Defining the mesentery as a new organ and what this means for understanding its roles in digestive disorders

J. Calvin Coffey & D. Peter O'Leary

To cite this article: J. Calvin Coffey & D. Peter O'Leary (2017): Defining the mesentery as a new organ and what this means for understanding its roles in digestive disorders, Expert Review of Gastroenterology & Hepatology, DOI: 10.1080/17474124.2017.1329010

To link to this article: http://dx.doi.org/10.1080/17474124.2017.1329010

Accepted author version posted online: 09 May 2017.

Submit your article to this journal

Article views: 5

View related articles

View Crossmark data
Defining the mesentery as a new organ and what this means for understanding its roles in digestive disorders

Authors: J. Calvin Coffey $^{1,2,3}$ and D. Peter O’Leary$^{1,2,3}$

Institutes

1 Department of Surgery, University Hospital Limerick, Limerick, Ireland
2 Graduate Entry Medical School, University of Limerick, Limerick, Ireland
3 Centre for Interventions in Infection, Inflammation and Immunity (4i), University of Limerick, Limerick, Ireland

Address for correspondence/reprints:
Professor J. Calvin Coffey, PhD, FRCSI,
Telephone: +353-61-482412 Fax: +353-61-482410
Email: calvin.coffey@ul.ie

Funding
This paper was not funded

Declaration of Interest
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.
1: Introduction

Categorisation of structures into tissues, organs and systems is arbitrary but has considerable utility as it provides a structural hierarchy within which one can more easily investigate and better understand human biology and disease. Until recently, this process was greatly hampered by an erroneous anatomical appraisal of the mesentery. Advances in our understanding of the mesentery now present scientific and clinical communities with new opportunities. Based on these, it is suggested that the mesentery be re-designated as an organ. Herein we challenge this concept and explore whether there are clinical benefits to redesignation.

2: Testing the mesenteric-organ model: what is the function of the mesentery and do abnormalities of this lead to disease development?

Our understanding of mesenteric anatomy was, until recently, incorrect. Not surprisingly, our understanding of its function is poorly developed and rudimentary. One of the specialised functions of the mesentery is to suspend a contractile intestine within the peritoneal cavity (avoiding direct contact with the abdominal wall) simultaneously maintaining systemic connectivity between intestine and body. The mesentery (and hence intestine) is maintained in a particular conformation through several mechanisms established during fetal development. When these are absent, or deficient, the mesentery twists leading to intestinal ischaemia and necrosis if uncorrected.

Continuity of the mesentery distal to the duodenojejunal flexure is a universal finding that is maintained even in settings of embryological abnormalities. Continuity lends itself to twisting, which is largely prevented by mesenteric attachment. This is where the right and left mesocolic regions of the mesentery flatten against and attach to the retroperitoneum. The medial aspect of the mesosigmoid and mesorectum also attach. In the absence of normal mesenteric attachment, the mesentery is suspended by its vascular pedicle alone, with a resultant tendency to twist around this. In the paediatric population, this occurs in the setting of non-rotation and is the commonest form of abdominal emergency in the first year of life. Management is mesenteric-based requiring restoration of normal mesenteric (and by definition intestinal) attachment and conformation.

A similar event can occur later in life as volvulus. Volvulus is a relatively common condition where a segment of intestine twists and becomes necrotic. Until recently, volvulus was attributed to the anomalous presence of a region of mesentery resulting in increased mobility of the intestine. As the mesentery is now regarded as continuous, the development of volvulus can no be longer attributed to the anomalous persistence of a mesentery in certain regions. Instead, volvulus arises when the differential between regions of attached and non-attached mesentery is such that the mesentery (and hence intestine) twists around the zone of attachment. Volvulus can be managed in an intestinal-sparing manner by attaching (called “pexy”) of mesenteric regions to the retroperitoneum.
Connectivity between the mesentery and systems of the body is a two edged sword (see below). For example, blood vessels contained within the mesentery are vulnerable to obstruction via embolus of thrombosis. This may lead to intestinal ischaemia which can be catastrophic.

3: Testing the mesenteric organ model: can model-based (i.e. mesenteric based) strategies be used in treating abdominal diseases?

If the mesenteric organ model held, then model-based (i.e. mesenteric-based) treatment strategies should lead to improved outcomes for patients. There is extensive evidence to support this suggestion. Surgeons have long advocated a mesenteric-based approach when operating for colon and rectal cancer.\textsuperscript{6,7} Total mesorectal excision is now the standard surgical approach in the management of rectal cancer. Emerging data demonstrates that inclusion of the mesentery during resection for Crohn’s disease, reduces recurrence rates.\textsuperscript{8} The mesenteric-based management of non-rotation and volvulus have been described above.\textsuperscript{4}

Mesenteric continuity and contiguity provide the surgeon with a universally applicable network of planes that permit safe and effective surgery. The craft-based goals, aims, techniques and activities of the intestinal surgeon can be universally explained using mesenteric descriptors.\textsuperscript{6}

Mesenteric-based treatment strategies are mainly surgical as pharmaco-therapeutic targeting of the mesentery is undeveloped at present. Experimental evidence indicates that cellular and molecular events in mesenteric lymph nodes have major roles in physiological and pathological states involving the intestine.\textsuperscript{9} It is feasible that future therapies may target mesenteric nodal events with a view to ameliorating abnormalities in the adjacent intestine.

4: Testing the mesenteric-organ model: does the stroma-parenchyma paradigm of organ structure hold for the mesentery and is it clinically relevant?

The question arises as to which mesenteric components correspond to epithelium (i.e. parenchyma) and stroma, and how these are altered in disease. Mesenteric abnormalities can be classified as parenchymal or stromal.\textsuperscript{3} Associated diseases and treatment strategies can be categorised accordingly. Mesenteric parenchymal abnormalities may arise from surface mesothelium and include mesenteric cysts, sclerosis and mesothelioma. Stromal abnormalities include panniculitis, cavitation syndrome, desmoid tumors and lymphoma.

Mesenteric cysts arise from the surface mesothelial lining of the mesentery and vary in size. Mesenteric sclerosis is characterised by hypertrophy of mesenteric mesothelium. There are several subtypes each with varying severity and related symptoms. Mesenteric panniculitis is a primary inflammatory abnormality of the mesentery. It can lead to abdominal pain and is usually managed conservatively. Mesenteric cavitation syndrome arises through prolonged antigen exposure causing lymphocyte depletion and nodal involution. It is not uncommon for lymphoma to be confined to the mesentery. Mesenteric desmoids can present particular diagnostic and technical challenges for the surgeon. Mesenteric mesothelioma is a rarer form of primary mesenteric malignancy with a poor prognosis.
Parenchymal and stromal abnormalities represent a substantive though understudied body of pathologies.

5: Testing the mesenteric-organ model: can certain diseases be categorised as mesenteric in origin and can the mesentery be affected by systemic diseases?

If the organ model concept is correct, mesenteric abnormalities could be arbitrarily categorised into those arising within the mesentery (primary mesenteropathies) and those that spread to involve mesentery (i.e. secondary mesenteropathies). Benefits to this system of categorisation of diseases should manifest in mesenteric-based diagnostic and management strategies. Mesenteric-based management strategies are well developed and established (see above). In contrast, diagnostic investigation of the mesentery is undeveloped. The radiological appraisal of the mesentery has been described as “difficult to reconcile with prevailing anatomical concepts.” This discrepancy is resolved when abdominal imaging is conducted against a background of mesenteric continuity. To demonstrate this, a mesenteric-based atlas of abdominal imaging was recently developed. This provides a mesenteric-focused standard which radiologists can now use to better interpret, diagnose or stage intra-abdominal disease.

The mesentery suspends the intestine away from the anatomic mainframe of the abdomen, whilst simultaneously maintaining connectivity with systems of the body. If the intestine was directly attached then it could not contract freely. Connectivity is a two-edged sword however, as systemic diseases can also affect the mesentery, i.e. “secondary mesenteropathies.” Intestinal tumors may directly involve mesentery or metastasise to mesenteric nodes. Although arbitrary, categorisation of mesenteric abnormalities as secondary mesenteropathies provides information on disease stage. Stage reflects prognosis and influences management decisions.

6: Testing the mesenteric-organ model: can the mesentery exert systemic effects and are abnormalities in these associated with disease development?

If the mesentery is an organ, then as with other organs, contributions to homeostasis and systemic diseases should be evaluated. This reveals the possibility of, as yet unproven, relationships between seemingly separate entities. For example, increased visceral adiposity is linked to development of atherosclerosis, diabetes mellitus, metabolic syndrome, dyslipidaemias, and hypertension. Increased visceral adiposity is linked to increased systemic C-reactive protein (CRP) and derangements in glycaemic control, fibrinolysis and coagulation. The mesentery is the largest contributor to visceral adiposity. It is feasible that alterations in mesenteric visceral adiposity contribute to derangements in CRP and glycaemic control and to each of the conditions listed.

Increasing data also suggest that the mesentery should be targeted in the setting of Crohn’s disease. Given the systemic manifestations of Crohn’s disease, it is feasible these may also subside with resection of the mesentery.
7: Future directions

Categorisation of the mesentery as an organ provides many practical and novel perspectives from which to view human biology in health and disease. Continuity between the small intestinal and right mesocolic mesenteric regions means there is substantive volume of lymphatic tissue at the ileocaecal level. This may explain development of right sided pain in mesenteric adenitis, volvulus of the ileocaecal region, the prevalence of ileocaecal Crohn’s disease, and worse outcomes with right-sided colon cancer.

The continuous mesentery provides, for the first time, an explanation as to how the right and left side of the colon are connected with the body. The mesentery is thus an important component of anatomical connectivity in the gastrointestinal system in particular, and in the body in general. In keeping with this, the two metre long zone at which the mesentery and intestine intersect, is highly relevant.

The neuro-anatomic basis of the gut - mesentery - brain axis is scientifically unchartered. Given the importance of this axis to overall homeostasis and disease processes, characterisation of mesenteric neuroanatomy is imperative.

8: In summary:

Anatomic and physiological centrality of the mesenteric organ is reflected in significant pathobiological contributions to commonplace abdominal and non-abdominal diseases. At present the only means of therapeutically targeting the mesentery is surgical. Increasing investigation of the role of the mesentery in diseases is likely to prompt development of mesenteric-focused radiological and pharmacotherapeutic means of medical intervention.
References:

Review describing the mesenteric organ and highlighting the emergence of the scientific study of the mesentery.

In depth description of modern understanding of mesenteric anatomy and how it relates to intestinal surgery.

Review of the embryological development of the mesentery in the context of the modern understanding of mesenteric anatomy.

*Description of the diagnosis and surgical management of non-rotation of the mesentery and intestine.

*Description of the diagnosis and management of intestinal volvulus.

**Article explaining how standardisation of colorectal surgery may be achieved by adopting universally applicable mesenteric-based anatomic principles.

**One of the earliest articles of the modern era to demonstrate how adoption of mesenteric-based strategies in surgery is associated with better outcomes for patients with rectal cancer.

**Review of the role of the mesentery in Crohn’s disease.

**Study demonstrating how defective lymphatic function can be corrected with VEGF-C stimulation and provide a potential therapeutic target for inflammatory bowel disease.

*Review of the radiological interpretation of the mesentery demonstrating how findings in abdominal imaging cannot be reconciled with previous interpretations of mesenteric anatomy.

**First radiological evaluation of abdominal imaging based on the modern interpretation of mesenteric and abdominal anatomy.
** Review linking visceral (and hence mesenteric) adiposity with systemic homeostasis and diseases.

*Study examining alterations in the mesenteric fat and its association with disease in Crohn’s disease.

** A review article demonstrating the contribution of the mesentery and its components in the pathogenesis and clinical management of Crohn’s disease.

** Clinical trial demonstrating that visceral fat area is associated with increased recurrence rates in Crohn’s disease.

**Clinical trial examining the histology of the mesentery before and after it has been surgically detached using a strictly mesenteric-based approach.