Key points

- The arterial supply to the splanchnic bed comprises three divisions of the abdominal aorta: the coeliac artery; and the superior and inferior mesenteric arteries.

- Under physiological conditions, blood flow in the splanchnic circulation is controlled via intrinsic (myogenic and metabolic) and extrinsic (autonomic and humoral) mechanisms.

- The splanchnic bed forms an important circulatory reservoir, which can be mobilized during periods of physiological stress.

- Disorders of the splanchnic circulation may contribute to the multi-organ dysfunction syndrome and vice versa.

- A number of techniques used in anaesthesia and critical care influence the distribution of blood flow in the splanchnic circulation.

The splanchnic circulation is a complex system. A number of important functions depend on its normal operation, including digestion and absorption within the gut, maintenance of the mucosal barrier, and successful healing of surgical anastomoses, but we have little quantitative information about its physiology because routine measurement in humans is so difficult. This article outlines some basic science and describes how influential the splanchnic circulation might be in our clinical practice.

Anatomy

The term ‘splanchnic circulation’ describes the blood flow to the abdominal gastrointestinal organs including the stomach, liver, spleen, pancreas, small intestine, and large intestine. It comprises three major branches of the abdominal aorta: the coeliac artery; superior mesenteric artery (SMA); and inferior mesenteric artery (IMA) (Fig. 1). The hepatic portal circulation delivers the majority of the blood flow to the liver.

Coeliac artery

The coeliac artery is the first major division of the abdominal aorta, branching at T12 in a horizontal direction ~1.25 cm in length. It shows three main divisions such as the left gastric artery, common hepatic artery, and splenic artery and is the primary blood supply to the stomach, upper duodenum, spleen, and pancreas.

Superior mesenteric artery

The SMA arises from the abdominal aorta anteriorly at L1, usually 1 cm inferior to the coeliac artery. The five major divisions of the SMA are the inferior pancreaticoduodenal artery, intestinal arteries, ileocolic, right colic, and middle colic arteries. The SMA supplies the lower part of the duodenum, jejunum, ileum, caecum, appendix, ascending colon, and two-thirds of the transverse colon. It is the largest of the splanchnic arterial vessels delivering >10% of the cardiac output and therefore has significant implications for embolic mesenteric ischaemia.

Inferior mesenteric artery

The IMA branches anteriorly from the abdominal aorta at L3, midway between the renal arteries and the iliac bifurcation. The main branches of the IMA are the left colic artery, the sigmoid branches, and the superior rectal artery. It forms a watershed with the middle colic artery and supplies blood to the final third of the transverse colon, descending colon, and upper rectum.

Physiology

Resting splanchnic blood flow (SBF) is typically 30 ml min⁻¹ 100 g⁻¹ of tissue, which equates to 25–30% of the cardiac output.
This may decrease to <10 ml min⁻¹ 100 g⁻¹ in low cardiac output states or peak locally at 250 ml min⁻¹ 100 g⁻¹ after a meal. The splanchnic circulation must therefore be highly adaptive. The mechanisms of physiological regulation of SBF are complex but the academic debate focuses primarily on three circulatory determinants: intrinsic, extrinsic, and humoral (auto-nomic nervous system, and circulating vasoactive substances).

**Intrinsic control**

The splanchnic vascular bed demonstrates an autoregulatory capacity similar to that seen in other vascular beds such as the renal and cerebral circulations. This ensures that a constant blood flow can be maintained across a wide variety of perfusion pressures. There are two proposed mechanisms: metabolic and myogenic control.

The metabolic hypothesis focuses on the balance between oxygen supply and demand rather than blood flow. Accumulation of metabolites such as H⁺, K⁺, adenosine or CO₂ during periods of poor supply and tissue hypoxia serve to produce vasodilation, thereby restoring blood flow. Alternatively increased delivery of oxygen to the tissues will result in vasoconstriction.

The myogenic hypothesis describes the mechanism by which vessels respond to an increase in transmural pressure or stretch by constricting, thereby restoring blood flow to baseline levels. This is mediated through opening of mechano-sensitive cation channels, principally sodium (Na⁺). The resulting depolarization activates voltage-gated calcium (Ca²⁺) channels elevating intracellular Ca²⁺ concentrations, thereby inducing smooth muscle contraction. Conversely the vessels relax and reduce their tone in response to a reduction in transmural pressure.

**Extrinsic control**

All of the splanchnic vasculature with the exclusion of the capillaries receive sympathetic innervation. The postganglionic fibres from the coeliac, superior mesenteric, and inferior mesenteric ganglia follow the path of the corresponding arteries. Sympathetic stimulation exerts a direct effect through the release of noradrenaline mediating α-adrenergic vasoconstriction. Alterations of blood flow in response to sympathetic stimulation follow a triphasic pattern. Initial reductions in flow return to near normal within minutes of stimulation followed by a reactive hyperaemia on cessation of activity. Sympathetic vasoconstriction plays an important role in the distribution of blood volume throughout periods of both physiological and pathological stresses such as exercise and major haemorrhage.

Parasympathetic innervations from the vagal and pelvic nerves synapse with postganglionic fibres in the gut wall. Parasympathetic stimulation increases intestinal motility and secretions, which indirectly increase blood flow. Release of nitric oxide (NO) upon activation of muscarinic receptors (M1) by acetylcholine in the endothelial layer leads to vascular smooth muscle relaxation and an increase in mucosal blood flow.

**Humoral control**

Circulating vasoactive mediators of the splanchnic circulation are legion and may be exogenous or endogenously produced (Table 1). The complex interplay of factors is evident during postprandial hyperaemia. Local production of vasodilator metabolites such as adenosine and CO₂ secondary to increased mucosal metabolic activity and consumption of O₂ lead to increased blood flow. In addition, the hyperosmolar conditions
exerted by the absorption of nutrients directly increases blood flow. Intracellular Na\(^+\) concentrations increase because of hyperosmolar intraluminal conditions. This results in activation of the Na\(^+\)/Ca\(^{2+}\) exchanger, increasing intracellular Ca\(^{2+}\) concentration, which in turn stimulates NO-mediated relaxation of vascular smooth muscle via activation of nitric oxide synthase. Many of the peptide hormones, including cholecystokinin, secretin, and gastrin, have vasodilatory properties. They are released locally during digestion and increase blood flow and gut motility.

### Disorders of the splanchnic circulation

#### Ischaemia-reperfusion injury and the gut origin hypotheses

Hypoperfusion is a common feature in anaesthesia and critical illness. Examples include low cardiac output states, vasodilatory or hypovolaemic shock, and abdominal compartment syndrome (ACS). In such situations, perfusion of other vital organs is often maintained at the expense of the splanchnic circulation. This renders the gut particularly vulnerable to non-occlusive mesenteric ischaemia. Reperfusion triggers a sequence of events beginning with the formation of reactive oxygen metabolites causing tissue damage and the activation and endothelial adhesion of polymorphonuclear neutrophils. The resulting increase in vascular permeability and release of inflammatory mediators into the systemic circulation is important in the development of the systemic inflammatory response syndrome (SIRS) and ultimately the pathophysiology of multi-organ dysfunction syndrome (MODS).

MODS is an important clinical syndrome associated with significant systemic insults such as trauma, pancreatitis, and sepsis, with a mortality in excess of 40%.

The majority of patients who develop MODS secondary to an insult will at some point in the process exhibit a septic response; however, it is recognized that in a significant proportion no precipitating bacterial focus will be identified.

The gut origin hypothesis describes the situation in which splanchic hypoperfusion and loss of gut barrier function may occur during the initial systemic insult. This hypothesis gained prominence with experimental evidence demonstrating that bacterial translocation during laparotomy or in pancreatitis is associated with an increase in infective complications. The link between bacterial translocation and ARDS/MODS is less conclusive with bacteria and endotoxin being identified in the portal blood of only 2% of trauma patients who later went on to develop MODS.

The suggestion that bacterial translocation and liberation of pro-inflammatory mediators may be independent of the disruption of gut barrier function is supported by the observation that in MODS, progressive dysfunction often begins with pulmonary changes, with acute lung injury being the initial clinical picture. This is contrary to the expectation that the liver may be the initial victim if gut derived bacteria or endotoxins were carried in the portal blood. The gut-lymph hypothesis attempts to resolve this paradox. In this model, pro-inflammatory mediators from the stressed or ischaemic gut are delivered to the systemic circulation via the mesenteric lymphatics in the thoracic duct bypassing the liver to the subclavian vein and then the lungs. This theory is endorsed by experimental data.

#### SBF in SIRS/sepsis

It is accepted that sepsis and acute intra-abdominal inflammatory conditions influence the SBF; however, the mechanisms are controversial. Microcirculatory conditions appear to be mediated by local metabolic and paracrine factors, indeed redistribution of blood between mesenteric and muscularis layers has been demonstrated. On the other hand, macrocirculatory flow is influenced predominantly by systemic circulatory conditions such as SVR and CO. Therefore, the precise circulatory milieu is a complex and dynamic process, the evolution of which is dependent on stage of disease (early or late), severity, or therapeutic intervention.

Systemic and microcirculatory disturbance is a prominent feature of severe acute pancreatitis (SAP) and is a key factor in the pathogenesis, progression, and outcome of the disease. At presentation, haemodynamic disturbance is a common feature. Circulating volume is reduced due to increased capillary permeability and third space losses while systemic vasodilatation has a profound influence. These features are common to all severe inflammatory conditions; however, they can be replicated by i.v. infusions of pancreas-derived enzymes such as trypsin, chymotrypsin, and elastase in the animal model.

Evaluation of the splanchnic microcirculation is complicated by the inability to directly measure blood flow and oxygenation in human disease. However, the impairment of the pancreatic microcirculation is recognized as an important factor in the pathogenesis and evolution of necrotizing pancreatitis. It occurs earlier and with greater severity than in self-limiting oedematous pancreatitis and appears to herald progression from mild to severe forms of the disease. Early vasoconstriction leads to reductions in blood flow, capillary stasis, and a loss of capillary density. Furthermore, endothelial dysfunction with activation and adhesion of leucocytes contributes to micro-vessel occlusion, while loss of endothelial barrier function results in increased capillary permeability. This allows migration of large molecules such as activated proteases into the pancreatic tissue causing further cellular destruction. Several therapeutic modalities have been identified which target the pancreatic microcirculation, including reducing the viscosity of blood, anticoagulation, and epidural anaesthesia. However, the influence on morbidity and mortality in clinical trials is inconsistent.

#### The splanchnic circulation in liver disease

The classic disruption of the splanchic circulation secondary to liver disease is portal hypertension (PH). This is most commonly
a result of cirrhosis; however, associated conditions include venous thrombosis, hepatic fibrosis, granulomatous disease (sarcoidosis, miliary tuberculosis), schistosomiasis, and right heart failure. The gold standard for assessing severity is the hepatic venous pressure gradient (HPVG), which is the difference between the free hepatic venous pressure and the wedged hepatic venous pressure. PH occurs when the HPVG exceeds 5 mm Hg. In the later stage of the condition in addition to PH patients with liver disease often have a hyperdynamic circulation characterized by vascular vasodilatation, plasma volume expansion, and increased cardiac output which maintains and exacerbates PH. The pathophysiology of vasodilatation in the hyperdynamic circulation is multifactorial but is ultimately secondary to an elevated production of vasodilators and an abnormal response to vasoconstrictors.7

Patients with PH may present acutely with a number of complications such as ascites, hepatic encephalopathy, hepatorenal syndrome, or spontaneous bacterial peritonitis, which generally are a result of blood that would normally be processed in the liver being shunted into the systemic circulation. Patients may also present with life-threatening haemorrhage from porto-systemic shunts such as gastric or oesophageal varices. These form not only as a direct effect of the increased pressure forcing blood into existing collaterals but also via revascularization under the influence of vascular endothelial growth factor.

The splanchnic circulation in anaesthesia and critical care

Inhalation and i.v. agents

Volatile anaesthetic agents have well recognized effects on systemic haemodynamics, but may also cause regional changes in blood flow to the splanchnic circulation. Despite the obvious importance of these changes, there is limited evidence regarding the effects of individual agents. Propofol and many of the volatile anaesthetics have vasodilatory properties, potentially increasing SBF. The literature does not report a consistent relationship between other i.v. anaesthetics (e.g. etomidate or thiopentone) and SBF. The degree to which changes occur depends on the agent which is being used. There are no data to link these findings with more significant outcomes, and firm conclusions regarding which agent is superior are impossible to make.

Ventilation and IPPV

Intermittent Positive pressure ventilation (IPPV) has well-described effects on the cardiovascular system, which may include a fall in cardiac output principally via a reduction in preload, predictably reducing splanchnic perfusion. The splanchnic circulation is also susceptible to more direct effects of positive pressure ventilation. The use of very large tidal volumes, high levels of positive end expiratory pressure, and high inspiratory pressures have been shown to reduce splanchnic perfusion. These effects appear to be due to increased hepatic venous pressures and mesenteric vascular resistance, with reduced portal blood flow. At normal ventilator pressures, adverse effects appear to be minimal. Sustained recruitment manoeuvres have been associated with a worsening in splanchnic oxygen delivery, despite improving arterial oxygenation. Spontaneous breathing efforts during airway pressure release ventilation have been shown to improve both cardiac output and splanchnic perfusion. Prone ventilation does not affect splanchnic perfusion, provided care is taken to avoid intra-abdominal hypertension. Permissive hypercapnia helps to maintain splanchnic perfusion.8

Sympathomimetic agents

Administration of vasoactive medications is a core component of treatment for a variety of conditions in which splanchnic perfusion may already be at risk. The variety of studies and endpoints of investigation make it difficult to draw clear conclusions about vasoactive medication use. Several receptor systems and their subtypes are important for the regulation of blood flow in the splanchnic circulation. In general, α1 stimulation causes vasoconstriction to a greater degree than α2, and β2 effects appear to be vasodilatory. Dopamine receptors are also present in the gut, principally DA1 and DA2, activation of which results in vasodilatation.

Norepinephrine (mainly α1 and β1 agonist) is the commonest drug used for augmenting the circulation in sepsis. Its effects on splanchnic perfusion appear to be minimal. Within the treatment of sepsis a further increase in mean arterial pressure (MAP) beyond 65 mm Hg did not improve or impair splanchnic perfusion. Phenylephrine (mainly α1) and epinephrine (α1 and β1) have been shown to reduce SBF, and also gastric markers of perfusion.9

Dobutamine (β1 and β2) and low-dose dopamine (DA1 and DA2, β1 and β2, α1 in high dose) all have vasodilatory effects on the splanchnic circulation, and have been shown to improve markers of perfusion. For many years, low-dose infusions of dopamine were used as a prophylactic and therapy for acute renal failure, using the logic that DA1- and DA2-mediated vasodilatation in renal and splanchnic beds would be protective. This was supported by the observation that dopamine promoted a diuresis; however, this is now widely acknowledged to be primarily a result of increased cardiac output due to dopamine’s β1 and β2 effects. Concerns over the potential harmful side-effects of dopamine including thyroid and pituitary dysfunction and immunosuppression and the lack of consistent data from the literature supporting its efficacy has meant that the routine use in high-risk surgery has become less widespread. In addition, from the available data, it would seem that the addition of dobutamine rather than dopamine to a noradrenaline infusion is superior for augmenting mesenteric blood flow.10

Vasopressin is utilized as a second line agent in the treatment of septic shock. It exerts its effect via G-protein coupled receptors (V1), and has been shown to be a vasoconstrictor in the splanchnic circulation. This property of vasopressin analogues is useful in the treatment of variceal bleeding and hepatorenal failure, but it is unclear what effect this may have in the treatment of a septic patient.

Regional anaesthesia

The relationship between regional anaesthesia (RA), in particular thoracic epidural anaesthesia (TEA) and SBF, is poorly characterized. This is of particular interest in colorectal surgery as many clinicians are concerned that direct reductions in tissue perfusion and worsening of tissue oedema as a consequence of fluid resuscitation while managing systemic hypotension might compromise vulnerable bowel anastomoses. Evidence suggests that TEA does not increase the risk of anastomotic leak and may in fact be beneficial.11 Human experimental data are limited, because of primarily difficulties with direct measurement. Furthermore, outcome data are conflicting. Sympathetic block might logically improve flow by reducing splanchnic vascular...
Laparoscopic surgery and the pneumoperitoneum

Normal intra-abdominal pressure (IAP) is 5–7 mm Hg although this varies during the respiratory cycle and may be as high as 14 mm Hg in the obese patient. Intra-abdominal hypertension is defined as an IAP >12 mm Hg while ACS occurs at pressures >20 mm Hg. The haemodynamic effect of laparoscopic surgery is principally determined by a number of factors including the insufflation pressure and the gas used. It is also worth noting however that laparoscopic surgery is more likely to use extremes of patient position such as head up or down for prolonged periods.

Clinical and experimental studies, with outcomes measured directly and indirectly, demonstrate that perfusion of the splanchnic organs is inevitably compromised by the pneumoperitoneum. The degree of this compromise is directly proportional to the pressure used. Typically insufflation pressures between 12 and 15 mm Hg are used during laparoscopic surgery, although this is tailored according to a variety of factors, and is a compromise between surgical access and potential haemodynamic compromise. It is of interest to note that deep neuromuscular block has been shown to facilitate laparoscopic cholecystectomy to be performed at lower insufflation pressures and was associated with better operating conditions when compared with moderate neuromuscular block.

The most widely used gas to establish pneumoperitoneum is CO₂. It has a number of favourable qualities because it is inexpensive, readily available, easily absorbed, and non-flammable. Argon and helium have been used as replacements for CO₂. These gases appear to have benefits experimentally; however, concerns over the potential for gas embolism and pneumothorax of non-absorbable gases mean that they are unlikely to be accepted as viable alternatives.

Laparoscopic surgery is well tolerated in fit patients, the majority of case reports of mesenteric ischaemia after operation have occurred in patients with significant cardiovascular co-morbidities. In this group, a number of strategies that aim to limit the impact of pneumoperitoneum have been advocated. The ‘dial-down’ approach uses standard inflation pressure which is sequentially reduced to find the lowest acceptable point. Alternatively, gas can be intermittently released from the abdomen during the procedure. Finally, the reverse Trendelenburg position should be avoided where possible because reduced venous return may compromise cardiovascular stability.

Monitoring and measurement

Splanchnic perfusion can be measured in a variety of ways; however, because of a variety of issues, monitoring has not become common in clinical practice. The use of indicator dilution with Indocyanine green (ICG) was first described more than 40 yr ago. This original application of this technique required hepatic venous catheterization to measure the post-hepatic concentration of ICG. From this the application of the Stewart–Hamilton equation (originally applied to calculate cardiac output using dye dilution) can be used to calculate an SBF, flow equals the amount of injectate divided by the area under the post-hepatic concentration curve. ICG is eliminated from the blood solely by hepatocytes. This process can be monitored non-invasively using the principle of pulse spectrophotometry and the optical absorption of ICG with a transcutaneous probe, allowing for assessment of liver function and splanchnic perfusion.

Gastric tonometry has been extensively studied as a monitor of splanchnic perfusion. This technique requires a gastric catheter to measure the concentration of carbon dioxide within the stomach and arterial measurements of carbon dioxide and bicarbonate. Using the Henderson–Haselbalch equation the gastric intramucosal pH (pHi) can be calculated. Alternatively the concentration difference between gastric and arterial carbon dioxide concentration (PgCO₂) can be calculated. Both pHi and PgCO₂ are prognostic indicators in the critically ill. Although not directly part of the splanchnic circulation assessments of the sublingual circulation have now been developed. This utilizes its greater accessibility within the gastrointestinal tract. The use of sublingual capnometry allows sublingual CO₂ to be measured (PsCO₂) which has been correlated with lactate concentrations and outcomes. At present, this remains an area of interest for the future without any clear evidence to support its widespread use. Laser Doppler flowmetry utilizes the frequency shift (Doppler principle) in a laser beam to measure flow. This has been used in trials to establish colonic blood flow, as have ultrasound-based Doppler measurements.

Supplementary feeding

Enteral nutrition has been established as an important part of the management of critically ill patients. Expert guidelines recommend that enteral feeding should be commenced early (<24 h) in all patients not expected to tolerate a full oral diet within 3 days. Under physiological conditions, oral alimentation results in a ‘postprandial hyperaemic response’, mediated primarily by local humoral and mechanical factors. The fact that this response is mirrored in critically ill patients receiving enteral nutrition raises safety concerns in the haemodynamically unstable patient. The first being the potential for triggering bowel ischaemia by an increase in oxygen demand exceeding supply, the second being the potential for the steal phenomenon whereby gut
blood flow increases at the expense of other ‘vital’ organs. Despite these anxieties, the benefits of early enteral nutrition appear to be apparent even in patients requiring vasopressor support. In contrast, SBF appears to be reduced during parenteral nutrition. This may be due to an increase in systemic basal metabolism resulting in diversion of blood towards systems with a higher basal metabolic rate.

**Conclusion**

Much of what we know about the physiology of the splanchnic circulation has been extrapolated from experimental studies because routine assessment of SBF in humans is impractical. Techniques for direct measurement are invasive while reliability issues hamper indirect alternatives. As such a thorough understanding of the splanchnic circulation during the perioperative period and critical illness remains elusive. Despite these problems, manipulation of splanchnic physiology is a fascinating area of research and therapeutic techniques for targeting the splanchnic circulation, such as RA in sepsis or SAP merit further investigation.

**Declaration of interest**

None declared.

**MCQs**

The associated MCQs (to support CME/CPD activity) can be accessed at [https://access.oxfordjournals.org](https://access.oxfordjournals.org) by subscribers to BJA Education.

**References**

2. Zani BG, Bohlen HG. Sodium channels are required during in vivo sodium chloride hyperosmolality to stimulate increase in intestinal endothelial nitric oxide production. Am J Physiol Heart Circ Physiol 2005; 288: H89–95