

HISTORY OF MEDICINE AND ANNIVERSARIES

TO CELEBRATE THE 500TH ANNIVERSARY OF THE BIRTH OF GABRIELE FALLOPIO (1523–1562)

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ABSTRACT

The article is dedicated to the 500th anniversary of the birth of the greatest physician and scientist of the 16th century Gabriele Falloppio (Fallopius), a revolutionary morphologist who made an invaluable contribution to the development of science, and one of the founders of fundamental anatomy. Although Falloppio is primarily known as an anatomist who described the uterine ("fallopian") tubes, his range of interests was much wider, and his contribution to anatomy was substantially more significant. Fallopius made many important discoveries in anatomy, and a number of anatomical structures bear his name. Also, Gabriele Falloppio was a talented teacher and a renowned medical practitioner, surgeon and pharmacist. It should be especially noted that Fallopius considered himself an apprentice of Andreas Vesalius. There is no data confirming the fact of their personal acquaintance, but there is documentary evidence of short-term correspondence between Fallopius and Vesalius. In his famous work "Anatomical observations" ("Observationes anatomicae", 1561), Fallopius pointed out Vesalius' mistakes and inaccuracies in anatomical descriptions, subjecting his "De humani corporis fabrica" to correct criticism. Vesalius' reply with compliments to Fallopius as a scientist has been preserved. In any case, the undoubted fact is that Fallopius was an adherent of Vesalius' methods in applied science and the teaching of anatomy, and consistently introduced them into practice throughout his life.

Key words: history of anatomy, history of medicine, Gabriele Falloppio, fallopian tubes, medical terminology

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К 500-ЛЕТИЮ СО ДНЯ РОЖДЕНИЯ ГАБРИЭЛЕ ФАЛЛОПИО (1523–1562)

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РЕЗЮМЕ

Статья посвящена 500-летию со дня рождения величайшего врача и учёного XVI века Габриэле Фаллопио (Фаллопия), революционера-морфолога, внесшего неоценимый вклад в развитие науки, одного из основателей фундаментальной анатомии. И хотя прежде всего Фаллопий известен как анатом, описавший маточные («фаллопиевы») трубы, круг интересов учёного был гораздо шире, а вклад в анатомию – несоизмеримо более значительным. Фаллопий сделал множество важных открытий в анатомии, ряд анатомических структур носят его имя. Кроме того, Габриэле Фаллопио был талантливым педагогом и известным практикующим врачом, хирургом и фармацевтом. Особо следует отметить, что Фаллопий считал себя учеником Андреаса Везалия. Данных, подтверждающих факт личного знакомства Фаллопия и Везалия, не имеется, но есть документальное подтверждение кратковременной переписки упомянутых учёных. В своём знаменитом труде «Анатомические наблюдения» («*Observationes anatomicae*», 1561) Фаллопий указал на ошибки Везалия и его неточности в анатомических описаниях, подвергнув корректной критике везалиевскую «*De humani corporis fabrica*». Сохранился ответ Везалия с комплиментами в адрес Фаллопия как учёного. В любом случае, несомненным фактом является то, что Фаллопий был приверженцем методов Везалия в прикладной науке и преподавании анатомии и последовательно внедрял их в практику на протяжении всей своей жизни.

Ключевые слова: история анатомии, история медицины, Габриэле Фаллопио, фаллопиевы трубы, медицинская терминология

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The year 2023 marks the 500th anniversary of the birth of Gabriele Falloppio (Latinized – Fallopius; 1523–1562) (Fig. 1), an eminent physician and morphologist, rightly considered one of the fathers of fundamental anatomy.



FIG. 1.
Gabriele Falloppio of Modena (Gabriele Fallopius Mutinensis). Portrait from the library of the botanical garden of the University of Padua, Italy [1]

For 1400 years, anatomists and surgeons, blindly following the voluminous writings of Galen (131–201), «saw what they believed» [2]. Galen did a lot of dissections and experiments, mostly on pigs and monkeys, because in those days dissection of humans was forbidden, which was the reason for the fallacy of many of his views. There were many excellent things in his writings – good descriptions of the skeletal and muscular systems, experimental studies of the function of the spinal cord by dividing it into successive levels in the pig, and so on. However, his views on blood circulation, for example, were pure conjecture, not to mention the fact that due to the lack of human material for study Galen had to extrapolate the features of the structure of animal organs to human anatomy [3]. For centuries, the study of human anatomy was reduced to the professor reading out Galen texts and students memorizing them, and the autopsy, if performed at all,

was performed by an assistant (demonstrator). The professor, for example, described the kidney as lobular and the liver as consisting of five segments (as in the pig and thus as in Galen's descriptions), although both organs presented during autopsy were smooth.

At the end of the first half of the 16th century, Andreas Vesalius (1514–1564) revolutionised traditional teaching methods. He taught at Padua, where he was appointed professor of anatomy at the age of 23. Vesalius personally dissected the human body and instilled in his students the truth that it was necessary not to «see what they believe» but to «believe what they see.» One of the merits of Vesalius is that he dared to criticize the anatomical views of Galen [4–7].

After Vesalius left the chair in 1544, the place was taken by his student Matteo Realdo Colombo (1516–1559), who continued the tradition of teaching his teacher. Colombo soon moved to the chair of anatomy in Pisa and then Rome, and in Padua he was replaced by another follower of Vesalius, Gabriele Fallopio, better known by his Latinized name Fallopius. He accepted a position as professor of anatomy and surgery, and became head of the botany department (in those days, it was not uncommon for one versatily gifted scientist to hold several positions).

Gabriele Fallopio was born in 1523 in Modena, an ancient city in Emilia-Romagna, Italy. He came from an impoverished noble family. His father Girolamo Fallopio was a jeweler by trade, but was in the military service for a number of years. It is also known that the mother of the future luminary of science was named Katerina Bergozzi. After the death of his father from syphilis, the family became impoverished, Gabriele was unable to continue his liberal arts education because of financial problems, and in 1542 he became a priest, following his uncle's example, in his parish of the Episcopal Church in Modena. However, the priesthood did not enthuse young Fallopius, although it improved his financial situation. After a few years he gave up his ministry and decided to devote himself to medicine [8, 9].

Having received an elementary liberal arts education, Fallopius became interested in anatomy, and, since there were no medical schools in Modena, he studied texts by Galen and Berengario da Carpi on his own, at the same time performing dissections of animals for educational purposes [10, 11]. In 1544, at the age of 21, Fallopius performed his first autopsy on a human cadaver under the leadership of Niccolo Macella. In those times, despite the liberalisation of the church's attitude to anatomical dissections (Pope Sixtus IV (1471–1484) was the first to allow dissection of human cadavers, namely the bodies of executed criminals, and then Pope Clement VII allowed to expand the scope of dissection possibilities), permission to dissect human beings was rarely granted to anyone, and it was necessary to have, besides a great desire to study anatomy, also influential friends to carry out one's intentions [10, 12]. Still, the 16th century was marked by the wide access of morphological scientists to dissection of the human body, which led to significant progress in the development of anatomy and medical science in general.

In 1545 Fallopius moved to Ferrara, where his teachers were Giovanni Battista Canano (1515–1579) and Antonio Musa Brassavola (1500–1555), the famous surgeon who first successfully performed tracheotomy. In parallel with his studies, Fallopius practised surgery for a time, but because of a number of lethal outcomes he abandoned the practice and resumed it only after being appointed head of the department of anatomy and surgery at Padua a few years later. In Ferrara from 1548 to 1549, Fallopius served as acting head of the department of pharmacy [9].

After Ferrara, Fallopius continued his activities at the University of Pisa, where in 1549, on the recommendation of the Duke of Florence Cosimo de' Medici, he became a lecturer and received the title of professor of anatomy [13]. Here he resumed the practice of surgery and taught anatomy until 1551. It should be noted that despite the efforts of the university administration to bring back the old ways of teaching based on Galen's texts, Fallopius taught in the progressive style of the school of Andreas Vesalius, in which he was warmly supported by the local students. The story survives of how in 1555 the university authorities attempted to revive the old style of anatomizing prescribed by statute, i.e., the junior lecturer was to read Mondino's "Anatomy" and the senior, Professor Vettor Trincavella (1490–1563), the theoretical lectures. Thus, Fallopius' role as an anatomist would have been downplayed. Trincavella's performance was eventually interrupted by students loudly chanting "vogliamo il Fallopio" ("we want Fallopio"), after which anatomy was completely in his hands [14]. Fallopius was a very bright teacher, with his character and manners he made a lasting impression on his contemporaries, all the more so when combined with an innovative approach to the educational process [3].

In parallel with teaching, Fallopius continued scientific research, dissecting with Medici's permission the corpses of lions in the Florence zoo, as a result of which he refuted Aristotle's opinion that these animals have no bone marrow [14]. While in Pisa, Fallopius conducted experiments to study the effects of opium, which was used at the time to carry out the execution of those condemned to death; as a result, the scientist was accused of vivisectioning a human being (in those days, such things happened to scientists-morphologists, in particular with Vesalius).

Then Fallopius moved to Padua, where in 1551, by order of the Venetian Senate, he headed the chair of anatomy, surgery and botany at the famous university. In 1556, Fallopius was admitted to the Medical College of Venice. Throughout his career, Fallopius performed quite a few dissections of human cadavers (he was allowed to dissect up to 7-8 cadavers per year) and animals - not only adults, but also fetuses, newborns, infants, and children - which allowed him to accumulate a large information baggage on anatomy [9].

In 1561, Fallopius published his work "Anatomical Observations" ("Observationes anatomicae"). The original plan was to publish a voluminous illustrated treatise, but the scientist's friend Pietro Manna (physician

to the Duke of Milan Francesco Sforza) advised him not to delay the publication of his discoveries, otherwise one of his contemporaries-colleagues would beat him to it. Thanks to this, a small book without illustrations was soon published, which later turned out to be the only one printed during Fallopius' lifetime and dedicated to his friend Pietro Manna [10, 11]. This work, in the best Vesalian tradition, describes a number of discoveries he made in human anatomy. These include a detailed description of the canal of the facial nerve («Fallopian aqueduct» or «aquaeductus Fallopii») and the chorda tympani (a branch of the facial nerve), as well as the «Fallopian hiatus» (in which the greater petrosal nerve passes), the bony labyrinth of the inner ear and, in particular, the semicircular canals and the cochlea. He first described the tympanic membrane and its relationship with surrounding bony structures. At that time two auditory ossicles were known, and Fallopius is the discoverer of the third of these, the stirrup. He also described the round and oval windows (fenestræ) and their communication with the vestibule and cochlea. Fallopius first discovered the communication between the mastoid cells and the middle ear [9]. These discoveries were realized thanks to a particularly careful method of dissection, developed by Fallopius and fundamentally different from the methods of his predecessors, who traditionally examined the skull cavity during autopsy in the last turn, which left no chance of freshness of the contents of the skull. Additionally, Fallopius used the most gentle methods of access to the base of brain and used special sharp-ground miniaturised instruments [10]. Fallopius more thoroughly than other researchers studied the ways of outflow of lachrymal fluid, described the topography of the ethmoid bone and the communication of its cells with the nasal cavity, as well as the structure of the sphenoid bone. Fallopius was also the first to describe the muscles of the soft palate, pharynx, and the pyramidal (later Fallopian) muscle [9]. He was the first to describe the anastomotic arterial ring at the base of brain, now known as the Willis' circle (polygon), in 1561, almost a century before Thomas Willis (1621–1675) [15]. Along with the above-mentioned topics, the book contains a section with a detailed description of the anatomy of female genital organs – vagina, hymen, ovaries, clitoris, and, of course, uterine tubes, which later received the name «Fallopian tubes» in honour of the scientist [6, 9]. The Russian translation of the fragment describing the fallopian tube can be found in our previous study [16]. Moreover, Fallopius described an obstetric anomaly in which the embryo implants in one of the tubes (ectopic, or tubal, pregnancy). To be fair, it should be noted that the fallopian tubes, although named after Fallopius, were described more than 1800 years earlier by Herophilus (although the latter erroneously believed that the functional role of the tubes is reduced to the transport of «female sperm» from the ovaries to the bladder). It was Fallopius who corrected this error many centuries later. But the inguinal ligament should rightfully be called the Fallopian ligament (although in a number of sources the inguinal ligaments are called «Fallopian arches»), because our hero

described it half a century before the French anatomist François Poupart (1661–1709) [12, 17, 18]. It should be especially noted that Fallopius, like Galen and Vesalius, found similarities between the male and female genital systems and noted the analogy between the clitoris and the penis, as well as common structural features of fallopian tubes and seminal ducts, but he interpreted the similarities and differences more correctly [9]. The scientist refuted the view that the ovary contains sperm and that the fallopian tubes are the functional analog of the male ejaculatory ducts; in his book in 1561, he wrote that the ovary contains oocytes that are fertilized by male sperm [13].

The interests of Fallopius covered practically all the systems of the human organism: nervous, vascular, digestive, urinary reproductive – as well as the patterns in their development. He described the ileocecal (named the Fallopian valve in his honor) valve, discovered the *valvulae conniventes* and the villi of the small intestine. He also paid much attention to the intricacies of the structure of the kidneys (first describing the tubules and calyces), ureters, and bladder, being the first to point out the three-layered architecture of its muscular tunic [9]. Fallopius made a significant contribution to anatomical terminology: he gave scientific names (which are still preserved today) to the vagina and placenta, proposed the terms “cochlea”, “labyrinth”, “hard and soft palate”, “tympenic membrane”, “cricoid cartilage”. His descriptions of the trochlear, trigeminal, vestibulo-cochlear and glosso-pharyngeal nerves were the best for his time [3]. Although it was not a systematic textbook, it covered a wide range of subjects with an emphasis on the skeleton, especially the skull, and muscles. In addition to the above organs and structures, the book contains descriptions of the carotid and vertebral arteries, the muscles of the head and neck (including the muscles of the external ear and masticatory muscles), as well as the muscles of the eyeball, and some muscles of the trunk and extremities. The scientist also touched upon the peculiarities of the structure of the scalp and face [9, 14].

Fallopius laid the foundations of embryology by investigating the process of tooth development (he described the tooth premordium and the process of replacing deciduous teeth with permanent teeth) and the mechanisms of primary and secondary ossification in the sternum, skull bones, and pelvic bone [6, 9]. He tried to explain the patterns of organismal development by studying the anatomy of embryos, fetuses, children and adults, thus introducing embryology as a method of studying anatomy. This method was then refined by two of his most famous students, Hieronymus Fabricius (Fabricius ab Aquapendente or Girolamo Fabrizi d'Acquapendente, 1533–1619) and Volcher Koyter (1534–1576) [12].

It is known that Gabriele Fallopio considered himself a disciple of Vesalius. Although in reality their acquaintance was limited to a short correspondence, in February 1561 Vesalius received a copy of Fallopio's “Anatomical Observations” with additions and corrections to Vesalius's *Fabrica*. By the end of the year, Vesalius had compiled a response to the “Anatomicarum Gabrielis Fallopii Observum

Examen”, commonly referred to as *Examen*. Vesalius was quite upset by Fallopius's reckless arrogance to criticize him; in his letter he tried rather clumsily and unsuccessfully to refute the Italian's arguments. But despite this, he recognized Fallopius as an equal in anatomical sectional practice [7, 13]. In hard times for Andreas Vesalius, when almost everyone turned away from him, and, in particular, the mentioned Colombo became one of the most zealous critics and persecutors of the scientist, only Gabriele Fallopio not only did not deny Vesalius, but, coming to the position of his predecessor in the chair at the University of Padua Realdo Colombo, called himself a follower and disciple of Vesalius and restored his traditions in teaching and science [19].

Notwithstanding the fact that Fallopius was a zealous follower of Vesalius, in his book he noted a number of errors and inaccuracies made by his idol, but he pointed them out in a mild and friendly manner, unlike his much more rigid contemporaries, including Vesalius himself, who criticised Galen quite sharply. In particular, Fallopius clarified information about the structure and function of the round ligament of the uterus, which Vesalius mistakenly believed to be a muscle; Fallopius also determined that the inferior vena cava drains blood from the liver, not the heart, and indicated the correct direction of the outflow of bile (Vesalius believed that the bile ducts open into the stomach). Historians of medicine believe that Fallopius made more discoveries than Vesalius, and Fallopius' research is more accurate. For example, Daremberg (Daremberg C.V., 1817–1872) in his “*Histoire des Sciences Medicales*” (Paris: Baillière, 1870) states, “Fallopius had the genius of invention, Vesalius the genius of method; in other words, Fallopius had genius, Vesalius had only knowledge.” And if in honor of Fallopius is named many anatomical formations, the name of Vesalius – only a small non-permanent hole in the large wing of the cuneiform bone. Fallopius, however, did not publish such a voluminous work as Vesalius, and did not attach much importance to illustrations, but he was the most serious researcher of anatomy, “the great tireless inventor”, as Haller (Albrecht von Haller, 1708–1777) called him, and in the polemic with Fallopius, the impartial critic Vesalius admits that his opponent was often right [5, 20].

In his book, Fallopius, following Vesalius, corrected the errors of Galen, who based most of his observations on the results of animal autopsies. This required a special courage, because in those days the ideas of Galen were dominant in anatomical science, and to contradict them was tantamount to heresy. Galen, in particular, believed that the lower jaw was made up of two bones, the sternum was made up of seven fragments, and the humerus was the second largest bone in the body after the femur. These (and a number of other) misconceptions were corrected by Fallopius [4, 9, 20].

Besides «*Observationes anatomicae*», following Fallopius' death, books on anatomy “*Exsitio in librum Galeni de ossibus*” (1570), “*Observationes de venis*” (1570), “*De humani corporis anatome compendium*” (1571) and “*De partibus similaribus humani corporis*” (1575), based on his lecture notes, were published [8].

A superb morphologist, Fallopio was also an equally outstanding clinician. He established the unity of the disease manifestations and refuted the hypotheses of other scientists who based its occurrence on the disorder of circulation and relationships of the main «humors» (fluids) [20]. Among the most famous studies of Fallopius is the study of the clinic, differential diagnosis and treatment of syphilis. And, it should be noted, perhaps his most famous clinical achievement was the introduction of the condom and concurrently conducted one of the first clinical trials at the time. According to the scientist himself, he tested the effectiveness of his proposed «device» - a small cloth pouch impregnated with a special composition – on 1100 men who had intimate relations with courtesans who were sick with syphilis, and then put the pouch on the organ for disinfection. As a result (according to the same Fallopius) none of the participants of the experiment were infected with the disease that was rampant at that time. The treatise «De Morbo Gallico Liber Absolutissimus» was published in 1564 and then repeatedly reprinted [8] (Fig. 2).

Another important contribution of Fallopius to clinical practice was the treatment of nasal polyps: he was

the first physician to use an ear mirror and to use sulfuric acid to remove polyps from the external ear canal. He wrote, but did not manage to publish, a number of practical manuals: treatises on ulcers, tumors and surgery, several therapeutic treatises on baths and thermal waters, on laxatives and on the composition of medicines, and a set of commentaries on Hippocrates' "On Head Wounds". These documents were manuscripts of Fallopius' lectures. In 1575, years after the author's death, they were published in Nuremberg by Volcher Koyter [8, 9, 16, 22]. With regard to infectious diseases, Fallopius, recognizing individual differences in susceptibility, declared that for ten persons exposed to an infection there were scarcely four who would become infected; thus, his great authority contributed to lessen the terror which epidemics inspired in Italy. As a successful surgeon as well as an anatomist, Fallopio was a masterful surgeon and recommended to his students the safe use of a trocar to puncture the anterior abdominal wall for ascites: that is, in the immediate vicinity of the iliac fossa rather than in the periapical region, as was commonly practised at the time. Fallopius ligated vessels and achieved rapid wound healing by using simple medicines [13, 20].



FIG. 2.

Title page of "De Morbo Gallico Liber Absolutissimus" 1566 edition (photo by Federica Viazzi) [21]

Among other things, Gabriele Fallopio served as director of the Padua Botanical Garden, the oldest in Europe, where he conducted research concerning the use of plants in pharmaceuticals. The plant genus *Fallopia* is named in his honour [12, 22].

With all this, Fallopius was dissatisfied with the salary he received while working in Padua, and in 1561 the scholar negotiated with the University of Bologna to move there with a salary of 400 scudi, which was double his previous income. But the move never materialized due to his sudden death at the age of 39 [9]. The cause of death of the great scientist is not precisely established. It is known that from 1556 to 1557, Fallopius suffered from chronic fatigue. By then, he had developed a chronic lung infection and, as he taught anatomy mostly in winter, his health was affected [12]. Some biographical works mention a probable complication of the scientist's hand wound during the autopsy or a «prolonged lung disease» and, alternatively, pleurisy, but the most likely hypothesis is tuberculosis. The great physician and anatomist was buried in the church of St. Anthony in Padua, but later, already in the XVIII century, due to repair work, the remains of Gabriele Fallopio were moved to a nearby monastery and placed in the tomb of his friend Melchior Guilandino [12, 13] (Fig. 3).

The story of a succession of anatomy pioneers doesn't end there. One of Fallopius' students, the Dutchman Volcher Koyter, became one of the founders of comparative anatomy and embryology, continuing the research begun by Fallopius into the patterns of human and animal development. Girolamo Fabrizi (Fabricius), who succeeded his teacher as head of the department in 1562 and made invaluable contributions to anatomy and embryology, opened the first ever permanent anatomical theater in Padua. Fabricius continued the tradition of teaching and research using human autopsy and in 1574 published his discovery of the presence of valves in the veins of the extremities.



FIG. 3. Tombstone on the tomb of Gabriele Fallopio, Chapter of the Convent of the Basilica of St. Anthony, Padua [23]

At the time, he did not realize their functional significance. However, one of his students was the young Englishman William Harvey (1578–1657), who in his later work used this discovery as an important part of his reasoning about the true nature of the blood circulation [2, 3].

Conflict of interest

The authors of this article declare no conflicts of interest.

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