ESSAY ON

IMMUNOLOGY OF THE GASTROINTESTINAL TRACT

Submitted for Partial Fulfilment of
Master Degree in Pediatrics

By
FATMA ABD EL-WAHAB ALI
M. B; B. Ch.
Faculty of Medicine
Ain Shams University

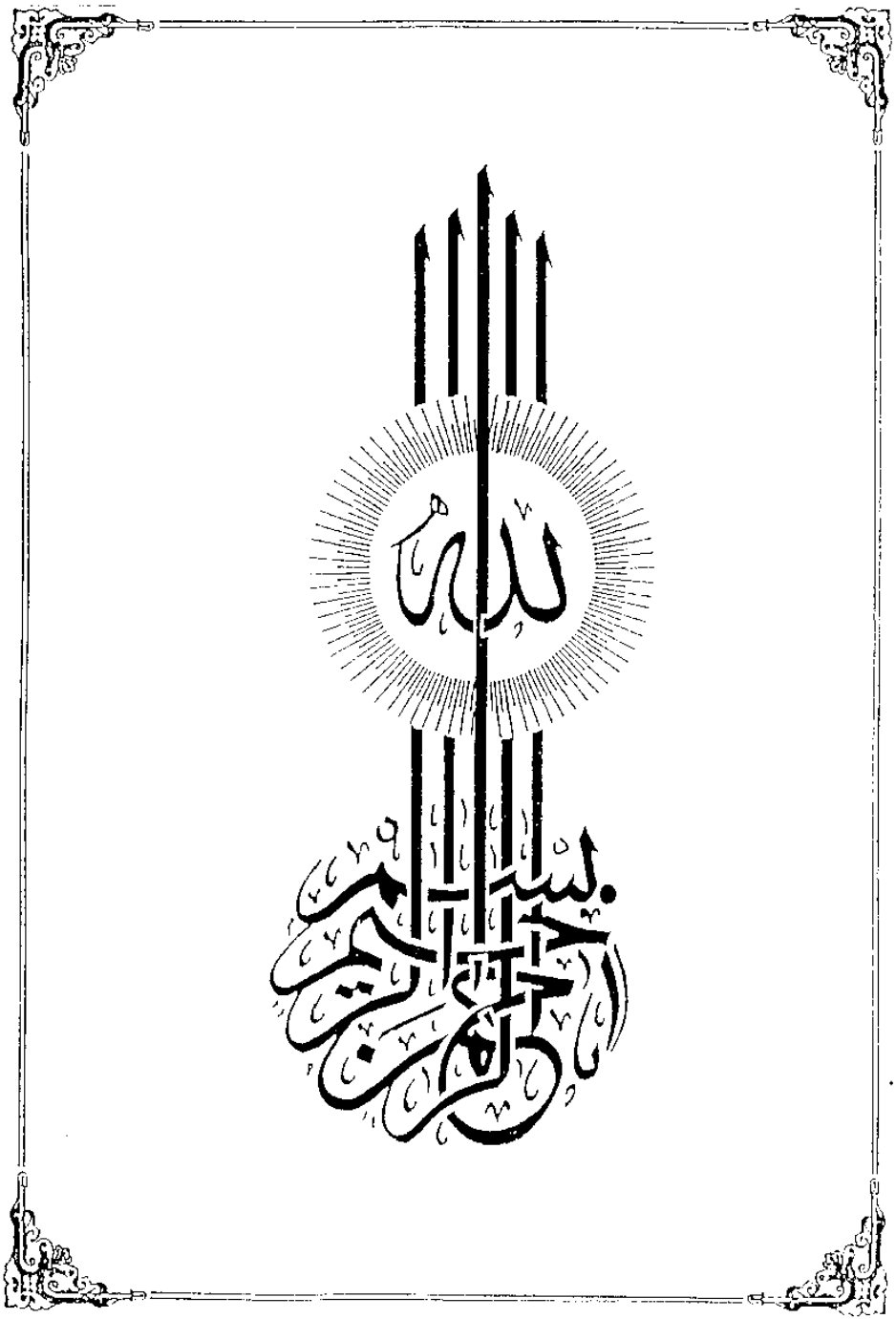
Supervised by
Professor Dr. MOHAMED AHMED AWAD-ALLA
Professor of Pediatrics
Ain Shams University

1984

بسم الله الرحمن الرحيم

« قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم »

سورة البقرة آية ٣٢



ACKNOWLEDGEMENT

I have to express my profound gratefulness and appreciation to my eminent professor Dr. Mohammed A. Awad-Alla Professor of Pediatrics Faculty of Medicine-Ain Shams University who suggested the item of this essay.

It was through his kind supervision, constant advice, support and encouragement and meticulous revision of every possible details, that this work could be brought to light.

Many thanks to all my colleagues for their help in performing this work.

TO MY PARENTS

TO MAY HUSBAND

TO MY CHILDREN

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INTRODUCTION

INTRODUCTION

The term immunity is now used to refer to any specific immune response to foreign substance "antigen" regardless whether or not that particular response has any protective value for that host. The activities of the immune system aim to protect against microbial invasion and maintain the integrity of higher organisms and aberrations of these activities can lead to diseases (Bowry, 1975).

The proliferation of information in both basic and clinical immunology and the increased awareness of the role of altered immune function as an etiology for certain gastro-intestinal disorders has focused new attention on the immune mechanisms of the gastrointestinal tract "Byrne, [illegible], 1980).

The concept of localized-intestinal immunity developed from Besredka's observation that oral immunization of rabbits with killd Salmonella organisms provided solid protection against fatal dysenteric infection, irrespective of the titres of serum antibody "Besredka, 1919).

In addition to the protection provided by the monolayer of epithelial cells and their mucous coat, the intestine, in common with exposed epithelial mucosa, has evolved a specialized form of local immunity. The essentials of the immune response viz, antigen handling and recognition, cellular and humoral responses, recruitment of effector systems, memory and regulation of tolerance have been adapted to function at external surfaces. Once the epithelial integrity of the mucosa is disrupted, ingested microflora, parasites, food antigens, toxins, drugs and bacteria from distal small and large intestine may enter the lamina propria. Knowledge of the physiology of intestinal immunity is central to our understanding of many gastrointestinal disorders. Manipulation of the intestinal immune system has produced the Sabin oral polio vaccine and the future offers further advances in the development of oral vaccines, in the management of chronic inflammatory conditions and food allergy, and in promoting intestinal parasite rejection. (Doe,1981).

For this reason the aim of this essay is to have a recent review to the immunology of the gastrointestinal tract "G.I.T.".

CHAPTER I

PHYSIOLOGY OF PROTECTIVE MECHANISMS IN G.I.T.

PHYSIOLOGY OF PROTECTIVE MECHANISMS IN THE GASTROINTESTINAL TRACT(G.I.T)

Gastrointestinal immunity:

The lamina propria is protected by both non-immune and immune mechanisms. The protective mechanisms may operate within the gastrointestinal lumen, at the mucosal surface or within the intestinal mucosa. Both immunologic and non-immunologic mechanisms of the gastrointestinal tract are important in preventing the penetration of the epithelial mucosal barrier by intraluminal substances such as dietary antigens, microorganisms and toxins. Their penetration into the intestinal interstitial space or general circulation may result in either local or systemic infection, allergy or autoimmune states. (Byrne, 1980).

Non-immunologic Mechanisms:

Several non-immunologic factors are important in limiting the antigenic mass thereby aiding the more classic immunologic mechanisms in preventing penetration of the mucosal barrier. These non-immunologic defense mechanisms include: secretions "mucins, gastric acid, bile salts" peristalsis and endigenous intestinal flora (Walker, 1976).

Various secretions of the digestive tract have a protective role. Mucus is secreted by goblet cells found throughout the digestive tract, protects the mucosa by lining it and by binding and lubricating the food particles. Being alkaline, it neutralizes acids present within the gastrointestinal contents. Mucins (glycoproteins and glycolipids) present in the mucus interact with biologically active materials to prevent microbial penetration of the intestinal mucosa (Strombeck and Harrold, 1974). They also inhibit microorganism proliferation by competitive inhibition for their attachment to epithelial cell surfaces. Without a receptor site, these organisms can be removed by peristalsis. A model for this has been demonstrated in the oral cavity, where salivary mucins inhibit the adherance of streptococcal, staphylococcal and lactobacillus organisms to the buccal mucosa, allowing for their removal by the washing action of saliva (Gibbon and van Houte, 1975).

Hydrochloric acid secreted by gastric parietal cells present in the antrum portion is an effective inhibitor of bacterial proliferation in the proximal gastrointestinal tract. In patients with achlorhydria or with gastric antral resection, bacterial over growth in the proximal

small intestine commonly occurs. These individuals also have an increased incidance of gastrointestinal infections. Acid peptic digestion i.e. hyper acidity in cases of peptic ulcer may prevent absorption of food antigens (Kraft & Rothberg, 1967).

Bile salts which are the Na and K salts of glycocholic and taurocholic acids which are derived from cholesterol which is formed mainly in liver. These bile salts inhibit bacterial growth in vitro. In vivo, a similar effect on anaerobic organisms occurs (Williams, Lehner, et 1975). These salts are anti-putre factive because they expose protein to its digestive enzymes, by an indirect way i.e. removal of the fat of proteins. In their absence, fat envelops protein preventing its digestion, and on reaching the large intestine, un-digested protein is acted upon by bacteria causing their putrefaction and production of offensive gases. They also stimulate peristalsis. (Sabri, ... 1980).

Propulsive peristalsis movement, consists of a wave of dilatation followed by a wave of constrictions travelling towards the distal end of the gastrointestinal segment. It is mediated by local axon reflexes, and the main

stimulus is the stomach or intestinal distentension which causes contraction above and relaxation below the distended segment and so the bolus is propelled forwards. Peristalsis is of primary importance in removing bacteria and other antigens from the gastro-intestinal tract. It limits bacterial proliferation and helps to prevent the toxic effects of stagnant intestinal contents (William, 1980).

The endigenous intestinal flora is important for normal digestion and absorption as well as for the prevention of colonization by pathogenic organisms. For example, short-chain fatty acids produced by both anaerobes and aerobes help to prevent colonization by Salmonella species (Meynell 1963) Further evidence for the importance of the endigenous intestinal flora is provided by studies in germ-free animals. When these animals are suddenly exposed to the external environment, severe gastroentritis and systemic infection usually develop. These flora is established early in the neonatal period and is dependant on environmental as well as dietary influences (Selner, Merrill, 1968). The proximal gastrointestinal tract is colonized by fucultative gram-positive organisms in concentrations