable us to capture images of the patient's internal organs.

Indeed, the way we diagnose a *secondary* headache continues the anatomo-clinical method first proposed by Morgagni in the Anatomical Theater in Padova: when, guided by symptoms, we make a diagnosis through neuroimaging, we carry out a "virtual autopsy" that enables us to view the organic lesion inside the living body, just like Morgagni taught to look for into the cadaver.

From the factual evidences I just presented, the attribute "cradle of modern medicine" recognized to Padova comes out as well deserved. Similarly, the Republic of Venice has to be considered the "cradle of public health".