CHRONIC PERSISTENT DIARRHEA

ESSAY

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By
Hanafy Abd El-Hamid Hanafy
M.B.B. Ch. (Assiut University)

Under Supervision of
Professor Dr. Khalil Abd El-Hadi Mourad
Professor of Paediatrics
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
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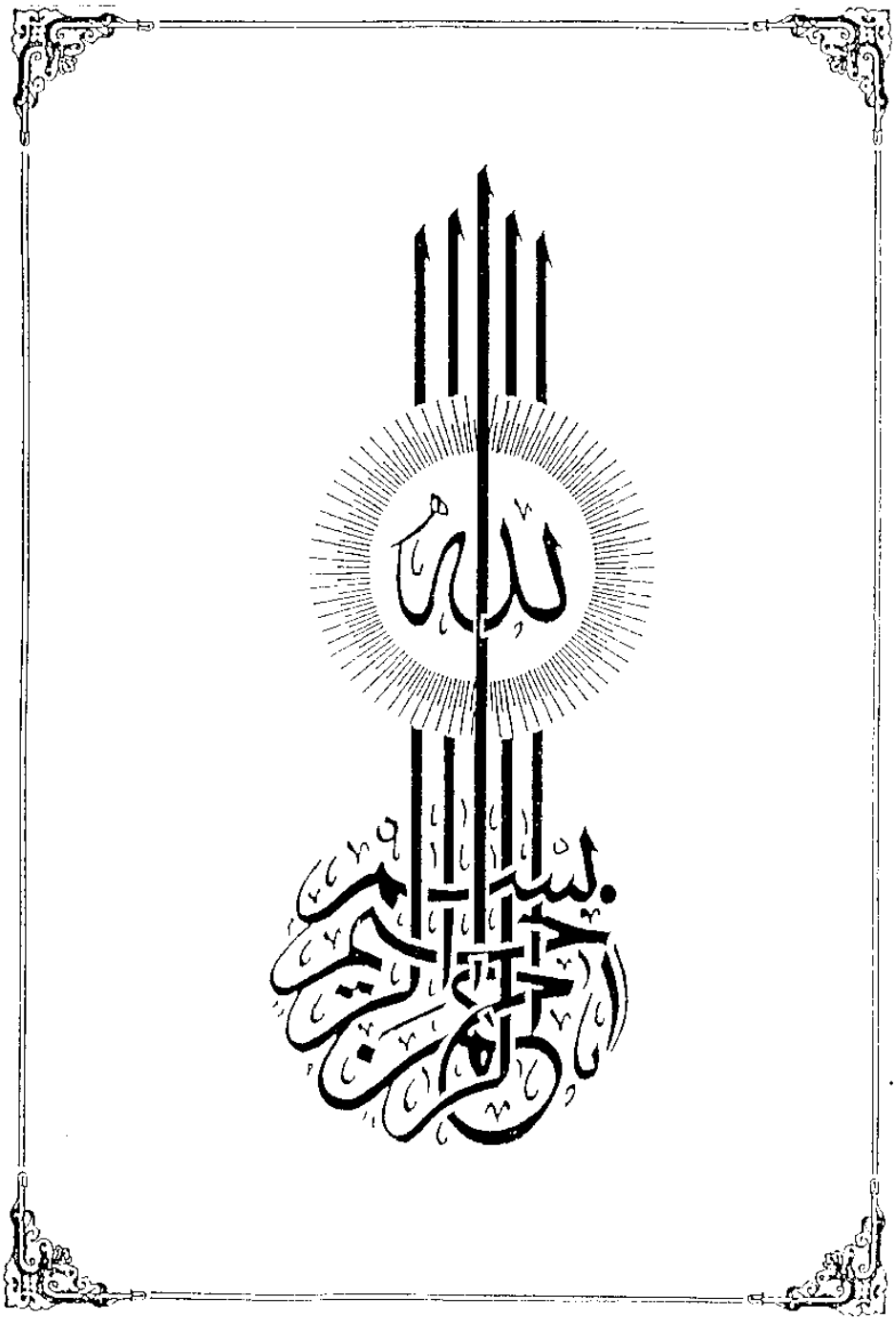

List of Abbreviations

CEN	Central enteral nutrition.
CPD	Chronic persistent diarrhea.
EAggEC	Entero Aggregative Escherichia coli.
EAEC	Entero Adherent Escherichia coli.
EPEC	Entero Pathogenic Escherichia coli.
ETEC	Entero Toxogenic Escherichia coli.
GEU	Gastero entritis Unit.
G Lamblia	Glardia Lamblia.
HIV^+	Human Immunodeficiency virus positive.
HIV^-	Human Immunodeficiency virus negative.
ION	Intermittent Oral Nutrition.
NCDDP	National control of diarrheal disease programe.
NCHS	National Center for Health Statistics.
ORS	Oral Rehydration Solution.
ORT	Oral Rehydration Therapy.
USA	United States of America.
WHO	World Health Organization.

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Aim of the Essay

Our essay will include :

- Etiology.
- Clinical manifestations.
- Investigations.
- Differential diagnosis.
- Treatment.
- Prevention.

Supervisor; Professor Dr. Khalil Abd El-Hadi Mourad

Prof. of Paediatrics,
Faculty of Medicine,
Ain Shams University.

INTRODUCTION
AND
AIM OF THE ESSAY

Introduction

Diarrhea that persists for more than two weeks after an apparent episode of infectious gastero-enteritis occur in 10-20 % of children less than 5 years of age in the developing world. In developed countries this may involve into the syndrome of intractable diarrhea of infancy.

Patients at risk in developed countries include; low birth infants, immigrants, those with failure to thrive and those less than 3 months of age with repeated episodes of diarrhea.

In most infants there is no other identifiable primary cause of diarrhea (Ulcerative colitis, persistent, infection) or Malabsorption (Cystic Fibrosis, celiac disease). Furthermore, the initiating infectious agent may be no longer be isolated from the stools, suggesting that secondary pathophysiologic mechanisms have become important in the continuation of diarrhea (Kliegman, 1992).

Episodes of PD although fewer in number than those of acute diarrhea, are more likely to have severe consequences.

PD is an important contributor to protein energy malnutrition and death in young children (WHO, 1988).

Management if PD remain difficult and pathophysiology is little understood, compared with acute diarrhea.

Although the clinical characteristics of PD have been described little is known about potential risk factors that may predispose the child to develop this condition. Such information is critical to our understanding its pathogenesis and to developing intervention to prevent persistence of an acute diarrheal illness (WHO, 1988).

ETIOLOGY OF CHRONIC PERSISTENT DIARRHEA

Etiology

Etiology of PD is complex (Wanke et al., 1991) and non of the clinical features or of the laboratory tests performed in the first week of diarrhea proved to be of value to identify cases that would become persistent (Lanata et al., 1991).

Agents isolated from acute and persistent diarrhea were similar, suggesting that other factors must be operative in the development of PD (Schorting et al., 1990).

It seems appropriate to focus on the intestinal epithelium as having a major role in the pathogenesis of prolonged diarrhea (Hamilton, 1984). Theoretically diarrheal illness may be prolonged by :

(a) Factors that continue to injure the intestinal mucosa or,

(b) Failure of the intestinal mucosa to heal after an acute episode.

In either event impaired absorption or abnormal secretion of solutes and water persists and the diarrhea is prolonged (WHO, 1988).

(a) Continuing mucosal injury :

Probable causes of continuing mucosal injury include micro organisms that either invade the mucosa or attach to its luminal surface. Clearly, the status of the host, mucosal barrier and capacity for microbial clearance, by immunological or other mechanisms, may influence vulnerability to continuing microbial damage (WHO, 1988).

Dietary constituents, notably disaccharides (especially lactose) and animal proteins, constitute another group of potentials of continuing intestinal mucosal injury. The role of the latter is most continuous, at present, since absorption of antigenically significant amounts of intact

protein has shown to occur in the experimental models of acute viral enteritis. Whether this triggers immune mechanisms that contribute to mucosal damage has, however, not been proved (WHO, 1988).

Altered intraluminal metabolism of bile salts has been suggested as a possible factor in persistent diarrhea.

In theory, malabsorption of bile salts in the terminal small bowel could result in excessive quantities reaching the colon, where they could influence fluid secretion, however the available evidence does not support this process as a major determinant of persistent diarrhea.

Also, small bowel bacterial overgrowth could lead to intraluminal de conjugation of bile salts, which in turn could cause fat malabsorption, but there are no controlled data on this issue (WHO, 1988).

(b) Delayed mucosal repair :

A major determinant of delayed mucosal repair, was demonstrated in animal models of acute viral and bacterial enteritis and was suggested by epidemiological data, in chronic protein-energy under nutrition. Whether impairment of the capacity of the gut epithelium to renew and differentiate contributes to the prolongation of diarrhea has not been established, nor has the possible therapeutic benefit of micronutrients such as zinc, iron, vitamin A, folate and vitamin B_{12} been determined. Nevertheless, clear evidence that malnutrition is a significant risk factor for persistent diarrhea suggest an important role for delayed mucosal repair and argues strongly for the importance of adequate nutrition in the management of this disorder (WHO, 1988).

Continuous mucosal injury may be due to persisting or recurring infection or may be food induced, either due to disaccharide intolerance or

due to allergy to animal proteins (Hamilton, 1984). In addition secondary bacterial overgrowth and altered bile metabolism have been suggested as causes of persistence (WHO, 1988).

Once mucosal injury has occurred small bowel dysfunction becomes self perpetuating (Kleinmann et al., 1989)$_{(a)}$.

Thus post enteritis enteropathy theoretically can be classified into :

1- Food sensitive enteropathy.

2- Infective enteropathy. (Walker-Smith, 1988).

1- Food sensitive enteropathy :

A- Carbohydrate intolerance :

Carbohydrate malabsorption in the diarrheal disease is probably due to mucosal damage. Leading to disaccharidase and other brush border enzyme deficiencies (Teichberg et al., 1978).

Among the disaccharidases, lactase is the most superficial, the most vulnerable, the first to be affected and the last to recover (Lebenthal, 1975)$_{(a)}$. The decrease in alpha glucosidases (sucrase and maltase) are less pronounced in all grades of mucosal atrophy (Rossi TM et al., 1980). In severe cases even monosaccharide (glucose, fructose and galactose) malabsorption occurs. Thus, lactose intolerance is a common finding in infant with PD and in a subgroup of patients it may be the only causal mechanism for the prolongation of diarrhea (Teichberg et al., 1978). Stools are characterized by an acidic pH and by presence of unabsorbed carbohydrates (Lifshitz et al., 1971).

Since carbohydrate intolerance during the acute stages of diarrhea, and diarrhea it self has adverse effects on the mucosal integrity, dietary carbohydrates may have a deleterious effect by aggravation diarrheal symptoms and prolonging mucosal injury and carbohydrate intolerance (Fig. 1).

The importance of monosaccharide intolerance is related to the use of oral rehydration solution which contains glucose (Kjellman and Rong, 1982).

Causes of carbohydrate intolerance :

Black et al. in 1988 summarized the causes of carbohydrate intolerance into the following : decreased disaccharidase concentration, loss of mucosal surface area and rapid transit time limiting the contact between the carbohydrate and the enzymes. The hyperosmolarity in the intestinal lumen may produce washing - off of intestinal disaccharidases.

In addition the systemic complications of the diarrheal process, such as dehydration, shock or malnutrition may also produce intestinal injury and secondary carbohydrate malabsorption (Lifshitz, 1977).

Bacterial overgrowth may also cause carbohydrate intolerance by depressing brush border disaccharidase activities.

Disturbance of transport of glucose and fructose have been correlated with the degree of bacterial contamination (Lebenthal, 1984).

Intestinal infection may lead to carbohydrate malabsorption by mucosal damage and disruption of the enterocyte (Lifshitz, 1977). Bacterial glucosidases hydrolyse the disaccharidases which are themselves glycoproteins (Perman and Modler, 1981).

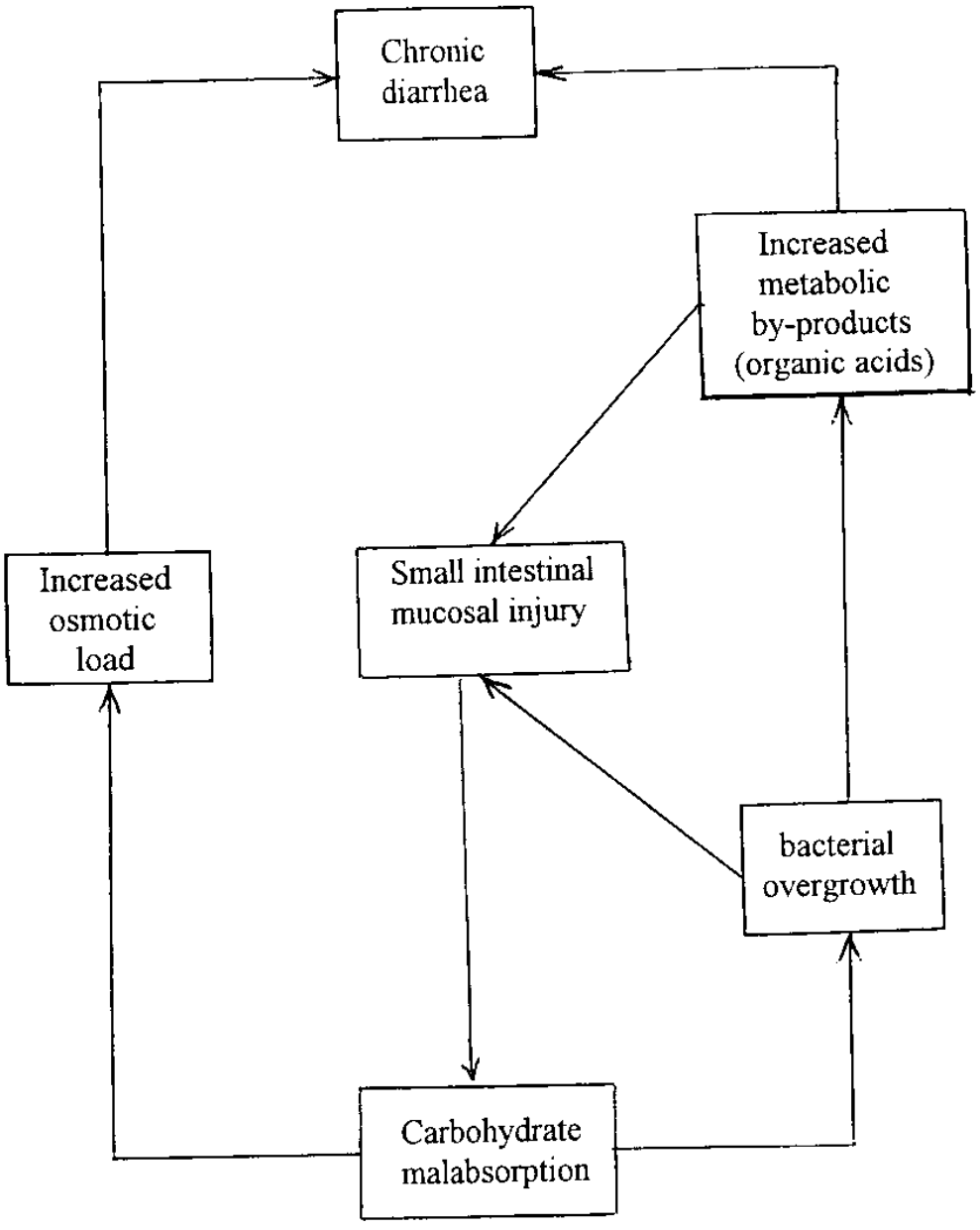

Fig. (1) : Inter-relationship of carbohydrate malabsorption and chronic diarrhea (Lebenthal, 1984).