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ABSTRACT. Abeloff MD, Gray R, Tarmey DC, et al. Randomized comparison of CMFPT versus CMFPT/VATHT and maintenance versus no maintenance tamoxifen in premenopausal, node positive breast cancer. An ECOG study. Proc Am Soc Clin Oncol 1991; 10, 43: abstr 47.

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Editoriale

Verso un futuro internazionale

La ricerca storico medica in Italia pare oggi aver trovato un canale divulgativo scientifico innovativo che sostiene apertamente la volontà espressa specialmente dai giovani ricercatori del settore: "apriamoci all'internazionalizzazione". *Medicina Historica* infatti, oltre ad aver ottenuto l'indicizzazione su Scopus già nel 2018, persegue le proprie ambizioni affermandosi all'interno delle classifiche del macro raggruppamento internazionale *Arts and Humanities* ed in particolare in quelle di *Medicine (miscellaneous)*, *History and Philosophy of Science* e *History*. Intendiamoci, questo rappresenta solamente l'inizio. L'inizio di una strada ancora lunga da percorrere ma riuscendo ancor meglio ad adattare il nostro veicolo ai modelli più aggiornati della letteratura scientifica internazionale non dovremmo più preoccuparci del tempo. La nostra rivista, espressione scientifica della Società Italiana di Storia della Medicina, attraverso la pubblicazione di articoli di ricerca delle tre principali divisioni del nostro settore scientifico disciplinare, MED/02 (Storia della Medicina, Paleopatologia e Bioetica), sottolinea, accresce e aggiorna le peculiarità che caratterizzano appunto la nostra ricerca.

Continuiamo così. Senza limitare la nostra aspirazione internazionale del far conoscere l'importante tradizione storico medica italiana al di fuori dei confini nazionali nelle sue diverse espressioni di ricerca scientifica.

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Editorial

Towards an international future

The historical medical research in Italy seems today to have found an innovative scientific spread channel that openly supports the will expressed especially by young researchers in our field: "let us open up to internationalization". In fact, *Medicina Historica*, in addition to having obtained indexation on Scopus as early as 2018, pursues its ambitions by establishing itself in the rankings of the international macro group *Arts and Humanities* and in particular in those of *Medicine (miscellaneous), History and Philosophy of Science* and *History*. But, this is only the beginning. The beginning of a road that still has a long way to go and if we could better adapt our vehicle to the most up-to-date models of international scientific literature we should no longer worry about time. Our Journal, a scientific expression of the Italian Society of the History of Medicine, through the publication of research articles of the three main divisions of our scientific disciplinary sector, MED/02 (History of Medicine, Paleopathology and Bioethics), emphasizes, enhances and updates the peculiarities that precisely characterize our research.

Let's keep going! Without limiting our international aspiration to make Italian historical medical tradition known beyond national borders in its various expressions of scientific research.

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Pancio of Controne (1275 ca.-1340), a Tuscan physician at the courts of Edward II and Edward III of England

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Abstract. This article focuses on the figure of Pancio of Controne, a 14th-century Tuscan physician who played a major role as archiater at the courts of the king Edward II (1307-1327) and Edward III (1327-1377). Through documents preserved in the English and Italian archives, it is possible to trace the biography of this illustrious physician and to reconstruct his social ascent and his economic activities. What emerges is a multi-faceted figure who devotes himself as much to medicine as to political and above all economic affairs, a range of activities that can be understood if they are read in the light of late medieval society and the Italian commercial expansion of the 13th-14th centuries.

Key words: medieval medicine, Lucca, Kingdom of England, Edward II, Edward III, court medicine

Introduction

The study of even one single figure, that of the lesser known Italian medieval physician Pancio of Controne from Lucca (†1340), can help understand the socio-cultural and economic aspects generally neglected by the more traditional forms of research into the late medieval history of Medicine.

In this paper, methodologically, we propose to investigate the biographical history of Pancio, as symptomatic of the condition of a successful 14th century physician, to develop the data obtained in a wider historical perspective and to reconstruct the socio-economic implications of the medical profession.

The historical sources of Pancio are not numerous but certainly important, above all to understand his economic activity during the English period of his life, when he became court physician under the reigns of King Edward II (1307-1327) and King Edward III (1327-1377).

The documents we analysed are stored in the Lucca State Archive (ASLu) – where there is an original copy of Pancio's will (1, 2), an essential source to reconstruct the social organization of his family – and in the English National Archives of the Public Record Office at Kew, London. In particular, the Patent Rolls, the Close Rolls under Kings Edward II and Edward III, and the Gascon Rolls in the years 1327-1338, are fundamental to understand how he handled his economic activities (3).

Birth and origins of Pancio

Pancio was born around 1275 in a village of *Controne*, a small region of the Lucca Apennines to the north of Lucca, in the valley of the Lima river. This is a mountainous area close to the Apennine chain, where people lived in various scattered villages. A very marginal area today, in the late Middle Ages it was important for at least two reasons: for its direct political link with the city of Lucca, and for its strategic position between Tuscany and northern Italy. At the beginning of the 13th century, Controne was one of the first mountain districts to fall under the direct control of the Commune of Lucca and to establish very close economic ties with the urban society. Furthermore, the position of the area, along the roads leading to Pistoia and to the Apennine passes, made it strategic for its connections with cities of the Emilia region, like Modena and Bologna (4).

Controne is also very close to Bagni di Corsena, a thermal bath that enjoyed a period of strong expansion in the 13th century, after the foundation in 1291 of a pilgrim hospital for thermal treatments, managed by a company of citizens from Lucca. From as early as 1299 the Hospital became direct property of the Commune of Lucca and, in 1347, the fatal year of the Plague, a dependency of the great urban Lucca Hospital of San Luca (5). This connection with thermal medicine, which developed strongly between the 13th and 14th centuries in Italy, may well have conditioned Pancio's choice of taking up medicine (6). Pancio is likely to have come into contact with medicine in the environment of local thermal baths, where it was certainly practised for the care of bathers; treatment was administered in the area of Val di Lima in stable manner starting from the late 1200s.

The family of Pancio was well rooted in this mountainous area. Pancio had probably been the richest member of his family and we may assume that his social position was truly remarkable, thanks to his studies and to the practice of the medical profession.

Education of Pancio

In the early Middle Ages Lucca already had an important local medical tradition, as can be inferred by some documents preserved in the Archiepiscopal Archive, where many physicians are recorded as witnesses in the Lombard, Carolingian and Ottonian parchments. In this period, the study of medicine was probably practised in the episcopal schools. After the year 1000 the medical tradition continued, and various physicians from Lucca were known: Rainerius, for example, was mentioned in a funerary epigraph of the 12th century housed in the Cathedral of Lucca (7). Bologna was the privileged university seat for the training of physicians from Tuscany, and from Lucca in particular (8). In the 13th century many students from Lucca were in Bologna; the *Studium* had a very close relationship with the medical tradition of Lucca, so that many prominent professors of medicine teaching in Bologna came from the Tuscan city. At the beginning of the 13th century Ugo Borgognoni (1180-1258) left Lucca for Bologna, where he gave impetus to the medical studies by teaching, in particular, surgery. He became a supporter of the antiseptic treatment of wounds, which he dressed with wine and bandages, in contrast with the still dominant Galenic theories according to which suppuration (*pus bonum et laudabile*) was necessary to heal a wound (9). Thanks to the activity of Ugo Borgognoni, the *Studium* of Bologna set up a course in medicine, institutionalized by Pope Honorius III in 1219 (10). Borgognoni's teaching was conducted in Bologna by his children Veltro, Francesco (†1301) and Teodorico Borgognoni (1206-1298) (11). Teodorico, the most famous of the medical dynasty, was the author of a fundamental text (*Cyrurgia*), in which he collected information about the surgical discipline of his time (12, 13). Another physician from Lucca documented as teacher in Bologna was Pellegrino of Bonaventura, described in documents of the Bologna Commune as "*lucensis, doctor et lector (o rector) artis physichae seu medicinae*", and who died in 1276 (11, 14).

Considering the strong link between Lucca and Bologna, confirmed by the arrival in the prestigious institution of Bologna of prominent medical personalities who moved from the Tuscan city, Pancio is likely to have followed the example of his compatriots. The training of Pancio at the University of Bologna is also confirmed by a passage contained in his will, where the University is indicated as the seat of the college for students, to be realized with his legacy.

Pancio as medical science writer

Pancio also devoted himself to scientific studies in medicine. With regard to the medical studies of Pancio we have the testimony of a famous contemporary physician, Gentile from Foligno (1272? -1348), professor of medicine in Bologna and in Perugia. In his book "*De febribus*" (On Fevers), *Quaestio* XI, he states that "…if fever derives from heart disease or if the heart only suffers fever" (*utrum febris sit passio cordis sive verum subiectum febris sit cor)*". Gentile reports the opinion of Pancio from Lucca according to whom the level of fever depended on a "liver disease". Gentile concluded by rejecting this solution and confirmed that "fever moves from the heart as the first cause". From this testimony, it appears that Pancio took an interest in the medical theory on the origin of fever. At that time, some illustrious physicians investigated the question, generally in agreement with the Galenic theory that identified the pathogenesis of fever in heart alteration. The theory of Pancio, traded by Gentile da Foligno, was quite original: fever depended on liver and not on heart disease. Furthermore, in the Malatesta Library of Cesena, one codex mentioned another *questio* of "*magistri Pacini de Luca*": whether fever can derive from the blood that remains in its own form "*utrum ex sanguine manente in propria forma sanguinis possit fieri febris*". A further opinion of Pancio about the origins of fever is reported in this *quaestio.* The problem is related to the pathogenesis of fever but is different from the theme discussed by Gentile da Foligno.

On the basis of these evidences, it is likely that Pancio wrote a general treatise on the origin of fevers, as suggested by Augusto Mancini, who found this mention in the Malatesta Library (2, 15). The dissertation of Pancio has gone lost, but it seems to have been known by the 14th century physicians.

First steps in the career of Pancio and his arrival in England

In 1309, before the English period, Pancio was remembered in Lucca in a particular public act against the Commune of Milan, a sign showing that he actively participated in the politics of his city and that he had become a relevant figure in his community of origin (16).

Before arriving in England, Pancio has had various experiences in Europe. In 1312, he was in fact in France at the papal court of Avignon, where he was working as doctor for the Florentine Frescobaldi family dedicated to merchandising in the Provençal land (3). The Frescobaldi were already well established in the London environment, where they probably introduced Pancio into the English scene.

At the beginning of the 14th century, the Lucca community in London was mainly composed by merchant-bankers. Lucca expanded its trade and financial services in Europe, especially in Rome, Sicily, Provence, France (Champagne), Flanders and England between the 12th and 13th centuries. In particular, Lucca had a monopoly for the production of silk fabrics in Western Europe during the 13th century. The production of luxury items in silk brought the merchants of Lucca into contact with the aristocratic elites, and the businessmen of the Tuscan city were easily introduced to the European courts. In 1284 Lucca was the seat of 22 merchant-finance companies constituted as lasting alliances between families, operating in international affairs (17, 18). Companies of Lucca had been present in London ever since the 13th century, and the Ricciardi bank was the most important in the English Kingdom at the time of Edward I (19, 20). In the first half of the 14th century, other important Florentine companies joined the Lucca companies, including the Frescobaldi, Peruzzi and Bardi companies, in which Pancio was also involved with business relations.

Pancio at the court of Edward II

Contacts of Pancio with the court of Edward II date back to 1317, when the king granted him a yearly sum of £25 (21: 57). The following year his salary quadrupled to £100, a sign confirming that his services had been highly appreciated (21: 199). In the following years Pancio received different forms of payment: in 1320 Queen Isabella granted him with a portion of the proceeds from the duty on wool, hides and woolfells collected at Southampton, the port on the English Channel from which exports for continental Europe departed, and he was also guaranteed the export rights on 80 wool sacks (22: 195). Pancio transferred the export privilege to the Florentine bank of the Bardi and raised money directing from them (22: 255). From the year 1322 Pancio obtained payments based on real estate and land income: the manors of Chiselborough in Somerset, Brambletye and Lavertye in Sussex, Plashes in Hertfordshire were granted to him for life, "as long as he should remain in the realm, for the good service which he had rendered to the King", and in place of the yearly grant of £100. If the income from these estates exceeded the yearly sum of £100, the balance had to be repaid to the Exchequer (23: 137). This way of managing the Archiater's payments from the King and Queen continued in the following years, and in 1326 he obtained confirmation of the grant deriving from the knights' fees pertaining to the same manors (23: 385).

The episode of Castruccio Castracani

Pancio of Controne never broke contacts with the Italian motherland and he was indeed a landmark for the Lucca population, which maintained commercial or political relations with London and with the English Royal Court. Among the businessmen of Lucca origin in England at the beginning of the 300s there were many political exiles, including Castruccio Castracani degli Antelminelli. During a brawl in London between 1301-1303 Castruccio, who was later to become one of the principal Ghibelline warlords in Italy and captain of the Lucca army, killed a compatriot, the merchant Ciato Ronzini. For this murder, Castruccio was forced to escape from England. In September 1325 he soundly defeated Florence in the battle of Altopascio and celebrated a Roman-style triumph in Lucca. He was named Duke of Lucca by the Emperor Ludovico the Bavarian and he was champion of the Italian Ghibellines and a leading international figure. Thanks to the intervention of Pancio on 12 December1325, Castruccio obtained the "card of forgiveness" from King Edward II, and therefore the grace of penalty of banishment from the English domains (2, 24: 200). Pancio obtained a similar grace a few days later, on 27 December 1325, for another compatriot, Levino Denuso of Lucca, who had killed a certain Iohannes Cacheger, probably under the same circumstances as those of Castruccio (24: 203). However, it is above all the episode relating to Castruccio of 1325 that shows the important political-diplomatic role of Pancio. The rehabilitation of Castruccio at the English court thanks to Pancio takes on the features of a real political act. Pancio played a diplomatic role that had a dual value, both for Lucca under Castruccio's dominion and for the English Kingdom. Pancio therefore exerted a strong influence on the king, and he firmly held his position at the royal court even after Edward III succeeded his father on the English throne in 1327.

Pancio at the court of Edward III

Starting from 1328 Pancio obtained a series of properties, partly deriving from those confiscated from Hugh le Despenser in 1326, such as the manor of Temple Guytyng in Gloucestershire. The properties were donated by King Edward III, at that time minor under the influence of his mother Isabella and her lover Sir Roger Mortimer (25: 95).

Pancio was involved in the management of the mint of Bordeaux in the years 1327-1332. Thanks to Pancio, in 1327 the king named his compatriot and partner Pellegrino of Controne "master of the King's mint in Bordeaux" (26: 39), and Giovanni Bonaguidi of Lucca "keeper of the dies of the king's mint" for five years (26: 39).

The name of another relative of Pancio first appears in the Gascon Rolls in 1331, when the king assigned Giovanni Nicola of Controne at the "office of assay of the king's money" (26: 43), and in 1332 at "the keepership of the dies of the king's mint" in Bordeaux, probably replacing Giovanni Bonaguidi (26: 44).

In the years 1336-1338 the King assigned to Pancho various responsibilities in Aquitaine, which he exercised through his agents, particularly in Agenais in 1336 as "keeper of the king's seal" (26: 48), and in Blaye in 1337-38 (26: 49).

In June 1333 the King granted to Pancio the farm of the city of Norwich (27: 50), and in March 1335 the custody of the manor of Brambletye in Sussex. The property already belonged to John de Seyntclere, who also had custody of the young heir of Seyntclere (25: 435).

A reference to a property held by Pancio in London, namely a tenement in the parish of Saint Maria Magdalen, Southwark, appears in 1336 (27: 678).

In 1338 Pancio went to the Low Countries, probably following the king during the very first phase of the Hundred Years' War; he then returned to England

and again to the king in November (28: 163). As real archiater, Pancio was probably with the king when Edward III was preparing the military raid in the kingdom of France from North in 1339 (29).

Pancio made huge profits thanks to his proximity to the king and queen. It is worth noting how Pancio, who had founded his wealth on the practice of the medical profession, became a leading protagonist of the English scene, reinvesting his fortunes and becoming a lender, in the same way as the large mercantile financial groups.

A change in the financial relations with the king began in 1337. The royal finances fell greatly with the start of the Hundred Years' War and therefore, after 1337, Pancio became a creditor of the king, who owed him the enormous sum of over £6465 (30: 192). In 1338 Pancio obtained permission to export 40 sacks of wool to Italy paying only fifty percent of the customs fees (30: 313), and receiving from the king another payment of £105 (30: 376), only a small proportion of the king's entire debt.

Pancio suffered the same failure to repay the debt suffered by the great Bardi and Peruzzi companies that failed in 1343 (only three years after Pancio's death) because of the debts contracted with King Edward III.

One of Pancio's last economic actions was the sale of the manor of Guiting to William de Clinton, Earl of Huntingdon, which took place on 9 September 1340, about one month before his death (31: 623).

After that event nine sarplars of wool, which had been prepared by the physician, were sent to Brabant, Belgium, on 8 October 1340 by order of the King, who expressed his gratitude and appreciation for Pancio's service (31: 556). In 1374, the King appeared to no longer be bound to Pancio, and the debt was recorded as discharged (3). Someone who lived after the physician must have bought Pancio's bound managing to get back the sum.

Death of Pancio and his will

Pancio died in the first days of October 1340. On 1 June, 1338, about two years before his death "*honorabilis et sapiens vir Magister Pancius de Controne, illustris domini Regis Anglie phisicus*" he wrote his will in London, in the sacristy of the priory of "Austin Friars" before Uguccio Sensii de Ficulli, an Italian notary operating in England. A complete copy of the will is housed at the Fund of the Opera of S. Croce, at the State Archive of Lucca (1, 2). This fundamental document reconstructs the social environment of Pancio, on the basis of information about his family, the links with his town of origin near Lucca and, of course, his aspirations at the end of his life. Many of the legates of Pancio awaited the return of the huge sums, not explicitly defined but recorded in his will as "*dueae magnae pecuniarum sumae*" that the King of England owed to Pancio. We know from Close Roll charts that the King's debt amounted to the incredible sum of £6465. Three hypotheses are made in the will: the first, according to which the king pays; the second, according to which the king does not pay so that the guarantee goods are sold; the third, according to which the king does not pay and the guarantee goods are not sold, and everything remains entrusted to the good will of the executors.

After having stated that he wants to be buried in the convent of the Franciscan Friars, the thought of Pancio goes to the king, to whom he wants to make a donation in gold, even though Edward III owed him a lot of money, and the credit would then affect all the legacies listed in his will. Information on Pancio's family can be evinced from this document: his father was a certain Pellegrino of Controne and his mother to a family of Rocca Mozzano, a little castle in the Serchio Valley, not far from the Controne region. He had a son called Gerardo, to whom he left his books, four brothers and a sister, called Agnese, with her daughter Bella. He left a sum of money as dowry for Bella and other grandchildren of marriageable age, and a long-term investment for his sister Agnese. More precisely, Pancio stated in his will that the executors should not award her with three hundred gold florins, but that the sum should be invested in a mercantile company so that the profit of the investment would be paid to the woman each year until her death, after which the sum was to pass to the other heirs of the testator. Pancio's nephew Iacopo, son of his brother Raimondo of Controne, was appointed executor of the will.

In the document, the Lucca physician, in addition to his relatives, appointed numerous people from Controne and others who in various ways rotated around him in the English period. For example, he allocated fifty gold florins each year to Guidone of the Ciocia for the time he had served him, and a hundred if he accepted to be one of his executors, besides assuring him food and drink. Two hundred florins and the «stuff» – to which he was entitled according to Pancio's provisions for each year – were assigned to Damiano di Paulo from Controne, for the expenses incurred for his journeys to Florence. To his valet Hariotto he allocated fifteen marks sterling, in addition to his horse, his bed, his weapons and the doublet he was obliged to wear on his own order; he ordered that his chamberlain Filippo de Ibernia, should receive ten marks and two clothes; he assigned one hundred pounds to the «apothecary» Giovanni of Lucca. The people mentioned in Pancio's will belonged to his retinue and if Hariotto and Filippo of Ibernia were foreigners, probably hired during his travels, the others were compatriots. He had therefore organized a kind of court, a sort of extended family of non-noble coterie that he could trust.

Through his testamentary dispositions, he sorted out his businesses, and the outstanding debts he had with the Hospital of Saint John of Jerusalem in London, with the bank of Peruzzi and Bardi, and with others. From the documents of the Close Roll it results that Pancio at least since 1325 had entertained various businesses (32: 339, 33: 103), including some loans, generally with his partners Peregrino of Controne and Azzolino Simonetti, with the priors of the Hospital of San Giovanni in London (32: 564). The idea that Pancio had lent his services to the Hospital of Saint John in London, as hypothesized by Della Capanna (34), must be discarded, as there seems to have been only a financial-commercial business relationship. Pancio also appears as witness in an important document drawn up on 4 January, 1335, which guaranteed the prior of the Hospital of Saint John many assets previously fallen under the control of the king.

Azzolino Simonetti was one of the most accredited bankers of Lucca in London, while his countryman and partner Pellegrino of Controne in 1327 was appointed by the king «master of the King's mint in Bordeaux», thanks to Pancio (26: 39). Both figures are present in many business documents stored in the Public Record Office.

Pancio could not personally follow his properties and respective incomes abroad; therefore, he appointed prosecutors, including Giovanni Marsuppini, a Florentine who came to England with one of the Florentine companies, and whom he sent even to Ireland to treat his economic interests.

Pancio recognized the importance of study for young people and expressed his desire to create an institution for them. He arranged for a house destined to twelve students to be purchased in the city of Bologna, with the sum returned by the king. In the Bolognese Committee, goods of the value of two thousand five hundred pounds of Bologna silver coins (*piccioli*) were purchased, and the income was to serve to support the students: three in grammar and arts, three in medicine, three in law and three in canon law. Iacopo di Raimondo of Controne, his nephew, heir and executor, was supposed to assess the qualities of the candidates. If he did not find a sufficient number of young people, he would have to fall back on others closer to the specified requirements. The students considered suitable, could stay in the house for no longer than seven years. The project was conditioned by the king's conduct, but had to be implemented even in the case of non-return of the debt, so that the executors had to sell the guarantee goods. In the case of death of Iacopo and his heirs, Pancio ordered that the Bologna Archdeacon of the time should intervene and take responsibility in the matter.

The debt of Edward III was not paid before Pancio's death and became essential for the complete execution of his wills. However, Pancio had stated that some of his wills should be carried out independently of repayment of the real debt, in particular the institution of the Bologna College. With this legacy, Pancio demonstrated a philanthropic will for the development of studies, truly remarkable for those times.

Alongside Giovanni of Montechiaro and Azzolino Simonetti, the banker of Lucca, as executors of the will, Pancio wanted his nephew Iacopo di Raimondo and some of his heirs of the Controneria, who were granted maximum discretionary authority over all the decisions to be made "*both here and across the sea of England*".

As it was customary for wealthy people, after having settled some pending debts, Pancio ordered the perpetual presence of a choir of four chaplains to celebrate Masses for the salvation of his soul and that of his relatives in the church of S. Martino in Lucca.

Conclusions

Pancio of Controne can certainly be considered a paradigmatic figure of a successful late medieval physician. He reached the pinnacle of success in the medical profession as English king's archiater, but it is difficult to explain his social ascent and his international success if we do not insert his figure in the business world of some Italian cities between the 13th and 14th centuries. Pancio of Controne is a son of the "13th century commercial revolution" (35). The Italian banking and commercial network allowed him to arrive at the English court, which had become the launching pad for the management of innumerable businesses alongside the profitable medical profession. In addition to his activity as king's physician in England, Pancio was engaged in numerous financial activities undertaken with some of the leading merchant bankers of the time, such as the Florentine Bards, or with Azzolino Simonetti, a well-known merchant and banker of Lucca.

His activities range from the medical art, which he practised for the Royal court (but probably also for other patients with high financial resources), and his commercial and money-lending businesses.

The Lucca medical tradition, started by Pancio in England, seemed to continue even after his death: in the 15th century Davino de' Nigarelli from Lucca also became archiater of the King of England Henry IV (7).

Acknowledgements

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The plague of 1630 in Modena (Italy) through the study of parish registers

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Abstract. The purpose of this paper is to study the impact this disease had on the community in Modena during the epidemic in 1630 and highlight the real course of the disease that brought Modena and whole Europe to its knees in the 17th century. The investigation was carried out by transcribing and studying the parish certificates of death for the period 1625-1635. This study confirmed that the plague epidemic in Modena began as early as 1629, and then exploded in the most virulent form since the beginning of summer 1630 and reached its peak in August of the same year, when it caused about seven hundred victims.

Key words: plague, infectious diseases, paleopathology

Introduction

Infectious diseases have accompanied humans since ancient times and have marked their history, sometimes in a catastrophic way. In particular, everyone has heard of or read something about the plague. Epidemics of plague have had significant demographic, economic, and social consequences for humanities. It is mainly recalled as a cause of high mortality in past times: the "black death" in 1348 or the great plague of 1630 narrated by Alessandro Manzoni in the *Promessi Sposi*. However, unlike the Black Death, whose aetiology is still controversial, for the plague of 1630 several proteins belonging to bacteria from the *Yersiniaceae* family, including *Y. Pestis*, deposited on the sheets of the autoptic registers of the time, have been detected (1). Plague epidemics have been recorded in European historical documents since the 6th century (2) and its traces were dated back to Neolithic by molecular data (3). Although rare in contemporary society, the plague is considered a re-emerging infectious disease (4, 5), characterized by cyclic epidemic phases. In fact, even today, newspapers and articles discuss about the plague as an active disease among rodents and, occasionally, among human beings. Many historians, doctors, epidemiologists and writers have ventured into the study of this disease, in telling its story and the impact of successive epidemics. Through a multitude of papers, spanning several research fields, many information about the spread of this disease in past and modern times were recovered. In fact, historical data and their elaboration (6-10) together with molecular methods and results (3, 11-13) contributed to improve the knowledge of this disease. These information are useful both to provide measures of disease management and also to hypothesize time and models of spread in the future.

The purpose of this paper is to study the impact this disease had on the community in Modena during the epidemic in 1630 and highlight the real course of the disease that brought Modena and whole Europe to its knees in the 17th century. The analysis of this territory is particularly interesting, as for northern Italy, it is considered the worst plague since the Black Death.

The Spanish and French troops involved in the Mantua succession war were in fact carriers of diseases that infected large areas. None of the communities included in the area at the intersection of Lombardy, Veneto and Emilia-Romagna has been spared from the mortality crisis. This was also an area where communication routes and exchanges were very well developed. These could have been the most important causes for spreading the disease so quickly (14). The survey was conducted on the data contained in the certificates of death preserved by the parishes located within the walls of the town of Modena in 1630 (15).

Unfortunately, the lack of absolute and certain data of the number of population within the town walls for the year 1630 is a significant limitation to this investigation.

Materials and methods

In the 13th century the town of Modena was surrounded by walls and the access was ensured by several gates. The four main gates, situated in the most important points for the access of goods and people, gave the name to the four town boroughs. These boroughs were divided into *Cinquantine*, which constituted districts whose aim was to organise the life of the inhabitants, for military and fiscal purposes (16). At the beginning of the 17th century, *Cinquantine*, since they already corresponded to the extension of a parish, were reduced to the corresponding modern parishes: Cathedral, Santissima Trinità, S. Pietro, S. Paolo, S. Giacomo, S. Barnaba, S. Biagio, Pomposa, S. Michele, S. Agata, Madonna del Paradiso, Santa Margherita, S. Giacomo Battista, S. Vincenzo, S. Lorenzo, S. Giovanni Evangelista, S. Giorgio. Each parish had the assignment of drawing up the certificates of death and marking them on special registers. These registers are an important source of information since they date back from the end to the 16th century, to the Napoleonic era, when they were suppressed. The registers of the year 1630 of the parishes of S. Agostino, S. Biagio, S. Francesco, S. Pietro and the Cathedral are still preserved in their respective archives, while the registers of the other parishes are located in the Diocesan Historical Archive of Modena-Nonantola.

The investigation was carried out by transcribing and studying the certificates of death for the period 1625-1635. The five years preceding 1630 and the five years afterwards were taken into consideration in order to clearly present the trend of mortality within the town. The following data were taken into consideration for each digitized death certificate (17, 18):

- day of death;
- month of death;
- year of death;
- name of the deceased:
- surname of the deceased;
- name of the parents;
- parish;
- burial place;
- sex of the deceased;
- age of the deceased (months and days in case of infants);
- cause of death;
- place of death (rarely indicated);
- provenance (in case of foreigners);
- any priest's notes.

The certificates of death recorded in the investigation amount to a total of 7,367.

Results and discussion

The analysis of the mortality trend in town, between 1625 and 1635, offers us a glimpse into the historical period and how mortality began to increase towards the end of 1629 and reached its peak in 1630 (Fig. 1). During the first five years examined, mortality accounted for around 500 deaths a year (in 1628 it decreased to 400) while in 1630 the number of deaths exceeded 2600. The very few deaths in 1631 are attributable to the fact that the plague brought to death before time individuals of poor health, who probably would have died of other causes if the epidemic had not occurred. It wasn't until 1635 that mortality surpassed 500 annual deaths again. The registers show a smallpox epidemic in the last year, which struck the youngest age group. The number of deaths of the single parishes (Tab. 1) shows that mortality reached its culmination in 1630 (Fig. 2), an increase as early as 1629, and then collapsed in 1631. The differences in the number of

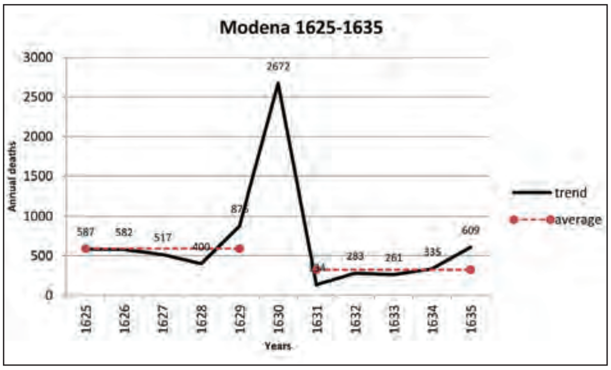

Figure 1. General trend of death (not just plague). Average 1625-1629 is 592,4 death/year, average 1631-1635 is 324,4 death/year, with decline of 45,2% after 1630.

deaths among the different parishes is due to the different size of the territory and the different number of inhabitants. The parish of the Cathedral was certainly one of the most numerous and important, therefore it is the one with the highest number of victims in 1630. Each parish hardly reached 50 deaths in 1631, but each of them had a slight increase towards the middle of 1634. The districts of the city within the walls were not affected simultaneously by the infection, but there is no way to establish exactly which district was struck first. The number of deaths began to increase in April, but only slightly and established itself in May in the district of the Cathedral, in S. Giorgio, in the Madonna del Paradiso, at Pomposa and in S. Pietro, and then increased significantly in all districts in June (19).

Giovanni Serra in his book *La peste nell'anno 1630 nel Ducato di Modena* (20) (The plague in the year 1630 in the Duchy of Modena), reports a total of 892 deaths within the walls of Modena in 1629. He also informs us that the total number of deaths that were declared in the Health lists and in the daily reports sent to the Duke's court, amounts to 4.057, of which, however, 3.623 died in the houses of Modena, 217 in the *Lazarettos* and 217 deceased belonged to the Jewish

Table 1. Number of deaths by year on individual parishes.

YEARS	NUMBERS OF DEATHS BY PARISH																
	S. Agostino	S. Barnaba	S. Biagio	S. Domenico	Cathedral	S. Francesco	S. Giacomo	S. Giovanni Battista	S. Giovanni Evangelista	S. Giuseppe	S. Lorenzo	S. Margherita	S. Maria della Pomposa	S. Maria della Trinità	S. Paolo	S. Pietro	S. Vincenzo
1625	11	61	1	26	112	33	48	3	28	48	27	17	72	28	25	34	13
1626	8	35	4	23	117	33	39	3	37	35	19	20	84	45	21	48	11
1627	17	49	1	24	80	47	41	6	40	19	14	17	52	36	13	38	23
1628	17	34	9	24	85	33	34	7	39	22	11	11	-	28	8	30	8
1629	36	70	68	44	170	74	49	13	60	6	20	29	26	32	61	90	28
1630	119	152	152	304	388	323	183	34	56	165	18	109	222	94	161	154	38
1631	3	-	-	10	31	14	12	2	5	16	1	-	-	10	13	11	6
1632	14	23	9	12	31	16	14	8	12	29	4	10	28	13	21	27	12
1633	9	16	18	11	30	21	14	3	8	20	8	4	29	19	18	24	9
1634	10	22	26	14	28	28	22	3	13	20	7	4	50	18	12	41	17
1635	22	34	30	26	77	43	43	8	26	46	15	-	86	39	38	70	6

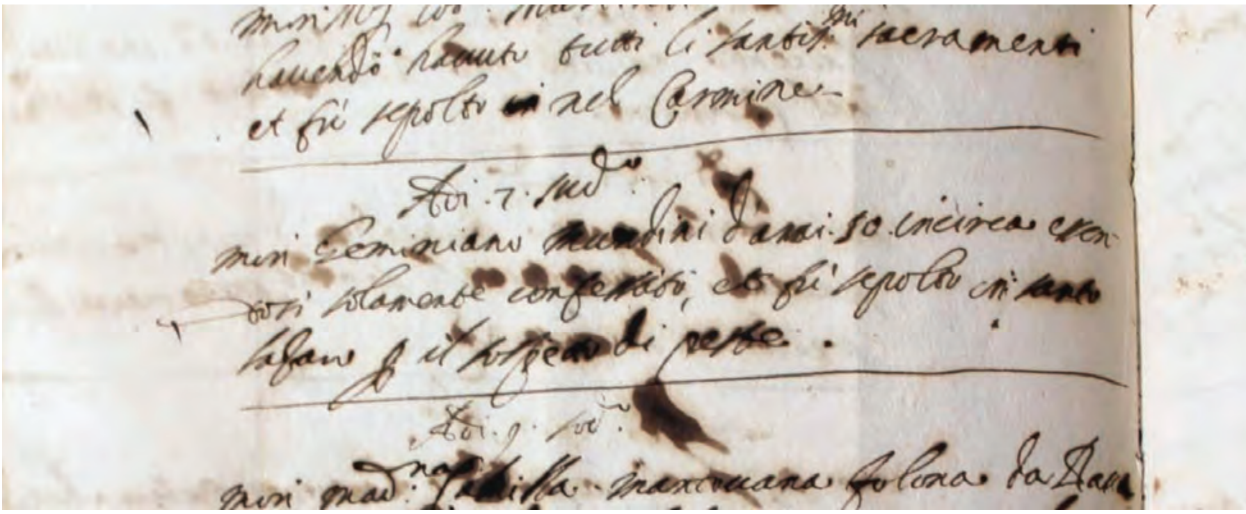

Figure 2. Death registration from the Parish of San Giovanni Evangelista, dated back to 7 July 1630, in which we read that Geminiano Mondini, aged 10, died for suspicion of plague (foto Diletta Biagini).

community. As for the mortality of the years preceding the infection, mortality rates within the town walls were obtained based on the data provided by Beloch (21), and therefore on a population of 20.000 inhabitants (Tab. 2). The mortality percentages show how the situation worsened in 1630 reaching 20,28%, if the data collected from the registers kept in the Diocesan Historical Archive of Modena-Nonantola are taken into account, and 40,57%, if instead we use Serra's data. This last one, suggested a much greater impact of the disease, since he stimated the number of individuals within the town as not higher than 10.000 (this is probably the closest to reality). It is clear that the large-scale epidemic suffered by Italy were characterized by very high mortality rates compared with those affecting contemporary Europe. If in fact, the 17th century English epidemic plague had mortality rates of 100-120‰, in Italy the most common was 300-400‰, As highlighted also in the case of Modena with the value of 407‰. The mortality rate was 330‰ in Venice, 443‰ in Piacenza, 615‰ in Verona (1629-1630); 490‰ in Genoa and 500‰ in Naples (1656-1657) (22-24). In the analysis of the registers the number of deaths in 1629 is 898, while 2.704 in 1630. During the summer months of 1630, when mortality reached its maximum extent, the parish priests, in many cases, stopped compiling the registers. The months in which the disease had the most severe impact were left as whole blank pages. In some places, the priest himself was a victim of the disease, consequently the compilation of the registers was postponed until the arrival of the new priest, who unfortunately was often unable to trace the data of the previous deceased. There are several registers featuring this void in the documentation, such as the parish of the Cathedral, S. Agostino and S. Pietro.

Table 2. Mortality rates within the city walls, calculated on a population of 20,000 and 10,000 inhabitants

Year	N. deaths	Percentage (population 20.000)	Percentage (population 10.000)
1625	590	2,9 %	5,9 %
1626	585	2,9 %	5,8 %
1627	526	2,6 %	5,2 %
1628	400	2 %	4 %
1629	898	4,4 %	8,9 %
1630	2704	13,5 %	27 %
1631	135	0,6 %	1,3 %
1632	291	1,4 %	2,9 %
1633	264	1,3 %	2,6 %
1634	336	1,6 %	3,3 %
1635	616	3 %	6,1 %

The collapse of the population was catastrophic. The seasonality of death in 1629 (Fig. 3) shows that this year is characterized by a very low mortality,

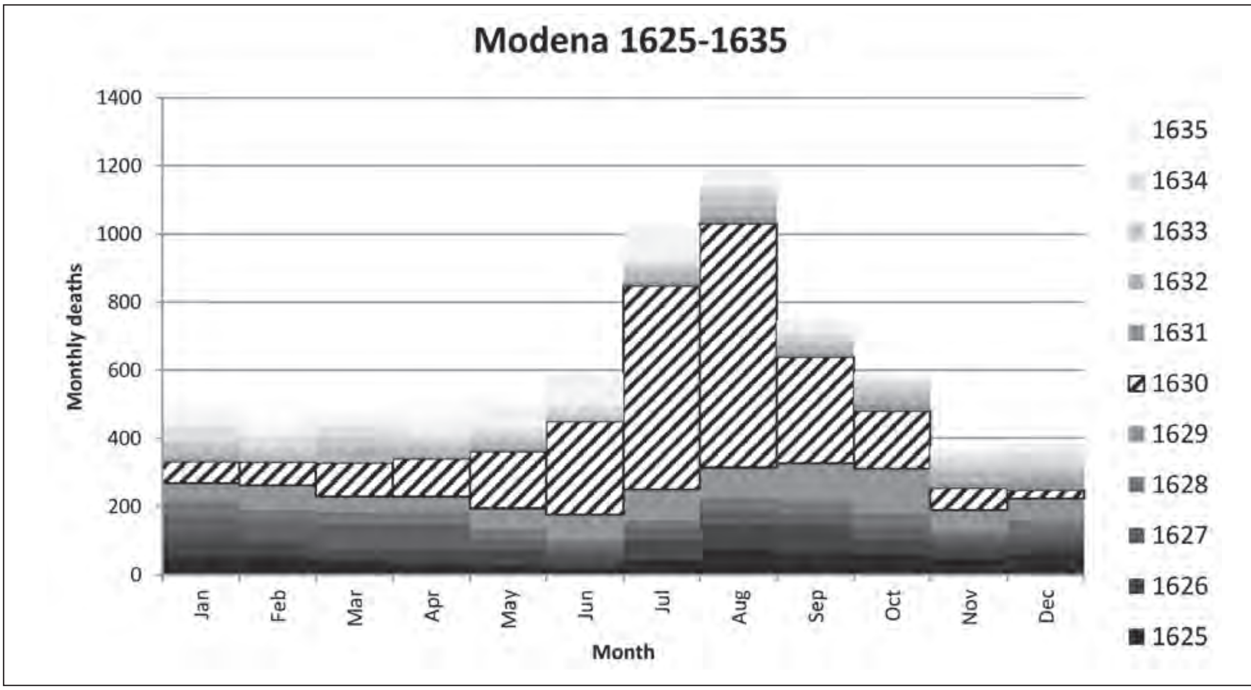

Figure 3. Monthly deaths over the period 1625-1635, in 1630 we observe an abnormal increase of mortality from May to October.

which is never higher than 100 deaths a month, except for the months of September and October. A slight increase is found starting from July to October, and then a decrease again in November and December. Indeed, although the contagion was already approaching, the city of Modena still enjoyed a certain tranquillity. Only towards November the Duke ordered the Magistrates of Gualtieri and Brescello to request the "*fedi di sanità*" of travelers. These documents, issued by doctors or health care professionals, also reported the physical characteristics of their owners in addition to their state of health. However, no further action was taken either in the city or in province. In fact, although it was known that the contagion spread to Brescia, Milan, Parma and Mantua, life in Modena seemed to flow quietly, so much so that at the end of May 1630 the borders were still open (25,26). It is clear that mortality in 1630, compared to the previous year, had been increasing since March, and then reached nearly 300 deaths in June, a time indicated by Serra as the beginning of the epidemic in town. Only from this month the court and the authorities began to admit the possibility of contagion even in the provinces of the Duchy. On day 13 of that month, Francesco I ordered the Magistrate of Health, Giacomo Spaccini, to organize "one or two lazzaretti" towards San Lazzaro. It was also arranged the closure with guards and ranchons of the borders in the area of San Martino, although the passes of Finale, Nonantola, San Felice, Montefiorino and Rubiera still remained open (27). Ten days later, contacts with Milan, Lecco, Bergamo, Pavia, Brescia, Vercelli, Toulouse, Guastalla were prohibited. Only from July 1630 very strict measures were finally adopted: capital punishment and confiscation of property for offenders against the prohibition of trade and circulation with such forbidden cities; ban on keeping animals within the walls of Modena; total ban on the movement of men and animals; prohibition of holding fairs and markets; ban on leaving home for the sick, for women and children; obligation to clean up roads and canals to remedy poor hygiene conditions; obligation to mark the homes of the sick with red crosses (28,29).

The Duke also claimed to be informed daily about deaths from plague in the city; the Magistrates of Health had to write a daily list, which contained the names of the dead and the total divided by non-Jews and Jews (Fig. 4). But now it was too late to try to stem the fierce epidemic. The highest peaks took

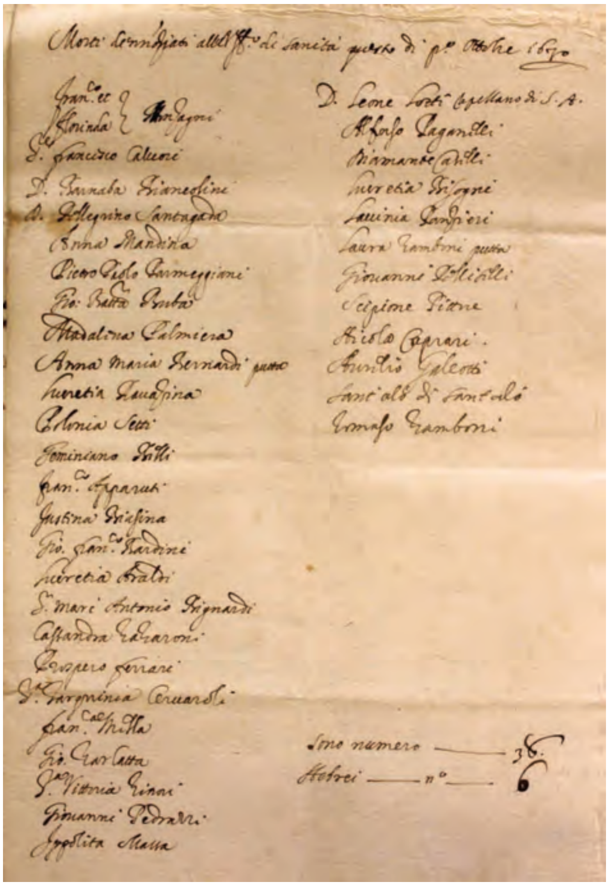

Figure 4. Daily list written by the Magistrates of Health, the names of the dead and the total deaths on October 1, 1630 are reported, divided between non-Jews and Jews. (foto Diletta Biagini)

place in July, with 599 deaths, and in August, with 717 deaths (Fig. 5). The number of victims remained rather high also in September, with 312 deaths, but also showed a slight decrease in the infection, which ended in November and December. During 1631, 135 people died over the year. This is because most of the population had been killed by the plague. Mortality in 1629 seems to increase especially in May and June, but then a rather constant trend is maintained. Mortality in 1630 is rather high compared to the previous years. The increase begins in May, and grows considerably in the summer months, until it collapses in November (Tab. 3).

As regards the age of the deceased, the population between 1 and 60 years of age was affected in almost equal measure during the plague epidemic, while almost all the parishes showed a lower number of deaths in the age range 0-1 years (14) (Fig. 6 and Tab. 4). Nevertheless, the age of the deceased is not recorded in all registers, so the picture presented here cannot be considered as completely exhaustive. During the plague of 1630 in Modena there were three hospitals for the plague patiens: one in S. Lazzaro, another in the Sgarzerie, and the third in the Stimmate district, all three financed for the conservators of the city. The bourgeoisie and nobility, with its own house equipped with separate rooms for the sick and healthy, could stay in their homes and be treated locally by doctors. Great surveillance was also applied to foodstuffs to be distributed to citizens: butchers had to sell healthy meat; the grain, flour, and bread suppliers were continuously checked directly by deputies appointed by the magistrates. Even the apothecaries remained under strict control of sanitary ware appointed by the conservators and had to be supplied with medicines in sufficient quantity for the needs. Given the tragic conditions of the population, the Duke of Modena had facilitated

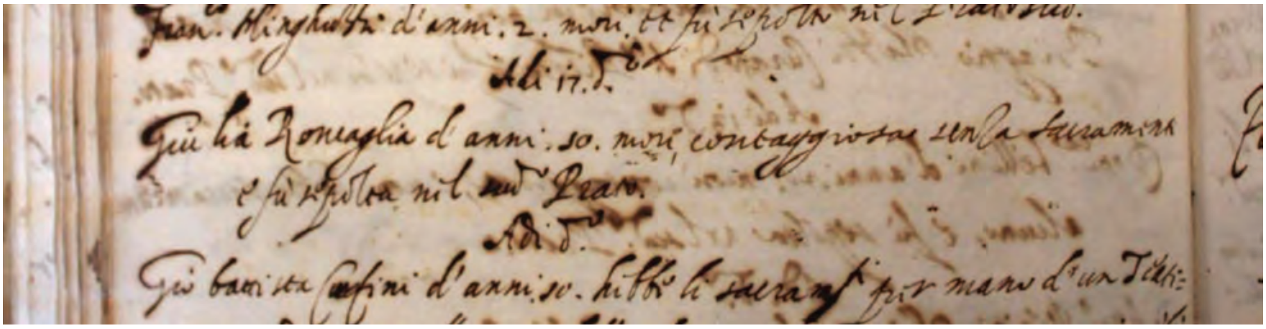

Figure 5. Death registration from the Parish of San Pietro, dated back to 17 August 1630, in which we read that Giulia Roncaglia, aged 10, died contagiously without sacraments (foto Diletta Biagini).

Table 3. Seasonality of death divided by the different years. The inverted winter/summer trend is evident. In the years before 1630 there are more deaths in winter, related to bronchopulmonary diseases, compared to summer. In 1630/31 this trend is reversed due to the plague. The same phenomenon of inversion recurs in 1635, year in which the city of Modena was struck by a smallpox epidemic.

	YEARS										
	1625	**1626**	**1627**	**1628**	**1629**	**1630**	**1631**	**1632**	**1633**	**1634**	**1635**
January	54	58	60	43	55	63	8	24	27	41	56
February	52	49	55	36	71	68	4	14	22	38	35
March	42	30	79	34	45	98	5	37	30	36	37
April	33	43	74	37	43	112	6	22	18	27	47
May	27	45	33	28	62	167	11	16	21	22	69
June	23	31	26	22	75	274	-	8	14	20	100
July	43	60	32	24	91	599	10	24	22	17	102
August	78	73	39	38	87	717	18	31	36	23	48
September	66	79	31	42	109	312	10	24	16	22	37
October	62	44	37	38	131	170	19	27	22	23	21
November	49	35	27	17	64	63	14	34	18	31	25
December	61	36	25	39	64	23	29	28	17	35	31

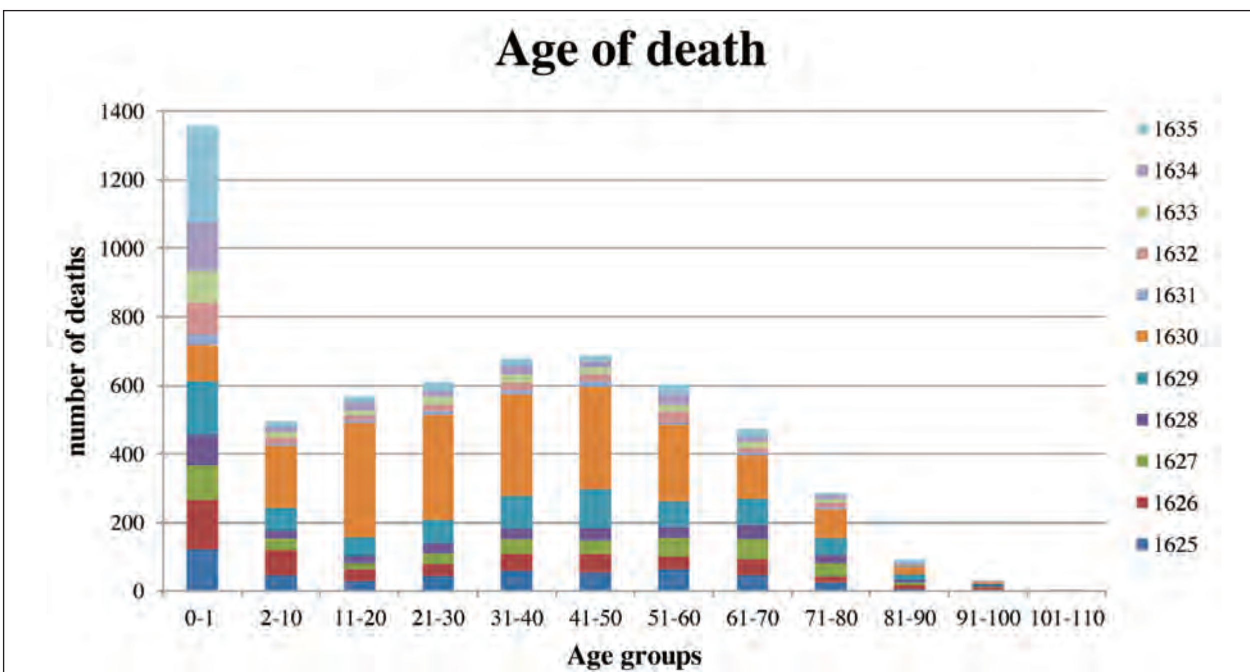

Figure 6. Representation of the number of deaths broken down by the different age groups of death in the years 1625-1635.

the way to make a will during the contagion: a notary with three witnesses, received the will of the testator, it was enough that the latter shouted it from the window or door. Outside the city, in the villas of the district, where a notary was not present, it was sufficient for the testator to declare his will to the pastor, or to the

Table 4. Age of death by age classes.

AGE CLASSES	NUMBERS OF DEATHS BY YEARS										
	1625	**1626**	**1627**	**1628**	**1629**	**1630**	**1631**	**1632**	**1633**	**1634**	**1635**
0-1	123	144	101	90	154	107	31	90	96	139	281
2-10	48	74	33	22	66	182	5	19	14	17	17
11-20	28	36	18	20	57	333	6	14	15	24	17
21-30	46	34	32	27	68	309	9	18	25	16	24
31-40	60	49	43	31	94	298	11	21	24	28	20
41-50	54	56	38	37	113	300	13	22	19	18	15
51-60	63	37	56	31	75	225	6	32	18	32	28
61-70	47	46	60	41	77	125	8	15	15	18	20
71-80	24	20	38	22	52	82	7	13	10	12	6
81-90	6	11	8	8	16	22	3	2	3	5	7
91-100	5	5	3	4	3	4	1	4	1	-	-
101-110	1	-	1	1	-	2	-	-	-	-	-

chaplain, in the presence of two witnesses. Historical sources make reference in particular to two cemeteries outside the walls, where the infected corpses were brought during the infection: the cemetery of S. Lazzaro (which was the cemetery of the Lazzaretto), outside Bologna gate, and the so-called "Prato novo", outside S. Agostino gate. Unfortunately, parish registers often simply report "buried outside", without specifying the place of burial. In addition to these two places, Roversella or Roverella (or Poverella?) and Verdeda are recorded in the sources. No correlation was identified between the parishes the deceased citizens belonged to and the places where they were buried. In fact, the parishes that buried their deceased outside Porta S. Agostino (one of the entrances to the town) seem to be as follows: S. Agostino, Cathedral, S. Domenico, S. Francesco, S. Giacomo, S. Giuseppe, S. Pietro and S. Vincenzo, while outside Bologna those of: S. Domenico, S. Giacomo, S. Giuseppe, S. Maria della Pomposa, S. Maria della Trinità, S. Pietro. The cemetery of Roversella was used only by two parishes: Cathedral and S. Francesco. The parishes not present in this list just bear the indication of the burial within the town walls, without specifying the place. Beloch (17) gives us some interesting facts about the plague-affected population in other Italian cities. In Lombardy more than a third of the population (38%) was struck by the plague, the city of Milan reached 40% of deaths, while 60% was even reached in Cremona. Major losses were suffered by Mantua, which in addition to the plague also underwent war and looting on the part of Lanzichenecchi. Parma lost about half of its population.

Conclusions

The analysis of the parish registers has confirmed that the plague epidemic in Modena began as early as 1629, and then exploded in the most virulent form since the beginning of summer 1630 and reached its peak in August of the same year, when it caused about seven hundred victims. Security measures by the authorities, were perhaps taken late, when the disease was already in the city. The town was massively affected, like the other cities of Northern Italy with very similar percentages. The epidemic in Modena lasted a slightly over one year, in fact already starting from November 1630, the mortality returns to levels that are even lower than those of the pre-epidemic time. This low number of deaths from 1631 to 1634 is probably due to the fact that, under normal conditions, individuals destined to die in these years had died early during the epidemic. Starting from 1635 the data foreshadowed a mortality increase due to smallpox, which can be deduced from the certificates kept in the parish archives. Smallpox particularly affected the youngest age group, accounting for a total of 420 victims between 0 and 10 of age. The district or parish that recorded the first cases of the plague, could not be identified also due to the limitations of the available documentation, nor did any clear mortality differences emerge between the different districts of the town. Based on our study data, it was estimated approximately that the plague epidemic in Modena caused the death of over a third of the population. This figure, compared with the values reported by Beloch, is not dissimilar or slightly lower than that recorded in other cities in Northern Italy affected by the disease such as Milan and Piacenza in which mortality reached 40%.

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ACAMo. Parrocchie soppresse nel XVIII secolo, S. Lorenzo, Morti
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Scholars and medicine in Sicily between the 18th and 19th centuries. Medical knowledge and universal history

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Abstract. Inspired by the Enlightenment-era ideal of reconstructing a history of universal knowledge, the 18th and 19th centuries also saw the emergence of universal literary histories in Italy that were dedicated to the totality of humanistic and scientific knowledge. Two scholars – a Sicilian and a Spaniard who had lived a long time in Italy - contributed with monumental works, of which a large part was reserved for Sicilian medicine and the progress thereof. This interest shows the island's intellectual ebullience and "openness" at the end of the 18th century, not only towards philosophical ideas from beyond the Alps, but also of European medical conceptions which, in many instances – on the island – were reinterpreted and "adapted" to the local culture and needs.

Key words: scholars, history of medicine, Sicily, 18th and 19th century

Introduction

Amongst the sources regarding the history of medicine in modern Italy, a particularly important position should be given to those works whose titles allude to "literary" histories or perspectives of "all" literature. These titles must not be deceptive in any way as the works themselves do not merely concern Italian (or foreign) literature and the history thereof but are, in fact, of much broader scope. Respecting an exquisitely enlightened encyclopaedic approach and within the concept of "literature", even in 18th- to 19th-century Italy works were published that embraced the *universal history* of the various fields of knowledge and scientific progress, following a vision inspired by the collective ideal of 18th-century culture. The history of "each" piece of literature in fact covered all "arts and sciences, sacred and profane, ancient and modern, general and particular […]; a philosophical outline of the progress it has made from its foundation to the present day… in each of its branches". This was the project as declared by the scholars - the authors of monumental works - who were mainly church-going men. Their works are therefore established within the concept of comparative conception which aimed to construct a "philosophical history", the objective of which was that to describe and explain the artistic and scientific progress of all humankind (1). It was obvious that the history of natural sciences would also cover the history of medicine, including that in Italy, which was reserved a prestigious position within the ambit of European medicine.

In this essay, I would like to consider the works of two humanists in particular, champions of the late Enlightenment culture, who were amongst the greatest forefathers of the distribution of knowledge (including that of the history of medicine). While in exile in Italy (Ferrara and Mantua, before reaching Naples) the Jesuit-humanist of Catalan origin Juan Andrés y Morell, dedicated his work *Dell'origine, progressi e stato attuale di ogni letteratura*, in seven volumes in its first edition of 1782-1799, and then reprinted with various updates – (and similarly updated compendiums) - (2) with integrations written by the author himself) to "all the disciplines". It is well known that the Jesuit order prohibited the practice of medicine. But this canon-dictated prohibition did not mean that the treatise on medicine had to be excluded from the all-encompassing study of the organisation of knowledge, and this ideal inspired Andrés' work which was linked to the Mediterranean culture and the fate of the Kingdom of Naples (where he was Prefect of the Royal Library). In the late Enlightenment age, Andrés was the founder of the so-called "Spanish Universalist School", the core principle of which was the spreading of the *totality* of knowledge within the framework of a universal *humanism*, which already between the 18th and 19th centuries stood out for its global vision of the world, culture and history.

While writing his literary work, Andrés indicated he was following in the footsteps of another great Sicilian scholar, who will be studied in this essay: Domenico Scinà, physicist and historian (and abbot) from Palermo whose work proposed to shed light on Sicily's important role in the progress of *all* sciences, including medicine.

Scinà and the history of medicine in Sicily

Having trained at the former Jesuit seminary in Palermo, Domenico Scinà was above all a scientist, the author of many different works of "general and specific" physics as well as a royal scribe upon appointment by Ferdinand of Bourbon. He taught mathematics in the Academy of Studies in Palermo and was part of the Commission of Public Education and Training in Sicily. His *Prospetto della storia letteraria di Sicilia nel secolo decimottavo* (1827) aimed, among other things, to illustrate the means "of public education and culture" (3). This prospectus legitimately covered all schools, no less medicine schools, apropos which – Scinà commented – the Catania school was left *unhonoured*. Founded in 1661, expanded in 1649 and restored in 1696, it was actually the Academy of Medicine in Palermo, which at the time was destined to "not prosper" as lacking both clinic and anatomical theatre. In the Academy of Modica, on the other hand, "one was kept busy by many medical issues", especially following a syphilis epidemic that slaughtered the city in the early 18th century. In order to eradicate it, local doctors – inspired by the ideas of the Cartesian philosopher and doctor Tommaso Campailla – catalogued a series of remedies deriving from the chemistry of the period. Campailla did all he could to cure syphilis, not merely limiting himself to the theoretical. In 1698 he introduced the fumigation stove known as the *botte*, within which patients were suffumigated with cinnabar and incense which were inhaled and absorbed by the sick. Through this practice, but also thanks to the success of some works on fevers and a treatise on physiology of a iatromechanical and Borellian nature (4), Campailla brought the Modica school to the forefront. This school also promoted the study of medicine, bringing it to other Sicilian cities as Catania was once again emerging following its calamitous earthquake. Within this context, around the middle of the century, Catania-born Agostino Giuffrida and the priest and doctor from Palermo, Giuseppe di Gregorio e Russo, fought to oppose the application of astrology in medicine. Like Campailla and many other scholars of the time, Giuffrida was also a man of letters; he composed a tragedy, held a chair in metaphysics (from which he was then relieved) and opposed Boerhaave's iatromechanics. As well as opposing the popular superstition that the moon somehow influenced health, Di Gregorio e Russo was also a broad connoisseur of the Newtonian viewpoint and keenly studied mineral waters. Specifically, he described the presumed curative properties of the spring of Acquasanta in Palermo, which seemed to contain cathartic salt, which had similar effects to those of Epsom salt.

At the time, there was no shortage of studies on mineral waters, on ferments (it was the season of van Helmont's "iatrochemistry": "everything in medicine was ferment, and everything fermentation", Scinà observed), on the purity of the air and cold water remedies for all diseases, and codes of pharmacopeia and public health were published (especially during the Messina plague in 1743). Another branch of studies – thanks to the work by the archpriest of Palma, then canon of the cathedral, Francesco E. Cangiamila – looked at promoting Caesarean sections in childbirth. This practice was sanctioned in the four volumes of the *L'embriologia sacra*, so-called as it concerned miscarriage and Caesarean sections, during which mothers and new-borns died and their souls had to be saved (5). This work included an "enlightenment" to instruct "zealous Pastors" how to act in such critical circumstances. Cangiamila was also the author of *Medicina sacra*, published posthumously in two volumes (1802) (6), through which he resolved to demonstrate that moderate penitence and Christian mortification led to a healthy body and long life. In Monreale and Palma, he promoted the procedure of Caesarean sections in order to impart sacrament to the mother and foetus, so as to baptise it before death and therefore save its soul. This book was a work on obstetrics by a religious man who probably had no official title as doctor but did have up-to-date scientific and technical knowledge in the field.

Surgery – which had progressed in the 16th century thanks to Filippo Ingrassia – developed significantly thanks to Gioacchino Parisi from Calatafimi, who was one of the first in Sicily to practice lithotomy operations (in just a few years he performed over 100). His method was published in 1728 and throughout the first half of the century prompted and maintained the discussion on the formation of gallstones and on the operations and instruments (canal dilator, conductor, lithotome, bistoury chaché, etc.) to be used to dilate and/or cut the bladder and the urethra and remove the stone (7). Huge steps forwards in urological techniques were also made with the perineum incision described in *Iscuria legittima* in 1752 (8), in which Parisi compared his technique for removing stones with that described in 1743 by the famous Parisian surgeon, the academic Pierre Foubert, in the *Nouvelle Méthode de tirer la pierre de la vessie*, with both of them using the *troicart*. In his reconstruction, Scinà mentioned all the illustrious foreign doctors who thought extremely highly of Parisi to demonstrate that his lauding of his fellow countryman and his progress in surgery had not been due to imagination or excessive patriotism, and to show that Sicily "could compete with even the most cultured nations in the field of lithotomy".

With the institution of new colleges, observatories and scientific offices, the reign of Ferdinand I of Bourbon saw great progress not only in medicine but in all natural sciences and in the medical ambit, theoretical systems started being "considered with disdain" as they did not rely on observations. However, the mechanistic position still dominated, as Scinà described with an ironic tone: "in our medical congresses between 1750 to 1760 you would hear nothing but triangles and parallelograms, there was no talk of disease and treatments other than with levers and counter-levers and doctors added geometry and statics to the affliction of the sick". This provoked a reaction by the Medical Academy of Palermo headed by Giuffrida, which quickly extended throughout Sicily from Partanna to Trapani. Within this context, the Modica school once again made a name for itself with very highly regarded doctors, including Michele Gallo and Gaspare Cannata, who was invited to Palermo in 1763 to fight an infection which then spread throughout the island. The number of anatomists increased under Giuseppe Mastiani, and anatomical dissections were undertaken and anatomical models of the eye, ear and skeleton were constructed.

In 1779, the Academy of Studies in Palermo – which was basically a university with teachings in law, theology and medicine and surgery - was reorganised and an anatomical theatre, wax anatomical museum and chemistry study were also created. The practice of anatomy was expanded, theoretical medicine was divided into physiology and pathology, and the veterinary chair was instituted. In academic year 1779/1780 lecturers were appointed for the two medicines – theoretical and practical – capped by teachings in Chemistry and Pharmaceutics, Surgery and Obstetrics, Anatomical Dissections and Practical Surgery and Anatomy (9). Considering, however, that medical students were first obligated to attend courses in Catania (because courses in the capital had no validity as credit towards degrees), very few students enrolled in Palermo and only in December 1871 did the king finally recognised the validity of teachings in Medicine (and Law).

Towards the end of the century, literary journals started being issued that contained articles on medicine, with discussions of electrology applied to the human body, in particular on effluviums and medicinal tubes with electrical properties. Despite the long-lasting influx of metaphysics and a primarily theoretical position in natural sciences, after 1780 things changed and, thanks to the two schools of Catania and Palermo, a more experimental attitude spread throughout the island. From this progress in natural sciences, medicine was the first to benefit: even if some doctors were still keen on Brownism both for the way of philosophising as well as for its apparent simplicity, there were also plenty of opponents. In Sicily, Jenner's discovery of the smallpox vaccine led to the writing of various doctrines describing infections and comparing smallpox with the plague, syphilis, shingles and other purulent diseases, reconstructing the history of the infection, the presumed origin thereof in Ethiopia and how to eradicate it. Thanks to his works on smallpox, Giuffrida's pupil, Francesco Maria Scuderi from Viagrande in Catania (10-11) was appointed the chair of practical medicine in Catania by King Ferdinand, generating rivalry and polemic, and even accusations of plagiarism. Scuderi became a true celebrity in Catania, where he continued to publish works inspired by the Hippocratic doctrine (12-13). Apropos of his understanding of fevers and contagion, it was said he had been directly influenced by Hippocrates and Empedocles, while in actual fact – Scinà observed – it was impossible that the notions present in that text came from the ancients - especially not Empedocles who was unaware of blood circulation. Concepts such as antagonistic force, innate heat, life force, etc., according to Scuderi came "from insects", which were the cause of life, health and disease, while Hippocrates believed that all illness came from the air.

The numerous works by authors of the Catania and Modica schools (including Eugenio Mollè-Mallo di Chiaramonte, Salvadore Fallica and Santoro Papa) indicated the *change* that was occurring in medicine, where "modesty and discretion" were replaced by increasing amounts of the most varied doctrines proposing to eradicate fever and epidemics – especially that of Catania in 1792-93, another that lasted three years in Cefalù, and finally one in Siracusa and Girgenti in 1793. Doctors of opposing thoughts provoked infinite polemics and refutations against each other in order for each to be "right". There were contradictory opinions between Brownians and anti-Brownians (first amongst them Giuseppe Mirone who, as well as teaching Chemistry in Catania, was a propagator of Brown's principles), showing not only that *political* medicine was gaining popularity, but also that the matter of medicine had improved; the first obvious effect of this was improved cleanliness in cities, with new provisions that prohibited burials within the city limits and proposed the planting of trees to dry up swamp areas. Hygiene laws and regulations were disposed regulating the maceration of hemp, rice and linen and the making of bread; the use of ventilators was introduced in hospitals; roads were cobbled; acid drinks were recommended to fight putrefaction.

Rosario Scuderi, nephew of the Scuderi smallpox scholar, wrote *Introduzione alla storia della medicina* (1794) (14), in which he proposed to bring order to the confusion of "facts", organising them in "separate groups" based on the dominating principles of each class. Through this formulation, the history of medicine became a succession of cameos, from which three frameworks in particular emerge: under the figures of Hippocrates, Asclepiades and Galen. Of no lesser interest are the frameworks dedicated to van Helmont, Boerhaave, Bordeu, Cullen and the vitalists. Thanks to Rosario Scuderi, the history of medicine became the "philosophy of the history of medicine", a philosophy in which elements of the doctrine of movement and contraction mixed with the influence of Bichat who considered pathologies the result of irritation or alteration in the vital action. This was therefore followed by therapy (*Programma di un sistema di medicina teorica*, 1804) (15) to restore vital action from disorder to its natural state.

There were not, on the other hand, so many publications regarding the field of surgery as this was limited to the merely practical - perhaps as dissections were still rather unrefined. Scinà observed that "the knife of anatomy was taken from the hands of the young" and there was no "growth and splendour in surgery, because there was no anatomy". On the other hand, manuals on obstetrics and the "treatment of cancers" abounded thanks, above all, to the work of Gaetano Merulla from Messina (16-17), who dictated his principles of obstetrics right up to his death in 1816. Extremely efficient in practice, these instructions were divulged as a sort of catechism for midwives all over Sicily. In his first volume, Merulla discussed the gifts and qualities of obstetricians, gave instructions and explained the principles of gynaecology; in the second book, he explained the mechanism of childbirth, the causes of miscarriage, the possible difficulties in difficult labours and the first treatment to be prescribed to new-borns.

Andrés and the book of anatomy and medicine

Having distinguished between literature and science – while keeping sight of a supposedly "universal knowledge" - the Jesuit Juan Andrés also dedicated a significant chapter to the discussion of "medicine and anatomy", the history of which was reconstructed from the past to the present day giving readers an idea of "journey of science". Andrés confessed to having written the chapter on anatomy with "trembling hand" and declared that in writing it he had appealed to two doctors who, however, had limited themselves to reading his text without adding anything (18). It is interesting how Andrés included news and notions of the history of medicine in almost every one of his volumes dedicated to the various disciplines that make up the whole of "each" literature - from physics to theology - even if the largest part devoted to medicine can be found in volume VII, *Scienze razionali e morali, politiche e mediche* (from hereon in I will quote from the 1840 edition, annotated by Alessio Narbone, Palermo, Stamperia Giovanni Pedone), where the IV chapter is dedicated to anatomy and the history thereof from ancient times to the early 19th century, in Italy and abroad. In this context, particular focus was placed on the history of Sicilian anatomy and surgery that Andrés aimed to complete following contributions by Antonio Mongitore (19), Scinà and other historiographers. Amongst the most important 19th-century Sicilian doctors was Giovanni Gorgone, founder of the clinical school of Palermo and author of memoirs and manuals for courses in descriptive and pathological anatomy; Gorgone also had the idea of building an anatomical theatre, gallery and library in the University.

The aspect that emerges most often from Andrés' historical reconstruction is the meticulous, even capillary, work in listing the various contributions - both of works and surgical operations, even the most curious. His encyclopaedism not only embraced the names of the great doctors and the various Sicilian and European schools - divided by current and including comparative and even veterinary anatomy - but also explored the details of works by little-known authors, even embalmers. Similarly for medicine, discussed in chapter V of the VII volume, in which schools and doctors (including foreigners, with the French in first place) are analysed considering the various sectors of medicine, from clinical to physiological, from pathology to "medical police", from hygiene to diet, from semiology to nosological classification, from therapeutics to practical medicine, without forgetting systems (homeopathic, cathartic, etc.) or pharmaceutics and the medical matter with its list of medicinal substances and the processes through which they are obtained. No less analytical was the part dedicated to medical encyclopaedias, dictionaries, journals and societies, also divided by nation and school. Within the Sicilian medical environment, Andrés observed that medical matters were usually discussed in essays on physics, literature, arts and science as well as in encyclopaedic journals and in scientific *Effemeridi*; but between the 18th and 19th centuries specific periodicals were established: for example the "Medical Journal" of Palermo followed by many other clinical "papers" and those dealing with medical-practical observations which, however, generally did not last long. This was followed by the list of biographies, lauds, memoirs and stories of Sicilian medicine, which usually fell within – as we have seen – the perspective of literary history, not least that in 1837 by Vincenzo Mortillaro, a former pupil of Scinà (20). Sicilian medicine appeared grandiose from its very beginnings, as testified in the *Dissertazioni dell'Accademia palermitana del Buon gusto*, published in Palermo from 1755. Andrés' objective was no exception, and it meant building up a vast collection of data and cognitions, aimed not only at completing an erudite work but a truly multidisciplinary one covering the inexhaustible list of observations regarding epidemics, classification of fevers and the broadest range of syndromes (a special place was reserved for syphilis), and the therapeutic procedures and public hygiene practices to remedy them.

Relying primarily upon Scinà's *Prospetto*, Andrés mentioned a large part of the authors quoted by him, with particular reference to the two Scuderis (uncle and nephew), in the universities of Palermo and Catania. He also mentioned the names of Gaetano Di Leo and Michele Foderà and other illustrious doctors who had trained abroad, particularly in France, to then return to the island bringing with them a precious luggage of knowledge and experience. Foderà, in particular, was a pupil of Magendie in Paris and gained notable acknowledgement beyond the Alps (21). Having obtained the chair at Palermo in 1841, his liberal ideas soon forced him to abandon it and return to France. Returning to Palermo in 1848, he participated in revolutionary uprisings and died soon afterwards. French frequentation explained the great interest in the doctrine of François Broussais, who had also made a name for himself in Sicily but around whom many doctors had now taken on a rather critical approach, questioning his doctrine on inflammation as it ignored other diseases, in particular those caused by miasmas. Among the wide range of epidemics on the island, one that had roused the most concern was scarlet fever; first recorded in Palermo in 1816 it was believed to have been caused by the "altered atmosphere" and was treated with laxatives, vomitives and antimony-based desoluamatives. But above all there was a real problem with *cholera;* in an attempt to eradicate it, two doctors were sent to Paris to then return to Naples and Palermo and publish, respectively, *Riflessioni* and *Istruzione popolare* explaining how to recognise it, avoid the spreading thereof, avoid contagion and treat it (22-24). The conclusive report on this epidemic is said to have been drafted by the Academy of Palermo and presented to the government in 1837 (25). It contained a *summa* with the statistics, medications, and treatments that were mainly anti-inflammatory but also stimulating and purgative.

Andrés commented that, if colleges taught the theory, "*spedali*" offered a chance for practice and so hospitals were the best places to heal. In Palermo, the city hospital had been founded in the 15th century and boasted a number of different clinics. This was followed by the number of specialities and confrontation with the *status* of Neapolitan hospitals. Special importance was given to health regulations, prevention, the management of public hygiene, particularly focussing on the building of cemeteries, bathrooms, mineral water springs and waste produce facilities. No less important observations were held for places reserved for "asphytics", that is to say violent or apparent deaths: such as the "observation chambers" in which a body was checked to ensure death. This had proved a real problem for medicine of the time. As well as treating the body, mental illnesses were also treated. Andrés followed the fate of the first "mad houses" in the 18th century: unhappy places in which lunatics were placed indiscriminately with the scabious, cankerous and consumptive, but which then became more decent and humane in the 19th century, thanks to philanthropist Pietro Pisani, renowned and lauded both in Italy and abroad (26). Finally, the matter of vaccinations: when Jenner's discovery was introduced in the English dominions, the two doctors who had practiced vaccinations in nearby Malta were called to Sicily to teach their Sicilian colleagues so that they could propagate it to uneducated people who had reacted badly to the idea of being vaccinated.

If regarding theory it was Broussais' doctrine that was put to the test (almost always to refute it), regarding practice it was Brownism that was judged, having been imposed for its simplicity. There was, in fact, no shortage of discussions imbued with the eclecticism that pervaded the island. In Palermo this diatribe did not spare the academies: the Academy of Good Taste founded in 1718 (reformed with the name of Academy of Sciences and Literature), the Academy of Anatomy, which was even older (1621) and dedicated to Iatrophysics (then Royal Academy for Medical Sciences, which was given the task to draft a *Topografia medica* of the city to provide an outline of the state of health and take provisions for public health) (27) and finally the Academy dei Chiari in Catania, as old as its counterpart in Palermo. Debates were also held in the medical schools that were established within the island's three universities, where the first chairs in legal medicine and medical policing were also founded. Less successful, however, was apparently the proposal of a "homoeopathic" Company inspired by Samuel Hanhemann's doctrine which had started to gain proselytes on the island from the first decades of the 19th century, following first the Austrian troops and then the work by Jules-Benoît Mure, who had arrived in Palermo in 1834 and published an essay on the homoeopathic treatment of cholera (28). The new transalpine approach was spread through the printing of annals and the establishment of dispensaries, in particular a *Dispensatorio omiopatico* in Palermo (29).

Concluding his panoramic treatise on the *status* and history of medicine in Sicily, Andrés formulated a *captatio benevolentiae*: if he had discussed anatomy and medicine, disciplines that were not strictly subjects in which he was an expert, and if he had forgotten some aspect of the immense matter taken in consideration, the reader was to remember that he, in fact, was "neither barber-surgeon nor anatomist", but that his intent was to stimulate the reader to study further, looking up the *sources* he quoted. His work aimed towards the "systematic recapitulation of everything", but with a very attentive focus on the present, and was pervaded by a great sense of progress by humanity. Though the path of history may be tortuous and subject to deviations, he was absolutely certain that in the end progress would triumph. This profession of intent also shows the great open-mindedness and sensitivity of humanist intellectuals in dealing with a "total" vision of knowledge, including medicine and the history thereof, but above all testifies the permeation (and popularity) of transalpine ideas in Sicily, not only on the social and political plain but also on that of science and history.

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Original article: history of medicine

The young Nicola Pende and the ambiguous adrenal gland: at the origins of Italian endocrinology

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Abstract. The thesis of Niccolò Pende, supported in 1903, bore the title: The alterations of the adrenal gland after resection of the splanchnic nerve. Studies on the adrenal glands were the main gate through which the Apulian clinician became one of the first scholars in the world to attempt a systematic organization of the endocrine glands and their functions. Six years after graduating, the treatise on the physiopathology of the adrenals placed Pende on the attention not only of the Italian medical class, but also of the newly formed American magazine *Endocrinology* and of Sir E. Schaefer himself. The idea of a close correlation between the nervous system and endocrine glands constituted the guiding idea by following which Pende built the systematic building of Italian endocrinology; however, it also constituted the limitation that prevented him - for example - from grasping the exact distinction between the functions of the cortex and medulla of the adrenal glands. The present contribution aims to underline the precisely ambiguous role that preconceived ideas play in the construction of scientific hypotheses.

Key words: Nicola Pende, endocrinology, adrenal gland, preconceived ideas

Introduction

When does a new scientific discipline come into being? When a medical speciality detaches itself from the corpus of general medicine to take upon itself the right to claim as separate and distinct not only Subject, Methods and Epistemology but also University Chairs, Sector Journals, Institutes, Schools? Is it possible to pinpoint a moment, a place, a figure that marks a caesura between a before and an after? Certainly, depending on the criteria cited by the historian to respond to these questions, different milestones may be identified: if one favours internal history, the history of ideas and concepts, the answer will be borne out by the reading of articles, treatises and, perhaps, by awareness on the part of coeval scientists – as I. B. Cohen would have said. If the material examined consists of the minutes of academic committees, financial reports, juridical summaries, scientometric criteria, then the so-named external history may or may not invalidate the conclusions reached by the first method. But unexpected factors may intervene, linked with the historian's sensitivity, his belonging to a national community or to a collective of thought. In this brief essay we shall examine, with criteria prevalently internal, the affirmation – wholly Italian – of the seminal role played by Nicola Pende in the birth of endocrinology, with specific reference to the episode that lay at its origin, seeking to point out how – setting out from an obscure physiopathological subject, the function of the suprarenal glands – he built up a coherent body of knowledge which, at least in Italy, has led to acknowledgement of the Apulian physician as founder of the discipline.

Nicola Pende was born in Noicattaro (Bari) on 21/04/1880. Having attended the Liceo-Ginnasio Cirillo in Bari he enrolled at the Faculty of Medicine in Rome where his teachers were Giovan Battista Grassi, Amico Bignami, Ettore Marchiafava and Luigi Luciani. In the laboratory of Michele Bufano he became acquainted with the experimental and biochemical methodologies that were to become so useful in his research activities. Graduating in 1903, he remained in Rome until 1909, when he obtained the post of assistant at the Institute of Pathological Medicine, University of Palermo. Giacinto Viola taught here, the second leading light of Italian constitutionalist medicine after Achille De Giovanni. Viola took Pende with him to Bologna after the war – in which the latter had been an army doctor in Bari, Rome and Padua – and as early as 1921 he returned to Sicily as head of Clinical Medicine at the University of Messina. In 1923 he was at the centre of a troublesome series of events for the position of full professor between Parma, Sassari and Messina, which ended up with a sudden call for a competition in Cagliari *ad personam* . But Pende was too late to take the position in Sardinia because meanwhile the Minister for Education, Gentile, called him to Bari , as first Rector of the then forming Università Adriatica Benito Mussolini. Here too Pende remained only a few months, being called to menage the Medical Clinic of the University of Genoa, where he founded the first Institute of Human Biotypology and Orthogenesis. In 1925 he took the chair in Rome for Medical Pathology and Clinical Methodology, and in December 1933 became senator of the Kingdom. In 1938 his signing of the Manifesto of Racial Laws led in 1944 to the order of forfeiture of the position of senator, a provision that was quashed four years later. Restored to the chair in Rome, he remained until 1956.- He died on 8th June 1870 in Rome.

Rome 1912

If the paper read at the XXII Congress of Internal Medicine in Rome was the one wholly published in the proceedings, then the moderators who sought to cut him short for exceeding the time limit could not, at bottom, be reasonably faulted. Sixty-seven very densely written pages suggest the duration of Pende's intervention, entitled "Internal secretions in relationships with clinical science". Certainly the task «entrusted him by his illustrious masters, to give *rapidly* and with a *critical spirit* a balanced account of positive endocrinological facts» (1) was onerous, and it may be that Pende (1880-1970) had in mind the address to the *British Medical Association* (2) with which Sir Edward Albert Sharpey-Schaefer had inaugurated the study of internal secretions as a physiological science – as well as clinical – seventeen years earlier (3, 4). But his masters, Edoardo Maragliano (1849-1940) and Achille De Giovanni (1838-1916), intervened in order that the thirty-two year old clinician might finish reading his paper. According to his son Vito Pende, on that occasion the great clinician Augusto Murri (1841-1932) exclaimed: «Behold a new sun rising!».

Effectively, Pende – who at the time was assistant to Giacinto Viola (1870-1943) at the Institute of Medical Pathology in Palermo – took upon himself the role of systemiser of «endocrinology which seems to us today rather a *true new science*, of the kind that reform, dominate and orient the medicine of an entire age» (1). Of this new science Pende attempted not only a complete summary but also put forward – in the final pages of his paper – a theory that was a «brief, general and unitary synthesis». Presented modestly as a draft, as a working tool, point of departure and meeting (1), the theory in reality concluded a decade of avant-garde – at least in Italy – experimental and clinical studies on the subject. For all that it was fleeting, this provisional theory contained a thread that would run through the whole scientific career of the Apulian clinician: the synergy between the *endocrine* and *nervous* systems, in particular the sympathetic section of the autonomous nervous system. The 1912 theory proposed the existence of a tropho-regulator system of the organism, consisting of the two cited systems and maintained in constant equilibrium between two antagonistic neuro-hormonal groups: accelerators and retarders of matabolism. Without entering into the details of this theory, it is worthwhile underscoring how it already clearly contains that which, in the decades to come, must have been Pende's correlative psycho-neural-endocrinology:

> Since the sympathetic nerve is connected to the psychic centres, we understand in what way a psychic trauma or a cerebral lesion may produce an

> endocrinal syndrome, Basedow's syndrome for example, if we admit the secreting influence of the sympathetic nerve on the hormone producing organs. On the other hand the facts, which we have already analysed elsewhere, demonstrate a great influence of hormones on psychic functions: which explains the onset of psychic syndromes due to a primitive hormonal disruption… our hypothesis may be applied to growth disorders, to metabolic disorders, the diseases of the visceral nervous system, and lastly to the pathogenesis of the highly complex syndromes of the endocrine glands. It perhaps allows us to orient ourselves even in the solution of the problem of determinism of morphological types and individual temperaments (1).

It seems to us that one of Pende's powerful, original and definitive ideas should be pointed out here. Victorius C. Medvei, author of a monumental history of endocrinology, places the beginnings of neuroendocrinology in 1936, with the *Croonian Lecture* by Francis H. Marshall (1878-1949) (5). On that occasion the British physiologist, a pupil of Schaefer, underlined the role, in the overall female reproductive hormonal balance, of the hypothalamus and of the nervous system in general.

Even more than being useless, in the history of science it is sickening to raise or lower the bar of a discovery, of an idea, along the axis of time, almost as if it were among the historian's most important duties. Even though this concept had peak moments in the 19th and part of the 20th century. And in any case, to understand how an idea, a research programme, a scientific paradigm took place at different times and in different places is not idle, above all when that programme of research was fertile and its various declensions took on different connotations, precisely in relation to the historical, social and political situation in which they were lived.

In Pende's case, that "determinism of individual types and temperaments" would lead in subsequent years to the theory of Biotypology and Orthogenesis on the one hand and, on the other, to his controversial idea of "race" which has weighed so heavily on the historical image of the Apulian physician. In Rome, in 1912, his ideas on the subject were already fairly clear. Referring to Charles Richet (1850-1935) who two years earlier advocated a "physiology of the individual", Pende expressed his wish:

> We hope for the conquest of what must be the goal and aspiration of future physiology and pathology, which is to say, the substitution of a physiology and pathology of the individual for the physiology and pathology of the species (1).

Moreover, in 1912 he asked to further backdate the origin of the idea of the neuroendocrine: «On this concept of the neuro-glandular concatenation we have been insisting for several years ... we maintain that these two systems, endocrine and sympathetic, are to be considered as a unitary apparatus: the endocrine-sympathetic apparatus» (1).

In truth this idea had been adumbrated precisely in his first scientific work, his degree thesis.

Rome 1903

Nicola Pende, Nicolò as he signed his first works, graduated at the age of twenty-three in Rome at the Institute of General Pathology, headed by Amico Bignami (6, 7), with a thesis entitled: *Alternations of the suprarenal gland after resection of the splanchnic nerve*. Amico Bignami (1862 - 1929), together with Ettore Marchiafava and Giovanni Battista Grassi, established the Italian road to the etiopathogenesis and anatomopathological study of malaria. There are traces of this research tradition in Pende's earliest scientific productions (e.g.: *Il liquido cefalo-rachidiano in alcuni casi di perniciosa malarica* published in 1906 in the medical section of the journal "Il Policlinico"). In Rome Bignami from 1900 led, as adjunct professor, the Institute of General Pathology where, over and above malaria, he carried out research on the nervous system, the haematopoietic system and, what is of interest here, work on the internal secretion glands in their reciprocal relationships and with the vegetative nervous system. A brief extract from the Pende's thesis appeared, on 28th November 1903, in the Practical Section of the Journal "Il Policlinico" (8), in which Pende claimed credit as first experimental pathologist of the suprarenal glands and their innervation: `study of the alterations that the suprarenal capsules undergo due to lesions of the nerves with which they are so abundantly provided, had not to my knowledge been attempted theretofore in any way by experimental pathology». Details of the experimentation in question would be supplied in the monograph of 1909 (9). Here, instead, the pathologist restricted himself to giving brief outlines of the experimental methodology in order to establish some fundamental concepts:

a) resection of the splanchnic nerve induces atrophy of the suprarenal medulla and this is the cause of the loss of production of Schaefer's "prodigious active principle". The conclusion was icastic, but somewhat hurried: «It is therefore appropriate to conclude in favour of the existence of regulatory nerves of trophism, independent of regulatory nerves of vasoconstriction, of the suprarenal capsules. But trophic nerves of glandular elements cannot but be secretory: therefore in the splanchnic and in the celiac plexus, together with the vasodilator nerves of the capsules demonstrated by von Biedl and with the vasoconstrictors demonstrated by my researches and by the recent plethysmographic research of Laiguel and Hallion, there are also the secretory nerves of the suprarenal capsules, nerves which heretofore had been merely presumed».

b) a hypothetical nervous aetiology of Addison's disease, caused therefore by resection of the splanchnic;

c) a feedback mechanism mediated by the same nerve for the compensation of pressure imbalances;

d) lastly, a hypothesis of specific secretion by the adrenal cortex "in connection with phenomena of reproductive life".

Rome 1552 - London 1855

Although published only in 1714, the *Tabulae Anatomicae* by Bartolomeo Eustachio (1520-1574) had remained unprinted in the Vatican Library since 1552. In these works the Roman anatomist illustrated the *glandulae renibus incumbentes* of which, in 1563 (10), he claimed to be the discoverer. Nonetheless, neither Eustachio nor a long procession of anatomists after him clearly put forward a function for the suprarenal glands.

This was the case with Casserio (1561-1616), Spigelio (1578-1625), Thomas Wharton (1612-1673) and Morgagni (1682-1771). Caspar (1585-1629) and Thomas Bartholin (1616-1680), father and son, were among the first to state that the *capsulae atrabiliariae* had a central cavity in which a mucus, precisely, of black bile, was secreted. Jean Riolan the Younger (1580-1657), basing his view on observation of the greater relative size of the glands during foetal life in comparison with adult life, hypothesised that their function was linked to embryonic growth, and this theory still had lasting echoes in Pende's day. Other Authors hypothesised functions linked to the position of the suprarenal capsules, and therefore with a regulatory secretion of the excretory function of the kidney (Joseph Lieutaud, 1703-1780), or as anastomotic deviator shunt of arterial blood incoming to the kidneys (Giuseppe Ippolito Pozzi 1697-1952).

Confirming this unsolvable knot, as early as 1716, the Academy of Sciences of Bordeaux established a competition aimed at clarifying the function of the suprarenal glands. Two years later, Charles de Montesquieu (1689-1755) pronounced thereon in *Discours sur l'usages des glandes rénales suivi de quatre résomptions*. Therein, the future author of *L'ésprit des lois* ran rapidly through both the historical hypotheses – such as that of the Bartholins, father and son – and those, some more original than others, put forward on the occasion of the prize.

> Most of the [competition] participants had only the merit of heartfelt, noble emulation, while others, more fecund, were no more fortunate: but these vain efforts are rather to be seen as proof of the obscurity of the subject and not of the sterility of those who dealt with it.

Thus there was a proposal that the suprarenal capsules secreted a substance which, on reaching the kidneys, induced the formation of a kind of its own bile; others hypothesised the function of filtration of the pararenal fats, or of further filtration of blood issuing from the kidneys. Yet others hypothesised a contractile function like the cardiac function for expulsion of a dense liquid; in any case, Montesquieu's conclusion was disarming:

> From all this we see that the academy will not have the satisfaction of awarding the prize this year and that this day is not as solemn as it was hoped to be… in spite of the experiments and the dissections which have been put before your eyes, we have become aware of the difficulty in all its breadth and have learnt not to wonder about the purpose not having been achieved. Perhaps one day chance will do that which all these researches have been unable to (11).

The good fortune invoked by Montesquieu would have to wait more than a hundred years, three hundred from Eustachio's discovery, before the suprarenal glands began to reveal their secret. And nearly all the histories of endocrinology that do not wish to go back to the Venus of Willendorf (one of the many Palaeolithic Venuses with exaggerated female attributes, almost certainly apotropaic of fertility, acrobatically interpreted as steatopygia by medical historians who are interpreters of a scientific historiography of days of yore) date the first clinical accounts of dysendocrinism to 1855 and the work of Thomas Addison (12). Addison (1795-1860), while studying "idiopathic" anaemia in 1849 – what would later take the name of Addison-Biermer's disease or pernicious anaemia – had proposed therein an etiopathogenic role played by the suprarenal glands, having found in several cases the lesion of these organs as the only anatomopathological evidence.

> It was whilst seeking in vain to throw some additional light upon this form of anæmia, that I stumbled upon the curious facts, which it is my more immediate object now to make known to the Profession; and however unimportant or unsatisfactory they may at first sight appear, I cannot but indulge the hope, that by attracting the attention and enlisting the cooperation of the Profession at large, they may lead to the subject being properly examined and sifted, and the enquiry so extended, as to suggest, at least, some interesting physiological speculations, if not still more important practical indications. The leading and characteristic features of the morbid state to which I would direct attention, are, anæmia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin, occurring in connexion with a diseased condition of the "supra-renal capsules. (13).

In fact the eleven cases of Addison, which presented the symptoms that later became the classic ones of the disease, all evidenced grave damage to the suprarenal capsules, due in six patients to tuberculosis, and in the rest prevalently to primary or secondary carcinomas. Six years later he published his monograph on the disease to which Armand Trousseau gave the name, precisely, Addison's disease (14). Six of Addison's eleven patients evinced tubercular lesions of the suprarenal glands. In the same year, while at the *Collège de France* Claude Bernard explained what he meant by internal secretions, C. E. Brown-Séquard began his experimental researches which were to lead him to putting forward a theory that took a long time to die, since Pende was still combating it in his monograph of 1909: the theory of the detoxifying role of the suprarenal glands themselves. Brown-Séquard experimented by removing the suprarenal capsules, thus causing the death of his animals – cats, mice, dogs, guinea-pigs – in an Addisonian crisis: in the space of 24 hours, after rapid death throes, the animals succumbed. So the capsules, connected in Brown-Séquard's view to the spinal centres, were indispensable to life, probably because they removed from the body a not better defined toxic substance whose remaining in circulation also explained the darkening of the patients' skin, a "melasma", presage of death (15). Still in 1856, Vulpian pointed out a "special matter" in the medulla of the suprarenal and in the veins of the organ, coloured by iron perchloride, a matter he considered responsible for the function of the glands (16).

Schaefer's "prodigious principle"

Not all scholars accepted Addison's disease as a definite nosological entity. For example, in Italy in

1863, R. Mattei in the *Sperimentale* denied its identification, perhaps due to a theoretical conservatism as supposed by R. S. Lavenson in an overview of acute suprarenal insufficiency of 1908 (17). The suprarenal glands eluded the understanding of physiologists and clinicians in the difficulty of pinpointing separate functions for the medullar and cortical: while Addison had pointed out a condition which only in the 1920s must have been correctly ascribed to the collapse of the production of substances produced in the cortical, the substance identified as agent physiologically produced by the suprarenal was the one identified by Oliver and Schaefer in 1894: a prodigious principle capable of causing sudden and considerable rises in pressure, both in the clinic and in experiments on animals. Schaefer had correctly identified the origin of his prodigious principle – which Abel and Crawford would shortly isolate, giving it the name of epinephrine (18, 19) – in the medulla of the suprarenal gland:

> Injection of a large dose of extract of the cortical substance has little or no effect, whereas extract of even a minute dose of decoction of the medullary substance produces the ordinary physiological results to a *prodigious* degree. We conclude therefore that the active principle of the extract is contained entirely in the medulla, the very small effects which we have sometimes got from extracts of cortex being probably to be explained by post-mortem diffusion of the medullary juice, or other accidental contamination (20).

But as for Addison's disease, the British physiologist noted only that extracts of diseased suprarenal gland had no physiological effect at all. The suprarenal remained ambiguous between hypertension and melasma. Even twenty years later, in his treatise on the endocrine organs, Schaefer initiated his chapter on the physiology of the suprarenal cortex as follows: «Little is known about the function of the cortex». Taking as given his clear distinction from the medullar on bases both histological and embryological, the only biochemical singularity was its considerable lipidic content and the only physiological annotation was related to a probable association with the sexual glands. However, «there is no evidence that any kind of active autacoid substance is produced by the cortical cells» (21). Whereas the medulla contained Vulpian's chromaffin bodies and the excitation of the splanchnic nerve induced the secretion of epinephrine by the medulla. Here – it was 1916 – Schaefer cited our man: «Pende found that section of the splanchnic nerves leads eventually to atrophy of the medulla» (21). The relationship between this fact and death by bilateral adrenalectomy remained an enigma: in witness of just how ambiguous the function of the suprarenal was, Schaefer hypothesised that adrenalin and melanin were substances in competition for a substratum, so the suppression of the production of adrenalin by medullary deficit induced hypersecretion of melanin.

Nicola Pende's Contribution

Schaefer's citation of Pende referred to the latter's degree thesis. Had Pende made no further contribution to the question? In fact in 1909 he had published a monograph on the suprarenal apparatus (9), a voluminous treatise that summed up the question from the viewpoint of international literature explored in a detailed manner and – even more importantly – laid forth the Apulian clinician's experimentations and the conclusions he hypothesised with regard to the physiological and clinical aspects of those glands.

On the subject of Addison's disease:

> Today the pathogenetic question of the disease is found more or less in the terms in which Addison himself, the creator of suprarenal pathology, put it in 1855… we do not yet know the clinical determinism of melanoderma…

And, on the subject of himself:

> I carried out a series of researches with the purpose of isolating, as much as is possible with experimental methods, the function of each of the two portions of the suprarenal gland, that is, the cortical and medullar… with a third series of researches aimed at studying the morphological physiological relationships between suprarenal apparatus and the other internal secretion

> glands… following the avenue disclosed and already so felicitously trodden in Italy by De Giovanni and his school (22).

Adrenalin – produced by the medullary portion of the gland – had already been isolated and described, and Pende hypothesised that the product of the cortical was a lecithin, which certainly had no relationship with blood pressure:

> I wanted to carry out research on the action of cortical extract on blood pressure in man, injecting in several subjects, subcutaneously, the watery glyceric extract of cortical substance from horses or oxen, isolated with maximum care from the medullary portion… pressure remained always unmodified (22).

Whereas the cortical extract «rapidly produced the return of forces and, what was even more impressive, the reappearance of menstruations» (22), so Pende hypothesised an important role played by cortical substance in "organic metabolism".

The clinician thus became physiologist and experimented intensely on animals (usually cats and dogs): having devised a technique to prevent the laboratory animal from dying immediately after removal of the suprarenals, he made a sort of surgical Addison (hypocorticosurrenalism) and, therefore, was able to verify how organotherapy with suprarenal cortical extract could attenuate asthenia, weight loss and cachexia and delay death. Moreover – let us not forget that the word "endocrinology" was coined in 1909 by Pende – great attention was paid to the relationships between the suprarenal ad other internal secretion glands, since this was the thread running through his entire research: the living organism is governed by a *consensus partium*, a harmony, which is embodied in the correlations between the endocrine glands, between this system and the autonomous nervous system and, again, of the latter with the neuraxis, finally reaching integration with the psyche. In Pende's intent, present right from these first writings and, with the years, increasingly consolidated, the constitutions of Viola and De Giovanni would be transformed into the harmonious somatopsychic unity of the tetrahedron. There are different pendian declensions of this platonic pyramid. The biotypological pyramid that distinguishes the aspects under which the living individual presents himself to the physician's examination: the morphological aspect, the humeral-functional aspect, the characterological-moral aspect and the intellective aspect. Another, more oriented towards constitutional harmonies is as follows: Hippocratic harmony, that is, the relationship between instinctual vegetative structures, substantiated by the vegetative nervous system and the endocrine glandular system and the affective and rational dimensions, having their fulcrum in the encephalic structures and in particular the diencephalon and hypothalamus; Thomistic harmony, the reciprocal give and take between biological I and spiritual I which found its fundamental material in the structures of Hippocratic harmony and thence was raised to the synthesis of psyche and body, constituting the indivisible unity of the human person. Christian personalism and medical personology; interpersonal harmony, that is, the agreement of solidarity resulting from altruism, foundation of human fellowship; and lastly, the harmony of Christian splendour that is the vertical dimension of this "regulated sympathy among bodies", the true philosophical leitmotif of Pende's work. But the tetrahedron recurs often in his copious literary production, in other forms which it would be tedious to recall here.

Against those who maintained the uniqueness of the active suprarenal principle, identified as adrenalin, and who therefore ascribed the deficiency thereof as being the cause of Addison's disease, Pende efficiently set forth a series of bibliographical and experimental evidence that centred above all on the difficulty of isolating *in vivo* the two portions of the suprarenal gland:

> Since 1895, Cybulski and Szymonowicz had maintained that the whole Addison syndrome, like the syndrome of experimental suprarenal insufficiency, might be simply explained with the abolition of the function of the medulla-suprarenal gland, a function which in those authors' view could be summarised in maintaining normal the functional tone of the vasomotor, cardiac and respiratory nerve centres and of the centres of muscle tone (23).

But, Pende points out, on the minuscule glands of a cat it is not possible to carry out an emptying of the medulla without also destroying the cortical and then:

> if the emptying is fatal, as is removal of the two capsules, this would appear to depend rather upon suppression of the cortical than the medullar, still largely represented by the paraganglia (22).

Pende had almost resolved the ambiguity of the suprarenal; it is a pity that a few lines on he added:

> We believe that the medullar substance and the cortical of the capsules constitute, at least in the higher animals, an anatomical and functional unity of which [*sic*] cannot be split by either the physiologist's knife or pathological processes (22).

and claimed that the experiences of Biedl (24) who had supposed that ablation of the cortical alone was responsible for the laboratory animals' death had need of being subjected to further controls.

However, a further experiment by Pende demonstrated that it is precisely the cortical which keeps the animal alive:

> I now made the following experiment: in kittens, I first removed the right capsule; after about a month I severed all the nerves of the other capsule. After this second operation, the results of my recent experiments being recorded, I supposed that atrophy of the medullar portion should occur more or less belatedly. On a third occasion, about three months after the second operation, I wholly removed the left capsule; I then expected to see the symptoms of cortical insufficiency added to those of medullar insufficiency (22).

And in effect things went as predicted: only after the third period did cachexia, deep asthenia and death occur. Loss of the medullar function was compatible with life, while that of the cortical function was not. We shall not go into detail about the clinician's further experiments; in 1909 Pende would have solved the problem but for his insistence on considering the two parts of the suprarenal gland connected "in the sense that the medullar cells cannot perhaps carry out a function efficient for the organism's life if not in the presence of a certain quantity of actively functioning cortical cells" (22). Why, when he had come so close to identification of the active principle of the cortical, did Pende insist on keeping together the role of the medullar in the genesis of suprarenal insufficiency both chronic and acute? We do not know and may only hypothesise that the vast literature on adrenalin, on "Schaefer's prodigious principle", prevented the young clinician from assigning a wholly new and independent role to his "lecithin" of the cortical. Moreover, his success in demonstrating the role of the autonomous nervous system in the production of adrenalin must have contributed to keeping the role of the medulla at a higher level. For all his life as a scholar Pende would assign a special place among his contributions to medical science precisely to the resection of the splanchnic nerve and the consequent lowering of blood pressure; and, for a long time, "Pende's operation" would remain on the rolls of surgical procedures as an anti-hypertension intervention (26, 27). But probably the idea that prevented him more than any other from seeing what was practically there before his eyes – i.e. the autonomous role of the cortical – was exactly that preconceived idea, that pre-inductive thought which according to William Whewell is indispensable for "holding together" empirical facts but which Claude-Bernard exhorted scientists to be ready to abandon when they went against the facts. Which is to say the idea that in the living organism *tout se tiens* and, therefore, not only the psyche with the central nervous system and this in turn with the vegetative and the latter with the endocrine glands, but also "within" the gland itself, medullar, cortical and glandular nerves constitute a coordinated, anatomical-functional unity. This is what happens when an idea in itself original becomes an obstacle to grasping the facts. To keep together cortex, medulla and suprarenal nervous system, Pende hypothesised a wholly new metabolic cycle: the cortical synthesised the lecithin, setting out from the toxic products of replacement of the nervous cell, with lecithin in turn utilised in the anabolic process of the nervous system. So an alteration of the cortico-suprarenal glandular function was simultaneously translated into both an insufficiency of the "primary neuro-dynamogenic material", with consequent asthenia, aboulia, apathy, and into a poisoning of the nervous system itself (Pende thus recovered by another way the hypotheses of Brown-Séquard) due to insufficient removal of toxic catabolites (22).

Thus both the cortical and medullar had a role in the metabolism of the nervous system. The concept was resumed and developed in the fourth chapter of the text, dedicated to the *Physiopathology of the suprarenal syndromes.* Here, after dealing with the two rival pathogenetic doctrines (the "sympathetic", that is, that lesion of the sympathetic was the cause of Addison's disease, and the "glandular", which held that it was caused by a medullar or cortical excretive defect), Pende put forward "his" hypothesis (22) which considered the suprarenal gland as indeed composed of three districts, cortical, medullar and nervous, but integrated, "indissoluble links of the same chain". So at the heart of the pathology there was a "lecithinogenous" defect of the cortical and an "adrenalinogenous" defect of the medullar, both under the influence of the vasomotor and vaso-secretory nerve centres (25). Coherently, melanoderma was ascribable to an injured sympathetic innervation and therefore to an injured medullar secretory function operating on the complex functional mechanism that regulates, through the chromatophore cells, the normal pigmentary tone of the skin (22). Here too Pende was deceived by the ambiguous suprarenal: skin pigmentation was indeed due to hyperfunction of the cells that produce melanin… but this had been related to the absence of a hypothetical inhibitory mechanism mediated by the sympathetic and by adrenalin.

Having "created" a syndrome, it would often be found by Pende in clinical contexts. This was the case - for example – of the "Pende's hyperthymic syndrome".

In the first half of the twentieth century, more than a million young Italians were found affected by a new disease: Pende's hyperthymic syndrome. According to the Apulian clinician, it was a case of hyperfunction of the thymus gland that caused a pathology analogous to Froehlich's adiposogenital syndrome: «For many years I have found that in the sphere of infantile growth, many youngsters – who are fat and tall from birth and have very small genitalia – in spite of being teenagers, look like big babies in their appearance, faces and temperament. These children are greedy, heavy water drinkers, lazy, and characterised by a persistent mental infantilism. Their serious anomaly of growth is due to a hyperfunction of the thymus gland». Thus wrote Pende in an unpublished manuscript (30). This undated manuscript can be probably dated to the last ten years of the clinician's life, owing to a reference to his return from Barcelona, where supreme honours had been rendered him in about 1965. In it, Pende wrote questions and answers, defining himself "the master of endocrinology and orthogenetic world medicine". Unfortunately. this Pendian contribution has also passed into the field of obsolete history, with the aggravating factor that the therapy envisaged by Pende – radiation of the thymus with X-rays – caused adenoma and carcinoma of the thyroid in a great number of these poor children. (28, 29).

The same determination Pende showed for the triadic etiopathogenesis of Addison's disease: in a clinical case sent to the journal *La riforma medica*, the clinician, at the autopsy, found all the signs of the aforementioned syndrome. The tubercular patient had died after showing the signs of Addison's disease; however, both the medullar and cortical of the suprarenals appeared little altered histologically, although "the two main suprarenal glands present, with regard to the cortex, a considerable deficiency in lipoid granulations" (31). The main lesion instead regarded the solar plexus, with a "hypertrophic sclerosis of the semilunar ganglia". In fact:

> Pende has already developed elsewhere the concept which considers Addison's syndrome as a disease of the entire suprarenal apparatus (cortical tissue, medullar tissue and sympathetic tissue); without such a unifying concept it is not possible to explain either the genesis of various symptoms of the disease or the anatomopathological finds so different from case to case (31).

So going back to the 1912 paper at the Congress of Rome, one clearly understands which clinical and physiopathological experiences fortified Pende in the concept that

> it is demonstrated for certain glands, such as the thyroid and the suprarenals, that the nervous system regulates the secretion thereof, by means of secretory and vasomotor nerves. This results from my own experiments, and those of Pellegrino and of Biedl… on the suprarenal glands (1).

Pende's endocrinology

Two years after the Rome paper, Pende began publication of the first edition of his monumental treatise *Endocrinologia. Patologia e Clinica degli organi a secrezione interna.* Although his then chief, Giacinto Viola, warned in the preface of the immaturity of some of the author's views (25), he in any case had to acknowledge that Pende's undertaking to write this treatise was extremely difficult, as demonstrated by the fact that his predecessors north of the Alps had discussed only particular aspects thereof (von Biedl only physiopathology; Wilhelm Falta only clinical aspects) (32). On the other hand, the importance of the treatise was borne out by the authoritative American journal *Endocrinology* (25) which, the year after publication, recognised that

> This is the largest and most comprehensive book on endocrinology that has come to our attention, transcending in size the well recognized monograph of Biedl (while the two volumes of the second German edition of the latter cover 1226 pages, nearly 300 pages are devoted to a bibliography). In going through Professor Pende's book it is very clear that he has given special study both in the laboratory and in current literature of all countries, and we regret very much that this book has not yet been translated from Italian.

A new medical specialisation was on the point of being established: Pende's treatise was not yet dogmatic – as Augusto Comte would have said – and he therefore had to:

1. resort to historical method, because it was a young science (33),
2. bring together everything that had been said and written in those years, compiling a huge bibliographical review,
3. unite a mass of experimental facts – his own and others' – in the attempt, effectively successful, at supplying an account as wide-ranging and profound as possible, of the knowledge of a subject which he himself had contributed to naming, precisely in his 1909 treatise.

For this reason a caveat in the introduction put the reader on his guard about the fact that the concepts set forth were to be understood as working hypotheses and not as endocrinological canons. In fact when many years later Pende was called upon to draw up the item "Endocrinology" for the Encyclopaedia Treccani, he would recover much of his introduction, continuing to distinguish the functions of the endocrine organs as "morphoregulating", "chemioregulating" and "neuroregulating", to which he added a "psychoregulating" function. The basic concept is that the endocrine system, together with the nervous system, is the structure of fundamental integration of the living organism. This integration envisages that psyche, central nervous system (for the life of relationships), the autonomous nervous system (for vegetative life) and endocrinal system should work in close coordination for the constitution of harmonious individual unity. In particular, just as the autonomous nervous system implements balance between accelerating functions (the sympathetic) and retarding systems (the parasympathetic), so does the endocrinal system, in its various glandular sectors, provide for the production of excitant-catabolic and excitant-anabolic hormones. We shall not go any deeper into the construction of the new science that Pende, at thirty-six, is entrusting to these pages, except to point out that it harks back to a noble genealogy in the constitutionalism of Viola and Achille De Giovanni, where it declares that:

> Our school therefore distinguishes two main and antithetical morphological types that represent the two forms of opposed deviation from the average morphological type: the long-limbed or micro-splanchnic type in which excessive development of the extremities dominates over the relatively deficient development of the trunk (microsplanchnia); and the short-limbed or megalosplanchnic type in which excessive development of the trunk (megalosplanchnia) dominates over the

> relatively deficient development of the limbs. The two types correspond to the third and first morphological combination, already distinguished by De Giovanni.

And it was from here that the ephemeral science of Biotypology and Orthogenesis would extend, which was to constitute the acme of Pende's production in the years to come.

As for the ambiguous suprarenal, the *Endocrinologia* devotes more than one hundred and thirty pages to it in which the author recovers all the scientific literature on the subject and, above all, claims the importance of his experiments (of 1909) on the question of innervation of the medulla and on the absence of capsules induced in animals.

In comparison with the 1909 text, Pende is now convinced that cortical and medullar produce different substances, the latter adrenalin, whereas the cortical perhaps produces not only lecithin but cholesteryl esters, in a word «cortical lipoids that actually represent products of secretion…. We can have no doubt about it, especially for reasons of analogy with what is also demonstrated today for the secretions, also of a lipidic nature, of other endocrine glands (genital gland etc.)» (25). The fact is – Pende is well aware of this although he himself is a victim thereof – that the physical action of these compounds is "obscured" by the comparison with adrenalin, for which an antagonistic action is hypothesised (hypotensive?) or, as suggested by Pende, an action aiding the adrenalin. Certainly the cortical secretion is seen to be in relationship with the processes of replacement and with the genital organs (25): «the clinical cases of hyperplasia or of cortical adenomas, coincident with early puberty and with phenomena of pseudohermaphroditism… the parallelism between hyperfunction of the genital endocrine gland and hyperplasia of the cortex render it more than probable that there exists a physical collaboration between it and the sexual glands» (25).

Pende's experiments were, coherently with the dictates of the "foetid Bernard kitchen" (34), experiments of destruction, capsular emptying, removal of part of the gland, then a whole gland, then both, rescission of the related nerves, experiments of grafting and implantation *à la* Voronoff (the Russian physician who, became very famous in the 1930s for his transplants of monkey glands in humans with view to achieving rejuvenation and the recovery of sexual potency) (35), organotherapy with homo- and allospecific glandular extracts. And if all the numerous authors who had dealt with the subject to date (1909) had not succeeded in obtaining engraftment of the complete capsule (but only the medulla), «I believe I have drawn attention to the fact that with appropriate technique, both medullar and cortical tissue may be equally engrafted» (25). Indubitably one of the merits of these works is, precisely, the personal and original synthesis between clinical practice and physiology, between sickbed and laboratory, to which may be added Pende's total mastery of the vast coeval literature on the subject.

As for the ambiguous suprarenal, for Pende it would remain as such, blocked as he was by his demand for functional unity of the gland. Experimental progress notwithstanding, even in 1925, Pende reaffirmed the impossibility of clearly separating the cortical from the medullar functions

> Can we now distinguish clinically the symptoms of hyposuprarenalism in hypocortical and in hypomedullar symptoms? A clear separation, for the reasons already mentioned of the mutual anatomical and functional relationships between the two tissues of the gland, is not possible (36).

Between 1927 and 1937, lastly, the role of the cortical of the suprarenal gland would be clarified, and acetate hydrocortisone would be synthesised (37).

In an article of 1945 (38) Pende would once more claim to be the founder of endocrinology:

> Endocrinology is a term I introduced in 1909 – and its synonyms are hormonology, incretology and science of the internal secretions of the endocrinal glands… in 1916 the first two great treatises on endocrinology come out, my own and that of the Englishman Schaefer. But as early as 1909 my monograph on the suprarenal apparatus and the parasympathetic organs was published, and in 1912 at the Congresso della Società Italiana di medicina interna in Rome, I summarised, in an

official paper, the basics of clinical endocrinology, which after forty years have remained more or less unchanged (38).

The court of the history of science

Was Pende's ambiguous suprarenal the lucky beginning of a discipline and, at the same time, a headstrong ideological error?

> One must avoid a possible equivocation when proposing the image of the court to characterise the function and meaning of a history of science which does not forbid itself scientific judgements of value. Judgement in this field is neither a punishment nor an execution. The history of the sciences is not the progress of sciences in reverse, that is, a prospect of the milestones of goals achieved, of which the truth of today would constitute the vanishing point. The history of the sciences is an effort to render understandable the extent to which certain notions or attitudes or methods, now outdated, were in their own day an advance, and consequently in what way does the outdated past remain the past of an activity for which we must preserve the name of science (39).

The idea of regulated 'sympathy' among organs dated back at least to Galen who, in the *De usu partium* had described part of anatomy from the organic nervous system: and he attributed to the wealth of anastomosis of this system, and therefore to the wide network of communications it established for circulation of the vital and animal spirits, the function of connecting mutually distant parts of the body, in such a way as to justify 'the suffering together' – for example – of the urinary tracts and stomach in renal colic. Meaning the *consensus partium*, the 'sympathy' between organs. Even earlier, Plato had underscored that there were several principles bearing government of the body, in particular the irascible and the concupiscible principles, the less noble, had been relegated – one to the chest, the other to the belly – to control the visceral and organic functions (40). In the early 19th century François Xavier Bichat, in the *Recherches* and even more so in the *Anatomie générale*, having defined life as a grouping of the functions that resist death, he divided these functions into two great systems:

– *la vie animale* or of relationships, including the functions necessary to maintain the living being in relationship with the external world, therefore the conscious and voluntary sense-motory context in a broad sense;

– *la via organique*, understood as the life of the organs, or vegetative life, including the functions of nutrition and reproduction. Obviously this was not of his own invention, being traceable to origins in the writings of Galen and Plato, but Bichat made a system of it and corroborated it, thanks to the great extent of his anatomical-autoptical observations. Furthermore, he assigned a "seat" to the Galenic spirits: animal spirits were localised in the cerebrospinal system while the vital spirits, vegetative life, the life of the organs, found its seat in the ganglionic system. Moreover, Bichat claimed the (moderate) independence of the two lives and the two systems. In the sense that the system of organic life (ganglionic) was wholly independent (autonomous) with regard to the system of the life of relation (cerebrospinal) (41). Subsequently Brown-Séquard was the first to suggest a close relationship between the autonomous nervous system and the humours secreted by the glands that poured their products into the circulatory torrent (42). The young Pende had tied himself to this idea and the experiments of his degree thesis, resumed between 1903 and 1909, had increasingly convinced him of the functional holism between these systems. This idea, certificated by the endocrinal effects of nerve resections, outlined a vast and original research project which saw, in the nascent science of hormones, the field in which to play for more than fifty years, in Italy and abroad, the role of initiator and founder of a school. As we have said, a fertile idea, but one which, like all a priori systematic ideas that adjust empirical observations and experimental facts to their Procrustean bed, in the case of the suprarenal it locked the Italian physician on the ambiguity of a cortical forcedly tied to the medullar and to the sympathetic nerve ganglia. Pende's experimentation therefore surpassed and was itself surpassed: the science of Nicola Pende opened the great chapter of Italian endocrinology and ended up miserably in an obstinate eugenic project for which he paid with scientific, political and moral ostracism. Endocrinology today is a scientific discipline whose history is ratified, while biotypology and orthogenesis have wound up in the cellar of obsolete histories (43), of interest in our times only to enthusiasts of "alternative", "holistic", "homeopathic" medicines and the like, who effectively acknowledge Pende – alas – among the noble founding fathers.

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Paolo Mascagni and Alessandro Moreschi: who discovered the vascular structure of urethra? Anatomy of an intellectual property dispute

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Abstract. In the beginning of the XIX century, when both vascular and cellular texture theories concerning the penis structure were still coexisting, three figures were involved in the controversy about the priority of the discovery of the vascular nature of human erectile tissues: Paolo Mascagni (1755-1815), represented by his pupil Tommaso Farnese (1780-1829), and Alessandro Moreschi (1771-1826). In the *Elogio del celebre anatomico Paolo Mascagni* (1816), Farnese attributed to his mentor the demonstration in 1809 of the continuity between arteries and veins and the description of venous plexuses, this term replacing the previous and misleading name of spongy body attributed to the inner part of penis. But in 1817 Moreschi inflamed the dispute, claiming for the priority of that discovery, with the publication of his anatomical work and a polemical essay against Farnese. Farnese promptly replied with *Note addizionali del Dottore Tommaso Farnese al suo elogio di Paolo Mascagni* (1818), where he reported a meeting with Moreschi in Bologna in 1810. In that occasion, Farnese explained a Mascagni's technique to perfuse urethral blood vessels that Moreschi would have plagiarized. Furthermore, Farnese also included eight testimonies claiming to have seen Mascagni performing such injections before 1810. The *Prodromo della grande anatomia*, a posthumous work of Mascagni edited in1819, includes a plate dedicated to the structure of the urethra and a comprehensive view of this scientific story. In short, Mascagni developed a technique to inject urethral blood vessels, but Moreschi was the first to publish an accurate work on this subject. For this reason, many Italian and international authors have attributed to the latter the discovery of the venous circulation of the urethra.

Key words: Paolo Mascagni, Alessandro Moreschi, anatomy

Introduction

For a scientist one of the greatest ambitions is to be remembered as responsible for scientific discoveries and technological progress. Often this desire has animated intellectual rivalries, concluding with unfair attributions of discoveries. It is sufficient to recall some of the most significant events of 20th century medicine. In 1962 James Watson and Francis Crick won, along with Wilkins, the Nobel Prize for Medicine for the discovery of the structure of DNA and its replication mechanism, while Rosalind Franklin's fundamental research was not rewarded. Also on the priority of the discovery of the virus responsible for AIDS a heated scientific controversy occurred, which ended in 2008 with the attribution of the Nobel prize to Montagnier and Barre-Sinoussi for the discovery of the HIV virus, but no recognition was given to Robert Gallo, whose work has made a fundamental contribution to the test that reveals the presence of the infection (1). Finally, the trademark possession rights of Stent's Composition, an innovative material for dental impressions, were examined in a court of law at the beginning of 20th century and the action is still used today as a reference in Anglo-Saxon case law (2).

The present paper deals with a classic dispute concerning the priority of an anatomical discovery. The subject of this controversy concerns the description of the vascular structure of spongy erectile tissue of male urethra. The first modern anatomical description of erectile tissues dates back to Andreas Vesalius (1514-1564) who illustrated male genitals in his famous masterpiece *De Humani corporis fabrica*. Vesalius denied the nature of cavernous bodies of the penis in terms of blood vessels, nerves, tendons, bones or ligaments, but he recognized the presence of venous (dark) blood, describing several fasciculi of arteries and veins closely interwoven, within an investing sheat (3).

After the discovery of the blood circulation described by William Harvey (1578-1657) in the famous *Exercitatio anatomica de motu cordis et sanguinis in animalibus* (4), published in 1628, and the microscopic identification of capillaries by Marcello Malpighi (1628-1694) in the *De pulmonibus observationes anatomicae*, published in 1661, it became clear the continuity between arteries and veins (5). It should be considered that in the *Dissertatio epistolica varii argumenti de cornuum vegetatione, utero, viviparorum ovis, plantis &c* Malpighi considered the structure of the penis as composed of diverticula or appendices of veins (6).

In the 18th century, the development of wax injection techniques and the creation of anatomical models contributed significantly to the anatomical discoveries and their demonstration.

However, in the late XVIII century this vascular disposition was not recognized in all organs. In some particular tissues, such as spleen and genitals, the anatomical continuity between arterial and venous system still had to be clearly demonstrated. This uncertainty favoured alternative hypotheses.

Albrecht von Haller (1708-1777), Regnier de Graaf (1641-1673), Frederik Ruysch (1638-1731), Guichard Joseph Duverney (1648-1730), Herman Boerhaave (1668-1738), and Marie François Xavier Bichat (1771-1802) interpreted the cavernous bodies of the penis and urethra as consisting of a loose and elastic spongy tissue (non vascular) arranged in several cells into which, during erection, blood is poured from the arteries, and from which it is afterwards removed by veins (cellular theory) (7).

On the contrary, the surgeon John Hunter (1728-1793), who also dealt with the concept of angiogenesis (8), in *Observations on certain parts of the animal oeconomy* observed that cavernous bodies were not spongy or cellular (9).

Accordingly, other authors, including Georges Cuvier (1769-1832), Friedrich Tiedemann (1781-1861), Bartolomeo Panizza (1785-1867) and Ernst Heinrich Weber (1795-1878), also recognized the vascular nature of the cavernous tissue (10). In particular, Pierre Augustin Béclard (1785-1825) provided the following definition of the erectile tissue:

The erectile, cavernous or spongy tissue consists of endings of blood vessels, especially vein roots, which, instead of having capillary tenacity, are more extensive, are very extensible, and united with many nervous nets (11).

In this crucial period, when both vascular and cellular texture theories concerning the penis structure were still coexisting, the controversy between Alessandro Moreschi and Paolo Mascagni's pupils for the priority of the discovery of the vascular nature of spongy bodies strongly rose (Tab. 1).

Protagonists of the controversy

Three figures were mainly involved in the controversy about the priority of the discovery of the vascular nature of human erectile tissues of genitals. The anatomists who claimed the priority of such a discovery were Tommaso Farnese, on behalf of late Paolo Mascagni, and Alessandro Moreschi.

Paolo Mascagni was born in Pomarance (Pisa) on January 25th, 1755. He studied medicine at the University of Siena where he graduated in 1778. Thanks to his mentor Pietro Tabarrani, the anatomical research became his main field of studies. He won great fame with masterpieces dedicated to the first complete description and illustration of the lymphatic system and became president of the *Accademia dei Fisiocritici*, deserving the title of *prince of anatomists*.

In 1784 he published *Prodrome d'une ouvrage sur le système des vaisseaux lymphatiques*. Then, in 1787 he

Table 1. Chronological and comparative list of publications and events referring to Paolo Mascagni and Alessandro Moreschi.

Year	Paolo Mascagni	Alessandro Moreschi
1785	Targioni Tozzetti stated that Mascagni performed the injections in urethral vessels since 1785.	
1787	Mascagni published *Vasorum lymphaticorum corporis humani historia et ichnographia*.	
1795	Mascagni published *Vasorum lymphaticorum historia seu totius operis pars prima*. Mascagni's observations, now dated back to 1795.	
1805	Most of the other witnesses remember to have participated in a similar demonstration during a lecture by the master in 1805.	
1809	Mascagni demonstrated the vascularization of urethra to Cuvier, organizer of the schools in the French Empire who was visiting Florence. Farnese's *Elogio* reported the date 1809, because it was the most univocally recognized.	
1810		Moreschi demonstrated the vascularization of the urethra in Bologna.
1812	Mascagni obtained his best anatomical model of urethra.	
1815		In August the scientific community recorded the discovery of Moreschi, dated December 1810.
1815	Mascagni died.	
1816	Farnese published *Elogio del celebre anatomico Paolo Mascagni toscano.*	
1817	Antommarchi published *Osservazioni intorno all'elogio del celebre Paolo Mascagni divulgato da Tommaso Farnese*.	
1817		Moreschi published *Cenni preliminari intorno alla scoperta della struttura vascolare del corpo dell'uretra e della ghianda* and *Commentarium de urethrae corporis glandisque structura*.
1818	Farnese published *Note addizionali del Dottore Tommaso Farnese al suo elogio di Paolo Mascagni*.	
1819	Antommarchi published *Prodromo della grande anotomia. Seconda opera postuma di Paolo Mascagni.*	
1821	Second edition of the *Prodromo della grande anatomia* was published by Farnese.	
1826		Moreschi died.

published the complete work in Latin and new insights into the lymphatic system were published in 1795 (12). In that period, Mascagni collaborated with Clemente Susini (1754-1814), at the Museum of La Specola in Florence, for the realization of anatomical wax models, now including the lymphatic vessels.

In his life he was professor of anatomy in Siena, Florence and Pisa. Besides the anatomical lessons, Mascagni was concerned with the ultimate preparation of the anatomical tables. Mascagni also conceived the idea to realize an ambitious dream of the anatomists: a complete and life-sized illustration of the human body. Nevertheless, political events delayed his purposes and upset his life. Unfortunately, he died on October 19th,1815 and his work was published posthumously (13-16).

Alessandro Moreschi was born in Milan on 1771 and studied in Pavia where he graduated in 1795. In 1802, thank to the Napoleonic decree date December 25th, he moved to Bologna where he taught Comparative Anatomy and Physiology. On July 20th 1803 he went back to Pavia. Again, on October 2nd 1804 moved to Bologna, where he remained until 1813 as a teacher of Human Anatomy. He was Rector of the university in the academic year 1809-1810.

During his stay in Bologna, he decided to separate the Ceroplastic Laboratory from the Anatomical Cabinet, giving life to a real museum collection in this university for the first time. Moreschi has shown to be attentive to the role of demonstration in anatomy with wax moulages and other types of preparations, helping to make the Bologna school important in this area. In anatomy his most remembered studies are those on the nature and function of spleen and urethra. Moreschi died on August 3rd,1826 (17,18).

Tommaso Farnese, a Mascagni's pupil, was essential in generating the dispute between his late master and Moreschi. He was born in Perugia on November 7th, 1780. He graduated in medicine in Bologna and moved to Florence, where he assisted Mascagni in the anatomical activity. In 1810 he moved to Milan, where he became a famous surgeon and for this he was invited in Russia. Then, he left Milan on September 22nd, 1828 to reach Vienna and finally Saint Petersburg but he was suddenly taken ill. In the spring of the next year he moved to Kazan, but during his travel he died before reaching Moscow on May 4th,1829 (19).

The controversy, first act. Farnese attributed the discovery of the venous plexuses of the urethra to Mascagni and Moreschi disputed against him on that subject

In *Elogio del celebre anatomico Paolo Mascagni toscano*, published in 1816, Farnese underlined merits and innovations of Mascagni in anatomy and physiology. In particular, among the most important discoveries, he attributed to his mentor the concept of continuity between arteries and veins and the description of intricate *venous plexuses*, this term replacing the previous and misleading name of spongy body attributed to the inner part of penis. This discovery, dated back to 1809, was made possible also by his ability to make wax injections in small-caliber vessels (20).

One year later Farnese's opinions were contested. In 1817 Francesco Antommarchi, one of the three Mascagni's anatomical dissectors in Florence, published *Osservazioni intorno all'elogio del celebre Paolo Mascagni divulgato da Tommaso Farnese* and he dated to 1795 Mascagni's discovery (21).

But in the same year, 1817, another figure entered officially the discussion and this time claiming for the priority of that discovery: Alessandro Moreschi. Indeed, this anatomist published *Cenni preliminari intorno alla scoperta della struttura vascolare del corpo dell'uretra e della ghianda creduta sin qui spugnosa o cellulosa ed osservazioni sull'Elogio del cel. Anatomico Paolo Mascagni, divulgato dal sig. Tommaso Farnese, Dottore in Medicina e Chirurgia, ecc* (22). As suggested by the title, there is a brief scientific description of his work on urethra and a polemical essay against Farnese.

In his book Moreschi also reported the record of his anatomical observations entitled *De penitiori urethrae corporis glandisque structura recens detecta*, already read on August 3rd 1815 at the *Istituto di Scienze, Lettere ed Arti* and published on August 11th, 1815 in the *Giornale Italiano*.

Furthermore, at the end of 1817, Moreschi hastened the publication of his anatomical work, solemnly written in Latin, *Commentarium de urethrae corporis glandisque structura*, another report read at the *Istituto di Scienze, Lettere ed Arti* on August 17th 1815 (23).

The text was well organized into 51 points, with 3 plates referring to urethral structure and including 3, 2 and 8 figures, respectively. Interestingly, drawings were realized by Filippo Bedettio in Bologna in 1811, and by Ignazio Altimo in Milan in 1817. In particular, table II depicted the pelvic region, with detailed figures concerning the *corpus urethrae vasculosum* (Fig. 1). At the end of the book, Moreschi dealt with blood vessels in spleen and pregnant uterus.

Moreschi also stated that he promptly included anatomical preparations referring to the new discovery. They were available to the students of the University of Bologna from 1810 to 1815. Some of the models were shown to the famous anatomist Antonio Scarpa

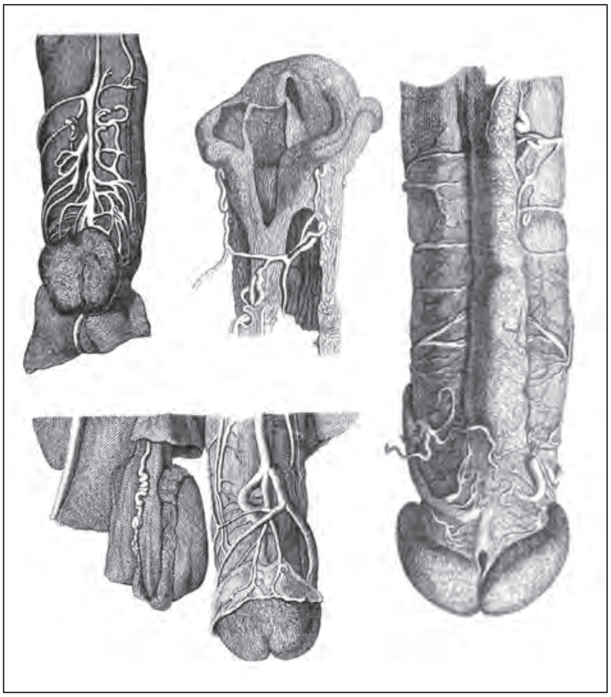

Figure 1. Some pictures taken from *Commentarium de urethrae corporis glandisque structura* by Alessandro Moreschi (1817).

(1752-1832) and were appreciated by him when Moreschi was hired by the University of Pavia in 1813 (22).

In 1817 Moreschi's research appared in two parts in *Annali Universali di Medicina* (24,25). Moreschi disputed various parts of Farnese's version. He was pitiless towards the fact that two Mascagni's pupils, Antommarchi and Farnese, reported so different dates concerning the Mascagni's discovery of the vascular structure of penis: 1795 and 1809, respectively. Furthermore, in a letter reported by Moreschi, professor Ottaviano Targioni Tozzetti (1755-1826) indicated the date 1785 and announced the publication of Mascagni's anatomical plates in the *Prodromo della grande anatomia*.

So, Moreschi also wondered why Mascagni supported the old cellular theory in his famous work on lymphatics, published two years later:

With microscopic observations and injections one demonstrates that arteries continues into veins and this is very evident. At the same way, one shows that they end into the cells that constitute the spongy tissue of clitoris and penis, and that the corresponding veins originate from the same cells. But the force of the heart moves the blood from arteries into cells and veins, and one can say that arteries continue directly into veins, merely through a dilation between them (26).

Moreschi concluded by stating that, although Mascagni has published many studies, no one of these supported the vascular theory of the urethra before 1810 and the Tuscan anatomist has not even claimed the paternity of the discovery after Moreschi broke the news to the scientific press in 1815. Indeed, Moreschi wrote that the discovery was made by him in Bologna in the presence of dr. Francesco Mondini (1786-1844), and doctor Tommaso Farnese, who was amazed and declared that Mascagni considered the two cavernous bodies of the penis as venous plexuses, but that no exclusive effect had ever been obtained on the body of the urethra. In a letter dated December 13th 1816, Moreschi's pupil Francesco Mondini confirmed that version (22).

The controversy, second act. Farnese's response to Moreschi's accusations

Farnese promptly replied to Antommarchi and Moreschi with *Note addizionali del Dottore Tommaso Farnese al suo elogio di Paolo Mascagni in risposta ai due scritti critici del Sig. Dottore Francesco Antommarchi e del Sig. Cavaliere Alessandro Moreschi* (27).

The dynamics of this controversy is typical of a classical spy story. Indeed, Farnese admitted to be aware, since the time of the *Elogio* writing out, of the Moreschi's reports dating back to the summer of 1815, but he provided another version about facts. According to him, the meeting was in September 1810. Farnese attended the Bologna anatomy cabinet when Moreschi, after a poorly achieved preparation, accidentally observed the real vascular structure of the urethra. Seeing him perplexed about the incident, Farnese informed him that Mascagni had already discovered the infinitesimal clusters of veins in the spongy body of the urethra and of the glans, and that he had called them venous plexuses. The discovery was made possible thanks to a technical precaution: injecting two substances of different colours into the venous and arterial vessels. Finally he informed him that Mascagni gave a demonstration to Mr. Cuvier the previous year.

Moreschi retried the operation on the horse's penis, but failed.

When Farnese went back to Florence, he informed his master about the meeting in Bologna with Moreschi. Farnese was oppressed by a sense of guilt for his incautious performance, but Mascagni knew how difficult was that injection and laughed at that episode.

To corroborate his version, Farnese included eight letters testifying that Mascagni injected venous vessels of the penis in the first decade of the nineteenth century. The witnesses were: Giovanni Battista Bellini, Pietro Betti, Paolo Casini, Cosimo Lazzerini, Paolo Francesco Acerbo, Enrico Acerbi, Antonio Targioni Tozzetti (1785-1856), Antonio Serantoni (1780-1837). The most important perhaps was the latter (who wrote on July 20th 1817) because he realized Mascagni's anatomical plates.

Among the letters the most complete chronological reconstruction, instead, is described by Antonio Targioni Tozzetti, who stated that Mascagni performed the aforementioned injections since 1785, most of the other witnesses remembered to have participated in a similar demonstration during a lecture by the master in 1805, and all of them confirmed that in the autumn of 1809 Mascagni illustrated the vascularization of urethra to Cuvier, zoologist learned in comparative anatomy, organizer of the schools in the French Empire who was visiting Florence. Farnese's *Elogio* reported the date 1809 because it was the most univocally recognized. Farnese reported that Cuvier made the same discovery, but in animals. Then, the two anatomists congratulated for having demonstrated the same structure in different experimental conditions, without claiming. According to Farnese, Mascagni had not yet published the discovery, because he wanted to be completely sure to demonstrate it.

One criticism raised by Moreschi was the fact that Mascagni did not respond to Moreschi's publications of the summer of 1815. But Mascagni was rather ill at the time, and perhaps he did not have time to consult the scientific literature, and on 19th October he died.

Nonetheless, in support of Moreschi, in 1818 an anonymous A.M. published in the Nuova *Biblioteca analitica di scienze lettere ed arti* a reply letter to Farnese. Two aspects are interesting. First, for the first time in this diatribe the copyright is claimed for those who first published a scientific discovery without giving too much importance to the observation date.

Second, an excerpt of a letter written by Cuvier on February 15th 1818 was including, where he thanked Moreschi for having given him a copy of his work, adding that he found it very interesting and decisive: … *permettez moi de vous remercier à mon tour de l'exemplaire que vous m'avez destiné, ainsi que de la manière honorable dont vous avez bien voulu parler de mes foibles travaux sur l'objet que vous traitez di profondement. Tout ce que j'ai vu depuis dans mes dissections me confirme dans l'opinion que vous défendez, et je suppose qu'elle n'éprouvera plus de contradictions* (28). A reply to those *Osservazioni* came to the defence of Mascagni in *Lo Spettatore*, where the letter of Cuvier was considered to be a common courtesy and not a response with scientific contents (29).

The controversy, third act. The posthumous works of Mascagni and the absence of protest by Moreschi

At the time of publication of the famous works on lymphatic vessels, it seemed that the real inner structure of penis was not completely clear to Mascagni. He suspected continuity between veins and arteries but, failing to prove it, confirmed the cell theory (30).

In 1816 a Mascagni's pupil, Giovanni Battista Bellini (1793-1853), translated into Italian the 1795 Latin edition of that work. In the chapter dealing with the anatomical question concerning the continuity between arteries and veins, Bellini wrote a very long and detailed note on this item (31). In the second edition of this translation, published in 1820, Bellini added further considerations to that note, taking now into account also the overt dispute between Moreschi and Farnese.

Bellini explained in detail the questions that led Mascagni to demonstrate the venous plexus of the urethra. He sensed that using corpses of children, the injected substances filled the vessels better because in the young the valves present in the veins are not yet functioning. Bellini wrote that the discovery took place at the end of 1795 and, in 1805, when he had them drawn, he called venous plexuses to replace the ancient name spongy body of the urethra (32).

Apart from his masterpiece on lymphatic vessels, Mascagni aimed to write a more comprehensive illustrated textbook, including both gross anatomy and microscopic observations. This project was not realized, but Mascagni's pupils organized plates and writings of their master and published posthumously three important works.

Two works were cured by Francesco Antommarchi (33-34). The latter work, published in 1819, was the famous *Prodromo della grande anatomia* and included macroscopic and microscopic observations of different parts of the human body, as well as comparative notes with plants and animals. Procedures and techniques were also illustrated. In the chapter II of this *Prodromo*, dealing with blood vessels, an accurate description was dedicated to the structure of erectile tissues. Since the dispute with Moreschi was known, again there is a chronological reconstruction of the facts. It is consistent with that provided by Bellini, even if Antommarchi given the first observations of the plexus to 1787.

The *Prodromo* was provided with a volume apart, including 20 plates realized by Antonio Serantoni. In particular, plate VII of this volume depicted male and female organs, and a plaster cast of spongy bodies of the urethra was shown (35) (Fig. 2). Some of these figures were also present in the *Note addizionali* by Farnese.

A second edition of the *Prodromo della grande anatomia* was published by Farnese. Plates and their captions were published apart. Only seven figures referred to the structure of penis, with detailed captions. In particular, a note underlined the dispute with Moreschi and the importance of the sophisticated technique adopted by Mascagni (36).

The vascular structure of penis was illustrated and described also in the posthumous Mascagni's

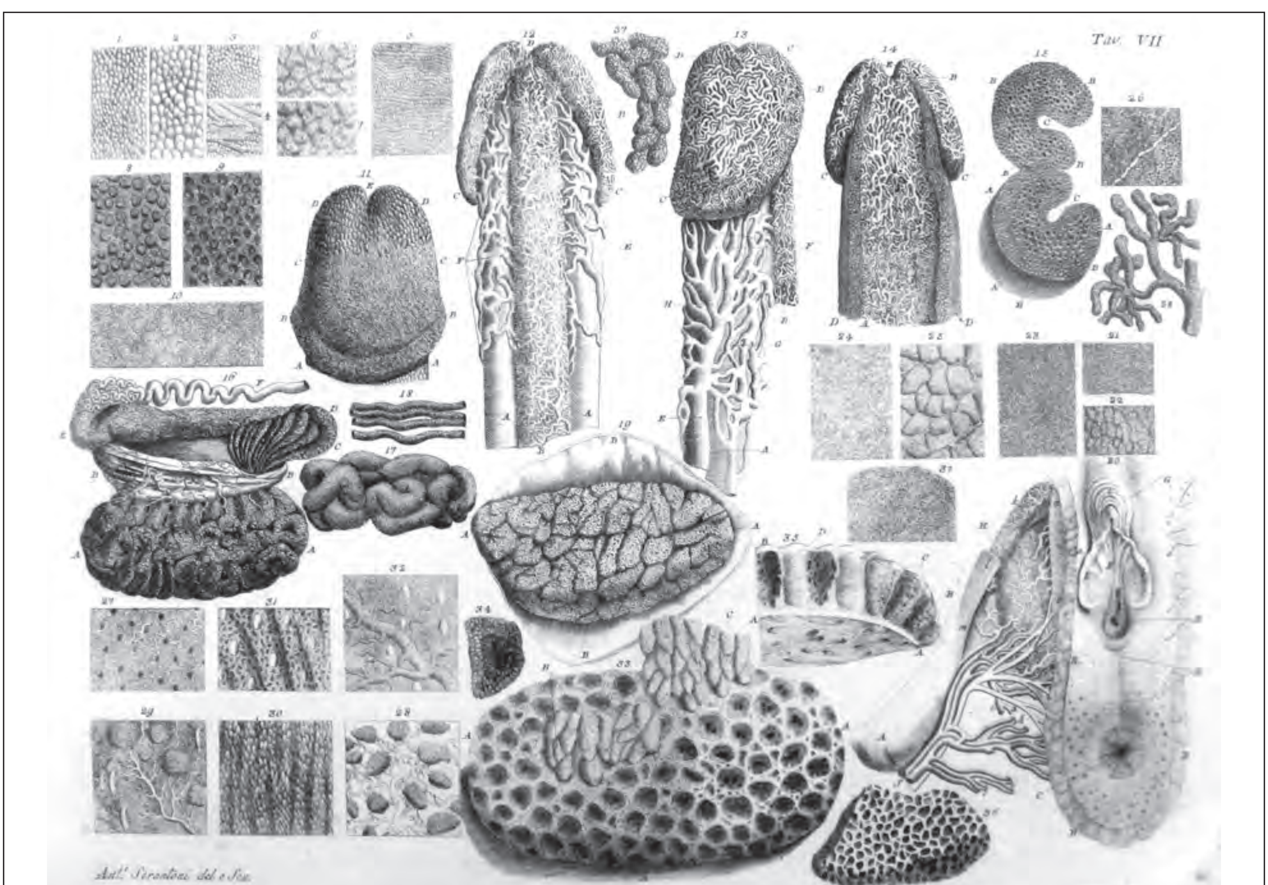

Figure 2. Plate VII taken from *Tavole figurate di alcune parti organiche del corpo umano, degli animali e dei vegetabili, esposte nel Prodromo della grande anatomia di Paolo Mascagni* by Francesco Antommarchi (1819).

Figure 3. Stratum Primum Tabula Specialis III taken from *Anatomia Universa* by Paolo Mascagni (1823-1831).

Anatomia Universa (37), edited by Mascagni's friends Andrea Vaccà Berlinghieri, Giacomo Barzellotti and Giovanni Rosini (Fig. 3), and in a cheaper edition of the Mascagni's anatomical atlas in Italian, with small-sized colour and black and white plates realized by Antonio Serantoni in 1833. In this work, new drawings were added. *Tavola particolare X* and *XII* of Plate XVII provided more informative details of the inner structure of penis (38).

Moreschi died in 1826. He and his pupils never again officially countered the clarifications that supporters of Mascagni gave to the facts.

The opinion of the scientific community

A large part of the testimonies collected so far were admittedly from pupils or collaborators of Moreschi or Mascagni, then it is difficult to evaluate the impartiality of their points of view. An impartial judgment could be sought in scientific societies chronicles, particularly foreign ones, and in the opinion of medical historians.

In the literature of that time, different opinions emerged. The *Biblioteca Italiana o sia Giornale di Letteratura Scienze ed Arti* a balanced comment on the *Note addizionali* by Farnese appeared in 1818, with a slight propensity to favour Mascagni's merits without doubting the good faith of Moreschi (39).

But historically, *this journal* was an Austrian pro-government journal, subject to censorship and propaganda. Therefore, in light of these considerations, it is not surprising that the article paved the way also in favor of Moreschi.

On *Medico-Chirurgical Transactions,* in 1819, the demonstrator of anatomy John Shaw (1792-1827) stated that he knew Moreschi's work and that he had a conversation with Antommarchi, but he does not quote Mascagni (40). Then, he realized that Italian anatomists did not extend their observations to the membranous part of the urethra. For this reason, he considered himself the first to demonstrate the vascular structure of this tract of the urethra, as also affirmed in a manual for the Student of Anatomy published in London and in the United States (41).

In 1824 *The Journal of Foreign Medical Science and Literature* published a very long a detailed review about Moreschi's *Commentarium* (42). This commentary really sang Moreschi's praises and never mentioned Mascagni. In that year the same text was published also in *The Edinburgh Medical and Surgical Journal* (43).

In 1825 the famous anatomist Johann Friedrich Meckel (1781-1833) published, with Jourdan and Breschet as co-authors, *Manuel d'anatomie générale, descriptive et pathologique*, a textbook then translated into many languages and distributed in English-speaking countries. Introducing the chapter dedicated to the anatomy of the urethra, he mentioned the work by Moreschi in the first note, as if it was the main and primary one, while Mascagni was not cited (44).

Mascagni was praised in the *New-York Medico-Chirurgical Bulletin* (1831) (45), and under the heading *erectile tissue* of *The Cyclopaedia of Anatomy and Physiology*, edited by Robert Todd (1809-1860), both Mascagni's and Moreschi's works were mentioned as important steps in this field of research. However, Moreschi's contribution and illustrations deserved a particular attention (46).

In his *Storia della medicina*, Francesco Freschi (1851) clearly attributed to Moreschi the discovery of the vascular nature of erectile tissues. He also stated that the anatomists Antonio Scarpa and Giovanni Antonio Palletta had the same opinion (47). This appears unlike, since Farnese (1816) dedicated his *Elogio* just to Palletta. Furthermore, in a letter without date addressed to Bartolomeo Panizza, Scarpa wrote: *Read the* Elogio of Mascagni *by Farnese at page 48 and you will find the confirmation of Moreschi's robbery. Anyway, Scarpa wanted further data form Panizza before releasing a final opinion on that matter* (48).

Conclusions

It is hard to decide the winner of this controversy. Probably as early as 1787 Mascagni began to have a correct view of the vascular anatomy of the urethra, different from the cell theory, but he had not published the discovery, because he wanted to be completely sure to demonstrate it. The certain demonstration was made possible by the improvement of the technique: different coloured injections were needed to distinguish arteries and venis and the procedure was better on corpses of young people.

The general accuracy of Mascagni's description has been since confirmed by the researches of Moreschi. The latter was the first to publish an accurate work on this discovery in 1815. Until 1815, nothing similar is described in the journals of the scientific societies, and in the publications of Mascagni the urethra does not.

One criticism raised by Moreschi was the fact that Mascagni did not respond to Moreschi's publications of the summer of 1815. But Mascagni was rather ill at the time, and perhaps he did not have time to consult the scientific literature, and on 19th October he died.

On the other side, Mascagni's works were mainly published posthumously and after the beginning of the dispute and in these books the real vascular nature of the urethra is clearly described, but we do not have objective elements to evaluate exactly when the observations (and what was really observed) were made. We must trust Mascagni' pupils reports who have admitted that the cellular texture theory was initially accepted. It is also true that neither Moreschi nor his pupils have ever told back to the clarifications made by Farnese in 1818 or criticized the posthumous publications of Mascagni.

For this reasons, as far as the opinion of the scientific community is concerned, we must consider that many Italian and international authors have attributed to Moreschi the discovery of the venous circulation of the urethra because they found only the well organized publications by him. On the contrary, those who explored historical aspects of the matter were able to appreciate Mascagni's work, as well.

The illustrations reported in Mascagni's and Moreschi's works really provided a vascular structure of the urethra. However, especially for microscopic details, we must consider that photos were not available. So, we have excellent drawings, then a mere interpretation of the real picture. Furthermore, the concept of microscopic examination is simply related to fine details, but we do not have histological preparations showing the vascular structure of urethral spaces, as in modern slides. Indeed, rather than microscopy, injection techniques and cast models were able to help our anatomists to understand the vascular nature of the urethral spongy tissue.

From the anatomical point of view to Moreschi the following merits are recognized**:** 1) That the glans consists of arteries and a very great number of minute veins, which pour their blood into the cutaneous dorsal vein; 2) That the urethra, and especially its posterior part, may in like manner be shown to consist of numerous minute veins, which terminate in a posterior branch of the dorsal vein, and communicate with the veins of the bulbous portion of the urethra; and, 3) That in the cavernous bodies, though also receiving blood-vessels, these are much less numerous, and are chiefly derived from the urethral vessels (49).

The History of Medicine teaches us to reflect on the past, on what has been done and what what we can do in the future, thus changing our behavior. The correct analysis of the past of medical science allows us to understand the progressive stages of medicine, helping to integrate and complete the preparation of those who will dedicate themselves to the medical profession (50,51). It is important to shed light on scientific disputes to allow history to tell the true course of events, recognizing to the scientists of the past their real merits and encouraging future doctors to intellectual honesty.

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Heterogenic transfusion in Italy. Historical review of a medical practice

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Abstract. In our paper, we present a brief historical review of the transfusion practice, with a particular emphasis on the Italian research between 17th century and the end of the 19th century. Centuries of experiments, attempts and hard achievement have marked the paths toward the comprehension of the transfusion practice. The blood types discovery was possible only thanks to hundreds of attempts. In our paper, we retrace part of the work of enlightened scientists, which leads to one of the most important discovery of the last centuries.

Key words: history of medicine, transfusion, blood type

Blood is an important fluid in human body that arouses our curiosity from ancient times. It was soon understood that the loss of blood could bring to death. Conversely, receiving blood could give new strength to a weakened body. Countless iconographic sources show blood in direct connection with an individual's health. Emblem of life and death, it was studied with both a scientific and a magical approach. In the history of medicine, it had often been the jumping off point for the study and the comprehension of the mechanisms behind human body.

First Hippocrates in the classical Greece and then Galen in the ancient Rome used blood in order to have insights into human physiology and into the onset of illness, within the framework of the so called humoralism (1). This theory was accepted and teached by the scientific community until the beginning of the 17th century (2). A turning point in the history of medicine resides in the discovery of the circulatory system and the cardiac activity by William Harvey (3). In his treaty "*Exercitatio anatomica de motu cordis et sanguinis in animalibus*", written in 1628, he refused the physiological system theorized by Galen. According to Harvey, the heart was the pump at the basis of the arterial and venous system, whereas Galen recognized to the liver this role. Two centuries later, in 1844 in Bruxelles, the *"Dictionnaire de Médicine et de Chirurgie Pratiques"* was published. It asserted that the circulation system of superior animals was based on a *fluide particulier* that moved without interruption in the best system by its own. That fluid was called *sang* and the system of vessels, which it flowed in, *appareil circulatoire*.

In vertebrates and in the human body the heart, a muscular organ, pumps blood trough divergent veins, called arteries, and collects it from convergent veins, called vessels. Arteries and blood vessels were connected to each other by small vessels called capillaries. This interpretation of the human circulatory system demonstrates how Harvey's theories were well received in the human physiology of the half of the 19th century.

Continuous researches during the century laid the foundation for a medical and surgical handbook for physicians containing the instructions for blood removal and transfusion. Bloodletting, intended as poured blood, in the light of its extensive use, was one of the most important practices in the history of medicine. It fell into oblivion only with the experience in the transfusion practice, intended as offered blood (4).

Physicians tried to transfuse blood into patients from animals, other humans and dead bodies. This bizarre transfusion attempts outline how this practice remained not well understood. An ancient reference of the use of blood comes from the "*Metamorphoses*", wrote by the ancient Rome writer Ovidio. In the seventh book named Medea, Cephalus and Procris, the witch, rejuvenate the old Aeson:

"Medea, when she saw this wonder took her unsheathed knife and cut the old man's throat; then, letting all his old blood out of him she filled his ancient veins with rich elixir. As he received it through his lips or wound, his beard and hair no longer white with age, turned quickly to their natural vigor, dark and lustrous; and his wasted form renewed, appeared in all the vigor of bright youth, no longer lean and sallow, for new blood coursed in his well-filled veins."

This myth allows us to comprehend that also in ancient times blood and transfusions were probably used for healing, even for the most intractable diseases, as reported in the *"Dictionarie des Sciences Médicales"* of the 1820.

It is worth mentioning the so called "world's first blood transfusion" performed in 1492 in Rome by Giacomo di San Genesio in order to save Pope Innocenzo III's life. The attempt ended with the death of three 10 years old donors and of the Pope himself. The Italian physician Francesco Folli made another attempt of transfusion in 1654 by inserting a silver cannula in the harm of the donor and a cannula made of bone in the arm of the recipient, connecting each other by an animal vessel. Folli was the first medician that proposed to transfuse nutrient and medicines directly in the circulatory system. Despite all experiments, until the discovery of blood type, transfusion remained a dangerous treatment with a mortality rate greater than 50% due to clots, bacteria, toxins and incompatibility reaction (5).

Geminiano Montanari in 1667 in Bologna conducted what was, probably, the first "real" transfusion in Italy. It was between two lambs and the experiment was replicated between a dog and a lamb the following year in Udine (6). Michele Rosa, at the end of the 18th century, in his *"Lettere Fisiologiche"*, demonstrated scientifically that it was possible to reanimate a bleeding animal, transfusing in its body an adequate quantity of blood. In the light of his discoveries, he proposed to use the transfusion practice in case of haemorrhage during childbirth, both for the mother and the child, and for the treatment of injured soldiers (7). This practice remained in use for over 200 years in the attempt to treat a wide range of diseases, such as anaemias, deficiency diseases, malaria, typhus, leprosy and haemorrhages. Finally, in 1818, James Blundell performed the first successful transfusion of human blood to a recipient for the treatment of a haemorrhage.

Thanks to the renewed confidence in transfusion due to Blundell, Giuseppe Albini, in 1871 in Naples, reintroduced the lamb blood transfusion, which was abandoned for over 200 years (8). In 1872, he wrote about the need to bring lambs to the battlefront so as to have fresh blood for the soldier's transfusions:

"I was in Milan in 1866, directed to the civil Medical-Surgical Ambulance camp. I firmly asked for one or more living lambs in my Ambulance, so as to use their hart or blood in transfusions with my emodrometro, saving soldiers life (9)." Albini described in detail that only the regiment physician was able to do the operation. He provided technological innovations such as the use of an elastic rubber tube connecting the two cannulas and a protocol to avoid the entry of air into the vessels and the blood coagulation.

Other Italian and European physicians supported this practice. Let us mention the Italian Luigi Luciani, the French Mathieu Moncoq and the German Ferdinand Heyfelder (10, 11). The latter in 1874 proposed to the European government the presence of flocks of sheep on the battlefields for the emergency transfusions of the soldiers. Luigi Luciani, the most known Italian physiologist of those times, conferred to Albini the value of the revival of the human-animal direct transfusions, the so-called heterogeneous blood transfusion. He developed in 1874 an instrument for this type of direct blood transfusions. A glass cannula was inserted in the carotid artery of a sheep or a goat and another blunt tip cannula was inserted in the human recipient vessel. Between the cannulas, a two-way valve allowed to control the blood transfer. Moreover, it was possible to choose the calibre of the instruments depending by the recipient's vessel and sodium bicarbonate was used as an anticoagulant. Luciani described every step of the procedure: how to choose the right vessel, how to do the transfusion and how to do the post-surgical therapy that comprehended the measurement of body temperature, of cardiac and respiratory activity, of blood pressure and an analysis of urine. Even if his proposal was original and valuable for the military medicine of the second half of the 19th century, clinical records showed that his method was often ineffective.

Despite many physicians disagreeing with this practice, considering it too dangerous for human's life, Luciani was always a strong supporter of it. To him, the danger resided in the fact that the practice had still to be consolidated among physicians, who were not always completely aware of it. Reporting his words:

"The unfounded risks and complexity of direct transfusion were only due to the scarse knowledge of its procedure."

Enrico Morselli wrote in 1876 *"La trasfusione del sangue"*, in which he transcribed the most important articles on transfusions published in the second half of the 19th century: all the scientific knowledge of this practice and the numerous attempts made by the physicians were summarized in his book. Despite his remarkable work on the subject, Morselli was sceptical towards transfusion. Indeed, even though he considered Luciani's work excellent, he affirmed that only few pathologies could be treated with this practice and that lamb's blood has "*the fewest analogies and the greatest number of dissimilarities with human blood*". Giuseppe Colasanti believed that heterogenic transfusion was too dangerous and suggested banning it from surgical practices (12). On the other hand, he was in favour of homogeneous transfusion. In the same years an eclectic Italian physician performed some new experiments in blood transfusion (13, 14)

Mario Giommi, chief surgeon in the Italian hospital of Gubbio, described in 1878 his direct experience with a patience suffering of scurvy, a pathology whose aetiology was unclear (15). The lack of knowledge of this illness leaded physicians to believe that the patient's physical decay was related to the blood and transfusion was seen as the only possible effective treatment. It seemed to reactivate the centres of the central nervous system, to improve the tissue remodelling and to change hematic parameters. Moreover, although other data of patients affected by pellagra or malaria showed how transfusion did not lead to a complete healing, it was possible to highlight a clear RBCs and HTC increasement. Giommi, in October 1877, performed a direct transfusion from a lamb to a woman affected by scurvy. He was fully satisfied by the results: the patient healed in twenty days. For this reason, he was in favour of this practice, even if it was not possible for him to assert that the transfusion was the main cause of the woman's healing. Indeed, the patient followed a healthy lifestyle: a rich and varied diet, plenty of wine, long outdoor walks, iron lactate and calcium phosphate powder consumption and a decoction saturated with Haller's elixir, also called "*acidum sulfuricum alcoholisatum*", composed from a part of sulfuric acid and three parts alcohol at 90°. In conclusion, he asserted that:

"*I cannot affirm to have improved blood's quality. Only an 80 g blood transfusion, even if arterial, cannot allow us to assert that.*"

A fundamental innovation for haematology came at the beginning of the 20th century thanks to Karl Landsteiner, a young researcher at the Institute of Anatomical Pathology of Wien that discovered blood types (16). This new knowledge has leaded to the abandon of the heterogeneous transfusion and animal blood has found other methods to be employed (17).

When transfusion was not a dangerous hazard anymore, blood could be safely donated. At the beginning of the 20th century, the foundation of the modern haematology was laid thanks to scientific researches on compatibility rules, thus opening new branches of research.

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Review article: history of medicine

The light of knowledge. Brief historical outline of some of the talented people who changed the destiny of the blind, from Haüy to Brail

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Abstract. In the 16th and 17th century the blind were considered unfortunates who could have no other future than to "*to be mocked by idle folk in the public square for their blundering and clumsiness*". Clearly no sort of instruction was considered for such people. The change came at the end of the 18th century, thanks to Valentin Haüy, a philanthropist and teacher of calligraphy, who had also been a pupil of the abbot Michel de l'Épée. short historical excursus from to Valentin Haüy to Charles Barbier de la Serre.

Key words: Valentin Haüy, Charles Barbier de la Serre, Michel de l'Épée

Historical outline: Haüy to Braille

In the 16th and 17th century the blind were considered unfortunates who could have no other future than to "*to be mocked by idle folk in the public square for their blundering and clumsiness*". Clearly no sort of instruction was considered for such people.

The change came at the end of the 18th century, thanks to Valentin Haüy (Fig. 1), a philanthropist and teacher of calligraphy, who had also been a pupil of the abbot Michel de l'Épée.

Haüy decided to use a new method of printing with mobile characters in relief to teach "*reading, music and a trade*" to blind children. He began to test the idea with his first blind student, a boy named François Lesueur (1). Subsequently, he published his findings in an article entitled *Essai sur l'éducation des aveugles* (Essay on the Education of the Blind). His desire to help blind children and give them the opportunity to obtain an education prompted him to present his project to the *Société philanthropique*, which recognized its educational merits and assigned him a house and a first group of twelve blind students (2).

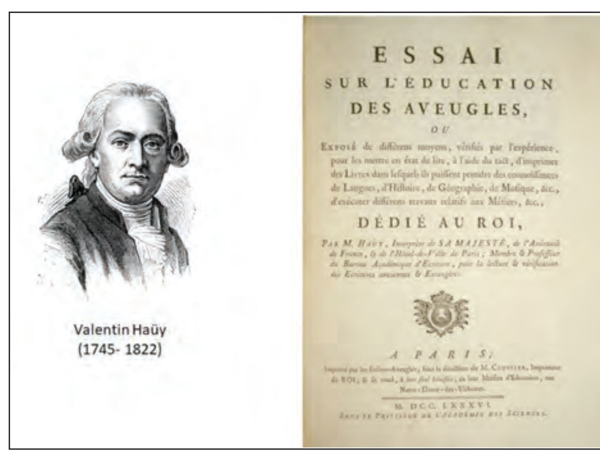

Figure 1. Valentin Haüy.

Haüy also wanted his blind students to be able to write, and took advantage of the progresses made in the field of printing to develop "*several models of tablets in wood with grooves and rods to frame the space for writing: they were used jointly with a card containing letters and numbers that served as models for the blind students to learn how to write them. Some had a frame on which the sheet could be fastened, with a row of holes along the sides* *to mark the space between the lines. The blind students, though they now had the ability to write, were not, however, able to read back what they had written and correct any errors*" (3).

The recognition of the validity of the methods he had developed and used enabled Haüy to obtain the title of *inventor of visual printing in relief* by the Academy of Science of Paris.

We can say without a doubt that those 12 students of Haüy were the first working group that led to the foundation of the *Institution nationale des jeunes aveugles*, the French school for the blind that is still operating today in Paris (4).

His passion and enthusiasm led Haüy to become the contact person and promoter for opening new schools for the blind in other parts of the world, including St. Petersburg and Berlin (5).

Haüy's studies of writing methods prompted the Austrian typhlologist and founder of the Vienna Institute for the Blind, Johann Klein (Fig. 2), to conceive and develop a new method of writing that made use of a punch, so that the characters could be perceived by the blind through touch (1).

At the same time, Maurice Ballu developed a method of writing that used lead blocks on which the letters of the alphabet were set in relief.

Klein and Ballu both realized that it was more practical to trace the letters with a dotted line rather than a continuous one (1).

Figure 2. Johann Wilhelm Klein.

The method that took the name of Ballu or Cubarithm was *a system of specular writing, slow to apply as the composition of each letter required the use of many dots.* It was a method that made it possible to write, using a special tablet, and to read back the composition of the text. Clearly, however, reproducing texts using this method was difficult because it would have required too much space.

The breakthrough came with the method developed by Louis Braille (Fig. 3) (6).

Louis Braille was born in Coupvray, in France, into a modest family, and lost his sight at the age of three as the result of an accident which occurred while playing with the tools his father used in his trade as a saddler.

Braille's family believed strongly in the importance of education, however, and he was taught to read, with the help of his father, who carved the letters of the alphabet for him in wood (7).

His active intelligence and enthusiasm for learning brought Louis Braille to the attention of the Abbot Palluy, the educator Becheret and the local nobility, who funded a scholarship to send him to the Royal Institute for the Blind (8).

Their belief in young Braille was not disappointed, as he turned out to be a model student, and in fact was hired, while still very young, to teach grammar, history, geography and mathematics at the school.

He was also a fine musician, and learned to play a number of instruments, later also becoming a music teacher of his blind students.

Although Braille's life was intensely busy "there was one idea that would not let him sleep": he wanted to find a method of writing for the blind that would

Figure 3. Louis Braille.

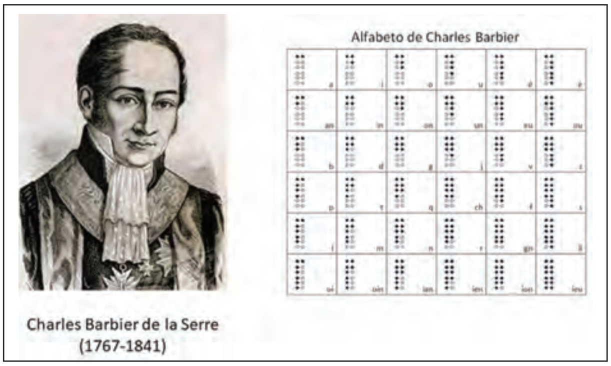

Figure 4. Charles Barbier de la Serre.

be simpler and faster than what was then in use. His first idea was to eliminate the continuous line using, instead, series of *dots* that would be more readily perceived by touch. His students welcomed the method, but he had to teach it to them in secret for many years because it was not accepted by many scholars and typhlologists, who accused him of developing a method that prevented direct communication between the writings of the blind and those of the sighted (9). The language he used was described as *encrypted, incomprehensible to anyone who did not possess the key.*

Braille's idea arose from the method developed by Charles Barbier de la Serre (Fig. 4), a military officer under Napoleon. He developed a system that used dots, which he considered more suitable for tactile identification. Barbier's alphabet used twelve dots and was based on the French phonemes. It was called "*night writing*" or "*sonography*" and was used in the military field to enable different divisions to communicate silently and in the dark. In order to write with the Barbier method a *sliding perforated stick was used, without any consideration of spelling, numbers and punctuation* (3).

In 1815 Charles Barbier de la Serre published an article entitled "*Essai sur divers procédés d'expéditive française contenant douze écritures différentes avec une Planche pour chaque procédé*" (Study of different procedures for writing French containing a dozen different methods of writing, each with its respective table for rapid execution). Barbier's method *was based on twelve dots in relief arranged on two vertical columns of six, in combinations according to a table that the students had to learn in advance, representing the letters and sounds of the alphabet* (3).

Braille studied and used the Barbier method to some extent, although he had several objections to it. He was critical of the complexity of the method and finally found the solution, inventing a system with just six dots in relief and sixty-three combinations to form *the letters of the alphabet, accented vowels, numbers, mathematical signs and punctuation* (3).

Thanks to the invention of Braille, in 1820, many texts were transcribed in Braille code and many blind children were able to approach the world of culture for the first time.

Soon after, new schools for the blind were opened all over the world, and it was thanks to the invention of Braille that the quality of life of these people changed radically (1,8).

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Review article: history of medicine

Thyroid surgery before the technological revolution: from Samuel Gross' "torrents of blood" to Paolo Miccoli's video-assisted thyroidectomy

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Abstract. "Can the thyroid gland…be removed with a reasonable hope of saving the patient?…If a surgeon should be so foolhardy as to undertake it…every step he takes will be followed by a torrent of blood, and lucky will it be for him if his victim live long enough to enable him to finish his horrid butchery…no honest and sensible surgeon would ever engage in it". With this renowned posthumous declaration, in 1886, Samuel D. Gross proposed that thyroid surgery should have been abandoned by surgeons. Despite this, subsequent improvements in anesthesiology, antisepsis strategies and better surgical instruments allowed to significantly decrease the mortality rates of this surgery to nearly zero percent, as is the case now. This paper aims at highlighting the most important steps and Mentors that led thyroid surgery to become one of the safest and most widespread surgical procedures.

Key words: thyroid surgery, Samuel D. Gross, Paolo Miccoli, Theodor Kocher, Theodor Billroth, minimally-invasive veideo-assisted thyroidectomy, MIVAT

Can you imagine how a person living before the first half of the nineteenth century could survive a giant-size thyroid goiter, or how he/she might be treated to avoid suffocation or strangling? The existence of goiter has been described since very early in recorded history. An enlargement of the neck was already reported in Chinese populations as far back as 2700 BC (1). Due to the widespread incidence of this disease, which is related to the low iodine content in the environment, goitrous people have long been depicted in drawings all over the world. Since goiter is an active and progressive disease, it is reasonable to assume that people with goiter reaching a certain age would likely display serious and life-threatening compressive complications from the significantly bulky disease.

So, back to our initial questions. How could doctors in the early ages deal with this sort of life-threatening problem? At a time when anesthesia did not exist, how could the primitive surgeon deal with a giant-sized, highly vascularized thyroid gland, a fully awake patient, and no electrocautery or proper surgical instruments designed to control bleeding?

The answer to these questions can now be found by looking back at centuries of surgical history.

Despite the well-known incidence of thyroid diseases, and the description of clearly-defined physiopathologic effects of the gland, the thyroid was not described in great detail until the XVI century, in the works of Andreas Vesalius (1514-1564) and Bartolomeus Eustachius (1520-1547). The latter was the first to use the term "isthmus" for the bridge that connects the two lobes of the gland. The gland itself was described by its Latin name ("glandulam thyroideam") only after the works of Thomas Warton (1614-1673), although he misinterpreted its role, and in his work "Adenographia", he was unable to distinguish the gland from the maxillary glands (1). Iconographically, the first anatomical representation of the thyroid was the one drawn by Leonardo da Vinci (1452-1519), that was depicted in a sketch currently hosted in the Royal Library, which was drawn around the year 1500 (https://www.rct.uk/collection/themes/publications/leonardo-da-vinci-the-mechanics-of-man): the Italian genius was nevertheless far from reality in his interpretation of its correct role in the human body (2).

Thyroidectomy before the nineteenth century

From a surgical point of view, some treatments to remove life-threatening bulky thyroid glands in cases of impending death due to compressive symptoms were carried out, most of which ended with distressing results in terms of intraoperative mortality. Among the primitive descriptions of thyroidectomies, we must cite the work of the Arabic surgeon Albucasis (936-1013) who performed surgery on opium-sedated patients with the help of a bag tied around their neck to collect the blood flowing from the incision. We must also mention the "noncutting operation" performed by Ruggero Frugardo (1140-1195) of the Salernitan Medical School, that included the use of setons, hot irons and caustic powders (all of which were used on the neck of an awake patient!). These techniques, together with others that were attempted in patients who were suffocating from large thyroid masses, were burdened by a degree of mortality that was not tolerable by the medical and surgical arts (2, 3). Operations on the thyroid were therefore long banned in several countries, and a report exists of a French surgeon who was imprisoned in 1646 (evidently after an "ante-litteram" litigation) for having performed a thyroidectomy in a patient who died immediately afterwards (3, 4).

The first description of a successful partial thyroidectomy dates back to 1791, and is attributed to Pierre-Joseph Desault (1738-1795) (5). Nevertheless, until 1850, the vast majority of surgical procedures performed on the thyroid proved to be either ineffective in managing the disease (e.g. ligature of the vessels of the superior pole, enucleations of the nodules, debulking of any sort) or burdened with a mortality rate as high as 50% (when more extensive procedures were attempted). The thyroid patient undergoing unfortunate surgery usually died of massive and uncontrollable bleeding or of acute asphyxia, while the luckier ones who survived the procedure usually died of other late complications such as infections or embolism (3,6).

These appalling results contributed to the idea, which was shared by many famous and skilled surgeons, that surgery of the thyroid was "not to be ventured upon" (7). In 1886, after his death, a statement by the American surgeon Samuel D. Gross (1805-1884) was reported: "Can the thyroid gland…be removed with a reasonable hope of saving the patient?…If a surgeon should be so foolhardy as to undertake it…every step he takes will be followed by a torrent of blood, and lucky will it be for him if his victim live long enough to enable him to finish his horrid butchery", concluding that "…no honest and sensible surgeon would ever engage in it" (3). This publication appeared, at that point, very late, since thyroid surgery in Europe was quickly changing…

"Modern" thyroid surgery: the impact of the German-speaking European school

The most important steps that led to the incredibly fast progression of thyroid surgery started in the 19th century, immediately after the posthumous statements from otherwise memorable surgeons: the introduction of anesthesia, the description and introduction of an antiseptic technique (Joseph Lister, 1867), and the introduction of surgical instruments designed to control bleeding (introduced in 1879 in Europe, much later in the US) (3,6,8-10).

Europe, and, more precisely, German-speaking countries such as Germany and Switzerland, were the core of the revolutionary development of thyroid surgery, mainly thanks to Theodor Billroth (1829- 1894) (Fig. 1) and Emil Theodor Kocher (1841-1917) (Fig. 2), two surgeons who hugely contributed to the improvements of modern surgery.

Emil Theodor Kocher and his impressive impact on mortality

Kocher held the chair of surgery in Bern, Switzerland from 1872 to 1917 (the year he died) and con-

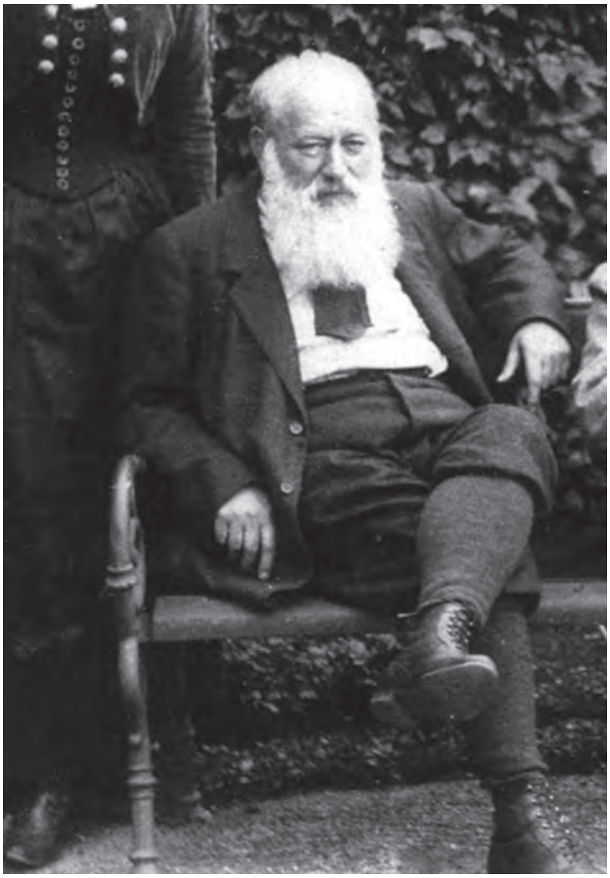

Figure 1. Theodor Billroth (1829-1894).

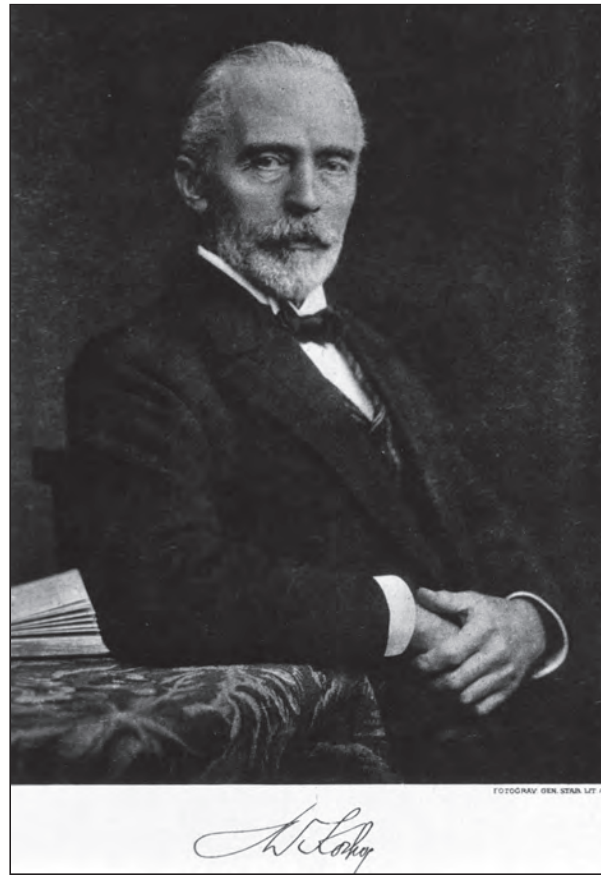

Figure 2. Emil Theodor Kocher (1841-1917).

tributed significantly to both the technique of thyroid surgery itself and the understanding of the physiology of the gland. He was awarded the Nobel Prize in 1909 for his "work on the physiology, pathology and surgery of the thyroid gland".

He was extremely curious and scientifically ready to accept new medical and surgical solutions, thus once he arrived in Bern in 1872, he introduced both antisepsis (which had only been described a few years earlier) in his operating theaters, and a surgical technique that was meticulous and respectful of the anatomical structures surrounding the thyroid. He also introduced chloroform anesthesia for his patients undergoing thyroid surgery, though with often unexpected results, since among the few mortalities in his initial experience there were some caused by the uncontrolled use of chloroform itself. He then decided to switch to a "safer" (at the time) type of local anesthesia, i.e., cocaine. Curiously, the incision that is currently used for thyroid surgery throughout the world, named after him, was adopted by Kocher only at the very end of his career, since he initially started performing surgery through an oblique incision in the neck, then through a vertical incision and only afterwards by the transverse incision that is still currently used.

In his hands, thyroid surgery mortality decreased from 13% at the beginning of his experience in Bern, to 0.5% at the end of his career, when he died in 1917. This astonishing result was not obtained easily, and presented several critical phases that required eventual improvements and relative technical adjustments (3).

Total thyroidectomy and the onset of cachexia strumipriva

After his first case series, Kocher was appalled when he met one of his patients and noticed how she had changed in what he called a "cretinoid way". The patient displayed a marked modification of her personality and had become psychically and physically slow, and she had also completely changed physical shape. Despite various attempts to cure her, she would never regain a normal quality of life. Based on this experience, he decided to review all his cases of thyroidectomy and concluded that "cachexia strumipriva" was present in all subjects who underwent total thyroidectomy: his conclusion was that total thyroidectomy should not have been indicated except in carefully selected cases (e.g. in the presence of malignancy). This unfortunate and sad evidence was extremely useful in understanding the many roles of thyroid hormones, and of hypothyroidism. All Kocher's reports perfectly exemplify how the effects and actions of several, if not all, endocrine glands could have been described in patients who underwent removal of the glands themselves (3, 4, 10).

Theodor Billroth and an inexplicable postoperative tetany

Unlike Kocher, Billroth, a German surgeon "positively godlike in demeanor" as described by the American, George Crile (1864-1943) (9), was an extremely daring surgeon who contributed to several innovations in abdominal and thyroid surgery. In his first six years as chairman of the Department of Surgery at the University of Zurich (1860-1866) he performed 20 thyroidectomies and reported a 40% mortality rate. Billroth then decided to abandon thyroid surgery, only to begin again some years later, after the benefits of anesthesia, antisepsis and the improvement in surgical instruments had been well established. After he moved to the University of Vienna, mortality rates in Billroth's hands decreased to 8% between 1877 and 1881. What was later found to be interesting with regard to Billroth's experience are the observations made by Anton Wolfler (1850-1917) and later by Anton von Eiselburg (1860-1939) and Eugène Gley (1857-1930) that patients operated on by the great mentor developed postoperative tetany which was likely caused by the removal of the parathyroid glands during surgery (10-12). The differences between Kocher and Billroth's surgical techniques, as well as an interpretation of their postoperative complications, are best described by another famous American surgeon, William Halsted (1852-1922), who wrote: «I have pondered the question for many years and conclude that the explanation probably lies in the operative methods of the two illustrious surgeons. Kocher, neat and precise, operating in a relatively bloodless manner, scrupulously removed the entire thyroid gland doing little damage outside its capsule. Billroth, operating more rapidly and, as I recall, with less regard for the tissues and less concern for hemorrhage, might easily have removed the parathyroids or at least have interfered with their blood supply, and have left fragments of the thyroid» (13). Halsted was among the first surgeons to publish a technique for parathyroid preservation (14). Billroth's postoperative tetany had been therefore solved after a few years…

"…Do you fancy a fried thyroid?" Or "how to cure postoperative hypothyroidism".

The problem Kocher had encountered was at least partially solved when, in 1891, George R Murray (1865-1939) injected an extract of the thyroid gland and later showed how it benefited patients who had undergone total thyroidectomy (15, 16). Immediately afterwards (1892), Frederick Y Fox (1856-1938) demonstrated that the same benefits were present when half a lightly fried sheep's thyroid obtained the same excellent results (17). These studies are now considered the cornerstones of modern replacement therapy with levothyroxine.

Thyroid surgery in the XX century: the "New wave" of surgeons from the New Continent

In the 20th century, thyroid surgery spread from Europe all around the world thanks to the many surgeons who had visited the two most famous European surgical schools and had been mentored by Kocher and Billroth. In this century, attention was focused more on the various diagnoses of thyroid disease requiring different preoperative and operative treatments than on the technique itself, which was at that time already fairly well standardized.

William Halsted's epiphany following his encounter with both Kocher and Billroth, helped him understand how one of the possible reasons American surgery was so underdeveloped as compared to the European schools, was the use of vascular clamps. In his observations, he concluded that “the value of artery clamps is not likely to be underestimated, since they determine methods and results impossible without them. They tranquilize the operator. In a wound that is perfectly dry…the operator, unperturbed, may work for hours without fatigue” (13). He therefore decided that a number of these clamps should have been present in every operating theater around his country, where they had previously been limited to very small numbers in very selected centers.

Thomas Dunhill (1876-1957) was an Australian surgeon who started working on patients with “exophthalmic goiter”, a condition that was considered extremely severe and was burdened by high rates of mortality in surgical case series, mainly due to the onset of uncontrollable atrial fibrillation. By 1910, Dunhill had reached an astonishing 3% mortality rate in his series of patients affected with this disease, while in London the standard mortality rate exceeded 30%. He was among the first surgeons to use and describe a thorough extracapsular dissection of the gland, although he performed a total lobectomy on one side and a subtotal lobectomy on the other, in patients undergoing surgery for toxic thyroid disease (18).

Charles Mayo (1865-1939), an American surgeon, is considered the father of American thyroid surgery: working with the famous endocrinologist, Henry Plummer (1874-1936), he was probably the surgeon with the largest case series. Their studies on hyperthyroidism are very well known, also because they were likely the first to use this definition for patients displaying “cachectic thyroid disease”. Mayo and Plummer further decreased the mortality of thyroidectomy in patients with hyperthyroidism (from 4% to 1%) thanks to the preoperative use of iodine compounds given to patients undergoing surgery (12).

Other pioneers contributed to the dissemination of the principles emerging in thyroid surgery, and among them, the most important surgical improvement was described by Frank Lahey (1880-1953), who advocated the full dissection of the inferior laryngeal nerve during every thyroidectomy, thus limiting its injuries to only 3% of his cases. Lahey’s technique for nerve dissection is still valid in modern thyroid surgery and is carried out to limit the incidence of postoperative vocal cord palsy (19).

The great mentors of thyroid surgery in the last decades of the XXth century

A relatively long time passed without any significant jolts in the field of thyroid surgery, but another “New wave” was brewing in Europe. Starting in 1971, a new current was taking shape in London, and more precisely at the Hammersmith hospital, where some prestigious British surgeons and endocrinologists met to organize what was the first Course on Endocrine Surgery dedicated to a European audience. This course, which was organized by Selwyn Taylor and Richard Welbourn, brought together a group of young endocrine surgeons from around the continent, all of whom would eventually become great mentors of the discipline in later years. This group was made up of the immense (in all senses) Charles Proye from Lille, Antonio Sitges-Serra from Barcelona, Sten Tibblin from Malmo, Hans-Dietrich Roher from Dusseldorf, and Matthias Rothmund from Mainz. In these courses (a regular appointment for anyone interested in the field of thyroid and endocrine surgery coming from all over the world in the ‘70s) the most recent knowledge the endocrinologists had merged with the technical notes provided by the most experienced and renowned British surgeons. In those years, London was attracting more and more experts in the field and creating further followers. The faculty included two other then-young American surgeons, Norman Thompson and Orlo Clark, who would later have spread their technical skills all over the new continent, becoming icons of the discipline, and founders of the American and International Societies that were to appear shortly afterwards (20).

In the 80’s and ‘90s, France became a fervent territory for endocrine surgery in general and thyroid surgery in particular, with the previously cited Charles Proye (1938-2007), Jean-Francois Henry from Marseille, Jacques Marescaux from Strasbourg, and Jean-Louis Kraimps from Poitiers.

Charles Proye was, as already stated, a huge figure in thyroid surgery. Trained by his mentor, Georges Lagache, he became a great mentor himself for hundreds of disciples all around the world. He always worked in Lille, where he would host surgeons coming from all around the globe. In his preoperative morning meetings you could hear several different languages (he could handle many of them, including his native Flemish), with people from nearby England, but also from the US, Mexico, Uzbekistan, Australia, New Zealand, Belarus, Switzerland, Germany and Italy, among others. He was a workaholic, working till all hours, 6 if not 7 days a week with the only exception of the Five Nations' match days, when his beloved French rugby team played (the signpost affixed on his office in the hospital claiming: "Closed for Five Nations match" was famous in those days). Charles Proye generously dispensed his unlimited knowledge and talent for research, and taught his skills about thyroid and parathyroid surgery every single day to whomever was willing to follow him into the operative room. Having the honor of assisting him on a surgery was always a gratifying moment. He was a fascinating man, a mentor for a lot of present-day thyroid surgeons, a friend to most of them, a scuba diver, a shark chaser, and, basically, one of those few who "invented" endocrine surgery as a discipline itself.

Proye contributed to the development of endocrine surgery in his country by being one of the founders of the extremely active French Association of Endocrine Surgery (AFCE) in 1989, as well as its first President (20), and became a founding member of the International Association of Endocrine Surgeons (IAES), and its President between 1997 and 1999. In his last years, still working hard despite an aggressive disease that was consuming him but not his untamed spirit, he became President of the French Academy of Surgeons (an honor he was very proud of) and was awarded the "Legion d'honneur". Despite the loss of the man, legends about him are still firmly rooted and widespread in operating theaters all around the world by his beloved disciples and friends (21).

France had indeed been the hub of endocrine surgery as a discipline, but in the last decade of the 20th century technology overtook science: laparoscopy impacted the surgical world…and the surgical world itself fell into turmoil.

The Italian revolution: the impact of an endoscope on thyroid surgery

At a time (late '80s to early '90s) when the biggest goal was to laparoscopically remove organs before other surgeons did, the thyroid was approached relatively late due to its limited anatomical region and the bulky instruments that could not be considered appropriate for such surgery. Despite these difficulties, two surgeons, both from Italy, reported their endoscopic approach to the neck: Cristiano Huscher, a pioneer of laparoscopic surgery (22), and Francesco Paolo Mattioli from Genoa, a true gentleman who, despite his advanced age, decided to dedicate himself to laparoscopic surgery and achieved excellent results (23). Nevertheless, these new techniques were clearly unsuccessful for the previously cited reasons: there was too little room in the neck for such instruments.

Many other surgeons also more or less successfully tried to perform endoscopic thyroidectomy via the neck, but always encountered major problems due to the fact that they wanted to adapt the neck region to the laparoscopic technique, and not the other way around. The main clinical problems, some of which were life-threatening, included: the CO2 pressure that was initially used was too high for a region (the neck) that is not confined, but that is in direct communication with the chest. This led to severe and long-lasting hypercapnia during operations which lasted more than 3 hours, often requiring postoperative recovery in the ICU. Another significant problem was the length of the surgical instruments: those dedicated to laparoscopic surgery were too long to be used in the neck region. Therefore, the main issue related to this was that the surgeon was performing a long operation in an anti-ergonomic position that could not be effective in terms of the fine movements required for this kind of surgery.

Then, in 1997, an Italian surgeon started to think that the thyroid was not the best choice organ of the neck on which to start developing a minimally invasive technique, when his surgical center was performing hundreds of…parathyroidectomies every year. Paolo Miccoli (born in Leghorn in 1947, but who always worked in Pisa, together with the immense endocrinologist Aldo Pinchera) (Fig. 3) then envisioned

Figure 3. Paolo Miccoli. Photo by: Philippe Eranian. With permission from Paolo Miccoli.

a technique that was not adapted to, but specifically created for the neck region. It involved dedicated instruments (that he designed together with his collaborators) and an endoscope smaller than the one commonly used for laparoscopy, i.e., a 30° 7mm caliber endoscope usually used by urologists for cystoscopy. The idea behind the technique was to take advantage of the endoscopic magnification (as high as 20x) during an operation in which the aim of the surgeon was to identify small lesions. In an effort to carry out a thorough exploration of the neck, he decided to make the 2cm incision on the midline, thus allowing him to work on both sides of the neck. To avoid the problem of hypercapnia, in a country where operating rooms used to be full of young surgeons wishing to observe, he decided that the best way to create the operative field was to rely on external retraction maintained by an assistant surgeon, and not on CO2 insufflation. The technique was therefore named "Minimally-Invasive Video-Assisted Parathyroidectomy", better known by the acronym MIVAP (24).

The die was cast and after a few months the technique was used for small-sized thyroid nodules, when a lobectomy was indicated mainly to perform diagnostic surgery, in the presence of a thyroid that was otherwise normal. The first series of MIVAT operations was published in 1999 (25), and the Pisa technique immediately spread throughout the world, with great help from the Roman School of Rocco Bellantone, who, together with his collaborators, published the description of their first case that same year (26), and several other studies in the years to follow. MIVAT was initially recommended for "diagnostic" surgery, thus only lobectomies were indicated, but within a few years it proved its value for total thyroidectomies (27, 28), for the treatment of thyroid cancer (29, 30), and for lymphadenectomy of the central neck (31). In just a few years this Italian technique spread throughout the world, and its effectiveness and reproducibility was shown in multicentric studies (32, 33).

Will other Mentors be able to override technological successes or will we be tied to 2.0 versions?

From that point on, the new millennium witnessed a major development of technology over the gigantic figures of Men, and, indeed, thyroid surgery advanced further and further, but new surgical techniques became more and more dependent on technical support (e.g. Leonardo da Vinci robotic system) or on derivatives of new surgical philosophies (e.g. the all-new transoral approach deriving from the Natural Orifice Transluminal Endoscopic Surgery). These new techniques are still under development and are far from being globally accepted, due also to the ethical issues they inevitably carry with them.

This is why we should never forget our origins or our Fathers since great Mentors and huge personalities will always override mere technology in a discipline that requires human contact between surgeons and their patients (34, 35).

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Bioarchaeology of the human remains of the so-called "*sailor*" from the site of the ancient ships of Pisa - San Rossore

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Abstract. The biological and taphonomic aspects of a human skeleton found along with that of a dog in Area 3 of the so-called Roman harbour of Pisa-San Rossore are here examined. Starting from 1998, in addition to other wrecks, the so-called "ship B" was brought to light. During the excavation, the skeletons of the so-called "sailor" and a dog were discovered under the loading, probably due to the sinking of the ship following a storm. Biological analyses of the human remains, carried out at the time of the discovery, revealed that they belonged to a male individual, who died when he was about 35-45 years old. The shape and strength of its skeletal structure, especially the muscular impressions of the limbs and the particular remodelling of the metatarsals and the phalanges of the feet, tended to confirm the hypothesis of his seafaring activity. Moreover, according to statistical analysis, the cranial shape falls within those of the ancient Pompeian population. The positions of the two skeletons, at the time of their highlighting, lead to the presumption of a sinking dynamic of the ship and of its loading more articulated with respect to what has been said and written so far. The present article aims to summarise the anthropological studies carried out on the sailor, throwing a new light on the taphonomic aspects of the discovery of the skeletal remains and reinterpreting the deposition and decomposition modalities of the two individuals.

Key words: roman port, wrecks, Pisa, human remains, bioarchaeology, sailor

Introduction

The archaeological site of the Roman ships of Pisa San Rossore is located about 500 meters from the medieval walls and 9 kilometers from the coast. In 1998, during the works to the train line connecting Rome to Genova, near the railway station of Pisa San Rossore, at a depth of about six meters, wooden artefacts belonging to a sanded boat dating back to the Roman age were found (1, 2). From that discovery, the site of the Roman ships of Pisa was born, unearthing thirty shipwrecks until its conclusion in 2016.

The shipwrecks site appears to be located within a secondary riverbed related to one of the branches of the ancient Auser river, which crossed the alluvial plain of Pisa. In this minor stream connected with the network of fluvial channels that characterized the alluvial plain, the ships coming from the various coastal landings transited to the city of Pisa (3).

In conjunction with exceptional flood events, caused by periods of intense seasonal rainfall and by the strong anthropic deforestation, the waters of the nearby Arno overflowed, flooding with large quantities of water and sediments this secondary channel, causing strong water movements that swept away everything they encountered.

According to the geological and archaeological stratigraphy, the deposits revealed several well-defined activities that can be divided in eight distinct phases, in a chronological range from the VI-V century BC to a period after the V century AD, five of which could be referred to traumatic events (3).

The phase of our interest is Phase IV (the Augusteo-Tiberian flood), which referred to a traumatic event that caused the sinking of a large number of boats, including ship <<B>> (4, 3). This wreck is of a medium-sized transport ship, about 9.50 m long and 4.30 m wide, made of oak and pine wood, which was unearthed inclined on one side. The ship kept part of the load *in situ* and the other portion was partially leaked from the boat at the time of the sinking. The origin of a part of the load (5), consisting of wine amphorae and a particular type of sand, seems to be related to the Campania region (3).

During the excavation of the fluvial bed sector, near the western side of the wreck, the almost complete skeletons of a man and a dog (SR2) were discovered lying next to part of the planking of the ship and to several finds referable to its loading (Fig. 1).

The present article aims to summarise the bioarchaeological analyses (6, 7) and to propose a reinterpretation of the taphonomic recovery conditions of the human and animal remains found on the fluvial bed, under the planking and the load of ship <<B>>. The taphonomic situation has so far been read as the outcome of a relationship between the two living individuals, being interpreted as the photograph of a familiarity between the two subjects and the man's attempt to rescue the animal. This is a hypothesis that this paper intends to question, in the light of the re-reading of the taphonomic data acquired during the excavation that suggest the non-contextual relationship of the two individuals, whose skeletons were found located in the same place but apparently without any living physical or temporal connection.

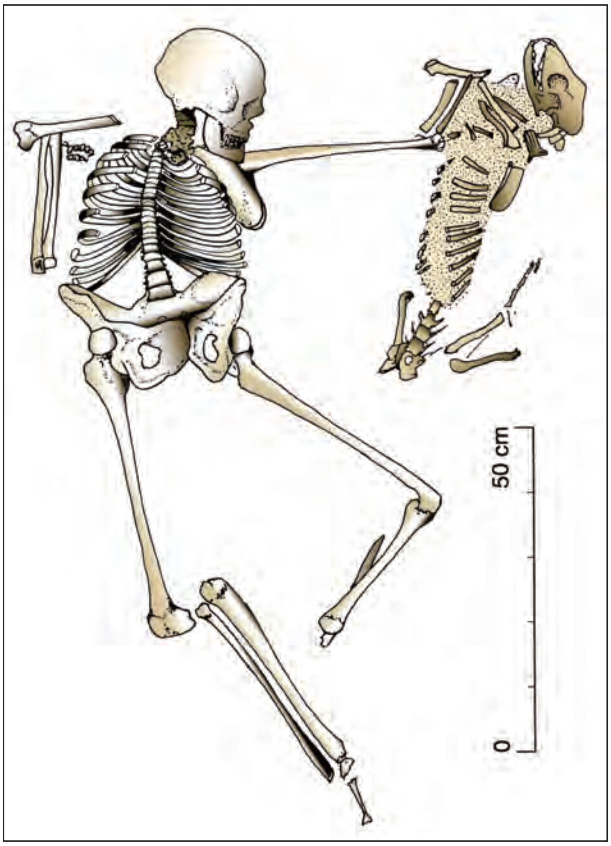

Figure 1. Plan of the skeletal remains (SR2) as found during excavation of the western sector of the ship <<B>>. The relationships between the two individuals, after the removal of the wooden elements of the planking, are shown (plan authors: Marta Abbado and Emilio Trinci; adapted by S. Ricci).

Materials and methods

The skeletal remains were very well preserved and almost complete in their anatomical parts, despite the long period of deposition in an underwater environment.

The human skeleton was subjected to anthropological analyses (6) and all the bones were macroscopically observed under good light, in order to describe their morphological features and highlight any changes and features suggesting possible pathological conditions. The remains were sexed on the basis of the pelvic morphology (8, 9); age-at-death was estimated from the degree of degeneration of the symphyseal surface of the pubic bones (10, 11). The height of the individual was estimated on the basis of the regression formulae by Trotter and Gleser (12). Anthropometric measurements have been collected using the standard metrics by Martin and Saller (13) and skeletal indices have been calculated.

For the final physiognomic reconstruction, the Manchester method (14, 15), commonly used in the forensic practice, was applied.

Results

The taphonomic aspects

The skeleton under study was unearthed in preserved anatomical position, in supine decubitus. The remains were found lying on a slight silt-sandy prominence on top of which rested the pelvis and the right lower limb. The position of the different skeletal districts revealed by the excavation was as follows. The skull was found turned to the left, maintaining a perfect anatomical connection with both the mandible and the first cervical vertebrae. The bones of the thorax were well preserved and maintaining a physiological position; the vertebrae were completely aligned, and the pelvic bones were still in tight connection. The upper right limb was parallel to the thorax, with the radius and ulna folded on the humerus and anatomically connected, but with the articulation of the elbow displaced. On the left, the humerus was perpendicular to the body of the subject. The lower right limb was stretched along the entire slope of the prominence and parallel to the body axis; the femoral head emerged from the acetabulum and the tibio-femoral joint of the knee was displaced. The right foot was missing. On the left, the femur formed an angle of about 90° with respect to the sagittal plane of the body, the tibia in turn was bent about 70° with respect to the femoral diaphysis. The left foot was found about a meter away from the tibio-talar joint. It appeared in anatomical connection, but lacking of several bones (6).

The skeleton of the man was discovered partially covered by a wooden stake about one and a half meter long, probably part of the planking of the ship or rest of an oar, placed above the skeletal remains, transversely to the sagittal plane of the body. The stake insisted on the bones of the right hand, passed over the anterior cervical trait, ending with its left extremity under the abdominal tract of the dog, which in turn was found in preserved anatomical position, partially covered by a large piece of wooden planking (Fig. 1).

The remains of the two bodies were then subjected to a negative cast, in order to preserve a plaster replica of their true position of recovery (6).

Bioarchaeology of the human remains

The skeletal remains, as first studied by Mallegni and colleagues (6) at the time of discovery, belong to a male individual, aged between 35-45 years, about 172 cm tall. The results of the anthropometric analysis and the calculated indices are reported in the appendix in full.

In brief, for what concern the index values, the cranium is defined as *mesocranic* (cranial index=78.19), *orthocranic* (vertico-longitudinal index=71.3) and *tapeinocephalic* (vertico-transverse index=91.2). The splanchocranium in the entirety of its parts, including the mandible, turns out to be low and wide (*hypereuriprosopus* and *hypereurienic*). The orbital cavities are high (*hypsiconchus*) and the nose of medium opening (*mesorrhinus*) with sinuous bridge and back and nasal septum slightly deviated to the left (Fig. 2).

The individual's postcranial skeletal system is very robust, more expressed by the upper limbs (humeral robusticity index=20.9; ulnar caliber index=14.9) compared to the lower limbs. The former, and in particular the humerus, are strongly marked by the action of the deltoid and biceps brachial muscles, responsible for the abduction of the upper limb (*m. deltoid*) and the supination and flexion of the forearm (*m. biceps brachialis*), with a more robustness displayed by the right limbs. The bones of the lower limbs are generally robust (femoral robusticity index=11.27; tibial robusticity index=23.38) (Fig. 3).

Figure 2. Cranium of the "sailor", lateral and frontal views. The masculine morphological features of the subject are evident (adapted from Mallegni et al. 2004, by S. Ricci).

Figure 3. Long bones of the upper and lower limbs of the individual. The strong muscular insertions on the diaphyses are clearly visible (adapted from Mallegni et al. 2004, by S. Ricci).

Of particular interest is also the study of the muscular attacks of the soles of the feet, especially those that during the march or in a situation of imbalance allow the contraction of the fingers. Unfortunately, the left foot is only partially preserved. Despite this loss, the remaining bones show very evident insertions, in the form of small tubercles and ridges, which mark the attacks of the adductor and flexor muscles and of the dorsal and plantar interosseous muscles (6).

As regards the oral conditions, the occlusal surface of the jugal teeth of both the upper and lower arches appear completely worn, with complete disappearance of the enamel cusps (6). Upper incisor teeth show extreme wearing that exposes the underlying dentine, abrading almost totally the crown up to the cervical area. The labial surfaces, in particular, exhibit extensive wearing in the form of a flat oblique plane of residual enamel towards the cervical area (Fig. 4). Microscopically, in these regions, the residual enamel displays micro-striations with a sinuous course (7). These striae are not observed on the crowns of the lower anterior teeth, which are preserved quite intact with very little signs of wearing in the buccal and lingual surfaces. Inferior teeth also show massive deposition of calculus on the cervical area and on the upper portion of the roots (Fig. 5). These teeth appear to have not been in-

Figure 4. Maxillary central incisors, labial view. The alveolar resorption and the uncovering of part of the roots is visible. The crowns are almost totally disappeared due to the extreme wear of the labial surfaces (adapted from Mallegni et al. 2004, by S. Ricci).

Figure 5. Mandibular anterior teeth, labial view. A strong layer of mineralized calculus covers the cervical and the upper radical areas (adapted by S. Ricci).

volved by the action that caused the extreme maxillary wearing, because they retain a strongly mineralized layer of calculus, which, in that case, would have been abraded and removed by the mechanical agent.

Discussion

The particularly strong muscular markings on the upper limbs suggest that the individual used to grab and manipulate materials and lift heavy loads. Then considering that on the right side the muscles acting on the forearm are more developed and shaped than those of the opposite limb, it would perhaps be hypothesized that the individual was right-handed.

Based on the lower muscular insertions, pretty pronounced at the level of the plantar region of the feet, a seafaring activity of the individual has been hypothesized. Indeed, these evidences suggest, based on a hypothetical reconstruction of biomechanics (16), that the individual was usual walking in frequent conditions of imbalance, probably on the wet ship's bridge, by contracting the plantar muscles to avoid slipping or falling (6). The individual was therefore renamed as the "sailor" of the Roman harbour of Pisa.

As to oral health, the almost complete disappearance of the enamel and dentine on the labial surfaces of the upper anterior teeth suggests that the subject used them to treat some coriaceous materials, possibly wood, or even vegetable fibres, probably manipulating by pressing them against dental crowns (6). This suggestion is supported by the micro-striations observed on the residual enamel, compatible with this activity (7).

Finally, the subject does not show signs of significant pathologies, highlighting how it was an adult individual at the height of his strength.

The measurements and the relative indices obtained on the various bone districts seem to fall within those that characterize the samples belonging to central-southern Italy and, in particular, to the Campania region (17), evidence that could confirm the archaeological hypotheses, obtained from the data on the origin of the amphorae of the ship loading and their content (3, 5). To investigate this hypothesis, calculation of Penrose's χ^2 through a set of some cranial measurements has been carried out. Craniometrics have therefore been used for the statistical analysis called the "*generalized distance*" of Penrose (18), which compares metric data of a set of ten features taken on the cranium under study, with those of a series of skulls from the excavations of Pompeii, published by Nicolucci (17). The statistical method, based on the calculation of standard deviation units starting from a set of repeated measures, is used to test whether an individual could be reasonably assigned to a given group. In this case, it tests whether the "sailor" from ship B, based on ten cranial measures, could be reasonably assigned to the group from Pompeii. The test reveals that the two group have a minimum distance in both size and shape and consequently that the subject shows a remarkable affinity with those from Pompeii.

Finally, a cast of the cranium was prepared in order to obtain a physical copy and allow for a physiognomic reconstruction of the subject. The Manchester method, developed and standardized in combination by Neave (14) and Wilkinson (15), was applied. The facial reconstruction of the sailor is shown in Fig. 6.

Figure 6. Physiognomic reconstruction of the sailor, starting from the cranium to the rebuilding of the facial soft tissue thicknesses on the positive replica, following the standardized Manchester method. The facial reconstruction was realized by Gabriele Mallegni, graphic rendering is by S. Ricci.

Taphonomic reading and reinterpretation

Firstly, taphonomic data indicates that the individual is in a primary position and therefore has decomposed in the place of the first location after death, brought to that site by the currents responsible for the shipwreck. The taphonomic data reading suggests that the subject has arrived on the fluvial bed carried by the currents and here, anchored by the planking of the ship, he died probably by drowning. The upper limbs have in fact a plastic position such as to suggest a voluntariness in the movement, rather than a post-mortal displacement: the position of the individual and his limbs therefore indicates that this dynamic occurred when the individual was still alive. Indeed, an attempt of the man to remove the stake from his body could be hypothesized, given the position of the upper right limb and of the related hand, which seem to grab the wood in the attempt to push it away. The effort would have been thwarted by the weight of the wreckage and of its loading, which in the meantime was falling outside the ship. The wooden stake, in this assumption, could have largely contributed to the rapid death of the man, anchoring him to the fluvial bed and preventing him from saving himself from drowning.

Moreover, the isolated position of the left foot suggests that this element decomposed at the site of the discovery, about a meter away from the tibio-talar joint, possibly separated from the rest of the body when it was still covered by the soft tissues, thus in the peri-mortem period.

The fate of the small animal, whose skeleton was found lying on the stake and in proximity to the upper left limb of the man, has perhaps had different paths before its death. The stratigraphic and taphonomic conditions of discovery of the man and the animal and the different physical relationships between their skeletons and the elements of the ship, tend to exclude the possibility of a physical and temporal contact between the two living individuals, rather suggesting that the two subjects would have arrived in the same place, perhaps dragged by the same currents, but in two different moments and with two different modalities (Fig. 7). In particular, it can be hypothesized that the body of the animal arrived next to the man at a later time at his death, perhaps brought to that place by the strong fluvial currents.

Figure 7. Reconstruction of the taphonomic sequence of the two individuals and of the superimposition of the wooden elements on the skeletal districts. Black line facilitates visualizing the bone elements, partially covered by the elements of the planking (adapted from Mallegni et al. 2004, by S. Ricci).

The remains of at least eight other individuals, both males and females, were found as isolated bones and represented only by the tibiae and femurs, probably due to the action of the river currents acting on the dried skeletal elements, activity that, due to fortuitous circumstances, did not act on the remains of the man and dog, perhaps protected by the planking of the ship and preserved until today.

Conclusions

The skeletal remains found under the planking of the wreck of ship B, thanks to the fortuitous circumstances of deposition, offer an overview of an ancient catastrophic shipwreck event, which occurred in the fluvial channel formerly connected to the Roman port network of Pisa.

The photograph that this discovery offers us is that of a man and a dog lying on the bed of the river under the load of the ship, placed close together, but yet separated by a wooden element from part of the planking. These two individuals, so far interpreted as linked by a relation of familiarity and in the act of helping each other during the last moments of life, probably found themselves close together in different ways and perhaps in circumstances subsequent to their death. The stratigraphy in fact suggests two different moments of deposition on the fluvial bed.

Here we have proposed a different reading of the taphonomic conditions that, in any case, does not make the story lose its fascination.

If the integrity of the other individuals recovered has been broken down by the currents of the river, the remains of the ship that caused their death have also allowed the exact image of the last moments of life of these two subjects to come untouched up to us.

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Appendix

In the following tables, the anthropometric measurements (based on Martin and Saller, 1957) of cranium and mandible, humerus, radius and ulna, femur, tibia and fibula, with the calculation of the related principal indices (indicated by a fraction between two numbers representing the two corresponding measures), are reported.

CRANIUM					R - L
1. (g-op)	188	25. Na-ops arc	285	*50. (mf-mf)*	15
2. (g-i)	177	26. *na-br arc*	134	*51. (mf-ek)*	39 - 39
4. (g-l)	183	27. *br-l arc*	126	*51.a. (da-ek)*	47
5. (n-ba)	97	28. *l-op arc*	25	52. *orb.height*	34,5
7. (ba-ops)	39	29. *na-br chord*	117	54. nas.breadth	24
8. (eu-eu)	147	30. *br-l chord*	113	*55. (n-ns)*	48
9. (ft-ft)	91	31. *l-op chord*	21	*59. (ecm-ecm)*	53
10. (co-co)	118	32(1a). *na-br*	53°	*60. (pr-alv)*	11
11. (au-au)	122	34. *ba-op*	8°	*61. (ect-ect)*	59
12. (ast-ast)	112	38. *cran.cap.po*	1450 cc	*62. (ol-sta)*	46
13. (ms-ms)	98	38d. *cran.cap.ba*	1510 cc 1576 cc	*63. (enm-enm)*	42
16. largh.for.occ.	28	*40. (ba-pr)*	86	64. *pal.breadth*	13
17. (ba-br)	134	*43. (fmt-fmt)*	100	72. (na-pr)	92°
18. (ba-ve)	137	*44. (ec-ec)*	95	73. (*n-ns)*	84°
20. (po-br)	120,63	*44a. sup.biorb.br.*	98	74. (*ns-pr)*	105°
21. (po-ve)	117,32	44(1). *naso-malar curve*	111		
22a. calotte height	106	*45. (zy-zy)*	112		
23. horiz.circ.gl	528	*47. (n-gn)*	113		
23a. horiz.circ.oph.	525	*48. (n-pr)*	67		
24. (po-br-po)	328	*49.a. (da-da)*	20		

Principal cranial indices	
8/1	78.2
17/1	71.3
17/8	91.2
47/45	66.1
48/45	39.2
52/51	88.5
54/55	50.0

Mandible	-	R	L
65. (kdl-kdl)	111	-	-
65.1. (krd-krd) o (crd-crd)	93	-	-
66. (go-go)	88	-	-
67. (ml-ml)	41	-	-
68. mand.length	72	-	-
69. (ifd-gn)	29	-	-
69(1). mand.height	-	28	28
69(3). mand.th.	-	115	120
70. (go-cd)	-	64	65
71a. min.r.br.	-	28	27
79. man.	112°	-	-
79(1a). (id-pg)	85°	-	-
79(1b). (id-alv)	72°	-	-

Humerus	R	L
1. max L	344	344
2. tot L	321	320
3. prox.ep.br		49
4. dist.ep.br	67	62
5. max.d.mid	26	25
6. min.d.mid	19	23
7. min.circ	72	69
8. head circ.	-	136
9. tr.d.head	-	41
10. sag.d.head	-	45
16. cond.diaf.	103,5	98
17.		
18. tors.	117°-	
Index		
7/1	20.9	20,1

Radius	R	L
1. max L	260	-
2. phys. L	247	-
3. min.circ.	53	-
4. tr.d.	20	-
5. sag.d	13	-
index		
3/1	20.4	

Ulna	R	L
1. max L	281	-
2. phys. L	252	-
3. min.circ.	42	-
11. sag.d	14	-
12. tr.d	18	-
13. sup.tr.d	22	-
14. sup.s.d	23	-
index		
3/1	14.9	

Femur	R	L
1. max L	452	451
2. phys. L	454	448
3. troch.max L	438	433
4. phys.troch. L	435	426
6. sag.d	28	28
7. tr.d	25	25
8. circ.mid	82	82
9. sup.tr.d	26	27
10. sup.s.d	36	31
15. neck tr.d	36	28
16. neck s.d	29	30
18. vert.d. head	45	45
19. tr.d. head.	45	45
20. circ. head	147	145
21. epic. br	79	77
28. tors.	15°	15°
29. neck-diaf.	135°	133°
index		
6/7	112	112

Tibia	R	L
1. max L	358	355
2. tot L	346	340
3. prox.ep.br	71	70
6. dist.ep.br	46	42
8. max.d.mid.	30	30
8a. s.d.f.n	33	34
9d. tr. med.	20,5	22
9a. tr.d.f.n	24	23
10b. min.circ.	81	83
index		
9a/8a	72.7	64.7

Fibula	R	L
1. max L	359	357
2. *max.d.mid.*	13	15
3. *min.d.mid.*	19	16
4a. min.circ.	41	38

Genome editing: slipping down toward Eugenics?

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Abstract. In this paper, I will present the empirical version of the slippery slope argument (SSA) in the field of genome editing. According to the SSA, if we adopt germline manipulation of embryos we will eventually end up performing or allowing something morally reprehensible, such as a new coercive eugenics. I will investigate the actual possibility of sliding towards eugenics: thus, I will examine enhancement and eugenics both in the classical and liberal versions, through the lens of SSA. In the first part, I will discuss the classical eugenics from a historical perspective and conclude that classical eugenics is morally deplorable; but by currently accepting genome editing I argue that it is not possible to 'slip' into classical eugenics. Then, I will analyze liberal eugenics: I will consider Habermas' and Sandel's objections to liberal eugenics and genetic human enhancement. Subsequently, I will reply to these arguments affirming that, although it is not possible to refuse any form of genetic enhancement, liberal eugenics would not consider the principles of justice, non-maleficence, and non-instrumentalization; hence, it should be considered not morally acceptable. In addition, I will support the thesis according to which the possibility of relapsing into liberal eugenics is more likely than relapsing into classical eugenics. Then, I will present a strategy that, while avoiding falling into the undesirable scenarios related to SSA, still accepts some application of germline genome editing of embryos and gametes. In such a way, I will show that even if we accept the plausibility of a certain slip into an undesirable scenario, SSA does not offer conclusive reasons to forbid any use of germline genome editing technique in both therapeutic and enhancement fields.

Key words: slippery slope argument, genome editing, classical eugenics, libera eugenics, genetic enhancement

Introduction: the slippery slope argument in the field of genome editing

The slippery slope argument (SSA) is one of the most relevant argumentative strategies in the discussion on human germline modification. SSA is widely considered throughout the bioethical debate: in fact, it is often used in relation to issues including abortion, euthanasia (1) and assisted fertilization. According to SSA, allowing germline genome editing treatments would lead to an uncontrolled sliding towards dangerous and undesired scenarios, such as an eugenics drift or the acceptability of enhancement practices; hence, in order to avoid such scenarios, germline genome editing treatments, for both therapeutic and enhancement aims, should be banned. In textbooks of logic and on writing in ethics, SSA is often classified as an informal fallacy, that is an argument whose stated premises fail to support their proposed conclusion (3). However, in this paper I will focus on the more compelling empirical or socio-psychological version of SSA (4-6): according to this version, due to the acceptance of germline genome editing, a gradual acceptance of genetic enhancement could infect the moral sensitivity of society, eventually leading to a new coercive eugenics. Indeed, some psychosocial features could make it difficult to clearly distinguish between ethically acceptable uses of genome editing, such as therapeutic uses, and unacceptable ones (7). Genome editing is the first technique that enables a positive modification of future generations and therefore requires careful analysis. I will discuss the concepts of eugenics, both in the classical and the liberal version, and of genetic enhancement, through the lens of SSA. Only after having carried out an in-depth ethical analysis of these concepts and having verified the actual undesirability of some scenarios and the real possibility of the occurrence of others, the soundness of the SSA can be assessed. Appreciating these concepts and the historical-cultural context will enable to understand which possible consequences could reasonably occur by allowing germline genome editing practice on human beings. Indeed, according to Anneli Jefferson, Empirical SSAs almost always require an assessment which takes into account the cultural and political context in which the argument is put forward (7). Therefore, I will present a strategy that, while avoiding falling into the undesirable scenarios related to SSA, still accepts some application of germline genome editing of embryos and gametes. In such a way, I will show that even if we accept the plausibility of a certain slip into undesirable scenario, SSA does not offer conclusive reasons to forbid any use of germline genome editing technique in both therapeutic and enhancement fields.

In this paper, I assume a mixed theory that accepts the "lexical" priority (8) of deontological reasons. From this perspective, a priori constraints on the production of maximum aggregate wellbeing are established on the thesis of the people rights. Such rights should be considered as claims that people have by nature or based on a certain agreement or original contract, and they cannot be violated in the name of better consequences for society. Once we assessed that a specific action does not violate any right, we have to evaluate whether its consequences do not lead to a future scenario in which rights could be violated. In this case, I maintain that we have good reasons, based on a deontological perspective, to prevent the beginning of this course of action. Furthermore, I also consider consequentialist reasons to evaluate two or more actions which respect people rights in both current and future scenarios. To assess which action is the most ethically legitimate, we should identity which action produces the best consequences from an aggregate wellbeing perspective. Indeed, according to the lexical priority, consequentialist reasons should be taken into account only after assessing that deontological ones are respected.

Specifically, the rights of liberty and autonomy should be guaranteed by fair equality of opportunity and this essentially translates into some limitation on the excessive accumulation of wealth and the guarantee of equal educational and health opportunities for everybody. I also assume that treating people as mere means and not also as ends in itself (9), even though for overall community wellbeing, is ethically questionable: despite rights-based ethical theories are often in contrast the Kantian idea, that is human dignity is an unnegotiable concept which does not depend on subject's freedom, I believe that these two models are not necessarily in contrast. It is reasonable to affirm that a person has the right not to be used as a mere mean by others, although this action could lead to positive or non-negative consequences for her: the right not to be exploited makes people able to consider themselves free and equal from a moral perspective.

The aforementioned strategy adheres to Tom Beauchamp's and James Childress' proposal which provides a common ground where both moderate deontologists and teleologists could converge (10). In short, I will take into account not only the principles of liberty, autonomy and non-instrumentalization but also non-maleficence, beneficence, and justice.

Eugenics: a controversial concept

During the second half of the 19th century, after the diffusion of Darwinian evolutionary theory, some disturbing proposals were formulated: one of these is eugenics which received concrete political and scientific application during the 1870-1950 period. In this period, the eugenics movement, originating in the United Kingdom, collected such a large consensus as to involve scientists and political institutions from all over the world. The term "eugenics" was coined by Francis Galton who called it "the science of improving stock, which is by no means confined to questions of judicious mating, but which, especially in the case of man, takes cognisance of all influences that tend in however remote a degree to give to the more suitable races or strains of blood a better chance of prevailing speedily over the less suitable than they otherwise would have had"(11). In his book Hereditary Genius, Galton studied the phenomena of the distribution of talent and the biological hereditariness, and came to two conclusive considerations: a) the number of talented person within families with a good social, moral and intellectual status is significantly higher than in the overall population; b) talent is distributed according to the Gaussian curve and therefore is reasonable to affirm that both the number of talented people and the number of individuals with lower intelligence would decrease over time due through a regression toward the mean (12). According to the author, moral and social norms of solidarity and compassion undermine the driving force of evolution, that is natural selection. This process contributed to human degeneration and it was exacerbated by another aspect: the tendency of so-called "unfit" individuals to reproduce more and, as a result, to outweigh the number of "fit" ones. As a consequence, Galton proposed some measures in order to save the fit traits of human species from an inevitable degeneration: a) positive eugenics, which aimed to guarantee and promote the reproduction between individuals with moral, physical and intellectual qualities above average; b) negative eugenics, which sought to prevent the increase of unfit persons through sterilization, abortion and contraceptive methods. It is important to remember that these measures, according to Galton, were not supposed to be the object of State imposition but of the citizens' free choice: from this perspective, the eugenics project was intended as a sort of civil religion (13). However, after the success of the Galtonian thesis around the world, the eugenics movement raised significant interest in different national states which promoted eugenics policies in both positive and negative form. The content of such programs varied according to the different states; nevertheless, over time there has been a widespread ideological-political use of the eugenics implications aimed at generating consensus. This "populist turn" mixed the original Galtonian convictions with ideological beliefs such as racism, classism, and nationalism (14). It was no longer the scientific genius that had to be sought through the eugenic practices but the purity of the race or the preservation of the middle class: in fact, coercive policies were introduced, e.g., restrictions on immigration, the prohibition of mixed marriages, racial segregation, and mandatory sterilization. Albeit these measures were also introduced by states such as Sweden and the USA, the emblematic case of the application of eugenics principles was certainly Nazi Germany. In this context, in order to preserve the purity of the "Aryan Race", mandatory sterilization programs and physical elimination of the unfit people were implemented; furthermore, mixed marriages between "Aryans" and Jews or other minorities were banned and finally the systematic extermination of ethnic, religious, and homosexual minorities was carried out (15).

Ethics of Eugenics

Overall, eugenics is a controversial chapter of human history, especially with regard to the relationship between ethics and science. Regardless of the different applications, the whole eugenic movement was based on ideological premises and scientific mistakes. The ideological premises are the following:

a) racism, i.e., a common belief spread during the 19th century that was systematically theorized by Joseph Arthur de Gobineau (16). According to such a belief, more equipped and less endowed races may be identified;

b) classism, according to which the richest persons are carriers of superior phenotypic traits, which are the expressions of genes in an observable way ranging from behavior through morphology and intellectual capabilities. Conversely, lower class individuals carry unworthy traits. Class discrimination started to be practiced around the 18th century (17);

c) nationalism, or the political conception that gives centrality to being part of a nation because of shared biological characteristics like common blood or social ones such as culture, language, religion, politics, and belief in a shared singular history (18). During the 19th century nationalism became one of the most significant political and social forces in history due to the ethnic and national revolution in Europe (19).

The scientific mistakes involved in this project were:

a) nowadays, as a consequences of DNA screening, it has been assessed that there is only one human race: Homo sapiens, though within which there are significant variations in the possible somatic traits as adaption to different contexts. Therefore, the belief according to which that only individuals with certain somatic traits can reach certain intellectual levels is deprived of any scientific support (20-22);

b) the eugenists believed that the condition of human beings in life reflected their abilities and this could be used to assess the quality of their genes. That is, the fact that certain individuals showed certain "social diseases", including poverty, prostitution, drunkenness and criminality, demonstrated that they were unfit and justified the exclusion of their reproduction. Today, the relationship between genetic basis and behavioral traits are still not clear, although recent studies suggest that some phenotypic behavioral traits, such as propensity to practice extreme sports (23) or having higher level of intelligence (24) may have a genetic basis. However, it is known that the majority of phenotypic traits depend decisively on a series of environmental factors: hence, predisposition caused by genes does not necessarily imply the realization of certain behavior;

c) eugenics advocates believed that human genetic pool was in decline because of social inclusion projects which were against evolution's natural tendency to favor the "fit" individuals . Hence, they believed that humanity needed an active contrast of such projects. However, there is no scientific evidence showing the existence of a relationship of inverse proportionality between civilization and genetic wellbeing. This was a scientifically unfounded convictions dictated by an irrational fear;

d) Finally, the prescriptions of eugenists for genetic improvement could not have had a significant effect on society. Having no way of identifying carriers of recessive genes and a sufficient knowledge of the genetic heritage, it was not possible to identify fit and unfit individuals. In some cases, the eugenists admitted the poor effect of eugenics but they argued that these results justified the interventions.

Due to these considerations, it is easy to acknowledge that the eugenics movement is ethically problematic and objectionable. In this period there was a constant violation of human rights: firstly through objectification, denigration, segregation, secondly with involuntary sterilization and finally, in the extreme case of Nazi Germany, through mass extermination. The eugenics movement perpetrated racial and class prejudice and this makes the negative reputation of this phenomenon well deserved.

Bold Liberal Eugenics

According to some bioethicists, classical eugenics is certainly morally wrong, but not because of the initial pursuit of improving the genetic pool of human beings (25); eugenics applications were ethically problematic because, in many cases, they did not leave individuals the possibility of formulating free and autonomous choices. Indeed, the main controversial aspect of eugenics was not considering rights, preferences and wishes of the individuals involved. On the contrary, some forms of genetic selection and genetic treatments currently available, or that will be available in the future, are morally defensible even though they share common traits with the eugenics movement. From this perspective, the social and cultural context of western democracies promotes the autonomy of individuals who are guided in their choices by their own view of the good: for instance, a couple may wish to have a child without Tay-Sachs or sickle-cell anemia and at the same time desire for it a specific eye or hair color. These choices would not be imposed by a third party but would be the result of a parents' free choice.

Enhancing the offspring through of germline modification could be considered morally appropriate if and only if the parents' decisions are free from impositions of the State. Allowing parents to choose the eye color or to enhance mathematical intelligence of their progeny should be morally on a par with allowing parents to teach their children certain religious values or force them to learn to play the piano. Therefore, a genetic change or an environmental influence, such as education, would have the same moral weight if they led to the same ends and had the same degree of desirability. In line with these arguments, Robert Nozick, within his philosophical theory of "minimal state", proposed a "genetic supermarket" allowing parents to design their children: "this supermarket system has the great virtue that it involves no centralized decision fixing the future humane type(s)" (26).

Moderate Liberal Eugenics

However, the promotion of parental procreative autonomy does not always make eugenics free from controversy. The advocate of a milder view of liberal eugenics, Nicholas Agar, states that not every type of genetic reproductive treatment should be considered ethically appropriate (27). In fact, such interventions could compromise the child's right to an open future. In other words, suppose a deaf couple would like to have a deaf child and a new genetic technology that enables the modification of early embryos to make them affected by permanent deafness is available; the couple does not conceive deafness as a physical impairment but as a sort of cultural identity that would guarantee a life experience as rich as that of a non-deaf individual. Instead, according to Agar, deafness would compromise a considerable number of opportunity for the future individual's life plan; such a restriction to the freedom of offspring is quite controversial, thus genetic treatments for this purpose should be prohibited. In general, treatments considered ethically appropriate should be only those that do not exclude life plans based on conceptions of the good life radically opposed to the parents' view. This is recommended because some parents' wishes could convey the prejudices of a certain historical age: John Mackie in this regard states: "*If the Victorians had been able to use genetic engineering, they would have made us more pious and patriotic*"(28). Sticking to my previous example, since the deaf couple's son will not be able to totally distance him or herself from the situation imposed by the parents, a germline modification aimed at intentionally imposing a trait such as deafness is not ethically appropriate. On the other hand, the enhancement of intelligence or of other functions which grant the future individual an increase in the opportunities for the realization of her life plan, could be considered morally defensible.

Habermas and the self-understanding of human nature

Liberal Eugenics is strongly criticized by Jürgen Habermas in his book *The future of human nature*. According to Habermas, genetic engineering blurs the dividing line between the nature *we are* and the organic equipment *we give* to ourselves. He affirms that there is a difficulty in distinguishing between negative and positive genetics, i.e., between the elimination of diseases and the enhancement of human abilities; within this context, liberal eugenics advocates deny to individuate a clear boundary according to the notion of illness and they preferer renouncing any limitation, promoting individual choice and market rules. This perspective is concerning because genetic engineering interventions that overcome the boundaries of therapeutic aims may undermine our ethical self-understanding as members of the human species and affect the self-understanding of a genetically programmed person (29).

The whole point of Habermas's critique is that liberal eugenics would compromise individual autonomy and equality between generations. Any form of genetic enhancement would disturb the moral self-understanding of the new individual who would no longer be able to conceive herself as an autonomous person, namely, the author and the responsible subject of her own life. In fact, the genetically modified individual would no longer have the possibility to consider herself as the undivided author of the her own life's conduct. As a result, she would not even have the possibility of being considered responsible for it. She would share the responsibility for her conduct with a third person who changed her genetic pool before her birth: hence, the programmed person could not conceive the programmer's intention as a natural casual fact. This could generate a sort of alienation from herself (29).

Furthermore, human dignity, conceived as the symmetry of the relations between human beings in which they recognize themselves as equal, would be violated. According to Habermas, dignity is not a quality that humans possess by nature, such as intelligence or eye color; on the contrary, dignity exists only within a community of moral beings who give themselves laws to all the relationships they have (29). As a consequence, liberal eugenics would not compromise only the self-understanding and the moral agency of the programmed person; it would also give rise to an asymmetrical interpersonal relationship that would jeopardize the possibility for human beings to conceive themselves as equal. Under normal circumstances, the social difference between child and parent, over the generations, is continuously cancelled with the growth of children; instead, the genetic dependence of a modified child by her parents establishes a social relationship that compromises the normal reciprocity of subjects who are equal in their moral value.

It could be noted that, with regard to the ethical autonomy to lead one's own life, the situations of the modified and the unmodified person are not so different: both never have the freedom to choose their genetic heritage which is configured as a given. However, Habermas states that the genetic programming of certain physical and psychical qualities raises critical issues to the extent that it fixes the modified individual to a certain life plan which is chosen by parents. From this perspective, the liberal analogy between genetically modifying a child and shaping it through education is not consistent; in fact, in the latter case, the child-student can always take a critical distance from the socialization process, making herself free in a retroactively perspective. Contrarily, genetic manipulations cannot be corrected ex-post: so a "critical self-(re) appropriation" by the individual is not feasible and no revisionist learning process is allowed. In this context, genetic engineering would promote a sort of unacceptable instrumentalization of human beings: the individual would not be considered as an end in itself, in the sense that he would not be considered the author of a conduct of life-oriented by its own claims.

In conclusion, according to Habermas, any positive eugenics interventions, such as PGD (Preimplantation genetic diagnosis) for non-medical reasons and germline genome editing treatments aimed to enhance the future child's characteristics, should not be allowed. However, this does not mean that every genetic treatments should be forbidden; indeed, with regard to genetic treatments for undoubtedly serious and universally recognized diseases, on which we can assume an implicit consent of the future individuals, Habermas considers such interventions legitimate. Furthermore, pre-implantation diagnosis for hereditary diseases imposing extreme suffering could also be considered ethically appropriate.

A reply to Habermas

Habermas seems to support the thesis that there are conclusive moral reasons against genetic enhancement; hence any genetic enhancement treatments should be considered illegitimate. However, this approach raises some objections. According to Allen Buchanan, Habermas provides no explanation of why a person who develops from a modified embryo *should* conceive herself or *should be conceived* by others as less free than other persons (30). That would be true if and only if germline genome editing rendered that individual incapable of living autonomously. As long as the genetic design does not destroy the biological basis for the individual developing in a being with the capacity for autonomy, the individual can be the "author" of her own life. This does not exclude that modified individuals can *still consider themselves morally different* from the unmodified individuals, or be considered morally different from those who are not modified. However, this is an empirical psychological prediction, not an obvious truth, and Habermas provides no argument in this regard. In addition, some psychological studies seem to show that Habermas' predictions are empirically false (31, 32): these pieces of research suggest that there is no negative effect on the psychological development of a child born after PGD for non-medical reasons compared to a naturally conceived child. Moreover, according to Julian Savulescu, even in cases of sex selection, children seem not to show signs of negative effects (33).

Habermas' argument according to which the genetically modified individual would be fixed to a certain life plan (FLPA) is particularly effective in reference to the bold liberal eugenics perspective, i.e., the position maintaining that parents should be allowed to decide privately any genetic modifications on embryos of their progeny without any limitations. However, Habermas' critiques become less effective with respect to the moderate position, where parents would have the possibility to modify progeny, yet not in complete discretion. Although Habermas' arguments are efficacious to several and bold genetic modifications, it does not follow that others genetic enhancements on progeny are ethically questionable.

In addition, it should be pointed out that fixing the future individual to a certain life plan does not mean undermining her autonomy. The FLPA should be considered ethically relevant regardless of the validity or otherwise of the argument according to which genetic enhancement would compromise the autonomy of the future individual. FLPA is consistent with Buchanan's view according to which both a manipulated individual and an individual generated without genetic manipulation would have a genome that is given and not chosen: in this context, both individuals have the same biological basis to be autonomous. Regardless of this, the attempt made by parents to intentionally tie the future individual to a given life plan, should be considered ethically questionable. To clarify this point, let us hypothetically consider an embryo that is modified in order to become the new genius of classical music: the individual derived from this embryo is surely autonomous, free to make life choices as indeed was Beethoven whose genome was certainly not modified; however, by manipulating that embryo, parents have made the future individual more inclined to classical music, thus predisposing her to a certain life plan. We cannot deny that our physical and psychical features shape our choices and our life plans, albeit not univocally. In our example, the individual who is manipulated to become the new genius of classical music at some point in his existence could "feel" a kind of affinity with classical music; being gratified by this, she could approach the world of music. In fact, there is a reasonable likelihood that a person who has an attitude for some activities is gratified in practicing them. On the other hand, it is unlikely that a person who has no talent for some activities finds in them a life plan or a great passion: human beings tend to pursue more frequently the activities that best suit their aptitudes. Additionally, being aware of the genome modification of the child and wanting for the child a specific life plan as a classical musician, parents would encourage the child to undertake the study of classical music; this would, even more, push the individual towards a future chosen by parents. In short, the fact that the autonomy of the enhanced individual is not harmed does not enable parents to carry out genetic interventions in full discretion. By fixing the offspring to a specific life plan, parents would consider their future son as a mere mean and not as an end in herself. However, this argument is insufficient to advocate an unconditional rejection of every form of genetic enhancement. In fact, providing the offspring with a greater nonspecific intelligence, which does not fix the individual to a specific life plan, would not seem a form of instrumentalization. On the contrary, providing a specific predisposition to classical music should be considered ethically questionable.

Michael Sandel: Mastery and Gift

Another prominent argument against enhancement is proposed by Michael Sandel in *The Case Against Perfection*. According to Sandel the core problem with genetic enhancement is the drive to mastery: "*what the drive to mastery misses, and may even destroy, is an appreciation of the gifted character of human powers and achievements*" (34). Eugenics and genetic enhancement, in fact, represent an unilateral triumph of wills over natural gifts, of domination over reverence, of modeling over contemplation. The Promethean impulse of domination pushes the individual to redesign nature, losing the capacity to accept human life as a natural gift. The urge to program and cancel the contingencies through genetic engineering corrupts parenthood as a social practice governed by rules of unconditional love. From this perspective, the maternal and paternal affection should not depend on talents and traits that the child possesses but on "an openness to the unbidden", that is a quality of character that restrains the impulse to mastery and control over progeny (34). As William May points out, parental love has two aspects: accepting love and transforming love. Accepting love affirms the being of the child, whereas transforming love seeks the wellbeing of the child: each side of parental love corrects the excesses of the other (35). However, according to Sandel, the balance between the two forms of love is undermined by genetic engineering. Furthermore, eroding the consideration of the sense of giftedness, genetic enhancement treatments could lead to a change of key terms of our moral vocabulary, namely, humility, responsibility, and solidarity (34). Firstly, if people became accustomed to genetic enhancement, the social foundation of humility would be weakened: that is because only the awareness that talent and skill are not entirely dependent on human beings, but also depend in part on chance, can reduce their propensity to *hybris*. Secondly, genetic enhancement could imply an increase in parental responsibility: parents would be responsible for having chosen or not chosen the characteristics of their children and this would call for a moral overload. Such a scenario could lead to the misuse of genetic testing or to the stigmatization of non-enhanced or disabled individuals. Finally, genetic enhancements would make it more difficult to cultivate the moral sentiment of social solidarity. Conceiving talents as fruits of fate, the individual will be more inclined to share the results obtained with people who, without their fault, do not have the same talents. The awareness that no one is fully responsible for her own success saves the meritocratic society from the comfortable certainty that success is the reward of virtue and that the rich are rich because they are more deserving than the poor: no longer offset by chance, meritocracy would become more severe and less understanding. Thus, the absolute control of the genome, according to Sandel, would undermine the solidarity that arises when men and women reflect on the casual character of their talent and their lucks.

A reply to Sandel

It is reasonable to say that also Sandel fails to offer a satisfactory argument against all forms of genetic enhancement. Firstly, according to John Harris, the concept of giftedness in quite controversial: in fact, it is not clear why we have to recognize and accept the gifted nature of normalcy but not the gifted nature of disease (36). Sandel could answer to this critiques affirming that medical intervention to cure or prevent illness, or restore the injured to health does not undermine the concept of life as a gift because it does not desecrate nature but honors it (34); by contrast, genetic enhancements would be considered as a form of hubris of the designing parents, in their drive to master the mystery of birth. By using the aforementioned expression of "openness to the unbidden", Sandel thus maintains that this is good when it is part of a non-disfiguring relationship between parent and child. However, he does not provide any convincing reason to ground this statement but only rhetoric reasoning (36), since Sandel does not give any reasonable criteria to draw the ethical distinction between therapy and enhancement: Harris suggests that there is a continuum between treating dysfunction and enhancing function which invites us to consider the benevolent motives and life-enhancing outcomes of both. (37).

Secondly, even assuming the sense of giftedness as a central human good, parents might want to genetically enhance their future son without having an impulse to mastery. For example, an increasing lifespan enhancement would not hide any inclination to dominate others and the sense of giftedness would seem preserved. Furthermore, for a hypothetical future individual who is potentially able to live much longer, more than anyone else, there would still be plenty of things to sustain the sense of giftedness. In fact, with Buchanan we can say that enhanced people would still die of accidents; wars presumably would still occur even though many of us would not want them to; deadly pandemics presumably would still arise, despite our best efforts to avoid them; people would still fall in love with people who do not love them and fail in every effort to make themselves loveable (30). These considerations seem to suggest that humility, responsibility, and solidarity would not be incompatible with every forms of genetic enhancement. However, it's reasonable affirming that seeking boundless enhancement exhibiting an impulse of domination incompatible with good human life should be considered a negative idea. There is no doubt that, at a certain point, the desire for a perfect child could corrupt the parents' virtue to still be open to welcoming others. Nevertheless, it seems difficult to argue that this concern provides a decisive reason against any form of enhancement.

General considerations on enhancement

Bearing in mind the above considerations, we can affirm that Habermas' and Sandel's arguments fail to provide a conclusive reason for rejecting genetic enhancement altogether. However, at the same time, we can take the recommendation of these arguments to formulate a neither too permissive nor too restrictive approach on genetic enhancement. In fact, as I said, some of the fears expressed by these two prominent philosophers are reasonable and noteworthy. As a consequence, we should adopt a view that evaluates the pros and cons or the risks and benefits of various forms of genetic enhancement through a case by case analysis. This view does not assume any kind of consequentialist or utilitarian outlook. It states that it is appropriate to take all considerations into account, not only with respect to the consequences but also with regard to a deontological perspective. Such an approach is quite similar to what Buchanan calls "Balancing view"(30). In order to support this approach, we need to redirect the ethics of enhancement by abandoning the questionable framing assumptions regarding a distinction between historical improvements and genetic enhancement.

Enhancement is here defined as the set of techniques aimed at improving certain abilities and functions over the normal human range. Therefore, enhancing human beings means allowing them to do what normal beings are not able to do. In these terms, we should note that enhancement cannot be limited to the genetic context but is omnipresent in human history. In fact, literacy and numeracy are among the most important cognitive enhancements: for example, literacy increases our cognitive abilities, allows us to understand the past through reading written archives and increases not only the mnemonic capacity but also the ability to reflect on our experiences and to give them meaning (30). From this perspective, historical improvements, even if they cannot be conceived as "genetic", must also be intended as forms of enhancement of human beings. Hence, there is no reason to believe that genetic enhancements are morally more problematic than historical ones.

The problematic aspect of enhancement is not in the enhancement in itself but in the ways in which enhancement is achieved. Indeed, enhancement treatments could be imposed on individuals who do not desire to receive them and this would compromise their autonomy. Furthermore, some enhancements could lead to situations of social injustice, inequality and discrimination of non-enhanced individuals: as Daniel Wikler notes, both classical eugenics and liberal eugenics raise important questions of justice with reference to the possible distortions of equity caused by the advantage gained to individuals through some improvements (25). This is why enhancement, both in the historical sense and in the genetic (or biomedical) sense, must not be rejected in itself. A balanced view is appropriate to evaluate case by case the ethical appropriateness of the specific types of genetic enhancements.

In light of these considerations, we can say that genome editing for enhancing progeny is morally appropriate to the extent that these treatments respect the principle of non-maleficence and the principle of non-instrumentalization of future individuals, and the principle of justice so that it does not create or exacerbate social divisions or unjustified inequalities in society. Consequently, Liberal Eugenics, especially in the more extreme formulations, should be rejected: even though the liberal eugenics argument is appealing because it promotes procreative autonomy of parents and refuses a specific "genetic ideal" promoted by the State, some genetic enhancing treatments might undermine the principles mentioned above.

Back to the Slippery Slope

It is worth repeating the undesirability of a slip toward an eugenics scenario in its classical sense: the eugenics movement, during the 1870-1950 period, perpetrated repeated violations of human rights, promoting ideologies such as classism and racism and violating the dignity of the human being. Actually, the return to classical eugenics seems unlikely. More precisely, a scenario in which human rights are continually compromised by coercive actions and by racial and class discrimination seems improbable. After the Second World War, western states paid great attention to human rights. Due to the atrocities committed by Nazi Germany, the centrality of the dignity and respect of the individual was reiterated in the "Universal Declaration of Human Rights" of 1948 (38). Furthermore, the spread of democratic values in the West and western Europe has changed the relationship between society and the individual: nowadays, a coercive intervention of society on citizens' body is considered inadmissible and every medical intervention, not only experimental but also therapeutic, is bound by informed consent (39). In addition, the disability, homosexual and ethnic minorities' rights movements have made enormous progresses in promoting greater awareness of such rights among institutions and public opinion since the second half of the twentieth century (40). Hence, there is a reasonable likelihood that permitting germline genome editing would not compromise the principles mentioned above to such an extent that this scenario is again realized. The historical assumptions of classical eugenics cannot be found in the mainstream thinking of contemporary western society and for this reason it can reasonably be argued that a similar movement cannot recur.

Nevertheless, in some regions of the world, ideological prejudices such as racism, nationalism, and classism are still widespread and, in this context, the regulation of new practices that improve the gene pool of the unborn child will have to be carefully analyzed.

Although a return to classical eugenics would be considered not likely to happen, supporting the possibility of a slide towards liberal eugenics seems instead more plausible. Indeed, accepting germline genome editing would pave the way to a future scenario in which it would be conceived morally acceptable to "shape" and enhance future individuals based on the parents' personal choices and wishes. The socio-cultural context may suggest the possibility of a progressive social acceptance of the perspective described above: the principles of procreative autonomy and pluralism, which are the basis of the liberal view, are widely recognized within western contemporary societies. Although we conceive sex selection for non-medical reasons as a negative selection, this practice is widely accepted from a moral standpoint by people in the countries where it is legally allowed; acceptance of other forms of genetic enhancement could, therefore, occur easily as soon as the technology reaches a sufficient level of progress. Furthermore, Sandel notes that contemporary American society already embodies some tendency to the exploitation of children who are subject to the wishes of their parents: the latter often demand too much effort from their offspring in sports and the school context (34). In line with Sandel's statement, Natalie Colaneri and colleagues observe that the diagnosis of attention disorders has increased dramatically over the last 20 years. According to the authors, this may be ascribed to an ambiguity of the diagnosis due to an unclear distinction between therapy and enhancement and, above all, high parental expectations of their children and the parents' way of conceiving of their style of parenting (41, 42). Due to the practical possibility of adhering to unlimited genetic enhancements, there is a plausible likelihood that they will be accepted inaugurating "a genetic supermarket" aimed at achieving the most disparate wishes of parents. Hence, the uncritical acceptance of germline modification would lead to the actual risk of a gradual acceptance of practices that could compromise the principles of justice, non-instrumentalization, and non-maleficence towards offspring. Nevertheless, I believe that there is a strategy for admitting germline genome editing treatments in order to enjoy the unquestionable advantages of this practice, without necessarily sliding towards an undesirable perspective.

Avoiding slippery slope argument: a proposal

The strategy here proposed stands in stark contrast to the libertarian perspective according to which genome editing, both in therapeutic and enhancing applications, should be regulated by purely market dynamics. However, it also rejects models that would allow only therapeutic interventions and prohibit all forms of enhancement.

I support a strategy that consists in admitting, as well as therapeutic interventions, some parental requests to genetically enhance their progeny. In order to be considered legitimate, genetic enhancement treatments should respect the following criteria: a) they must not conflict with the interests and well-being of the future individual (principle of non-maleficence); b) they must not violate the principle of non-instrumentalization of offspring (principle of non-instrumentalization); c) they must not generate unjustified inequalities or undermine access to any social positions for other non-enhanced individuals (principle of justice).

However, it could be reasonably objected here that in this way the SSA in its empirical version is not avoided at all. Allowing, at first, certain enhancements could lead to a scenario in which many other enhancements would eventually be allowed, thus ending up in accepting the perspective of liberal eugenics. This strategy would not provide any conceptual distinction and effective methods to avoid the possibility of a psycho-social acceptance of an undesirable scenario. To guarantee the purposes of the strategy, and at the same time avoid to slipping "down to the slope", it is appropriate to set up an *advisory and authorization body*: its main purpose would be to assess which enhancements are legitimate and which are to be considered inappropriate, through a case-by-case analysis.

With the aim of developing this proposal more comprehensively, I briefly recall the case of the Human Fertilization and Embryology Authority (HFE Authority). The latter is a public body of the United Kingdom Department of Health which regulates *in vitro* fertilization practices, artificial insemination, gamete and embryo cryo-conservation, and human embryo research. This body includes not only doctors, researchers, scientists but also economists, jurists, bioethicists, religious authorities, and individuals who report personal experiences in the area of assisted reproduction. Established in 1990, the HFE Authority has the task of supervising and regulating medical treatments associated with technological developments in this field (43). Therefore, it is not a matter of entrusting to a body only the implementation and monitoring of the legislative requirements; HFEA has the power to regulate in good part the medical treatments associated with technological developments in the sector (44). The institution of such authority not only makes laws (and ethical and social considerations) suitable for a field of medicine subject to rapid changes but also allows a case-by-case approach to evaluate the interests at stake (45). Parents make requests to the HFE Authority; the requests are analyzed by a committee which can provide or deny authorization to the requested practice. In the context of genetic interventions, I support an authorization model that is in contrast to the laissez-faire regime that characterizes liberal eugenics, which subordinates all interests to the principle of parental procreative autonomy. An example of HFE Authority work is the case of Nicole Maserton's parents, a 3-year-old girl who died in an accident. Shortly after her death, parents contacted the HFE Authority to be allowed to use PGD in order to select a female embryo. Already having four male sons, they wanted to "rebuild the female dimension" of the family. In this case, the HFE Authority did not authorize the request, because it did not consider the practice of sexual selection acceptable for purposes other than that of avoiding genetic disorders (46).

The HFE Authority experience is significant to face the issue of genetic treatments and enhancements of progeny. From this perspective, the authorizing body should examine the parents' requests for enhancing children and evaluate their compliance with the principles of non-maleficence, non-instrumentalization, and justice. Moreover, the possible social consequences resulting from the authorization body's decisions should be considered. The authorization body should also provide support and consultancy service (47) to couples intending to enhance their future children: in this way, it would promote the parents' autonomy to decide in a fully informed way but also consider and guarantee the interest of future individuals and society. Additionally, such a committee should guarantee equity among society avoiding social division and unjustified inequality.

Conclusions

It has been argued that the SSA, in its empirical formulation, cannot always be rejected. Indeed, convincing arguments exist in order to show that admitting certain genetic manipulation practices may lead to the acceptance of inappropriate interventions. However, it is wrong to deduce that the general prohibition of germline genome editing is the only way forward. In my opinion, the strategy proposed offers a reasonable embankment to the slide towards liberal eugenics. The Authorization model appears convincing because it would allow greater procreative autonomy and would promote a reasonable control in the field of human genetic enhancement, which inevitably harbors significant risks. While a general prohibition appears unjustified, an excessive form of laissez-faire could lead to the progressive acceptance of a scenario in which the principles of justice, non-maleficence and non-instrumentalization would be continually violated, making genetic interventions ethically unacceptable and not desirable. In light of this, the establishment of a body composed by experts who assess the ethical and social appropriateness of the individual enhancement cases is a strategy that deserves to be taken into account in new genome-editing techniques' debate.

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Voices from the past defending Criminal Anthropology

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Abstract. From the second half of the nineteenth century the anthropometric identification system has been used to analize not only the crime itself but also to investigate and to construct anthropological criminal categorization.

Key words: criminal anthropology, skull of criminals, anthropometry

Criminal anthropology from the second half of the nineteenth century took the first steps towards the analysis of the criminal, reserving him the highest attention. The focus to analyze not only the crime itself but also to investigate the kind of criminal, because the penalty should not be perceived as a means to fight crime but a means of defense against the real enemy, the criminal (1).

In the chronicles of this period, as in all periods, even in the current one, an increase in criminality and in particular in recidivism was recorded. Not only the growth of the army of criminals was considered a threat to civil society but also the increase of resistance of the individual criminal.

For the followers of Criminal Anthropology, it was therefore necessary to proceed with the identification of the criminal. From the anthropological point of view, morphological analysis of the physical anomalies could diagnose a particular psychiatric disorder especially if related to a criminal tendency (2). Among those who defended a rigorous scientific method at the service of identifying the criminal type was Raffaele de Notaristefani (Naples, 20th October 1861 - Rome, 13th December 1933), an Italian magistrate and deputy prosecutor of the King (3).

The author pronounced that already in his time there were sure, infallible, even if at the same time experimental, means to establish the identification of an individual with the one who had a conviction. With sure means, he referred to the anthropological measures. The author claimed, like so many others, that it was necessary to become familiar with these tools in order to create a public conscience.

Anthropometric measures had to fit within scientific investigations and legislative provisions.

Many scholars of the time were not open to news. Others, on the other hand, confused the anthropological measures aimed to identify the criminal with those anthropometric and physiognomic signs that Lombroso and his followers believed to be characteristic of the criminal. Others, ~~as~~ Luigi Lucchini and Enrico Ferri, wanted to introduce the application of Bertillonage in Italy.

The system planned by Alfonso Bertillon, presented at the Rome Penitentiary Congress, had been applied with great success in Paris since the year 1883. This system obtained very successful results that the American doctor Paolo Riccardo Brown enthusiastically exclaimed:

"Quételet and Bertillon are among the greatest benefactors of the human race and the jurists and criminologists of future centuries will be amazed when they read about the […] ignorance of those nations, which do not immediately adopt this wonderful anthropometric identification system. As recorded by Notaristefani, the Bertillonage system was based on the same way in which naturalists of the time classified the animal and plant kingdoms, or rather in identifying the characteristic elements of the specimen, considering that, in humans, bones which belonged to adult individuals, represent the maximum immutability among the anatomical districts.

Furthermore, Bertillon affirmed that within 100,000 individuals only 10 might have the necessary similarity in the proportions of the principal measurements of their body […].”

It is clear that anthropometry had to take this into consideration for the identification and recognition of criminals.

Brown also quotes Quételet, the Belgian scholar who also participated in the creation of a work on anthropometry. While trying to perfect the morphological-anthropological and anthropometric investigative method, several objections were raised by a faction of the scientific community, in a specific psychiatric way of that time.

In particular, in the Experimental Journal of Phreniatry and Legal Medicine of 1901, we found an interesting contribution by Professor Angelo Zuccarelli who defended Criminal Anthropology from several critics exposed by a part of psychiatry (4, 5). In particular, he reported that for Criminal Anthropology, through the discovery of degenerative features during the autopsies of criminals it was possible to counter the objections addressed to the discipline, but these degenerative features were also found in many socially normal individuals (6,7). The author also reported the work of Dr. Motti on the diagnoses (8) of the skulls of criminals, which clearly showed the degenerative evidence expressed by Criminal Anthropology. In particular, the presence of the internal occipital or wormian dimple, enormous thickness of the cranial dimples and complete intraparietal parietal bones, were the features that better represented the criminal type.

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A light in the dark: the history and ethics of a therapeutic relationship

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Abstract. The therapeutic relationship is like a tailor-made dress: specific for the individual patient. Its objective is the well-being of the patient and the overcoming of his difficulties; in some cases the goal is to teach the patient to take care of himself. The therapeutic relationship can also have a positive value for the therapist, in the context of a reciprocity, which learns from the patient some teachings that he gives himself to the patient. In the therapeutic relationship there can be some issues linked to new and unexpected difficulties and which can be overcome with a careful examination of one's defense mechanisms.

Key words: patient doctor relationship, therapeutic relationship

After years of good health, a patient of mine, a blind lady, contacted me to tell me that she had been diagnosed with breast cancer. This was painful news. My first reaction was one of anger: this woman had already been unlucky in life, she had been born blind and now she had to face a cancer; I felt this new turn of events was utterly unfair, as she had already been given her share of suffering. However, there was something else in my being upset that I could not put a finger on, I felt a certain discomfort. It was a thought that stuck in my mind.

I thought back on the past therapy with her. She had come to me at a very low time in her life, as she was searching for personal autonomy despite her disability. We had embarked on a path together. We had succeeded in overcoming her fears, the ghosts of the past that stumbled around in the darkness of her life and blocked her more than the non-perception of light. I had managed to convince her to take classes to learn to walk unaided, manage household chores, use gestures in conversations.

Then we progressed even further. Together we had steadily raised the bar of her goals: learning to travel alone, going to concerts, visiting museums, listening to books. The therapy for her 'low' times was personalised (1), I started with the question 'what would please you when you feel sad?' at which she would reply for example: 'I'd like to feel something soft because life is rough.' So, the therapy would be to feel and stroke a silk or cashmere fabric, or wear perfume to bed, listen to soothing music before going to bed, listen to a good book.

She cast off the grey smock she had worn over her many years in a boarding school and a residential institution, and began to choose clothes, shoes, accessories, displaying a keen and surprising good taste and, most importantly, feeling happy. She learnt to listen to her needs and to strive to achieve her wishes, she learnt to trust herself and others, while standing up for herself.

Over time, we smiled at many things together, with the help of her self-irony, and she would say to me: 'Professor, we must admit I'm blind and it's a constant struggle ... but I'm happy to fight for myself, in order to feel well'. She realised that her therapy was to take care of herself. So we progressed from the search for autonomy to working on achieving a good quality of life, while maintaining awareness of diversity and managing her disability.

Over time I realised that there was a lot of reciprocity in her therapy. Her therapy was good for me, too. I encouraged her, explained to her the dynamics underlying her limits and together we found the strategies to overcome them; she responded with courage, enthusiasm, determination, and in so doing she also stimulated and encouraged me, in my personal and professional life. I remember that in those days I often dreamt that I was swimming against the current, and yet I did not feel tired, I wanted to continue. The outcome of her therapy was successful… for both of us. We found light in the dark.

And now what? Would we go back to square one? Not really. We would not have to redo what we had already done; we would have to do something different, walk a new path: I would have to stand by her in her suffering, in her pain, and accompany her to the end of her days. No more perfumes, silk, cashmere, music, books, but pain, nausea, vomiting, hair falling out, the body changing as it slowly fades away. I finally understood that the unclear thought in my head was a strong temptation to avoid this new commitment: the confrontation with the suffering and death of a patient, which confronts me with the limits of our existence. I wondered for a while whether I would be up to this task or I should entrust it to the dedicated cancer care team. But then I realised that mine was a rationalisation to avoid getting fully involved and facing with her the crucial challenge, that of life in a new, different, disturbing darkness.

And so here we are, together, dealing with a wobbly healthcare system, as I help her to book tests, chase the surgeon, choose the type of surgery and then …. we'll take things as they come. As Hoffman (2) wrote, I will listen to the sound of her silence, because silence is also comforting and therapeutic. And perhaps we will once again see the light together in the dark.

References

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