Chapter 1

NATURE AND PROPERTIES OF THE HUMAN GASTROINTESTINAL IMMUNE SYSTEM

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I. INTRODUCTION

The surface of the adult human gastrointestinal tract has been estimated to make up some 200 to 300 m^2. 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 Besredka[3] when he demonstrated that rabbits, after oral immunization with killed Shiga bacillus, were protected against fatal dysentery irrespective of the serum antibody titer. Davies[4] 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 Besredka[5] and Pierce.[6]

The interest in local immunity was significantly revived in the 1960s when it was reported by Tomasi and Zigelbaum[7] 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

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