DISACCHARIDASE ENZYMES DEFICIENCY IN IRRITABLE BOWEL SYNDROME

THESIS

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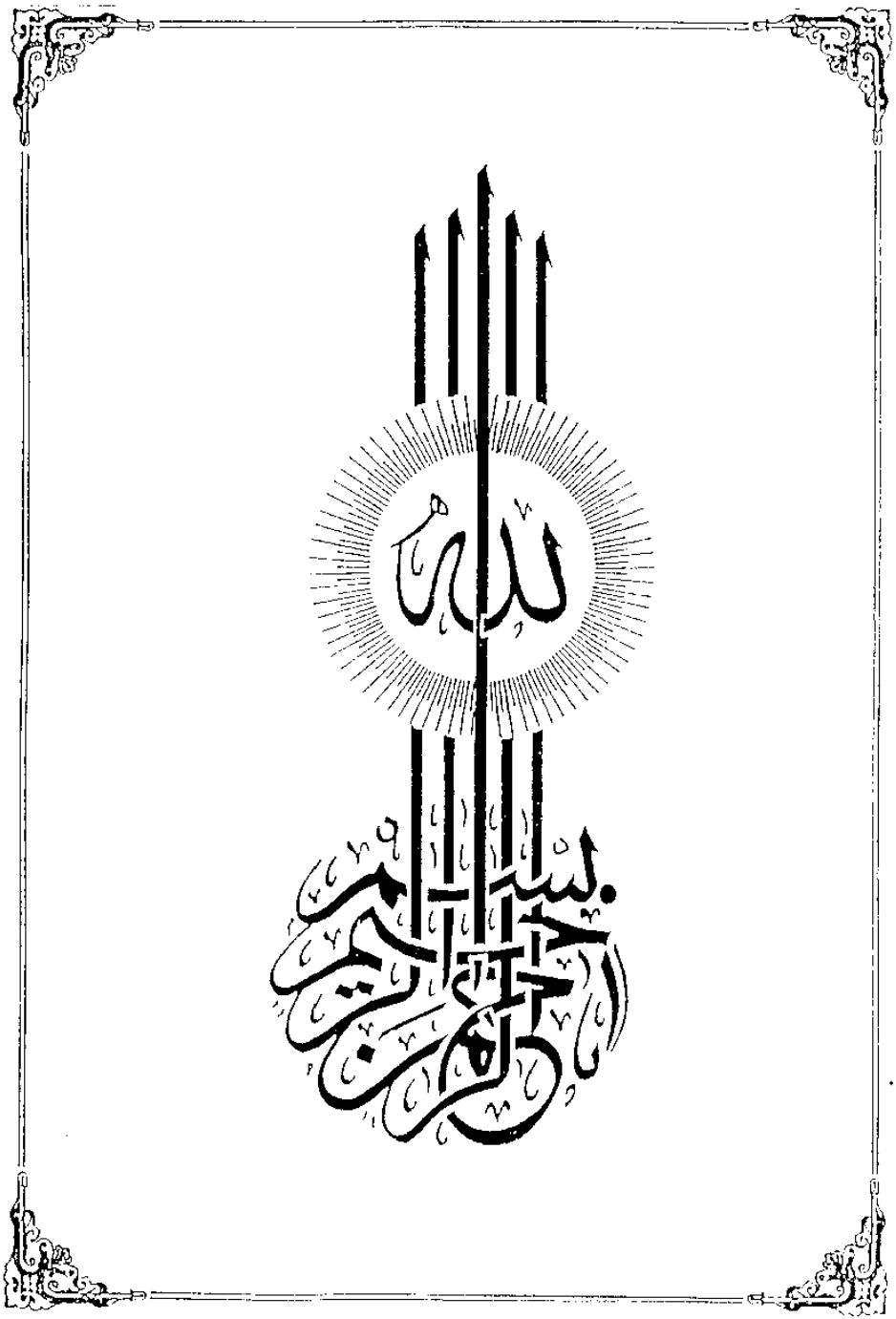

C O N T E N T S

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INTRODUCTION

I N T R O D U C T I O N

The irritable bowel syndrome is the most common gastro-intestinal disease in clinical practice and although not a life threatening illness, it causes great distress to those affected and a feeling of helplessness and frustration for the physician attempting to treat it.

The pathogenesis of the irritable bowel syndrome is unclear. Evidence for infection, autoimmunity, or food allergy or stress factors are known to play a role. Enzymatic deficiencies particularly may be a contributing factor.

It is the purpose of this work to demonstrate the incidence of lactase deficiency in these patients and to compare this with normal control group.

ANATOMY OF THE COLON

NORMAL ANATOMY AND PHYSIOLOGY OF THE COLON

NORMAL ANATOMY (1)

1. General Consideration:

The colon is a hollow muscular organ which joins the small bowel at the ileocaecal valve. The length of the colon from the end of ileum to the anus is approximately 1.5 meters long.

The length varies considerably from patient to patient and is in general related to the size of the subject. The most proximal of the colon, the caecum, is of larger caliber than the remainder of the colon and is nestled in the right iliac fossa. The caliber of the colon decreases as it proceeds distally such that the luminal diameter of the sigmoid colon is considerably less than that of the caecum; increase in the caliber occurs in the rectum, however, that portion of the organ is somewhat dilated relative to the colon proximal to it.

The divisions of the colon are as follows:

The caecum is the proximal-most end of the colon and consists of the blind pouch adjacent to the iliocaecal valve.

The appendix arises from the caecum. The ascending colon extends from the caecum to the hepatic flexure. The transverse colon, from the hepatic flexure to the splenic flexure (which is situated slightly higher in the abdominal cavity than the hepatic flexure) and the descending colon extends from the splenic flexure to the sigmoid loop. The begining of the sigmoid portion of the colon is not a rigidly defined landmark. Similarly, the rectosigmoid junction usually defined by a rather sharp angulation of the colon from the redundant sigmoid loop to the straightened rectum, is not always so clear.

2. Morphology:

The colon exhibits, through most of its length, several distinct morphological layers seen in the remainder of the gut. These are the mucosa, muscularis mucosa, submucosa and musculosa and serosa. Several features of these layers are peculiar to the colon, however, the mucosa of the large intestine differs from that of the small intestine in several respects. It has no villi in post-natal life. The crypts of Lieberkuhn are deeper and therefore the mucosa is thicker. The crypts contain no paneth cells and have more goblet cells than does the small intestine. The surface epithelial cells are tall columnar in type. Some goblet cells are scattered

among the epithelial cells. The lamina propria is very sparse since the crypts take up most of the mucosal space. A scattering of round cells is present in the lamina propria normally. The muscularis mucosa is present immediately at the base of the crypts. The submucosa has no important distinguishing features. The muscularis propria does however. The entire colon wall is relatively thin, owing mainly to the fact that the longitudinal muscle is gathered into three bundles called taeniae coli, which run longitudinally, leaving the majority of the colon wall with only circular muscle fibres. Begining at the caecum, the taeniae coli develop from the base of the appendix into three flat bundles extending along the colon. They are not as long as intestinal wall itself of which they are composed and hence they are responsible for gathering the wall of this part of the bowel into sacculations or haustrations. If the taeniae are cut or stripped away, the bowel immediately elongates and the sacculations disappear. The three taeniae extend from the caecum to the rectum, where they spread out at the rectosigmoid junction and fuse to some extent so as to form a more continuous muscle coat of longitudinal fibres around the rectum. Viewed from the anterior aspect, one taenia traverse the length of the colon on the anterior wall, the

other two are posterior, one on the superior aspect and one on the inferior aspect of the transverse colon with corresponding relationship in the ascending and descending colon.

The serosa, along the colon and upper part of the rectum, leaves the surface of the intestine at irregular intervals to form little peritoneal sacs which enclose fat. These peritoneal redundancies large from the external surface of the bowel and are termed appendices epiploicae. Part of the caecum and all of the ascending colon are retroperitoneal, but the transverse segment of the colon has a mesentry, the transverse mesocolon. The descending part of the colon lacks a mesentry, but the sigmoid colon possesses mesenteric support, the sigmoid mesocolon. The transverse colon interrupts the greater omentum extending from the stomach, and is therefore enfolded in it.

ANO-RECTUM:

The rectum begins, by convention, at the termination of the pelvic or sigmoid mesocolon. It is somewhat dilated relative to the sigmoid colon and its mucosa is smoother than that of the rest of the colon. The mucosa of the rectum is thrown up into three folds, the valves of Houston. Two of

these valves are situated on the left and one on the right. They are shelf-like folds consisting of mucosa, muscularis mucosa, submucosa and circular muscle of the muscularis propria, but not longitudinal muscle. The distal 7-8 cm of the rectum are not covered by peritoneum since they are below the peritoneal reflexion; there is therefore no serosa for this portion of the rectum. In the distal rectum, two muscle bundles are present which make up the internal and external anal sphincters. The internal anal sphincter is a continuation of and an enlargement of the circular muscle of the colon. Overlapping it, and external to it, with a thin layer of transverse muscle interposed, is the external sphincter, composed of striated muscle in several bands.

The anal canal is recognized proximally by the sharp demarcation between rectal mucosa and anal mucosa the denate or pectinate line. Just proximal to that margin, the mucosa is thrown into several longitudinal folds, the columns of Morgagni terminating in the anal papillae, between which are a series of small folds so called anal valves, each of which somewhat resembles a leaflet of an aortic semilunar valve. The concavities of the small pockets so formed are called rectal sinuses. At this point the merging lamina propria and submucosa contain many convolutions small veins. A very common

condition, internal haemorrhoids, is the result of the dilation of these veins so that they bulge the mucous membrane inwardly and encroach on the lumen of the anal canal. The internal and external anal sphincters overlap the anus and distal rectum and effected closure of the anus.

The muscles of the pelvic floor are closely related to the anal rectum and are involved in the function of defaecation. These muscles are the elevator ani, the ileococcygeus and pubococcygeus.

3. Blood supply:

The arterial supply to the colon is variable, but a classic pattern does exist and is as follows: the superior mesenteric artery supplies the caecum, right colon, and transverse colon to a variable extent all the way to the splenic flexure. The inferior mesenteric artery supplies the descending and sigmoid colon and the proximal portion of the rectum. Important anastomosis usually occur between the superior and inferior mesenteric arteries. Additional supply to the rectum includes the middle and inferior haemorrhoidal arteries which arise from the internal iliac arteries.

The venous drainage of the caecum, right colon, some of the transverse colon is by way of the superior mesenteric vein in a pattern similar to that of the distribution of the superior mesenteric artery. Similarly, the left colon is drained by the inferior mesenteric vein. These veins are of course a part of the portal system and therefore deliver their blood to the liver. The proximal portion of the rectum is drained by the superior haemorrhoidal vein which flows into the portal system via the inferior mesenteric vein. The middle and distal portions of the rectum are drained by the middle and inferior haemorrhoidal veins respectively, which flow to iliac veins and are consequently a portion of the systemic system. Anastomosis occurs with superior haemorrhoidal vein, however, and thus the potential for flow into the portal system from the distal portion of the rectum is present. Therefore, the presence of both internal and external haemorrhoids may reflect portal pressure.

4. Lymphatics:

Throughout the colon a rich network of intra-mural lymphatics is present in the submucosal and subserous layers. These drain into the external lymphatics. For the colon, there are generally four groups of external lymphatics. There

are the epicolic lymphatics which lie on the colon itself, the paracolic lymphatics which are located along the marginal artery, the intermediate lymphatics located along the main colic vessels and branches and the principle lymphatic glands along the superior and inferior mesenteric blood vessels trunks.

For the proximal part of the rectum, the lymphatic flow is upward accompanying the superior haemorrhoidal and inferior mesenteric vessels to the aortic lymphatic glands. From the midportion of the rectum, the drainage is laterally along the middle haemorrhoidal vessels to the internal iliac glands. The inferior portion of the rectum and of the anus drain downward and out to the inguinal glands or the internal iliac glands.

5. Nerves:

The colon is supplied by the autonomic nervous system, both sympathetic and parasympathetic branches. In the right colon and the transverse colon, the preganglionic cells bodies of the sympathetic supply are in the lateral columns of the lower sixth thoracic segments of the spinal cord. Axons from these cell bodies synapse in the coeliac, preaortic and superior mesenteric plexi. The postganglionic fibres then proceed