

Research Article - History of Anatomy and Embryology

## Historical considerations regarding the first descriptions of pancreas' anatomy

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### Abstract

The descriptions of the term “pancreas” as well the macroscopic anatomy of the pancreas throughout Antiquity, Byzantium, Middle Ages and Renaissance are displayed. In particular, the original phrases of famous physicians of that period as regards the anatomy of the pancreas are presented: Hippocrates, Aristotle, Herophilus, Galen, Rufus of Efesus, Julius Pollux, Oribasius, Bartolomeo Eustachio, Andreas Vesalius, Gabriel Fallopius, Johann Georg Wirsung, Francis Glisson, Giovanni Domenico Santorini.

### Key words

Pancreas, anatomy, history.

Hippocrates, the so-called “Father of Medicine” (about 460-375 BC) considered and described the lymph nodes as “glands”. A speculation has been made as regards the awareness of “pancreas” by Hippocrates. In his treatise “About glands” Hippocrates wrote: «Τά δ' ἄλλα οκόσα ἀδένας ἔχει μόνον, οἶον ἔντερα, ἔχει γὰρ καὶ ταῦτα ἀδένας ἐς τὸ ἐπίπλου μείζονας, τρίχας οὐκ ἔχει», which means: “There are other parts of body that contain only glands, such as intestines. Those parts contain great glands into epiploon (omentum), but they do not contain hair” (Mandilaras, 1992). However, that statement is obscure, and it is not certain that such a gland correspond to “pancreas”.

Aristotle (about 384-322 BC), the great Greek philosopher, in his famous treatise entitled “Historia Animalium” stated the following: «Ἐτι ἄλλαι ἀπὸ τῆς μεγάλης φλεβός ἀποσχίζονται, ἡ μὲν ἐπὶ τὸ ἐπίπλου ἡ δ' ἐπὶ τὸ καλούμενον πάγκρεας. Ἀπὸ δε ταύτης πολλαὶ φλέβες διὰ τοῦ μεσεντερίου τείνουσιν. Πάσαι δ' αὐταὶ εἰς μίαν φλέβα μεγάλην τελευτώσιν, παρὰ παντὸ ἔντερον καὶ τὴν κοιλίαν μέχρι τοῦ στομάχου τεταμένην. Καὶ περὶ ταῦτα τὰ μόρια πολλαὶ ἀπ' αὐτῶν σχίζονται φλέβες», which means “Some veins arise from the great vein, one running onto the epiploon and one onto the so-called pancreas. From the great vein numerous veins are directed to the mesentery. All these veins end to a great vein extending from the intestine to the stomach (presumably that vein is the portal vein). And around these anatomical structures many veins are bifurcated” (Mandilaras, 1994). As it is evi-

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dent, Aristotle did not make any particular mention to the structure and function of the pancreas, referring only to the fact that this organ is surrounded by veins that presumably correspond to the superior mesenteric vein and splenic vein. Thus, it is apparent that prior to Herophilus from Chalcedon, Aristotle utilized the word "pancreas". However, it has been stated that the word "pancreas" was popular at the time of Aristotle in the field of zoological study, and has not been authorized as an anatomical term at that time, since the word had been utilized tentatively (Tsuchiya et al., 1997).

It is widely said that the first description of the pancreas is attributed to Herophilus of Chalcedon (about 335-280 BC), the famous anatomist who is considered as the "Father of Anatomy" (Wain et al., 1958; Busnardo et al., 1983). Galen in his treatise entitled "De Semina" mentioned: "The residues pass from the stomach to the bowels; in addition the bile arrives from the liver and from some other glands (presumably the pancreas) located there comes a viscous fluid, similar to saliva. There is a considerable controversy among anatomists regarding these glands, started by Herophilus and Eudemos, and therefore I better close here my discussion" (Kuhn, 1821; Howard, 2002). It is certain that Herophilus and Eudemos did not name the organ and it is not sure whether the term "other glands" is attributed to the pancreas or the mesenteric lymph nodes.

Rufus of Efesus (about 100 AD), a prolific teacher, anatomist and physician, who had the misfortune of being cast in the shadow of Galen, in his work entitled "On the names of the parts of the body" writes as regards the pancreas: "Ἡ δὲ παρὰ τὴν πρῶτην τοῦ εντέρου ἐκφύσιν κειμένη σαρκὲ διαπίμελος καὶ αδενώδης, πάγκρεας" which means: "The first structure (flesh) adjacent to the first portion of the intestine is glandular and is called pancreas". However, there is no Rufus' mention relevant to the structure and potential function of the pancreas.

Galen (about 130-200 AD), the great Greek physician and surgeon, considered that this organ supports the blood vessels, as all lymph nodes were thought to do. Moreover, Galen missed the duct of the pancreas although he discovered both the vein and artery leading to this "spongy flesh" (Siegel, 1968). Galen in his work "On the usefulness of the parts" and in the "Fourth book" stated: "Indeed, in many animals something of a glandular nature is found at this point (anatomical site of pylorus), which increases the constriction, particularly when the stomach exercises its retentive faculty and is actively engaged in digestion, gathering itself together, contracting, and clasping and compressing its contents". It is not clear if the organ of "glandular nature" corresponds to pancreas or other anatomical structure. Daremberg, who was a famous editor and translator of the great works of Galen, considered that presumably the peculiar shape of the pylorus in the ape may be what was meant. In another point of the same work Galen claimed: "...the omentum is attached to the spleen and the part called the pancreas, as well as to the outgrowth (the duodenum) leading to the small intestine, the mesentery, the colon and the curve of the stomach itself" (May, 1968). Moreover, Galen in his work entitled "De venarum arteriarumque dissection" stated: «...καὶ τὸ πάγκρεας, ὅπερ ἐνιοὶ καλλίκρεας ὀνομάζουσι· ἀδὴν δ' ἐστὶν οὗτος ὑποβεβλημένος ταῖς ἐνταῦθα κατασχιζομέναις ἀρτηρίαις καὶ φλεψίν», that means "...and the pancreas which some physicians call kallikreas: that gland is supported and surrounded by bifurcated arteries and veins". In another text of the aforementioned Galen's work, Galen claimed: «...ικανῶς γὰρ αὐτὴ (ἡ φλέβα)

μικράς και πολλάς ἐν τῇ διόδῳ τριχοειδεῖς φλέβας εἰς το πάγκρεας εκφύει», that means "...that vein supply pancreas, with small and numerable capillary veins" (Kuhn, 1821). So, someone may conclude that Galen did not pay any particular attention to the structure as well the function of pancreas. He considered the pancreas as a glandular anatomical structure overlying arteries and veins, which supply and support it.

Julius Pollux, who was a lexicographer and teacher of the second century AD, in his famous treatise called "Onomasticon" wrote as regards the pancreas : "... ιατροῦς δε και αδένας τινάς καλοῦσιν... μάλιστα περὶ βουβώνας τε και μασχάλας και σιαγόνας και μεσεντέριον..." that means : "... physicians call these organs glands... that are located at inguinal, axillary region, jaws and mesentery" (Pollux, 1846). Pollux, precisely as Hippocrates, referred to "glands" in the mesentery which correspond to the lymph nodes of this anatomical region. However, someone may speculate that some of these glands, likely, represent the "pancreas". Oribasius (about 320-390 AD), who was personal physician to the Emperor Julian, in his excellent treatise termed "Collectiones Medicae" provides a well-organized anatomy based on Galen's notes. In that work as regards the pancreas he wrote: "... και διὰ τοῦτο ἡ φύσις αδενώδες τι σῶμα δημιουργήσασα, το καλούμενο πάγκρεας, υπεσώρεσεν ἅμα τα περιέβαλεν (αγγεία και νεύρα) ἐν κύκλῳ... κι ἀρρηκτα διὰ παντός φυλάττεσθαι...", which means "... and for that reason the nature created a glandular body, the so-called pancreas, that surrounds like circle the vessels (superior mesenteric) and nerves... and protects them" (Oribasius, 1556). It is apparent that Oribasius paid attention only to the protective role of the pancreas with respect to the surrounding superior mesenteric vessels and nerves.

Bartolomeo Eustachio (1520-1574 AD) provides us with the first known anatomical drawing of the pancreas demonstrating the posterior surface of a dog's pancreas. That drawing was published in his work "Tabulae Anatomicae" that was edited in 1714 by the physician Giovanni Mario Lancisi with his own explanations (Eustachio, 1728; Singer, 1957). Andreas Vesalius (1514-1564 AD), the great reformer of the Anatomy in Renaissance, in his epic treatise entitled "On the fabric of the human body" published in Basel in 1543 provided the scientific community with a figure where the pancreas is shown as a U-shaped organ within the mesentery. Vesalius wrote: "...in humans it is rather white and reaches to the portal vein and the rami of arteries ... to protect them and to serve as a support for the stomach" (Howard et al., 2002; Vesalius, 1453). Thus, Vesalius accepted the Galen's claim that the pancreas serves as a "bed for the stomach to lie upon" and as a protector for the surrounding vessels. Gabriel Fallopius (1523-1562 AD) who was pupil of Andreas Vesalius and taught anatomy at the University of Padua in his work entitled "Anatomical Observations" published in 1561 stated as regards the pancreas the following: "If there was true (that pancreas protects the stomach), then this organ would be completely useless in animals which do not go about upright, because in them the pancreas lies above the stomach... It (pancreas) is placed beneath (the splenic vein) like a cushion and protects against everything that could squeeze it together (Fallopius, 1561; Beger et al., 2008).

Johann Georg Wirsung (1589-1643 AD) as a medical student and protector to Professor of Anatomy Vesling, on March 2<sup>nd</sup>, 1642, in Padua executed an autopsy on a murderer named Zuane Viaro della Badia who had been hanged the day before. The autopsy was witnessed by two medical students, Thomas Bartholin and Moritz Hoff-

man (McClusky et al., 2002). The autopsy of the criminal was executed privately at San Francesco Hospital that was part of a monastery (Howard et al., 2002). Wirsung did not publish his discovery, however he engraved his discovery on a single copper plate and made approximately seven identical copies, sending them to famous anatomists in Europe expecting their opinion (Beger et al., 2008). In these letters, Wirsung stated that the pancreatic duct perforated the duodenum in a location just nearby to the bile duct. Wirsung was asking the anatomists whether that canal is an artery or a vein: he claimed that he never noted blood within the duct, and the contained fluid dyed the silver probe just as the bile does (McClusky, 2002; Howard et al., 1998). Unfortunately, Wirsung was murdered while entering his house at night on August 1643, presumably as a result of a quarrel over whom was the first to discover a duct. He was killed by a Belgian student, named Giacomo Cambier (Pai, 2002). Rumors existed that period that Vesling, because of jealousy, had something to do with Wirsung's death, rumors that have not been proved (Howard et al., 2002). Moritz Hoffman five years after Wirsung's death claimed that in September 1641, prior to Wirsung's discovery, he noticed such a duct during a dissection undertaken on a turkey. Hoffman never published his findings. Hoffmann stated that Wirsung would never have paid attention to such a duct, if they had not made a conversation about Hoffman's discovery (McClusky et al., 2002). Albrecht von Haller claimed that Hoffman was honored for his discovery by most of the Germans, and every year a feast celebrated his discovery (Howard et al., 2002). It was Johan van Horne (1621-1670), Professor of Surgery and Anatomy at Leiden, who in 1685 honored Wirsung and was the first who attributed Wirsung's primacy in the duct's discovery by applying the name "Wirsung's duct" (Beger et al., 2008). Cecka et al. (2013) have suggested that Zuane Badia, the cadaver in whom Wirsung made his discovery, suffered from chronic pancreatitis, since the main pancreatic duct in healthy pancreas is frequently difficult to find even if we know what we are searching for. On the contrary, in chronic pancreatitis the duct is dilated.

Francis Glisson (1597-1677 AD) was Professor of Physics at Cambridge and one of the great physicians at the seventeenth century, mostly known for his work on liver and rickets (Persaud et al., 2014). Glisson in his famous treatise "Anatomia hepatis" stated for pancreas the following: "Pancreatis quidem temperies videtur humida, laxa, flaccid, et moderate calida; estque vapor illius necessario consimilis, nempe humidus et relaxans. Humor quoque, quem de se emittit, videtur ejusdem temperiei esse, scilicet lenis et lubricus, minimumque adstringens: ut ab illius effluviis parum admodum soliditatis, roboris, aut firmitudinis, partibus vicinis expectandum fit" which means: "Pancreas character is moist, loose, floppy and moderately warm; and due to its similarity (comparison with the liver) it is surely moist and loose. Moreover, the juice that it gives off (pancreatic fluid) seems to be of the same character, mild and fluid, minimally sticky. So that from its secretion only little strength, power and stability should be expected for the adjacent organs" (Glisson, 1654).

The discovery of the accessory pancreatic duct was attributed to Giovanni Domenico Santorini (1681-1737 AD) who was appointed Professor of Anatomy at the Medical College of Venice when he was 22 year old (Kleinerman et al., 2014). Santorini executed several hundred duodenopancreatic dissections with the assistance of magnifying glass. Santorini utilized in his drawings a scale providing the true size of the anatomical structures. Santorini mentioned that the second duct was not a vari-

ant, but a normal finding (Beger et al., 2008; Flati et al., 2002). That normal anatomical element was published in a Santorini's book entitled "Observationes Anatomicae: quibus inventorum plurima, tabularum non modica accessio adjuncta est" that was edited in 1775, 38 years after Santorini's death (Beger et al., 2008). In that treatise Santorini named that duct "superior pancreatic duct" and wrote as regards its anatomy: "the duct... (that) has its small origin from the longitudinal duct... runs into the duodenum, about two fingers above the orifice of the main duct". Prior to Santorini, Frederick Ruysch observed a second duct describing it as anatomical variation (Howard et al., 2002). Furthermore, it has been said that Albrecht von Haller (1708-1777) mentioned the presence of the minor pancreatic duct prior to Santorini's discovery, however he too considered that duct as an anatomical variant (Haller, 1757).

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## References

- Beger H., Warshaw A., Buchler M., Kozarek R., Lerch M., Neoptolemos J., Shiratori K., Whitcomb D. (2008) *The Pancreas: An Integrated Textbook of Basic Science, Medicine, and Surgery*. 2nd edition. Blackwell Publishing, Oxford.
- Busnardo A.C., DiDio L.J., Tidrick R.T., Thomford N.R. (1983) History of the pancreas. *Am. J. Surg.* 146: 539-550.
- Cecka F., Jon B., Kaska M. (2013) Was the Wirsung duct discovery facilitated by intemperate alcohol consumption in 17<sup>th</sup> century Italy? *Pancreatology* 13 suppl.: 542.
- Eustachi B. (1728) *Tabulae Anatomicae. Praefatione, ac notis illustravit Joh. Maria Lancisius. Typis Bartholomei Locatelli, Venetiis.*
- Faloppius G. (1561) *Observationes anatomicae. Apud Marcum Antonium Ulmum, Venetiis.*
- Flati G., Andren-Sandberg A. (2002) Wirsung and Santorini: The men behind the ducts. *Pancreatology* 2: 4-11.
- Glisson F. (1654) *Anatomia hepatis: cui praemittuntur quaedam ad rem anatomicam universe spectantia, et ad calcem operis subjiciuntur nonnulla de lymphae-ductibus nuper repertis. Du-Gardianis, Londini.*
- Haller A. (1757) *Elementa physiologiae corporis humani. Vol. VI, book XXII. Grasset, Bern.*
- Howard J.M., Hess W., Traverso W. (1998) Johann Georg Wirsung (1589-1643) and the pancreatic duct: the prosector of Padua, Italy. *J. Am. Coll. Surg.* 187(2): 201-211.
- Howard J.M., Hess W. (2002) *History of the Pancreas. Mystery of a Hidden Organ.* Kluwer Academic, New York.
- Kleinerman R., John A., Etienne D., Turner B., Shoja M.M., Tubbs R.S., Loukas M. (2014) Giovanni Domenico Santorini (1681-1737): A prominent physician and meticulous anatomist. *Clin. Anat.* 27: 545-547.

- Kuhn D.C.G. (ed). (1821) Galen, Opera Omnia. Vol.22. C. Knobloch, Leipzig.
- May M.T. (1968) Galen on the Usefulness of the Parts of the Body. Cornell University Press, Ithaca.
- Mandilaras B. (Ed.) (1992) Aristotle, Opera Omnia, About Glands. Athens, Kaktos.
- Mandilaras B. (Ed.) (1994) Aristotle, Opera Omnia, About the History of Animals, book C. Athens, Kaktos.
- McClusky D.A., Skandalakis L.J., Colborn G.L., Skandalakis J.E. (2002) Harbinger or hermit? Pancreatic anatomy and surgery through the ages - Part 1. World J. Surg. 26: 1175-1185.
- Oribasius (1556) Collectaneorum artis medicae liber, quo totius corporis humani sectio explicatur, ex Galeni commentariis. Apud Guil. Morelium, Paris.
- Pai S.A. (2002) Our medical past. Death and the doctor. Can. Med. Assoc. J. (CMAJ) 167: 1377-1378.
- Persaud T.V.N., Loukas M., Tubbs R.S. (2014) A History of Human Anatomy. 2nd edn. Charles C. Thomas, Springfield.
- Pollux J., Bekker I. (1846) Onomasticon. Prostat in Libraria Friderici Nicolai, Berolini.
- Rufus of Efesus (1983 edn.) De partibus corporis humani. Duphar Hellas, Athens, Paris.
- Siegel R.E. (1968) Galen's System of Physiology and Medicine. S. Karger, Basel.
- Singer C. (1957) A Short History of Anatomy and Physiology from the Greeks to Harvey. Dover Publications, New York.
- Tsuchiya R., Fujisawa N. (1997) On the etymology of "pancreas". Int. J. Pancreatol. 21: 269-272.
- Vesalius A. (1453) De humani corporis fabrica libri septem. Ex officina Ioannis Oporini, Basileae.
- Wain H. (1958) The Story Behind the Word. Some Interesting Origins of Medical Terms. Charles C. Thomas, Springfield.

Pancreas anatomy. View Media Gallery. Embryology. The pancreas develops as 2 buds (outpouchings) of endoderm from the primitive duodenum at the junction of the foregut and the midgut. The pancreas is prismoid in shape and appears triangular in cut section with superior, inferior, and anterior borders as well as anterosuperior, anteroinferior, and posterior surfaces. On the cut surface of the pancreas at its neck, the main pancreatic duct lies closer to the superior border and the posterior surface. The head of the pancreas lies in the duodenal C loop in front of the inferior vena cava (IVC) and the left renal vein (see the following images). Surgical considerations. The following should be kept in mind when considering surgical intervention in pancreatic disorders His was the first description of the posterior superior pancreaticoduodenal, branch of the gastro-duodenal artery to the posterior arcade. Haller also described the A. pancreatica magna suprema, a vessel which has a veq-frequent occurrence but is perhaps more commonly recognized at present as the dorsal pancreatic artery. The following description of the pattern of arterial blood supply to the pancreas and the statistical analysis of variants in this pattern is based on detailed dissection by the authors of 150 specimens. Exocrine pancreas, the portion of the pancreas that makes and secretes digestive enzymes into the duodenum. This includes acinar and duct cells with associated connective tissue, vessels, and nerves. Figures 1-13 depict the gross anatomy of the pancreas and its relationship to surrounding organs in adults. It is customary to refer to various portions of the pancreas as head, body, and tail. The head lies near the duodenum and the tail extends to the hilum of the spleen. We will adopt the convention that right and left (unqualified) will be used in the first sense in the legends for gross anatomy (indicating the subject's right and left side). Figure 1. The gross anatomy of the human pancreas can vary. Figures 1A and 1B are two normal human pancreases from autopsies of adults.