

Chapter 1

NATURE AND PROPERTIES OF THE HUMAN GASTROINTESTINAL
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TABLE OF CONTENTS

I.	Introduction.....	3
II.	Defense of the Gastrointestinal Mucosa.....	4
	A. General Outline	4
	1. Immune Exclusion.....	4
	2. Immune Regulation	4
	3. Immune Elimination	5
	B. Igs in Gastrointestinal Juice.....	5
	1. Nature of SIgA.....	5
	2. Function of SIgA	6
	3. SIgM.....	7
	4. IgG, IgD, and IgE	7
	C. Innate Resistance Mechanisms.....	8
	1. Nonimmunological Factors.....	8
	2. Cooperation Between Nonimmunological and Immunological Factors	9
	D. Cellular Aspects of the Secretory Immune System.....	9
	1. Ig-Producing Cells in Health and Disease.....	9
	a. Normal Mucosa	9
	b. Diseased Mucosa.....	11
	(1) Celiac Disease and Similar Lesions	12
	(2) Circulating Antibodies in Celiac Disease.....	14
	(3) Pathogenesis of Celiac Disease	15
	(4) Chronic Gastritis.....	16
	(5) Inflammatory Bowel Disease.....	18
	(6) Antibody Production in Inflammatory Bowel Disease	18
	(7) Miscellaneous Large Bowel Disorders	19
	2. Gut Epithelium in Health and Disease.....	19
	a. Normal Mucosa	19
	(1) SC-Mediated Transport	19
	(2) HLA Expression and T Lymphocytes.....	20
	b. Diseased Mucosa.....	22
	(1) SC-Mediated Transport	22
	(2) HLA Expression and T Lymphocytes.....	23
	3. Role of the Liver in Secretory Immunity.....	26
	a. Hepatic IgA Transport	26
	b. Removal of Circulating Immune Complexes.....	28
	c. Clinical Aspects	28
III.	Generation and Regulation of Secretory Immunity.....	28
	A. Developmental Aspects of Mucosal Defense	28



1.	Gut Closure, Breast-Feeding, and Secretory Immunity.....	28
a.	Perinatal Immunity.....	28
b.	Benefit of Breast Milk	29
c.	Variables in the Development of Gastrointestinal Immunity	30
2.	Nutrition and Secretory Immunity.....	32
3.	Immunodeficiency and Mucosal Defense	32
a.	IgA Deficiency.....	32
b.	Generalized B Cell Deficiency	35
B.	Mucosal Barrier Function in Health and Disease	36
1.	Penetration of Antigens.....	36
a.	Magnitude and Routes of Gastrointestinal Antigen Uptake.....	36
b.	Effects of Immunization on Gastrointestinal Antigen Uptake.....	36
c.	Antigen Uptake in Gastrointestinal Disease	37
2.	Role of Mast Cells and IgE.....	38
a.	Identification of Mucosal Mast Cells	38
b.	Mucosal Mast Cells and IgE	38
c.	Mast Cells in Gastrointestinal Diseases	39
d.	Nature and Function of the IgE-MMC System	39
e.	The IgE-MMC System, Mucosal Barrier, and Food Allergy.....	42
3.	Local Immunological Homeostasis	43
a.	Normal Homeostasis in Gastrointestinal Mucosa	43
b.	Altered Homeostasis in Gastrointestinal Mucosa	43
4.	Fate of Formed Immune Complexes	45
a.	Modes of Eliminating Immune Complexes	45
b.	Effects of Mucosal and Systemic Immunity	46
C.	Induction of Secretory Immunity	46
1.	Nature and Role of Lymphoepithelial Structures	46
a.	The Epithelium	46
b.	Developmental Aspects.....	49
c.	Lymphoid and Accessory Cells.....	49
d.	Functional Aspects	50
2.	Cell Traffic in the Secretory Immune System	51
a.	Emigration of Lymphoid Cells from MALT	51
b.	“Homing” Mechanisms.....	53
c.	Extravasation and Retention of B Cells in Gut Mucosa	54
d.	Role of MALT	54
3.	Cellular Interactions Determining Enhanced or Reduced B Cell Responsiveness	55
a.	T Cell-Regulated Generation of IgA Precursor Cells.....	55
b.	Proliferative Generation of IgA Precursor Cells	56
c.	Induction of Systemic Hyporesponsiveness.....	56
4.	Proliferation and Differentiation of B Cells in Gastrointestinal Mucosa	57
a.	Local Development of IgA Immunocytes	57
b.	“Second Signals” for Proliferation and Terminal Differentiation.....	60
5.	Interactions Between Local and Systemic Immunity	60

6.	Modes of Stimulating Secretory Immunity	61
a.	Form of Antigen and Vaccine Administration.....	61
b.	Current Avenues of Vaccination Research.....	62
IV.	Conclusions	62
	Acknowledgments	64
	Abbreviations.....	64
	References	65

I. INTRODUCTION

The surface of the adult human gastrointestinal tract has been estimated to make up some 200 to 300 m². Throughout this large area, intimate contact takes place between the host organism and a wide variety of dietary substances and their breakdown products as well as microorganisms, parasites, exogenous toxins, and enzymes. The mucous membrane must permit the exchange of substances between the gut lumen and the "milieu interieur" of the body but, at the same time, inhibit the penetration of potentially noxious agents.¹ Besides the mechanical barrier, an exclusion function is exerted by a great number of humoral and cellular factors.² These factors work together more or less in concert and can partly substitute for each other. It is usual to distinguish between nonspecific and specific defense mechanisms. The former are innate, whereas the latter depend on passively or actively acquired cellular and humoral immunological components.

The existence of a protective local immune system functioning fairly independently of systemic immunity was proposed in 1919 by Besredka³ when he demonstrated that rabbits, after oral immunization with killed Shiga bacillus, were protected against fatal dysentery irrespective of the serum antibody titer. Davies⁴ was subsequently able to detect antibodies against the dysentery bacillus in stools from infected patients several days before such antibodies were present in serum. These and other pioneering studies on local immunity have been discussed by Besredka⁵ and Pierce.⁶

The interest in local immunity was significantly revived in the 1960s when it was reported by Tomasi and Zigelbaum⁷ that the predominating immunoglobulin (Ig) in external body fluids was IgA; this secretory IgA (SIgA) was shown to have unique immunochemical and physicochemical properties.^{8,9} Shortly afterward, Crabbé et al.¹⁰ demonstrated an isotype distribution of intestinal Ig-producing cells strikingly different from that previously found in other lymphoid tissues; mucosal IgA immunocytes were remarkably predominant — being more than 20 times as numerous as IgG-producing cells. This finding has been repeatedly verified.¹¹ The first direct evidence indicating that the mucosal IgA immunocytes produce dimers rather than monomers was obtained in 1973 by Brandtzaeg.¹²

In 1970 we pointed out that IgM also appears in exocrine fluids because of active secretion.¹³ SIgM was later shown to be associated with the same epithelial secretory component (SC) and to follow the same intracellular route through glandular epitheliums as SIgA.^{14,15}

In 1974 a common epithelial transport model was proposed for dimeric IgA and pentameric IgM.^{16,17} The "joining" (J) chain had been identified a few years earlier as a unique polypeptide shared by these two Ig polymers.^{18,19} Our original suggestion that the J chain and epithelial SC represent the "lock and key" in the selective external translocation of IgA and IgM has recently been firmly established.²⁰

Knowledge about the functional role of SIgA has improved considerably since its

Chapter 2

INTESTINAL UPTAKE OF ANTIGEN — IMMUNOLOGICAL CONSEQUENCES

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TABLE OF CONTENTS

I.	Introduction.....	88
II.	Intestinal Uptake of Antigens.....	88
	A. Antigen Uptake in Neonates	88
	B. Antigen Uptake in Adults.....	89
	1. Protein Molecules.....	89
	2. Polysaccharides	90
	3. Inert Particulates.....	90
	4. Microorganisms	91
III.	Route of Antigen Entry into the GALT	92
	A. Nonspecific Uptake	93
	B. Persorption.....	93
	C. Role of Peyer's Patch in Antigen Uptake	94
	D. Cellular Uptake	95
	E. Origin of Absorptive Epithelial Cells	95
	F. Villus Uptake	96
	G. Antigen Transport	97
IV.	Immunological Responses to Ingested Antigens.....	99
	A. Oral Immunization	100
	B. Responses to Infectious Agents.....	100
	C. Immunization and Antigen Uptake.....	101
	D. Systemic Tolerance	101
V.	Summary and Conclusions	103
	References	103

Chapter 3

MECHANISMS OF SECRETORY IgA RESPONSES

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TABLE OF CONTENTS

I.	Introduction.....	112
II.	The Cellular Composition of the PP and the Gut Mucosa.....	113
	A. PP	114
	B. Intestinal Mucosa	114
III.	Empirical Observations on the Generation of SIgA Responses.....	115
	A. Primary Responses	115
	B. IgA Memory	116
IV.	Regulation of IgA Production.....	117
	A. Mechanism of Heavy Chain Class Switch.....	117
	B. Role of Environmental Antigens	118
	C. T-Cell Dependence of IgA Responses.....	119
	1. The Role of T Cells with Fc Receptors for IgA.....	120
	2. The Role of T Cell-Derived Soluble Factors.....	120
V.	Summary and Conclusions	121
	References	122

