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Modern Data on the Structure and Functioning of the Immune System of the Gastrointestinal Tract

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ABSTRACT: The article considers lymphoid nodules and lymphocytes of the mucous membrane of the digestive system providing local immune protection in norm, pathology and experiment. It is necessary to study the quantitative ratio of various immunoglobulins with cell populations of lymphoid accumulations of the gastrointestinal tract both under normal and pathological conditions. Special attention should be paid to the immune structures of the digestive system in animals and humans.

KEYWORD: plasma cells, Peyer's plaques, lymphoid tissue, Epithelial cells, intraepithelial lymphocytes (IEL), T- and B-lymphocytes

The mucous membranes of the gastrointestinal, bronchopulmonary and urogenital tracts have a total area of at least 400 m^2, covered with a single layer of epithelial cells. These shells are a barrier between the internal environment of the macroorganism and its environment containing a large number of allergens and microbes capable of penetrating the epithelium, penetrating into the macroorganism and causing various infectious and allergic diseases in it. Therefore, almost all mucous membranes contain a certain number of immune system cells, often (but not always) organized into structural formations [1,2].

Of considerable interest is the elucidation of the relationship of morphological, cytological changes with the content of various immunoglobulins in the mucous membrane and blood plasma under the influence of hydrological, balneological and mineralogical factors. The question of the ratio of epithelial cells of the gastrointestinal mucosa with lymphocytes (villi, crypts, folds, nodules, etc.) in animals and humans needs to be purposefully investigated.

The maturation of various populations in the lymphoid nodules of the small intestine provides cellular and humoral immunity. B-lymphocytes of Peyer's plaques are precursors of plasma cells secreting all 5 classes of Ig A, which in their own plate of the mucous membrane provide a local immune response. Especially in this regard, the importance of plasma cells as a source of synthesis of secretion of immunoglobulins and antibodies is great. When antibodies act on B-lymphocytes, they transform into immature and mature plasma cells, followed by the formation of antibodies.

Plasma cells are localized in the stroma of the villi and in the own plate of the mucous membrane of the small intestine. Basically, plasmocytes are located under intestinal epithelial cells, around the components of the lymph-bearing and microcirculatory channels. Plasmocytes are single-celled protein glands that form immunoglobulins.

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70-80% of the plasma cells of the intestinal mucosa's own plate contain Ig A 20-22%, Ig M 4% and consider local plasma cells of the mucosa to be the "first line of defense" synthesizing Ig A. It is the difference between rich and diverse microflora and antigens that contributes to the development, improvement and differentiation of lymphoid clusters of the gastrointestinal tract as a result of their constant antigenic stimulation from the lumen of the gastroenteric system.

Plasma cells are mainly grouped around the intestinal glands, but their morphological ratio along the entire length of the gastrointestinal tract has not been studied both under normal conditions and under the influence of water, spa, physical and pharmacokinetic agents. Of theoretical and practical interest are the ratios of the spectrum of cells and the composition of intestinal juice, the relationship of histotopography of lymphoid tissue and intestinal glands. Questions need to be clarified about the participation of lymphoid cells in the formation of intestinal juice, its composition, properties and the nature of their relationship in the norm, experiment, pathology and the effects of spa, physiotherapy and balneological factors, taking into account the intestinal microflora.

Physico-chemical factors, the nature of nutrition and other environmental influences, up to geo- and geleo-, are caused by the influence of electromagnetic fields through the neuro-endocrine system. Glucocorticoids and ACTH in high concentrations inhibit the formation of antibodies and inhibit the development of allergies, and somatotropin and mineral-corticoids enhance antibody formation.

Especially T-lymphocytes depend on the action of the somatotropic hormone. There is a synergy between T - lymphocytes, thymus, somatotropic and therotropic hormones, and there is antagonism with respect to T - lymphocytes, thymus and ACTH.

In terms of protecting the body from antigens coming through the mucous membrane of the digestive tract, single and group (Peyer's plaques) lymphoid nodules, lymphocytes of the mucous and submucosa of the stomach, small and large intestine, which secrete secretory and cellular immunity, are essential.

When stimulated by antigens (of food, microbial, viral origin) of immunocomponent B cells of Peyer's intestinal plaques, specific antibodies enter the corresponding secrets. Stimulated mature plasma cells migrate through mesenteric lymph nodes into the thoracic stream, then settling in submucosal secretory zones, both in those that have had contact with the antigen and in intact ones. Similarly, the process of antigenic stimulation occurs in the mucous membranes of the respiratory and genitourinary tracts of all systems that constantly communicate in the salivary glands, are produced far beyond the oral cavity. The issues of regulation of immune reactions in the gastrointestinal mucosa have not been sufficiently studied. The assumption of the importance of peptide compounds of endocrine releasing hormones in the regulation of cellular immune reactions opens up great prospects.

It seems promising to us to study the morphology of the lymphoid organs of the gastrointestinal tract, when exposed to peptides, gastrin, secretin, hormones in terms of the relationship of the morphofunctional state of the stomach, intestines and endocrine organs. The question of the ratio of lymphocytes and intestinal epithelium (intestinal glands, villi, folds) deserves special attention, because there are different views on this issue in the literature. The lymphoid system of the gastrointestinal tract participates in the control of the function and proliferation of intestinal and gastric epithelium. Inhibition of the function of Peyer's plaques causes a decrease in the concentration of differentiated intestinal epithelium.

According to modern data, argyrophilic and agretophilic cells of the digestive system belong to endocrine cells, where serotonin (EC cells) is produced, an endorphin-like substance like in the brain,

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and all cells are called enteroendocrine cells together. The gastroentero-pancreatic endocrine system (GEPES) produces hormones: serotonin, secretin, substance, vasoactive intestinal polypeptide (VIP), glucagon, insulin, somatostatin, GEPES secretes the contents into the bloodstream, intestines into the intestinal cavity. In our opinion, the ratio of endocrine cells and their secretion with the lymphatic bed, intestinal glands, macrophages, lymphocytes, lymphoid formations, intestinal microbes should be carefully investigated, because they provide a variety of local and general immunological reactions of the mucous membrane.

The expansion and deepening of ideas about the role of individual links of immunity in the pathology of the digestive organs has allowed today to come close to the problem of active immunocorrection. Despite some progress in gastrointestinal immunology, many facts have not yet been the subject of in-depth study, interesting, promising hypotheses have not been proven.

Immunological, morphological and physiological barriers of digestion can be considered to consist of 6 barriers: 1) luminar (in the lumen of the gastrointestinal tract there are lymphocytes, macrophages, enzymes, antibodies-immunoglobulin, etc.), 2) interepithelial lymphocytes, 3) in the thickness of the mucous membrane, 4) in the thickness of the submucosal base (lymphocytes, macrophages, plasma cells, antibodies, lymphoid nodules, etc.), 5) mesenteric lymph nodes, 6) in the lumen of the thoracic duct.

To correct immunological disorders in animals and humans, it is necessary to have a thorough knowledge of the anatomy of the vascular bed, the macro- and microscopic structure of single and group lymphatic follicles of the small intestine, which play an essential role in the digestive process, lymphocyte circulation, immunoglobulin synthesis, antigenic and antimicrobial reactions. When studying the macro- and microscopic anatomy of the lymphoid nodules of the small intestine, we found that single nodules occur in the thickness of the mucous membrane and submucosal base. There are interspecific and intraspecific features in the sizes of single and group nodules and their lymphatic networks.

Currently, several lymphoid formations associated with the mucous membranes are distinguished: lymphoid tissue associated with the intestine - GALT; lymphoid tissue associated with the bronchi - VALT; lymphoid tissue associated with the nose - NALT, which include paired lymphoid formations of the Pirogov-Waldeyer ring, lymphoid tissue associated with the Eustachian tube - TLT. All together, these lymphoid structures create a functionally unified, relatively autonomous immune system - lymphoid tissue associated with mucous membranes - mammoth (mucosa-associated limfoid tissue) [8], and in this system, epithelial cells of the mucous membranes are not immunologically passive structures, but participate in the presentation of antigen (AG) CD4+ and CD8+ -lymphocytes [4]. The secretory immune system, sometimes also called local immunity, provides an integral connection between organs that have mucous membranes, and it is relatively independent of systemic immunity. In each of these organs, inductive and effector, or secretory, zones are isolated, where primed T and B cells mainly migrate from the inductive zones and where these cells carry out their effector functions. The main characteristic feature of all the structural formations of the lymphoid system associated with mucous membranes is the synthesis of secretory Ig A - immunoglobulin B by lymphocytes, which is determined only in the secretions of the mucous membranes and is normally not detected in peripheral blood. This immunoglobulin is quantitatively prevalent in humans and mammals. 4-5 g of this protein is synthesized daily and released onto the surface of the mucous membranes, which is significantly more than the amount of IgG and IgM synthesized [13Despite some territorial disunity between the systemic immunity, represented by central (thymus and bone marrow) and peripheral (spleen and lymph nodes) organs, and lymphoid tissue associated with mucous membranes - mammoth, all major groups of the immune system, thanks to the unique ability

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of immunocytes to migrate and recycle, function as a whole, and lymphoid tissue and lymphoid organs of the gastrointestinal tract (gastrointestinal tract) are closely functionally related to both systemic immunity , and with other components of the MAST. The immune system of the gastrointestinal tract is characterized by some features that somewhat distinguish it from other peripheral organs of immunity and other structures of the gastrointestinal tract. First of all, the immune system of the gastrointestinal tract is most strongly developed in comparison with similar structures that make up the mammoth. This system, like no other, is in the closest contact with a huge flow of microbial and allergenic material coming from the intestinal lumen, and serves as the first barrier to this flow. Features of the structure and cellular composition of the gastrointestinal immune system In the gastrointestinal immune system, inductive and effector zones are distinguished. The first one consists of Peyer's plaques, a vermiform process and solitary follicles, the second one consists of its own plate (Lamina rhorgia) and epithelial cells of the intestinal mucosa. In accordance with the names, the recognition-presentation of antigen and the formation of a population of antigen-specific T- and B-lymphocytes occur in the inductive zone; in the effector zone, the synthesis of immunoglobulins by B-lymphocytes, cytokines by monocytes/macrophages, T- and NK-lymphocytes, i.e. they perform their effector functions. Peyer's plaques play an important role in the functioning of the immune system of the gastrointestinal tract. They consist of T- and B-zones with the presence of germinal centers in the B-zone. Their cellular composition does not differ significantly from that of any peripheral lymph node. In the immune system of the gastrointestinal tract, Peyer's plaques perform two important functions: the priming of "virgin" T- and B-lymphocytes and the direction of differentiation of B-lymphocytes towards the synthesis of IdA. The first function is carried out with the help of a unique morphological structure characteristic only of Peyer's plaques - the follicular-associated epithelium, the main feature of which are the so-called M-cells [12, 13]. These cells have short cytoplasmic processes and form, as it were, an intraepithelial pocket, in which, in addition to the M-cell itself, there are macrophages, dendritic cells, T- and B-lymphocytes. The main role of Mclets is the capture and transport of AG inside the peyre plaques. AG is captured by them by endocytosis or phagocytosis, transported through the entire M-cell with the help of an actin network in vesicles and released into a pocket by exocytosis. The latter is the main site where the presentation of AH by macrophages, dendritic cells and B lymphocytes to T cells takes place. Currently, it has been established that the transport of both soluble and corpuscular AH by M cells is the most important factor in the induction of an immune response by lymphoid cells of the gastrointestinal tract. Epithelial cells as an effector zone of the immune system of the LCG consist of two closely related components - intraepithelial lymphocytes (VEL) and epithelial cells themselves - enterocytes, which, as it was recently established, are not immunologically inert components. It turned out that between the epithelial cells, closer to the basement membrane, there is a huge amount of VEL: for every meter of the mucous membrane there are about 1.6 • 106 such cells. 80-90% of VEL are mainly CD+ cells, among them 4 subpopulations can be distinguished: CD4-C8+, CD4+CD8-, CD4+CD8+, CD4-C8- [10]. VEL are characterized by two very important features [5] that significantly distinguish them from other components of the gastrointestinal immune system: - the presence among CDZ+ T-lymphocytes of an increased number of cells carrying the CD8+ receptor (up to 75%), while in peripheral blood the number of these cells does not exceed 35%; - the presence among CDZ+ T-lymphocytes of an increased number of cells carrying the y/ 5-antigen-recognizing receptor (up to 40%), in other lymphoid organs the number of such cells is no more than 10 %. A significant part of such T-lymphocytes has the CD4-C8-phenotype, the remaining part contains the CD8+ marker.

Summing up the analysis of the cellular composition of the intestinal lymphoid tissue, I would like to note two important features. The first is that the lymphoid formations associated with the intestine

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contain more T cells than all other lymphoid structures of the body combined. It was initially assumed that the cause of the excess of T cells in the intestine are food and microbial AG. Sterile mice treated with autoclaved food have undeveloped lymphoid tissue in the intestine with an almost complete absence of α/β-T cells, although γ/δ-T cells were in normal numbers in the epithelium. Hence, it is concluded that the main stimulus for the development of the bulk of intestinal lymphoid tissue is not food, but microbial AG, with the exception of the epithelium, where food AG is important for the formation and development of T cells [7]. However, this does not mean that food AG is not recognized by the T cells of Peyer's plaques. Currently, it has been established that the recognition of food AG occurs and this leads to the so - called oral tolerance

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