International
Congress Series 555

STOMACH DISEASES

CURRENT STATUS

Editors:

Y. M. F. van Maercke
E. M. J. van Moer
P. A. R. Pelckmans

STOMACH DISEASES
CURRENT STATUS

Proceedings of the 13th International Congress on Stomach Diseases, Antwerp, May 1–2, 1981

Editors:
Y.M.F. VAN MAERCKE
E.M.J. VAN MOER
P.A.R. PELCKMANS
University of Antwerp, Belgium

1981

EXCERPTA MEDICA, AMSTERDAM-OXFORD-PRINCETON

International Congress Series No. 555
ISBN Excerpta Medica 90 219 0500 0
ISBN Elsevier North-Holland 0 444 90228 7

Library of Congress Cataloging in Publication Data
International Congress on Stomach Diseases (13th : 1981 :
Antwerp, Belgium)
Stomach diseases.
Includes indexes.
1. Stomach--Diseases--Congresses. 2. Gastrointestinal system--Diseases--Congresses. I. Maercke, Y. van. II. Moer, E. van. III. Pelckmans, P. IV. Title.
[DNLM: 1. Stomach diseases--Congresses. W3 IN662H 13th 1981s / WI 300 I61 1981s]
RC816.157 1981 616.3'3 81-15237
ISBN 0-444-90228-7 (Elsevier North-Holland)
AACR2

Publisher:
Excerpta Medica
305 Keizersgracht
1000 BC Amsterdam
P.O. Box 1126

Sole Distributors for the USA and Canada:
Elsevier North-Holland Inc.
52 Vanderbilt Avenue
New York, N.Y. 10017

Printed in The Netherlands by CASPARIE-AMSTERDAM

13th International Congress on Stomach Diseases

Organized by:

European Association for Gastrocamera Diagnosis and Endoscopy

in cooperation with:

Flemish Society for Gastroenterology
Pelgian Society for Endoscopy

Congress President:

Yvan van Maercke

Congress Vice-President:

Charles Dive

Welcome address

The 13th International Congress on Stomach Diseases is the first meeting in the field of gastroenterology to be held at the University of Antwerp. Our University is a young one; it emerged from the planning stage less than ten years ago and our Academic Hospital has now been fully operational for only one year; therefore, we feel proud indeed to welcome such a distinguished international gathering.

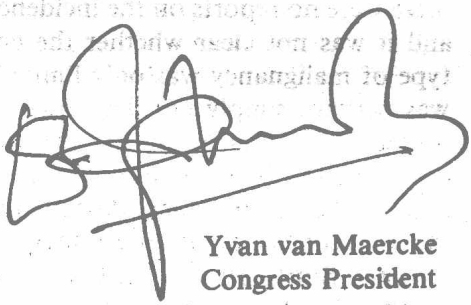
The European Society for Gastrocamera Diagnosis and Endoscopy, which I have had the honor to preside for the past two years, was founded in Berlin in 1970, at the initiation of Professor Oshima from Tokyo. At the time it had struck members of the Japanese school that there were no reports on the incidence of early gastric cancer in Europe and it was not clear whether the epidemiological distribution of this type of malignancy was only limited to Japan, or whether the disease was perhaps simply not diagnosed as such in Europe. Therefore, the first aim of the European Association for Gastro-camera, as it was then called, was to find the answer to this question. Within the Association, a school evolved which thoroughly familiarized itself with gastro-camera techniques; its most prominent members were Professor K. Heinkel, Stuttgart; Dr. W. Bergemann, Berlin; Professor H. Reissigl, Innsbruck; Dr. W. Mockel, Cologne; and Professor J.M. Kimmig, Stuttgart. Within a very short time, the Association's first aim was achieved when it was established that early gastric cancer did occur in Europe but escaped detection, owing to a lack of suitably adapted diagnostic techniques.

For ten years now, our Association has made efforts to get this message through, and this has been done by organizing 12 symposia and 16 courses, all relating at least partly to the use of the gastro-camera. Over the past 10 years, progress in the field of endoscopy has been extensive, and new areas have been explored, such as the small intestine and the colon; and as the fields of investigation became wider, it was decided in 1980 that the Association would attempt to tackle these problems as well. Hence, its present name: 'European Association for Gastro-camera Diagnosis and Endoscopy'. Because of this change of strategy, I could opt for a broad selection of problems to be dealt with at the present congress. For our Association this means that we are following a new path, with new aims and objectives.

I believe to be acting in the spirit of this congress by confining myself to what is essential; I would therefore conclude my introductory

remarks by expressing my gratitude to the European Association for Gastro-camera Diagnosis and Endoscopy for giving the opportunity to organize this congress and for its substantial financial support; the Flemish Society of Gastroenterology and the Belgian Association for Endoscopy for their share in the organization of the Congress; the Belgian authorities, the University of Antwerp, the National Institute of Scientific Research, the Ministry of National Education, the Ministry of Flemish Culture, the pharmaceutical industries, especially Janssen Pharmaceutica. A special word of thanks should go to Her Excellency Mrs. de Backer, Minister of Flemish Culture, for her willingness to elucidate the position of the Flemish community today.

Finally I would thank all those whose cooperation made it possible for me, personally, to fulfil my tasks in the organization of this meeting: the secretaries, for ably carrying out a variety of tasks; my colleagues, for taking over a part of my clinical activities; and, last but not least, my wife, Rita, for her delicate and creative help.



Yvan van Maercke
Congress President

Contents

III. MOTILITY OF THE GASTROINTESTINAL TRACT

IV. ENDOSCOPY, LASER AND GASTROINTESTINAL BLEEDING

V. EARLY GASTRIC CANCER

VI. POSTERS

PHARMACOLOGICAL CONTROL OF GASTRIC ACID SECRETION IN DUODENAL ULCER DISEASE

Stanislaw J. Konturek and Janusz S. Swierczek

Institute of Physiology, Medical Academy, Krakow, Poland

Secretion of gastric acid is generally considered to play a paramount role in the production and maintainance of gastroduodenal ulcerations and most current therapeutic measures, irrespective whether pharmacological or surgical are designed to reduce this secretion.

This review will briefly discuss major gastric secretory disorders in duodenal ulcer (DU) disease and their pharmacological treatment.

Gastric acid secretory capacity

Since the classic study of Card andMarks in 1960 (2) the gastric acid response to maximal stimulation is considered to reflect the "parietal cell mass" and is used as an index of the number of these cells in the stomach. DU disease consists of heterogenous group of disorders due to a variety of genetic and environmental causes. An increased secretory capacity is one of these disorders and concerns only a portion of DU patients. In the majority of DU patients, the secretory capacity to secrete acid does not differ, however, from that in healthy subjects. This overlap of maximal secretory data corresponds well with the old study of Cox (3) who found that only a portion of DU patients examined show greater number of the parietal cells than control subjects without ulcer disease. In addition to increased secretory capacity, DU patients may secrete more acid because of the hypersensitivity of the parietal cells to exogenous and endogenous stimulants (5).

The question remains whether DU patients showing relatively higher secretory capcity and greater sensitivity to secretory stimulation respond in some unusual way to secretory inhibitors and whether their secretory capacity can be affected by the prolong medical therapy. These questions have been answered only recently when potent gastric inhibitors such as H_2-blockers became available. Indeed, it was reported that metiamid is less effective inhibitor in DU patients than in healthy subject suggesting that gastric secretion in DU is more resistant to secretory inhibition than in normal subjects (14).

The question of whether the increased secretory capacity in DU patients could be changed by prolong treatment with potent gastric inhibitors seems to be important because both the "breakthrough" recurrences during maintenance therapy and recurrences after ceassation of treatment with H_2-blockers has been attributed to the increased secretory capacity to secrete acid and pepsin.

Spence et al. (13) reported that 3 months treatment reduced somewhat the maximal secretory capacity. Other studies, including our own, gave different results. Six week treatment with ranitidine fail to reduce significantly gastric acid secretory capacity in DU patients (8). It can be concluded that a secretory capacity remains unchanged even after prolong treatment with potent antisecretory compounds such as H_2- receptor blockers. On the other hand, it has been reported that following ceassesion of the prolong cimetidine treatment, the parietal cells show an increased sensitivity to secretory stimulants (1).

Cephalic phase of gastric secretion

The regulation of gastric secretion in the intact stomach is one of the most complex physiological processes in the body. Secretion of acid depends upon the interplay of various neural and humoral stimulants and inhibitors. The major physiological stimulant of acid secretion is an ingestion of meal and the digestive period of secretion can be clasically devided into three partly overlapping phases, the cephalic, gastric and intestinal.

The cephalic stimulation "turns on" gastric secretory processes in response to various stimulants acting in the region of head. Since it involves the excitation of vagal nerves which may show higher "tone" or "drive" in DU patients, one should expect that this patients should secrete more acid in response to cephalic stimulation than healthy subjects. Indeed, the mean peak acid output in response to this stimulation tends to reach higher values in DU patients as compared with healthy controls. This does not seem to reflect, however, any more vig rous reaction of the stomach to vagal stimulation but probably results from greater secretory capacity as evidence by higher rates of pentagastrin induced maximal secretion in these patients (5, 11). The sham-feeding induced peak acid secretion was closely correlated with the peak acid response to pentagastrin in both healthy subjects and DU patients.

According to classic concepts, the cephalic phase stimulation of gastric secretion is mediated entirely by vagal nerves and involves at least two components; 1. direct cholinergic stimulation and sensitization to other stimuli and 2. vagal release of gastrin. The first component seems to be quite well documented but evidence for the vagal release of gastrin is inconclusive.

Although the controversy regarding the vagal release of gastrin remains, there is little doubt that atropine, which presumably blocks the muscarinic receptors, significantly raises serum gastrin response while reducing acid secretory response to sham-feeding (7). This has been interpreted that vagal nerves contain cholinergic inhibitory fibers for the G-cells which are block by atropine leaving unopposed stimulatory pathway and causing an increase in serum gastrin response to sham-feeding. It is of interest that pirenzepine, a novel and highly selective antimuscarinic blocker is capable of suppressing gastric acid response to sham-feeding without affecting serum gastrin level (7). This indicates that the concept of the inhibitory cholinergic nerves for the G-cells is questionable, and

probably, various subclasses of muscarinic receptors are available.

Although it is generally accepted that Ach plays a major role in direct vagal activation of parietal cells during caphalic phase stimulation, there are some indications that histamine and H_2-receptors may also be involved in this stimulation. H_2-receptor antagonists such as cimetidine or ranitidine, are capable of complete suppression of sham-feeding induced gastric secretion without affecting serum gastrin level (8). This could be explained that either histamine is released by vagal excitation and plays a predominant role in vagal stimulation of parietal cells or that histamine is a final mediator of cholinergic stimulation of these cells. It remains to be established which of these concepts is correct.

Gastric and intestinal phases of gastric secretion

The presence of food in the stomach is the most potent stimulant of acid secretion due to activation of the secretory machanisms of both gastric and intestinal phases of gastric secretion. The postprandial secretory rate may reach, particularly in DU patients, the level similar to that obtained by maximal stimulation by gastrin or histamine.

The major components of gastric secretion induced by the meal in the stomach include - 1. gastric distention activating reflexes with efferents to both the parietal cells and G-cells, 2. direct chemical stimulation of the parietal cells and G-cells by peptic digest, 3. the release of histamine in the gastric and intestinal mucosa. The mechanism of intestinal phase, which overlaps the gastric phase is not fully explained but the release of various stimulants sach as enterooxyntin, gastrin and histamine may be implicated. DU patients tend to release more gastrin after a meal and to exhibit more prolong postprandial secretion than healthy subjects.

Since the gastric phase provides most of the stimulation for the oxyntic glands in the postprandial period, most of the studies related to the pharmacological action of various drugs were performed during this particular phase. Anticholinergics are considered to be rather poor inhibitors of postprandial secretion and are known to enhance rather than inhibit gastrin response to feeding. Recent studies with pirenzepine at dose level, which has negligible side effects, show that this drug is effective inhibitor of meal-induced secretion and, unlike atropine, suppresses serum gastrin response (10) If this finding proves to be correct, our view on the role of muscarinic receptors in gastrin release and in gastric acid secretion will require modification.

In spite of rather minor role attributed previously to histamine in gastric or intestinal phases of acid secretion, the most effective inhibitors of postprandial secretion appear to be H_2-receptor antagonists. Since these agents do not affect serum gastrin response to a meal, the major mechanism of the inhibitory action on acid secretion is a direct suppression of the activity of the parietal cells. Indeed, the electrone-microscopic examination of the parietal cells has shown that the treatment with cimetidine produces an ultrastructural appearance of resting state, despite continuing secretory stimulation.

The spectrum of gastric inhibitory effects of H_2-blockers is rather wide. These agents not only inhibit histamine stimulated gastric secretion but also suppress the secretory response to all secretagogues so far studied (8) . This ubiquitous nature of gastric inhibitory effects of H_2-blockers has clear therapeutic implications but so far it remains unexplained. It has been suggested that these general inhibitory effects indicate the involvement of histamine as final common mediator for all other secretagogues of the parietal cells. It is of interest that in "in vitro" studies, H_2-blockers are direct inhibitors of the isolated parietal cells. They were found to suppress histamine but not gastrin induced secretory activity of these cells. This actually contrasts with the observation in vivo where H_2-blockers are actually effective against all modes of secretory stimulation (12) .

The pharmacological analysis of the type of interaction between H_2-blockers and various secretagogues shows, that the kinetic of gastric acid inhibition by these drugs depends upon the type of secretagogues used. In man, H_2-blockers appear to inhibit competitively histamine induced secretion but non-competitively - pentagastrin induced secretion. This disagrees with an unified concept that H_2--blockers abolish histamine mediation in the action of other secretagogues and suggests the possibility that the drug may remove only sensitization of these cells.

Prostaglandins (PGs) and gastric secretion

PGs of E and I series are generated throughout the gastrointestinal tissues particularly in the stomach. Methylated analogs of PGE_2 are the most potent inhibitors of gastric acid secretion. These methyl analogs not only have gastric antisecretory actions several times greater than those occuring naturally but also they are effective after oral or intraintestinal administration. They are highly effective particularly against meal stimulated gastric secretion and have a unique ability of preventing the usual postprandial rise in serum gastrin level. Their inhibitory action probably results from direct action on both the parietal cells and the G-cells. Recent studies on the isolated parietal cell preparation showed that PGs reduce histamine but not gastrin stimulated secretory activity of these cells (12) . In addition, PGs exhibit "cytoprotective" effect on gastrointestinal mucosa which will be the subject of special lecture during this meeting.

One of the most striking phenomenon which is evident in the pharmacological control of gastric acid secretion is the interaction and summation of the effects of various inhibitors. The combination of gastric inhibitors such as H_2-blockers and anticholinergics was shown to augment and prolong the inhibitory action of the individual drug acting alone. Similar additive interplay was described between methylated PGE_2 analogs and anticholinergics. The basis for the combination of histamine and cholinergic blockade is the presence separate receptor sites for histamine and cholinergic stimulants on the parietal cells. Such a combination of gastric inhibitors may be clinically valuable because it allows to reduce the dose of interacting drugs and reach more prolong inhibitory effect on gastric acid secretion.