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SANTORIO SANTORIO (1561–1636) – THE PIONEER OF MODERN CLINICAL SCIENCE

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ABSTRACT

The career of Santorio Santorio (1561–1636) marked the beginning of modern medicine. Born in Capodistria, a territory of the Venetian Republic (now called Koper, a town on the coast of Slovenia), Santorio was not only a student, physician, and a professor of theoretical medicine at the University of Padua, but he also introduced measurements and mathematics into human experimentation. By means of a weigh scale, he conducted studies on more than ten thousand people (including Galileo Galilei) over a 30 year period. It was his habit to measure his daily body weight, along with the quantity of ingested food and drink, as well as the quantity of bodily discharge (urine and feces) so that he was able to calculate the amount of insensible perspiration which he then used as a dual indicator to characterize health and disease and to cure patients after knowing their physical parameters including their pulse and body temperatures.

His main work was De Statica Medicina, a well received book which had more than 40 editions during the 17th and 18th centuries and which was translated into English, Italian, French and German. It was a slight volume, but it was praised by Boerhaave, von Haller and Lavoisier. It was this praise and recognition which granted to Santorio the definition of Galilean, by many historians of medicine including Salvatore De Renzi, Castiglioni, Pucinotti and Pazzini.

Santorio embodied the modern physician-scientist. He used a vast number of people as the subjects of his experimental work and immediately transformed discoveries and new technologies into medical devices using the data originating in basic science. It

is the case that the information reported in his book was quickly put to use to help patients. He also introduced self-experimentation in medicine, an important issue even nowadays. Although he was aware that the university took credit for his work, he respected the institution from which he obtained a salary for life even when he stopped the teaching there. He demonstrated his modernity: he was a pioneer in granting money for yearly scholarships to the University of Padua through his last will and testament.

Keywords: Santorio Santorio, insensible perspiration, weighing machine, thermometer, pulsilogium, hygrometer, self-experimentation, last will and testament, University of Padua

SANTORIO SANTORIO (1561–1636) – OČE SODOBNE MEDICINSKE ZNANOSTI

IZVLEČEK

Poklicna pot Santoria Santioria (1561–1636) je zaznamovala začetek sodobne medicine. Rojen v Kopru (Capodistria, kot se je že tedaj imenovalo mesto na področju Beneške republike), Santorio ni bil le študent, zdravnik in profesor teoretične medicine na Univerzi v Padovi, temveč predvsem znanstvenik, zaslužen za uvedbo meritev in uporabo matematike pri eksperimentiranju na ljudeh. S pomočjo tehtnice je v tridesetletnem obdobju opravil raziskave na več kot deset tisoč ljudeh (med temi Galileo Galilei). Na podlagi dnevnega merjenja lastne telesne mase, količine zaužite hrane in pijače, pa tudi telesnih izločkov (urina in blata) je Santorio ugotavljal raven t. i. »nezaznavne perspiracije«, ki mu je služila kot indikator za opredeljevanje bolezenskih stanj in za zdravljenje pacientov, ko je zanje pridobil podatke o osnovnih telesnih parametrih, vključno s frekvenco srčnega utripa in telesno temperaturo. Izsledke svojih raziskav je objavil v knjigi De Statica Medicina (O medicinskem merjenju, 1614), ki predstavlja prvi sistematični študiji temeljev metabolizma. Delo je imelo v 17. in 18. stoletju več kot 40 izdaj in je bilo prevedeno v angleški, italijanski, francoski in nemški jezik. Čeprav knjiga ni bila najbolj obsežna, je požela pohvale s strani Boerhaaveja, von Hallerja in Lavoisierja. Zaradi številnih priznanj za življenjsko delo so Santoriu mnogi zgodovinarji s področja medicine (Salvatore De Renzi, Castiglioni, Pucinotti in Pazzini) podelili naziv »Galilejevec«. Santorio pooseblja modernega zdravnika – znanstvenika. V svoje eksperimentalno delo je kot merjence vključil veliko število ljudi, svoja spoznanja in nove tehnologije pa neposredno uporabil za izdelavo medicinskega inštrumentarija. Delo Santoria je imelo veliko aplikativno vrednost, saj so se podatki, o katerih je poročal v svoji knjigi, s pridom uporabljali pri zdravljenju in pomoči bolnikom. Prav tako je v raziskovanje uvedel samoeksperimentiranje, kar ostaja še danes aktualna tema v medicinski znanosti. Čeprav se je zavedal, da mu univerza veliko dolguje za opravljeno delo, je vedno kazal veliko spoštovanje do institucije, od katere je prejemal dohodek, tudi potem, ko je prenehal s poučevanjem.

Svojo izredno modernost je izkazal tudi s tem, da je na podlagi svoje poslednje volje in oporoke zagotovil denarna sredstva v obliki štipendij perspektivnim študentom na Univerzi v Padovi.

Ključne besede: Santorio Santorio, nezaznavna perspiracija, tehtnica, termometer, pulsilogium, vlagomer, samoeksperimentiranje, oporoka, Univerza v Padovi

SANTORIO SANTORIO – A TIMELINE

Santorio Santorio (1561–1636), the founder of modern clinical science, was a talented fellow and a charismatic professor of theoretical medicine in Padua, which in those days was the most renowned university in Europe (Table 1). Students from abroad came to Padua where they were organized in national groups. Students were attracted by the level of tolerance shown by the local Catholic Church, and who considered Padua an area deeply linked to the professionalism and charisma of the professors. Copernicus and Harvey are just two examples of the excellent physicians who received training in Padua.

Although Cosmacini (1987) may be right in defining the period between 1550 and 1650 as a time of crisis, it should be noticed that the ideas of Leonardo, who had been a solitary scientist in life, had only just begun to fertilize scientific thought. In addition, Copernicus published *De Revolutionibus Orbis Coelestium* in 1543, just before his death, and in 1545 the University of Padua, in parallel with the University of Pisa, planted the first herb garden (*giardino dei semplici*) where the famous Professor Anguillara cultivated some two thousand medicinal plants. Pisa and Padua were soon followed by Bologna in 1568, the same year in which Ulisse Altrovandi established a garden of simplex in the *Alma mater Studiorum*.

It is likely that there was no dramatic shortage of creative ideas at that time and that the only pressing problem was the plague which caused the deaths of twenty per cent of the inhabitants of Italy in the year 1630, numbers which also include the Republic of Venice.

Table 1. Timeline of Santorio Santorio (1561–1636).

1561	Birth of Santorio Santorio (March 31) and of Francis Bacon. Falloppia authored *Observationes Anatomicae*
1562	Eustachius discovers galactophorus ducts in the horse
1563	Death of Falloppio, Professor of Botany, Anatomy and Surgery at the University of Padua
1564	Birth of Galileo Galilei, death of Vesalius, Paracelsus and of William Shakespeare
1565	Death of Conrad Gessner, the German Pliny, Father of Zoology, author of *Historia Animalium*
1566	Death of Leonardo Fuchs

1567	Death at Louvain of Thomas Fyens, one of the strongest opponents of Copernicus
1568	Death of Amatus Lusitanus, the first to report on purpura, Ulisse Altrovandi founded the Botanical garden at the University of Bologna
1569	Death of Nicolò Massa, Professor of Anatomy in Venice
1570	Pope Pius V excommunicated Queen Elizabeth I
1571	Battle of Lepanto, Birth of Kepler
1572	Pope Gregory XIII, Night of Saint Bartholomew
1573	Cyprus from Venice to Ottoman Empire
1574	Death of Batholomaeus Eustachius, Foundation of the University of Leyden
1575	Santorio Santorio entered the University of Padua, Ambroise Paré *Opera Omnia*
1576	Foundation of the University of Helmsted
1577	Birth of Jan Baptista van Helmont, Death of Realdo Colombo
1578	Foundation of the University of Altorf
1579	Birth of William Harvey
1580	Death of Marco Aurelio Severino and Gianfilippo Ingrassia
1581	Galileo Galilei registered at the University of Pisa on September 7 being no. 1471 in the rolls
1582	Santorio Santorio received his medical degree
1583	Andrea Cesalpino published *De Plantis,* Gerolamo Mercuriale *De morbid puerorum*
1584	Birth of Paolo Zacchia
1585	Jacques Guillemeau published the *Hereaux Accouchement des Femmes*
1586	Marcello Donati, *De Medica Historia Mirabilia*
1587	Death of Christobal Acosta, famous navy surgeon
1588	Giovambattista della Porta publishes *Magia Naturalis* making reference to lenses; death of Bernardino Telesio, the first strong opponent of Aristotle
1589	Birth of Johann George Wirsüng
1590	Death of Ambroise Paré
1591	Prosper Alpinus, *De Medicina Aegyptiorum*, Venice
1592	Galileo Galililei Professor of Mathematics at the University of Padua. Giovanni Mocenigo denounced Giordano Bruno to the Tribunal of the Inquisition in Venice
1593	The Senate of Venice with 142 votes for and 30 against, transfers Giordano Bruno to the Roman Inquisition.
1594	Fabrizio of Acquapendente completes the *Amphitheater*
1595	Scipione Mercurio published the *Comare* (Midwife)
1596	Birth of René Descartes
1597	Gaspare Tagliacozzi, *De curtorum chirurgia per insitionem*
1598	William Harvey registered at the University of Padua
1599	Death of Realdo Colombo of Cremona who discovered pulmonary circulation
1600	Vatican sentenced Giordano Bruno to death.

1601	Athanasius Kircher, German Jesuit, inventor (magic lantern), was born
1602	Santorio Santorio, *Methodus Vitandorum Errorum Omnium Qui in Arte Medica Contigunt*
1603	Foundation of the Academy of Linx-eyed in Rome
1604	Basilius Valentinus, Leipzig, *The Triumphal Chariot of Antimony*
1605	Ippolito degli Obizzi published *De Nobilitate Medici Contra Illius Obtrectatores*.
1606	Death of Girolamo Mercuriale
1607	Foundation of the University of Giessen
1608	Galilei discovers Jupiter's planets; Birth in Naples of Giovanni Alfonso Borelli
1609	Galileo informed by a letter written by his brother in law of the construction of a spy-glass based on a report from Flanders
1610	Galileo Galilei in Venice, *Sidereus Nuncius*
1611	On October 6 Santorio Santorio made a Professor at Padua to cover the first chair of theoretical medicine
1612	Santorio Santorio, *Commentaria in Artem Medicinalem Galeni*
1613	Death of Paolo Sarpi
1614	Santorio Santorio, *De Statica Medicina*
1615	A copy of *De Statica Medicina* sent from Santorio to Galilei with a letter dated February 9
1616	Santorio elected president of the Collegio Veneto which conferred degree of laureate
1617	Fabbrizio d'Acquapendente published *Opera Chirugica*
1618	Harvey nominated physician In extra ordinary to James I
1619	Death of Fabrizio d'Acquapendente
1620	Théophile Bonet born
1621	Bartolomeus Eustachius, *De Formatione Ovi et Pulli*
1622	Thomas Willis born; Tommaso Campanella published *Apologia pro Galileo* at Frankfurt
1623	Galileo Galileo, *Saggiatore*
1624	Birth of Thomas Sydenham
1625	Santorio Santorio, *Commentaria in Prima fen Primi Libri Canonis Avicennae*
1626	Birth of Robert Boyle and Francesco Redi; death of Francis Bacon
1627	Cardinal Richelieu began the siege of La Rochelle
1628	Harvey published *De Motu Cordis*
1629	Santorio Santorio published the *Commentaria in Primam Sectionem Aphorismorum Hippocratis* and *De Remediorum Inventione*
1630	Death of Kepler; plague in Venice
1631	Birth of Richard Lower
1632	Trial and sentencing of Galilei
1633	Birth of Bernardino Ramazzini

1634	Birth of Denis Dodart, French botanist, member of the Académie of Sciences at Paris and physician to Louis XIV, author (1725) of *De Medicina Statica Galllica*
1635	Foundation of the Academy of France
1636	Death of Santorio Santorio due to a urinary disease on February 26

The time of the academies

The time of Santorio was the time of the birth and initial flourishing of the academies which were instrumental in promoting innovation in philosophy and science. This was a goal missed by universities because of their difficulties in breaking the links with the past. The following are just a few examples. In 1511 in Cosenza, Southern Italy, Aulo Giano Parrasio founded the *Accademia Cosentina*, the first Italian Academy which was subsequently reshaped by the philosopher of nature Bernardino Telesio, a laureate in philosophy and mathematics at Padua in 1635, the year Cardinal Richelieu founded the *Académie Française*.

Before Santorio's birth, Giovambattista della Porta founded the *Academia Secretorum Naturae* in Naples between 1550 and 1560, whereas the *Accademia Olimpica* was founded in Vicenza in 1555. In his palace in Rome in 1603, Duke Federico Cesi founded the *Acccademia dei Lincei*. In 1652 at Erfurt, the *Academia Leopoldina* was founded (*Sacri Romani Imperii Academia Caesarea Leopoldino-Carolina Naturae Curiosorum*). In 1657 Giovanni Alfonso Borelli, in association with Torricelli, founded the *Accademia del Cimento*. The motto of the latter was *provando e riprovando*, which translates to "experiencing and experiencing again". Finally, in 1662, the Royal Society in London joined the golden list of the academies and three years later began the publication of the *Philosophical Transactions*.

The time of the great trials

It was also the time of the great trials started by the tribunals of the Inquisition. Among them were those trials against Giovambattista della Porta, Galileo Galilei, Giordano Bruno, and Tommaso Campanella. The trial against Galileo Galilei confirmed that the University of Padua was a bonded area, and the same happened with Naples in 1224 at the time of Frederick II of Hohenstaufen. Thus political freedom was granted to students in Padua, however the Republic of Venice carefully examined the report of Giovanni Mocenigo before the local Tribunal of the Inquisition against Giordano Bruno and the Senate of the Republic in 1693, with a vote of 142 yes and 30 no, decided to put the philosopher into the severe hands of the Roman Inquisition.

Santorio in the Morosini's drawing room

Santorio was certainly fortunate to be part of the group of people who commonly met in the drawing room of the Morosini Palace in Venice. It was a place which was

familiar to him since during his early studies, he had shared tutors with Paolo and Andrea Morosini. There it was common to encounter individuals of various cultural origins. This list of distinguished individuals included Fra Paolo Sarpi, a mathematician, anatomist and advisor to the Republic of Venice who was a constant presence at Morosini Palace, as well as the aforementioned Giovambattista della Porta, a friend of Paolo Sarpi, and a Neapolitan scientist of great reputation in the field of optics. There he also met Galileo Galilei, who was a professor at the University of Padua. It is certain that Santorio also met Gio-Francesco Sagredo, a friend of Galilei, who was also a frequent attendee, as was the great physician and professor of the Padua Studium, Gerolamo Frabrizi d'Acquapendente, who mastered anatomy and surgery. The friendly atmosphere of the Morosini home provided a more than adequate environment for cultural exchange, thus it is not surprising that the inter-disciplinary debate met the conditions necessary to generate new ideas, to pass from the usual to the innovation.

When Santorio Santorio received the title of Professor of Theoretical Medicine (1611), Galilei had published the *Sidereus Nuncius*, Copernicus had broadened the sky and with his heliocentric theory, he took a swipe at the centrality of the earth in the heavens (*De Revolutionibus Orbium Coelestium*, 1543). As well, Friedrich Johannes Kepler had published *Astronomia Nova.*

It was a great time for science. Its spirit can be felt by reading the words of the great Italian poet, Giacomo Leopardi, who in *Le Operette Morali,* commented Copernicus achievements. *"It will not simply consist of a physical change, as it might be argued. It will fall not only on physics, it will induce changes in the ranking dignity of things and in the order of the entities. It will affect even the goals of people and this will cause great changes in metaphysics which deals with speculative part of the knowledge. As a result men will be able to discuss correctly, they will be and will behave at variance with the men they had previously been, or presumed to have been theretofore"*. The *zeitgeist* caught by Leopardi really corresponds to the changes occurring after Galileo Galilei. As pointed out by Mario Gliozzi (1962) *"the change in mentality caught by Leopardi attains perfectly to the direction of physics after Galileo Galilei. The opponents were forced to answer to observations with other observations, to experiments with other experiments, to mathematical demonstrations with other mathematical demonstrations. They were forced to ask questions no longer on Aristotle's book, even the Peripatetic of that time contributed to reject the principle of authority, thus facilitating the work of Galilei's disciples"*.

At this time it should be pointed out that Santorio was nominated Professor of Medicine at Padua because of his talent and professionalism and was therefore given a good salary, exceeding that which Galilei had received the year before (eight hundred ducats against five hundred and thirty). Santorio was a man aware of his talent, and he was also aware that being a professor at the University of Padua was not the reason for his success. He was highly sought after for consultations simply because he was the best. However the university which indeed greatly valued his talent and nearly doubled his salary at the time of his second contract. It is not insignificant that when Paolo Sarpi underwent an assassination attempt through a dagger blow of the Roman

Curia (*Stilo Romanae Curiae*), he asked for and received assistance from both Fabrizio d'Acquapendente and Santorio Santorio.

The advent of a science based on measurements and numbers

In the *Ecclesiastes* we learn that everything is based on numbers and weights *Omnia in numero et pondere*. It was a concept finally taken into account in science during the seventeenth century. It was during that time that the study of anatomy aimed at understanding organ function, thus leading to a radical revision of Galen's physiological doctrine. Biological data were extensively analyzed in order to answer physiological questions. Scientists were no longer happy with the disclosures on organs anatomy and structure. They began to be interested in the work of the various organs. The first step was the transition from descriptive anatomy to functional anatomy. This had occurred mainly after Galilei had introduced the concept of the book of nature written in mathematical terms (*Il Saggiatore*), that is a science based on measurements of natural phenomena.

De Statica Medicina

In 1614, Santorio published *De Statica Medicina*, a slim volume printed by Niccolò Polo (Table 2). The second edition in 1615 was printed by Marcus Antonius Brogiollum. It was written in the form of aphorisms a long-lasting series of experiments. Santorio had built a weigh scale. As reported by Guthrie (1945) "*in the weighing machine Santorio literally passed a great part of his life. Seated in this weigh scale, eating and even sleeping in it*", Santorio took precise notes of his body weight, the weight of his foods and drink, weights of urine and feces. This allowed him to calculate insensible perspiration, a factor used to investigate health and disease. Santorio Santorio provided a new insight into an old problem, as he wrote in the preface:

"It is a new unprecedented event in medicine, to be capable of measuring insensible perspiration with accuracy. No philosopher, no physician did dare to investigate this peculiar aspect of the medical doctrine. I made the first attempt. I can anticipate that there will be many opponents against this new art and they will try to discredit it."

Table 2. Structure of De Statica medicina.

Section	*Topic*	*Aphorisms (no.)*
1.	On weighing and insensible perspiration	140
2.	On air and waters	61
3.	On food and drink	105
4.	On sleep and waking	70
5.	On exercise and rest	36
6.	On sex	42
7.	On affections of the soul	48

His investigations on the role of diet were analytical and took into consideration many confounding factors including sleep, waking hours, physical exercise, sexual activity, age, state of health, diseases, locations, atmospheric conditions, temperature and humidity. He also made use of his newly developed thermometers and hygrometer. According to Salvatore De Renzi (1846, 1848), Professor of Medicine and Historian at the University of Naples, no one studied perspiration with the same exactness, however, it is the case that to some extent Santorio's studies were detrimental to practical medicine due to the rushed use of deductions converted into results made by his followers and plagiars. Santorio demonstrated by means of such experiments that perspiration is absolutely essential to the living human machine and exceeds all other body evacuations. According to him, a ratio of 8 pounds of foods and drink to 3 of perspiration was an indicator of a healthy status, thus perspiration was factor used to determine health and used as an indicator for both the state of health and the presence of disease. Disease originated either due to reduced perspiration or due to reduced sensible losses. Thus diuretics, cathartics and diaphoretics came of age. The weigh scale became the instrument capable to disclose diseases as well as to prevent them. In patients with a moderate intake of food and drink, without reduction of sensible losses, an increase in body weight indicated the presence of disease due to reduced perspiration.

"Such things and many more were put into mathematical forms by Santorio Santorio, which greatly influenced contemporary physicians who were lit by a new light which could not be derived from the old precepts of Galen" (De Renzi, 1846).

In the entry on physiology of the *Encyclopédie* of Diderot and d'Alembert (*Encyclopédie*, 1778) Albrecht von Haller, the founder and director of the Academy of Göttingen wrote:

"This scientist did not want to teach us how he had collected the huge amount of data which are the fundaments of his work. A book so small in size but requiring so much work and experiments had not been written before."

It is evident that although Haller appreciated the content of *De Statica Medicina*, he did not like its presentation in the form of aphorism. Elsewhere, in the entry on anatomy (*Encyclopédie*, 1776) the work of Santorio was mentioned appreciatively, however, the form of its presentation was criticized. *"He departed from vague ideas from the past and drove perspiration to weight and nature giving dignity to this secretion, and derived from it news on the healthy state. However he used aphorisms and did not provide details."*

Modestino del Gaizo, a Neapolitan scientist at the end of the ninetheenth century, made it clear that Lavoisier made *De Statica Medicina* the starting point of his studies on perspiration. Since at the time of Santorio only a few scientists attributed a weight to air, nothing was known on the origin of water and on the origin of CO_2 the scientist was obliged to simplify a complex problem. However, Santorio opened the field (Del Gaizo, 1869).

According to Arturo Castiglioni, Santorio *"[...] in the field of medicine was the first and most happy innovator, the most courageous initiator of that method of exact investigation to which medical sciences owes the greatest successes. The foundation stone upon which has been built the entire structure of modern medicine"* (Castiglioni, 1920). According to Castiglioni Santorio was a Galilean, one of the Galileans who met great

success in medicine, the other being Giovanni Alfonso Borelli the author of *De Motu Animalium*. However, Santorio never declared Galilei the originator of his science: Galilei, like the vast majority of his contemporaries held firm to the writings of Galen.

"Paracelsus, Vesalius, Harvey and Santorius earned their living by the teaching of the writings of Galen and to a great extent practiced medicine that could be easily qualified as Galenism" (Eknoyan & De Santo, 1996).

Francesco Puccinotti pointed out that Santorio *"does not cite Galilei and Acquapendente, with whom, in their last years as professor, he had become a colleague. […] In 1608, Galileo discovered Jupiter's satellites at the same university in Padua and his new method was applied to physiological anatomy by Fabrizio d'Aquapendente. However Santorio in the commentary to the 17th question to the comment to Avicenna states that "the earth rests"* (Pucinotti, 1962).

Furthermore in "In De Remediorum Inventione *Santorio did not quote Falloppia or d'Acquapendente but a certain Doleoni who left no special trace in the annals of history. It is likely that Santorio had difficulties in abandoning the old doctrines and making the move into the new ones*".

However in *De Remediorum Inventione,* Santorio quotes his *De Methodo Vitandorum Errorum* on three separate occasions to make clear his interest in mechanical and experimental doctrines (11).

Also according to Adalberto Pazzini, Santorio *"made full use of the Galilean method. The birth of instruments to measure must be a direct fruit of the labours of great Italian scientists. Being the nature written in mathematical terms it could be indagated through numbers which was the answer provided by the instruments. Santorio is credited with the introduction of clinical instrumentation by applying the thermometer to measure a fever". "Santorio also invented the pulsilogium to measure the frequency of the pulse using numbers"* (Pazzini, 1962).

With *De Statica Medicina,* Santorio opened a new methodology scrutinizing human metabolism. Everything was based on accurate measurements, on balance studies, and on the full use of calculations. A more than appropriate number of patients were enrolled for the studies. No less than ten thousand people sat on the scale, including Galileo Galilei, as anyone can learn from a letter written by Santorio to Galilei dated 1615, accompanying the gift of a copy of *De Statica Medicina* (Ongaro, 2001a). In that letter, Santorio also suggested to Galilei that he read aphorisms no. 2 in section 1 and aphorism LXXIV in section 3.

The former reads: *"If the doctor who has the care of another health is acquainted only with sensible supplies and evacuations but knows nothing about the waste made daily by insensible perspiration, he will deceive his patient and never cure him."*

The latter reads: *"Excessive amounts of food and drink, ingested for long periods of time, hide the acrimony of retained perspiration and also cause distempers of some of the less considerable parts, which manifest and degenerate into serious diseases when bodies are purged or fasted."*

Giorgio Baglivi wrote in *Canones de Medicina Solidorum ad Rectum Statices Usum* that *"De Medicina Statica and De Motu Cordium are the two pillars of modern medicine."*

De Statica Medicina met with a great success during the 17 th and the 18th centuries (Kuriyama, 2008). The second edition was reprinted some forty times. There were translations into English (1676), Italian (1704), French (1722) and German (1836). Herman Boerhaave from Leyden pointed out that in the field of medicine "*no medical book attained this perfection*" (Boerhaave, 1753).

Currently, the scientific message regarding perspiration has nothing to teach, however as Giuseppe Ongaro points out (Ongaro, 2001b):

"Although medicine based on weighing body weight is no longer an actual medical doctrine, the method which drove Santorio to introduce it remains important. The great merit of Santorio was the introduction of quantitative experimentation in medicine, thus opening the route to mathematical and experimental analysis of physiological and pathological phenomena."

Santorio against astrology in medicine

Of course Santorio has many other primacies in the clinical sciences. The first and not the least important was the rejection of astrology in medicine.

Falsa esse Astrologiam divinatricem, *Predictiones astrologorum esse irritas et vanaa*, and *Astrologia esse chimeram*. In other words, *"diagnostic astrology is false; the predictions of astrologists are risible and of no value; astrology is a chimera"* (Del Gaizo, 1889).

Santorio's primacy in self-experimentation

Another primacy of Santorio is in self experimentation. As thoroughly discussed in 1996 by Lawrence K. Altmann, scientific editor of *The New York Times* (Altmann, 1996):

"The earliest self-experimenter I have discovered was an Italian scientist – Santorio of Padua, the father of the science of metabolism". *Santorio lived from 1561 to 1636, the age of Shakespeare and William Harvey's discovery of the circulation of the blood. It was an era when the scientist's great difficulty was finding suitable instruments to measure changes in basic physiological functions. Santorio was probably the first physician to use a thermometer to measure the temperature of the body. Santorio also used a steelyard, a type of large portable balance, to discover insensible perspiration. The bearded Santorio placed his work table, his bed, and all his other daily necessities upon his steel yard balance. Over a thirty-year period he experimented on himself to determine how his body responded to various physiological and pathological conditions. Each day he weighed himself and the amounts of foods he ate and drank, as well as his bodily discharges. From these measurements, Santorio determined that there was always an appreciable difference between the weight of the food and drink he consumed and what his body lost as waste and sweating. Santorio's self-experiments taught us about what is known as insensible perspiration."*

For Altman the real followers of Santorio in self-experimentation were John Hunter, the English surgeon and professor of St. George's Hospital in London who inoculat-

ed himself with material from a patient with gonorrhoea and Werner Fossmann who placed a catheter into his own heart on nine occasions, while developing cardiac catheterization (Altman, 1996).

The pulsilogium and the clinical thermometer

Santorio certainly took advantage of his exchanges in the drawing room of the Morosini Palace in Venice. He made use of Galilei's principle of isocrony of the *pendulum* as well as of his experiments with the thermoscope. In 1583, Galilei observed the oscillation of the chandelier in the Cathedral of Pisa and measured them making use of his pulse. Santorio constructed a *pulsilogium* (pulsiloge, pulsometer), a stop-clock used to measure the pulse which was assembled following the principles of the pendulum.

It is probable that Galilei assembled the first tool to measure temperature, more a tool designed for termoscopy than a thermometer, and without a scale. Santorio developed a clinical instrument and, much more, identified the locations on the human body where to measure clinical temperature. He suggested taking one's temperature in the palm of the hands, in the mouth, from the exhaled breath of the patient who engaged in open-mouth breathing. In addition, Santorio also made a suggestion on the timing of the measurements in connection with fevers. Thus clinical thermometry belongs to Santorio.

According to Modestino Del Gaizo (1889), *"Galileo invented the thermometer; Santorio diffused its use [...]. Santorio modified the thermometer of Galileo for physico-pathological investigations and for application to the mouth and for rendering it more sensitive. Santorio was the first who attempted to use the thermometer in medicine on a large scale*".

"There is great merit in Santorio. Galilei invented the thermometer, Santorio Santorio made it popular. Santorio modifies Galilei's thermometer for phsyiopathological studies, to adapt it to body surface, to the mouth, to make it more sensitive. Santorio is the first who attempts to propagate a more frequent use of the instrument in medicine. An instrument about which even Malpighi and Borelli wrote" (Del Gaizo, 1889).

Santorio also studied the environment. Besides measuring temperature *"diagnoscendo temperature calida vel frigide aeris*", he attempted *using four different procedures to evaluate humidity. [...]. For which he used, as hygroscopic means, either bodies with absorptive power, and even the thermometer, since he might have argued that a decrease in temperature was an indicator of what we now call the relative humidity of hygrometric state"* (Del Gaizo, 1889).

Santorio left money for scholarships in his last will

In his last will and testament, Santorio left money to the Morosini family, remembering his early days with the shared tutors. More importantly, he also left money to the University of Padua for ten scholarships, part of these to be conferred to students born in Capodistria. This gives an insight into his magnanimity, the respect he had for the

new generation and for the University of Padua, which lived on citizenship taxes and on duties paid by wagons and cars entering in the city.

Santorio, a modern physician-scientist

Santorio, the founding father of metabolism (Eknoyan, 1999) embodied the characteristics of a modern physician scientist experimenting on patients, departing from patients needs, trying to cover the gap between a basic discovery (pendulum, thermoscope) and the time this discovery inspired an instrument used for cure (*pulsilogium*, thermometer) and making full use of already disposable instruments such as a weighing machine to unseat diseases before they could clinically manifest.

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