SPLANCHNIC ISCHEMIA AND MULTIPLE ORGAN FAILURE

Edited by
Adrian Marston
Gregory B. Bulkley
Richard G. Fiddian-Green
Ulf H. Haglund

Splanchnic Ischemia and Multiple Organ Failure

Edited by

Adrian Marston

MA DM MCh FRCS MD
Consultant Surgeon,
The Middlesex and University College Hospitals, London
Senior Lecturer in Surgery,
University College and Middlesex School of Medicine, University of London, England

Gregory B. Bulkley

MD FACS
Mark M. Ravitch Professor of Surgery,
Director of Surgical Research,
The Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

Richard G. Fiddian-Green

MA BM BCH FRCS FACS
Professor and Chairman,
Division of General Surgery, University of Massachusetts Medical Center, Worcester, Massachusetts, USA

Ulf H. Haglund

MD PHD
Professor and Chairman,
Department of Surgery, Uppsala University Hospital, Uppsala, Sweden

The C. V. Mosby Company
St. Louis * Washington, D.C. * Toronto

1st edition, 1st printing

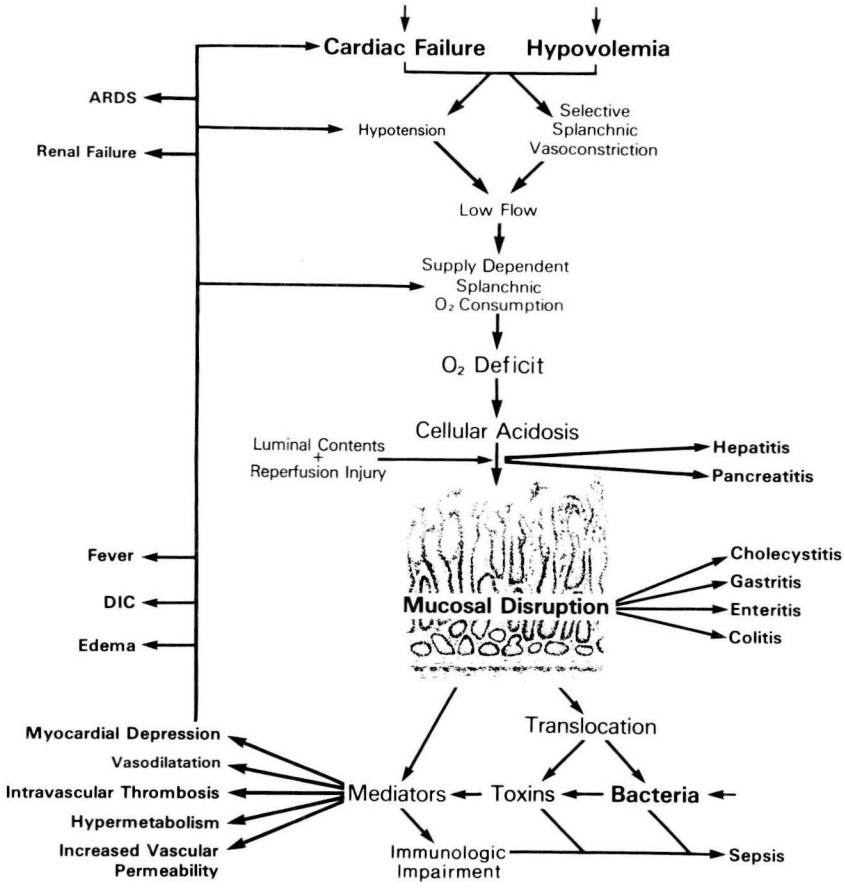
Distributed in the United States by
The C. V. Mosby Company
11830 Westline Industrial Drive
St. Louis, Missouri 63146
U.S.A.

Distributed in Canada by
The C. V. Mosby Company, Ltd.
5240 Finch Avenue East
Scarborough, Ontario
CANADA M1S 4P2

ISBN 0-8016-5523-4

Typeset in Baskerville 10/11 pt by Butler & Tanner Ltd
Printed and bound in Great Britain for Edward Arnold, the educational, academic and medical division of Hodder and Stoughton Limited, 41 Bedford Square, London WC1B 3DQ by Butler & Tanner Ltd, Frome

Splanchnic Ischemia and Multiple Organ Failure



Causes and effects of Splanchnic Ischemia

Contributors

Dag Arvidsson MD, Senior Registrar: Department of Surgery, Uppsala University Hospital, Uppsala, Sweden

Robert W. Bailey MD, Assistant Professor of Surgery: University of Maryland School of Medicine, Baltimore, Maryland, USA

Haim Bitterman MD, Post Doctoral Fellow in Ischemia: Shock Research Institute of Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Anders Borgstrom MD PhD, Assistant Professor of Surgery: Department of Surgery, Malmo General Hospital, Sweden

Gregory B. Bulkley MD FACS, Mark M. Ravitch Professor of Surgery, Director of Surgical Research: The Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

John L. Cameron MD FACS, Warfield M. Firor Professor and Chairman, Section of Surgical Sciences: The Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

Nicholas D. Carr MS FRCS, Lecturer in Surgery: University College and Middlesex School of Medicine, University of London, England

Jeffery A. Clemens MD FACS, Fellow in Surgery: The Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

Richard G. Fiddian-Green MA BM BCh, FACS FRCS, Professor and Chairman, Division of General Surgery: University of Massachusetts Medical Center, Worcester, Massachusetts, USA

Mitchell P. Fink MD, Associate Professor of Surgery and Anesthesiology, University of Massachusetts Medical School; Director, Surgical Intensive Care Units: Department of Surgery, University of Massachusetts Medical Center, Worcester, Massachusetts, USA

D. Neil Granger PhD, Professor of Physiology: Louisiana State University, Shreveport, Louisiana, USA

Matthew B. Grisham PhD, Assistant Professor of Physiology: Louisiana State University Medical Center, Shreveport, Louisiana, USA

Karen D. Crissinger MD PhD, Assistant Professor of Pediatrics and Physiology: Louisiana State University Medical Center, Shreveport, Louisiana, USA

Nelson J. Gurll MD, Professor of Surgery: Department of Surgery, University of Iowa College of Medicine, Iowa City, Iowa, USA

Ulf H. Haglund MD PhD, Professor and Chairman: Department of Surgery, Uppsala University Hospital, Uppsala, Sweden

Christopher C. Kibbler MA MB MRCP, Senior Registrar: Department of Clinical Microbiology, The Middlesex and University College Hospitals, London, England

Peter R. Kvietys PhD, Associate Professor of Physiology: Louisiana State University Medical Center, Shreveport, Louisiana, USA

Iain McA. Ledingham MB ChB MD FRCSEd FRCP (Glas) FRSE, Professor of Intensive Care, University of Glasgow; Honorary Consultant, Western Infirmary: Department of Surgery, Western Infirmary, Glasgow, Scotland

Allan M. Lefer PhD, Professor of Physiology; Chairman of the Department of Physiology: Jefferson Medical College, Philadelphia, Pennsylvania, USA

Ove Lundgren MD PhD, Professor of Physiology: University of Göteborg, Göteborg, Sweden

Michael A. Maddaus MD, Medical Fellow: Department of Surgery, University of Minnesota Medical School, Minneapolis, USA

John C. Marshall MD FRCSC, Assistant Professor of Surgery: Dalhousie University, Halifax, Nova Scotia, Canada

Adrian Marston MA DM MCh FRCS MD, Consultant Surgeon, The Middlesex and University College Hospitals; Senior Lecturer, University College and Middlesex School of Medicine: London, England

Jonathon L. Meakins MD DSc FRCS(C) FACS, Professor of Surgery and Microbiology: McGill University, Montreal, Canada

Carol L. Miller PhD, Professor of Molecular Genetics and Microbiology; Professor of Surgery: Division of Surgical Research, University of Massachusetts Medical Center, Worcester, Massachusetts, USA

John G. Mosley BSc MD MRCP FRCS, Consultant General and Vascular Surgeon: Leigh General Infirmary, Leigh, Lancs, England

Paul E. O'Brien MD FRACS, Professor of Surgery; Chairman, Department of Surgery, Monash University: Monash Medical School, Victoria, Australia

John Pegington MD FRCS, SA Courtauld Professor of Anatomy: Department of Anatomy and Developmental Biology, University College London, England

John Maurice Porter MD FACS, Fellow in surgery: The Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

Graham Ramsay MD FRCS, Senior Registrar, Department of Surgery, Western Infirmary, Glasgow, Scotland

Richard L. Simmons MD FACS, Professor and Chairman, Department of Surgery, University of Pittsburgh, Pennsylvania, USA

Marc S. Sussmann MD, Fellow in Surgery: The Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

Gyongyi Szabo PhD, Post Doctoral Fellow of the Immunology Program, University of Massachusetts Medical Center, Worcester, Massachusetts, USA

Kenneth M. Taylor MD FRCS FRCSE FSA, Professor of Cardiac Surgery, University of London; Professor and Chief of Cardiac Surgery, Royal Postgraduate Medical School: Hammersmith Hospital, London, England

Selwyn M. Vickers MD, Fellow in Surgery: Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

Carol L. Wells PhD, Assistant Professor, Departments of Surgery and of Laboratory Medicine and Pathology: University of Minnesota Hospital Center, Minneapolis, Minnesota, USA

Jia Yan Wu PhD, Post Doctoral Fellow of the Immunology Program, University of Massachusetts Medical Center, Worcester, Massachusetts, USA

Introduction

The concept of the gastrointestinal tract as an internal 'siege mechanism' owes as much to fashion as to science. Sir Arbuthnot Lane, a famous British surgeon of the 1920s, is remembered for his early use of the internal fixation of fractures, but is almost better known for his theory of 'autointoxication' by bacteria, which led to the widespread and remunerative practice of removing the healthy colon from the wealthy patient. This was lampooned in Bernard Shaw's play *The Doctor's Dilemma*.[1] The dilemma persists. Many years later, and with much more scientific justification, Dr Jacob Fine and his team in Boston produced the concept that absorption of bacterial endotoxin from the GI tract was responsible for death from 'irreversible shock', following all manner of physical stresses, especially trauma and hemorrhage.[2] This theory, again, was disputed and rejected.[3] When it became possible to visualize the living circulatory anatomy of various organ systems, and to measure their blood flows, the idea was advanced that a compromised intestinal circulation might render the body susceptible to all the consequences of an infarcted gut, following a fall of pressure in the splanchnic bed.[4]

Over the years many such speculations have been disproved; but recently, because of advances in care of the critically ill, interest has reawakened in the potential of the alimentary tract as a focus of multiple organ failure. This has come about through a fruitful communication between anatomists, physiologists, microbiologists, immunologists and scientifically minded physicians. Such a group was convened by Dr Richard Fiddian-Green of the University of Massachusetts and met in the (perhaps rather unlikely) venue of Monte Carlo, in September 1987.

Although the idea of the present book was born at that meeting, it does not represent the proceedings of a symposium. Such publications are rather like travel snapshots in that, while of great interest to the participants, they seldom capture the imagination of those who were not there. However, as the publishers, Edward Arnold, had been responsible for producing two previous books on the intestinal circulation,[5,6] this was a convenient opportunity to synthesize the new knowledge and exciting developments which had taken place since the publication of *Intestinal Ischaemia* in 1976. Adrian Marston was appointed as Senior Editor, and Gregory Bulkley, Richard Fiddian-Green and Ulf Haglund as Sectional Editors. In addition to those present in Monte Carlo, experts have been recruited widely from America and Europe to cover areas not dealt with at the meeting.

After the usual introductory material, the book is designed in four sections. Part I is concerned with the normal state of the splanchnic circulation, including the gross and microscopic anatomy, mechanisms of regulation of blood flow and of absorption and insorption, and direct methods of measurement of flow.

Part II examines the causes and effects of disturbances of this normal state. A first sub-section is concerned with the ways in which general events in the body can affect the gut. These include mechanical vascular occlusion, vasospasm, and the release of vasopressor materials. The second sub-section describes the intimate events which take place in the gastrointestinal tract, as a result of these influences. This includes the role of mucosal hypoxia, the effect of oxygen-derived free radicals, of locally released enzymes, and of bacterial products. The final sub-section is devoted to the systemic consequences of such pathology including the systemic release of endotoxins and myocardial depressant factors, the activation of the arachidonic

acid/thromboxane pathway, and the role of the damaged bowel in immunosuppression.

Part III deals with the clinical syndromes resulting from the mechanisms previously described, including acute and chronic ischemia of the small intestine, ischemic colitis and syndromes outside the bowel which are now being recognized as ischemic in origin.

Finally, Part IV draws the whole of the preceding material together, and identifies the central role of the gut in the pathogenesis of multiple organ failure. This includes the detection and prediction of systemic syndromes by the examination of mucosal flow, the overall stragety practised in the modern intensive care unit, and the detailed clinical care of the patient with the threatened bowel.

Adrian Marston
Gregory B. Bulkley
Richard Fiddian-Green
Ulf H. Haglund

References

1. Shaw G B. *The Doctor's Dilemma*. London, 1906.
2. Fine J, Frank E D, Rutenberg S H, Schweinburg F B. The bacterial factor in traumatic shock. *New Eng J. Med* 1959; **260:** 214–16.
3. Einheber A. Recent progress and present problems in the field of shock. *Fed. Proc.* 1961; Supp 9: 170–1.
4. Marston A. The bowel in shock. *Lancet* 1962; **2:** 365–7.
5. Marston A. *Intestinal Ischaemia*. London: Edward Arnold.
6. Marston A. *Vascular Disorders of the Gastrointestinal Tract*. London: Edward Arnold, 1986.

Contents

C *Systemic mediators of splanchnic origin*

III SPLANCHNIC ORGAN INJURY SYNDROMES

IV MULTIPLE ORGAN FAILURE SYNDROMES

1 SPLANCHNIC VASCULAR ANATOMY AND PHYSIOLOGY

1

Macroscopic anatomy

Adrian Marston and John Pegington

This chapter is concerned with the gross and macroscopic structure of the intestinal arteries, veins and lymphatics (lacteals), but mainly with the arteries, upon whose integrity depends the effective function of the alimentary tract as an absorptive, excretory, propulsive and endocrine organ. The basic outlines of this complicated structure were worked out by classic studies over a hundred years ago[1] using the Vesalian techniques of formal cadaveric dissection. Later authors[2–4] defined the detailed architecture of the system. However, such formal methods tell us little about the working of the living, moving human body, and nothing of the subvisual components of the circulation on which function depends. To conventional dissections have now been added *diaphanization* techniques[5] and radiologic studies using selective arterial catheterization. The *microvasculature* has been further analyzed by means of injection of prepared specimens,[6] by corrosion casts and by induced *x-ray fluorescence*.[7] These techniques are discussed in Chapter 2.

There are three components to the splanchnic arterial tree. First are the *main vessels* arising from the aorta, which are of great clinical importance but, because pressure within them is virtually identical to central (left ventricular) pressure, have little influence on blood flow. Second are the visible, surgically accessible, vessels, knowledge of whose anatomy is essential in clinical practice – referred to in this book as the *intermediate vessels*. The *microcirculation* is the final common pathway of arteries, capillaries and venules, and has a lymphatic component. Events here, the actual territory of oxygen exchange, are the true determinants of intestinal function.[8] This, too, is discussed in Chapter 2.

The main arteries

The three main visceral arteries correspond to the embryological areas of the gastrointestinal tract: the foregut, midgut and hindgut. Of these, much the largest is the midgut, which is that part of the alimentary system which emerges into the extra-embryonic celom during the eighth week of fetal life on the axis of its main vessel, the *superior mesenteric artery* (SMA). The arteries to the foregut (the *celiac axis*, CA) and the hindgut (the *inferior mesenteric artery*, IMA) convey relatively less blood to the intestine, and, through collateral pathways, their distribution extends into extracelomic structures (Figs 1.1–1.6). Patterns of blood supply to the gut are variable, and in only one-half of cases is the 'classic' arrangement found.[9] For this reason it is sometimes difficult to distinguish between an anatomical difference and an abnormality caused by disease.

The celiac trunk (axis)

The celiac trunk emerges from the front of the aorta at the level of the first lumbar vertebra (see Fig. 1.2). The aorta is bridged by the median arcuate ligament of the diaphragm just above the origin, and the trunk may be kinked at this point, with a poststenotic dilatation below. The clinical significance of this variant, however, has caused dispute. The trunk is surrounded by the celiac plexus of nerves which are connected to the right and left celiac ganglia on the sides of the vessel. The plexus and ganglia receive inputs from the greater and lesser splanchnic nerves, the vagi and the phrenic nerves. The pancreas and the splenic vein lie below the trunk. Some fibres of the suspensory ligament of the diaphragm (ligament of Treitz) may surround the origin of the vessel.

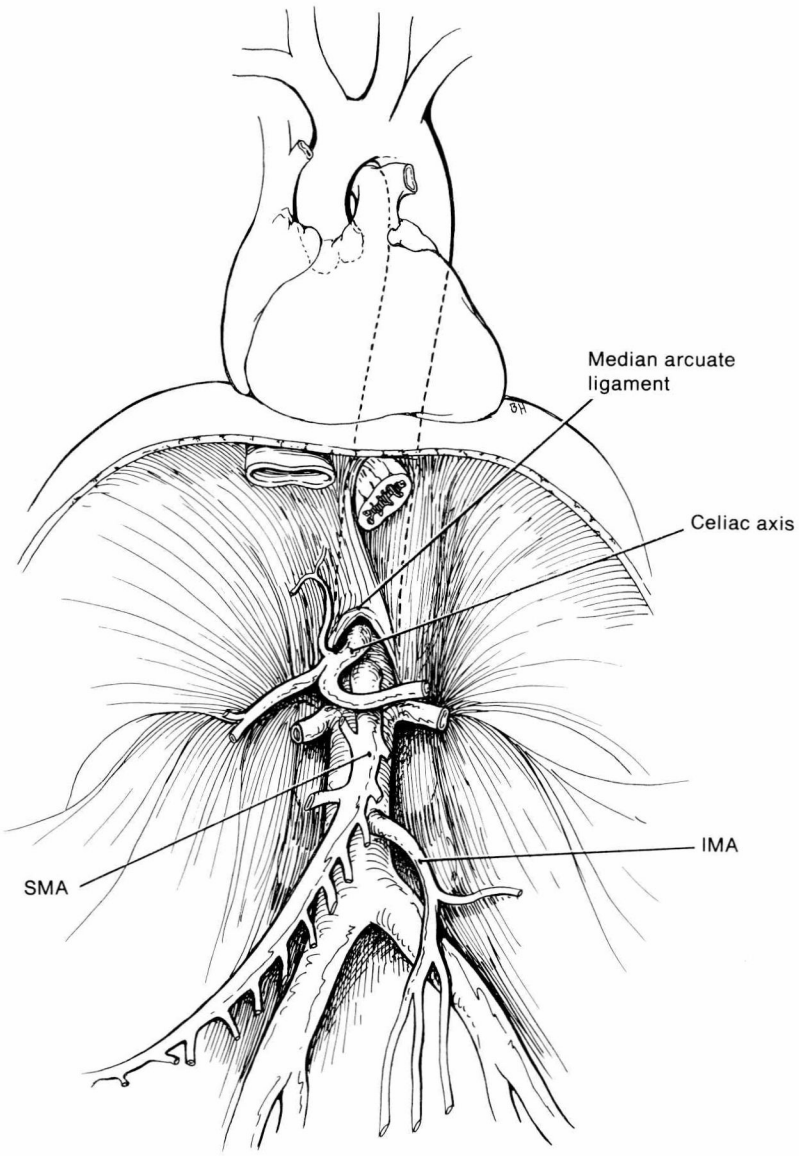


Fig. 1.1 The visceral branches of the aorta.

The celiac trunk is only about 1.25 cm long, and immediately divides into three branches, the splenic, left gastric and hepatic arteries. Occasionally, however, a branch or branches may arise independently from the aorta, or additional branches such as the inferior phrenic and superior mesenteric vessels may arise in common with the celiac trunk.

The *splenic artery* runs upwards and to the left behind the omental bursa and the stomach, and continues along the upper border of the body and tail of the pancreas. It enters the hilum of the spleen between the two layers of the lienorenal ligament where it divides into five or more segmental branches. The splenic artery is unusual in that it does not run a direct course but is tortuous throughout its length. This feature can sometimes be put to surgical use, in that the spleen may be removed and the splenic artery mobilized, straightened out and brought down to other parts of the mesenteric circulation to irrigate an ischemic area. Pancreatic

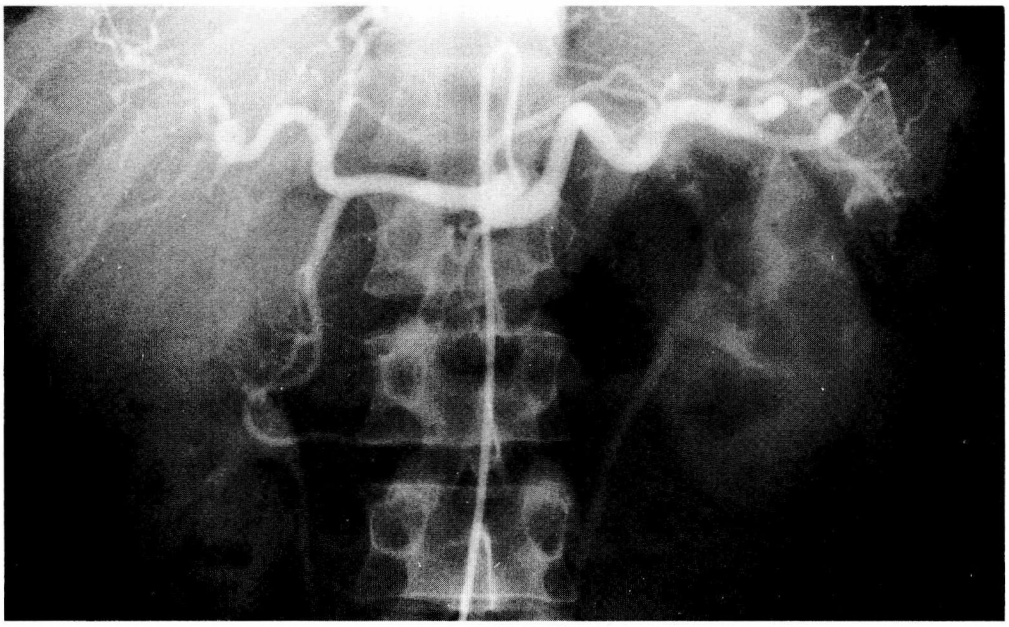


Fig. 1.2 Selective angiogram showing distribution of the CA.

branches arise from the splenic artery along the upper border of that organ. One of these, the dorsal branch, is large and divides into right and left branches. The right branch travels between the neck and uncinate process of the pancreas and anastomoses with branches of the anterior superior pancreaticoduodenal artery: the left branch travels along the inferior border of the pancreas towards the tail. Two named pancreatic branches are the arteria pancreatica magna and the arteria caudae pancreatis which supply blood to the body and tail of the organ respectively. Five or more short gastric branches of the splenic artery (vasa brevia) arise near its termination, pass between the leaves of the gastrosplenic ligament, and are distributed to the fundus of the stomach. They anastomose with the left gastric and left gastroepiploic arteries. The left gastroepiploic artery arises from the splenic artery close to the splenic hilum. It sends several long branches through the gastrosplenic ligament to the greater curvature of the stomach and ends as a large omental branch which anastomoses with the termination of the right gastroepiploic artery. It should be noted that the omental branches of the gastroepiploic arteries do *not* supply branches to the transverse mesocolon even though this is adherent to the greater omentum. The posterior gastric artery, a fairly large vessel, is often found arising from the middle of the splenic artery and reaches the back of the stomach in the gastrophrenic fold of peritoneum.

The *left gastric artery* runs upwards and to the left from the celiac axis, behind the omental bursa, to reach the cardiac end of the lesser curvature of the stomach. The vessel gives several esophageal branches which travel upwards through the esophageal opening of the diaphragm and these often supply twigs to the cardiac part of the stomach. The main trunk of the left gastric artery turns downwards between the layers of the lesser omentum and often divides into upper and lower branches. The upper branch supplies the upper part of the lesser curvature and connects with the esophageal arteries, the phrenic branches of the aorta and the lower intercostals. The lower branch runs down to anastomose with the right gastric artery around the pyloric antrum. The left gastric artery sometimes gives an important supply to the liver via a large accessory left hepatic artery which runs across the lesser omentum. An accessory left gastric artery may arise from the left branch of the hepatic artery, travel between the layers of the lesser omentum, and reinforce the blood supply along the lesser curvature.

The *hepatic artery* runs to the right, along the upper border of the head of the pancreas, to the first part of the duodenum. Here it gives off the large and

important gastroduodenal artery, which grooves the pancreas as it runs down behind the first part of the duodenum to the left of the common bile duct. The gastroduodenal is usually the first branch of the hepatic artery.[10] The vessel sometimes gives a supraduodenal branch to the first part of the duodenum, and during its retroduodenal course supplies pyloric and duodenal branches, and twigs to the head and uncinate process of the pancreas. It ends at the lower border of the first part of the duodenum by dividing into right gastroepiploic and superior pancreaticoduodenal branches. The section of the hepatic artery between the celiac trunk and the origin of the gastroduodenal artery is known as the *common hepatic artery*. After giving off its gastroduodenal branch, the main trunk of the hepatic artery turns upwards to reach the liver, and this section of the vessel is known as the *hepatic artery proper*. The hepatic artery proper leaves the duodenum and travels upwards in front of the epiploic foramen in the free edge of the lesser omentum. Here it lies in a variable relationship to the portal vein and common bile duct, but usually lies in front of the portal vein and to the left side of the bile duct. The right gastric artery or leash of vessels most frequently arises beyond the origin of the gastroduodenal artery. It descends in the lesser omentum to the lesser curvature of the stomach and anastomoses with the left gastric artery. Near the hilum of the liver the hepatic artery proper divides into right and left branches which supply the respective 'lobes' of the liver. It should be noted that these 'lobes' do not correspond to the classical lobes based on the surface marking of the falciform ligament attachment. The hepatic artery, portal vein and bile duct divide and subdivide within the liver to supply segments, but the divisions of the hepatic veins do not follow the pattern of the hepatic triads. The cystic artery is usually a branch of the right branch of the hepatic artery. An accessory cystic artery may arise from the common hepatic artery. The superior pancreaticoduodenal arteries are usually two in number: one lies in front between the pancreatic head and the duodenum and the other behind. The arteries anastomose with branches of the inferior pancreaticoduodenal vessels. The superior pancreaticoduodenal artery supplies blood to the pancreatic head and duodenum, and to the lower end of the bile duct.

In the non-cirrhotic liver some two-thirds of the oxygen and nutritional requirements are met by the portal vein, so that occlusion of the hepatic artery is relatively well tolerated. It used to be thought that interruption of this vessel led invariably to necrosis of the liver; but such is not in fact the case, and the hepatic artery is quite frequently tied deliberately, as part of the treatment of metastatic tumours. Conversely, when the SMA is occluded, the hepatic artery may contribute significantly to the blood supply of the gut, without any deleterious effect on liver function. Variations in the origin and branches of the hepatic artery are fairly common. An accessory left hepatic artery sometimes arises from the left gastric artery, and on other occasions an accessory right hepatic artery comes from the SMA and runs upwards behind the portal vein to the porta hepatis.

The superior mesenteric artery

The superior mesenteric artery (SMA) is clinically by far the most important vessel of the alimentary tract. It arises from the front of the aorta 1 cm below the celiac trunk, just above the renal arteries and at the level of the L1/2 intervertebral disc (see Figs 1.3 and 1.4). At its origin it is crossed in front by the body of the pancreas and the splenic vein. It is separated from the aorta by the left renal vein. At its origin it is 1–5 cm in diameter. It runs downwards immediately in front of the uncinate process of the pancreas, and then passes in front of the third part of the duodenum to enter the mesentery of the small intestine. This area can sometimes be seen on a barium study as a band of translucency running vertically across the duodenum. If the proximal duodenum appears dilated, this normal finding may be misinterpreted as representing an obstruction, to which clinical symptoms are then attributed. In fact, the syndrome of 'duodenal ileus' has little factual evidence to sustain it, and has never been confirmed by endoscopy. This band of translucency probably also accounts for the mythical 'sphincter of Ochsner' analogous to the high-pressure zones at the ileocecal valve and rectosigmoid junction.

The SMA continues in a curve within the mesentery towards the right iliac fossa where it anastomoses with one of its own terminal branches, the ileocolic artery. The convexity of the curve of the artery is usually directed downwards and to the left. The SMA is accompanied on its right side by the superior mesenteric vein, and as it travels within the mesentery it crosses the front of the inferior vena cava and the right ureter. Occasionally a fibrous remnant of an embryonic artery which runs to the yolk sac is found running between the terminal part of the SMA and the umbilicus.

The origin of the SMA, lying well back in the