AIN SHAMS UNIVERSITY
FACULTY OF MEDICINE

The diagnostic and prognostic value of cell maturity of duodenal ulcer

Thesis
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By

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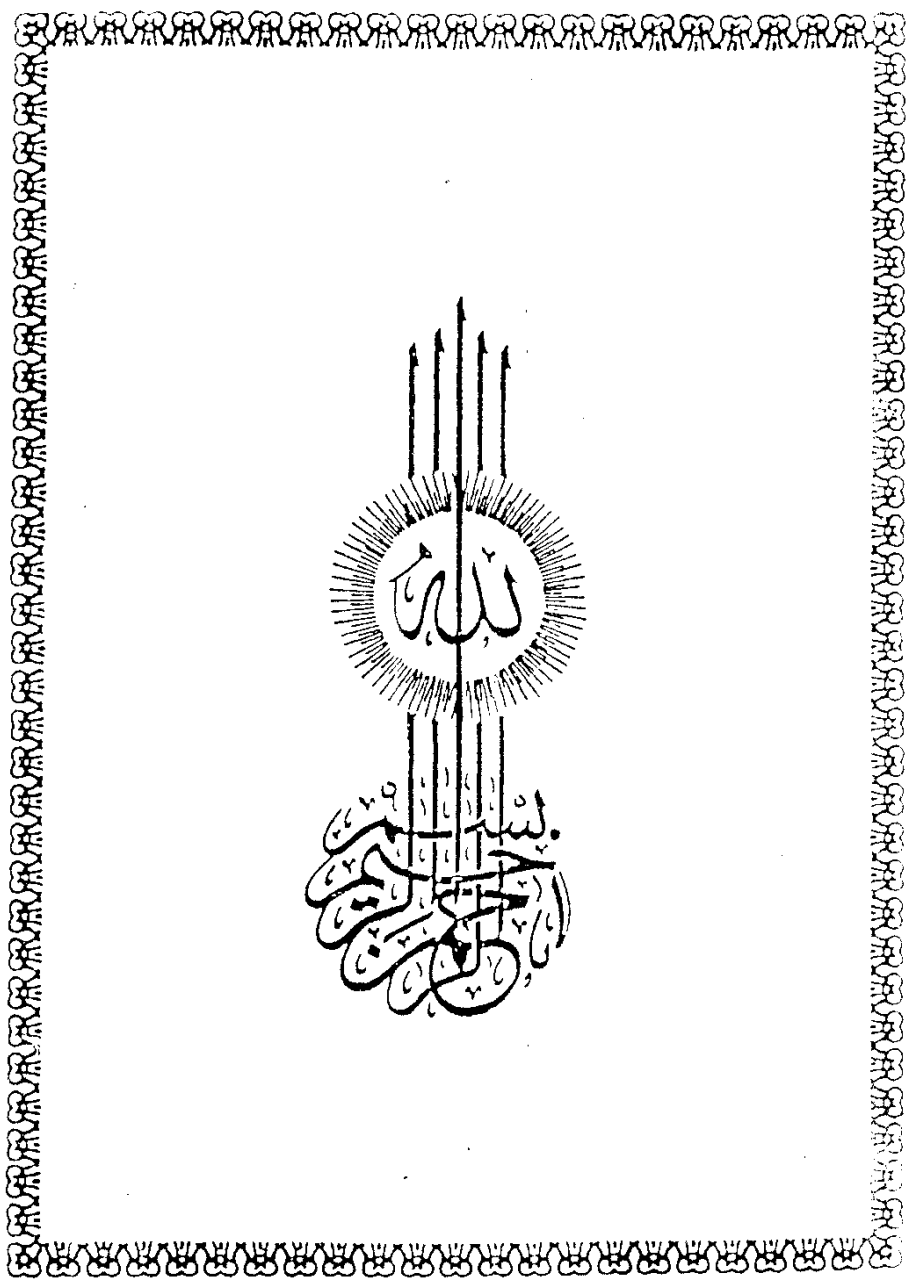

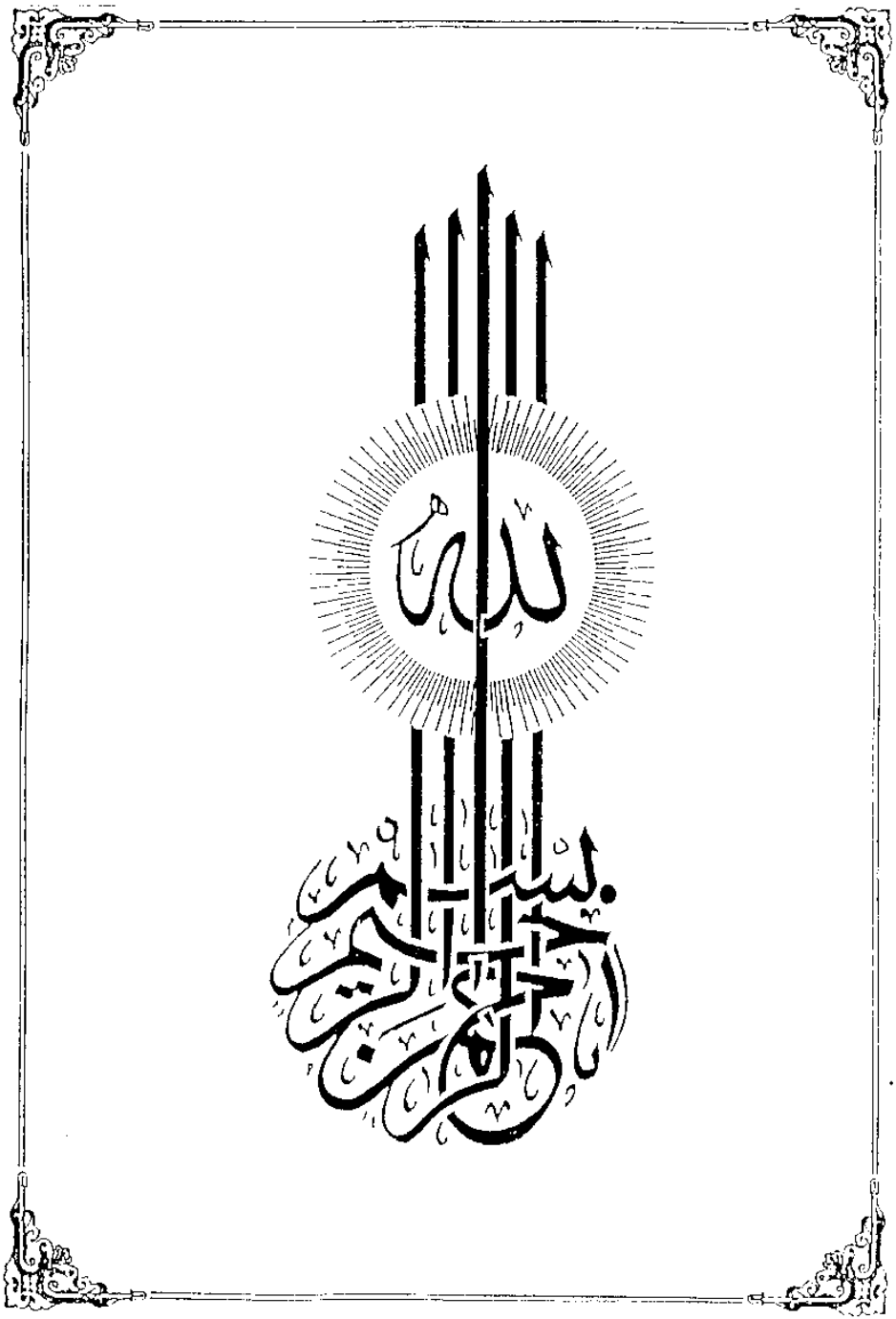

I N D E X

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AIM OF WORK

The frequency of peptic ulceration was estimated as 8.3% for men and 3.9% for women. (Sleisenger, 1973).

Many factors were planed to be predispossing for aetiological factors:

1- Mucosal hypoxia
2- The blood flow
3- Decrease the mucosal resistance.
4- ABO blood groups secretory states.
5- The mucosal barrier.
6- Reflux disturbance of pottassium pump all were deeply investigated.

Pringle (1971) reported that mucous from patient with duodenal ulcer has a higher viscosity than mucous from normal.

Max at 1970 and Sleisenger 1973 proposed that in about all people with duodenal ulcer has asmall defects in the mucous membrane of the stomach and duodenum occurs frequentily because of food trauma yet rarely if even are these diffects converted into chronic peptic ulcer, and so the repair of each defects must depends on the rate of removal of surface epithelial cells.

Suggested that defects in removal could thearitically play a role in the conversion of small errosion into chronic ulcers.

This value was not deeply investigated and so it become the aim of the work.

ETIOLOGY AND PATHOGENESIS OF DUODENAL ULCER

Peptic ulcer is the most important organic gastrointestinal disease. The cause of peptic ulceration remains unknown, but clinical studies have demonestrated a number of important factors, such as hypersecretion of acid and pepsin and impaired mucosal resistance, which are probably influenced by hereditary, psychological or dietary factors. It seem likely that the development of an ulcer is usually the result of the interaction of several factors, and the relative importance of these varies in different forms of peptic ulceration. In duodenal ulceration, hypersecretion of acid and pepsin may be of prime importance, whereas in gastric ulceration damage to the mucosa seems to be of greater consequence. Whatever the predominant factor in the causation of a particular ulcer, the effect of this factor would be expected to be diffuse, whereas the ulcer is usually discrete and single. To explain this Kirk (1977) has postulated that the presence of the ulcer in some way inhibits the development of further ulcers or extension of the existing one.

Gastric Secretion:

The secretion of acid and pepsin is necessary

for the development of a peptic ulcer. This topic has been extensively reviewed by Baron (1972) and Wormsley (1974) clinical experience supports this concept in that benign ulcer does not develops in the Zollinger-Ellison syndrome in which there is hypersecretion of acid. Furthermore, most ulcers heal after surgery or during treatment with cimetidine, both of which markedly reduce acid output.

Many different abnormalities of acid secretion have been described in duodenal ulcer (Grossman, 1978), but in most of these the evidence is conflicting, probably because duodenal ulcer disease is a heterogeneous group of disorders (Rotter & Rimoin, 1977). It is agreed, however, that patients with duodenal ulcer as a group secrete more acid, both basally and in response to a variety of stimuli, than do normal subjects. This is due to an increased number of parietal cells which may be a hereditary feature of the disease, or it may result from hyperplasia of these cells.

Several other studies suggest that acid hypersecretion is of importance in the aetiology of some duodenal ulcers. Prospective studies on ulcer-free

subjects with high acid or serum pepsinogen levels show a high incidence of duodenal ulcer (Novis et al., 1973). Whilst it is difficult to measure duodenal pH accurately, many studies do show that duodenal ulcer patients as a group have a lower pH for longer periods than control subjects, both in the fasting state and in response to food. This abnormality is a reflection of gastric hypersecretion, since it does not occur in those duodenal ulcer patients with a normal acid secretion (Rune & Viskum, 1969). There are data to suggest that the acid response to meat is greater and more prolonged in duodenal ulcer subjects than in normal subjects, but this has not been confirmed in all studies (Grossman, 1978).

Many other factors may contribute to hypersecretion in duodenal ulcer (Grossman, 1978), for example:

1- An excessive drive to the secretion of acid; blood gastrin levels are higher after eating in duodenal ulcer subjects than in controls.

2- Increased sensitivity of parietal cells; this has been shown with pentagastrin stimulation and with endogenously released gastrin (Lam et. al., 1980).

3- Impaired inhibition of acid secretion.

However, these abnormalities have not been confirmed in all studies and their role remains undetermined.

Mucosal resistance:

Normal acid secretion in many patients with duodenal ulcer has led to speculation that there is reduced mucosal resistance to ulceration in these patients. It is a function of the normal mucosa to prevent re-entry of hydrogen ions and the movement of sodium ions across the mucosa. Davenport (1967) used the term "mucosal barrier" to describe these functions and this concept has been reviewed by Ivey (1971). The barrier can be breached by intestinal juices and some exogenous agents such as aspirin and alcohol. When the barrier is broken, there is a fall in the electrical potential difference across the mucosa and sodium ions accumulate in the lumen of the stomach as a result of their exchange for hydrogen ions. However, the potential difference probably reflects the net flux of several ions moving in opposite directions across the gastric mucosa (Fromm, 1979).

There has been much debate on the structure and function of the barrier. The structural integrity of the epithelium is important; this depends on the tight junctions between epithelial cells and the surface lipoprotein layer of the epithelial cells, the latter being disrupted by aspirin, and the normal cellular turnover, which may be influenced by some ulcerogenic drugs. Urogastrone which inhibits acid secretion also promotes epithelial growth (Bower et. al., 1975), and it is possible that this and other factors are important in maintaining mucosal integrity. Of major importance in the protection of the mucosa is the alkaline state of the mucosa, since acid secretion must be accompanied by production of an equivalent amount of bicarbonate which diffuses into the small vessels of the mucosa. In addition, the surface epithelial cells actively secrete bicarbonate into the surface "unstirred layer" and this layer may be sufficient to prevent hydrogen ions reaching the epithelium. Bicarbonate secretion is stimulated by prostaglandins which are synthetised in the gastric mucosa; ulcerogenic drugs inhibit the synthesis of prostaglandins, thus decreasing bicarbonate secretion. (Johansson et. al., 1980). Many prostaglandins protect the mucosa of the

stomach and intestine from becoming inflammed and necrotic when it is exposed to noxious agents; this has been called "cytoprotection" and may operate through several mechanisms (Robert, 1979), including the secretion of bicarbonate.

THE EITIOLOGY:

INCIDENCE OF DOUDENAL ULCER:

Duodenal ulcer is a common disease affecting 6-24% of all males and 5-12% of all females during life time, (Leviy and Fuente 1963). Salib (1970) put the incidence of duodenal ulcer in Egyptians as 5-10% of adults between 20-40 year of age. Both duodenal and gestric ulcers have a greater prevalence in men than in women (Grossman et. el., 1976). Duodenal ulcer is commoner than gastric ulcer all over the World (Bockus, 1974). The ratio of gastric to duodenal ulcer is 1 : 9 but both occur together in 5% of Egyptian ulcer patients (Salib, 1970).

AGE INCIDENCE:

Duodenal ulcer occur at any age from childhood to old ones. In the newborn ulcer evidenced by the occurence of melaena neonatorum. In infancy and early childhood the ulcer is of acute variety usually present with perforation or haemorrhage without any history of previous symptoms (Billington, 1965).

SEASONAL INCIDENCE:

Periodicity or recurrence of ulcer symptoms

promoting medical advice. Such symptoms usually appear for the first time or are exacerbated in the winters and autumn months. These seasonal variations are noticeable in England but are not so marked in Egyptian patients (Elsherif, 1962).

GENETIC FACTORS AND DUODENAL ULCER:

Convincing evidence of the separate inheritance of duodenal ulcer was found by Dolland Kellock (1951). They shown that the relatives of Duodenal Ulcer patients tend to have duodenal ulcer. The incidence of Duodenal Ulcer in the relatives of patients with the disease is about three times that expected in the general population. The increase incidence in relatives of Duodenal Ulcer patients in due to polygenic basis, also, must be due to an environmental factors. (Jensen, 1972) has found that genetic and environmental factors are about equal in the importance in this disease.

There are three genes concerned in duodenal ulcer patients:

1- The gene which determines blood group O.

2- Thegene for non secretion of blood group substances in saliva, and gastric juices.