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Structural and Functional Features of the Immune System of the Small Intestine (Literature Review)

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Summary

The article is devoted to the review of foreign literature on the structure and functioning of Peyer's plaques. Located in the intestinal wall, the lymphoid system associated with the mucosa ensures the development of an immune response in response to the penetration of pathogenic agents and provides immunological tolerance towards food components and commensal bacteria.

Relevance. In the immune system of humans and all mammals, 3 main groups of organs can be distinguished: - central organs of immunity (thymus and bone marrow); - peripheral organs of immunity not associated with the gastrointestinal tract (spleen and numerous lymph nodes); - lymphoid tissue and lymphoid organs associated with the gastrointestinal tract (GIT). As you know, the main role of the immune system is to maintain the constancy of the internal environment of the body by eliminating foreign agents of an antigenic nature. The immune system of the gastrointestinal tract is no exception in this regard, and its main task is to prevent the penetration of microorganisms and allergens into the intestinal mucosa. At the same time, the immune system of the gastrointestinal tract is characterized by a number of features that somewhat distinguish it from other peripheral organs of immunity (1). The central organs of the immune system in ontogenesis are formed from the intestinal tissue, for example, the thymus - from the 3rd and 4th pharyngeal pockets. However, due to the unique ability of immunocytes to migrate and recirculate, all three main groups of the immune system function as a whole, and the lymphoid tissue and lymphoid organs of the gastrointestinal tract are closely functionally related to other components of this system. Another feature of the immune system of the gastrointestinal tract is that it is in closest contact with the huge flow of microbial and allergenic material coming from the intestinal lumen, and is practically the first barrier to this flow (2).

However, there are various environmental factors that directly influence the formation of the immune structure of the small intestine. For example, the monotony and stereotypical nature of lesions of internal organs in people with chronic alcohol intoxication makes it possible to identify a number of pathological signs that reflect chronic alcoholism, which makes it necessary to distinguish between the pathology of internal organs, which forms the main and immediate

causes of death, and pathology, reflecting toxicosis (3). And so on, some harmful environmental factors threaten the formation of lymphoid tissue of the immune system.

In addition, various synthetic drugs affect the formation and restoration of the internal environment of the intestinal system (4). Other antibiotics used or administered orally act by specific mechanisms. Essentially, antibiotics are distinguished, and there are four main mechanisms: inhibition of bacterial cell wall synthesis, interaction with cell membranes, interference with protein synthesis, and inhibition of nucleic acid replication and transcription. Antibiotics can affect pathogenic bacteria. Accordingly, antibiotics can also affect normal bacteria that colonize the human body. The number, structure, and function of the microbiota may change in response to antibiotic treatment. Significant changes in human gut microbiota may be associated with repeated antibiotic use (5)

The aim of the study is to analyze the literature data on the structure and functions of Peyer's patches in the formation of the immune system of the small intestine.

Material and methods

We used information sources on the development of ISS at an early age, as well as materials related to the structure and functioning of Peyer's patches.

Conventionally, in the immune system of the gastrointestinal tract, inductive and effector zones can be distinguished. The first consists of Peyer's patches, appendix, and regional lymph nodes; the second consists of its own plate (Lamina propria) and epithelial cells of the intestinal mucosa. As their names suggest, recognition, antigen presentation, 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 (6).

The presence of morphologically separable tissue structures in the human small intestine was described as early as 1645 by the Italian surgeon Mark Severino, but they received their final name in 1667 by the Swedish anatomist Konrad Peyer 32 years later. In humans, they reach sizes up to several centimeters (1). The number and size of Peyer's patches change throughout life. The formation of Peyer's plaques in humans begins already at 14-16 weeks of fetal development - at this time, separate accumulations of T- and B-lymphocytes appear, and by 19 weeks dendritic cells migrate to this area. Peyer's patches become macroscopically visible only by the 24th week, but their lymphoid follicles still do not contain germinal centers. Their development begins after birth, when there is an increase in antigenic load as a result of food intake and the appearance of microbiota in the intestinal lumen (2). By the 30th week of pregnancy, the number of Peyer's patches in the small intestine increases to about 60, and after birth their number increases continuously by about 4 times by the age of 15–25 years (7). Morphological features and the sequence of processes of formation of Peyer's patches at the stage of intrauterine development have been studied in detail using the example of rat embryos. During this period, lymphocytes and blast cells are located diffusely, nodules are not detected. Plasmacides are not detected, macrophages, both light-optically and electron-microscopically, are detected in isolated cases. Mitotically dividing cells are found among clusters of blast and stromal cells. It should be assumed that the number of cells in the lymph nodes increases from time to time due to the division of diffusely located cells, as well as their migration from the circulating blood. Peyer's patches have now been proven to play an extremely important role in the immune system of the gastrointestinal tract. They, like any lymphoid formations, 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. But they are characterized by a unique morphological structure - follicular-associated epithelium, the main feature of which is the so-called M-cell. This cell has short cytoplasmic processes and forms, 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 M cells is to capture and transport antigen within Peyer's patches. The antigen is taken up by them by endocytosis or phagocytosis, transported across the M cell by the actin network in the vesicles, and released into the pocket by exocytosis. The latter is the main site where the antigen is presented by macrophages, dendritic cells and B-lymphocytes to T-lymphocytes. It has now been established that the transport of both soluble and particulate antigens by M cells is the most important factor in the induction of an immune response by lymphoid cells of the gastrointestinal tract. B-lymphocyte precursors, having received a signal from antigen-presenting cells, migrate to the B-zone of Peyer's patches, where they actively proliferate.

Morphologically mature Peyer's patches are clustered lymphoid follicles, each covered by a specialized follicle-associated epithelium. The lymphoid follicles of Peyer's patches are primary or secondary if there is a germinal center and consist mainly of B-lymphocytes and follicular dendritic cells. The interfollicular zone mainly includes T-lymphocytes, as well as macrophages and dendritic cells (4). A feature of Peyer's patches is the absence of afferent lymphoid ducts. Migration of immune cells to Peyer's patches is carried out through venules with a high content of endothelium, located in the interfollicular region (5). The general principles of organization of Peyer's patches correspond to the characteristics of the organized lymphoid tissue of the mucous membranes. The regulation of the functioning of Peyer's patches, which are sensors of the intestinal immune system, is carried out not only due to irritants coming from the intestinal lumen, but also due to various neuropeptides and hormones. They influence the differentiation of lymphocytes (6) and the formation and secretion of immunoglobulins (7). An important structural feature of Peyer's patches is the follicle-associated epithelium, which is a tissue barrier between the underlying lymphoid follicles and the contents of the intestinal lumen. The cellular composition of the follicle-associated epithelium differs from the villous epithelium of the small intestine: the bulk consists of enterocytes, goblet cells and specialized M-cells, while fewer digestive enzymes are expressed on the surface of enterocytes, and the mucin layer on the surface of the follicle-associated epithelium is thinner, even compared to interfollicular villi (8). These factors increase the likelihood of interaction with pathogenic structures that enter the body with food. The function of the follicle-associated epithelium is to capture and transport antigenic structures from the intestinal lumen to the immune cells located below. This process can be carried out with the help of M-cells, as well as with the help of cells of the immune system located under the follicle-associated epithelium.

The immunocompetent cells of the lymphoid nodules of the gastrointestinal tract, unlike similar other immune organs that are not related to the gastrointestinal tract, are distinguished by the highest, ten times greater than in other organs, ability to migrate. The antigen from the intestinal lumen is transported through M-cells to the region of the Peyer's patch dome. There, with the help of a macrophage, T- and B-lymphocytes are presented. (9,10) Activated, they are delivered through the lymphatic pathways to the mesenteric lymph nodes, the spleen. Subsequently, T- and B-lymphocytes enter the lamina propria of the mucous membranes of the gastrointestinal tract, respiratory and genitourinary systems, lacrimal, salivary, and mammary glands. T-lymphocytes are predominantly located between epithelial cells, B-lymphocytes are differentiated mainly (80%) by JgA-secreting plasma cells (12,13,15). Based on this, the grouped lymph nodes should be considered as the main activator of the immune properties of both the gastrointestinal tract and the lungs, urinary tract. Stimulation of the immune system of the small intestine by normal microflora leads to an increase in the level of sJgA in the secret of the bronchopulmonary tract, cervix, elimination of bacterial vaginosis, remission of bronchopulmonary diseases (17,18).

Peyer's patches of the small intestine are an important (but not the only) source of IdA-synthesizing plasma cells for almost all mucous membranes and glandular organs. This led to the

isolation of a special, relatively autonomous organ of immunity - mucosa-associated lymphoid tissue (MALT) (19,20). This leads to one fundamentally important conclusion: stimulation of the immunocompetent cells of Peyer's patches can lead to the activation of the immune system not only of the gastrointestinal tract, but also of the lungs, urinary tract, etc. If mice are injected intragastrically with the immunostimulant glucosaminylmuramyl dipeptide (licopid), a synthetic analogue of the cell wall component of all bacteria, then in L. rga both the respiratory tract and the small intestine there is a significant increase in the number of IgA-synthesizing cells. Such mice become resistant to oral infection with a virulent culture of S. dublin and to intranasal infection with a lethal dose of influenza virus. Stimulation of the immune system of the human small intestine leads to: - an increase in secretory IgA in the secretions of the bronchopulmonary tract and cervix; - the disappearance of bacterial vaginosis; - to the disappearance of condylomas of the cervix; - to a significant improvement in the clinical condition and prolongation of remission in patients with chronic nonspecific lung diseases.

Conclusion

Thus, grouped lymphoid nodules are an important tool for the dialogue of the macroorganism with antigens of microorganisms and food components. Developing and activating under their influence, they provide an optimal relationship between the central and peripheral organs of the immune system, a barrier function on the way to the introduction of foreign antigens by activating its humoral and cellular links, and the development of tolerance.

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