

Structural and Functional Features of Peyer's Plates in the Formation of the Immune System of the Small Intestinal (Literature Review)

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Resume: The article is devoted to a review of foreign literature on the structure and functioning of Peyer's patches. The lymphoid system located in the intestinal wall, associated with the mucous membrane, 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.

Key words: immune system, small intestine, Peyer's patches

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 that are 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 respect 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 intestinal tissue, for example, the thymus - from the 3rd and 4th pharyngeal pockets. However, due to the unique ability of immunocytes to migrate and recycle, 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 connected with other components of this system. Another feature of the gastrointestinal immune system is that it is in the closest contact with a huge flow of microbial and allergenic material coming from the intestinal lumen, and it is practically the first barrier to this flow (2).

However, there are various environmental factors that directly affect 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 allows us to identify a number of pathomorphological signs reflecting chronic alcoholism, which has the need to distinguish the pathology of internal organs forming the main and immediate causes of death, and pathology reflecting toxic (3). And so on, some harmful environmental factors endanger 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, used or administered antibiotics act by peculiar mechanisms. Essentially, antibiotics are distinguished, and there are four main mechanisms: inhibition of bacterial cell wall synthesis, interaction with cell membranes, interference in protein synthesis and inhibition of nucleic acid replication and transcription. Antibiotics can act on pathogenic bacteria. Accordingly, antibiotics can also affect normal bacteria that colonize the human body. The number, structure, and functions of the microbiota may change in response to antibiotic treatment. Significant changes in the human gut microbiota may be associated with repeated use of antibiotics (5)

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

Material and methods

We used information sources dedicated to the development of ISS at an early age, and materials related to the structure and functioning of patches Peyer.

Conditionally, the inductive and effector zones can be distinguished in the immune system of the gastrointestinal tract. The first one consists of Peyer's plaques, appendix and regional lymph nodes; the second one consists of its own lamina (Lamina propria) 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(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 a size of up to several centimeters (1). The number and size of Peyer's plaques vary throughout life. The formation of Peyer's plaques in humans begins already at 14-16 weeks of intrauterine development – at this time, separate clusters of T- and B-lymphocytes appear, and by week 19, dendritic cells migrate to this area. Peyer's plaques become macroscopically distinguishable only by the 24th week, but their lymphoid follicles still do not contain germinative centers. Their development is initiated after birth, when there is an increase in the antigenic load as a result of food intake and the appearance of microbiota in the intestinal lumen (2). By the 30th week of pregnancy in the small intestine, the number of Peyer's plaques grows to about 60 and after birth their number continuously increases by about 4 times by the age of 15-25 (7). Morphological features and sequence of processes of formation of Peyer's plaques at the stage of intrauterine development were studied in detail on the example of rat embryos. During this period, lymphocytes and blast cells are located diffusely, nodules are not detected. Plasmocides are not detected, macrophages, both light-optical and electron-microscopically, are found in isolated cases. Mitotic dividing cells are found among clusters of blast and stromal cells. It must be assumed that the number of cells in lymph nodes increases from term to term due to the division of diffusely located cells, as well as their migration from the circulating blood. Currently, it has been shown that Peyer's plaques 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 germ 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 - the 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 the capture and transport of antigen inside Peyer's plaques. The antigen is captured by them by endocytosis or phagocytosis, transported through the M-cell with the help of an actin network in 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 corpuscular antigens by M cells is the most important factor in the induction of an immune response by lymphoid cells of the gastrointestinal tract. The precursors of B-lymphocytes, having received a signal from antigen-presenting cells, migrate to the B-zone of Peyer's plaques, where they actively proliferate.

Morphologically mature Peyer's plaques are grouped lymphoid follicles, each of which is covered with a specialized follicle-associated epithelium. The lymphoid follicles of Peyer's plaques are primary or secondary, if there is a germinative 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 plaques is the absence of afferent lymphoid ducts. The migration of immune cells into Peyer's plaques is carried out through venules with high endothelium located in the interfollicular region (5). The general principles of the organization of Peyer's plaques correspond to the characteristics of the organized lymphoid tissue of the mucous membranes. Regulation of the functioning of Peyer's plaques, which are sensors of the intestinal immune system, is carried out not only due to stimuli coming from the lumen of the intestine, but also due to various neuropeptides and hormones. They affect the differentiation of lymphocytes (6) and the formation and secretion of immunoglobulins (7). An important structural feature of Peyer's plaques is the follicle-associated epithelium, which is a tissue barrier between the lymphoid follicles located below 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 immune system cells located under the follicle-associated epithelium.

Immunocompetent cells of the lymphoid nodules of the gastrointestinal tract, unlike similar other immune organs not related to the gastrointestinal tract, are distinguished by the highest, ten times greater than in other organs, the ability to migrate. The antigen from the intestinal lumen is transported through M-cells to the area of the Peyer's plaque 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 their own plate of the mucous membranes of the gastrointestinal tract, respiratory and genitourinary systems, lacrimal, salivary, mammary glands. T-lymphocytes are predominantly located between epithelial cells, B-lymphocytes are differentiated mainly (80%) by JgA-secreting plasmocytes(12,13,15). On this basis, grouped lymph nodes should be considered as the main activator of the immune properties of both the gastrointestinal tract and the lung, urogenital tracts. Stimulation of the immune system of the small intestine by normal microflora leads to an increase in the level of sJgA in the secretions of the bronchopulmonary tract, cervix, elimination of bacterial vaginosis, remission of bronchopulmonary diseases(17,18).

Peyer's plaques of the small intestine are an important (but not the only) source of plasmacytes synthesizing IgA for almost all mucous membranes and glandular organs. This gave rise to the isolation of a special, relatively autonomous organ of immunity - lymphoid tissue associated with mucous membranes (mucosa-associated lymphoid tissue - MALT) (19,20). This leads to one fundamentally important conclusion: stimulation of immunocompetent cells of Peyer's plaques can lead to activation of the immune system not only of the gastrointestinal tract, but also of the pulmonary, urogenital tracts, etc. If mice are intragastrically injected with the immunostimulator glucosaminylmuramyl dipeptide (lycospide), a synthetic analogue of the cell wall component of all bacteria, then a significant increase in the number of IgA —synthesizing cells occurs in L. rga of both the respiratory tract and the small intestine. Such mice become resistant to oral infection with the 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: - to the disappearance of bacterial vaginosis; - to the disappearance of cervical condylomas: - 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 the antigens of microorganisms and food components. Developing and activating under their influence, they provide optimal interconnection of the central and peripheral organs of the immune system, barrier function on the way of introduction of foreign antigens by activating its humoral and cellular links, the development of tolerance.

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