MEDICAL TREATMENT OF PEPTIC ULSER

THESIS

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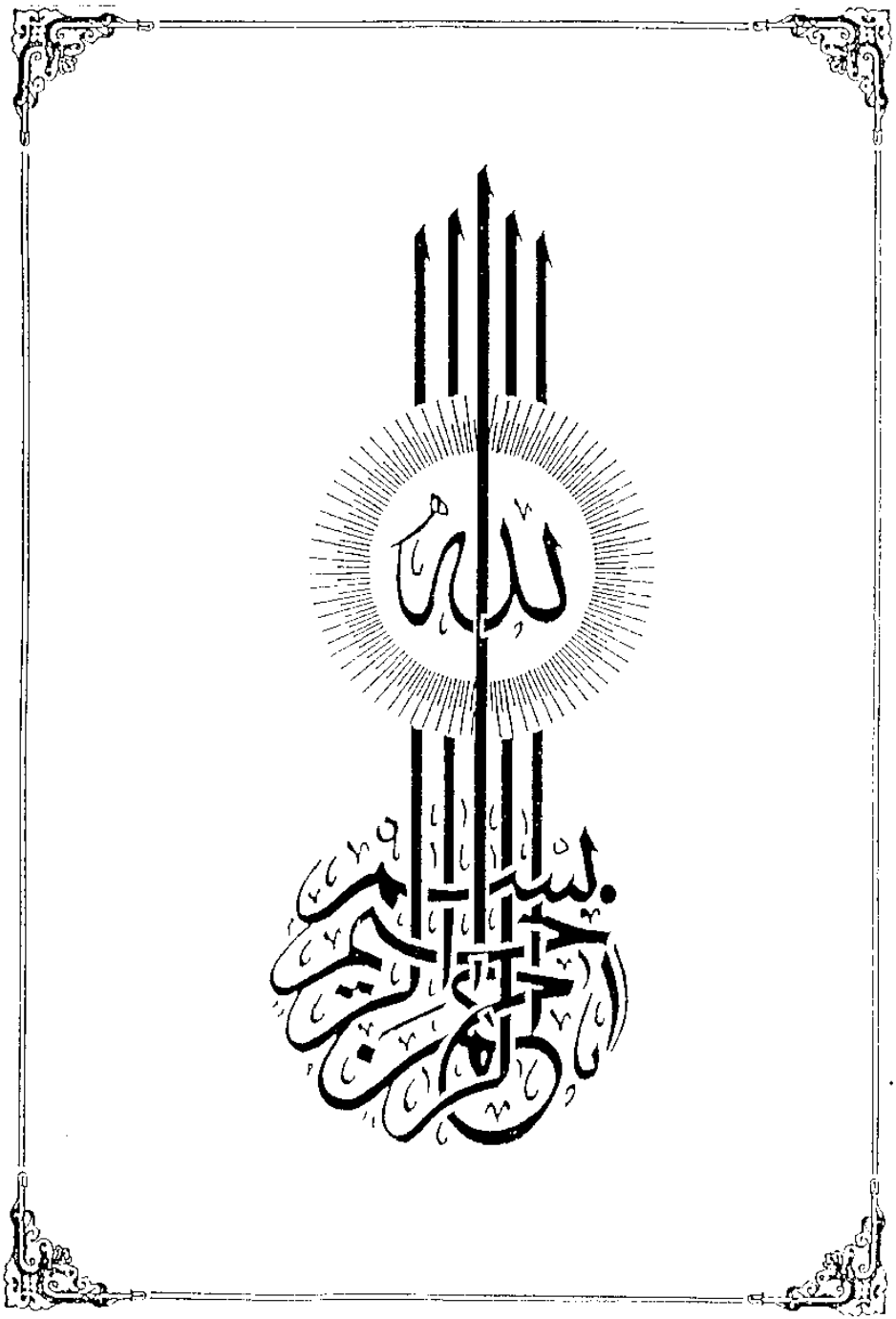
CONTENTS

	Page
INTRODUCTION	
I . APPLIED PHYSIOLOGY OF THE STOMACH	1
II. EPIDEMIOLOGY AND ETIOLOGY OF PEPTIC ULCER	8
III. PATHOGENESIS OF PEPTIC ULCER	16
IV . MEDICAL TREATMENT OF PEPTIC ULCER	21
1. Drugs to relief pain :	
A. Anticholinergics	23
B. Antacids	25
2. Drugs promote healing:	
A. Substances that cause blockade of Histamine H_2- receptor :	34
B. Liquorice derivatives	45
- Carbenoxolone	45
- Ulcedal and Caved-S	48
3. Miscellaneous Drugs :	
. Colloidal Bismuth	49
. Gefarnate	50
. Prostaglandins	50
. Esterogen	50
. Pepsin Antagonists	51
. Trithiozine	51
. Proglumide	52
. Pifarnine	52
. Tricyclic Antidepressant Trimipramine.	52



	Page
. Metoclopramide	52
. Sulpiride (Dogmatil)	53
. Diet	54
. Hospitalization	55
. Interdiction of Smoking	55
V . SUMMARY	56
VI . METHODS AND MATERIALS	62
VII. REFERENCES	84
VIII. ARABIC SUMMARY	

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INTRODUCTION

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Peptic ulcer is one of the commonest diseases which may be acute or chronic benign ulceration occuring in a portion of the digestive tract that is accessible to gastric secretion.

Other than the requirement for acid and pepsin, the cause of peptic ulcer at any level of the gut remains obscure.

Other factors in peptic ulceration (beside the presence of gastric acidity) include hypersecretion of hydrochloric acid and decrease tissue resistence. Peptic ulcer may occur during the course of drug therapy (phenylbutazone, salicylates, reserpine, and indomethacin).

It may occur as a result of critical illness or severe tissue injury such as extensive burns or intracranial surgery (stress ulcer), and may be associated with endocrine tumours producing gastrin, which stimulate hypersecretion of hydrochloric acid and a very refractory peptic ulcer diathesis (Zollinger-Ellison syndrome, gastrinoma).

The latter is the only type of peptic ulcer whose cause and pathogenesis are fully known.

(John V. et al., 1979).

APPLIED PHYSIOLOGY OF THE STOMACH

Applied physiology of the stomach

- Secretory function :

Gastric juice is a colourless transparent fluid, though occasionally it may be turbid by suspended mucin and desquamated epithelial cell. Its specific gravity is 1002 - 1007. The 24 hours volume of gastric juice collected from intact stomach of normal man under basal fasting conditions is about 1 : 1.5 liters.

Chemically the gastric secretion is a complex and variable mixture of water, inorganic ions, usually hydrochloric acid, bicarbonate ion (when acid is absent) and inorganic constituents including enzymes and their precursors, several types of mucus and intrinsic factor of castle (Bockus, 1974).

- Mechanism of Gastric Secretion :

It is generally accepted that gastric juice is the result of two types of secretions : a component actively produced by the parietal cells and consisting of a slightly hyperosmotic secretion of hydrochloric acid and potasium chloride and a non parietal component possibly of extra cellular origin and virtually identical in composition to interstitial fluid.

The rate of gastric secretion is related to mucosal blood flow, although agents such as histamine

and gastrin may exert stimulatory effect without producing alterations in the circulation.

(James E.Mc Guigan, 1980).

- Regulation of gastric secretion :

Two substances activate the parietal cells to secrete acid : the hormone Gastrin which reaches the parietal cell by way of the blood, and the neurohumor Acetylcholine which is released at the parietal cell by the postganglionic endings of the vagus nerve. (Morton I. Grossman, 1975).

- Gastrin :

The most potent known stimulant of gastric acid secretion, secreted by specialized cells (G-cells) scattered among the mucus cells of pylonic gland and consists of a family of polypeptides, present in cells of the antral phylonic glands. The major form of tissue gastrin is (G 17) containing 17 amino acid residues.

Gastrin II is a form in which the tyrosyl residue is sulfated at position 12, and gastrin I is the nonsulfated form. The two-thirds of circulatin, gastrin consists of "big gastrin" or G-34 which contain 34 amino acids, the final 17 of which are identical to G-17.

The major hormonal stimulus to gastric acid secretion after feeding is due to G-17, (James E. Mc Guigan, 1980).

In patients with duodenal ulcer serum gastrin concentration is normal in the fasting state and greater than normal after feeding. Patients with gastric ulcer tend to have elevated concentrations of fasting serum gastrin. (Morton I. Grossman, 1975).

- Vagal Action :

It enhances gastric acid secretion by 1. directly stimulating parietal cells. 2. stimulating release of gastrin into the circulation and 3. lowering the parietal cell threshold to circulating gastrin concentrations.

- Role of Histamine :

Histamine is present in large concentrations in mast cells in the parietal cell-containing regions of the gastric mucosa.

Some have suggested that histamine is the "final common pathway" for cholinergic and gastrin stimulation of parietal cell acid secretion.

The role of histamine on acid secretion has been renewed by the discovery of H_2- receptor antagonists which inhibit the action of histamine on H_2 receptors (located on gastric parietal, cardiac atrial, and uterine smooth - muscle cells).

Most of the available data support the concept that 1. histamine plays a role in stimulating acid secretion 2. it acts in concert with gastrin and cholinergic activity, but 3. it is probably not the final common effector molecule in the stimulation of parietal cell secretion. Food ingestion is the major physiological stimulus of gastric acid secretion.

(James E. McGuigan, 1980).

Traditionalby, gastric acid secretion has been divided into three phases :

- Cephalic phase :

Represents the secretory response to the sight, smell, taste and anticipation of food it is mediated by the vagus which in turn leads to acid secretion by stimulation of parietal cells directly and by an increased release of gastrin.

- Gastric phase :

Is induced by the presence of food in the stomach and it involves stimulation of chemical and mechanical receptors in the gastric wall luminal contents. Mechenical distention of the stomach stimulates gastric acid secretion but not gastrin release, this mechanical effect inhibited by atropine and appears to be mediated by vagal reflexes.

Proteins of food promotes acid secretion by increasing gastrin release.

Oral glucose and fat cause slight increase in serum gastrin but do not stimulate gastric acid secretion.

- Intestinal phase :

Is due to the entry or presence of food within the lumen of the small intestine, it has been proposed that food in the small intestine induces release of an intestinal hormone, which stimulate gastric acid secretion and is believed to be distinct from gastrin.

Ingestion of coffee stimulate gastric acid secretion. Inhibition of acid secretion may be by acid in the stomach or duodenum, by hyperglycemia or by hypertonic fluids or fat in the duodenum.

Reduction of the intragastric pH to 3.0 produce a partial inhibition of gastrin release, further reduction to pH 1.5 or below blocks the release of gastrin to almost all stimuli.

. Acid in the duodenum inhibits gastric acid secretion by stimulation of secretin release which is contained in the cytoplasm of cells (S cells) in the mucosa of the small intestine.

. Fat in the duodenum appears to inhibit acid secretion by the intestinal release of gastric inhibitory peptide (GIP) or cholecystokinin (CCK).

. Peptides have been identified in the mucosa of gastro-intestinal tract which have the capacity to inhibit gastric acid secretion.

These peptides include somatostatin, glucagon, vasoactive intestinal peptide (VIP) and urogastrone.

(James E., 1980).

- Enzyme secretion :

Pepsin is formed by the chief cells of the stomach, there are variety of pepsinogens and pepsins in gastric juice pepsinogens have been classified by immunochemical techniques as either PGI (present in chief and mucous cells in the body and fundus of the stomach) or PG II (located in cells of the pyloric glands, Brunner's glands of duodenum, mucous cells of the gastric cardiac glands, and the same cells in which PGI is found.

Both PGI and PG II are found in plasma, while only PGI can be detected in urine.

Cholinergic action is particularly potent in promoting pepsinogen secretion.

Parietal cells also secrete intrinsic factor.

Other proteolytic enzymes present in the gastric juice are cathepsin and gelatinase.

Non proteolytic enzymes such as carbonic anrydrase, urease, lysozyme and lipase are also present in the gastric juice.

- Mucous secretion :

It is secreted by gastric mucosa cells, it is a gelatinous material which coats the mucosal surface. Mucous secretion is enhanced by mechanical or chemical irritation and by cholinergic stimulation. Gastric mucous contains mucopolysaccharides and glycoproteins, including blood group substances. (James E., 1980).