

PRACA POGLĄDOWA
REVIEW ARTICLE

COMPARATIVE HISTOLOGICAL STRUCTURE OF THE GASTROINTESTINAL MUCOSA IN HUMAN AND WHITE RAT: A BIBLIOGRAPHIC ANALYSIS

PORÓWNANIE HISTOLOGICZNEJ STRUKTURY BŁONY ŚLIZOWEJ PRZEWODU POKARMOWEGO CZŁOWIEKA I BIAŁEGO SZCZURA: ANALIZA BIBLIOGRAFICZNA

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ABSTRACT

Introduction: According to numerous domestic and foreign researchers, morphofunctional structure of the digestive system of humans and rats have much in common, therefore, rats are used as the laboratory animals during the experiments.

The aim of the paper was the comparative study of the histological structure of the gastrointestinal mucosa in human and white rat through the bibliographic analysis of the publications.

Materials and methods: The material for the investigation was current publications on the study of the histological structure of the intestine mucosa in human and white rat by analyzing, synthesizing and generalizing the resulting data.

Review and discussion: Histologically, the gastrointestinal mucosa in white rat is similar to the human one. The gastrointestinal mucosa in white rats (with the exception of the generic difference in the structure of the stomach and the caecum), in its histological structure, is quite similar to the human one, to be studied in the experimental simulation of the specific lesions of the digestive system.

KEY WORDS: digestive system, mucosa, white rat, comparative histology

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INTRODUCTION

The paper has been written within the research scientific work, carried out at the Department of Human Anatomy of the Higher State Educational Establishment of Ukraine "Ukrainian Medical Stomatological Academy", entitled "Age-related aspects of the structural organization of the organs of the human immune system, glands of gastrointestinal and urogenital system in normal condition and pathology"; State registration number 0116U004192.

Currently, under the influence of the pathogenic ecological situation, the aggressive effect of food and various chemical agents on the gastrointestinal mucosa, there is a rapid growth of chronic diseases of the digestive system. Consequently, the novel trends in the investigation of the histological structure of the digestive tract of humans and mammals, and white rats, in particular, have emerged in recent years, since outbred white rats are the main model for reproducing human pathologies in experimental conditions and preclinical testing of the new drugs [1, 2, 3].

THE AIM

The aim of the paper was the comparative study of the histological structure of the gastrointestinal mucosa in

human and white rat through the bibliographic analysis of the publications.

MATERIALS AND METHODS

The material for the investigation was current publications on the study of the histological structure of the intestine mucosa in human and white rat by analyzing, synthesizing and generalizing the resulting data.

REVIEW AND DISCUSSION

Generally, the mucous membranes have the common structure. Their base is represented by the layer of compacted fibrous connective tissue, which is known as lamina propria. On the side of the cavity the latter is covered with a layer of epithelium forming a barrier between the content of the lamina propria and the underlying connective tissue, which is the interstitial compartment of the internal environment of the body. The important detail is the presence of a basal membrane between the epithelium and the connective tissue, which serves as an elastic support for the epithelium and a barrier for filtration and diffusion of

substances [4]. In addition, the muscle plate belongs to mucosa, which occupies the boundary position between it and the submucous layer of loose fibrous connective tissue. The term "mucosa" is justified by the fact that throughout the digestive tract it is covered with a thin layer of thick viscous liquid, or mucus, which is the product of the secretion of the intramural glands and individual goblet cells that are the derivatives of the covering epithelium. Mucus, being a complex composition of glycosaminoglycans with proteins, performs mainly protective function for the mucosa. At the same, along with such ubiquitous purely mucous glandular formations, in gastrointestinal mucosa there are also intramural glands with more complex cytophysiological properties of secretory granulocytes, which, by the chemical composition of their secretion, determine the physiological properties of its respective segment. However, separate islets of lymphoid tissue known as lymphoid nodules are somehow related to the epithelial formations (covering epithelium and glands) of gastrointestinal mucosa. The publications report that, generally, the structure of gastrointestinal mucosa in human and rat is almost the same, though with some particular differences [5, 6, 7].

First of all, this difference is related to stomach, because rat stomach is two-cavity one. Due to the fact that its mucosa is separated from the muscle coat by a well-marked submucous layer, it, when emptying the stomach, forms numerous folds. The stomach filling leads to smoothing out the majority of them; only the more constant ones remain, two or three of which are the most typical. The transition of such folds of the esophagus into the pylorus can be observed. These folds often restrict a relatively deep longitudinal groove, the so-called "gastric path", which in the state of contraction of the stomach serves as a direct channel for conducting water and liquid solutions from the esophagus to pylorus and duodenum. At the border with the latter, gastric mucosa forms an annular fold, transforming the cavity of the pylorus into an oval hole. The presence of this fold is due to the tone of the pyloric sphincter, with the reduction of which the complete closure of the annular fold occurs, which leads to dissociation of the stomach and duodenum.

According to the publications [8, 9, 10], the thickness of the gastric mucosa varies within 2-3 mm, which depends on its functional state. Its connective tissue lamina propria is covered with a simple high (columnar) secretory epithelium. Therefore, the entire epithelial cover of the gastrointestinal mucosa is naturally regarded as a continuous glandular field producing a mucous secretion, a thin layer of which covers its entire surface. This layer of mucus forms a protective barrier to mucosa against damaging by hydrochloric acid and pepsin.

The analysis of this surface, using a binocular loupe, has shown that its entire area is dotted with an infinite number of small depressions, dimensions of which do not exceed 2 mm. These are the so-called gastric pits; on their bottom there are 2 or 3 holes, which are the orifices of the gastric glands. Noteworthy, the gastric pits along the periphery are bordered with thin, cylindrical folds, restricting

small, polygonal gastric fields. Due to the fact that venous microvessels are laid within their connective tissue base (under the epithelium), these gastric fields become more distinct when filled with blood.

There are innumerable simple branched tubular glands in the thickness of the gastric mucosa, which with their ducts enter into the gastric pit. The total secretion, which is produced by these glands, is called gastric juice, characterized by high acidity, due to the presence of hydrochloric acid in it. The increased acidity of this medium is detrimental to microflora. Despite this, some pathogenic microorganisms can exist in this aggressive environment, for example, *Helikobacter pylori* [11].

Importantly, the gastric glands, having a fundamentally identical structure, still differ among themselves in some cytophysiological properties of secretory glandulocytes depending on their location in the stomach. By this feature they are divided into three groups: cardial, fundal and pyloric. Cardial glands are located in mucosa in the circumference of the esophagus coming into the stomach, being actually a complete similarity of the esophageal glands, which differ from all other gastric glands by small sizes and simplicity of structure. Their acini consist of mucous cells (mucocytes), among which some parietal cells are located.

The most numerous are the fundal glands or, more correctly, the proper gastric glands, since they are distributed in its mucosa throughout the area from the cardial to the pyloric part. These glands produce almost all enzymes and hydrochloric acid, as well as some mucus. With their acini they reach the muscle plate of mucosa; they are the so-called fundal segments of the glands. Their middle segments are called cervical parts, and the short excretory duct that flows into the gastric pit is known as the isthmus. This division of each gland into three segments, being conditional, serves to determine secretory cells different by the cytophysiological properties, which are represented mainly by three types: mucous (mucocytes), zymogenic or major, and parietal. At the same time, the first of them are located mainly in the wall of the cervical part of the gland, and in the isthmus they convert into the integumentary epitheliocytes of the gastric pit, which, nevertheless, preserve the mucinogenic properties. The location of the zymogenic (main) cells is the fundal segments of the gastric glands; these cells are called main because they produce proenzyme pepsinogen, which in the acidic medium turns into an active form, pepsin is the main component of gastric juice. Acidic medium in the stomach is created, as is known, due to the production of hydrochloric acid by special cells, namely, parietal exocrine cells, which are located in all sections of the gastric glands, occupying a parietal position, outside of the mucous and main cells. Additionally, in the wall of the gastric glands there are more rare cellular elements that refer to the diffuse endocrine system. The publications report, that some of them serve as the receptor cells, reacting to the content of the stomach, and others - to its functional state (gastric dilatibility) and the chemical composition of the microenvironment. The content of the secretory granules of these endocrinocytes

is released into the connective tissue of lamina propria mucosa and then enters into blood microvessels [4, 12, 13].

The deepest layer of gastric mucosa bordering the submucosal layer is the muscle plate consisting of bundles of smooth muscle cells located along all directions in the plane of mucosa. Throughout the length individual bundles, which, permeating the thickness of mucosa, pass between the glands, ended in the basal membrane of their excretory ducts and integumentary epithelium. Due to the contractile activity of these smooth muscle structures, adaptive dynamic plasticity (change in thickness and shape) of mucosa itself, as well as an increase in secretion of glands secreted from the excretory ducts. Consequently, the gastric mucosa has its own autonomic contractile system. At the same time, the stomach as a whole has a common muscular membrane, which is separated from mucosa by a loose submucosal layer. Regulation of secretory and contractile function of the stomach is carried out through the intramural section of the autonomic (vegetative) nervous system, represented mainly by submucosal and muscle plexuses.

Generally, the contractile activity of multidirectional bundles of smooth muscle fibers in the gastric wall gives it the properties of a “mixer” in which a uniform mixing of food with gastric juice occurs. Its acid medium is an indispensable condition for the processes of primary enzymatic digestion (hydrolysis) of proteins and milk caseation. In this case, the products of this enzymatic process become soluble in water, and the resulting liquid mixture is called gastric chyme (pulp). The duration of the digestive process in human stomach takes about 4 hours, after which the pyloric flap opens and the gastric chyme is evacuated to the next section of the digestive tract, which is the duodenum.

It is known, that the first level of mucosa protection is the morphophysiological barrier, which is represented by the integumentary epithelium and its derivatives, namely, glandular structures. If the barrier is ineffective, the factors of the inherent immunity are included in the protection process, followed up (in the event of its insufficiency), by the adaptive reactions of the immune system, so-called immune system of gastrointestinal tract mucosa, which is mainly represented by associations of lymphoid tissue with epithelial structures, represented mainly by single and group (Peyer’s plaques) lymphoepithelial nodules. But the latter occur only in mucosa of small and large intestine, as well as in the appendix, whereas they are completely absent in the stomach, as reported in the publications [12, 14]. In this case, gastric mucosa in this regard should not be included in the concept of the immune system of the digestive tract. Apparently, it has other methods of protection due to the high level of acidity of the gastric juice, as well as the mucous secretion of the glands and the integument epithelium. Incidentally, the publications on clinical immunology identifies the term “mucosa immune system” as mucosal immunity [8, 15], which in our opinion may be acceptable only for the gastric mucosa. However, it should be taken into account that in this sense this notion is not entirely sufficient, since in the mechanisms of protecting the gastric mucosa, along with the acid-mucosal factor, the

effector elements of the immune system are engaged, to which predominantly T-lymphocytes and secretory Class A immunoglobulin, which arise in response to immunization from the inductive section of the immune system of the digestive tract mucosa, which is represented by single and group lymphatic (lymphoid) nodules of small and large intestines, and appendix. This is one of the examples of “mucosa immune solidarity” phenomenon. It appears that gastric mucosa in some cases, shall possess these manifestations of immune reactions in the form of diffuse aggregations of the immunocompetent cells. This site is the connective tissue of gastric mucosa lamina propria.

Thus, the gastric mucosa, although it does not have such specialized lymphoepithelial formations as lymphoid nodules (single and group), but being associated with the general system of digestive tract immune reactions, should be included into the plan of our investigations.

According to the literature, stomach of white rats is not unilocular, in contrast to humans; it is separated into esophagus section or proventriculus and other, the larger section, which is actually a proper stomach. These two sections are partially divided by a well-defined ridge. It is believed that proventriculus is intended primarily for bacterial digestion, while the main section is responsible for enzymatic processing of food. Generally, the mucous membrane of proventriculus is of the same structure, i.e. the covering epithelium, lamina propria and the muscle plate is distinguished in it. The epithelial cover is of particular interest, since it, according to the literature, refers to a multilayered squamous keratinizing epithelium, consisting of 3 to 6 layers [5, 12, 16]. This indicate that in rats, the multilayer squamous non-keratinizing epithelium of esophagus mucosa acquires the properties of keratinization in proventriculus, which may be due to increased mechanical effects on mucosa in this part of the digestive tract. But it is not known which process causes these effects. After all, if we admit that the bacterial digestion is carried out in the proventriculus, then it hardly requires an increased load caused by its muscle membrane. The second feature of the proventriculus mucosa is the absence of any glandular structures in it, although a lot of them are found in the esophagus gets. In this regard, this part of rat digestive tract is called non-glandular, which is absent in humans.

The boundary between the proventriculus and the main part of stomach is defined by transition of multilayer squamous keratinizing epithelium into high (columnar) simple epithelium, which is characterized (similar to the human one) by cytological features of mucous secretion. According to the publications, the superficial relief of the white rat’s mucous membrane of the main part of the stomach is similar to human one due to the numerous cluster-based stomach pits, entering into the gastric glands [10, 16]. Unfortunately, this information is only mentioned in the literature without cytologic analysis. However, this part of the stomach, in contrast to the proventriculus, is defined as the forestomach. The immunohistochemical analysis has shown that in normal mucous membrane of white rats forestomach has three types of mucins (MUC1, MUC,

5AC, MUC6) with specific zoning, similar to the human gastric mucosa. This gives the grounds to hypothesize that white rats' proventriculus could be the anatomical substrate in the experimental simulation of different pathological gastric states [13].

Mucous membrane of the human small intestine in its common structure possesses specific features and some morphological peculiarities in its different parts. The common anatomical sign is the presence of the longwise numerous transverse-circular folds, due to the loose submucosal interlayer and the tonus of smooth musculature. But their number and degree of pronouncedness gradually decreases towards the distal department of the iliac. In the duodenum the folding of the mucous membrane is somewhat different since from the medial wall of the descending part there is a permanent longitudinal fold, which is inferiorly becomes higher and ends with a large papilla. It opens with one common orifice of the biliferous duct and the pancreatic duct. Slightly higher from it there is the second papilla of the smaller size, on which the additional pancreatic duct is opened.

Mucous membrane of the small intestine in a straighten state is opaque and velvet due to the innumerable micro (1 mm) finger-shaped or foliate papillae, called the intestinal villi. They contribute to the enlargement of the absorbing surface of the covering epithelium of the small intestine. The longest microvilli are in the duodenum and jejunum, whereas they become 2/3 shorter in the distal segment of ileum. This is the reason of gradual decline of absorbing capacity of mucous membrane of the small intestine.

Between the villi, at their base, in a proportional quantity there are tubular invaginations of the epithelium which penetrate into a depth of the lamina propria. They are known as the intestinal crypts, being essentially the simple intestinal (Lieberkuhn's) glands. In the duodenum they perforate the depth of the mucous membrane and bifurcate in submucous layer, and are specified as the Brunner's glands.

The epithelium of the mucous membrane of the small intestine, covering the intestinal villi and lining the glandular crypts, is represented by mainly (approx. 90%) single layer of high (columnar) microvillious cells. The distinctive feature of these cells is that their apical plasmolemma forms numerous, densely grouped microvillous projections, which, microscopically, resemble brush limbus. Cytologically, the similar masses are the hallmark of adaptation of these cells to the massive transmembrane transfer, which is the basis for the absorbing function of mucous membrane of small intestine [4, 17]. Among these cells less numerous goblet cells (approx. 10%) are evenly distributed. At the same time endocrine cells are few in numbers. The special focus is on Lieberkuhn's crypts because their bottom (terminal) parts contain stem (cambial) cells, the mitotic activity of which the permanent renewal of all types of enterocytes occurs during the process of differentiation. Additionally, acidophilic exocrine cells (Paneth cells) are distinguished in the glandular crypts.

Generally, the digestion in the small intestine consists of two interrelated processes: the final nutrient digestion

(mainly proteins, polysaccharides and fats) and absorption of hydrolysis final products through intestinal epithelium: amino acids, saccharides and glycerids. Such processes start in the duodenum from the moment when the chymus from the stomach is exposed to bilis and pancreatin. The last one has alkaline reaction that is necessary for neutralization of chymus acidic medium. As the digestion in the duodenum is hold with the help of secretion of glands out of digestive tract, it was named as distant or cavitory digestion in contrast to mucosal one held on the covering epithelium. The optimal act of cavitory digestion needs certain time for chymus staying in the duodenum. Its form and stable condition fit better than other parts of small intestine.

Absorbing of hydrolysis final products without antigenic specificity is holding over the total length of small intestine through the limbic epithelium of intestinal villi of connective tissue membrane where the central lymph capillary is surrounded by blood vessels. The lymph capillaries of intestinal villi absorb the products of fat hydrolysis as chylomicrons, just as blood vessels get other substances. Such absorbing selectivity remains unclear.

Mucous membrane of small intestine has more developed local representation of immune system as in terms of lymph epithelial assembly called lymphoid nodules.

Usually they are in a form of single nodules or aggregations. The first ones are represented in the form of whitish projections with the dimensions of a millet grain, evenly distributed longwise the small intestine. Their aggregations, widely known as Peyer's plaques, are attributable to the iliac only. Usually they have oblong shape from 2 to 10 cm. Their amount (20-30) has inverse dependence on the size. Each mass is the aggregation of single lymphoid nodules that cause surface tuberosity. As a rule they are in the mucous membrane from the side of ileum opposite to the place of mesentery attachment. The rest of the surface is covered with single lymphoid nodules. It confirms that the concentration of lymphoid tissue on the approach to large intestine is increasing due to rising of gastrointestinal microflora.

Numerous publications confirm that the abovementioned description of human mucous membrane of small intestine is similar to white rats' one. The single disadvantage of these publications is in poor illustrative description [7, 15, 17, 18, 19].

In the place where the iliac enters into the large intestine there are two folds (superior and inferior), which form a kind of wing valve, preventing fecal entry into small intestine. Throughout the rest length the mucous membrane of the large intestine is smooth due to the absence of the intestinal villi. But in comparison with small intestine it is thicker due to deeper proliferations of the covering epithelium similar to crypts of small intestine. The covering epithelium of large intestine mucosa is represented as a layer of high (columnar or prismatic) cells, limbic epitheliocytes, which are the morphological proof of absorbing function of mucous membrane. But the amount of such cells is less per unit area, than in the small intestine; the greater part of the covering epithelium is occupied by the goblet cells, the amount of which is increasing towards

the rectum. Almost the same ratio of abovementioned cells has the epithelium of large intestine crypts. It should be noted, that in comparison with the similar masses of small intestine, according to the publications, the crypts of large intestine do not contain Paneth cell, but they are found in the child age [4, 15]. However, this conclusion is not decisive according to our previous studies [20].

To generalize the issue on cytophysiological properties of the covering epithelium of large intestine mucosa, it can be concluded that all surface, the area of which, increased by hundred times due to its individual proliferations into the subjacent lamina propria in the form of crypts, is represented by the continuous filed, secreting mucus. Its main chemical components are mucins, i.e., glycosaminoglycan compounds (mucopolysaccharides) with proteins, bifurcated chains of which are capable of binding water.

Moreover, the colon mucosa contains a large number of lymphatic nodules; however, no aggregations of the Peyer's plaques are found (in contrast to the ileum. The exception is vermiform appendage (appendix) mucosa, where the concentration of lymph nodes is significantly higher than in other parts of digestive tract [21, 22].

Human vermiform appendage is an integral part of the caecum, the length, form and position of which vary individually in a wide range [20, 23]. At the same time it is subjected to apparent changes with age that linked with involutive processes of other lymphoepithelial masses of immune system such as thymus and tonsils.

The publications report that the structure of the colon mucosa in white rats is similar to human one [16, 18, 20]. The exception is an issue of the rectum and appendix. The caecum in white rats is more prominent as compared to other parts of the gastrointestinal tract; moreover, it doesn't have anatomically developed appendix, in contrast to other rodents. However, the publications report that its mucosa contains the high concentration of lymphoid nodules. Consequently, we hypothesize that the functions of bacterial digestion and immunological surveillance on microflora were not subjected to the anatomical separation in this part of the rat colon during the process of phylogenesis.

CONCLUSIONS

Therefore, according to the publications, the white rats gastrointestinal mucosa (apart from generic difference in structure of stomach and caecum) is histologically similar to the human one to be an object of experimental modeling of pathological conditions of digestive system. In the course of bibliographic analysis we could prove, that these varietal masses have common structure of disease resistance, the immune system of gastrointestinal mucosa demands more detailed review.

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