

# The Gastrointestinal System at a Glance



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# Preface

## How to use this book

This book presents a graphic scaffold for further detailed study and is an aid to revision. Therefore, it will be useful for students approaching a subject for the first time, particularly as part of an integrated systems-based medical curriculum. The diagrams will make abstract concepts more memorable and help the student to recall details that might otherwise be lost in plain text. The student may further annotate the diagrams with additional details from lectures, tutorials and self-directed study, to help with later revision.

## Organization of the book

The book is organized in four parts, starting with a structural and functional overview of the main components of the gastrointestinal system, followed by consideration of integrated gastrointestinal function, which requires some preceding basic knowledge. Clinical examples are included throughout these early chapters highlighting the practical importance of each subject.

The third and fourth sections are more clinical, and cover the most important gastrointestinal and hepatobiliary diseases and the main aspects of diagnosis and treatment. Fundamental pathophysiological mechanisms are emphasized.

## Anatomical and clinical detail

The anatomical diagrams are functional representations, and not exact reproductions, and they are used to illustrate how structure supports function.

Similarly, specific diseases are discussed to demonstrate pathogenic mechanisms and general principles, rather than to provide exhaustive detail. This book should be used to understand the normal physiology, how it goes wrong in disease, and the principles underlying modern clinical practice in gastroenterology and hepatology.

Satish Keshav

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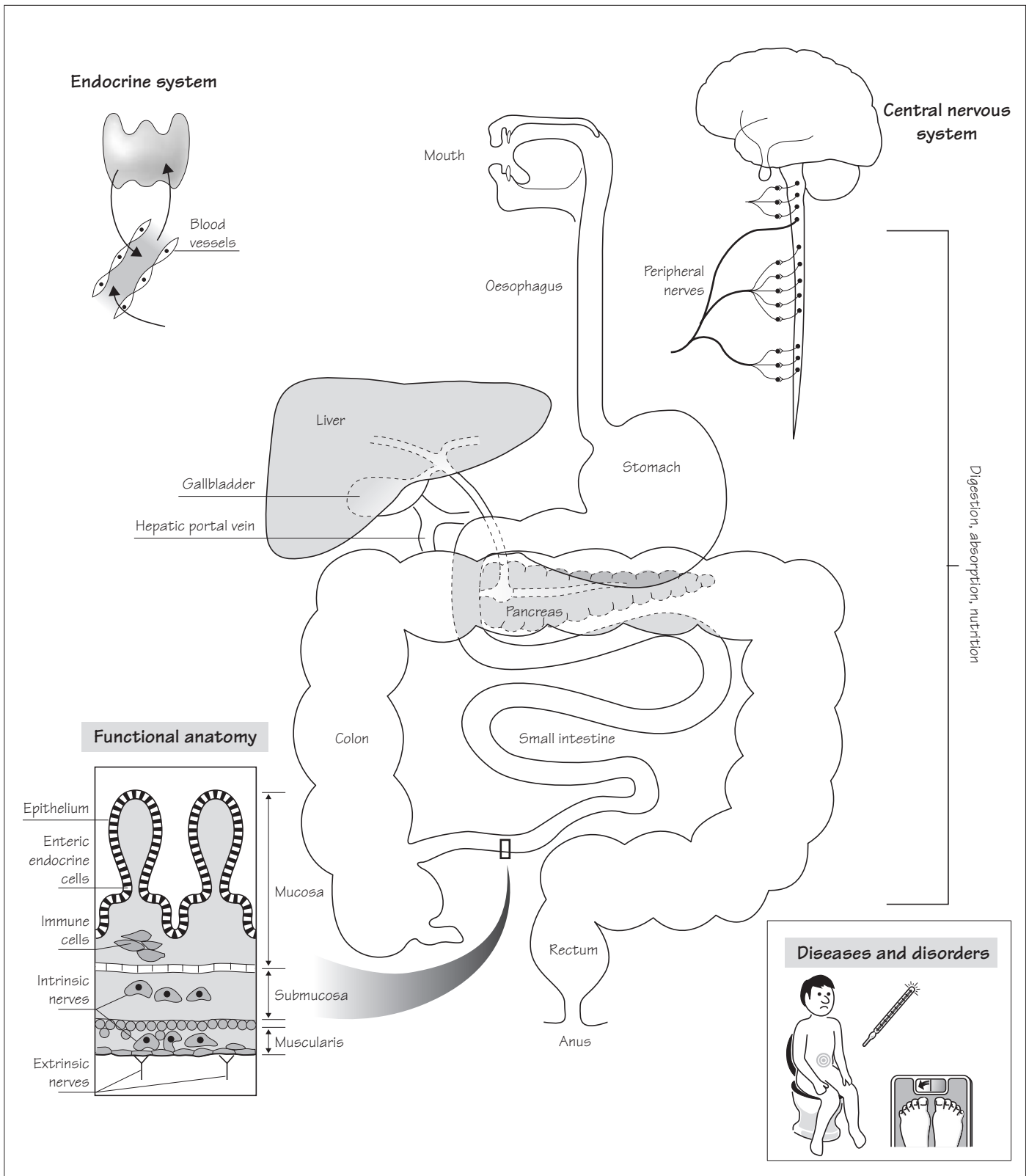
pertinent questions and useful comments. I also thank Michael Stein, who suggested this book, and Camilla and Vijay, who helped me to complete it.



# List of abbreviations

ACh	acetylcholine	HIV	human immunodeficiency virus
AFP	$\alpha$ -fetoprotein	HNPPC	hereditary non-polyposis colon cancer
AIDS	acquired immune deficiency syndrome	5HT	5-hydroxytryptamine
ALP	alkaline phosphatase	IBD	inflammatory bowel disease
ALT	alanine transaminase	IBS	irritable bowel syndrome
ANCA	antineutrophil cytoplasmic antibodies	IF	intrinsic factor
5ASA	5-aminosalicylic acid	Ig	immunoglobulin
ASCA	antibodies to <i>Saccharomyces cerevisiae</i>	IL	interleukin
AST	aspartate transaminase	IMMC	interdigestive migrating motor complex
ATP	adenosine triphosphate	IPSID	immunoproliferative small intestinal disease
ATPase	adenosine triphosphatase	K <sup>+</sup>	ionized potassium
BAT	bile acid transporter	LPS	lipopolysaccharide
BEE	basal energy expenditure	MAD-CAM	mucosal addressin-cell adhesion molecule
BMI	body mass index	MEN	multiple endocrine neoplasia
BMR	basal metabolic rate	Mg <sup>2+</sup>	ionized magnesium
BSE	bovine spongiform encephalopathy	MHC	major histocompatibility complex
Ca <sup>2+</sup>	ionized calcium	MOAT	multispecific organic anion transporter
cAMP	cyclic adenosine 3',5'-cyclic monophosphate	MRA	magnetic resonance angiography
CCK	cholecystokinin	MRCP	magnetic resonance cholangiopancreatography
CD	Crohn's disease	MRI	magnetic resonance imaging
CEA	carcino-embryonic antigen	NA	noradrenaline
CFTR	cystic fibrosis transmembrane regulator	Na <sup>+</sup>	ionized sodium
cGMP	cyclic guanosine monophosphate	NAPQI	<i>N</i> -acetyl- <i>p</i> -benzoquinone-imine
CGRP	calcitonin gene-related peptide	NO	nitric oxide
Cl <sup>-</sup>	chloride ion	NSAIDs	non-steroidal anti-inflammatory drugs
CO <sub>2</sub>	carbon dioxide	OAT	organic acid transport
CoA	coenzyme A	PBC	primary biliary cirrhosis
CRC	colorectal cancer	PET	positron emission tomography
CRP	C-reactive protein	pIgA	polymeric immunoglobulin A
CT	computerized tomography	POMC	pro-opiomelanocortin
CTZ	chemoreceptor trigger zone	PSC	primary sclerosing cholangitis
DA	dopamine	PT	prothrombin time
DMT	divalent metal transporter	PY	peptide Y
DNA	deoxyribonucleic acid	RNA	ribonucleic acid
ECL	entero-chromaffin-like	SBP	spontaneous bacterial peritonitis
EHEC	enterohaemorrhagic <i>Escherichia coli</i>	SC	secretory component
EPEC	enteropathogenic <i>Escherichia coli</i>	SGLT	sodium-glucose co-transporter
ERCP	endoscopic retrograde cholangiopancreatography	sIgA	secretory dimeric immunoglobulin A
ESR	erythrocyte sedimentation rate	STa	heat-stable enterotoxin
ETEC	enterotoxigenic <i>Escherichia coli</i>	TECK	thymus and epithelial expressed chemokine
FAP	familial adenomatous polyposis	TGF $\beta$	transforming growth factor $\beta$
Fe <sup>2+</sup>	ferrous iron	TIPSS	transjugular intrahepatic portosystemic shunt
Fe <sup>3+</sup>	ferric iron	TNF $\alpha$	tumour necrosis factor $\alpha$
GABA	$\gamma$ -amino butyric acid	TPN	total parenteral nutrition
$\gamma$ GT	$\gamma$ -glutamyl transferase	tTG	tissue transglutaminase
H <sup>+</sup>	ionized hydrogen	UC	ulcerative colitis
H <sub>2</sub> O	water	USS	ultrasound scanning
H <sub>2</sub> R	histamine receptor type 2	VC	vomiting centre
HCG	human chorionic gonadotrophin	VIP	vasoactive intestinal peptide
HCl	hydrochloric acid	VLDL	very low-density lipoproteins
HDL	high-density lipoproteins	WHO	World Health Organization
5-HIAA	5-hydroxyindole acetic acid		

# Introduction and overview



## Structure and function

The gastrointestinal system comprises the hollow organs from mouth to anus that form the gastrointestinal tract, the pancreas, which mainly secretes digestive juices into the small intestine, and the liver and biliary system, which perform vital metabolic functions in addition to their contribution to digestion and absorption of nutrients.

### The intestinal tract

A hollow tubular structure into which nutrient-rich food is coerced, and from which wastes are expelled, is found in the most primitive multicellular organisms, from the hydra onwards. In humans, the tract is highly specialized throughout, both structurally and functionally. The mouth and teeth are the first structures in this tract and are connected by a powerful muscular tube, the oesophagus, to the stomach. The stomach stores food after meals and is the site where major digestive processes commence. The small intestine is the main digestive and absorptive surface. The large intestine acts mainly as a reservoir for food waste and allows reabsorption of water from the mainly liquid material leaving the small intestine. It is not essential for life and, paradoxically, is affected by a number of common, serious diseases, such as inflammatory bowel disease and colorectal cancer.

### The pancreas

Digestive enzymes are produced in many parts of the gastrointestinal tract, including the mouth (salivary glands) and small intestine (enterocytes), although the exocrine pancreas is the most prodigious producer of digestive enzymes. Pancreatic failure causes malabsorption, which can be reversed by artificial enzyme supplements.

### The liver and biliary system

Without the liver, survival is measured in hours, and no artificial system has yet been devised to substitute for hepatic function. The liver is the largest solid organ in the body and its essential functions include regulation of protein, fat and carbohydrate metabolism, synthesis of plasma proteins, ketones and lipoproteins, and detoxification and excretion. Via the hepatic portal circulation it receives and filters the entire venous drainage of the spleen, gastrointestinal tract and pancreas. Through the production of bile, it is also essential for digestion and absorption, particularly of dietary fats and fat-soluble vitamins.

## Integrated function

The gastrointestinal system is controlled by both intrinsic and extrinsic neuronal and endocrine mechanisms. Enteric nerves and endocrine cells are particularly important in coordinating motility, digestion and absorption, and in regulating feeding and overall nutrition, including the control of body weight.

The gastrointestinal system presents a huge surface area that has to be protected against injury, particularly from microbial pathogens that are

ingested with food and from the large population of commensal bacteria that populate the intestine. The mucosal immune system is critically important in regulating how the intestine responds to these challenges, providing protection and not reacting inappropriately to normal components of the diet.

## Diseases and disorders

Nausea, vomiting, diarrhoea and constipation are common symptoms and their basic pathophysiology illustrates important aspects of gastrointestinal function.

Gastrointestinal symptoms are frequently not associated with any discernible pathological abnormality. These medically unexplained symptoms are often labelled functional disorders and, as our understanding of gastrointestinal physiology becomes more sophisticated, we may discover new explanations and treatments that are more effective.

Gastrointestinal system infections are common and are associated with significant morbidity and mortality worldwide. They range from self-limiting food poisoning to life-threatening local and systemic infections. Even peptic ulceration is most frequently caused by infection, with the *Helicobacter pylori* bacterium.

For some major diseases, such as inflammatory bowel disease, the aetiological agent has not been identified, despite rapidly advancing genetic and molecular research. Conversely, coeliac disease, another serious and common gastrointestinal inflammatory disease, is caused by a well-characterized immune response to wheat-derived proteins.

Colon cancer is a major cause of cancer-related death and our molecular and cellular understanding of its pathogenesis, and the pathophysiology of other gastrointestinal, pancreatic and liver tumours, is rapidly increasing.

Liver damage is often caused by infections or drugs and may be acute or chronic. Acute liver disease can rapidly progress to liver failure, or can resolve, either spontaneously or with appropriate treatment. Chronic liver disease may cause cirrhosis, which is characterized by a variety of signs and symptoms and changes throughout the body, including the effects of hepatic portal venous hypertension.

The gastrointestinal system is essential to nutrition, and disordered nutrition is a major issue worldwide – both through undernutrition and starvation and through overnutrition, which causes obesity, possibly the single most important modern health problem in the affluent world.

## Diagnosis and treatment

Clinical assessment, including a focused history and examination, is the foundation of diagnosis. In addition, the gastrointestinal system can be investigated by endoscopy, radiology and specific functional tests. Endoscopy and radiology may also be used therapeutically, and pharmacotherapy and surgery for gastrointestinal disorders exploit many unique features of the structure and function of the system.