Lecture

Morphology and physiology of salivary glands.

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Abstract: This article discusses the issues of classification and morphology, ultrastructural features of their cells, embryogenesis. The importance of saliva for the normal functioning of the oral cavity is described.

Keywords: salivary glands, oral fluid, saliva, salivation.

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1. Introduction

The oral cavity is constantly washed with saliva, which performs various functions that ensure the normal functioning of the oral organs: providing local immunity, maintaining the normal condition of the teeth (providing them with calcium and phosphates), moistening the oral cavity, participating in digestive processes, endocrine, excretory, regulation of water-salt homeostasis, etc. [1-3]. Understanding the structure and functions of the salivary glands is relevant for such specialized specialists as dentists [4, 5], otorhinolaryngologists, oncologists [6], maxillofacial surgeons [7], plastic surgeons [8], chemo- and radiotherapists, pathologists [9], etc. [10].

2. Embryogenesis of salivary glands and disorders of their development

The source of the development of salivary glands is the epithelium of the oral cavity. Connective tissue stroma develops from mesenchyma. The submandibular gland is laid at 6-7 weeks of intrauterine development. The parotid gland and sublingual are laid at 8 weeks. At birth, the glands already secrete saliva. Violation of the bookmark and subsequent development of the salivary glands leads to malformation – aplasia. With heterotopia, the gland lining shifts compared to the norm, while the topography of the gland is disturbed, which can complicate surgical interventions [11].

Among the possible pathologies in the duct system, agenesis and aplasia occur. Hypoplasia and atresia of the main ducts are very rare. On the contrary, intra-nodal (intranodal) heterotopias are quite common [12], tumors of the salivary glands occupy 3-5% of all tumors of the head and neck [13]. Extranodal heterotopia is rare, but it can involve the pituitary gland and the lower jaw, the lower part of the neck, and the thyroid gland. In 20% of people there are additional parotid glands, separated from the main gland, but adjacent to the excretory duct of the parotid gland (Stensen's duct).

3. Classification and general principles of the structure of the salivary glands

The salivary glands are divided into the glands of the vestibule of the mouth and the glands of the oral cavity proper. The glands of the oral cavity include 3 pairs of large salivary glands (parotid, submandibular and sublingual) [5]. Salivary glands located in the mucous membrane of various parts of the oral cavity (buccal, labial, tongue glands, palatine tonsils, larynx, pharynx) are called small salivary glands [14].

3.1 The large salivary glands

The large salivary glands are complex, branched alveolar (parotid) or alveolar-tubular (submandibular, sublingual) glands, have one principle of anatomical organization – a branched system of excretory ducts and secretory terminal sections (Fig. 1).

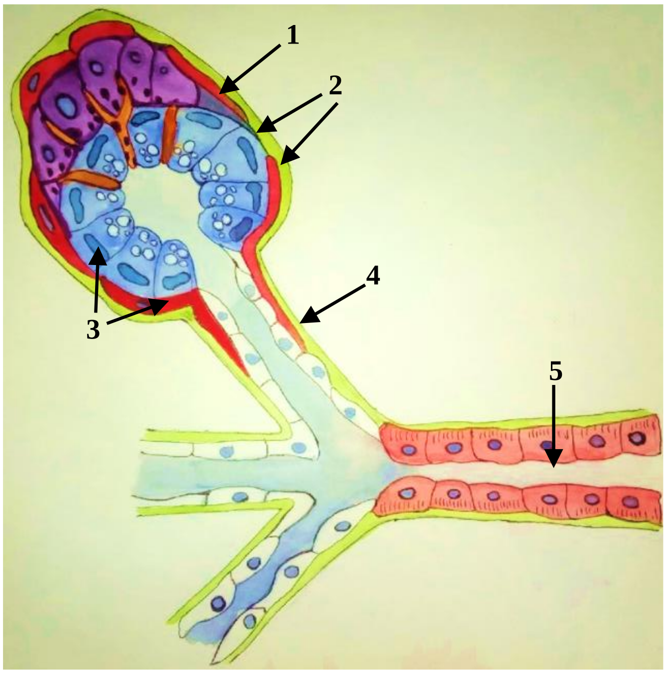

Figure 1. Diagram of the structure of the secretory department and ducts of the salivary gland. 1 – serous cells; 2 – mucous cells; 3 – myoepithelial cells; 4 – insertion duct; 5 – striated duct.

Inside the lobules, there are intra-lobular excretory ducts and numerous secretory terminal sections. All connective tissue structures form the stroma, and epithelial cells (ducts and secretory departments) form the parenchyma of the gland [15]. The secretory divisions of the salivary glands consist of secretory and myoepithelial cells, are divided into protein (serous), mucosal (mucosal) and mixed (protein-mucosal). The protein end sections have a rounded shape in the form of alveoli with a narrow lumen. They consist of serous cells shaped like a truncated pyramid. The cell nucleus is rounded, the cytoplasm contains a well—developed granular endoplasmic network that provides basophilia when sections are stained with hematoxylin and eosin (Fig.2), the Golgi complex, numerous mitochondria in the basal part of the cell and an abundance of apically located secretory granules rich in protein - ptyalin (amylase), lysozyme, lactoferrin [15].

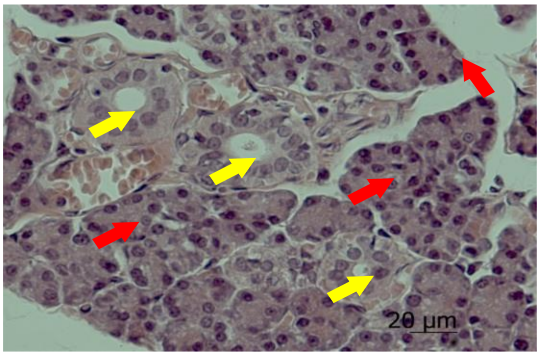

Figure 2. Protein secretory departments. Red arrows – secretory departments, yellow arrows – excretory ducts. Parotid salivary gland. Stained with hematoxylin and eosin. Magnification x 300.

The mucous end sections predominate in the sublingual salivary gland (Fig. 9). They are larger and lighter than the protein ones, have a tubular shape. Mucous cells resemble protein cells in shape, but their nuclei are located basally and are not round, but flattened, there are fewer mitochondria in the cytoplasm, a less developed granular endoplasmic network, but a significantly more significant Golgi apparatus, which indicates a greater proportion of the carbohydrate component in their secret. Most of the cytoplasm is filled with a mucous secretory product having a light cellular appearance [11, 16-18].

The mixed terminal sections consist of 2 types of glandular cells – protein and mucous, especially clearly visible in the submandibular salivary gland (Fig. 4, 8). Protein and mucous cells are located in the mixed secretory department alternately, directing the mixed secret into the duct.

Many authors point to serous half-moons, or Gianuzzi half-moons (Fig. 4), which are only a consequence of the preparation of the drug, that is, an artifact [11].

Each terminal section is surrounded by myoepithelial cells, which have a process shape, in their cytoplasm there are numerous contractile actin and myosin filaments, as well as intermediate filaments that belong to the cytokeratin family, which makes it possible to indicate the source of their development ectoderm, not mesenchyma. The contraction of these cells promotes the excretion of saliva from the terminal sections [19].

The excretory ducts transport and modify saliva before it enters the oral cavity. In the large salivary glands, insertion, striated, interlobular and common excretory ducts are represented [15]. The insertion ducts form the beginning of the duct system, they are thin tubes lined with a single layer of cubic cells (Fig.3). On sections stained with hematoxylin and eosin, they differ in basophilic coloration and small diameter (less than the diameter of the secretory department). The insertion ducts are very well developed and branched in the parotid salivary gland [11].

The insertion ducts merge with each other, forming striated excretory ducts (Fig. 3), lined with a single layer of prismatic or cubic cells, the basolateral membranes of which have a pronounced folding (striation) due to mitochondria located between numerous folds of the plasmolemma.

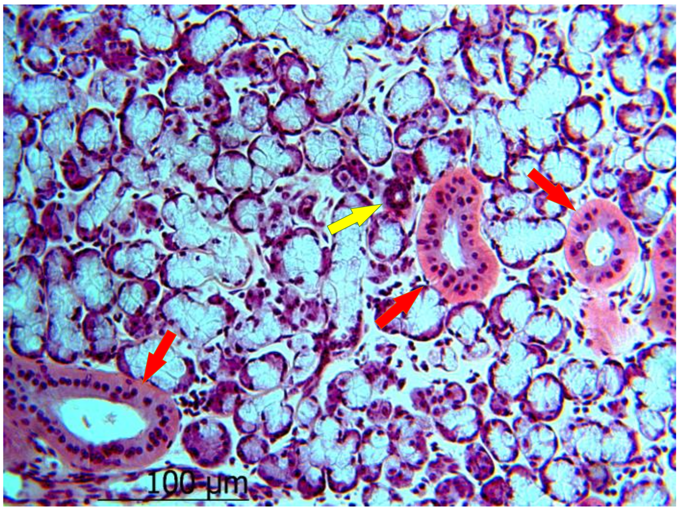

Figure 3. Striated ducts (red arrows) and insertion duct (yellow arrow). Stained with hematoxylin and eosin. Magnification x 200.

The striated excretory ducts connect to each other, forming intra-lobular ducts (Fig. 4) of a larger diameter, lined with a double-row or double-layer epithelium. The excretory ducts extending from the lobules combine to form interlobular excretory ducts, which are lined with a multilayer cubic epithelium Fig. 5).

The common (main) excretory duct of the gland approaches the mucous membrane of the oral cavity, opens on its surface, its mouth is lined with a multilayer flat epithelium.

The interlobular connective tissue forming the stroma of the glands contains fat cells, vessels, nerves and interlobular excretory ducts [20, 21]. The small salivary glands are located in almost all parts of the oral mucosa, except for the gums and the anterior part of the hard palate. They are predominantly mucous by the nature of the secretion, their ducts are not differentiated into inset and striated. Despite its small size, the importance of small salivary glands is due to their ubiquity in the oral mucosa and their abundance [22].

3.2 The small salivary glands

The small salivary glands also play an important role in the formation of protective functions and moistening of the mucous membrane due to the composition of the saliva secreted by them [23, 24]. They produce about 70% of saliva mucins and a significant amount of immunoglobulins (mainly secretory IgA), salivary acid phosphatase and lysozyme, preventing the colonization of microorganisms on the surface of teeth and the occurrence of infections. The structure and function of the large and small salivary glands are potentially affected by alcohol and drug use, as well as poor nutrition, aging and radiation therapy of the head and neck [25, 26].

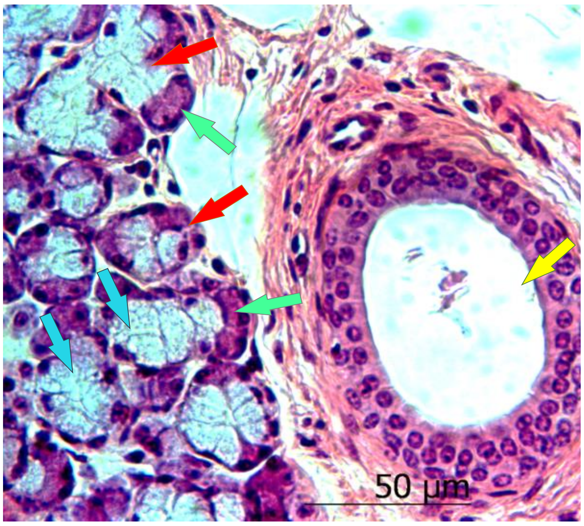

Figure 4. Interlobular excretory duct (yellow arrow); mixed secretory sections (red arrows), which consist of mucosal (mucous) cells (blue arrows) and serous cells forming serous Gianuzzi half-moons (green arrows). Stained with hematoxylin and eosin. Magnification x 300.

4. Saliva and oral fluid

The salivary glands produce saliva, which when it enters the oral cavity is called oral fluid [27]. It contains the secret of the large and small salivary glands, the contents of the dental grooves, bacteria, food particles, leukocytes, etc. Oral fluid has bacteriostatic properties, protects teeth by participating in the remineralization of enamel, forms a protective film of calcium-binding proteins, facilitates articulation of speech and the act of swallowing, moistening a lump of food. Due to a pH of 5.9-7.6, saliva has buffering properties that ensure the neutralization of acids. The components of the oral fluid are involved in the process of blood clotting and wound healing due to the presence of clotting factors and epidermis growth factor in it [28].

4.1 Salivation

Salivation of large salivary glands is carried out reflexively. Small salivary glands secrete constantly, moistening the mucous membrane of the oral cavity. Regulation of salivation is carried out by nerve centers located in the medulla oblongata, hypothalamus and cerebral cortex. The formation of a conditioned reflex mechanism occurs when visual, auditory, and olfactory receptors are irritated. In humans, conditioned reflex secretion of saliva can also begin with the memory of delicious food. When parasympathetic nerve fibers are stimulated, a large volume of watery saliva with a low protein content and high concentrations of electrolytes is secreted [29]. When sympathetic nerve fibers are stimulated, a small volume of viscous saliva with a high content of mucus is released [30].

The secretion of saliva in the glands takes place in two stages. At the initial stage, acinar cells form a primary isotonic secret – primary saliva. Then, the primary secretion is modified in the ducts of the glands, depending on its composition and physiological needs – secondary saliva. By the striated cells of the excretory ducts, excess hydrogen, chlorine and sodium ions from the gland duct are reabsorbed back into the blood using passive transport, which leads to a decrease in the acidic reaction of saliva. And potassium ions and HCO3- from blood serum and tissue fluid selectively enter saliva by active transport, increasing its alkaline reaction. Due to this mechanism of regulation, the pH of the saliva secreted may differ significantly from the always stable blood pH value of 7.4 [31].

Normally, a person releases up to 2 liters of saliva per day. Due to the strengthening of both salivary reflexes and spontaneous salivation, the amount of saliva can increase several times (hypersalivation). Hypersalivation is observed in people suffering from Parkinson's disease, epidemic encephalitis, cerebrovascular accident, stomatitis, toxicosis of pregnant women, helminthiasis, trigeminal neuralgia. At the same time, increased salivation (ptialism) may be such that the patient is unable to swallow saliva. A decrease in saliva secretion (i.e. hyposalivation) is accompanied by dryness of the oral mucosa — xerostomia, often complicated by caries, stomatitis, fungal infections. Hyposalivation (hyposialy, sialopenia) and asialia (i.e. extreme hyposalivation) are symptoms of both common diseases (septic conditions, pneumonia, diabetes, malignant anemia, typhoid and typhoid fever, etc.) and pathology of the salivary glands proper, their inflammation (sialodenitis), blockage of the excretory ducts (sialolithiasis). With age, the salivary glands may be subject to atrophic changes, which often leads to hyposalivation, and as a consequence, to xerostomia. [32].

During the SARS-COV-19 pandemic, salivary glands were found to be susceptible to coronavirus infection. Thus, several studies have shown that saliva and destroyed epithelial cells of the salivary glands may contain SARS-COV-2 [21, 33]. This is of great diagnostic importance, since the detection of coronovirus in the material obtained from the mucous membranes is possible only at the initial stages of the lesion, when there are no clinical symptoms, and the isolation of viruses into saliva can help with the verification of the virus strain at an early stage of clinical manifestations [5].

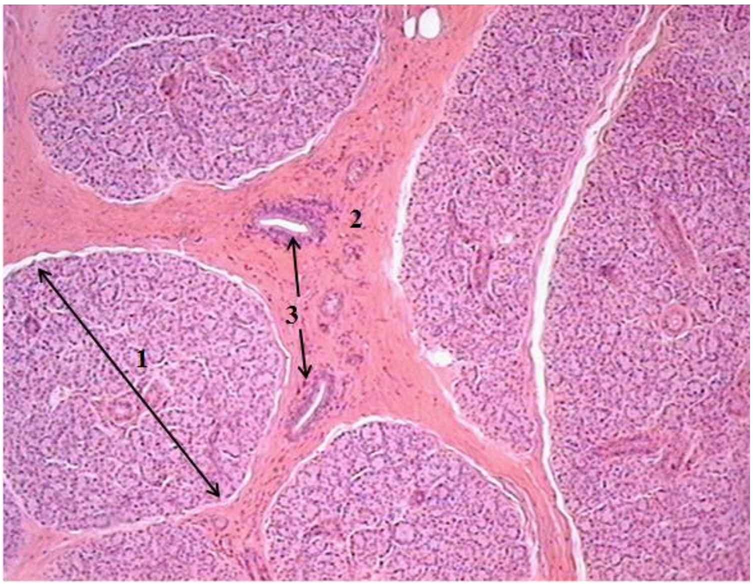

Figure 5. Parotid salivary gland, lobules (1), interlobular connective tissue (2), interlobular excretory ducts (3). Stained with hematoxylin and eosin. Magnification x 150.

4.2 The parotid gland

The parotid gland is the largest salivary gland, has a mass of 20-30 g, produces 30% of the total amount of saliva. The connective tissue capsule of the gland is well developed, numerous partitions depart from it, which divide the gland into lobes and lobules (Fig. 5). The parotid salivary gland produces a protein secret, therefore, basophilia is characteristic of secretory cells when stained with hematoxylin and eosin [25].

On electron microphotographs, numerous secretory granules are visible in the apical areas of serous cells, (Fig. 6, 7) filled with an electron-dense product. In saliva produced by the parotid gland, there is a high level of the enzyme saliva amylase (ptyalin) and secretory IgA. The main excretory duct (Stensen's duct, Stenon's duct) of the parotid salivary gland opens into the oral cavity near the second molar of the upper jaw.

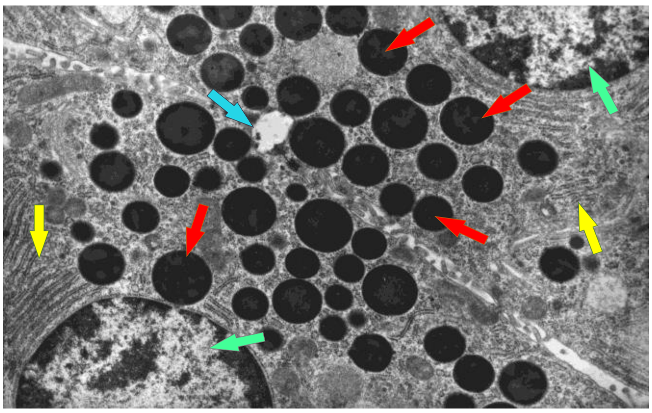

Figure 6. Ultrastructure of parotid salivary gland cells before meals: secretory granules (red arrows), granular endoplasmic network (yellow arrows), cell nuclei (green arrows) and the lumen of the secretory department (blue arrow). Magnification x 5300.

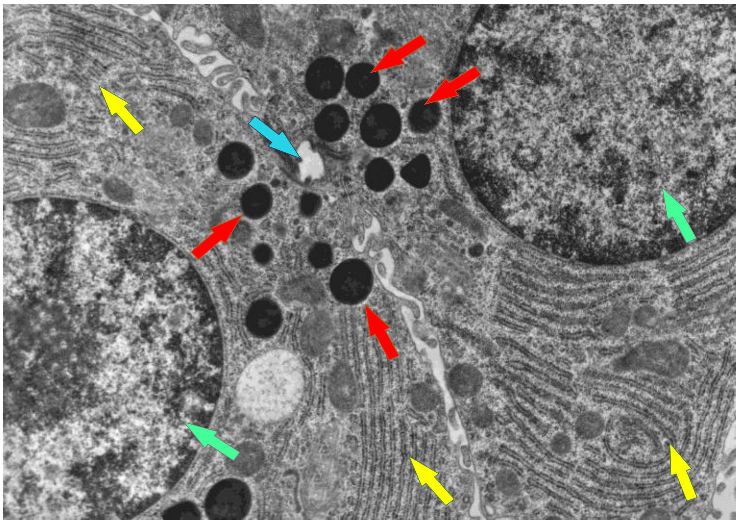

Figure 7. Ultrastructure of parotid salivary gland cells in the conditioned reflex phase of saliva secretion during meals: secretory granules (red arrows), granular endoplasmic network (yellow arrows), nuclei of neighboring cells (green arrows) and acinus lumen. (blue arrow) Magnification x5300.

4.3 The submandibular gland

The submandibular gland is much smaller than the parotid gland, has a mass of 12-15 g, but produces approximately 60% of the total volume of saliva. This gland is mixed with a predominance of the serous component (Fig. 8). The striated excretory ducts of the submandibular gland are significantly longer than the ducts of the parotid or sublingual glands; as a result, numerous cross-cut profiles of these excretory ducts are visible on histological sections, which is a characteristic feature of the submandibular gland. The main excretory duct is called Wharton's duct (Wharton's duct), it opens into the oral cavity under the tongue at the frenulum with a thickening – a sublingual caruncle [32].

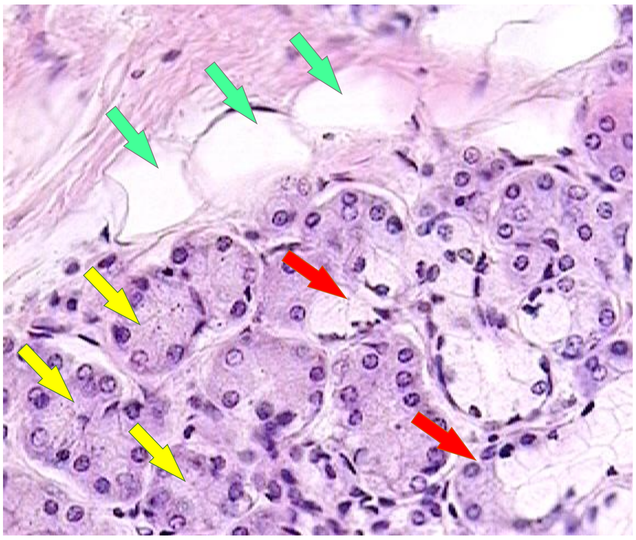

Figure 8. Submandibular salivary gland: mixed terminal divisions (red arrows), serous terminal divisions (yellow arrows) and fat cells (green arrows). Stained with hematoxylin and eosin. Magnification x 375.

4.4 The sublingual gland

The sublingual gland, the smallest in the considered group of salivary glands, almond-shaped, produces only about 5% of the total volume of saliva, in which the mucous component predominates. On a preparation stained with hematoxylin and eosin, the sublingual gland looks very light due to the abundance of mucous secretory departments (Fig. 9). The sublingual gland has a loose connective tissue capsule, and its system of excretory ducts does not form a common excretory duct. Several excretory ducts open in the area of the bottom of the oral cavity and along the course of the excretory duct of the submandibular gland [35].

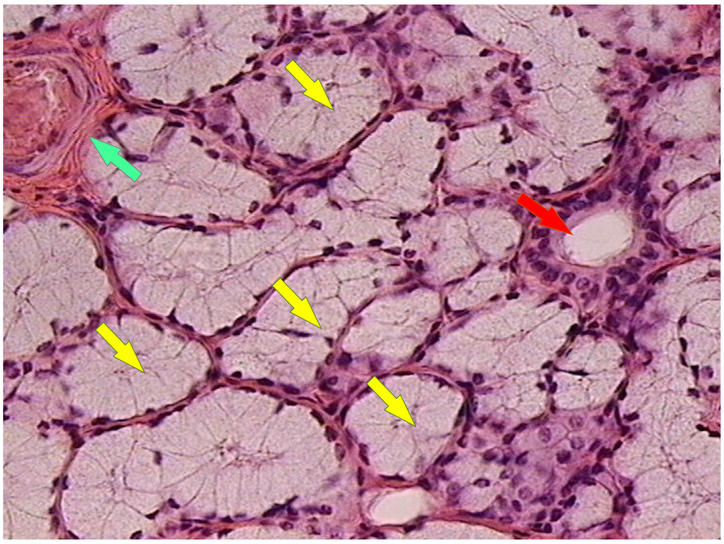

Figure 9. Sublingual salivary gland: mucous end sections (yellow arrows), intra-lobular excretory duct (red arrow) and artery (green arrow). Stained with hematoxylin and eosin. Magnification x 375.

Relatively recently, the tubal, or Eustachian glands, located in the submucosal base of the auditory tube, which a number of scientists refer to the salivary glands, have been described. These glands contain mixed (serous-mucous) secretory departments that play a physiological role in the lubrication of the nasopharynx and when swallowing. However, localization of these glands and saliva secretion is not carried out in the oral cavity, which means that it is impractical to refer them to salivary glands. [36, 37,38].

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