preface

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Widespread use of 24-hour esophageal pH monitoring has left little doubt that gastroesophageal (acid) reflux is an almost universal and daily occurrence even in asymptomatic healthy subjects. Nevertheless, only a small percentage of the population at risk develops reflux esophagitis and an even smaller number demonstrates evidence of severe (macroscopic) disease. These observations serve to emphasize the importance of mechanisms other than the antireflux barriers (i.e. the lower esophageal sphincter, acute angle of His, etc.) as determinants of reflux disease. Antireflux barriers are indeed the first line of defense designed only to limit the frequency and volume of contact between gastric contents and the esophageal epithelium. When this fails, a second line of defense known as esophageal clearance comes into play. This defense, composed of esophageal peristalsis for volume removal and swallowed salivary secretions for acid neutralization, is designed to limit the duration of contact between gastric contents and the esophageal epithelium. However, esophageal clearance is not instantaneous and it is inoperable during sleep. Thus, the total daily time for acid contact with the esophagus may be considerable, necessitating an additional defense to avoid significant injury to the epithelium. This third line of defense is commonly referred to as tissue resistance. That tissue resistance is effective in epithelial protection against acid is best illustrated by experimental studies in which antireflux barriers and esophageal clearance mechanisms are bypassed. In such studies, the esophageal epithelium may be exposed to acid for substantial periods of time, but despite this, exhibits little if any morphologic evidence of injury.

Unfortunately, relatively little work has been done on esophageal mucosal resistance compared to the gastroduodenal one. As a consequence, improvement of mucosal resistance has been rarely attempted as a therapeutic goal in the treatment of esophageal lesions, acid neutralization or inhibition being the first logic approach, due to the damaging effect of acid onto the esophageal mucosa.

Some interesting work however has recently focused on how esophageal squamous epithelium resists attack by acid, and the underlying biochemical mechanisms of epithelial disruption are being clarified. To gain new insights into these physiologic and pathophysiologic processes, we organized a symposium at the 4th International Congress of OESO, which took place in Paris during the 1st week of September 1993. There, world renown scientists presented an in-depth review of the current status of the knowledge.

With the ever-increasing number of volumes of conference proceedings, the criticism is often made that they are poorly organized or edited, or that they appear on the market so long after

the meeting that the contents are out of date. These criticisms are irreconcilable: the editing of a journal supplement necessarily causes months of delay. Nevertheless, we believe that this issue with its updated papers should contribute to a better knowledge of such clinically relevant, but often forgotten, topic. Increasing understanding of the physiologic mechanisms of defense

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indeed will surely contribute to find out the right place for mucosal protective compounds in our therapeutic armamentarium.

The esophageal epithelium maintains its integrity by epithelial defenses which are made up of structural and functional components. Structural components are the physical barrier consisting of cell membranes and intercellular junctional complexes. The functional ones include cellular defense against acidification and epithelial repair. In addition to these defensive mechanisms, there is an effective immunologic system composed of aggregated and nonaggregated lymphoid cells that constitutes the first immunologic barrier to luminal antigens. The function of this gut-associated lymphoid tissue, which is present in the esophagus as well as in other parts of the gastrointestinal tract, is just beginning to be appreciated. All these components of esophageal defense together with the measurement of transmucosal potential difference as an index of mucosal integrity are thoroughly reviewed and presented with many original observations and thoughtful comments by the contributors to this supplement. We are indebted to all of them for having agreed to share with us their knowledge and for providing us with excellent manuscripts despite their many daily commitments. We also wish to thank all the participants who contributed significant time, ideas and enthusiasm. Ultimately, it was them who made the symposium a great success. Among them are not only the speakers but also those investigators in the audience who made valuable criticism and stimulated the lively discussion.

We sincerely hope that new thoughts or ideas may arise from a reading of the present issue. Its publication, and the purpose of the original symposium, will then have been justified. We would like to thank Mr. Peter Roth and Mr. René Müller of S. Karger AG, Basel for their excellent cooperation during the publication of this supplement. We also acknowledge the help of Michèle Liegeon and Sabina Cavagni in collecting the manuscripts for this issue, nagging authors to submit their papers, organizing the contents and interacting with the referees and the publisher. Moreover, we are grateful to Houdé Laboratories, Paris, who supported the symposium and helped us to back the publication costs. Last but not least, our sincere gratitude goes to Dr. Iva Pelosini and Dr. Enzo Grossi at Bracco SpA, Pharmaceutical Division, who rendered this publication possible. They have grasped the scientific significance of the topic from the very beginning and made huge efforts to make these proceedings available to the medical community.

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