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Review Article

Mesentery — a 'New' organ

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The mesentery is the organ in which all abdominal digestive organs develop, and which maintains these in systemic continuity in adulthood. Interest in the mesentery was rekindled by advancements of Heald and Hohenberger in colorectal surgery. Conventional descriptions hold there are multiple mesenteries centrally connected to the posterior midline. Recent advances first demonstrated that, distal to the duodenojejunal flexure, the mesentery is a continuous collection of tissues. This observation explained how the small and large intestines are centrally connected, and the anatomy of the associated peritoneal landscape. In turn it prompted recategorisation of the mesentery as an organ. Subsequent work demonstrated the mesentery remains continuous throughout development, and that abdominal digestive organs (i.e. liver, spleen, intestine and pancreas) develop either on, or in it. This relationship is retained into adulthood when abdominal digestive organs are directly connected to the mesentery (i.e. they are 'mesenteric' in embryological origin and anatomical position). Recognition of mesenteric continuity identified the mesenteric model of abdominal anatomy according to which all abdominal abdomino-pelvic organs are organised into either a mesenteric or a non-mesenteric domain. This model explains the positional anatomy of all abdominal digestive organs, and associated vasculature. Moreover, it explains the peritoneal landscape and enables differentiation of peritoneum from the mesentery. Increased scientific focus on the mesentery has identified multiple vital or specialised functions. These vary across time and in anatomical location. The following review demonstrates how recent advances related to the mesentery are re-orientating the study of human biology in general and, by extension, clinical practice.

Introduction

The mesentery is the organ in which all abdominal digestive organs develop, and which maintains these in systemic continuity in adulthood (Figure 1). Interest in the mesentery was re-ignited with Heald's demonstration that tumour recurrence following rectal cancer surgery was dramatically decreased if the mesorectum was removed [1]. The mesorectum is a region of the mesentery. Heald's work was the true start of mesenteric-based surgery. This garnered further attention with the development of minimally invasive techniques of surgery (i.e. endoscopy and laparoscopy). Whilst Heald concentrated on the mesorectal extremity of the mesentery, Hohenberger focused on the mesocolic region, and showed that intestinal tumour recurrence was minimised, if the mesocolon was surgically excised intact [2]. Heald and Hohenberger thus prompted a renaissance in the study of the mesentery and abdominal anatomy. Their findings led to work demonstrating that the mesentery below the duodenum (the initial segment of the small intestine) is continuous, and that the large and small intestine are centrally connected to the rest of the body, by the mesentery. As these findings clarified its shape, they marked the true start of the scientific study of the mesentery and led to the proposal it be reclassified an organ [3–13] (Figure 1).

Neither mesenteric continuity, nor direct connection with abdominal digestive organs, can be anticipated from conventional anatomical teaching [14] (Figure 2). The latter holds that there are multiple mesenteries, and that all abdominal digestive organs are individually and centrally connected to

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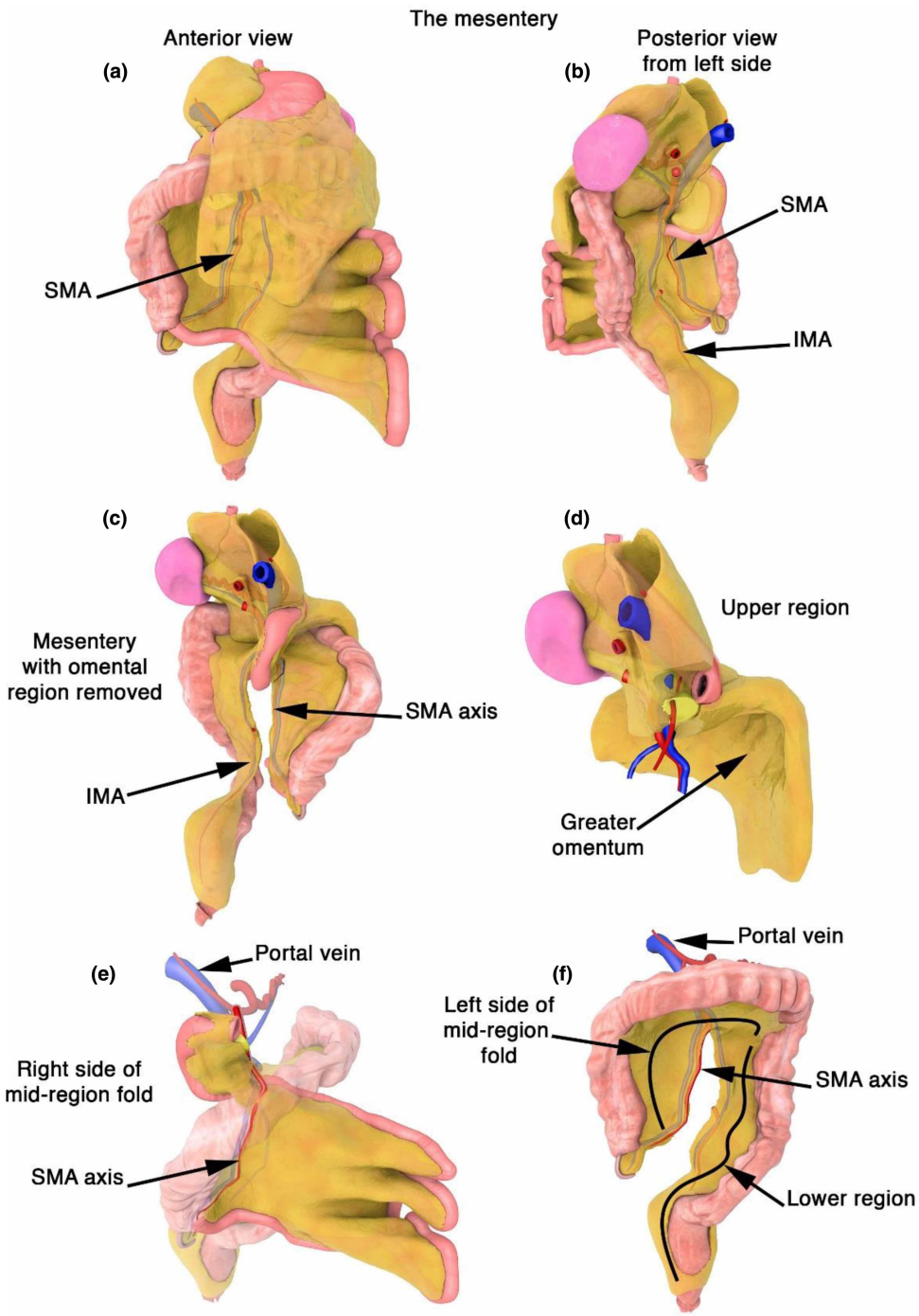

Figure 1. The human adult mesentery.

(**a**) The complete mesentery. (**b**) Posterior view of the complete mesentery. (**c**) Posterior view from the right side of the mesentery with the greater omental component of the upper region removed. (**d**) Upper region of mesentery detached from the remainder of the mesentery. (**e**) Mid and lower region of the mesentery with the upper region removed. The image comprises 'ghosted' and highlighted areas. The highlighted region corresponds to the embryological right side of the mid-region fold. During development the right side is located on the right side of the superior mesenteric artery. A switch then occurs whereby the periphery of the right side ends up positioned to the left of the artery. (**f**) Mid and lower regions of the mesentery. In the adult, the left side of the fold is peripherally on the right of the artery, but centrally on the left. On the left, it corresponds to the flexure. The latter continues distally as the lower region of the mesentery.

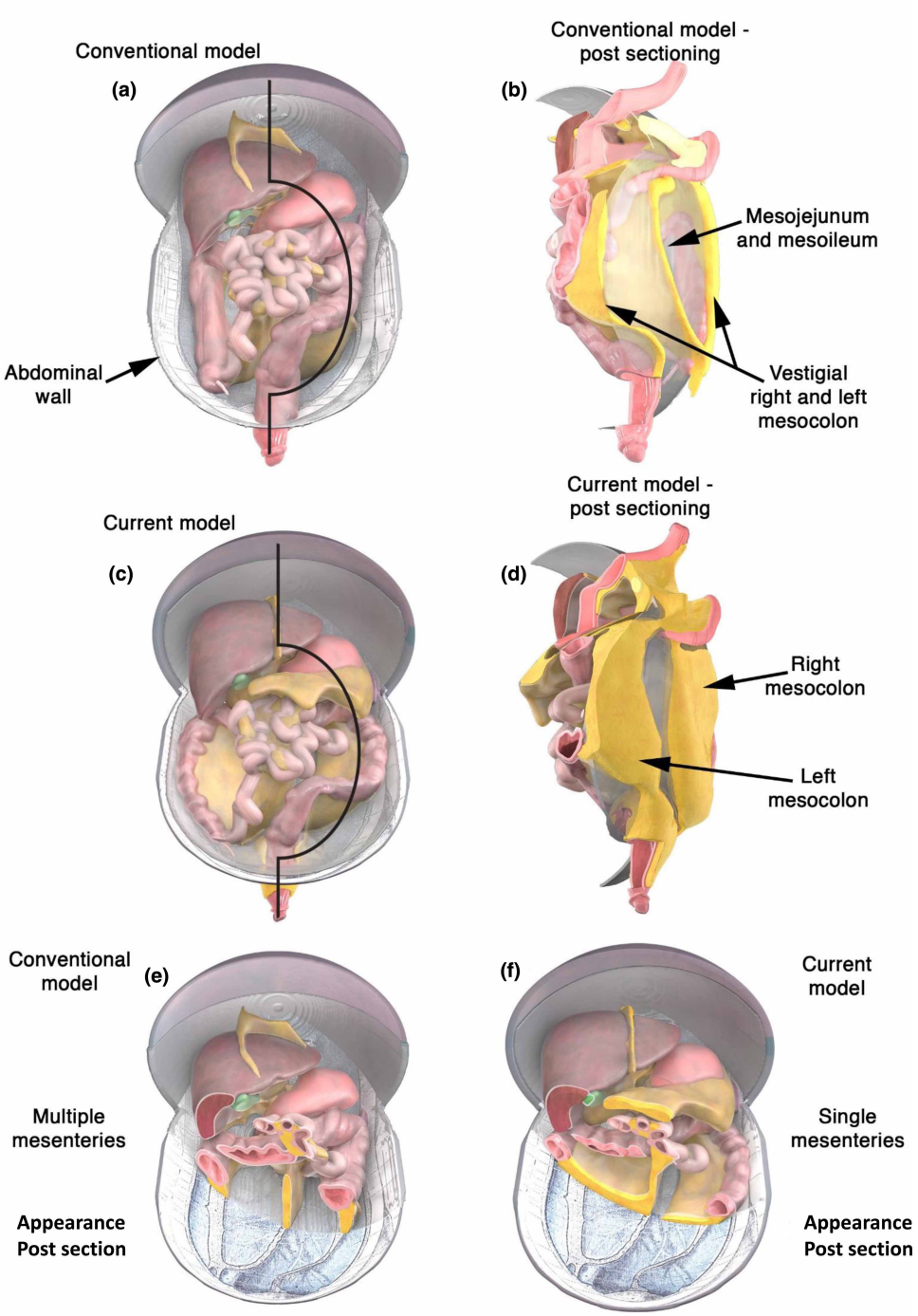

Figure 2. Comparison of conventional and current interpretations of mesenteric anatomy.

(**a**) Digital reconstruction demonstrating the conventional (peritoneal) model of abdominal anatomy in which there are multiple mesenteries. (**b**) View of the conventional model when sectioned along the line in (**a**), and viewed from behind (left to right). Multiple mesenteries as well as vestigial right and left mesocolon are apparent. (**c**) Digital reconstruction demonstrating the current (mesenteric) model of abdominal anatomy. There is one mesentery and all abdominal digestive organs are directly connected to it. (**d**) View of the current model when sectioned along the line in (**c**), and viewed from behind (left to right). Although several regions of the mesentery are apparent, these are different regions of one mesentery. (**e**,**f**) Side by side comparison of conventional (**e**) and current (**f**) models of abdominal anatomy. The models are conceptually 'set' into the abdomen. The background image in each abdomen is the image that provides the start point of conventional descriptions of mesenteric and peritoneal anatomy.

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the rest of the body, by a network of peritoneal derivatives [15–20]. More recently, attention turned to the mesentery above the duodenum with a similar clarification of how upper abdominal organs are centrally connected (Figures 1 and 2). It is now recognised all abdominal digestive organs are mesenteric in embryological origin and that this close relationship is retained into adulthood where the mesentery is their *primary* connection to the body [21]. In the following, we summarise current knowledge regarding the growth, form and function of the mesentery in the human.

Development of the mesentery

The program by which the mesentery develops continues to challenge scientific and clinical communities. As a result, it is important to first clarify how the mesentery develops. A stylised animation has been included to assist in interpreting the description that follows (https://vimeo.com/419869016/b0139b86c9). The animation demonstrates some of the morphological changes the periphery of the mesentery undergoes, during development.

The early mesentery comprises a double layer of the mesothelium (i.e. peritoneum) connected along its full length to the posterior wall of the developing coelom. This composition forms the mainstay of the conventional definition of the mesentery, i.e. the mesentery is a double layer of peritoneum connecting the small intestine to the posterior abdominal wall [22,23]. The conventional model also argues that multiple regions of the mesentery regress during development, leaving gaps between separate mesenteries in the adult [22,23] (Figure 2). Recent recognition of mesenteric continuity (see above) prompted re-appraisal of mesenteric development. This can be achieved by examining the reconstructed foetal mesentery at several time points during development (Figure 3) [24].

Early during development, the mesentery becomes highly cellular. It remains a continuous and composite organ thereafter [25]. These properties mean it can be systematically investigated. A mesenteric fold develops at the mid-region level, subdividing the mesentery into upper (pre-fold), mid (fold) and lower (post-fold) regions (Figure 3a,b) [26]. The upper region indents on the right side and expands leftwards to form a bursa. As it does so, it overlaps the upper and left sides of the central zone of the mid-region fold (Figure 3a–c). In tandem with this, the fold fans out and its sides switch position relative to the superior mesenteric artery (SMA) (Figure 3). After the switch, the side of that fold that is centrally on the right of the vessel, is peripherally on the left of the artery [24]. The side of the fold that is peripherally on the right of the vessel, returns centrally to continue on the left of the vessel, as the splenic flexure [24] (Figure 3f–h). Importantly, the embryological right side of the mid-region fold contains the endodermal forerunner of the duodenum, jejunum and ileum (Figure 3). The embryological left side of the mid-region fold contains the endodermal forerunner of the right and transverse colon (Figure 3). Switching of the position of the sides of the fold thus explains the final positioning of the intestine from the duodenum to the descending colon.

A further, secondary fold also occurs along the right side of the mid-region fold. This is a left to right folding of mesentery and intestine at the junction between developing mesoduodenum and mesojejunum. As a result, the periphery of the mid-region fold (and its derivatives) overlap the front of the central zone (Figure 3h). Once these conformational changes have occurred, the inferior wall of the upper region bursa apposes to the upper surface of the mid-region (Figure 3a–c). Although regional changes in shape continue to occur throughout life, these do not alter the overall foundational shape described above.

As mentioned, the mesentery first comprises two mesothelial cell layers. The space between these, the 'intramesenteric space' [27,28], is quickly and densily populated by cells derived from the posterior abdominal wall (Figure 4a–d). Soon after this event, a demarcation occurs between cells of the mesentery and those of the posterior abdominal wall (Figure 4a–d). Demarcation means the mesentery has separated from the posterior wall. Continuity between both is retained at (1) surface mesothelia (i.e. peritoneum) and (2) vascular trunks (Figure 4a–d). At the zone of demarcation, the mesentery and posterior wall remain apposed. The zone of demarcation (i.e. apposition) of the mesentery and posterior wall then propogates laterally, displacing the mesothelial continuity at the junction between mesentery and abdominal wall (Figure 4a–d) [27]. Propogation occurs to the left of the midline at upper and lower mesenteric regions. At the mid-region level, it progresses centrifugally from the centre of the abdomen to the right iliac fossa (Figure 4e–g). At the completion of propogation, the surface mesothelial continuity that was originally located in the midline, is positionally relegated to the periphery of the mesentery and its conjugate organs. At the periphery, it marks the anatomical limit of the apposition of the mesentery and posterior wall. In the adult, surface mesothelial continuity is represented by a

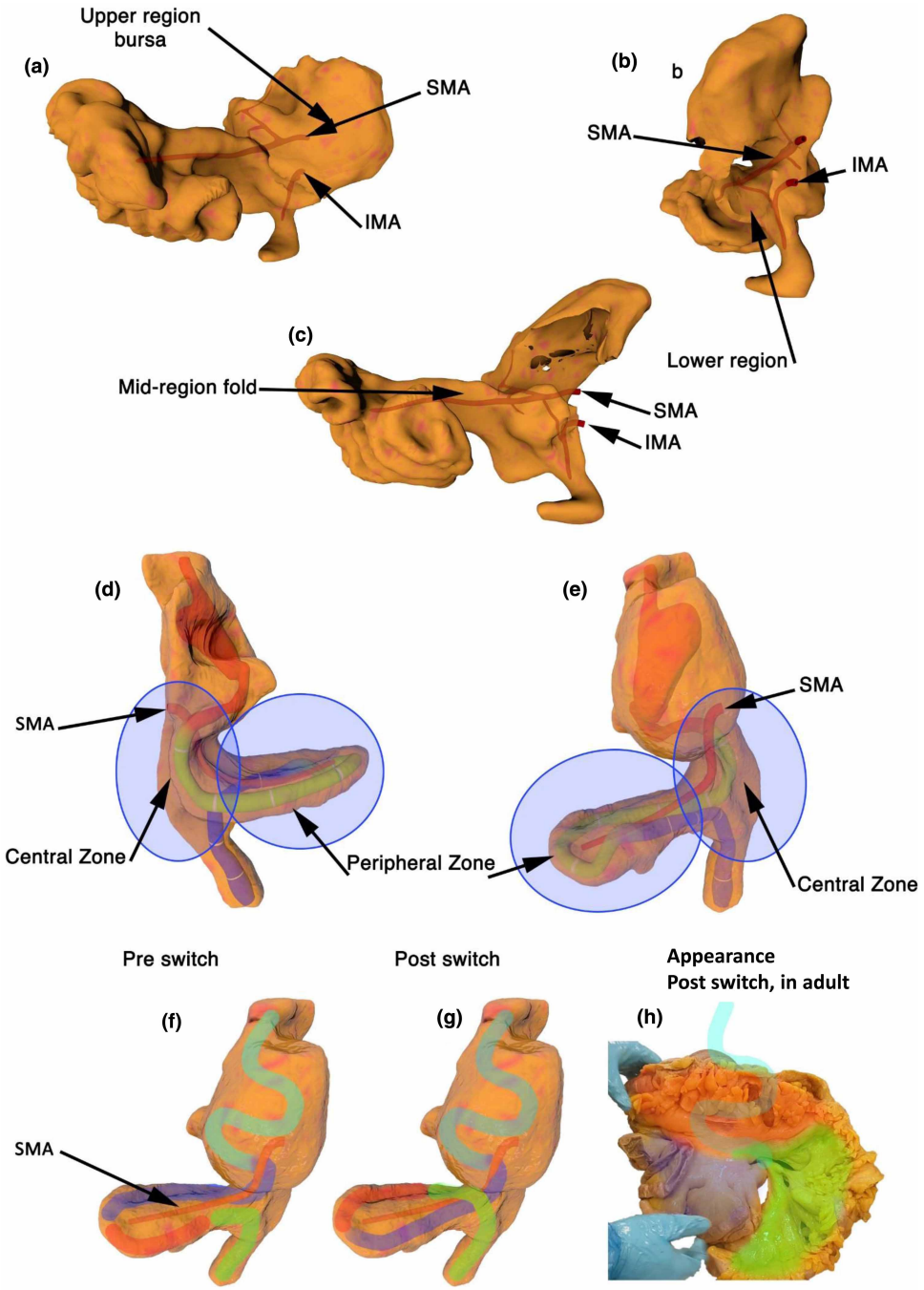

Figure 3. Digital reconstructions of the mesentery during development. Part 1 of 2

Early in development a mid-region fold subdivides the mesentery into upper (**a**) (pre-fold), (**b**) mid (fold) and (**c**) lower (post-fold) regions. The anatomy of the mid-region fold is of considerable importance. The central zone (**d**) of the fold is closest to the posterior abdominal wall. It fans out anteriorly as the peripheral zone (**e**). The mid-region fold is bisected into the right and left sides by the superior mesenteric artery. During subsequent development the upper region expands and overlaps the mid-region fold anteriorly and on the left side (**a**–**c**). These relationships become apparent when the upper region is conceptually hinged upward and off the central zone of the mid-region (**b**,**c**). (**f**) Reconstruction of the early mesentery. Regions of the developing endoderm are colour-coded. The appearance corresponds to that observed prior to switching of the sides of the fold. The endodermal forerunner of the duodenum, jejunum and ileum are coloured blue, and are positioned in the right side of the fold. The endodermal forerunner of the right and transverse colon are coloured red and are positioned in the left side of the fold. (**g**) Appearance of the developing intestine (and by definition the left and right side of the mesenteric fold) after

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Figure 3. Digital reconstructions of the mesentery during development. Part 2 of 2

switching of sidedness between central and peripheral zones. (**h**) Appearance of the periphery of the mesentery in the adult setting. The post-switch position of the sides of the fold are retained into adulthood.

mesothelial bridge (termed 'reflection') between surface mesothelium of the abdominal wall (parietal peritoneum) and surface mesothelium of the mesenteric domain (visceral peritoneum) (Figure 4).

Abdominal digestive organs (i.e. liver, spleen, pancreas and intestine) are mesenteric in embryological origin in so far as they develop within, or on, the developing mesentery (Figure 4) [24]. This topographical relationship is of considerable importance and is retained into adulthood where the mesentery is the primary mechanism by which all abdominal digestive organs are centrally connected [29]. Whilst these organs developed in a midline structure (i.e. the mesentery), propagation led to their being distributed to the left and right of the midline (Figure 4e–g).

Mesenteric anatomy

In the adult human, the mesentery is continuous [4–6,30] and, like the developing mesentery, is subdivided into three regions by a mid-region fold. These are the upper (pre-fold) region, mid (fold) region and lower (post-fold) region [31–33] (Figure 1). The upper region is sac shaped with an anterior wall corresponding to the greater omentum. The mid-region is fold shaped. The fold has right and left sides, as well as central and peripheral zones (Figure 1e,f). The right side of the fold commences centrally on the right of the SMA. It fans out peripherally, but on the left of the SMA (Figure 1e). The left side of the mesenteric fold commences peripherally on the right of the vessel, but returns centrally to the left side of the SMA (Figure 1f). There it (i.e. the mesentery) corresponds to the splenic flexure, and it is where the fold continues distally as the lower region of the mesentery. The latter consists of the left mesocolon, mesosigmoid and mesorectum (Figure 1f) [34].

Normally in the adult setting, the fold-shaped conformation of the mid-region is not readily apparent. This requires clarification. The main (i.e. primary) fold undergoes a further, secondary left to right folding, at the junction between mesoduodenum and mesojejunum (Figures 1f and 3h). As a result of left to right folding, the periphery of the primary fold acquires a diagonal orientation, overlapping the right side of the central zone and right iliac fossa. The right side of the central zone comprises mesoduodenum and the head of the pancreas. The area of the mid-region fold that overlaps the central zone corresponds to the hepatic flexure. Primary and secondary folding thus explain several anatomical realities in the adult. They explain why the hepatic flexural region of the transverse mesocolon overlaps the anterior surface of the duodenum and head of the pancreas (Figures 1f and 3h). They also explain the positioning of the ileocaecal junction (and related structures) in the right iliac fossa.

In the adult, the left side of the central zone is in direct view as the splenic flexure (Figures 1f and 3h). However, the upper surface of the central zone is not apparent due to its apposition to the inferior wall of the upper region (Figure 3a). This relationship is disrupted during bursectomy, when the inferior wall of the upper region is detached from the underlying mesentery. Following bursectomy, the left side of the central zone of the mid-region is fully exposed (Figure 3a) [35].

Given all abdominal digestive organs develop on or in the mesentery [24] the positional anatomy of each, including that of associated vasculature, is explained by their relationship with the mesentery. This is an extremely useful concept as it greatly simplifies abdominal anatomy. For example, the pancreas is positioned in the right side of the central zone of the mid-region (Figure 5a,b). The neck of the pancreas is located in the confluence between the upper and mid-region and the body of the pancreas is located in the posterior wall of the upper region. The inferior mesenteric vein is located in the left mesocolon in which it tracks proximally to the splenic flexure. There, it is positioned at the medial margin of the central zone of the mesenteric fold. It continues proximally to the apex of the central zone to merge with the superior mesenteric vein. The abdominal intestine (i.e. from oesophago-gastric to anorectal junction) follows an overall double spiral trajectory (Figure 5c–e). This is explained by the anatomical positioning of the intestine at the periphery of the mesentery. As the latter follows a double spiral course, so too does the connected intestine (Figure 5c–e).

The mesenteric model of abdominal anatomy

Combining mesenteric-based anatomy proximal and distal to the duodenum leads to a single and general model of abdominal anatomy. The mesenteric model of abdominal anatomy is fundamentally based on

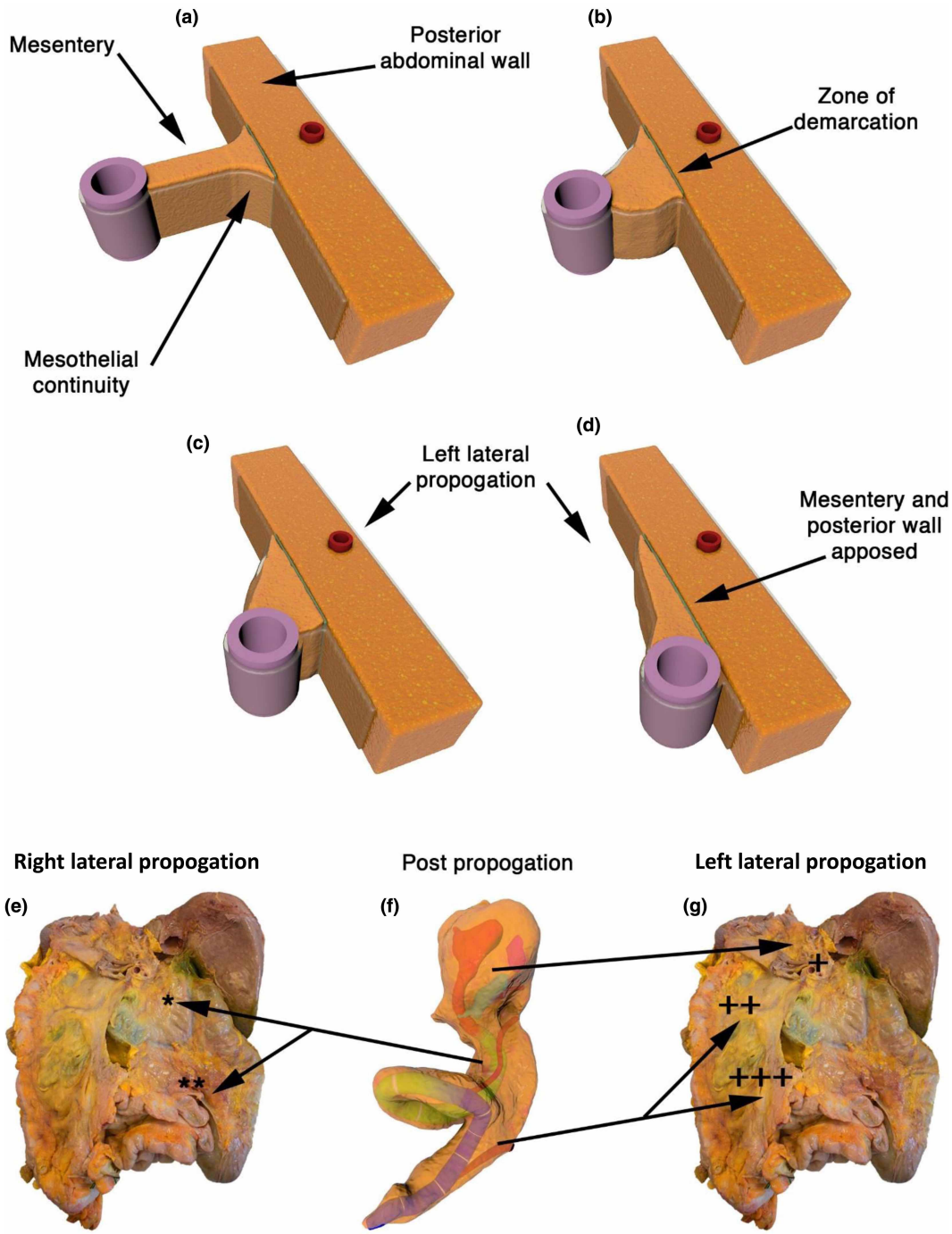

Figure 4. Mesenteric propogation.

(**a**–**d**) Schematic demonstration of the relationship between the mesentery and posterior abdominal wall after demarcation of both. Following demarcation (**b**) the mesentery and posterior abdominal wall appear apposed. Propogation of the zone of demarcation (without disruption of the surface mesothelia), explains how the zone of apposition between mesentery and abdominal wall develops (**c**,**d**). (**e**–**f**) Illustrations demonstrating the direction in which each region of the mesentery appears to propogate. (**e**) The mid-region fold (central and peripheral regions) are represented by the mesoduodenum (*) and right mesocolon (**) and propagate to the right of the midline. (**g**) The upper region (represented by the posterior wall of the upper region (+), left side of the central zone (++) and lower region (+++)) each propagate to the left of the midline. In this manner, organs that are directly connected to the mesentery (i.e. originally midline in position) becoming distributed throughout the three-dimensional space of the abdomen.

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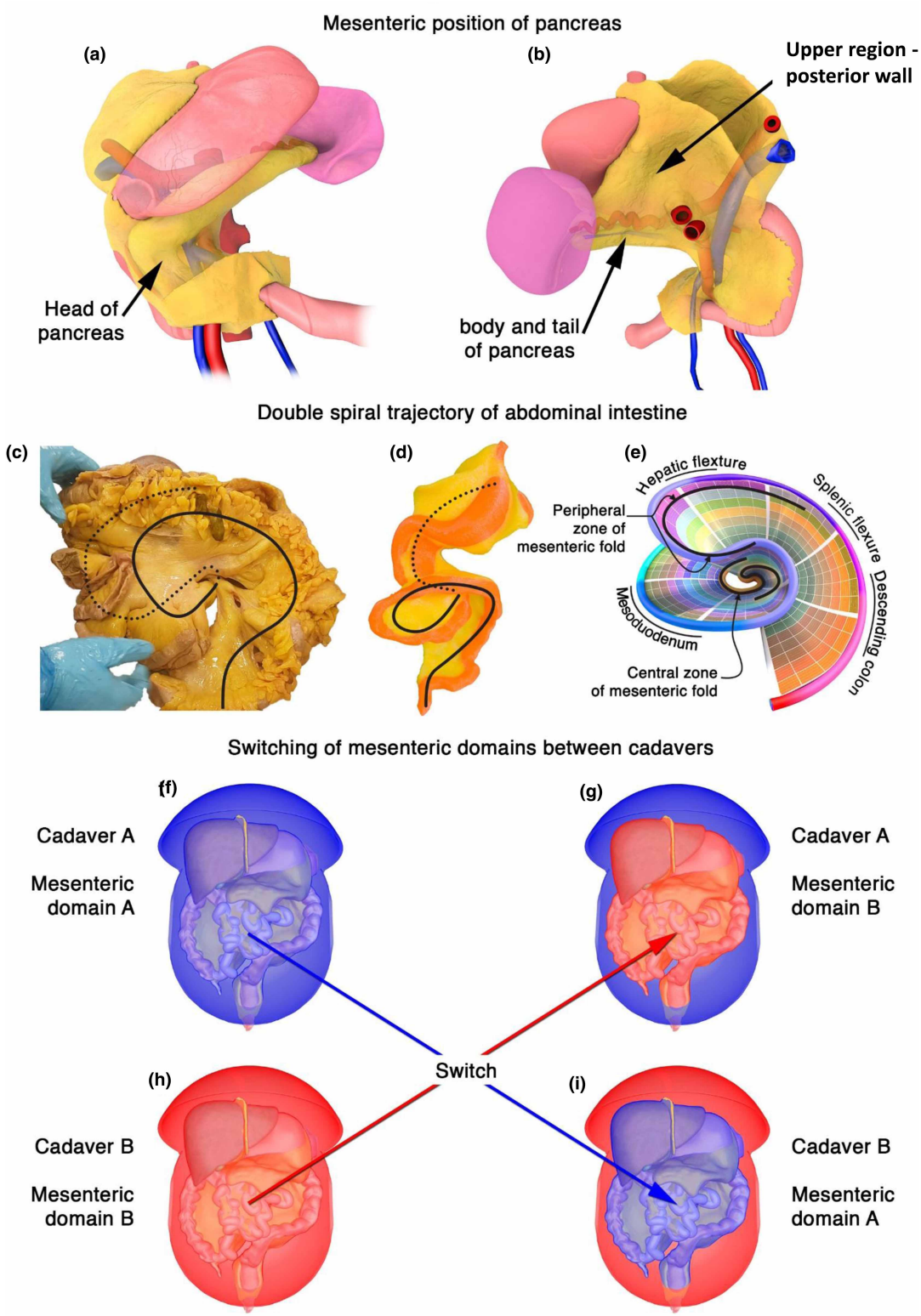

Figure 5. Schematic illustration of the position of the pancreas on the mesentery. Part 1 of 2

(**a**) The head of the pancreas is located at the right side of the central zone of the mid-region. This region of the mesentery, corresponds to the proximal extremity of the mid-region fold and is the anatomical continuity between upper and mid-regions of the mesentery. (**b**) The body and tail of the pancreas are positioned in the posterior wall of the upper region. (**c**–**e**)

Figure 5. Schematic illustration of the position of the pancreas on the mesentery. Part 2 of 2

Illustrations demonstrating the double spiral trajectory of the periphery of the mesentery (and hence the intestine) *in vivo* (**c**), in 3D print format (**d**), and in schematic format (**e**). (**f–i**) Illustrations demonstrating switching of the mesenteric domain between two cadavers. Removal of the mesenteric domain leaves the non-mesenteric domain but switching of mesenteric domains between cadavers fully restores abdominal anatomy in each.

(1) mesenteric continuity and (2) direct connection between mesentery and each abdominal digestive organ [29,32] (Figure 5f–i). Continuity and direct connectivity mean that abdominal digestive organs and mesentery, collectively comprise a single anatomical unit, the 'mesenteric domain of the abdomen (Figure 5f).' The genito-urinary organs are outside of this unit and are positioned on the musculoskeletal mainframe of the abdomen. Collectively, these can be termed 'non-mesenteric domain of the abdomen.' Removal of the mesenteric domain from a cadaver radically alters abdominal anatomy. However, replacing the mesenteric domain, or switching domains between cadavers fully restores abdominal anatomy, albeit with the mesenteric domain of a different cadaver (Figure 5e–i). Comparative studies of several animal species point to mesenteric continuity and direct connectivity with abdominal digestive organs. Collectively, these findings indicate the mesenteric model is not be unique to humans but may also apply across a range of animal species [27,36–38].

The mesenteric model of abdominal anatomy explains the peritoneal landscape [32]. According to the conventional model, the peritoneal landscape is extremely complex being comprised of sacs, recesses, pouches, cavities and fossae (Figure 2) [17–20]. The anatomical boundaries of these are called folds, membranes, reflections and even ligaments [19]. The mesorectum and mesocolon are often described as 'misnomers [39–43].' This approach reflects persistent adherence to the conventional definition of the mesentery (i.e. as a duplicature of the peritoneum) [17–20,27]. Clarification of mesenteric anatomy demonstrates that peritoneum corresponds to (1) surface mesothelium of the non-mesenteric domain (i.e. the parietal peritoneum), (2) surface mesothelial of the mesenteric domain (i.e. the visceral peritoneum) and (3) the mesothelial junction between both (the peritoneal reflection) [27]. The mesenteric model of abdominal anatomy is thus the first to comprehensively reconcile abdominal embryology, anatomy, surgery and radiology [3,9,44].

The mesentery as an organ

The counterargument to the mesentery as an organ normally commences with a common definition of the word organ; an organ is a (somewhat independent) part of the body that performs a vital or specific function [45–47]. The counterargument is also based on the fact that physical linkage of body components, enabling transport or communication and possession of multiple tissues, do not meet requirements for designation as an organ [46,47].

We will address each point in the following. Before doing so, it is important to recap the definition of the mesentery. It is the collection of tissues that supports the development of all abdominal digestive organs and that maintains these in systemic continuity in adulthood [24,32]. Importantly, it is no longer adequate to define the mesentery as 'a duplicature of the peritoneum that connects the small intestine to the posterior abdominal wall.' That definition ignores several key properties of the mesentery (see preceding sections) [30,33,36,37].

The main objection to the idea of the mesentery as an organ relates to its function, and whether that can be described as vital or special. Mesenteric function varies depending on the time point in question (i.e. during or after development) and the region in question (i.e. upper versus middle or lower regions). During development, the mesentery contributes actively and directly to the development of each abdominal digestive organ [24]. The contributions of the mesentery to organ development are comprehensively detailed in 'Mesenteric Organogenesis,' a series of state of the art reviews compiled in a focussed issue of Seminars in Cell and Developmental Biology [21]. Some of these structural, cellular and molecular inputs are highlighted in the following [24,48,49]. Mesenteric lymph-angiogenesis precedes and then drives intestinal lymph-angiogenesis [50,51]. Mesenteric production of BMP influences intestinal tissue mechanics [48]. Mesenteric events lead to differential compressive forces that in turn are required for gut tube looping [48]. Mesenteric contributions to intestinal development can be recapitulated in the sea cucumber model. Some species of sea cucumber can be induced to expel their intestine but retain mesentery. Following this, they redevelop intestine at the margin of the mesentery. The histological features of this remarkable program have been elegantly worked out by

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García-Arrarás and colleagues [52,53]. During development, mesenteric production of cytokines leads to co-ordinated migration of cells from the neural crest, across the mesentery, to the developing enteric nervous system [54,55]. Primordial germ cells migrate in a similarly co-ordinated manner but in the opposite direction [56]. The yolk sac is continuous with the mesentery at the omphalo-mesenteric duct. Early during development, yolk sac contents are distributed via the mesentery to developing organs [49]. Developmental contributions persist into adulthood in the form of histological elements shared between mesentery and digestive organ, at the anatomical interface between both [3,57,58].

Direct contributions of the mesentery, to the composition of abdominal digestive organs, also occur in the adult human setting. The adult human mesentery contains adipose stem cells that are highly proliferative, phagocytic and can drive inflammatory responses in the adjacent intestine [59]. In Crohn's disease, the mesentery extends beyond its normal anatomical boundaries to overlap the surface of the connected intestine. This is termed creeping fat or fat wrapping, and it is pathognomic of Crohn's disease [60]. Mesenteric fat wrapping induces an accumulation of connective, lymphatic and neurologic tissue in the underlying intestinal wall [61–64]. This effect is tightly and topographically coupled. As a result, surgeons increasingly rely on mesenteric disease manifestations to guide them as to where the intestinal disease is present, and what should be resected.

The mesentery supports the development and viability of several organ types in the adult. Splenunculi are an accessory form of the spleen that can arise anywhere in the mesenteric frame [65,66]. They occur in ∼10% of the adult population (Figure 6a). The mesentery can support splenic regeneration following splenectomy or traumatic rupture [67]. The mesentery can support teratomas, heterotopic pancreata and ectopic pregnancy. Heterotopic ossification refers to the development of an ossifying pseudotumor of the mesentery, mostly following surgery or trauma [68]. Heterotopic pancreata are a rare but functional pancreatic tissue normally found in the small intestinal region of the mesentery [69]. Experimental data from numerous animal model settings demonstrates that when tissues are transplanted into the mesentery, they can remain viable and develop functions. These findings prompted investigation of the mesentery (and regions of it) as a biological scaffold in which tissues and organs can be engineered [70–73].

Defects in mesenteric contributions to intestinal development result in intestinal atresia (i.e. failure of a segment of the intestine does not develop). Normal intestine develops on either side of the atretic segment [39,69]. This is an important observation as it indicates that intestinal development depends on local inputs. In keeping with this, atresia is *always* accompanied by a defect in the adjacent mesentery. Just as the mesentery is continuous along the intestine, atresia can occur anywhere along the intestine. There are varying grades of severity of atresia. This indicates that mesenteric inputs are required to maintain several aspects of intestinal development.

In the adult human setting, the intestine requires mesenteric inputs to survive, but the reverse does not hold. If the intestine is removed, the mesentery will remain viable. The surgical management of ulcerative colitis and Crohn's disease involves amputating the intestine at the mesenteric margin (termed 'close resection')[3,57,61]. Many of these patients require reoperation at some point. This provides an opportunity to examine the mesentery that had been left *in situ* in the preceding operation. When this is done, the viable mesentery is always apparent. In abdominal trauma, minor disruption of mesentery compel the surgeon to consider excision of the associated intestine. This is due to the fact that that if the intestine is left *in situ* it may rapidly necrose. The mesentery continues to expand and elongate throughout life. This property was elegantly described by Byron Robinson and although it can contribute to many pathologies in the adult (e.g. volvulus, stomal prolapse and hernia formation) it has received little focus [27].

Vital and special functions vary by region in the adult human mesentery. The ileocolic mesentery corresponds to the tip of the mid-region fold (see above). The greater omentum corresponds to the anterior wall of the upper region. The mesorectum is the anatomic extremity of the mesentery. Cellular and molecular events in ileocolic lymph nodes are critically important in determining inflammatory and immunological activities in the intestinal mucosa [74–77]. They are required in normal immune responses to environmental pathogens [78,79]. The immunological importance of the ileocaecal lymphatic watershed is reflected in the frequency with which patients develop right iliac fossa pain during infections with campylobacter, mycobacterium, salmonella, escherichia coli and numerous other bacterial species. It also explains the high incidence of mesenteric adenitis in patients with systemic viral, bacterial, fungal or parasitic infections. Excessive immunological responses in the ileocolic mesentery are primarily responsible for the development of Crohn's disease in this location. The greater omentum is also highly functional [80]. It has several physiological and immunological

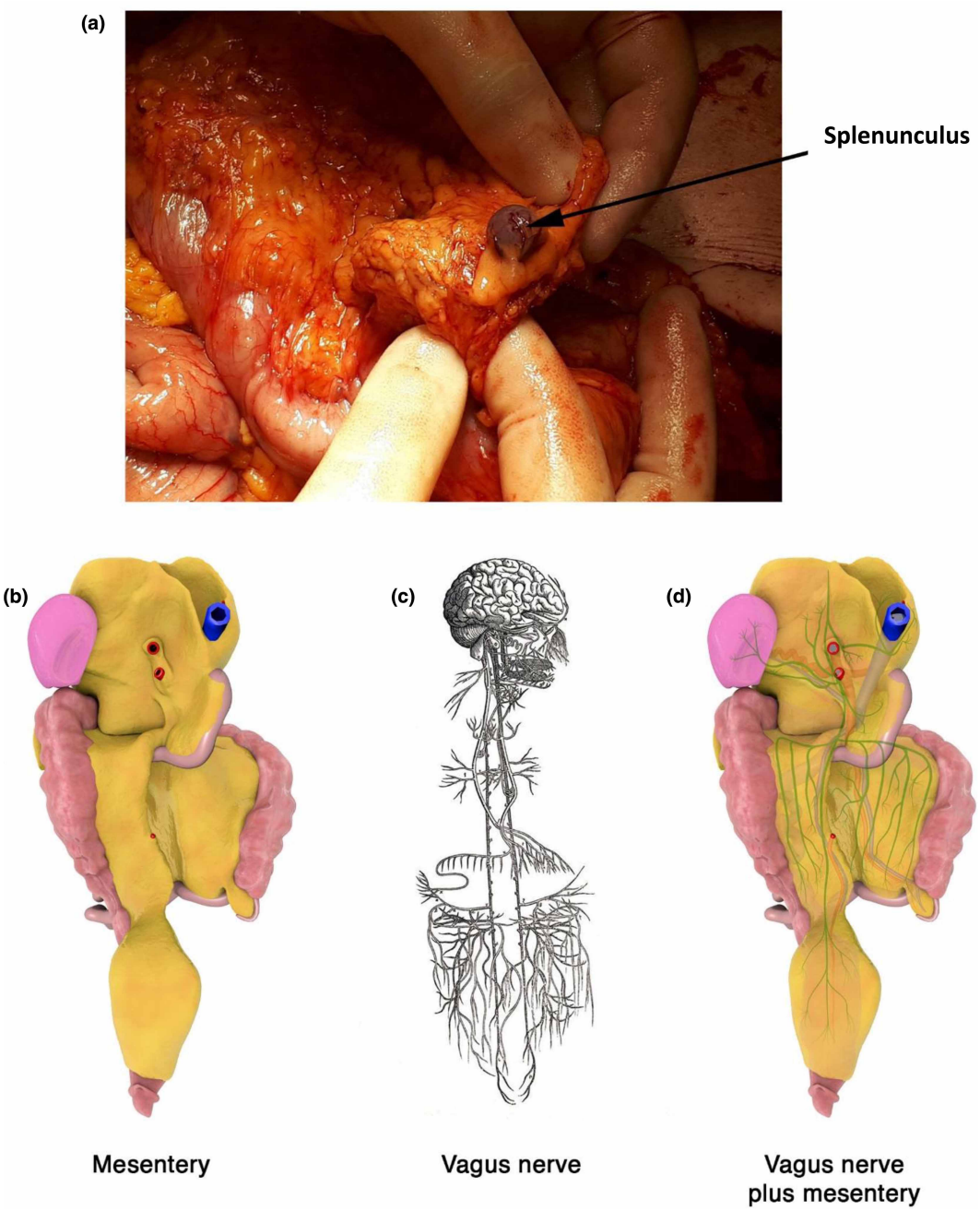

Figure 6. The mesentery, spenunculi and vagus nerve.

(**a**) Intraoperative photograph of an accessory spleen (termed a splenunculus). (**b**) Posterior appearance of the mesentery. (**c**) Vesalius' depiction of the gross anatomy of vagal and sympathetic nerves to the abdomen [88]. (**d**) Combination of (**b**,**c**) to demonstrate a putative overlap in the topographical anatomy of both mesentery and vagus nerve.

activities but also acts directly to adhere to and wall off regions of intra-abdominal contamination. Cell-based immunological activities in the mesorectum directly influence intestinal mucosal events. Given these, removal of the mesorectum is emerging as an important element of the surgical treatment of inflammatory disorders of the rectum [81].

If one adheres to the standard definition of the mesentery as a duplicature of peritoneum connecting the intestine and abdominal wall, then it is reasonable to refute the idea that it is an organ [45–47]. As mentioned

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above, that definition ignores numerous properties of the mesentery [15,16,19,20]. The mesentery is structurally independent with an autonomous arterial inflow and venous drainage. This is apparent during the Cattel–Braasch and Mattox approaches to medial visceral rotation (surgical techniques used to access the great vessels intraoperatively) as well as during the Rokitanski method of autopsy and during multi-visceral transplantation [82–85]. Arterial inflow to the mesentery and mesenteric domain, represents a substantive proportion of cardiac output, and occurs at the coeliac trunk, and superior and inferior mesenteric arteries [86]. Venous drainage occurs via the hepatic veins, at their junction with the inferior vena cava. Mesenteric shape and continuity are remarkably conserved across humans, even in the most complex of congenital abnormalities. In malrotation (where the mid-region fails to undergo the switch-process described above) the shape of the upper and lower regions remain normal. Although mesenteric continuity and direct connectivity with abdominal digestive organs) are conserved across species of the animal kingdom [27,36,37], mesenteric shape varies between species.

Data regarding the functions of the mesentery are increasing rapidly. Mesenteric functions are underpinned by extensive gene and protein expression. Over 50 cytokines are produced in the mesentery. These include ghrelin, adiponectin, resistin, adipophilin and many others. Cellular activities are supported by molecular activities. A large number of enzymes are produced by the mesentery. It is not known if these, in conjunction with surface receptors, subserve specialised or general functions, or both [8].

In 1899 Byron Robinson presciently argued that although the standard definition of the mesentery was as 'old as anatomy itself,' it was incorrect. He also argued that unless the definition was abandoned, '..no advance in the knowledge of the mesentery can be expected.'[27]. Unfortunately, he was accurate in his predictions [22,39–42,87] and mainstream anatomical and surgical texts continued to adhere to the conventional definition [22,23,39–42]. It can be argued that, adherence to the standard definition of the mesentery has impeded not only mesenteric science, but also our understanding of human biology in general. This is explained as follows. All abdominal digestive organs are directly connected to a single mesentery. This means the mesentery provides a linkage mechanism between abdominal digestive organs. In addition, it collectively links all these organs, to the body. A linkage mechanism is an essential component of any functioning system. The elements of a system cannot function in concert, unless they are connected. The mesentery is the anatomical platform on which all abdominal digestive organs are integrated in the systems that collectively generate the human body. Integration commences (or ends) at a histological level in the digestive organ itself. In the mesentery, integration is concentrated into prominent lymphatic, vascular and neurological elements. The mesentery can thus be compared with a biological circuit board by which digestive organs are integrated in the body. Unless we understand the mesentery, we cannot hope to have a complete understanding of the mechanism by which the human body works.

Future directions

Recent findings on the mesentery have significantly enhanced our understanding of the biological composition and organisation of *homo sapiens* in general [10]. They shed light on how we function (as a biological system). If future studies of digestive organs are to be conducted in the correct biological context, this should be done with reference to the region of mesentery with which the organ is connected. Whilst this article focused on the abdominal mesentery, similar findings are emerging in relation to a thoracic mesentery and conjugate organs. In keeping with this, a potential overlap may occur between the topography of branches of the vagus nerve, and the shape of the *ex vivo* mesentery (Figure 6b–d). We speculate this overlap could point to a possible role for the mesentery, in assisting in the coordination of higher level functions. If that intriguing suggestion held, then the renaissance in the science of the mesentery (sparked by Heald and Hohenberger) could also have implications for who we are.

In summary

Clarification of the growth and form of the mesentery are opportunities that enhance our understanding of human biology and, by extension, clinical practice. As Byron Robinson argued over a century ago, it is no longer appropriate to define the mesentery as a double fold of peritoneum connecting the small intestine to the abdominal wall. It is the organ which supports embryological development of all abdominal digestive organs, and which, following birth, maintains all abdominal digestive organs in systematic continuity.

Summary

- The mesentery develops as a single, composite organ in an on which all abdominal digestive organs develop and remain connected to.
- Abdominal digestive organs are mesenteric in embryological origin and anatomical location.
- Abdominal organs are organised primarily along mesenteric (and not peritoneal) lines.
- Specialised functions of the mesentery vary in terms of time point in life, and in anatomical location.
- The science of the mesentery enhances our understanding of human biology in general and clinical practice in particular.

Competing Interests

The authors declare that there are no competing interests associated with the manuscript.

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Abbreviations

SMA, superior mesenteric artery.

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