It was over ten years ago that we identified the need for an introductory gastroenterology textbook that would be useful to students, residents, family physicians and specialists. We decided this textbook should be relatively concise and readable, with appropriate figures, tables and algorithms, providing a logical and practical approach to patient management. It should cover the pathological basis of gastrointestinal and hepatobiliary disease, provide a list of learning objectives and be well indexed. We intended the book would not replace the standard encyclopedic tomes or excellent in-depth reviews, but would instead present a complementary first step to the vast and exciting field of gastroenterology. We also recognized that there was a place for important topics such as the clinical trials that form the basis of much of our modern practice and the crucial new area of molecular biology as it applies to clinical practice and patient care. We also thought it important that such a tribute to Canadian gastroenterology be made available in both official languages, English and French. And we considered it essential to bring out such a textbook in a timely manner and at a modest cost.

The first four editions of the resulting *First Principles of Gastroenterology* were sponsored by Astra and then AstraZeneca. For this, we are most grateful. When they chose not to continue their support, we were absolutely delighted that Janssen-Ortho enthusiastically agreed to support this important educational tool with an “arms-length” grant to fund the current publication and distribution of this 5th Edition of *First Principles*. The book will be available to all medical students in Canada, as well as to medical residents, gastroenterologists and family physicians. The current edition has remained true to our original tenets, having been well-received by the community of learners. Our intent in the 5th Edition is to not only update the information, but
to enhance the text with more tables and figures to better convey the basics of
gastroenterology. This represents a major revision, under a new publisher, The
Medicine Group, as a sign of our personal commitment to an ever-changing
discipline that keeps us all enthralled.

We appreciate the continued endorsement of the Canadian Association of
Gastroenterology and the Canadian Association for the Study of the Liver. To
our readers, we welcome your suggestions and comments – this textbook is at
the forefront of medical knowledge and we are eager to use modern teaching
and communication methods to help you remain at the forefront.

To all our chapter captains and contributors, thank you most sincerely for
your excellent contributions. It is a pleasure working with you and we look
forward to many future years of successful collaboration.

Alan B.R. Thomson
Eldon A. Shaffer
To Jeannette – kind and caring, bright and energetic, you have taught me the meaning of family, of commitment, always; to James, Matthew and Allison, Jessica and Matt, and Ben – through your youthful idealism, compassion for others, friends and fun, you have shown me the hope for the future and the promise of a better tomorrow; to Tom, Gary and Ivan – for your support, acceptance, encouragement, mentoring and friendship; to Robin – fellow teacher and author, for showing me the value of the spoken history and recorded memories, helping me to make my own writing perhaps more enjoyable.

To Beryl, a wife who has made me a better person and a more caring physician; to my talented daughters, Andrea, Emily and Alexandra, who have embarked on careers that will help people with their health and their decisions in life; to my father, Henry, a compassionate family physician, now deceased, who was my role model and influenced many of my colleagues; and to mentors like Douglas Kinnear, Donald Small and Clarence Guenter, whose stature as doctors, scientists and leaders in medicine I attempted to emulate.

To Janet Chlebo – for believing in this project, for believing in us, for your understanding, knowledge and wisdom; to Sarah Thorp – for her energy and enthusiasm in seeing this project to completion; and to our patients, whom we have the privilege of helping. May this book in some small way provide knowledge, and may our dedicated spouses, children, friends and colleagues support our art of medicine and of life, compassion and justice.

It is both in caring for and caring about our patients and for each other that we truly become good persons and great physicians.

A.B.R. Thomson
E.A. Shaffer
Endorsement

The Canadian Association of Gastroenterology and its members are proud to endorse the 5th edition of *First Principles of Gastroenterology*. This highly successful text is written for the undergraduate and graduate student of gastrointestinal and liver disease, and for the practicing clinician providing digestive health care to patients. The disciplines of gastroenterology and hepatology, like all of medicine, are continuously evolving. This text provides a comprehensive and current review of these disciplines, and will serve as an invaluable resource for students and practitioners alike. The Canadian Association of Gastroenterology hopes that you find it informative and stimulating.

William J. Paterson, MD
President, Canadian Association of Gastroenterology

It is my pleasure to endorse this 5th edition of *First Principles of Gastroenterology*. This Canadian-authored textbook has been an indispensable guide to both established practitioners and to numerous residents as they enter and progress through their training. This latest edition, as with the previous versions, incorporates a Canadian viewpoint, which is often different from that of the USA or Europe, where the other major textbooks originate. This edition maintains the tradition of excellence developed in previous editions. Finally, the authors of the section on liver diseases highlight the excellence of hepatology in Canada.

Morris Sherman, MD
President, Canadian Association for Study of the Liver
Contents

Dedication v
Preface vii
Endorsements ix

1 Common Symptoms and Signs in Gastroenterology. 3

1 Introduction / W.G. Thompson and C. Dubé 3
2 Globus / C. Dubé and W.G. Thompson 4
3 Heartburn and Regurgitation /
   C. Dubé and W.G. Thompson 5
4 Dysphagia / A.S.C. Sekar 6
5 Dyspepsia / C. Dubé 8
6 Nausea and Vomiting / M.C. Champion 9
7 Anorexia / M.C. Champion 12
8 Gas and Bloating / W.G. Thompson 13
9 Constipation / C. Dubé and W.G. Thompson 16
10 Diarrhea / W.G. Thompson 19
11 Malnutrition / D.G. Patel 22
12 Acute Abdomen / J.M. Watters 24
13 Chronic Abdomen / W.G. Thompson 28
14 Jaundice / L.J. Scully 30
15 Ascites in Chronic Liver Disease / L.J. Scully 32
16 Gastrointestinal Bleeding / A. Rostom and C. Dubé 33
17 Abdominal Mass / S. Grégoire 37
18 Proctalgia Fugax / W.G. Thompson 40
19 Examination of the Abdomen / R.F. Bursey, J.M. Fardy, D.G. MacIntosh and N. Saloojee 41
Suggested Reading List 48
Practice Points 48

1 Introduction 49
2 Essential Physiologic Concepts in Nutrition 49
3 Clinical and Laboratory Features of Protein-Energy Malnutrition 55
4 Effects of Malnutrition on the Gastrointestinal Tract and Pancreas 56
5 Dietary Therapy in Gastrointestinal Disease 59
6 Dietary Therapy in Liver Disease 63
7 Nutrition Intervention 65
References 78
Suggested Reading List 78
Objectives 78

3 Pharmaceutical Research and Clinical Trials: The Basis for New Knowledge. B.G. Feagan and A. Archambault 79
1 Introduction 79
2 Clinical Research Regulations and Supervision 79
3 Clinical Drug Development 80
4 Methodology in Clinical Research 82
5 Planning a Clinical Trial 83
6 Informed Consent Form and Ethical Issues 85
7 Clinical Monitoring 85
8 Institutional Review Committee (IRC) 86
9 Reporting the Results of Clinical Research 86
10 Conclusion 86
Bibliography 87

1 Introduction 88
2 Anatomy 88
3 Physiology 90
4 Symptoms and Signs of Esophageal Diseases 94
5 Investigations Used in the Diagnosis of Esophageal Disease 97
6 Anatomic Variants 101
7 Gastroesophageal Reflux Disease (GERD) 105
8 Nonreflux-Induced Esophagitis 113
9 Disorders of the Oropharyngeal Phase of Deglutition 116
10 Motor Disorders of the Esophagus and Lower Esophageal Sphincter 119
11 The Esophagus as a Cause of Angina-Like Chest Pain 123
12 Esophageal Neoplasms 125
13 Miscellaneous Disorders of the Esophagus 130

Suggested Additional References 135
Objectives 135

1 Introduction 138
2 Anatomy 138
3 Gastric Physiology 142
4 Gastritis 145
5 Pathophysiology of Peptic Ulcer Disease 153
6 NSAIDs and Gastric Duodenal Diseases 160
7 Helicobacter Pylori and Peptic Ulcer Disease 162
8 Non-Variceal Gastrointestinal Hemorrhage 164
9 Gastric Malignancy 168
10 Other Gastric Diseases 172

Suggested Reading List 173

6 The Small Intestine. H.J. Freeman and A.B.R. Thomson 175
1 Gross Anatomy and Histology of the Small Intestine 175
2 Small Intestinal Motility 177
3 Principles of Absorption 178
4 Absorption of Vitamins and Minerals 178
5 Absorption of Water and Electrolytes 183
6 Absorption of Fat 192
7 Absorption of Carbohydrates 194
8 Absorption of Protein 199
9 Malabsorption or Malabsorption 202
10 Acute Diarrhea 209
11 Chronic Diarrhea 225
12 Disaccharidase Deficiencies 232
13 Gluten-Induced Enteropathy (Celiac Disease) 234
14 Short Bowel Syndrome 242
10 The Colon. G.K. Turnbull, S.J. Vanner, M. Burnstein and J. Burke
   1 Introduction 357
   2 Physiology of the Colon / S.J. Vanner 357
   3 Specific Colonic Diseases / G.K. Turnbull and J. Burke 364
   4 The Anal Canal / M. Burnstein 395
   5 Lower Gastrointestinal Bleeding / S.J. Vanner 408
   Suggested Reading List 414
   Objectives 414

11 The Pancreas. F. Habal, H. Gaisano and P. Rossos 417
   1 Anatomy 417
   2 Physiology 419
   3 Pancreatic Function Tests 423
   4 Pancreatitis 428
   5 Carcinoma of the Pancreas 443
   6 Pancreatic Islet Cell Tumors 450
   7 Pancreas Divisum 452
   8 Cystic Fibrosis in the Adult 453
   Objectives 458

12 The Biliary System. E.A. Shaffer and J. Romagnuolo 460
   1 Gallstone Disease 460
   2 Cholecystitis 470
   3 Acalculous Gallbladder Disease 477
   4 Diseases of the Bile Ducts 480
   Objectives 487
   Learner Workbook 489

   1 Liver Structure and Function / E.A. Shaffer and R.P. Myers 491
   2 Approach to the Patient with Liver Disease / J.B. Simon 500
   3 Evaluation of Abnormal Liver Enzyme Results in Asymptomatic Patients / J.P. Villeneuve 513
   4 The Liver and Drug Disposition / P. Paré and J.P. Villeneuve 522
5 Congenital Hyperbilirubinemias / P. Paré 527
6 Acute Viral Hepatitis / P.T. Grover and M. Ma 530
7 Chronic Viral Hepatitis / P.T. Grover and V. Bain 548
8 Alcoholic Liver Disease / F. Wong 567
9 Non-Alcoholic Fatty Liver Disease / G. Kichian and W. Wong 574
10 Drug-Induced Liver Disease / J.B. Simon 579
11 Inherited Liver Disease / E.A. Roberts and P.C. Adams 585
12 Cholestasis / J. Heathcote 589
13 Cirrhosis of the Liver / J. Heathcote 596
14 Portal Hypertension / S.S. Lee and S.K. Baik 601
15 Ascites and Spontaneous Bacterial Peritonitis / F. Wong 612
16 Hepatic Encephalopathy / L.J. Worobetz 623
17 Hepatorenal Syndrome / K.M. Peltekian 629
18 Liver Transplantation / L.B. Lilly, N. Girgrah and G.A. Levy 632
19 Neoplasms of the Liver / L.J. Worobetz 643
20 Liver Disease in Pregnancy / R.P. Myers and E.A. Shaffer 651
21 Vascular Disorders of the Liver / L.J. Worobetz 658
Suggested Reading List 662
Objectives 667
Practice Points 671
Research Agenda 677

14 Manifestations of Gastrointestinal Disease in the Child. 681
M. Robertson, J.D. Butzner, H. Machida, S.R. Martin, H.G. Parsons and S.A. Zamora

1 Functional Gastrointestinal Disorders with
   Abdominal Pain / M. Robertson 681
2 Vomiting and Regurgitation / M. Robertson 685
3 Chronic Constipation / M. Robertson 695
4 Growth Failure and Malnutrition / M. Robertson, S.A. Zamora and H.G. Parsons 701
5 Acute Diarrhea in Children / J.D. Butzner 710
6 Cystic Fibrosis / H. Machida 718
7 Approach to the Jaundiced Neonate / M. Robertson and S.R. Martin 725
Suggested Reading and/or References 735
Objectives 736
The Applications of Recombinant DNA Technology in Gastrointestinal Medicine and Hepatology: The Basic Paradigms of Molecular Cell Biology.


1 Introduction 738
2 Eukaryotic Gene Structure and DNA Replication 741
3 Eukaryotic Gene Transcription and Post-Transcriptional RNA Processing 764
4 Protein Synthesis and Post-Translational Processing in Eukaryotic Cells 782
Abbreviations 809
References 809
Acknowledgements 814

List of Contributors 817
Index 825