HISTORY OF MEDICINE AND ANNIVERSARIES

JEAN PECQUET (1622–1674). TO THE 400TH ANNIVERSARY OF THE BIRTH

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ABSTRACT

The article is dedicated to the 400th anniversary of the birth of the outstanding French anatomist, physician and philosopher Jean Pecquet (1622–1674). Pecquet's biography is connected with the city of Dieppe, where the future scientist was born and got his primary education, and with Paris, where he made his main discoveries in anatomy. Throughout his life, Pecquet collaborated with many prominent scientists of that time (Jacques Mentel, Louis Gayant, Jean Riolan (the Younger)), including not only physicians and anatomists, but also physicists such as Blaise Pascal, Edme Mariotte, Marin Mersenne and Evangelista Torricelli. Pecquet's most famous discovery is the chyle cictern, or cisterna chyli. The structure was named after of the scientist – "Pecquet's reservoir (cistern)". But more revolutionary discovery made by Pecquet is revealing and proving the fact that the lymphatic ducts flow into the superior vena cava indirectly through the venous angles and refuting the conventional opinion on the drainage of lymph into the liver. An important help in Pecquet's anatomical research and experiments was his passion for the physical and mathematical sciences. In collaboration with Edme Marriott, Pecquet studied the structure of the eyeball and turned out to be more foresighted, because, unlike Marriott, he correctly understood the role of the retina in the functioning of the eye as an organ of vision. Pecquet was one of William Harvey's supporters regarding his concept of blood circulation. He introduced cutting-edge at that moment technologies into the anatomy methodology, including animal experiments in vivo, and made a fateful contribution to the progress of anatomical science.

Key words: *history of medicine, history of anatomy, Jean Pecquet, lymphatic system, thoracic duct, blood circulation*

Received: 18.12.2022
Accepted: 29.05.2023
Published: 11.07.2023

For citation: Fominykh T.A., Kutia S.A., Zakharova A.N., Malov A.E. Jean Pecquet (1622–1674). To the 400th anniversary of the birth. *Acta biomedica scientifica*. 2023; 8(3): 224-231. doi: 10.29413/ABS.2023-8.3.25

ЖАН ПЕКЕ (1622–1674). К 400-ЛЕТИЮ СО ДНЯ ЕГО РОЖДЕНИЯ

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РЕЗЮМЕ

Статья посвящена 400-летию со дня рождения выдающегося французского анатома, врача и философа Жана Пеке (1622–1674). Биография Пеке связана с г. Дьепп, где будущий учёный родился и получил начальное образование, и с Парижем, где он совершил основные свои открытия в анатомии. На протяжении жизни Пеке сотрудничал со многими выдающимися учёными того времени (Жак Ментель, Луи Гайан, Жан Риолан – младший), в том числе не только с врачами и анатомами, но и с физиками, такими как Блез Паскаль, Эдм Мариотт, Марен Мерсенн и Эвангелиста Торричелли. Самое известное открытие Пеке – млечная цистерна, cisterna chyli, или цистерна грудного протока. В честь учёного данная структура носит его имя – «резервуар (цистерна) Пеке». Но более революционным открытием Пеке является то, что он, опровергая устоявшееся мнение о дренаже лимфы в печень, обнаружил и доказал факт впадения лимфатических протоков в верхнюю полую вену опосредованно через венозные углы. Важным подспорьем в анатомических исследованиях и экспериментах Пеке явилось его увлечение физико-математическими науками. В содружестве с Мариоттом Пеке занимался изучением строения глазного яблока и оказался более прозорливым, т. к., в отличие от Мариотта, правильно понял роль сетчатки в функционировании глаза как органа зрения. Пеке был одним из сторонников Уильяма Гарвея в отношении его концепции кровообращения, внедрял передовые на тот момент технологии в методологию анатомии, в том числе эксперименты на животных in vivo, и в целом внёс судьбоносный вклад в прогресс анатомической науки.

Ключевые слова: *история медицины, история анатомии, Жан Пеке, лимфатическая система, грудной проток, кровообращение*

Статья поступила: 18.12.2022
Статья принята: 29.05.2023
Статья опубликована: 11.07.2023

Для цитирования: Фоминых Т.А., Кутя С.А., Захарова А.Н., Малов А.Е. Жан Пеке (1622–1674). К 400-летию со дня его рождения. *Acta biomedica scientifica*. 2023; 8(3): 224-231. doi: 10.29413/ABS.2023-8.3.25

The year 2022 marks the 400th anniversary of the birth of Jean Pecquet (9 May 1622, Dieppe (Normandy) – 26 February 1674, Paris), a French scientist, anatomist, physician and educator who made indisputable contributions to anatomy and physiology (Fig. 1). As a child, Pecquet attended a Catholic school in Dieppe, then studied at the Jesuit College of Rouen. There he met Adrien Auzout and Blaise Pascal, with whom he shared interests in mathematics and natural philosophy. After graduation, the young man started looking for a job. His first employer was a noblewoman who employed Pecquet as a practicing physician in 1641. There is evidence that at that time the future scientist performed autopsies, the information about which he recorded (Memoirs of the Royal Academy of Surgery). When the woman moved to Paris, she took Pecquet with her. There, the elderly Marquise reportedly paid for anatomy lessons that Pecquet took from Louis Gayant, a renowned anatomist and president of the Paris Society of Surgeons. However, in 1646 the patient passed away and so the doctor was forced to find a new employer. According to history, the autopsy of his dead mistress was performed by young Pecquet himself [1, 2].

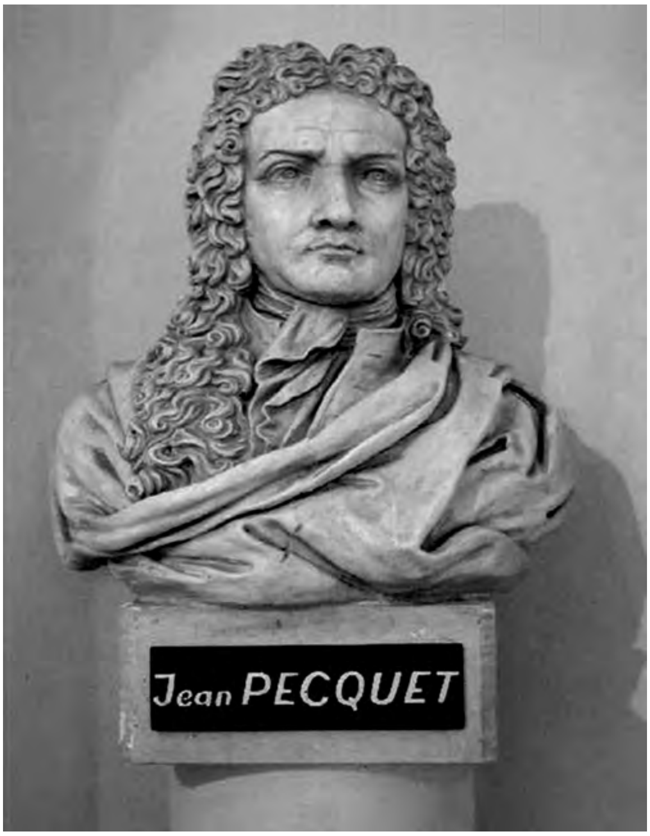

FIG. 1.
The bust of Jean Pecquet [3]

In 1645, the rector of the Jesuit college in Clermont (today, the Lycée Louis-le-Grand), which was part of the University of Paris, offered Pecquet a teaching (tutor) position, providing him with the financial means to further his studies. There the future scientist received a Master of Arts degree, necessary for admission to the Faculty of Paris [1]. Pecquet met many interesting people during that period, notably Marin Mersenne and Evangelista Torricelli, who were conducting research in acoustics, gravity and vacuum fields. By the mid-1640s Pecquet, probably through Pascal, had gained access to the circle of the famous physicist and mathematician Marin Mersenne, and, judging from the evidence of their correspondence, they became very close. Pecquet also met Mersenne's nephew Pierre, then a student at the University of Paris. Thanks to his acquaintance with Mersenne, Pecquet attended the Bourdelot Academy, later called the "true school" of medicine, and, according to some sources, by the mid-1640s he was conducting anatomical demonstrations (autopsies) there together with the surgeon of Saint-Côme Paul Emmerez [1]. In 1648, Mersenne introduced Pecquet to François Fouquet, physician to the faculty of Paris, Bishop of Agde, and his older brother Nicolas Fouquet (1615–1680), an official who was rapidly rising through the ranks of Cardinal Mazarini's administration at the time. The influential nobleman Nicolas Fouquet (superintendent of finance in France, 1653–1661) took Pecquet into his service and contributed to his further education. For this purpose, Pecquet travelled to Rome and returned to Paris in 1648. He was not only Fouquet's personal physician but also his confidant and friend; they discussed scientific, medical, and literary matters freely. In parallel with his practical medical work, Pecquet continued his medical research, which he had begun in Paris in 1646, and in 1651 he began work on his thesis, which he continued in Montpellier, where he received his doctorate in 1652 [2, 4].

Pecquet made extensive use of animal experimentation in his anatomical studies. When Jean Pecquet stepped into the Paris Faculty of Medicine in 1647, at the age of twenty-four, he already knew how to perform dissections. Most historians view the faculty by the 1640s as a dying institution steeped in the doctrines of Galen, which, under the leadership of Jean Riolan the Younger, refused to accept William Harvey's (1578–1657) theory of the blood circulation [1]. Between 1647 and 1650, Pecquet, with the support of his Parisian teachers Mentel and Mersenne, performed more than a hundred autopsies on various animals (bulls, horses, pigs, etc.). It is worth noting that Jacques Mentel (1599–1671) concluded in 1629, based on dissections of dogs, that mesenteric lymphatic vessels flow into the thoracic duct before entering the bloodstream [5].

Pecquet performed the majority of the autopsies at Fouquet's residence in Paris. Pecquet dedicated the book published as a result of these studies to François Fouquet as it was, in his words, "born in your house" [1, 6]. Thus, in 1647 (although A. Cunningham [7] believes that it happened in 1642), opening the chest of a living dog, he found a white fluid resembling milk, which he later interpreted as lymphatic fluid. He found that the structures conducting this "milky juice" end in the superior vena cava and, on the other side, in a reservoir or lumbar cistern (called cisterna de Pecquet in French-speaking countries) behind the stomach. This discovery was made by accident: the white fluid that Pecquet initially mistook for pus after the removal of the dog's heart, but further investigation showed that the fluid appeared as a result of damage to a lymphatic vessel (thoracic duct) flowing into the venous angle [8, 9]. As a result, the scientist first described the thoracic duct he discovered and the differences between a vein and a lymphatic vessel [7, 10–12].

Thus, as a student, Pecquet challenged the prevailing notions of the time and took up not the "silent and frozen science" of cadaver anatomy, but the anatomy of animals – dogs, cattle, pigs and sheep. Using a living dog in the experiment, he showed the following:

1. If the heart is removed, pressure on the mesenteric root causes lymph to be released into the superior vena cava.

2. Lymph is channeled to the subclavian veins by two paravertebral channels, which swell when their distal ends are ligated.

3. The origin of the ascending lymphatic ducts is in the prevertebral and subdiaphragmatic ampullae – "this the sought-after sanctuary of chyle, this hard to palpate reservoir".

4. The posterior part of the "pancreas of Azelli" consists of lymph nodes.

5. The mesenteric lymphatic vessels do not go to the liver (a fact confirmed by Glisson in 1654), and the inferior vena cava, incised above the liver, shows no signs of lymph [5, 6].

By the way, the English anatomist Francis Glisson (1597–1677), who was engaged with his pupil George Joyliffe (1621–1658) in similar studies, claimed that he was the first to prove that lacteals are not connected to the liver. Glisson wrote that Joyliffe was "busy with other practice" an was unable to publish his findings, stating that the new knowledge of the course of the mammary glands was obtained on behalf of his pupil [13, 14].

The discovery made by Pecquet as a result of experiments on animals was soon confirmed by other scientists, his contemporaries, but already on humans. Thus, Pecquet's colleague and associate, surgeon and anatomist Louis Gayant, soon repeated the study of the patterns of lymphatic drainage during the autopsy of a soldier killed in a fight with a comrade [14]. Nicholaes Tulp at Amsterdam described the thoracic duct and Pecquet's reservoir; Vesling (Padua) and Folli (Venice) made the same observation. There is an important testimony of the famous physicist Gassendi, who was present when Peyrac performed an autopsy on the corpse of a man who had just been hanged. To see the vessels of the criminal better, Peyrac fed him before the death sentence. Pecquet claims to have learnt this fact from Gassendi himself, who told him about it when they met in Paris. Thomas Bartholin, soon after the publication of Pecquet's work, demonstrated the human thoracic duct in Copenhagen; Jan van Horn did the same in Leiden in 1651. But while Bartholin gave Pecquet the praise he deserved, van Horn did the opposite. He officially appropriated the discovery and made no mention of Pecquet. Although there is a version that he was simply not familiar with Pecquet's work and thought he had made an independent discovery. Coincidentally, van Horn performed ligature experiments to prove that the chyle does not drain into the liver, as did Pecquet [15–17].

In the fundamental work "Experimenta nova anatomica, quibus incognitum hactenus chyli receptaculum, et abeo per thoracem in ramos usque subclavios vasa lactea deteguntur. Eiusdem dissertatio anatomica de circulatione sanguinis, et chyli motu" ("New anatomical experiments, in which a hitherto unknown reservoir of milky juice and milky vessels branching from it through the whole thoracic cavity up to the subclavian vein were discovered") (Fig. 2) Pecquet described the thoracic duct with its valves and reservoir, the so-called *cisterna chyli* (*receptaculum chyli*), which was later named Pecquet's cisterna in his honor.

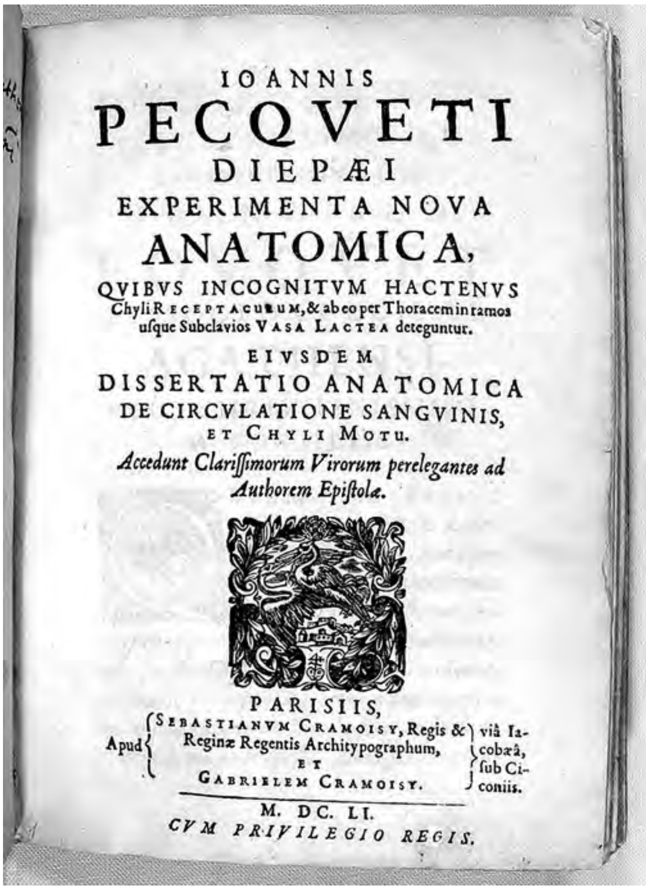
IOANNIS
PECQVETI
DIEPÆI
EXPERIMENTA NOVA
ANATOMICA,
QVIBVS INCOGNITVM HACTENVS
Chyli Receptaculum, & abeo per Thoracem in ramos usque Subclavios Vasa Lactea deteguntur.
EIVSDEM
DISSERTATIO ANATOMICA
DE CIRCVLATIONE SANGVINIS,
ET CHYLI MOTU.
Accedunt Clarissimorum Virorum perelegantes ad Authorem Epistolæ.
PARISIIS,
Apud Sebastianvm Cramoisy, Regis & Reginæ Regentis Architypographum, et Gabrielem Cramoisy. via Iacobæâ, sub Ciconiis.
M. DC. LI.
CVM PRIVILEGIO REGIS.

FIG. 2.
Frontpage of Jean Pecquet's "Experimenta nova anatomica" [21]

Importantly, he also definitively established that the intestinal duct containing milk-like fluid (lymph) flows into *cisterna chyli*, and then the lymph enters the thoracic duct, and not into the liver, as Azelli and other anatomists before him mistakenly thought [4, 18, 19]. Despite its relatively small volume and only one illustration, this work is considered the key point in research on the lymphatic system.

The scientist refutes Galen's ideas of hepatocentrism and refines Azelli's discovery. Numerous anatomists (Valleus, Harvey, Conring, Bartholin, and also Riolan the Younger) have argued on this point, stating that some of the lacteals scattered in the mesentery converge in the pancreas, some in the liver, some in the vena cava, and others in the portal vein. Riolan the Younger in particular supported Azelli's view that the "milky glands" drain into the liver, and rebuked Harvey for not thinking the same way. Pecquet demonstrated that chyle does not collect in any of these locations (Fig. 3) [2, 15, 20].

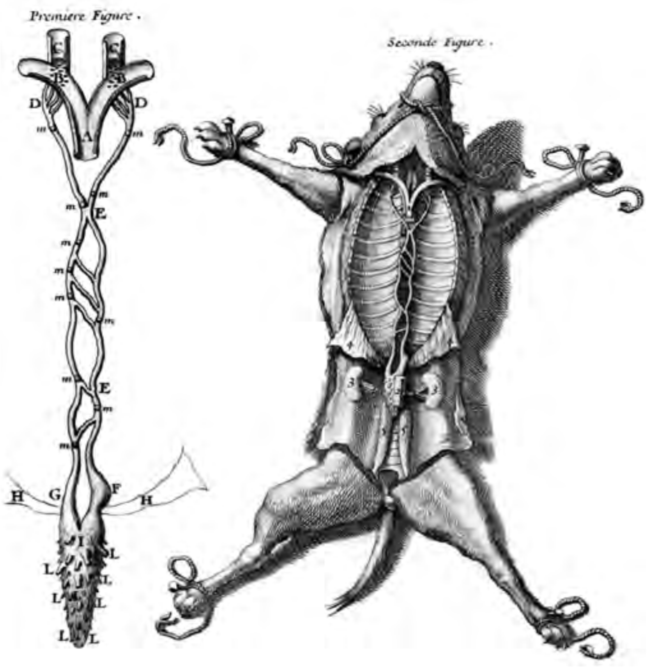

FIG. 3.
Dog's thoracic duct (from Jean Pecquet's «Experimenta nova anatomica», 1651) [21]

In the same work, in the "physico-mathematical" section, Pecquet describes experiments with vacuum conducted by means of a Torricelli tube. Evangelista Torricelli (1608–1648), student of Galileo, proposed an experiment in 1643 that investigated a phenomenon noted by Galileo in his Discorsi: a suction pump could only lift water to a certain height. Galileo argued that the internal force of a vacuum allows a column of water to rise until, stretched to its limit, it collapses under its own weight. Torricelli filled tubes of different lengths with mercury and inverted each over a bowl filled with the same liquid. In each case, the mercury fell into the tube to the same height, leaving an empty space at the top of the tube, which Torricelli claimed must be a vacuum, despite longstanding arguments that a vacuum could not exist in nature [1]. Pecquet witnessed a modification of the experiment belonging to the mathematician Gilles Personne de Roberval. The experiment consists in placing a deflated fish bladder in a vacuumized torricelli tube: as soon as it is in the empty space at the top of the tube, the bladder, working like a tiny balloon, inflates due to the elasticity of the air or "elatery" (the English translation of his work of 1653 is "elastrum"). As the upper part of the tube is almost empty, the tiny amount of air remaining inside the bladder expands and fills the bladder [22]. Pecquet introduced the concept of air elasticity ("elatery") as part of these experiments.

Pecquet had a number of reasons for resorting to such experiments: firstly, to explain the movement of chyle or digested food in a mechanical way within the body, without resorting to attraction solely as a result of elasticity and pressure, such as from respiration. Thus, elasticity is used here qualitatively rather than quantitatively in terms of pressure and volume. Another process associated with "elatery" is digestion, in which the fibres of the stomach and intestines expand and contract, "as in elatery". Another topical area concerns the "elatery" of blood vessels – both arteries and veins. Pecquet believed that immediately after cardiac systole, the arteries swell; the same happens to the veins when blood enters them. At one time, Harvey devoted attention to this issue, opposing Galen's views: Galen argued that arteries move because of the ability transmitted to them by the heart, and "ability" is called by the term *technicus* associated with his philosophical position. Harvey, on the other hand, argued that the arteries fill up because of the blood flow. Pecquet's analysis modified this dichotomy, as he attributed a more active role to the walls of arteries and veins: they were no longer purely passive vessels, but contributed to the movement of blood, facilitating by their dilation and contraction the activity of the heart [22].

These experiments had a profound influence on Pecquet and his ideas about the correlation between blood and lymph circulation. Pecquet later claimed that the knowledge he gained from dissecting human cadavers was "silent and cold" and that he gained "true knowledge" (*veram scientiam*) only by dissecting living animals. This technique allowed Pecquet to realize the mentioned discoveries in anatomy [1].

Pecquet may have been the first to introduce the concept of elasticity into anatomy, but he was not the last in the seventeenth century: other scientists followed his lead in various forms, some of which resonate with our current views and some of which do not. In those days, many researchers believed that physical and mathematical knowledge was necessary for a better understanding of anatomy. "New (or mechanistic) anatomy", of which Pecquet was also an adherent, refuted a number of statements existing at that time in anatomy. For example, the discovery of the thoracic lymphatic duct "deprived" the liver of its ability to produce blood and required a rethinking of its pathology [10, 11, 23]. Pecquet also formulated his reasoning on blood transfusion, capillary function and vascular permeability, by his own studies of the circulatory system confirming Harvey's theory of blood circulation. In his original work on blood circulation, William Harvey argued that the primary engine of blood circulation is the pulsation of the heart. Describing blood flow in the veins, Harvey argued that the movement of the ventricles of the heart "is sufficient to distribute the blood throughout the body and to drain it from the vena cavae". Thus, for Harvey, a single heartbeat was enough to "draw" blood from the vena cava, despite the fact that the vena cava is the largest vein of the body, into which almost all other veins drain blood, Harvey was virtually silent about the patterns of blood circulation within it. One of the first anatomists to specifically state venous blood flow was the young scientist Jean Pecquet in his book "Experimenta nova anatomica..." (Paris, 1651). In this book, Pecquet included a thesis on the problem of blood circulation in veins. There he claimed that the initial impulse of cardiac contraction was insufficient to explain the return of blood to the heart through the veins (what today is called venous return). More importantly, in some parts of the venous outflow, Pecquet noticed that the blood moved in a direction opposite to the direction of its own weight or, to put it in modern terms, against the law of gravity. This opposite movement of blood is particularly problematic in upright humans and animals because more than half of the blood flows upward to the heart through the inferior vena cava. How can such a large amount of blood move upward without the initial impulse of the heart? [23].

In his work, Pecquet shows the "circular movement of blood throughout the animal's body" by means of ligatures applied to arteries and veins. Similar experiments have been carried out before him, but Pecquet shows great originality in methodology and in the directness of his conclusions. He starts with arteries and veins in general. If a ligature is applied to the femoral, brachial, or carotid artery of a living animal, the vessel empties beyond the ligature, but becomes swollen on the side towards the heart; and if it is opened beyond the ligature there is no hemorrhage, whereas a puncture on the side towards the heart causes profuse bleeding. But a similar experience on the femoral or brachial vein gives the opposite result: the vein shrinks towards the heart and swells towards the periphery; a puncture below the ligature is accompanied by hemorrhage, and above it has no effect. To make sure that the blood flowing from the wounded vein came from the arteries, he applies a ligature to the appropriate artery for the duration of the hemorrhage. When this ligature is tightened, the bleeding from the vein first diminishes, and then ceases; but when it is relaxed, the bleeding begins again with the same intensity. As part of these experiments, Pecquet was able to disprove the idea of Riolan the Younger that "portal vein blood does not pass through the liver into the vena cava". By studying blood flow in the portal vein using ligatures, Pecquet proved that blood entering the liver through the *v. porta* leaves the organ through the hepatic veins flowing into the inferior vena cava [24].

With the publication of "Experimenta nova anatomica..." in 1651, Pecquet's position on the Faculty of Paris was no longer secure. Apparently, the author did not receive permission from the faculty to publish because he was a student, which constituted a breach of etiquette [1]. The publication created a great sensation in scientific circles. Even Harvey questioned the importance of Pecquet's work. In writings dated 1652, Harvey stated that he had observed these "milky glands" (perhaps even before Aselli), but doubted their importance in the circulation process. Ironically, he believed that the network of mammary glands was "too extensive" to move all the nutrients from the digestive tract into the bloodstream. Harvey believed that while an embryo can receive nourishment from the umbilical veins, an adult can receive nourishment to the liver via the mesenteric veins [17, 20]. Pecquet's work also received harsh criticism from the influential Riolan the Younger, causing Pecquet to retire to Montpellier, where he completed his medical research and submitted his finished thesis on 23 March 1652. Pecquet was famous in Montpellier, where he gave public anatomical demonstrations, and remained there, coming occasionally to Paris, until 1654. After receiving his doctorate, Pecquet practiced successfully in Paris and even became a physician at the court of Louis XIV. In particular, he served as personal doctor to the Marquise de Sévigné and Jean de la Fontaine [1, 2, 12].

While the discoveries of Harvey and Azelli in the anatomy of the lymphatic system caused a burst of activity in the scientific world of that time, the work of Jean Pecquet, first published in Paris in 1651, served as a stimulus for subsequent studies by Thomas Bartholin and Olof Rudbeck [9]. It is important to note that by the mid-seventeenth century, comparative anatomy had become not only a descriptive but also an experimental discipline. Pecquet's work combined dissection and mechanical philosophy and paved the way for the mechanical theories of bodily functions that dominated the second half of the century [1].

In 1661, Nicolas Fouquet was arrested for abuse of official position. Pecquet, as his personal physician, voluntarily followed his master to the Bastille until February 1665. Fouquet was then transferred to the prison of Pignerol (where he died in 1680), and Pecquet was ordered to go to his sister in Dieppe. He was to remain there until further notice. This stay lasted a year before King Louis XIV and Secretary of State Jean-Baptiste Colbert concluded that Pecquet was not to blame for his master's misdemeanours. Colbert went even further by nominating Pecquet to the French Academy of Sciences as an anatomist in 1666, enabling him to participate in the blood transfusion experiments conducted at the Academy between 1666 and 1667. In the academy, the scientist had a difficult time: despite the fact that by that time Pecquet was already famous, he was a native of a provincial university and he had to fight with representatives of the Faculty of Paris, who believed that only doctors who came from this faculty could practice their art. Pecquet was one of the doctors who founded the Royal Chamber of Physicians of Provincial Universities. A few years later, between 1666 and 1670, Jean Pecquet was appointed personal physician to the king, which provided him with a solid career [2, 6].

Already a member of the Academy, Pecquet carried out research on the eyeball with Edme Marriott, the discoverer of the blind spot, and published with him in 1668 the work "Nouvelle découverte touchant la veüe". Unlike Marriott, Pecquet believed that the retina, not the vasculature of the eye, was the main formation responsible for vision. He also experimented with mercury tubes because he suspected that atmospheric pressure affected blood circulation [2].

Summarizing the above, it can be stated that the work of Jean Pecquet has had a decisive influence on the formation of the modern concept of body structure. With his demonstration of the thoracic duct, Pecquet launched one of the strongest attacks on Galenism: "since blood does not flow into the liver, the liver cannot carry out the cooking process of converting chyle into blood". As a consequence, the liver has lost its privileged role in the body. In addition, Pecquet proved that the flow of chyle (lymph) is circulatory. In 1653, the Danish anatomist and physician Thomas Bartholin, in his work "Vasa lymphatica", supported Pecquet's conclusions and showed that the vessels described belonged to a new vascular system called the "lymphatic system". Finally, Pecquet's three-year experiments on living animals raised the problem of assessing the impact of dissection on the life sciences. Moreover, the attempt to adapt physical research to medicine shows the importance of co-operation between physicians and mathematicians in the foundation of "mechanistic anatomy" and, more generally, in the development of late seventeenth-century medicine [10].

Conflict of interest

The authors of this article declare the absence of a conflict of interest.

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