Progress report

A historical perspective on the discovery of the accessory duct of the pancreas, the ampulla ‘of Vater’ and pancreas divisum

SUMMARY The discovery of the accessory duct of the pancreas is usually ascribed to Giovanni Domenico Santorini (1681–1737), after whom this structure is named. The papilla duodeni (ampulla ‘of Vater’, or papilla ‘of Santorini’) is named after Abraham Vater (1684–1751) or after GD Santorini. Pancreas divisum, a persistence through non-fusion of the embryonic dorsal and ventral pancreas is a relatively common clinical condition, the discovery of which is usually ascribed to Joseph Hyrtl (1810–1894). In this review I report that pancreas divisum, the accessory duct and the papilla duodeni (ampulla ‘of Vater’) had all been observed and the observations published during the 17th century by at least seven anatomists before Santorini, Vater, and Hyrtl. I further suggest, in the light of frequent anatomical misattributions in common usage, that anatomical structures be referred to only by their proper anatomical names.

The human pancreas forms during the seventh week of embryonic development by the fusion of two pancreatic primordia, one dorsal and the other ventral.\(^{1-4}\) Each of these two primordia contains a duct, opening into the duodenum. After fusion, the distal part of the main duct of the pancreas (‘Wirsung’s duct’) is formed from the duct of the ventral pancreas, and its proximal part from the proximal portion of the duct of the dorsal primordium. The distal portion of the embryonic dorsal pancreatic duct often regresses. In many cases, however, this portion persists despite normal fusion of the two primordia, and in these cases there will be an accessory pancreatic duct (‘duct of Santorini’). A fairly common congenital anomaly (up to 5–8% of patients undergoing endoscopic retrograde cholangiopancreatography (ERCP))\(^5\) is the failure of the two primordia to fuse. This condition is known as pancreas divisum, and manifests itself as two ‘independent’ glands with two separate ducts. In these cases therefore, drainage of the larger, dorsal pancreas into the duodenum is entirely through the accessory duct and accessory papilla. Anomalies of the pancreas and its ducts may have clinical importance. For example it has been suggested\(^5\) that pancreas divisum might play a predisposing role in a substantial proportion (up to 25–6%) of otherwise unexplained (for example, in relation to alcohol abuse or cholelithiasis) chronic and relapsing acute pancreatitis. The discovery of pancreas divisum has until now been ascribed to Joseph Hyrtl (1810–1894) who wrote in 1866:\(^6\)

‘... fand sich in der hinteren Wand der Bursa omentalis ein Neben-Pancreas, von der Grösse und Form einer Mandel.’ (. . . there was, in the
posterior wall of the omental bursa, an accessory pancreas, of the size and shape of an almond).

The accessory duct of the pancreas is named after Giovanni Domenico Santorini (1681–1737) who in his Septendecim Tabulae (published posthumously by Michael Girardi in 1775) produced a clear drawing of the pancreas and its accessory duct (Tabula XIII) and a clear description of this duct.

An embryological interpretation of the presence of an accessory duct and of pancreas divisum was not afforded until at least 1812, when Meckel reported that the pancreas arises from the fusion of dorsal and ventral primordia in the embryo. For this reason, early descriptions of cases of pancreas divisum and of the accessory duct often do not make a clear distinction between the two. Although such a distinction could have clinical importance since in pancreas divisum pancreatic drainage may be impaired, this distinction may be of less relevance from the embryological point of view, and a whole gradation of 'penetrance' of pancreatic duct anomalies has been described. From the clinical point of view, the (somewhat arbitrary) criterion for distinction between the two types of anomaly is whether or not the accessory duct and the main duct are in communication.

Early descriptions

Pancreas divisum and the Accessory Duct

The earliest published description of an accessory duct is that of Thomas Wharton (1614–1673) (Fig. 1a), who, in his Adenographia of 1656 states about the pancreas: '... in diversis animalibus plurimum variat. In piscibus aliquibus, ad pennatorum genre, duplex, cum duplicie ductu, ab utroque extremita in unum truncum coeunt...'. (... it is variable in different animals. In some fishes and winged creatures it is double with a double duct, which unite at the other extreme in a single trunk...).

By this time, however, Johan Rhode (1587–1656) (Fig. 1b) had already (1646 and 1647) made his own observations of two cases of patent accessory ducts in Man, but his description was not published until 1661 (Fig. 2): 'XXX. Ductus pancreaticus geminus. An. 1646. 15. Januar. in cadavere mulieris e valetudinario Patavino ductus pancreaticus manifeste geminus in duodenum intestinum migravit. Anni sequentis Januario 24 in virili cadavere idem obvenit'. (15 January, 1646. In a female cadaver from the hospital in Padua, the pancreatic duct was clearly double leading into the duodenum. The next year, on 24 January, I found the same in a male cadaver). This is the earliest description of the accessory duct of the pancreas in man (for biographies of Wirsung and Rhode see references 10 and 11).

In 1664, the Danish anatomist Niels Stensen (Fig. 1c) also reported cases of double pancreatic ducts in birds, and the same year Regnier de Graaf (Fig. 1d) made a similar observation in animals and in man (the following quotation is taken from a contemporary, 1676 English translation): '... There are some animals which have only one single pancreatid duct. Others there are which have it double, and lastly some have three, when the ductus is single; sometimes it enters with the ductus biliarius into the intestinum duodenum, and sometimes a part. When the ductus is
Historical perspective on the pancreas

Fig. 1  (From top, left to right) (a) Thomas Wharton (1614–1673) oil painting by unknown artist c.1650. (b) Johan Rhode (1587–1659) engraving from his De acia dissertatio, 1672. (c) Niels Stensen (1638–1686) oil painting by unknown artist, after an anonymous oil painting in the Clergy House, Schwerin. (d) Regnier de Graaf (1641–1673) engraving by P Pinchard. (e) Frederik Ruysch (1638–1731) aged 86, engraving by I Wandelaar, 1723. (f) Franciscus de le Boë Sylvius (1614–1672) aged 45, engraving by C van Dalen Jr, 1659. (g) Samuel Collins (1618–1710) at age 67, engraving by W Fairthorne from his Systeme of Anatomy, 1685.

(a, printed with permission of the Royal College of Physicians, London, b, c, e, f and g printed with permission from the portraits collection of the Wellcome Institute Library, London; d from the University Library, Cambridge).
duplicate, sometimes one, sometimes both meet together with the ductus biliarius in the intestine. But when the ductus is three-fold sometimes one only, sometimes two and sometimes all three enter into the intestine by the same passage, and also therein lie a contained humour'. . . 'in Men and Dogs we find it sometimes double'. . . 'As often as these two ducts happen in the Animals now cited, for the most part they are conjoined in the Pancreas, so that the one being blown up, the other will swell; yet we find them so constituted in Man, that they are not joyned together although both be extended to the extremity of the Pancreas almost in the same Longitude and Magnitude'. This latter statement makes it plain that Graaf is referring to the accessory duct in what we would now classify as a case of *pancreas divisum*. The following year (1665), Frederik Ruysch (Fig. 1e) made similar observations, but is careful to point out that Graaf had already described the same.

Graaf had received his inspiration from Franciscus de le Boë Sylvius (1614–1672) (Fig. 1f), who in 1679 published his *Opera Medica*, in which he also makes a passing reference to duplicate pancreatic ducts.

In 1685, Samuel Collins (Fig. 1g) published his massive *Systeme of Anatomy . . .* (Fig. 3). Within it are contained detailed descriptions (more than four chapters) of the anatomy of the human pancreas, observed variations in its structure, and cases of pathology. Among them, the following unambiguous description of *pancreas divisum*: 'A man for the most part hath but one Pancreatick Duct, and rarely two, which was discovered in a Woman Dissected in the Colledg Theatre, who had two Pancreas, and two Ducts (inserted into the Duodenum at some little distance) between which in the middle way, the Hepatick Duct was implanted into the first small Gut'. He describes the accessory pancreatic duct thus: 'The Excretory Vessels are numerous, and begin in small Capillaries, . . . and from these Minute Capillaries, do branch themselves and grow greater and greater, as they approach the middle of the Pancreas, where they unite, and concenter for the most part in one common Duct, and rarely in two, and then they are of unequal bigness; the greatest running along the middle, and the smaller a little below, and do both coalesce near the Duodenum . . .'.

The number of publications on the pancreas and its ducts at around this time was such that it astonished some 17th century observers as much as it will the modern anatomist. One author, Johann Nicholaus Pechlin (who wrote under the pseudonym of Janus Leonicenus Veronensis), reacted by publishing, in 1673, a work entitled *Metamorphosis Aesculapii et Apollinis Pancreatrici*, a caricature of the vast proliferation of works on the pancreas, with Wharton, Aselli, Wirsung, Graaf, and Sylvius as his main targets. Graaf’s description of the double pancreatic ducts (the same as I quoted above) is condemned as ‘horribilis cacophonia’, and Wirsung’s, Wharton’s and Aselli’s work as ‘aequivocationes and cacographia’.

**THE PAPILLA DUODENI (AMPULLA ‘OF VATER’)**

The *papilla duodeni* (=hepatopancreatic ampulla, =ampulla ‘of Vater’) is named after Abraham Vater (1684–1751), who published a description of this region in 1720. That Vater was its discoverer has already been disputed, and the honour transferred to GD Santorini himself. According to Velasco-Suarez, the ampulla ‘of Vater’ should be known as
Fig. 3  Title page of Samuel Collins’s A Systeme of Anatomy of 1685, and pages 399 and 400 in Volume I, containing descriptions of the papilla duodenii, of double pancreatic ducts and of a case of pancreas divisum (from the Library of the Anatomy Department, Cambridge).
‘Santorini valves’, because of Santorini’s description.7 As early as 1685, however, Samuel Collins16 already provides a clear description of the ampulla: ‘... the Termination of the Pancreatrick Duct is inserted, about four Fingers below the Pylorus, where a Prominence, or little Teat, may be discovered near the flexure of the Duodenum, about the egress of the Porus Bilarius in Man, and in Dogs at a Fingers breadth distance below the entrance of the Hepatrick Duct (into the Duodenum) into which it is sometimes inserted’. It should be pointed out that Andreas Vesalius had already given an obscure account of this region in 1543.20 Furthermore, Velasco-Suarez himself (albeit somewhat obtusely) acknowledges that Santorini was not the first to have observed the valves in the ampulla: ‘... the valves discovered by Santorini in 1720 and made known by Vesalius in 1543 ...’.19

Comments

Did Santorini know about the observations of the earlier anatomists? One interesting insight into the answer to this question comes from examination of the Bibliotheca Anatomica of Leclerq and Manger (1st ed 1685, 2nd ed 1699),21 a splendid compendium of writings of many contemporary and earlier anatomists. Both editions of the Bibliotheca Anatomica contain references to supernumerary pancreas and to double pancreatic ducts, including some of the works of Wharton, Ruysch, Stensen, and de Graff. (Wharton’s chapters 10 and 11, where he reports his double pancreatic ducts, are not included, but Graaf’s text is included in full, with two pages – pp. 212–213 of the 1699 edition – on the pancreatic ducts). Lorenzo Bellini (1643–1704), probably one of Santorini’s teachers,22 was recommended this book by Marcello Malpighi himself, as evidenced by extant correspondence between the two.22–24 A more bizarre direct link between Santorini and Malpighi is that one of Santorini’s editors, Giorgio Baglivi, performed the necropsy on Malpighi’s own body in 1694.22 Bellini finally obtained a copy of the book in 1699 and was impressed by it. It was in 1699 that the 2nd edition appeared, and at this time Santorini was a medical student (as he received his doctorate two years later). It is very likely, therefore, that Santorini was acquainted with this book in his student years. Furthermore, Santorini’s 1775 editor, M Girardi, makes reference to Graaf’s discovery (ref. 7, p. 150): ‘Quamquam Graaffius, qui accuratio caeteris Spartam hanc excoluisse videtur, duplicis pancreatis ductus ...’. (Although Graaf with exactness and perfection saw the double pancreatic ducts ...). Girardi chose to place this reference to Graaf just before Santorini’s description of the accessory duct, and justifies Santorini’s observations by considering them to be ‘better’ than Graaf’s.

It is worth remembering that the importance assigned to priority is a comparatively recent preoccupation. Questions of plagiarism and priority would have been much less likely to have arisen in the 17th–18th centuries. As it is obvious that by the end of the 17th century pancreas divisum, the papilla duodeni and the accessory pancreatic duct were all well known, it seems a mystery how the observations of these early anatomists have been forgotten and how the discoveries have been misattributed to later anatomists, who not even always had improved upon the detail of the earlier accounts. In the case of Collins’s work, a possible explanation may be found in that his work was only published in English, a language which
continental anatomists were unable to read. For example, in his Histoire de l'Anatomie, Portal\textsuperscript{22} attempts to conceal that he never read the book: Collins (Samuel), Anatomiste Anglois. Systema anatomicum. Lond. 1685, in-fol. Il y a peu de details Anatomiques qui concernent l'homme; l'auteur s'est plus etendu sur l'anatomie des oiseaux et des poissons, dont il a decrit les ecailles et leurs glandes cutanes; il a depeint le trou borgne de la langue, et les papilles nerveuses . . . . (Collins. English Anatomist . . . . There are few anatomical details concerning Man; the author is more interested in the anatomy of birds and fishes, of which he described the scales and their cutaneous glands . . . .) It is less easy to understand why the observations of Wharton, Rhode, Graaf, Stensen, Sylvius, and Ruysch, who did write in Latin, have been forgotten. This is especially puzzling since Santorini's/Girardi's 1775 work,\textsuperscript{7} which is widely quoted does acknowledge Graaf's findings. One reason might be, once again, the language of the texts. Most of the writings of this period are in Latin, and only a few contemporary anatomists are willing to take the trouble to read them.

Conclusions

The foregoing discussion shows that at least seven 17th century anatomists were aware of the existence of an accessory pancreatic duct 'of Santorini' before Santorini's own observations. They were also aware of the anomaly now known as pancreas divisum long before Joseph Hyrtl, who is generally credited with the first description of this condition in 1866. One of these anatomists, Samuel Collins, in 1685, published a clear description of the ampulla 'of Vater' before Vater's own description in 1720. In the light of these observations I suggest that hitherto these structures be referred to only by their proper anatomical names: ductus pancreaticus accessorius (accessory duct of the pancreas), pancreas divisum, pancreas accessorium, ampulla hepatopancreatica (hepatopancreatic ampulla) and papilla duo- deni major and minor, as defined in the Nomina Anatomica.

This review started life as a lecture on the history of pancreas divisum delivered to the International Workshop on Pancreas Divisum in London on 13 December, 1984, and organised by Drs P B Cotton and J Lowes and Mr R C G Russell. I am grateful to Drs Cotton and Lowes for the invitation to attend and for having initiated my interest in this subject. The research I have done would not have been possible without the generous help given by the staff of several libraries: the Anatomy Department, Cambridge, the Cambridge University Library, the Whipple Museum Library (Cambridge); the British Library Reference Division (London), the Wellcome Institute for the History of Medicine Library (London), the Library of the Royal College of Physicians (London). I must also single out the help of Mr W Simons, librarian to the Department of Anatomy, Cambridge, for his enthusiastic help, and that of the Audio-Visual Aids unit in the same department who carried out much of the photographic work for the lecture and this review.

Claudio D Stern

Department of Human Anatomy,
South Parks Road, Oxford OX1 3QX.
Historical perspective on the pancreas

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C D Stern

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