STUDY OF CAMPYLOBACTER PYLORIDIS IN PEPTIC ULCER DISEASE

THESIS

Submitted For Partial Fulfillment Of The Master

Degree Of Internal Medicine

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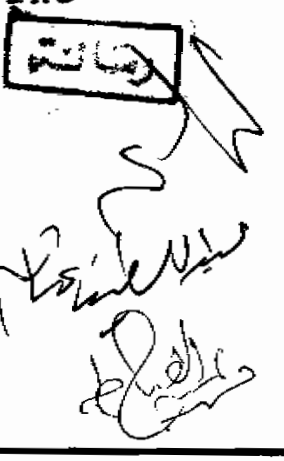

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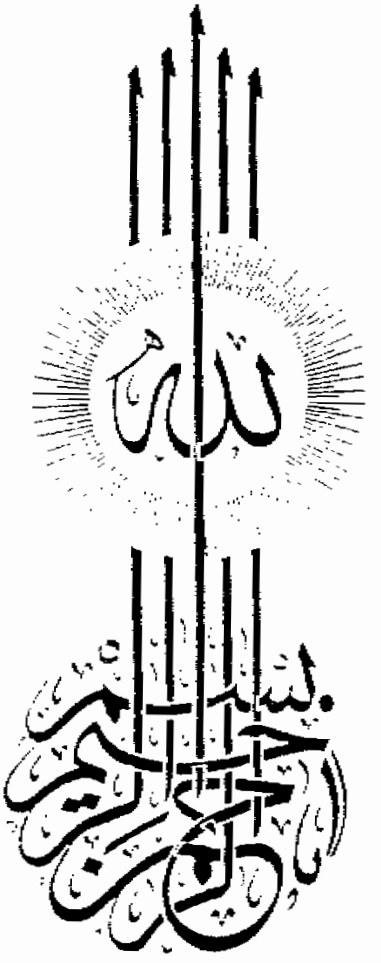

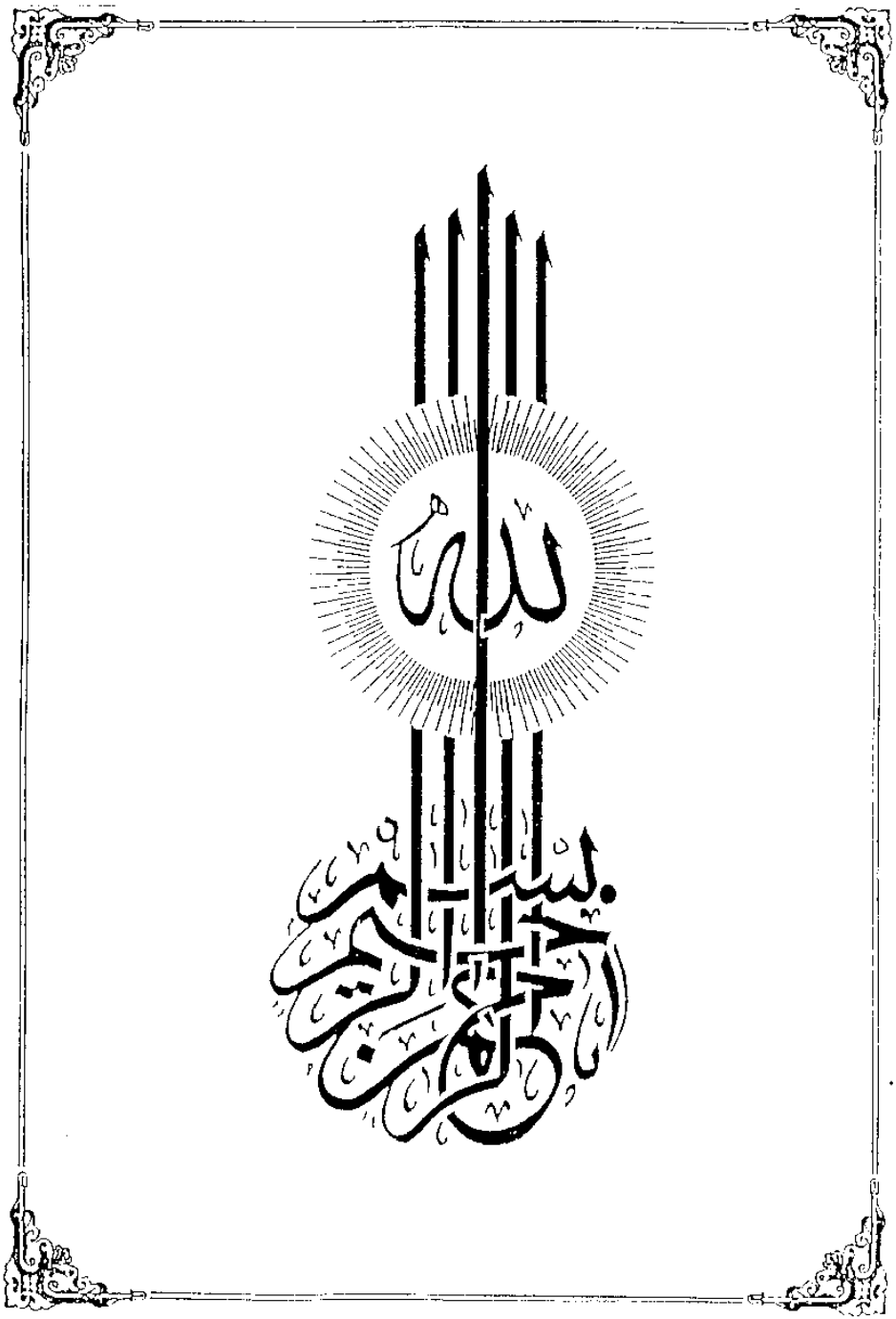

ACKNOWLEDGMENT

I wish to express my deepest gratitude to DR. MOHAMED ABDEL FATTAH TAHA, Assistant Professor of Medicine, Ain Shams University , Faculty of Medicine, for his advice , guidance and consultation throughout the course of this study.

I also wish to express my sincere gratitude to DR . IBRAHIM KHALIL ALI Assistant Professor of Clinical Pathology , for his encouragement, support and helpful directions during this study.

I am sincerely grateful to DR. MOHSEN MOSTAFA MAHER Lecturer of Medicine for his unfailing support and continuous advice.

I would like to thank DR. TAREK HASHEM Lecturer of Pathology , MR. MOHAMED AL ENANY and MR. MAGDI RIAD who helped me so much in performing the practical part of this study.

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INTRODUCTION
AND
AIM OF WORK

Introduction and aim of work

Gastric spiral bacteria have been repeatedly observed, reported, and then forgotten for at least 45 years (Doenges, 1938 and Ito, 1967) In 1940 Freedburg and Barron stated that " Spirochaetes " could be found in up to 37% of gastrectomy specimens, but examination of gastric suction biopsy material failed to confirm these findings (Palmer, 1954). Since that time, the spiral bacteria have rarely been mentioned, except as curiosities (Ito, 1967), and the subject was not reopened with the advent of gastroscopic biopsy.

Recently, Spiral organisms have been seen in the stomach and they are closely associated with gastritis and duodenal ulceration (Rollason et al. 1984). The provisional name of Campylobacter pyloridis had been assigned to this new organism (Marshall and Warren, 1984).

The initial data on C.Pyloridis are exciting. At this early stage its cultural requirements are becoming established as are its associations with gastritis and duodenal ulceration (Price et al., 1985).

These results prompted us to do the present study in twenty patients with duodenal ulcer and ten control subjects (ulcer free) in a trial to discover Campylobacter pyloridis in the duodenal and antral mucosa and to confirm the association between these bacteria and duodenal ulceration.

PEPTIC ULCER

Peptic Ulcer

Although our present knowledge of the etiology of peptic ulcer is incomplete, information from studies in humans and in experimental animals indicate that acid-pepsin is crucial for development of peptic ulcer. The presence or absence of peptic ulcer is determined by the delicate interplay between gastric acid secretion and mucosal resistance. Peptic ulcer is produced when the aggressive effects of acid-pepsin dominate the protective effects of gastric or duodenal mucosal resistance (McGuigan, 1983).

The evidence for this internal turmoil, so often ending in defeat, is epidemiological (identifying groups of individuals at risk) and pathophysiological (indicating which individuals are at risk) (Wormsley, 1983).

The epidemiological evidence is that there is a fairly strong association between gastrinomas and duodenal ulcers, an association which is assumed, to be based causally of the gastric hypersecretion evoked by the gastrinoma (Ellison and Wilson, 1964).

An alternative approach to establishing the aetiological involvement of aggressive gastric juice

is experimental. After showing that gastric juice digested the legs of frogs and ears from rabbits (Dragstedt, 1978), large amounts of hydrochloric acid were poured into the stomachs and duodenum of dogs, without producing ulcers, other than in exceptional circumstances (Robert, 1974).

On the other hand, experimental duodenal ulcers can be produced by mimicking gastrinomas, using slow-release parentral administration of histamine, or gastrin (Robert, 1974). Of course, the most important (alleged) evidence for the involvement of aggressive and defensive factors in the aetiology of duodenal ulceration has been derived from what are considered the pathophysiological 'disturbances' encountered in patients with duodenal ulcer.

Patients with duodenal ulcer have excessive amounts of acid in the duodenal bulb (Rhodes and Prestwich, 1966); attributable to excessive secretion of gastric juice (Wormsley, 1974), as well as abnormally rapid emptying of excessive amounts of gastric juice from the stomach into the duodenum (Malagelada, 1979).

The stomach secretes too much gastric juice because there is an excessive mass of parietal cells in patients

with duodenal ulcer. There parictal cells are abnormally sensitive to secretory stimuli, perhaps because gastric inhibitory factors are not acting normally. There may, in addition, be excessive stimulation of the parietal cells by abnormally large amounts of circulating gastrin both in the basal and postcibal state and also as a result of vagal activity. The increased amounts of gastrin are released because the number of antral G cells and the antral content of gastrin of patients with duodenal ulcer is greater than normal and because acid in the antrum does not inhibit release of gastrin normally (Wormsley, 1983), The excessive amounts of intraduodenal acid do not elicit sufficient or even normal amounts of bicarbonate because the release of secretin from the small intestine is defective (Thompson and Swieczek, 1977), in part because the threshold for secretin release is greater than normal in ulcer patients (McLoughlin et al , 1978).

Add to this collection of apparantly positive evidence for the aetological importance of noxious gastric juice the negative evidence that ulcers heal and apparently remain heald if gastric secretory capacity is therapeutically reduced (surgically or with drugs) and one has the classical proof for what, at present, purports to be the erosive aetiology of ulcer disease (Wormsley 1983).

Factors which play an important role in the development of peptic ulcer

Hereditary factors

Patients with peptic ulcer often have a family history of the disease and sometimes this is striking. Melrose and Wallace (1965) reported a family in which 14 of 30 members, extending over three generations, had had severe duodenal ulceration with hypersecretion of acid.

A review of the genetic of gastric and duodenal ulcer provides strong evidence that they are separate disorders (Rotter and Rimoin, 1977). The relatives of gastric ulcer patients have three times the expected number of gastric ulcers, but duodenal ulcers occur with the same frequency as in the general population. Relatives of duodenal ulcer patients also have three times the expected incidence of duodenal ulcer without any increase in gastric ulcer. Blood group O and non secretor status are associated with duodenal ulcer but not with gastric ulcer. Thus, group O non secretors are two and a half times more likely to develop a duodenal ulcer than secretors of group A,B and AB (McConnell, 1966). Blood group O is associated

with hypersecretion of acid (Langman-and Doll, 1965).

Until now the correlation of peptic ulcer with HLA-antigens (B5, B12, BW 35) is controversial.

The chances of relatives of duodenal ulcer patients having active duodenal ulcer or a scarred duodenal bulb was reported to be significantly higher than in relatives of patients without duodenal ulcer (Tarpila et al, 1982).

Racial incidence

A recent study showed no difference between the white and non white population living under the same circumstances (Kurata and Haile, 1982).

Life events and stress

On the basis of clinical experience and expermental data which show that emotional factor can infleunce gastric secretion, blood flow and motility, stress, worry and overwork have come to be associated with peptic ulceration (David and Nill, 1982).

There are frequent studies on the role of psyche in the pathogenesis of peptic ulcer disease which appears to be controversial. Recently, Magni et al (1982) suggest

a role of psyche in duodenal ulcer and acute gastroduodenitis. Peters and Richardson (1983) describe two patients in whom symptoms and radiological evidence of gastric ulcer followed stressful life events. Other studies e.g Piper et al (1978) and Thomas et al (1980) from australia found no temporal relationship between chronic gastric ulcer and stressful life events.

Smoking and Peptic Ulcer

It is strongly suspected, but not proven, that smoking is an aetiological factor in gastric and duodenal ulceration (Harrison et al, 1978). Patients with peptic ulcer are more likely to smoke than a control population (Friedman et al, 1974); stopping smoking aids the healing of gastric ulcers but does not prevent relapse (Piper et al, 1975). The raised intraluminal pressure exerted by the pyloric sphincter falls during smoking, and bils reflux into the stomach is increased (Rees and Rhodes, 1977).

Sonnenberg and Hüsmert (1982) concluded that nicotine increases blood supply to the gastric mucosa relatively to the reduced gastric secretion. Nicotine is either not associated with the development of peptic ulcer or It exerts its ulcerogenic action via other mechanisms than change of acid secretion and gastric mucosal blood flow.