The mesentery: structure, function, and role in disease

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Systematic study of the mesentery is now possible because of clarification of its structure. Although this area of science is in an early phase, important advances have already been made and opportunities uncovered. For example, distinctive anatomical and functional features have been revealed that justify designation of the mesentery as an organ. Accordingly, the mesentery should be subjected to the same investigatory focus that is applied to other organs and systems. In this Review, we summarise the findings of scientific investigations of the mesentery so far and explore its role in human disease. We aim to provide a platform from which to direct future scientific investigation of the human mesentery in health and disease.

Introduction

One of the earliest depictions of the mesentery associated with the small bowel and colon was generated by Leonardo Da Vinci.[1,2] The Da Vinci mesentery was continuous and appeared to converge centrally. Over the following four centuries, medical illustrators, surgeons, and physicians drew the mesentery as it appeared in situ, suggesting contiguity. In 1879, Toldt[3] identified a mesentery associated with the ascending and descending colon and showed that, although these structures were flattened against the posterior abdominal wall, they remained separate from it. He did not, however, combine these findings to identify mesenteric contiguity.[4] Toldt's findings were highly accurate, but were summarily ignored during the 20th century.[5] Instead, the 1885 findings of Treves[6] were preferred. He concluded that the ascending and descending colon do not normally have an associated mesentery.[7] The resulting depiction in most anatomical, embryological, surgical, and radiological literature of the next century was a fragmented mesentery, present only at the small-intestine, transverse colon, and sigmoid colon.[8–10] Indeed, some publications continue to depict the presence of a right or left mesocolon as being anomalous.[11–18]

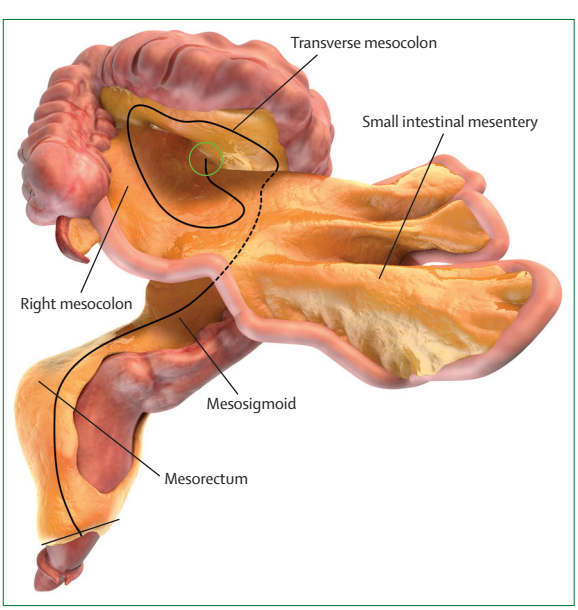

***Figure 1*: Digital representation of the small and large intestines and associated mesentery**

The mesentery associated with the small intestine and colon is now regarded as contiguous (figure 1).[2] It emerges from the superior mesenteric root region and fans out to span the intestine from duodenum to rectum; however, the continuity can be seen only when the mesentery is exposed in a certain way. Dividing the peritoneum provides access to a plane formed by the mesentery and underlying fascia. When peeled away from the fascia, the mesentery emerges as a discrete entity (figure 1). Repeating this process from duodenum to rectum reveals the entirety of the mesentery. Of note, this approach has been used in colorectal resection for many years to permit safe intestinal resection.

Mesenteric contiguity was first demonstrated in an observational cohort study of patients undergoing total mesocolic excision,[19] in which the entire mesocolon is detached from the posterior abdominal wall. Similar observations were made in a cadaveric study of this approach, by the same authors.[20] Mesenteric contiguity is also apparent in embryological variants, such as non-rotation or malrotation, situs inversus, and mesenteric atresia. Mesenteric, peritoneal, and fascial contiguity were confirmed with datasets available in the Visible Human Project,[2,21] which provides cross-sectional photographs of human anatomy without alteration and in full colour, with corresponding axial CT images. From these datasets, the mesentery was identified in full, enabling development of a radiological atlas of the normal contiguous mesentery against which abnormalities can be compared.[22]

Clarification of the mesenteric anatomy was used to derive a surgical nomenclature applicable to all forms of resectional colorectal surgery.[22–26] This terminology is increasingly being used worldwide to describe the individual steps involved in mobilising and resecting the intestine.[27–32] The adoption of a universal nomenclature has notable benefits, including standardisation of the resection process, permitting valid comparisons in clinical trials. Such comparisons have so far been lacking, and related surgical literature is dominated by trials comparing types of mesenteric-based surgery (total mesorectal excision, complete mesocolic excision) with ill-defined approaches collectively referred to as "conventional" surgery.[33] A standardised nomenclature may also be repeatedly used

in the educational setting. Thus, the colorectal community can now be systematic in performing and teaching intestinomesenteric mobilisation and resection. The most relevant implication of mesenteric contiguity was that it permitted, for the first time, systematic investigation of the mesentery and, by definition, its related structures.[2] Previously, mesenteric research had been done under several unrelated headings, but the discovery allowed seemingly disparate findings to be brought together under the heading of mesenteric science.

Exciting opportunities for investigation are now emerging in relation to the role of the mesentery in health and disease.[34] Mesenteric events are important in the pathobiology of diverse abdominal and non-abdominal disorders, including colorectal cancer, inflammatory bowel disease, diverticular disease, cardiovascular disease, diabetes, obesity, and metabolic syndrome.[35–37] We therefore summarise the scientific findings of the mesentery's role in health and disease and explore the directions future investigations might take.

Anatomy and embryology

The mesentery distal to the duodenojejunal flexure is a contiguous and extraretroperitoneal organ (figures 1–3).[23,38] It is compactly folded in a spiral conformation within the peritoneal cavity. The small intestinal mesentery is mobile, whereas the right mesocolic region is flattened against the posterior abdominal wall. It then changes conformation to continue as the transverse mesocolon, with another change in conformation at the splenic flexure to continue distally as the left mesocolon (figure 1). The left mesocolon and medial region of the mesosigmoid are flattened against the posterior abdominal wall (figure 4),[2] whereas the intestinal margin of the mesosigmoid is mobile and elongates in tandem with the sigmoid colon. These two regions of the mesosigmoid converge distally at the pelvic brim and extend into the pelvis as the mesorectum (figure 4), which anatomically terminates in the distal pelvis.

The shape of the mesentery is remarkable. It emerges from the "root region" (as named by Treves), which corresponds to the attachment of the superior mesenteric artery to the aorta.[2,6] The mesentery distal to the duodenojejunal flexure can be viewed as similar to a handheld fan, with the central pivot point corresponding to the origin of the middle colic artery from the superior mesenteric artery.[20] From this point, the mesentery extends radially up to the intestinal margin. It elongates along with the intestine and folds repeatedly, making the intestinal margin extremely long. The body of the fan consists of regions in the following sequence: small-intestinal mesentery; right, transverse, and left mesocolon; mesosigmoid; and mesorectum. The right and left mesocolic regions and the medial mesosigmoid region curve onto and are flattened against the posterior abdominal wall. They are held attached in these regions by Toldt's fascia and the peritoneal reflection

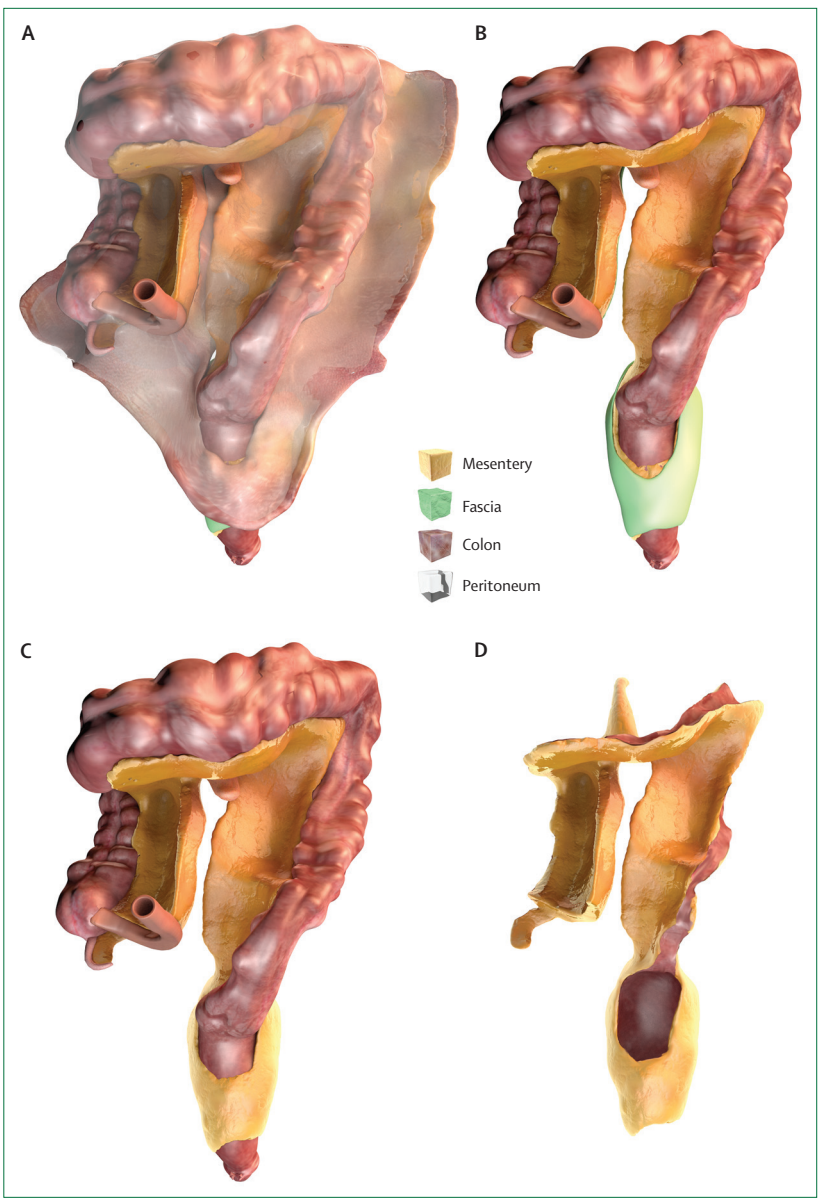

Figure 2: **Digital representations of peritoneum, mesentery, fascia, and intestine**
(A) Peritoneum, mesentery, fascia, and intestine. (B) Mesentery, fascia, and intestine. (C) Mesentery and intestine. (D) Mesentery.

(figures 2–4).[20,21] Intervening regions of the fan (ie, the small-intestinal mesentery, transverse, and mesosigmoid) are contiguous with attached regions but are mobile and not flattened against the posterior abdominal wall. Suspension and mesenteric attachment prevent the intestine from collapsing into the pelvis.

It is feasible that the intestine and mesentery are contiguous from the diaphragm to the pelvic floor.[20] Accordingly, the mesogastrium and mesoduodenum (containing the pancreas) are thought to be continuous with the mesentery of the jejunum, ileum, and colon, although this alignment needs confirmation in future studies. The transverse mesocolon consists of a

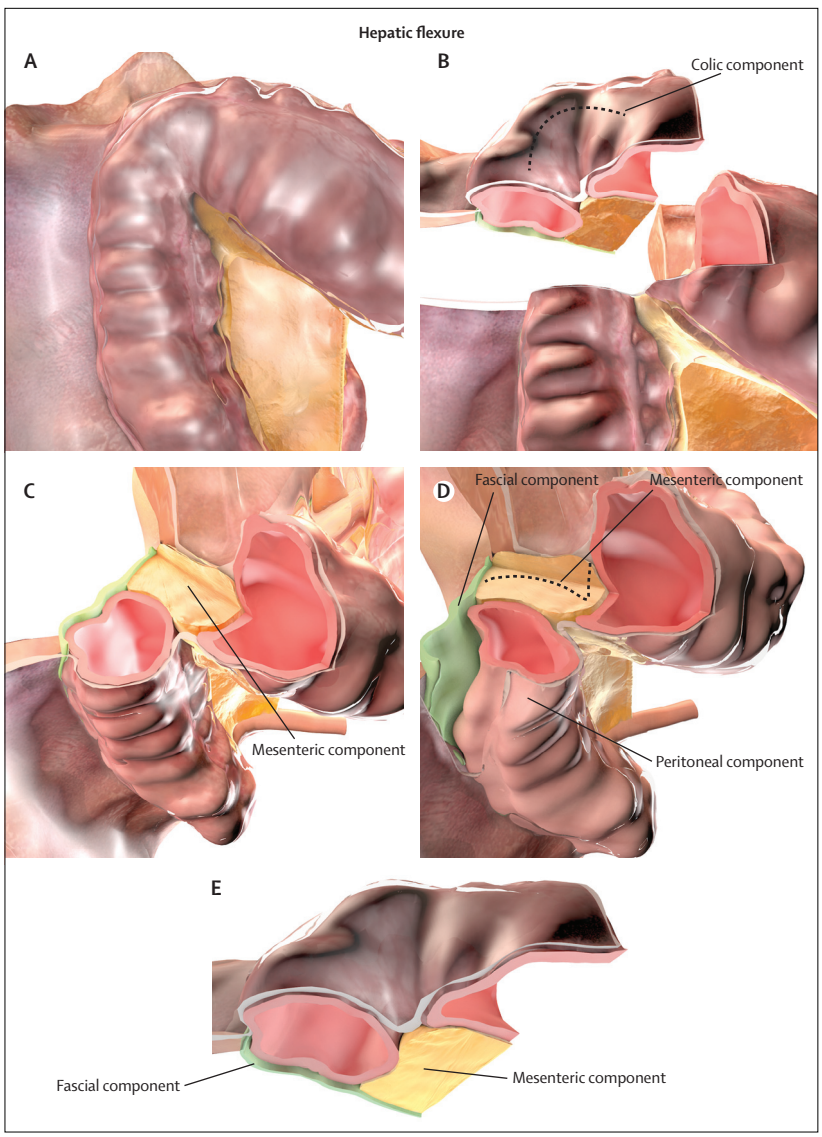

Figure 3: **Anatomical components of the hepatic flexure**
Snapshots from a digital sculpture showing (A) undisturbed hepatic flexure, (B) flexure separated from contiguous structures highlighting the colic component, (C) view of contiguous mesentery, (D) divided peritoneal component of flexure, and (E) fascial component of flexure.

confluence between the mesenteric components of the hepatic and splenic flexure and the middle colic adipovascular pedicle.[20] It forms a caudal limit to the lesser sac. The greater omentum adheres to the cephalad surface of the transverse mesocolon and partially obliterates this space.

The latest depiction of the mesentery helps with understanding of flexural anatomy (figure 3). There are six flexures: duodenojejunal, ileocaecal, hepatic, splenic, and those between the descending and sigmoid colon and the sigmoid and rectum (figures 3, 4).[24] All six have contiguous intestinal, mesenteric, peritoneal, and fascial components (figure 3). This knowledge greatly simplifies technical aspects of colorectal surgery in these regions.

Suspension of the mesentery prevents the intestine collapsing into the pelvis, and is mediated by vascular connections (ie, the superior and inferior mesenteric vessels). Suspension is further aided by mesenteric attachment, that is the apposition or flattening of mesenteric regions against the posterior abdominal wall.[20,21] The right and left mesocolon and the medial mesosigmoid and mesorectum are apposed or attached to subjacent abdominal wall or surrounding pelvis (figure 4). If attachment does not occur, the intestine and mesentery are suspended at vascular pedicles alone and thus prone to twisting with vascular occlusion. This phenomenon occurs in non-rotation or malrotation, discussed later, and is the commonest cause of death due to abdominal crises in the first year of life.

Although contiguous, the peritoneal reflection has several names, according to the anatomical region: the peritoneal reflection, Jackson's membrane, the anterior reflection, the Pouch of Douglas, and the lateral peritoneal reflection (figure 2).[24]

Toldt's fascia is also contiguous (figures 2–4),[20,21,24] as confirmed by high-magnification and high-definition intraoperative imaging during laparoscopic (and in particular robotic) surgery,[20,39] and has various names for the different regions. Where it surrounds perirenal fat, it is frequently referred to as Gerota's fascia. Beneath the left and right colon it is called Toldt's fascia.[24] At this point it has been erroneously called the vestigial right and left mesocolon. Beneath the right and left mesocolon it is also referred to Toldt's fascia. Continuing under the mesosigmoid, into the pelvis, and separating the mesorectum from the bony pelvis, the fascia is called the mesorectal fascia. Where the mesorectum terminates above the pelvic floor, a space occurs. Where the fascia fills this space, it is termed Waldeyer's fascia. Given Toldt's contributions to this field, we propose that the entire fascial layer be collectively referred to as Toldt's fascia, with the different regions denoted by the region of associated mesentery (ie, mesosigmoidal, mesorectal, mesocolon, and mesenteric regions).

The universality of contiguity in adult human beings indicates that the embryogenesis and development of the mesentery is one of the most conserved processes in human embryology. Broadly speaking, the intestine develops from the endodermal germ layer, whereas the mesentery derives from the mesodermal germ layer.[40] The processes involved in the embryological development of the mesentery were previously based on classic anatomical theories that attempted to reconcile mesenteric regression, fragmentation, and discontinuity.[41,42] These included the sliding and regression theories,[43–45] neither of which gained a foothold in the mainstream scientific literature. According to the regression theory, the dimensions of the embryological dorsal mesentery are such that, with relative lack of further growth, and with future growth of the right and left colon, their respective mesenteries regress and

become vestigial. According to the sliding theory, as the right and left colon adopt their final lateral positions they pull their respective mesenteries with them until these take up their final location as vestigial mesenteries posterior to the right or left colon respectively.

With contiguity now revealed, the embryological development of the mesentery, peritoneal reflection, and fascia need to be reappraised. Fortunately, the adult structure is far simpler than that previously proposed, and might be more easily explained by mechanical and cellular events. By reverse engineering its development with the adult shape as a starting point, mesenteric embryology can be simplified into a set number of key processes: suspension at points of vascular connectivity; differential elongation of regions of the intestine and mesentery with a resultant counter-clockwise rotation of both, mesenteric flattening against the posterior abdominal wall, and development of Toldt's fascia and the peritoneal membrane to maintain attachment in this conformation. Understanding of the anatomy of the entire mesentery provides new anatomical endpoints to which embryologists should work to further characterise the development of the mesentery and associated structures.

Histology

The fundamental histological elements of the mesentery are the surface mesothelium, the connective tissue lattice, and adipocyte populations housed in the interstices of the lattice. So far, little is known about the cellular components of these elements.

In regions where the mesentery is flattened against or attached to the posterior abdominal wall, Toldt's fascia is present in between.[23] Although the fascia contains minute vessels and lymphatics, the sites of origin and termination of these have yet to be confirmed. Histological and scanning electron microscopic analyses in this region have shown that Toldt's fascia is a true fascia in the anatomical sense.[21] It is interposed between the visceral peritoneum of the overlying mesocolon and the parietal peritoneum of the retroperitoneum. In the past, the terms visceral and parietal fascia were incorrectly applied to these mesothelial layers.[46] As they are epithelial and not mesenchymal, they are not fascia in the anatomical and surgical sense. Thus, the terms visceral and parietal peritoneum should be used to reference these mesothelial layers.[47]

At the intersection between the intestine and the mesentery, the mesenteric mesothelium continues onto the intestine and contributes to the cellular component of the outer layer, the serosa. Additionally, the connective tissue of the mesentery contributes to, and is contiguous with, that of the serosa.[48] From the serosa, connective tissue septations extend into underlying muscle and submucosa, meaning that the mesenteric and intestinal connective tissues are contiguous. Classic histological studies from Toldt[3–5] pictorially hinted at this arrangement,

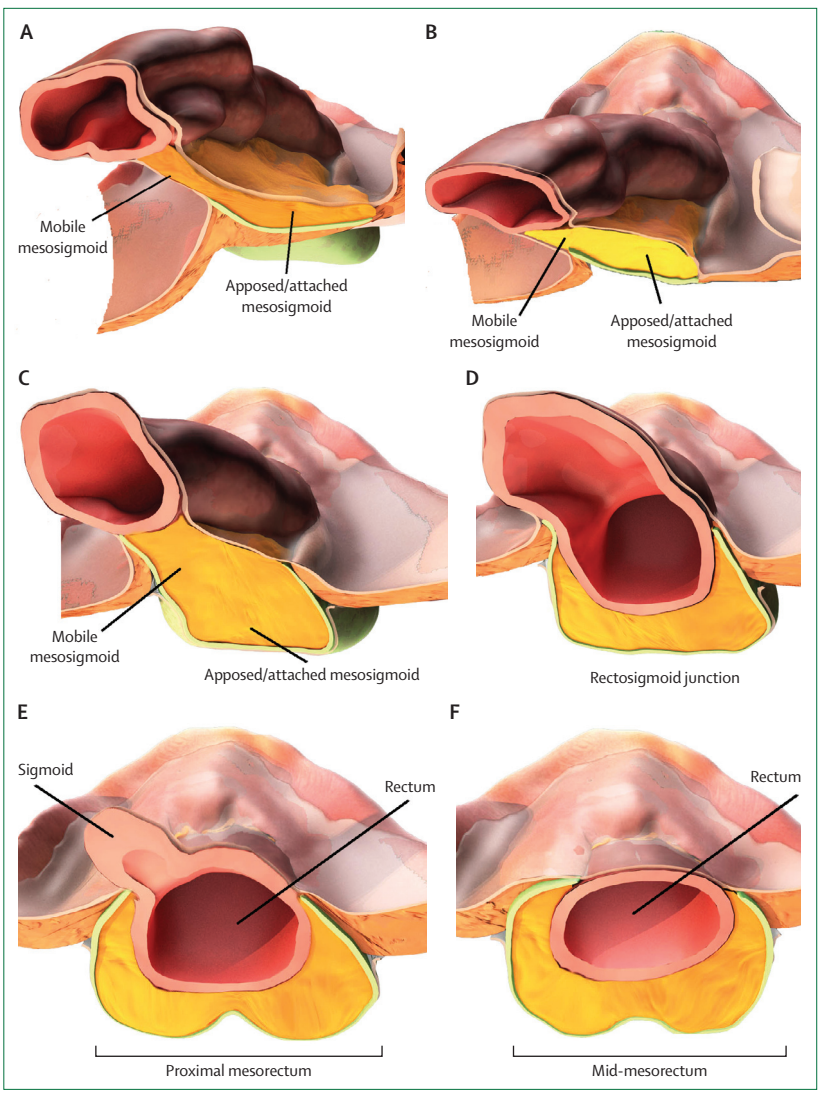

Figure 4: **Axial (craniocaudal) views of mesosigmoid and mesorectum**
(A) Upper mesosigmoidal, (B) mid-sigmoidal, (C) distal mesosigmoidal, (D) rectosigmoidal, (E) proximal, and (F) mid-mesorectal levels.

which is a remarkable achievement given the limit of imaging resolution possible at the time.

For many years, the interface between the body and intestine (or environment) was postulated to be represented by lymphovascular and neurological elements embedded in the submucosa. Little, if any, reference was made to the intersection between the mesentery and intestine. However, it is now recognised that this histological overlap is the true intestinal hilum (ie, where blood vessels enter or leave) and spans the intestine from duodenum to rectum.[21]

Physiology

The anatomical distinctiveness of the mesentery is mirrored by unique functions. The mesentery suspends much of the intestines from the posterior abdominal

wall,[19] preventing it from collapsing into the pelvis when standing upright. Intestinal transit would probably be slowed or possibly even cease without this attachment. Mesenteric attachment facilitates suspension of the colon,[20] allowing it to adopt a spiral conformation. It is feasible that mesenteric suspension and attachment were important developments that facilitated vertical ambulation in *Homo sapiens*, although examination of mesenteric attachment in lower-order species is needed to confirm or refute this suggestion.

The mesentery is interposed between the intestines and the body,[20] making it is optimally positioned to sample intestinal (ie, environmental) cues and mediate local responses, systemic responses, or both. Mesenteric nodes sample bacterial components derived from the adjacent intestine[49] and regulate migration of B cells, T cells, natural killer cells, and dendritic cells to nearby intestinal mucosa.[50] However, owing to the sporadic way in which mesenteric-based feedback mechanisms have so far been identified, they are not fully understood. Additionally, many of the findings were made in animal studies, and how they translate to the human context needs to be confirmed.

Mesenteric production of C-reactive protein is an important determinant of systemic concentrations. C-reactive protein regulates glycaemic and lipid metabolism. Data suggest increasingly that mesenteric events contribute to the regulation of systemic fibrinolytic, inflammatory, and coagulation cascades.[51–53]

The mesenteric mesothelium is the single largest expanse of mesothelium in the human body. It has transformative capacities that might be relevant to tissue repair (ie, after surgery) and various disorders (ie, hernia and adhesion formation).[54] The mesenteric mesothelium is a stem cell niche that has undergone remarkably little investigation. Understanding of the enteromesenteric component of the peripheral nervous system is also deficient.[55–57] No studies have comprehensively characterised the mesenteric component of the peripheral nervous system in adults. Postganglionic nerves leave the three major abdominal ganglia to reach the intestine, but their trajectory is poorly characterised. Given the relevance of the mesentery to intestinal function and overall homoeostasis, neurological studies of the mesenteric component of the enteric nervous system should be given increased emphasis.

Role in disease

Improved understanding of the normal mesenteric shape enables identification of mesenteric abnormalities,[20] which in turn permits investigation of the relation between mesenteric abnormalities (position and nature) and disease. The multilevel contiguity between the mesentery and adjacent organs provides a structural platform to maintain homoeostasis, but also provides a means for disease spread. A mesenteric-based approach to disease classification therefore has broad applicability. We provide a brief description of its application to several common disorders, including primary[58–63] and secondary[64–69] mesenteric abnormalities (mesenteropathies).

Primary mesenteropathies

Primary mesenteropathies arise from the mesentery itself, owing to its intrinsic properties. Examples are volvulus, non-rotation, superior mesenteric artery thrombosis, sclerosing mesenteritis (of which there are several subtypes), and mesenteric cysts.[58–63]

Volvulus

As detailed in the section on anatomy, the intestinal margin of the mesentery elongates in tandem with the intestine. This property predisposes to volvulus (twisting or torsion) of the mesentery and the attached intestine. Volvulus is prevented by flattening and attachment of alternating regions of the mesentery to the posterior abdominal wall. For example, attachment of the right mesocolon reduces the risk at the ileocaecal junction. Volvulus can occur anywhere that mesenteric attachment is incomplete or inadequate. The medial region of the mesosigmoid is attached, whereas the lateral region is mobile (figure 4). If the differential in length between the attached and mobile regions is sufficient, a volvulus occurs. Rarely, volvulus develops in the transverse mesocolon and colon for the same reason.

Non-rotation (also known as malrotation)

If the mesentery does not rotate as normal during embryological development, mesenteric attachment does not occur and the adult conformation is abnormal (figure 5). Instead, the intestine and mesentery are suspended at vascular pedicles alone, and the mesentery twists around these points of connection. The result is a catastrophic volvulus of the mesentery and intestine. Non-rotation (malrotation) is the most common cause of fatality due to abdominal crises in the first year of life.

Internal herniation related to mesenteric defects

Mesenteric defects or gaps can act as routes for intestinal herniation. This disorder might arise postoperatively (eg, after intestinal resection), or spontaneously (eg, due to mesenteric atresia). After intestinal resection, the resultant mesenteric defect should be closed if it is narrow and risk of herniation is high.

Vascular mesenteropathies

Vascular mesenteropathies are among the most common mesenteric disorders, and include acute occlusion of the superior mesenteric artery and thrombosis of the superior mesenteric vein.[58,59] The major vessels of the mesentery are the superior and inferior mesenteric arteries and veins. The manner in which these subdivide or branch is variable. For example, a right colic artery arising directly from the middle colic artery is seen

in only 25% of the general population.[70] Vascular mesenteropathies can be catastrophic since they might lead to rapid and extensive necrosis of the small intestine. Occlusion of the superior mesenteric artery can be embolic or can arise as a result of thrombus formation on an atherosclerotic plaque.

Mesenteric cysts

Cysts on the mesentery are uncommon and arise after mesenteric mesothelial proliferation (figure 5). Mesenteric cysts can be asymptomatic, although sudden expansion secondary to haemorrhage can lead to severe abdominal pain.[71,72]

Cellular mesenteropathies

The pathologies discussed earlier have a mechanical basis. Increasing data point to the occurrence of cellular mesenteropathies.[73] The concept of cellular mesenteropathies is supported by findings in sclerosing mesenteritis and adhesion formation.[74] With increasing investigation of the histological basis of the mesentery in health and disease, further examples of this disease subtype are likely to emerge.

Mesenteric mesothelium can undergo mesenchymal transformation, contributing to local mesenchymal populations and activities. Abnormal mesothelial proliferation is driven by chronic inflammation, and is a feature of mesenteric lipodystrophy, mesenteric panniculitis, and IgG4-related sclerosing mesenteritis.[75–77] Synchronous mesothelial and mesenchymal proliferation occur when adhesions form after surgery. It is feasible that mesothelial proliferation provides a cellular basis to the mesothelial (ie, hernia) sac. The hernia sac is an important anatomical component of most forms of abdominal hernia.

Secondary mesenteropathies

Secondary mesenteropathies arise from extrinsic sources and might occur due to direct (ie, contiguous) or systemic spread of a disease process. Examples include mesenteric involvement in intestinal malignancy or inflammation (ie, diverticular disease).[64–69]

Intestinal malignancy

Intestinal malignancy can lead to various secondary effects in the adjacent mesentery. Lymphatic contiguity between the mesentery and intestine provides a means for disease spread. Lymphatic spread to mesenteric nodes is thought to be an important mechanism for the systemic spread of intestinal tumours.[78] Additionally, intestinal tumours might invade or perforate into the contiguous or nearby mesentery.

Crohn's disease

Mesenteric fat wrapping and thickening are prototypical of Crohn's disease. The classic view of Crohn's disease is that it is as an intestinal disorder (figure 5),[79] making

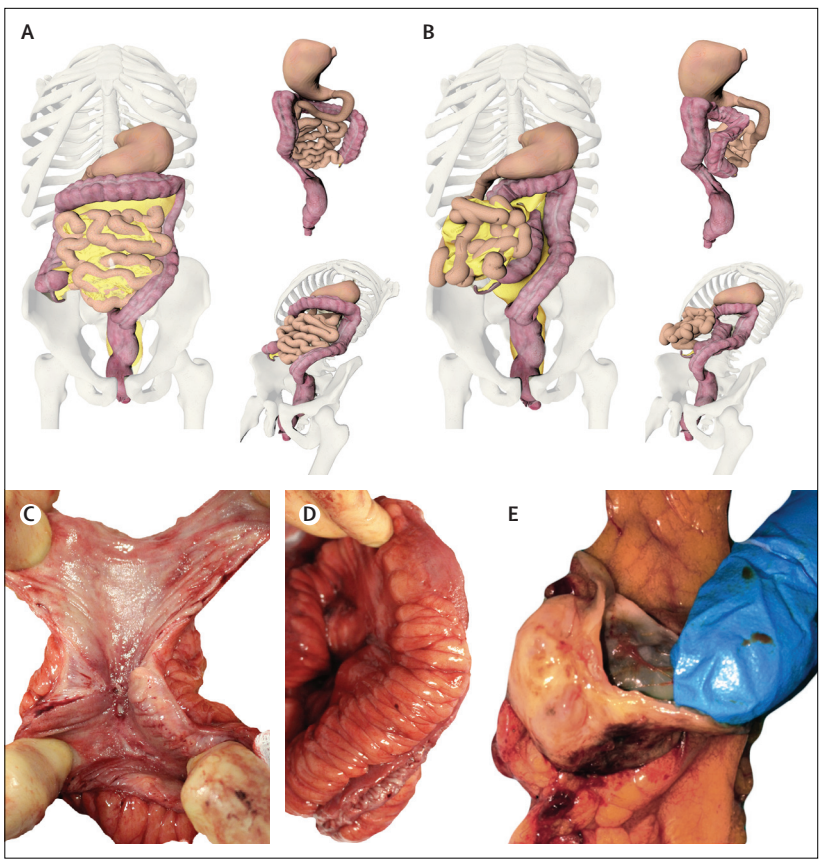

***Figure 5*: Primary mesenteropathies**

(A) Various views of the conformation of the normal mesentery and intestine. (B) Various views of the intestine and mesentery in non-rotation (ie, malrotation). (C) Mucosal and (D) mesenteric transition zones in a postoperative resection for Crohn's disease. (E) Mesenteric cyst seen in a postoperative specimen.

associated mesenteric abnormalities secondary. However, some findings suggest that mesenchymal abnormalities can extend from the mesentery into the subjacent intestine,[80] in which case, Crohn's disease might be a primary mesenteropathy. Mesenteric inputs explain the transmural appearance of Crohn's disease as well as the origin of mesenchymal cells responsible for the disease.

Obesity, diabetes, atherosclerosis, and metabolic syndrome

The clinical relevance of the mesentery is not confined to abdominal disease.[68,81,82] It is the single greatest contributor to visceral adiposity,[83] which regulates systemic concentrations of C-reactive protein.[49] Dysregulation of systemic C-reactive protein has an important role in the pathobiology of obesity, atherosclerosis, diabetes, and metabolic syndrome.[84] Studies should be done to investigate whether increased mesenteric adiposity is a primary or secondary pathobiological event in these disorders.

Mesenteric-based diagnostics

Mesenteric diagnostics aim to identify and assess (or stage) mesenteric abnormalities by non-invasive or minimally invasive means. However, the mesentery is anatomically

remote and, at present, can only be assessed by radiological or surgical means.[22,23] Radiological approaches are regarded as particularly complex due to the concept of mesenteric discontinuity. Abdominal radiologists continue to face challenges when they attempt to reconcile the radiological appearance of the mesentery with classic appraisals of mesenteric anatomy. In the 1980s, Oliphant and Berne[85] proposed mesenteric contiguity with "a posterior abdominal core", and Dodds and colleagues[86] suggested that the entire mesentery was extraretroperitoneal. Their hypotheses resonate with current understanding of mesenteric anatomy. Nevertheless, most updates on mesenteric and peritoneal radiology still lead off with the assertion that it remains difficult.

Clarification of mesenteric and peritoneal structure has provided a basis on which to examine the radiological appearance of the mesentery systematically, in normality and disease. Advances in abdominal CT and MRI mean that the flexural and non-flexural regions of the mesentery can be reproducibly identified in adults with normal anatomy, embryological variations, and abdominal diseases.[23] Although gaining traction, these advances have yet to be included in educational programmes.

Endoscopic visualisation can be used to map the mesentery and could facilitate transintestinal biopsy in a similar way to transrectal prostate biopsy. Transintestinal mesenteric biopsy would provide diagnostic data on secondary mesenteric disorders (eg, cardiovascular disease, diabetes, obesity, metabolic syndrome, and Crohn's disease). Endoscopic mapping during colonoscopy can provide endoscopists, on a patient-by-patient basis, with a trajectory along which the large intestine may be traversed with minimum discomfort to the patient.[87] By combining longitudinal and axial positions, polyp location might be pinpointed to guide future investigation or resection.

Mesenteric-based therapeutic strategies

The anatomical remoteness of the mesentery is such that surgery is the only means of altering it. Surgical manipulation of the mesentery is well developed in so far as surgeons have long recognised the importance of removing it as part of intestinal resection. Jamieson and Dobson[88] showed as early as 1909 the importance of removing the lymphatic drainage of the colon during resection for colon cancer. Miles[89] showed similar benefits in treatment of rectal cancer. In 1982, Heald and colleagues[90] found that removing an intact mesorectal package was beneficial in surgical management of the rectum. Likewise, Hohenberger and colleagues[91] showed the importance of removing an intact mesocolic package in resection of colon cancer.

The detachment and disconnection of an intact mesenteric package by surgeons for many years is striking because it was at odds with the reference surgical and non-surgical texts which stated that persistence of a right or left mesocolon was anomalous.[9,10] Identification and confirmation of mesenteric contiguity led to resolution of disparity between surgical approaches[17] and provided a common anatomical basis for the concepts of total mesorectal excision, total mesocolic excision, and complete mesocolic excision. Indeed, it provides an anatomical foundation for good-quality resectional surgery from the duodenum to rectum.

Clarification of mesenteric anatomy will have many benefits for colorectal surgery. Surgery can be more systematised,[28] which in turn will allow tailoring of educational information and lead to standardisation of the surgical process. Systematisation will also facilitate rigorously controlled randomised trials, which have long been called for but have not so far been possible.

The range of diseases that can be treated with mesenteric strategies is increasing.[92,93] Recommendations that the mesentery should be included in resections for Crohn's disease have been largely ignored due to the dangers (eg, extensive haemorrhage) associated with division of the Crohn's mesentery. Reoperation rates remain as high as 40% after resection for Crohn's disease.[94,95] However, data suggest that margin positivity and reoperation rates can be substantially reduced if resection is guided by mesenteric-based strategies.[34]

Mesenteric pharmacology is poorly developed. Few data are available on drug pharmacokinetics or pharmacodynamics within the mesentery. Early findings in mouse studies suggest that infliximab can alter the mesenteric cytokine environment.[96] With increasing recognition of the central functionality of the mesentery, the number of studies is likely to expand.

Conclusions and future directions

Clarification of mesenteric structure has raised many questions, but has simultaneously provided a platform from which to direct future investigations across natural and applied sciences. Various anatomical and other features of the mesentery need to be detailed. Contiguity of lymphatic, neurological, vascular, and connective tissue means that the mesentery occupies a central position.[21,97] Whether the mesentery should be viewed as part of the intestinal, vascular, endocrine, cardiovascular, or immunological systems is so far unclear, as it has important roles in them all. Its effects are being investigated at haematological, immunological, endocrine, metabolic, and other levels.[98–101] Many, but not all, organs have a distinct functional unit. The functional unit of the mesentery is unknown, and whether a distinctive cell type is primarily responsible for its functionality should be investigated.

Several anatomical questions also remain unanswered. For example, although early data suggest that the mesentery proximal to the duodenojejunal flexure is contiguous with it, this is still unclear. If this is the case, discovering the mesenteric factors that drive development of the pancreas in one mesenteric region and not in another will be of great interest. If the proximal mesentery

Search strategy and selection criteria

We searched PubMed and Ovid with the terms "mesentery", "peritoneum", "peritoneal AND reflection", "mesocolon", "fascia", and "Toldt's AND fascia." All papers identified that were published from Jan 1, 1858, to Aug 1, 2016, were included, without language restriction. Additional papers were identified from reference lists in retrieved papers. Other material of relevance was identified from the personal records of the authors. Abstracts presented at international meetings were included only if they had been published.

is contiguous, the anatomical correlate of the meso-oesophagus could also be investigated. The relation of the greater omentum to the remainder of the mesentery should be re-examined.

Mesenteric mesothelial plasticity and transformation contribute to several disorders, including adhesion and hernia formation. Focusing research on the molecular and cellular cornerstones of mesothelial plasticity might reveal that related events, such as postoperative adhesion or hernia sac formation, can be altered. The multilevel contiguity of mesentery and adjacent structures is being investigated as a route for the spread of disease. Connective tissue contiguity could explain the development of musculoskeletal, ocular, and cutaneous abnormalities in intestinal diseases, such as ulcerative colitis and Crohn's disease, and might also account for so far unexplained patterns of pathogen and disease spread.

Continued development of radiological and endoscopic mesenteric diagnostics will improve the staging of abdominal diseases by non-invasive and minimally invasive means. Endoscopic mesenteric sampling aims to provide clinically relevant data in an array of abdominal and non-abdominal disorders and will be addressed in studies.[34,87] It is anticipated that these data will culminate in the development of non-invasive mesenteric-based therapies (ie, mesenteric pharmacotherapeutics), which might obviate surgical intervention. Mesenteric pharmacology remains poorly developed, partly due to the relative inaccessibility of the mesentery, but mainly due to little investigation. Understanding of drug activities within the mesentery and mesenteric pharmacokinetics and dynamics is needed.

In summary, advances in understanding of the mesentery now enable a rigorous and scientific study of it. Accordingly, benefits to gastroenterology are anticipated by improved diagnostics and an expansion of therapeutics in general. Benefits to radiological appraisal of the abdomen will be achieved by increased accuracy in the interpretation of abdominal disease. Pathology will benefit from enahnced comprehensive understanding in an array of abdominal and non-abdominal conditions. In surgery, it is expected that surgical technique, standardisation of the craft component of abdominal surgery, and its future scientific investigation will all be improved.

Contributors
JCC conceived the idea of the review on the basis of findings reported by him and his group. The manuscript was written by JCC and critically reviewed and edited by DPO. The literature review was done by JCC and DPO and the review bibliography was populated by DPO.

Declaration of interests
We declare no competing interests.

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