set forth in this text are in accord with current recommendations and practice at the time of
publication.
However, in view of ongoing research, changes in government regulations, and the constant flow
of information
relating to drug therapy and drug reactions, the reader is urged to check the package insert for
each drug for
any change in indications and dosage and for added warnings and precautions. This is particularly
important when
the recommended agent is a new and/or infrequently employed drug.

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This book is dedicated to our wives, Matilde and Maddalena.
They are the only ones who really know how much time we spent on it.
C.S.
G.B.P.

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Foreword

For too long a time, and for too many physicians, the clinical physiology
of the stomach has been no more than a synonym for the physiology of acid
secretion. For the elderly gastroenterologist, to whom gastric function of ten
means no more than the hydrogen ion (and the respective validities of MAO
versus PAO), this book should come, if not as a revelation, then as a salutary
shock. For younger colleagues, it will be a welcome panorama of the contemporary clinical physiology of the human stomach.

Gastroenterology is waking up from the prolonged obsession with the suppression of acid as the ultimate therapy, and entering the real world where all aspects of organ physiology and pathophysiology need to be considered in the management of organ dysfunction. As - at least in the developed world - ulcer disease diminishes in incidence at the same time as treatment becomes ever more effective, so do patients who present with benign, nonulcerous, but troublesome gastric disorders claim an ever-increasing proportion of the gastroenterologist's time and effort. To understand these problems, we need to consider all aspects of what the stomach does and how this can be assessed by the clinician. This is, in essence, the territory claimed by this book.

What primary function is served by the human stomach? 'Digestion' is the reflex response, but as the pernicious anaemia patient can testify, achlorhydria is not a functional problem. It is to the gastrectomised patient that we must look for the answer. The stomach allows us the luxury of ingesting a large meal in a short time, while releasing it into the small intestine at a slow and controlled rate which does not overwhelm the digestive and absorptive process. While the food is resident in the stomach, it is preprocessed so that solids are dispersed into small particles with a surface area that is large in relation to their volume and thus readily accessible to enzymatic attack. Viewed in this way, the importance of the motor function of the stomach is obvious, and this forms the second part of this book.

The stomach can be considered as a reservoir, a mechanical grinder, and a hopper that feeds the digestive tube. Yet the digestive function cannot be ignored. The exocrine secretions, acid and pepsin, are not crucial to the function of the stomach, but they aid in the mechanical breakdown of nutrient solids. Yet, at the same time, they threaten the integrity of the stomach itself; when this integrity is compromised, inflammation and ulceration are the result. We now have a clearer understanding of the auto protective secretory functions of the stomach, in the form of mucus and bicarbonate secretion. In health, protective secretions are sufficient to maintain the integrity of the 'gastric mucosal barrier', but it is easily appreciated that breakdown can occur for a number of reasons; not merely an excess of acid and pepsin, but also a fault in the mucus-bicarbonate barrier. All these
mechanisms need to be taken into account, as they are in the first part of this volume, if we are to understand the pathophysiology of the individual patient, and to devise appropriate treatment. We need also to remember that medicine is not only about science; it is about people who live within specific cultures. It has long been known that the stresses inherent in society disturb gastric function. Moreover, for much of our contemporary world, it is a melancholy fact that hedonistic impulses are often satisfied by substances - tobacco and alcohol - that threaten the delicate balance of efficient digestion and mucosal protection in the stomach. To give realistic advice to our patients, we need to understand how to adjust the balance between the physiology of the stomach and the social ecology of its owner. This approach is reflected in the altered approach to clinical measurement, utilising methods that are less invasive, or even noninvasive. This is not simply because of greater sensitivity towards the potential hazards of intubation, instrumentation, and radiation, but also because of increasing awareness that if the perturbations of gastric physiology by the environment are to be understood, then the constraints of that environment should be, if possible, maintained during the study and not replaced by wholly artificial conditions. To give a single example, it has been possible to study moment-to-moment changes in gastric function in patients in whom motion sickness is being induced using the noninvasive technique of electrogastrography. It would be foolish, however, to abandon established techniques altogether in favour of new technology; such methods are still under evaluation and should be regarded as adjuncts and not alternatives to existing models of study. Nor, as we are reminded within these pages, should we neglect the advantages that flexible endoscopy has given us in being able to directly examine gastric tissue. The control mechanisms of the stomach are not easily accessible in the clinical context. As far as neural control is concerned, we can only deduce changes in neural control from altered function of the mucosal and muscular effector cells. But, with the benefit of sensitive and specific assays for
regulatory peptides, at least some of the controls are accessible. Two decades ago, the study of gut hormones did not just grow, it exploded. Now that the dust and smoke have subsided, we can see that two peptides are of peculiar relevance to gastric function; moreover, unlike most of the other putative 'hormones', they are not diffusely distributed throughout the nervous system as regulatory neuropeptides, but are confined to the gastroduodenum. Gastrin has an unquestioned role in the control of acid secretion, while motilin has the unique property of inducing the powerful contractions of the fasting stomach that are alone capable of expelling solid residues. The discovery that erythromycin and its macrolide analogues can restore the propulsive function of the stomach in diabetic neuropathy through their action on motilin receptors gives a new relevance to the physiology of an otherwise somewhat enigmatic polypeptide.

At this point, I must declare an interest. I was honoured to be invited to serve as chairman of the symposium which gave birth to this book. The less than onerous duties of a scientific obstetrician were lightened by the company, who are the authors of this book, and by the pleasures of the ancient village of Sirmione, almost but not quite a floating island in the calm waters of Lake Garda. On that day, the shore of the lake and the distant Alps were obscured by mist. Out of that mist, has emerged the fully-grown progeny, which is this book. I can only hope that it will serve to dispel the obscurity which has concealed many aspects of gastric function from our colleagues in clinical gastroenterology.

London, June 1990 David Wingate

Preface

In recent years, the proliferation of gastroenterologic procedures has broadened the diagnostic and therapeutic options available to the clinician; it has also increased the need for a standardized approach to their selection, technique and interpretation. From time to time one is thus justified in attempting a critical overview of the available methodology and its clinical relevance. This idea prompted us to bring together in a symposium a number of the leading experts in the field, known for their direct personal experience
and their acknowledged clinical and scientific expertise. The meeting was held in Sirmione on Lake Garda, Italy, in April 1988, under the auspices of the annual Congress of the European Association of Gastroenterology and Endoscopy (EAGE), and aroused strong interest both on account of the issues addressed and the outstanding quality of the presentations.

In light of the consent obtained, we felt it worthwhile to compile a series of reviews to further consolidate the mass of general and specific information existing in the field. Our original idea was to collect manuscripts of the speeches presented at the symposium to merely publish a book of proceedings. Later, we realized that a more complete work could be of help for all the colleagues involved in the everyday investigation of gastric function. We therefore planned additional chapters covering all the important gastric parameters, some of which are often neglected in clinical practice. Additional distinguished scientists enthusiastically joined us in this adventure and we now present to the reader what we hope will become a reference book.

Both secretory and motor functions of the stomach are reviewed with the aim to present complete and concise information regarding technical procedures, indications and interpretation of results. In addition, the pathophysiology and measurement of the digestive hormones (i.e. gastrin and motilin)

Preface

involved in the physiologic regulation of gastric secretion and motility are surveyed. Finally, an approach to gastric functions by endoscopy and biopsy is also described. This book, which includes much of the information difficult to collect from other scattered sources, will be of interest to gastroenterologists and digestive surgeons engaged in the everyday clinical investigation of gastric function. Gut physiologists and pharmacologists will find it extremely useful in selecting the appropriate technique to study the effect of physiological or pharmacological stimuli on the secretory and motor functions of the human stomach.

We would like to thank the staff of S. Karger AG Medical and Scientific Publishers, Basel, especially Mrs. Denise Greder and Anke Rogal, for their efficiency in the publication of this volume. They have shown infinite patience in their willingness to accept continually shifting deadlines. We are indebted to our referees who kindly reviewed the papers and greatly helped us in the editorial work. Our sincere gratitude goes also to Glaxo Italy for their financial backing of publication costs. We have been fortunate to obtain contributions from top flight experts. Without all of them, this book would never have gone to press.