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# WHO DISCOVERED THE LYMPHATIC SYSTEM?*

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*ABSTRACT*

*The 17th century saw several emerging and almost simultaneous discoveries in the field of lymphology by Asselli, Pecquet, Bartholin and possibly Joliffe. However, Olof Rudbeck (1630-1708) of Sweden, a true scientific genius, who mastered botany, chemistry, physics, mathematics, astronomy, music, drawing, architecture and engineering, and became the Rector of the Faculty of Upsala, was probably the first anatomist to consider correctly the lymphatic circulation as an integrated system of the whole body.*

The discovery of the lymphatic system came comparatively late in the history of medicine, probably because of the transparency of lymph and the difficulty of seeing lymphatic vessels during gross dissections. Whereas many ancient civilizations identified some components of the lymphatic system including the chyliferous vessels, lymph nodes and the larger lymph vessels, none conceived of the lymphatic system as an extensive vascular network. Traditional Chinese medicine alludes to a global liquid circulation. These descriptions are likely more "energetic" than precisely physiological. They define the circulation of the "water element" through the kidney (Chen) and bladder meridian (Pang Kouang). The liquids of the body (Jinye), as opposed to the blood (Xue), take a controversial trajectory throughout the twelve main meridians of the body. Similarly, in ancient medicine of India (Ayurveda), the concept of "Raja" that may be translated as "interstitial liquid" or lymph simply represented one of seven "Dathus", or systems of the body, that underlie disease states. In ancient Egypt, which was to influence the anatomical concepts of the Greek civilization, the heart (Haty) contained liquid and "Metou" as vessels transported and distributed organic substances namely, water, air, blood, mucus, saliva and feces throughout the body (1-5).

The Greeks surely discovered some components of the lymphatic system. Thus, Hippocrates (460-377 B.C.) spoke of "white blood" and used, for the first time, the expression "chyle" and defined a "lymphatic temperament" (6-9). Aristotle (384-322 B.C.) later identified structures containing transparent fluid termed "sanies." Probably the first insight into lymphatics emanated from Alexandria by the illustrious physicians Herophilus and Erasistratus (10-13). Herophilus (335-280 B.C.) coined the word duodenum ("long as 12 fingers"), the prostate ("in front of the bladder"), and discovered intracranial cisternae. He also noted the existence of mesenteric lymph nodes and "milky veins" (lacteals). He wrote: "For ... [Nature] has made, in the whole of the mesentery, peculiar veins, destined for the nourishment of the intestines ... these veins

*Laureat of the Medical Faculty of Paris. This article is partly excerpted from "The Discovery of the Lymphatic Sytem and of Manual Lymph Drainage" that received a medal from the Medical Faculty of Paris VI, France.


*Fig. 1. Portrait of the learned abbey Pierre Gassendi who only 12 years after Asselli's discovery confirmed the presence of "white veins" in the mesentery of man.*

terminate in certain glandular bodies, whilst all the rest are carried upwards to the portae" (14,15).

Erasistratus of Chios (310-250 B.C.), sometimes referred to as the "father of modern physiology," dissected many cadavers. He concluded that food stuffs were digested and fragmented into numerous droplets termed "chyle" and thought that the chyliferous vessels transported alternatively air and milk. Cited by Galen, he wrote: "We may see arteries, on suckling kids [goats], full of milk." These arteries were called lacteals ("ductus lactei").

Whereas the illustrious Galen of Pergamon (131-201 A.D.), did not discover the lymphatic network, he brought forth concepts that were considered immutable for over 1400 years. He recognized that arteries and veins were different structures, that these vessels carried blood and not air, but he erroneously proposed that the adult liver was a blood-forming organ and transformed nutrients into blood.

During the European Renaissance, Charles Estienne (1504-1564) in France identified mesenteric lymph nodes (Wickersheimer), Nicolas Massa of Venice (1532-1569) observed lymphatic vessels of the kidneys, and another Italian, Bartolomeo Eustachius, in 1563 described the thoracic duct of a horse and its termination in the left subclavian vein, naming it the "Vena alba thoracis" (De Vena sive pari) (16). Eustachius failed to appreciate the meaning and the function of this "vein" because he did not locate its subdiaphragmatic origin.

The historical rediscovery of the mesenteric vessels and the first official differentiation between lymphatics (chyliferous vessels) and veins was made in 1622 by the Italian physician/surgeon, Gasparo Asselli (1581-1626) when by chance he observed the "venae albae et lacteae" of a well-fed dog. He later confirmed the observation in cats, sheep, calves, cows, horses and goats, but, of interest, not in humans. Asselli never questioned Galen's misconception of the blood forming role of the liver and also thought that chyliferous vessels terminated in the "pancreas glandulosum" or "pancreas of Asselli." His single publication "De lactibus sine lacteis venis. Novo invento" was published posthumously in 1627, just one year before the historical publication of William Harvey's "De Motu cordis." "De lactibus sine lacteis venis" was probably the first anatomy book with color prints (17-19).

In 1624, Johann Vesling (1598-1649) recognized lymphatic vessels in humans and the book "Anatomy of the Body of Man," published in 1653 after his death, showed the first illustrations of human lymphatics (20,21). Twelve years after Asselli's discovery, Nicolas Claude Fabrice of Peiresc, Principal Court Judge in Aix en Provence (south France), confirmed the presence of lymphatics in man. With the help of the learned abbey Pierre Gassendi *(Fig. 1)*, they opened a body of a prisoner, who had recently eaten, one and a half hours after his hanging; they found, as expected in the mesentery, "white veins."

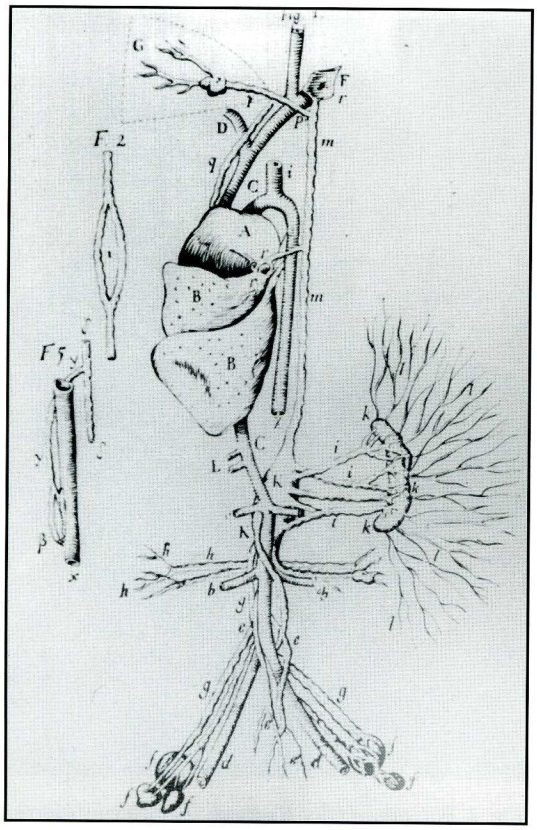
In 1629, several years before Jean Pecquet's famous discoveries (vide infra), Jacques Mentel of France (1599-1671), based on vivisection of dogs, reported that mesenteric lacteals terminated in the thoracic duct before gaining access to the bloodstream.

John Pecquet (1622-1674) from Dieppe (France) described in 1647 the "receptaculum chyli (cisterna chyli)" or "receptaculum Pecquet" in a canine (22-27). At the time he was just 25 years old, and in 1651, before he even finished medical studies, he published "Experimenta Nova Anatomica." He clearly illustrated the continuum of the chyliferous vessels with the cisterna chyli, the thoracic duct and the communication with the left subclavian vein, and recognized the lymphatic link to large mesenteric nodes. He also suggested the importance of respiration in the circulation of "chyle" and described the presence of valves within lymphatics. Pecquet was unable to demonstrate continuation of mesenteric lacteals with the liver (in contrast to mesenteric veins) and thereby began to challenge the ideas of Galen concerning the function of the liver.

Olof (Olaus in Latin) Rudbeck (1630-1708) was a true scientific genius having mastered botany, chemistry, physics, mathematics, astronomy, music, drawing, architecture and engineering, and ultimately became the Rector of the Faculty of Upsala. He was probably the first anatomist to recognize the lymphatic system as part of the circulation *(Fig. 2)*. Born in the little town of Vasteras in Sweden, Olof was the son of Johannes Rudbeck, the bishop of King Gustav Adolph, and Professor of Anatomy at the University of Upsala (28,29). At the University in 1648, Rudbeck was a brilliant and independent student. It was said that he didn't just passively receive information but rechecked and verified everything on his own initiative. His teacher of physiology was the renowned Neils Stensen (Steno or Stenius).

In 1650, at the age of 20 years, Rudbeck watched the preparation of a newly slaughtered calf. When the heart was removed, Olof saw white liquid dripping from the superior vena cava, and when he searched for the origin of this fluid, he discovered the thoracic duct. He dissected this duct retrograde until he observed a slight dilatation that he termed "saccus lacteus" or "vesicula chyli." Rudbeck made this discovery independent of the work of Pecquet, Mentel and Vesling. During the ensuing two years, Rudbeck continued vivisections and defined the continuation of the lacteals, vesicula chyli and the thoracic duct terminating in the central veins of the neck. He performed more than 400 animal dissections including cats, dogs, calves, sheep, goats and wolves. He termed these vessels "vasa serosa" and "ductus serosi" because they carried not only chyle but also straw-colored liquid. He emulated the physiologic techniques of Harvey using strategically placed ligatures and came to understand that

*Fig. 2. Portrait of Olof Rudbeck (painting by Martin Mitjens) who was the first to recognize the lymphatic system as part of the circulation.*



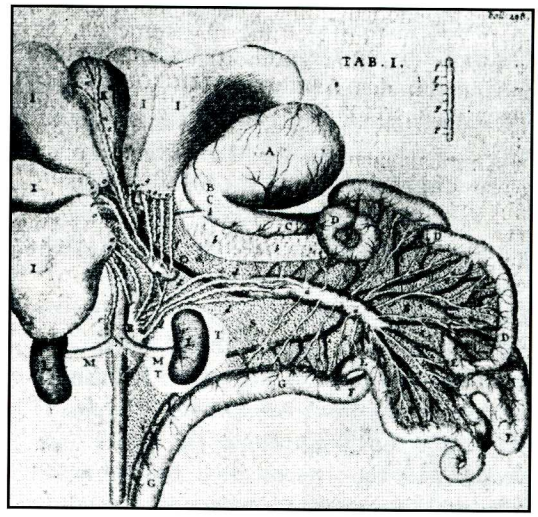



*Fig. 3. Rudbeck's drawing of the lymphatics of the liver, the lacteals, cisterna chyli and thoracic duct (1659) taken from P. Bartels "Das Lymphgefässsystem" Verlag von Gustav Fischer (1909).*

the lymphatic network is a system of closed vessels similar to the arteries and veins. Later, he found lymphatics of the liver and their retrograde connection with the vesicula chyli and lymphatic drainage of the colon, rectum and esophagus, the lymphatics of the spermatic cord, lungs, abdominal wall and around the crural vein and later within the chest *(Fig. 3)*. He clarified the existence of lymphatics throughout the body, their connections with lymph glands and their termination in central (thoracic) ducts and finally in the jugular subclavian veins of the neck. With the ligature technique, Rudbeck unequivocally substantiated that lymph flowed along the portal vein but away from the liver, and probably was the first to refute the blood-forming role of the liver, against the established dogma of the "divine" Galen.

In April 1652, Queen Christina of Sweden, the "illustrious virgin of Europe," stopped in Upsala, and Stensen asked Olof Rudbeck to demonstrate before the royal court the lymphatics of a dog. Among those present were the Queen's physicians Bromsius, Palmeron, Wullen, and many important personalities from the University of Upsala. Likely also present was Thomas Bartholin, a student. On this occasion, Bromsius informed Rudbeck of the work of Pecquet who had lectured in Stockholm a little earlier. Later Bromsius provided Rudbeck a copy of Pecquet's book.

In 1652, one month after this demonstration, Rudbeck submitted his medical thesis "De circulatione sanguinis." He was then only 22 years old, but he dared to write in opposition to Galen's teaching, "An Hepar

sit sanguificationis organum? Negatur." Approximately 14 months later, Rudbeck published the discoveries concerning the "vasa serosa" in a 48-page book entitled, "Nova Exercitatio Anatomica, Exhibens Ductus Hepaticos Aquosos, et Vasa Glandularum Serosa, nunc Primum Inventa, Aeneisque Figuris Delineata" or "New Anatomical Investigation demonstrating the Aqueous Efferent Ducts of the Liver and the Serous Vessels of the Gland, Now for the First Time Discovered and Described with Illustrations" (30,31).

In a "dedicatory Epistle" he explained that "the glands of the body draw out from the blood a serous liquid like a residue; by what means this is done, however, and [by] what channels they then rid themselves of the fluid, was obscure: fortune has revealed this to me. For glands situated near the crural veins, the sides of the heart, the esophagus, and the mammary veins, carry a water liquid to the chylous ducts by virtue of certain vessels."

In the first chapter, he explained using the physiologic technique of Harvey, "when I placed a ligature around the portal vein and the bile duct, sometimes ducts (lymphatic) became visible, distinctly engorged between the liver and the ligature, but collapsed below the latter." In the second chapter, Rudbeck noted the existence of "numerous valves which open in an outward direction." In chapter nine, he raised "the significance of this discovery for medical practice," in discussing the etiology of edema and ascites. He wrote, "I think it not unlikely that pathological changes in these vessels may give rise to disease and particularly to ascites if they become obstructed by viscid, thick or mucoid fluid. Their occlusion causes swelling of the glands.... The swelling increases daily as long as the vessels can stand the pressure." And later "... any glands which have these vessels may cause a watery dropsy."

After this work was published, Rudbeck traveled in Europe, and it was in a shop in Hamburg, Germany (1653) that he came across the book of the Danish anatomist


*Fig. 4. Portrait of Thomas Bartholin who coined the term "vasa lymphatica." Before that, lymphatics were named "vasa serosa," "ductus serosi," or simply the "aqueous vessels." Ultimately he engaged in a bitter dispute with Rudbeck over priorities of discoveries about the lymphatic circulation.*

Thomas Bartholin entitled "Vasa lymphatica, nuper Hafniae in animantibus inventa, et hepatis exsequiae." Rudbeck, known for having a bad temper, immediately considered Bartholin's work as plagarism, and an atmosphere of violent animosity rapidly developed between the two men (32).

Thomas Bartholin *(Fig. 4)* was a second son of the noted Caspar Bartholin the first, whose respected atlas "Anatomicae Institutiones" was continued by Thomas (33). Bartholin traveled widely in Europe and in 1644 published "De Unicornu" in which he described the application of unicorn horns for headaches. After receiving a medical

doctorate in 1645, he published a second version of his father's "Anatomica" (1647) in collaboration with Sylvius. Jean Riolan (1577-1657), a highly respected authority in anatomy at the University of Paris, was a vigorous opponent of modernity. He vehemently opposed the discoveries of Asselli, Harvey and Rudbeck particularly as they refuted established dogma promulgated by Galen. Riolan specifically reproached Bartholin for introducing in "Anatomica" the discoveries of other anatomists without citing sources and for not initiating original research (34-36).

Ironically, Bartholin supported Galen concerning the role of the liver. Moreover, he believed that part of chyle drained towards the liver and part to the thoracic duct although he wrote to a friend (1652) that he hesitated to radically transform the theories of the "Ancients."

Around 1652 or 1653, as Rudbeck had previously demonstrated, Bartholin came to realize that periportal lymph in contrast to portal blood carries fluid away from the liver, and he probably understood that the "aqueous vessels" were part of the same system as the lacteals. Bartholin designated these vessels "vasa lymphatica" and the fluid that they carried "lympha" which means limpid, clear, or transparent. He tried to confirm his discoveries in humans but only after dissecting eight cadavers (1654) did Bartholin finally visualize lymphatics in man.

Bartholin hurried to publish his results in May 1653 (37). He first put the date of February 28 in his publication but in the next edition, Bartholin added "anno 1652." As soon as Rudbeck saw Bartholin's book, Rudbeck maintained that the publication year was 1653 (the same date as publication of the book) and not 1652 as Bartholin claimed in the second edition. Bartholin did not reply personally to the dispute but rather sent his student Bogdanus to defend him (38,39). This confrontation between Rudbeck and Bartholin lasted until at least 1661 (40-47).

Historical events led to popularization of

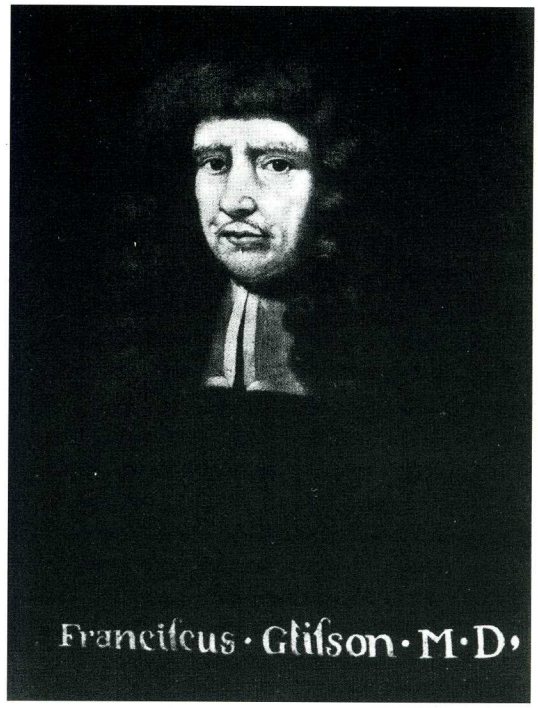



*Fig. 5. Portrait of Francis Glisson, the noted hepatologist, who maintained that his student Joliffe recognized the circulation of lymph before Rudbeck and Bartholin. This claim seems dubious.*

the word "lympha" from Bartholin probably because he was an important figure who frequented the royal court. Moreover, his discoveries had a large following and his students, namely Bogdanus and Moinichen, traveled widely in Europe demonstrating the "vasa lymphatica." Whether Bartholin carried out his experiments in 1652 or 1653, it seems that priority of the discovery of the lymphatic circulation should be attributed to Rudbeck because, at the time, presentation before the Queen of Sweden and physicians of the court was equivalent to official recognition and, in that sense, formal publication.

Rudbeck returned to Upsala in 1654. In 1661, at the age of 31 years, he became Rector of the University of Upsala and remained a leading authority for many years. His interests moved into botany and with the help of his children and students he illus-

trated more than 6000 accurate botanical drawings, some of which were published in the first volumes of his never completed "Campus Elysii." Rudbeck had wide interests and activities. He expanded the University, enlarged the library, erected buildings, and elaborated a water system. Known as the leading engineer in his country, Rudbeck even built by himself 50 compasses for the Swedish navy during the time of the war.

Near the end of his life, Rudbeck's attention was drawn towards possible mythological origins of Sweden as "the Atlanticus." In three enormous volumes, published between 1679 and 1702, the first of 891 pages, he tried to demonstrate that the origin of Sweden itself was directly related to the Greek story of Atlantis.

A final controversy surrounding the discovery of the lymphatic system is the alleged contribution of Georges Joliffe or Jolivius (1618-1658). In his famed text "de hepate" (1654), Glisson *(Fig. 5)* claims that his student Joliffe discovered as early as 1650 the lymphatic system and the "aqueous humor" present inside its vessels long before Rudbeck and Bartholin and that Joliffe deemed the function of these vessels was to carry "humor" throughout the body (48). It is difficult, however, to confirm and reconcile this attribution because Joliffe's thesis was never published, and he died at a comparatively young age.

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