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Thomas Bartholin (1616-1680): Danish anatomist and his cardinal contributions towards the discovery of the lymphatic system

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SUMMARY

Thomas Bartholin (1616-1680) was the most famous member of the celebrated Bartholin family of Copenhagen and made outstanding contributions in anatomical sciences during the 17th century. As a student he was exposed to the academic environment of eminent European universities like Leiden and Padua, which significantly contributed to his progressive outlook towards advances in medical sciences. He was an ardent proponent of William Harvey's theory of circulation and adopted Harvey's method-based approach for his own scientific experiments. Bartholin undertook multiple dissection of human cadavers and noted that *lacteals* (carrying whitish lymphatic fluid) and *vasa lymphatica* (carrying clear lymphatic fluid) were not entering the liver (the prevalent theory during that period). Rather, he observed, they were draining into the thoracic duct, which in turn empties its contents into circulating blood by opening into left subclavian vein. His findings corroborated those of Jean Pecquet, who had reported similar observations in animals. Bartholin's efforts were critical towards the discovery of the lymphatic system in humans and establishing the same as an independent component of the circulation system. Bartholin was a prodigious writer and his most remarkable anatomical treatise was *Institutiones Anatomicae*, which also included a text authored by his father Caspar Bartholin, the Elder. In his lifetime, he wrote numerous letters in which he discussed his findings in details with his colleagues and contemporaries. He was a trendsetter, as he published most of these communications as valid scientific documents for future references. His exploits were instrumental for the evolution of anatomical sciences to the form familiar today.

Key words: Anatomy – Medicine – Harvey – Circulation – Lymphatics – *Institutiones Anatomicae*

INTRODUCTION

Thomas Bartholin (1616-1680) was a Danish anatomist and physician (Fig. 1), who belonged to the celebrated Bartholin family that made outstanding contributions towards the development of anatomical sciences and medicine in the 17th and 18th centuries (Hill, 2007). Bartholin was the torch bearer of the Paduan School of anatomy teaching, initiated by Andreas Vesalius (1514-1564), whereby the dissector himself was the orator, thus involving the convergence of two individual skills as an educator (Porzionato et al., 2012). In fact Bartholin adopted a more evolved version of the Vesalian approach, i.e. to communicate exactly the findings of dissection. Hereby he followed the footsteps of Johann Vesling (1598-1649), another illustrious anatomist from Padua, thus liberating the anatomical sciences from the shackles of theoretical and often inaccurate Galenic principles (Mønster-Kjaer, 2009)

Bartholin absolutely relied on dissection-based

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Fig 1. A portrait of Thomas Bartholin. Image in public domain

findings for his anatomical experiments. Although he was an ardent dissector, however he was often enamored by the intricacies of the human anatomy, which is evident in his following lines (Bartholin, 2015):

"Beautiful is what which we see
More beautiful is that which we understand
But most beautiful is that which is not intelligible"

Probably his inclination for the unfound, unexplored and unexplained was the true motivation behind his anatomical findings.

In this article, a review of literature was undertaken to present a biographical sketch and a brief account of the scientific exploits of Thomas Bartholin, the most famous member of the Bartholin family. It was hypothesized that such a review would be relevant to anatomical education in the 21st century, as medical educators are in search of avenues for effective utilization of classical teaching methods like cadaveric dissection (Ghosh, 2016).

METHODS

An extensive literature search was undertaken for this study, and standard search engines such as PubMed, Scopus, Google search, Google scholar and Wikipedia were referred to for relevant published materials. The following terms were used during literature search: "Thomas Bartholin", "Bartholin", "biography of Bartholin", "Bartholin and anatomy", "lymphatic system", "lymphatics", "Bartholin and eponyms", "Letters of Bartholin", "Institutiones Anatomicae", "Anatomy in Renaissance" and "Dissection and Bartholin". Published texts of Bartholin and their translations into English were consulted from online libraries while conducting the present study and wherever applicable have been appropriately referenced. The images used in the text were procured from the internet and it was ensured that all the figures included in this study are in the public domain.

EARLY LIFE AND EDUCATION IN EUROPEAN UNIVERSITIES

Thomas Bartholin was the second of the six sons of Caspar Bartholin the elder and his spouse, Anne Fincke, who was the sister-in-law of noted anatomist Ole Worm (1588-1654) (Hill, 2007). The lineage of the illustrious family showed its glimpses in young Bartholin, who unfortunately lost his father at the age of thirteen (Porzionato et al., 2013). His uncle Ole Worm was quick to identify the flair in him and took on the responsibilities of educating his nephew. Bartholin enrolled at the University of Copenhagen in 1634, and after spending three years there he embarked upon an academic tour of the European universities in 1637 (Porter, 1963). His first stop was at the University of Leiden, the Netherlands, which attracted scholars from all over Europe due to the cosmopolitan environment and progressive views in the academic domain. Bartholin was particularly attracted to the Anatomical Theatre in Leiden, where human dissection was carried out in presence of general audiences (Grendler, 2004). In 1640 he went to France and visited the universities of Paris and Montpellier. The medical faculty at both places ensured a strong adherence to the Galenic tradition, and the scientific approach to anatomy which was characteristic of the Renaissance period, primarily initiated by Andreas Vesalius, was strictly forbidden there (Tubbs et al., 2007). Such rigid and authoritative academic environment disappointed Bartholin and he left for Padua, the most prominent university in Europe in the field of medicine during that period (Suitner, 2016). There he studied medicine under the guidance of the famed anatomist Johann Vesling. He assisted Vesling in anatomical dissections at the famous anatomical theatre in Padua (Ghosh, 2014). Bartholin was charmed by the academic freedom and the intellectual atmosphere at Padua, expressed in his own words: "this paradise on earth" (Bartholin, 2015). In 1645, on his way back to Copenhagen, he reached Basel, which also played a significant role in molding his approach (Porter, 1963). Bartholin was impressed by the anatomical dissection being conducted in public with the spectacle lasting for five days, a ritual started by Swiss anatomist Caspar Bauhin (1560-1624) (Ghosh, 2016).

PROFESSIONAL CAREER IN COPENHAGEN

Bartholin was keen to apply his experiences at Leiden, Padua & Basel and upon returning to Copenhagen in 1647, he started conducting anatomical dissections in presence of distinguished guests, professors, physicians and even general public in the anatomical theatre within the University premises under the patronage of King Frederick III (Holck, 1993). Bartholin was one of the earliest practitioners of bioethics in the dissection hall as he urged spectators to behave with dignity while dissection was undertaken and the audience was requested to refrain to laughing and talking (Porter, 1963). Later Bartholin was appointed as the Chair of Anatomy at the University of Copenhagen, and in 1654 succeeded his uncle Ole Worm as the Chancellor of the University. He had the privilege of serving as the *medicus primus* of Copenhagen from 1656, upon the death of his maternal grandfather Thomas Fincke (Behnke, 1980). It was in the same year that Bartholin had to give up his anatomical duties due to repeated attacks of renal colic, a condition which troubled him from his young age. Now all his efforts converged towards documenting his communications addressed to his contemporaries, thus exploring deep into his anatomical finding and replying his critics (Cunningham, 1997). In 1661 Bartholin was elected *Professor Honorarius*, whereby he was relieved from his academic duties. Subsequently in 1663, he moved to the estate of Hagestedgaard, 75 kilometers from Copenhagen. However his house in Hagestedgaard was destroyed by a fire in 1670, leading to loss of a large number of his valuable manuscripts (Rhodes, 1957). He was appointed Royal Physician to King Christian V in the same year (Behnke, 1980). In 1675, he received an invitation to become Professor of Anatomy at the prestigious University of Padua, but Bartholin had to decline on account of his ill health (Mønster-Kjaer, 2009). His health continued to deteriorate, and in 1680 Bartholin sold his estate and returned to Copenhagen, where he breathed his last. His mortal remains were buried at the Church of Vor Frue Kirke in Copenhagen (Rhodes, 1957).

INFLUENCE OF HARVEY'S CONCEPT OF CIRCULATION ON BARTHOLIN

In early 17th century Europe, scientific concepts in medicine were still based largely on ancient philosophical and theological explanations based on Galenic principles. Galen's interpretation of anatomy and medicine was primarily shaped by animal dissections and remained uncontested till the middle of 16th century (Ghosh, 2015). It was around this period that Andreas Vesalius documented his observations based on human dissections in his seminal work *De humani corporis fabrica*, which challenged the core of Galenic principles. However, a section of anatomists were aggressively opposed to the acceptance of new findings and consequently, among many theories, Galen's understanding of the physiology of the circulatory system endured till the beginning of 17th century (Joutsivuo, 1997). Nevertheless, around this period experimentation began to find foothold as a legitimate component of scientific investigation. Accordingly, during the early part of 17th century the most sought after issue that emerged in medicine was William Harvey's theory on the circulation of blood (Lubitz, 2004). Harvey (1578-1657) was an English physician who documented a detailed account of the systemic circulation in his work *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus,* which was published in 1628. The essence of his theory was the existence of a unified circulatory system for both arterial and venous blood, with the heart being the sole regulating organ of the system (Androutsos et al., 2012). This was in sharp contrast to Galen's theory, as he believed that the circulation consists of two separate systems for distribution of arterial and venous blood. According to Galen, venous blood was generated in the liver, from where it was distributed and consumed by all organs of the body. He was of the opinion that the circulation of arterial blood was regulated by the heart and eventually the blood was regenerated either in the liver or the heart, thus completing the cycle (Karamanou et al., 2015). Harvey adopted a methodology based on scientific experiments to establish his findings, and in accordance with this approach he manipulated the functioning of the heart in living as well as dead animals. His experiments involved isolating parts of the heart, ligating and dividing arteries and also exerting pressure on veins on either side of the valves. He observed the beating heart in living animals and noted the synchronized contraction of the ventricles, thus dispelling Galen's theory that blood was forced from one ventricle to the other. Harvey further established his viewpoint by undertaking dissection of the inter-ventricular septum, which showed an absence of any gaps or perforations. He even removed the heart from a living animal which continued to beat thus establishing his theory that it primarily acts as a pumping organ and not as a sucking organ, as was documented by Galen. Finally, with the help of mathematical data collected from his experiments, Harvey was able to prove that blood continuously moves around in circulation (thus refuting the centuries-old Galenic principle that blood was consumed in the organs and peripheral parts of the body), and this is regulated by the heart by its pumping activity (Ribatti, 2009). Incidentally Harvey's circulation theory was received with a great deal of controversy among his colleagues as well as contemporaries, mostly because of their rigid adherence to ancient doctrines. However, Harvey's theory found support from a section of anatomists who were open to new ideas and recognized the significance of application of scientific methods in establishing theories (Aird, 2011). Among this group, Thomas Bartholin was an ardent proponent of Harvey's theory and this could primarily be attributed to his exposure to a cosmopolitan and progressive academic environment in the universities of Leiden and Padua, regarded as pillars of medical education in those days (ElMaghawry et al., 2014). Bartholin was greatly influenced by Harvey's exploits and adopted his method-based approach for scientific experiments (Fig. 2). He studied Harvey's theory in detail, which inspired him to further exploring of the details of human circulation (Grell, 1993).

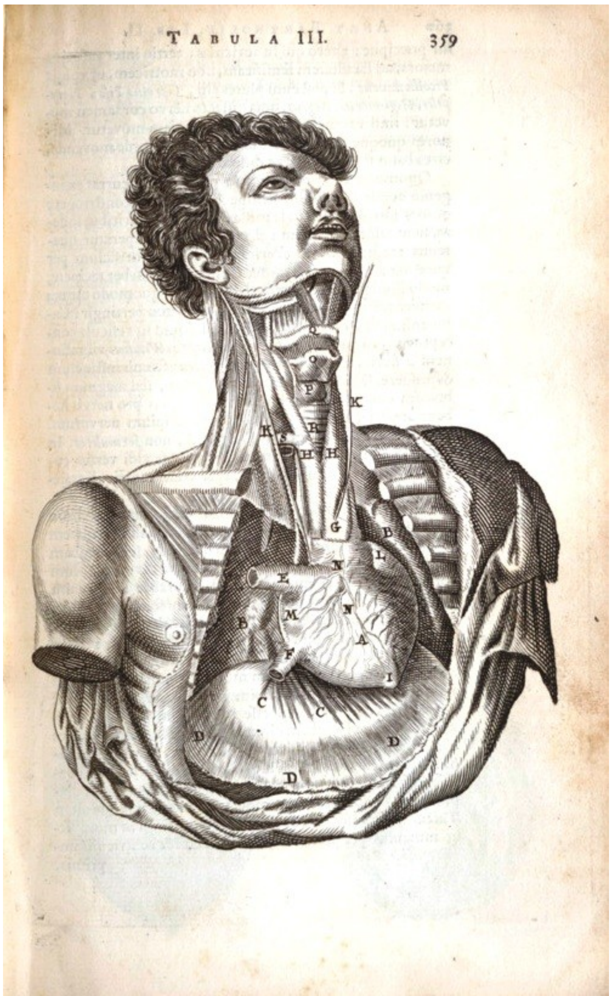

Fig 2. Illustration plate from Bartholin's *Institutiones Anatomicae* showing the heart as a prominent anatomical structure and as the sole regulating organ of the circulatory system. This was in accordance to Harvey's theory on circulation and a significant deviation from the Galenic principle that circulation was regulated by both heart and liver. Image in public domain.

BARTHOLIN'S EXPERIMENTS ON LYMPHATICS AND PECQUET'S WORK

During the 17th century, the science of anatomy was the primary domain of medical research and this period witnessed major innovative breakthroughs such as the introduction of the experimental method with which William Harvey established his theory of blood circulation (Arráez-Aybar et al., 2015). Being a young anatomist, Bartholin was prompt to note the significance of Harvey's findings and his interest in the circulatory system was further ignited by Italian physician Gaspare Aselli's (1581-1626) work on lymphatics, which was regarded in many ways as important as Harvey's work. Although Aselli had described the lymphatics, the course and function of these vessels were not fully understood (Loukas et al., 2011). Bartholin undertook some dissections while he was working in Leiden to determine the origin of lacteal vessels, but did not follow up his work until years later (Porter, 1963). In 1650, Bartholin dissected the corpse of a waiter and observed the lymphatics of the mesentery. Following this, he, along with his uncle Ole Worm, also noted the white distended chyle ducts in fish (Chickly, 1997). While he was undertaking these preliminary experiments, his brother Rasmus (1625-1698), who was in Paris at that time, communicated with him regarding Jean Pecquet's (1622-1674) work on lymphatics, which was published as *Experimenta Nova Anatomica* in 1651 (Bartholin, 2015). Pecquet reported that the lacteals actually drain into the cysterna chyli (previously the prevalent theory was that the lacteals drain into the liver), and from there the chyle is conveyed to the thoracic duct, and then the lymphatic system empties into the circulating blood by draining into the left subclavian vein (Régnier, 1999; Suy et al., 2016) . Although Pecquet's findings were based on his observations in animals, Bartholin realized the significance of these new observations and concentrated his efforts towards corroborating these findings in humans (Loukas et al., 2011).

DISCOVERY OF THE HUMAN LYMPHATIC SYSTEM

Bartholin undertook multiple human dissections during this period and came across new vessels (vasa lymphatica) which contained clear fluid as compared to the cloudy consistency of chyle, which was present in the lacteals. He noted that these vessels do not enter the liver, rather they carry their contents away from liver and drain into the blood system in a manner similar to the observations of Pecquet. Bartholin published the results of his experiments in 1653 as *Vasa Lymphatica* (Bartholin, 1675; Suy et al., 2016). In the same year Swedish anatomist Olaf Rudbeck (1630-1702) published similar findings independently as

Nova Exercitatio Anatomica, which triggered an intense priority dispute (Ambrose, 2007). It is generally accepted that Rudbeck was the first to demonstrate the lymphatics in human, as he had presented his findings at the Royal Court of Sweden in 1652. However, Bartholin is credited as the first to publish his results (Chickly, 1997; Eriksson, 2004). Moreover, Bartholin continued with his experiments in a quest to further unravel the anatomy of the lymphatics. In the later part of 1653, Bartholin published his *Dubia Anatomica*, an account of additional experiments performed by him on lymphatics particularly involving the lymphatic system of the breast, which he had observed in the cadaver of a young woman (Bartholin, 1675). Although an epidemic of plague had affected Copenhagen at that time thus making human dissection a risky exercise, Bartholin prioritized scientific quest above anything else. He achieved breakthrough in 1654, when he dissected the emaciated body of an alcoholic who had died of tuberculosis (Bartholin, 2015). After having exposed the mesentery, he found to his great delight the lymphatic vessels (Fig. 3). He realized that the lacteals and vasa lymphatica (which were earlier observed separately) were actually elements of the same system, and the difference in consistency of their fluid content was due to difference in fat concentration. In the same year, Bartholin published his observations as *Vasa Lymphatica in Homine Nuper Inventa* (Bartholin, 1675). His work won accolades from anatomists across Europe (including Pecquet) and established him as “the eye of the anatomists” (Cunningham, 1997). Bartholin’s efforts were critical for identifying the anatomical details of the lymphatic system in the human body, and proved instrumental in establishing lymphatics as an independent component of the circulation system.

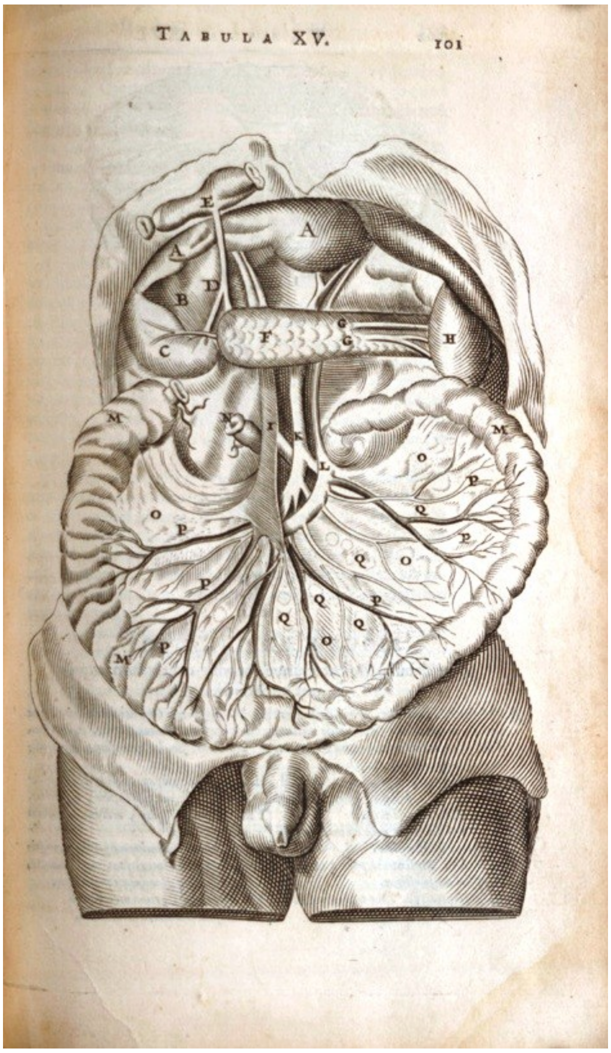

Fig 3. Illustration plate from Bartholin’s *Institutiones Anatomicae* showing lymphatic vessels from the mesentery draining into the cisterna chyli. This was a seminal finding as the prevalent theory in those days was that the lymphatics from the mesentery drained into the liver. Image in public domain.

PUBLISHED WORKS IN ANATOMY

Thomas Bartholin was considered the greatest anatomist of his time, a reputation achieved by his teaching but even more by his publishing. His fame across Europe rested more on his literary works than on his scientific achievements (Holck, 1993). His inclination towards communicating his findings is reflected in his own words: “It was my desire not only to find but also to communicate to others what nature has created” (Bartholin, 2015). His most popular work was his anatomical text *Institutiones Anatomicae,* which was widely used across Europe, as is evident from the number of editions and multiple languages in which it was translated (Fig.4). *Institutiones Anatomicae* was first published by Bartholin in 1641: it was largely a revised and updated edition of the text authored by his father, Caspar Bartholin the Elder, first published in 1611. The illustrations included were mostly from published works of Vesalius and Iulius Casserius (1552-1616). Notably the text included the observations made by Harvey regarding the circulatory system (Bartholin, 1645). Bartholin published revised editions of this book in 1645, 1651, 1666 and 1674, and with each edition the quality of the work improved, as new findings were included. In these subsequent editions, Bartholin gradually replaced the older illustrations (representing the Vesalian tradition of being more artistic than scientific) with newer ones, which were more scientific with focus on anatomical details (inspired by the trend followed by Johann Vesling in his *Syntagma Anatomicum*) (Bartholin, 1675). These changes introduced by Bartholin possibly ensured the popularity of the text over a considerable period of time. His first published original work was a monograph on dissecting aneurysm, *Anatomica Aneurysmatis*

Fig 4. Image of the cover page from Bartholin's *Institutiones Anatomicae.* This anatomical treatise was first published in 1641 and because of its popularity across Europe the text was published as multiple revised editions. The above image is from the fifth revised edition of the text which was published in 1674. Image in public domain.

Dissecti Historia, which was published in 1644 (Bartholin, 1662). Between 1654 and 1661, Bartholin published a collection of case histories of unusual anatomical and clinical structures, including descriptions and illustrations of anomalies and normal structures as the *Historarium Anatomicarium Rariorum Centura,* in six volumes (Bartholin, 2015). One such case description presented the clinical picture which was later classified as a congenital syndrome of multiple abnormalities produced by trisomy of chromosome number 13 by Klaus Patau in 1960 (Bartholin, 1654). Presently the condition is referred to as Bartholin-Patau syndrome. It was in *Historarium* that Bartholin first introduced the term 'Ossa wormiana' or 'wormian bones' after his uncle Ole Worm, who was first to make a detailed description of accessory or supernumerary bones present within the cranial sutures and fontanelle in a letter addressed to Bartholin (Ghosh et al., 2016). Bartholin also edited *Acta Medica et Philosophica Hafniensa*, one of the earliest medical journals from 1671 till his death in 1680 (Bartholin, 1675).

COMMUNICATIONS ACKNOWLEDGING FELLOW ANATOMISTS

Bartholin was never shy of giving due recognition to Pecquet, as he acknowledged the importance of Pecquet's findings as precursor and catalyst to his own experiments on the lymphatic system. In 1654, he published a collection of his letters as *Spicilegium Secundum Ex Vasis Lymphaticis* and dedicated the same to Pecquet (Bartholin, 1660). These communications were documented primarily to counter the criticism by French physician Jean Riolan (1580-1657), who was the head of medical faculty at University of Paris, one of the strongholds of Galenic teaching, and hence a harsh critic of the works of Harvey, Pecquet and Bartholin (Suitner, 2016). He never detached himself from scientific advancements related to the circulation system and kept a close watch on findings reported by his contemporaries. He promptly acknowledged the importance of Italian physician Marcello Malpighi's (1628-1694) discovery of the capillaries as the communication between arteries and vein, which Malpighi documented in his text, *De Pulmonibus*, published in 1661 (Ito, 1996). He wrote two letters to Malpighi whereby he endorsed the findings and also recognized that Malpighi's observations were critical in providing the crucial link in Harvey's findings, and it actually helped in presenting the complete picture of the circulatory system. These two celebrated were published in *De Pulmonum Substantia et motu* in 1663 (Bartholin and Malpighi, 1663).

CONCLUSION

Thomas Bartholin was one of the cardinal figures of anatomy in the 17th century. He devoted his life to scientific research in medical sciences and made concerted efforts to share his findings with his contemporaries. Moreover, he ensured that his communications were published so that these could be accessed by future generation of physicians. In that sense, he could be considered a pioneer of modern day scientific writing. Bartholin's experiments contributed to understanding of the anatomical details of the lymphatics and went on to establish lymphatic system as an independent element of human circulation. The contributions of such anatomists were instrumental in the evolution of anatomical sciences and development of modern medicine.

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REFERENCES

AIRD WC (2011) Discovery of the cardiovascular system: from Galen to William Harvey. *J Thromb Haemost*, 9 (suppl 1): 118-129.

AMBROSE CT (2007) Rudbeck's complaint: a 17th-century Latin letter relating to basic immunology. *Scand J Immunol*, 66: 486-493.

ANDROUTSOS G, KARAMANOU M, STEFANADIS C (2012) William Harvey (1578-1657): discoverer of blood circulation. *Hellenic J Cardiol*, 53: 6-9.

ARRÁEZ-AYBAR LA, NAVIA-ÁLVAREZ P, FUENTES-REDONDO T, BUENO-LÓPEZ JL (2015) Thomas Willis, a pioneer in translational research in anatomy (on the 350th anniversary of Cerebri anatome). *J Anat*, 226: 289-300.

BARTHOLIN T (1645) Institutiones Anatomicae. 2nd Ed. Franciscum Hackium, Leiden.

BARTHOLIN T (1654) Historarium anatomicarum rariorum centuria I et II. The Adrianus Vlacq, The Hague. pp 326.

BARTHOLIN T (1660) Spicilegium ex vasis lymphatics. Petrum vanden Berge, Amstelodamum.

BARTHOLIN T (1662) Thomae Bartholini Cista Medica Hafniensis. Mathiae Godiccheni, Hafniae.

BARTHOLIN T (1675) Thomae Bartholini Acta medica & philosophica hafniensa anni 1673. Sumptibus Petri Hauboldi, Hafniae, pp 376.

BARTHOLIN T (2015) The Anatomy House in Copenhagen. Niels W. Brunn (ed). Museum Tusculanum Press, Copenhagen, pp 224.

BARTHOLIN T, MALPIGHI M (1663) De pulmonum substantia & motu diatribe. Henrici Godiani, Hafniae.

BEHNKE O (1980) Review of the history of the University of Copenhagen and the Faculty of Medicine. *Dan Med Bull*, 27 (suppll 1): 1-4.

CHICKLY B (1997) Who discovered the lymphatic system. *Lymphology*, 30: 186-193.

CUNNINGHAM A (1997) The Anatomical Renaissance: the resurrection of the anatomical projects of the ancients. Scholar Press, pp 283.

ELMAGHAWRY M, ZANATTA A, ZAMPIERI F (2014) The discovery of pulmonary circulation: From Imhotep to William Harvey. *Glob Cardiol Sci Pract*, 2014: 103-116.

ERIKSSON G (2004) Olaus Rudbeck as scientist and professor of medicine. *Sven Med Tidskr*, 8: 39-44.

GHOSH SK (2014) Johann Vesling (1598-1649): Seventeenth century anatomist of Padua and his Syntagma Anatomicum. *Clin Anat*, 27: 1122-1127.

GHOSH SK (2015) Evolution of illustrations in anatomy: a study from the classical period in Europe to modern times. *Anat Sci Educ*, 8: 175-188.

GHOSH SK (2016) Caspar Bauhin (1560-1624): Swiss anatomist and reformer of anatomical nomenclature. *Ital J Anat Embryol*, 121: 159-164.

GHOSH SK (2016) Cadaveric dissection as an educational tool for anatomical sciences in the 21st century. *Anat Sci Educ*, [Epub ahead of print] doi: 10.1002/ase.1649.

GHOSH SK, BISWAS S, SHARMA S, CHAKRABORTY S (2016) An anatomical study of wormian bones from the eastern part of India: is genetic influence a primary determinant of their morphogenesis. *Anat Sci Int*, [Epub ahead of print] doi: 10.1007/s 12565-016-0342-1.

GRELL OP (1993) Medicine and the Reformation. Psychology Press, pp 197.

GRENDLER PF (2004) The Universities of the Renaissance and Reformation. *Renaiss Q*, 57: 1-42.

HILL RV (2007) The contributions of the Bartholin family to the study and practice of clinical anatomy. *Clin Anat*, 20: 113-115.

HOLCK P (1993) The Bartholinian era-anatomy at the time of Christian IV. *Tidsskr Nor Laegeforen*, 113: 3694-3696.

ITO K (1996) Marcello Malpighi's theory of medicine. *Nihon Ishigaku Zasshi*, 42: 49-59.

JOUTSIVUO T (1997) Vesalius and De humani corporis fabrica: Galen's errors and the change of anatomy in the sixteenth century. *Hippokrates (Helsinki)*, 1997: 98 -112.

KARAMANOU M, STEFANADIS C, TSOUCALAS G, LAIOS K, ANDROUTSOS G (2015) Galen's (130-201 AD) conceptions of the heart. *Hellenic J Cardiol*, 56: 197-200.

LOUKAS M, BELLARY S, KUKLINSKI M, FERRAUIOLA J, YADAV A, SHOJA MM, SHAFFER K, TUBBS RS (2011) The lymphatic system: A historical perspective. *Clin Anat*, 24: 807-816.

LUBITZ SA (2004) Early reactions to Harvey's circulation theory: the impact on medicine. *Mt Sinai J Med*, 71: 274-280.

MØNSTER-KJAER I (2009) Thomas Bartholin, theological anatomy in the 17th century-religion and science in Danish history of Medicine. *Dan Medicinhist Arbog*, 37: 9-19.

PORTER IH (1963) Thomas Bartholin (1616-80) and Niels Steensen (1638-86) –Master and pupil. *Med Hist*, 7: 99-125.

PORZIONATO A, MACCHI V, STECCO C, PARENTI A, DE CARO R (2012) The anatomical school of Padua. *Anat Rec (Hoboken)*, 295: 902-916.

PORZIONATO A, MACCHI V, DE CARO R (2013) The role of Caspar Bartholin the Elder in the evolution of the terminology of the cranial nerves. *Ann Anat*, 195: 28-31.

RÉGNIER C (1999) Jean Pecquet (1622-1674) and his cistern. *Rev Prat*, 49: 125-128.

RHODES P (1957) The Bartholin Family. *BJOG*, 64: 741 -743.

RIBATTI D (2009) William Harvey and the discovery of the circulation of the blood. *J Angiogenes Res*, 1: 3.

SUITNER R (2016) Radical reformation and medicine in late Renaissance: The case of the University of Padua. *Nuncius*, 31: 11-31.

SUY R, THOMIS S, FOURNEAU I (2016) The discovery of the lymphatics in the seventeenth century. Part iii: the dethroning of the liver. *Acta Chir Belg*, 116: 390-397.

TUBBS RS, LINGANNA S, LOUKAS M (2007) Jacobus Sylvius (1478-1555): Physician, teacher and anatomist. *Clin Anat*, 20: 868-870.