Clinical Management of Salivary Gland Disorders

Louis Mandel

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Dedication

The seeds for this book have been germinating within my mental field for many years. Its materialization was made possible only through the genes that I inherited from my Hungarian immigrant parents. Their nurturing, direction, work ethic, and sacrifices paved the way for me to achieve a professional education. Simultaneously, it facilitated my recognition of these indispensable qualities in the woman I courted and married, Mary Damiani. In turn, Mary and I endeavored to implant these values into our two children, Susan and Richard. The results have not been disappointing. They both have meaningful lives and successful careers. I have taken pride in their principles and accomplishments, and it is to Susan and Richard that I dedicate this book. It is one avenue made available to me, albeit insufficient, to express my love for them, something that I may not have always adequately demonstrated.

Although in truth the family always comes first, there are individuals whose interactions with me served as a continued inspiration and incentive for my writing, teaching and study, my students. Their thirst to learn galvanized my patient investigations. Standouts include, but are not limited to, Drs. David Alfi, Ashley Houle, Daria Vasilyeva, and Vicky Yau. In addition, I will be forever grateful for the opportunities afforded to me by my superior, Dr. Sidney Eisig, and for my friendships with Murray Slochover, Carl Nelson, Ian Hu, and George Minervini. They all contributed to making my life complete.

Preface

My interest in salivary gland disorders originated when I was a graduate student many years ago. Consequently, I have had ample opportunity to evaluate patients victimized by a wide variety of salivary gland diseases. Inevitably, I developed "smarts" or what is referred to as clinical expertise. In addition to my examinations of the more familiar salivary gland afflictions, my experiences have allowed me to become familiar with a group of salivary gland conditions that nowadays are seen infrequently. Surgical (acute) parotitis and HIV lymphoepithelial cysts represent examples of this cohort of salivary gland problems. Furthermore, the passage of time has allowed me to accumulate and evaluate a collection of false/positive patients. I have attempted to incorporate into this text the knowledge that I have acquired from my exposure to the full gamut of salivary gland disorders and to those entities (the false/positives) that mimic salivary gland pathology.

A huge step forward in my ability to evaluate salivary gland disorders occurred in 1988 with the establishment of the Columbia University Salivary Gland Center. The impetus for its establishment came from Dr. Irwin Mandel (no relation of mine, just a coincidence in names) who had a background in biochemistry and was interested in the biochemistry of saliva. I am a clinician and he thought that we would make a perfect team, we did. As you peruse this book, you will note that some chapters allude to salivary chemistry, a reflection of Dr. Irwin Mandel's influence upon me.

In addition, the continued value of sialography in the diagnosis of salivary gland disease has been recognized. Examples of its place in diagnosis have been sprinkled throughout the chapters. Sialography is a venerable diagnostic technique whose scope has gradually been impinged upon by other imaging (CT scan, MRI, etc.) approaches. Nevertheless, it has a significant place in the salivary gland diagnostic armamentarium. It is unrivaled in its ability to image normal/abnormal ductal patterns as they relate to glandular disorders. Mastering the technique will reward the clinician.

The reader should look upon this book's compendium of salivary gland disorders as only opening the door to the subject. The text should serve as a guide in attaining a diagnosis and in mastering pathophysiology. Digestion of this information should

be followed by a pivot to current scientific journals for recent updates. The derived information should then be filed away in the reader's intellectual memory bank. Clinical expertise will now develop and can be added to the investigator's diagnostic abilities.

New York, NY, USA Louis Mandel, DDS

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Chapter 1
Anatomical Considerations

Letty Moss-Salentijn

Abstract The general anatomy and histology of human major and minor salivary glands are described. The sublingual glands and all minor glands develop in the submucosa close to the sites of the oral mucosa where the openings of their excretory ducts are located. Particular attention is paid to the development of the submandibular and parotid glands. The final anatomical location and morphology of these glands, as well as the lengths of their excretory ducts, are influenced by the rapid facial growth and development, and the spatial restrictions imposed by the developing muscles, nerves, and organs that are present in this shared connective tissue space.

Introduction

Saliva is the product of a collection of major and minor salivary glands, which by their secretory activity contribute to the maintenance of a healthy oral environment.

Saliva plays a key role in maintaining oral health under normal conditions. If conditions change, for example, in sedated patients in intensive care, a rapid shift in oral flora may occur to Gram-negative species. This may subsequently spread into the respiratory tract, causing pulmonary afflictions.

While a detailed description of the composition and role of the salivary constituents is beyond the scope of this chapter, we note here the principal functions of these constituents (Fig. 1.1):

- Affecting the processing of food prior to swallowing.
- Protecting mineralized tissues against demineralization and stimulating remineralization.
- Providing innate and acquired immune protection against micro-organisms.

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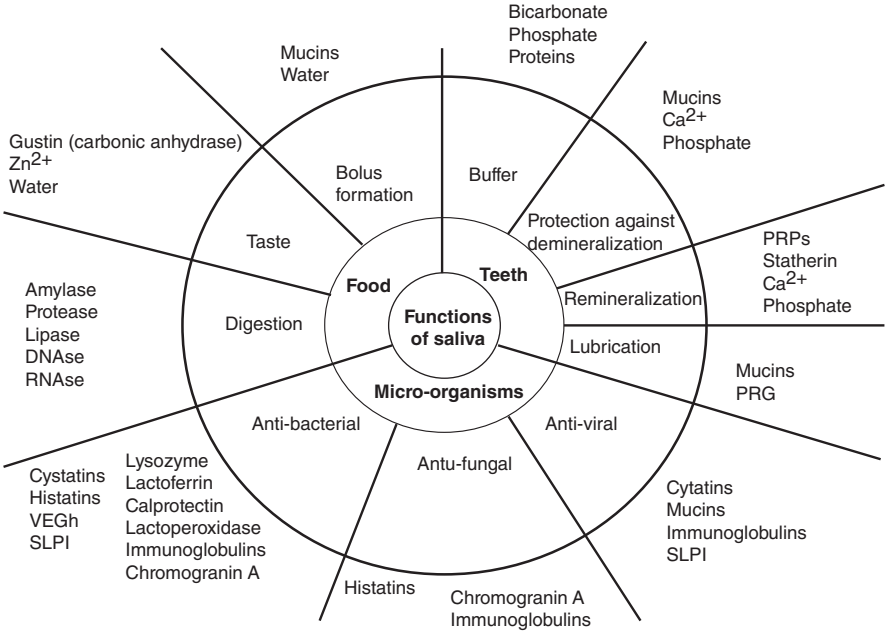

Fig. 1.1 Functions of saliva [1]

Traditionally, a distinction has been made between three pairs of *major* glands, the parotid, submandibular, and sublingual glands, and numerous *minor* salivary glands.

While these glands all have in common that they release their product into the oral cavity, the parotid and submandibular glands are not located directly below the oral mucosa, but at some distance, which necessitates the transport of saliva via lengthy excretory ducts: of the parotid (Stensen) with an opening on a papilla of the buccal mucosa near the second maxillary molar and of the submandibular gland (Wharton) which opens on the surface of the sublingual papilla. The smallest of the major salivary glands, the sublingual glands, are well developed in only about 65% of cases where a distinct anterior "major sublingual gland" is present [2]. The anterior major sublingual gland and a collection of minor sublingual glands that are located immediately below the sublingual oral mucosa have separate excretory ducts that open along the top of the sublingual fold (Rivinus). If an excretory duct of the major sublingual gland is well developed (Bartholin), it may join the submandibular duct (Wharton) and open on the sublingual papilla [3, 4].

Numerous minor salivary glands are found immediately below the oral mucosa in almost every location of the oral cavity. These glands are named according to their respective locations: **sublingual**: 8–20 in the floor of the mouth, **lingual**: directly below the ventral lining mucosa of the tongue and the dorsal specialized mucosa—particularly numerous near the lingual tonsil, **labial**: in the submucosa

below the lining mucosa of the lips, **buccal**: directly below the lining mucosa of the cheeks, **palatine**: directly below the masticatory mucosa of the hard palate and the lining mucosa of soft palate, and **glossopalatine**: particularly rich near the tonsil. Finally, a rare developing gingival gland has been described [5].

In many of these locations, no submucosa is present. If a submucosa is present, the minor salivary glands are located in that layer.

General Structure

Salivary glands are organs that consist of epithelial and connective tissue components. The epithelial components are responsible for the production, modification, and transport of saliva, while the connective tissue components provide physical support and carry the neurovascular supply needed for the function of the glands.

Epithelial Component

The *epithelial component* resembles a tree in which the major branches and the "trunk" are the largest (excretory) ducts. The principal excretory duct opens into the oral cavity, while the "leaves" are the acini where the production of saliva begins. The intervening "branches" and "twigs" are part of the ductal system, through which the secretory product is moved and modified until it reaches the oral cavity as saliva [6] (Fig. 1.2). This epithelial structure is most visible during the fetal period when the salivary glands are still developing. When cytodifferentiation of the epithelial cells of the acini and the ductal system is completed, the epithelial components seem to dominate the histology of the lobules.

A well-known diagram that was published in 1924 by Braus [7] (Fig. 1.3) illustrates the principal cellular details of the epithelial components of a salivary gland (mixed seromucous):

- Acini—these may be serous or seromucous in nature.
- Intercalated ducts—long in serous glands and short or non-existent in seromucous glands.
- Striated ducts—longer in serous glands.
- Excretory ducts.

In the major salivary glands, the acini, intercalated ducts, and most of the striated ducts constitute the *parenchyma* of the lobules of the salivary gland and are therefore described as intralobular.

The remaining lengths of the striated ducts and the excretory duct system run in the connective tissue between the lobules and are therefore described as interlobular.

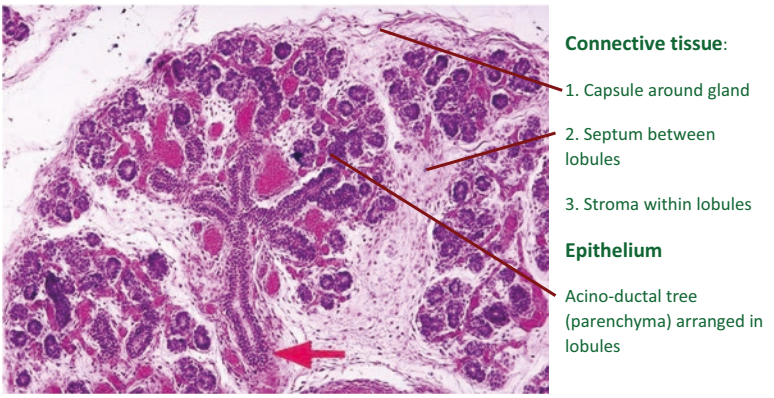

Fig. 1.2 Developing major salivary gland in a human fetus showing the distal epithelial components forming an acino-ductal tree intralobularly and one of the excretory ducts (red arrow) interlobular in a connective tissue septum. Original magnification 32 × [6]

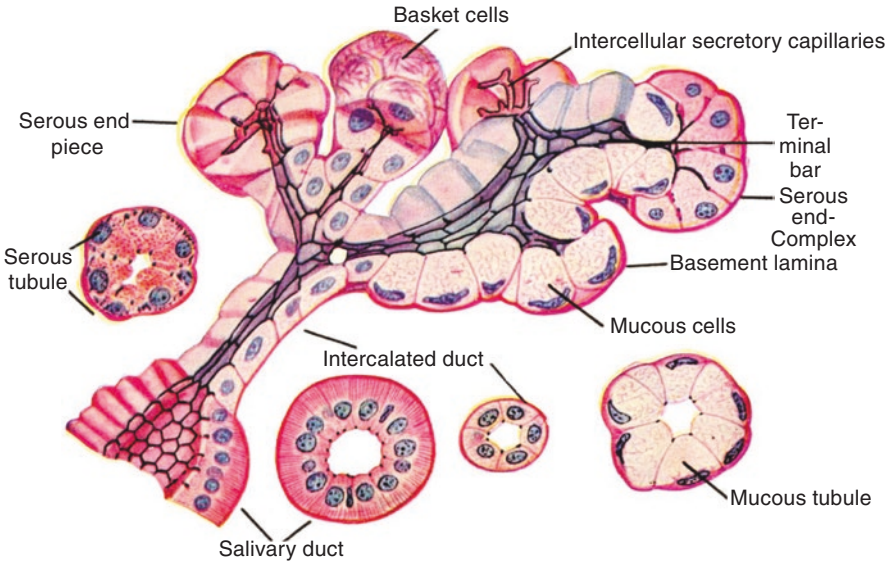

Fig. 1.3 Diagram. After a reconstruction by Vierling: Braus H (1924). Anatomie des Menschen. Berlin, Springer Verlag. Adjusted nomenclature: basket cells: myoepithelial cells: Mucous tubule: seromucous acinus (sectioned). Salivary duct: striated duct. Serous tubule: serous acinus (sectioned). Serous end piece: serous acinus (in 3D)

Connective Tissue Component

The *connective tissue component* forms a connective tissue *capsule* around the entire glandular mass. From this capsule, several *connective tissue septa* extend into the mass of the gland, between the lobules. These septa contain the interlobular ducts and the major neurovascular supply of the glands. A fine *connective tissue stroma* is present within the lobules and surrounds all the intralobular epithelial components. The stroma carries an abundant capillary supply and the afferent and autonomic nerves that supply the glandular tissue.

The epithelial components of the minor salivary glands generally are limited to seromucous acini and excretory ducts. A few cells resembling striated duct cells may be present in the excretory ducts. As will be discussed below, most minor salivary glands have seromucous acini, except for the purely serous von Ebner glands that are associated with the circumvallate and foliate papillae of the tongue.

The minor glands do not have distinct connective tissue capsules. In most cases, the connective tissue of these glands is limited to connective tissue stroma that surrounds the epithelial parenchyma and carries the vascular and neural elements needed for the epithelial functions.

Salivary Gland Development

The major glands start to develop during the embryonic period: the parotid glands (4–6 weeks) are first, and the sublingual glands are the last (8 weeks). The minor salivary glands begin their development slightly later, during the third prenatal month.

The salivary glands develop as the result of a series of epithelio-mesenchymal interactions that lead to an initial ingrowth of *solid epithelial strands* into the underlying mesenchyme, at the future site of the opening of the excretory duct into the oral cavity. The ductal system continues to expand by forming a series of successively smaller branches that will become striated ducts, intercalated ducts, and finally the terminal buds: the future acini. Thus, the pattern of development runs in a direction that is opposite to the production, flow, and secretion of saliva.

The pattern of development is characterized by several stages:

1. **Morphodifferentiation stages:** pre-bud, bud, and pseudoglandular: epithelial cord growth and successive rounds of branching of the solid cord [8–10].
2. **Canalicular stage**: During this stage, a hollowing or cavitation of the solid cord [11] leads to the formation of lumina in the developing glandular ducts.
3. **Terminal stage**: cytodifferentiation [12].

Eventually, *bulbous terminals (acini) are formed* at the ends of the strands during the third prenatal month. These terminals are the future acini.

The complexity of the growth and differentiation of the components of salivary glands has been studied by many investigators during recent decades. The selected

references will provide some insight into the current literature on this topic. However, a full picture of the signaling cascades that are required in salivary gland development is still incomplete [13].

Finally, stabilizing effects of elements of the extracellular matrix: fibroblasts and collagen, and the basal lamina components: laminin and nidogen, are needed to support branching morphogenesis [13]. While the stages of morphogenesis have been well-studied, little is known about the factors that control cell differentiation in the terminal stage. Those factors differ from the ones that control the morphogenesis stages.

Salivary Gland Anatomical Relationships

Developmentally, a salivary gland starts proliferating from the future site of the oral opening of its excretory duct to become the tree-like structure that was described above. This process of growth and development occurs during the same period during which the surrounding tissues are proliferating and establishing their respective territories. So, the final "space" in which a fully developed gland is located is a compromise between the domains that are needed by the gland and its neighboring structures, tissues, and organs. Notably, it is subject to individual variation. The differences in thickness of the connective tissue fasciae which serve as packing structures between the salivary glands and the surrounding tissues and organs reflect these compromises in the establishment of such domains.

The patterns of vasculature and innervation of the salivary glands similarly need to be considered within the frame of the glandular development. Thus, while the function of the salivary glands usually is described from the distal-most acini to the oral openings of the excretory ducts, the arterial supply and venous drainage of the glands follow the pattern of the duct system in reverse, with the blood vessels entering the mass of the gland near the excretory ducts in a way that is somewhat like a hilum [4].

As noted before, there is no consensual agreement in the literature concerning some gross structural details that are potentially important in surgical procedures [3]. The descriptions that follow are general. Detailed studies based on extensive dissections may be found in [14, 15] and to a lesser extent in [2].

Parotid Gland

The parotid gland is the largest of the three major salivary glands. The shape of this gland is variable, and more than those of the other major glands, it is determined by the neighboring structures that define the space into which the gland has grown. The gland occupies the space between the posterior surface of the mandibular ramus and the sternocleidomastoid muscle. It extends vertically from a level below the external auditory meatus to a level below the angle of the mandible and extends anteriorly, covering the posterior part of the masseter muscle, where it is wedged between the skin and the muscle. The excretory duct (Stensen) of the gland runs in an anterior

direction across the external surface to the anterior border of the masseter muscle, where it curves medially and crosses the buccinator muscle before opening near the second maxillary molar on the buccal mucosa (Fig. 1.4).

The fetal development of the acinotubular structure of the parotid gland occurs during intensive growth of the facial region in the late embryonic and fetal stages, in a limited anatomical space, simultaneously with the development of the future facial muscles. The muscles are formed by myoblasts that have migrated from the second pharyngeal arch to their locations in the developing face along with related branches of the facial nerve which undergo variable branching as needed by the developing muscles. This fetal jigsaw puzzle results in a gland that has a more complicated gross anatomical organization than that of other salivary glands and with less fascial definition.

The peripheral connective tissue capsule around the parotid, if present, is of minimal thickness. The skin and the other surrounding structures, that form the walls of this tight parotid space, supply the deep cervical fascia which provides connective tissue packing material for biomechanical protection and support.

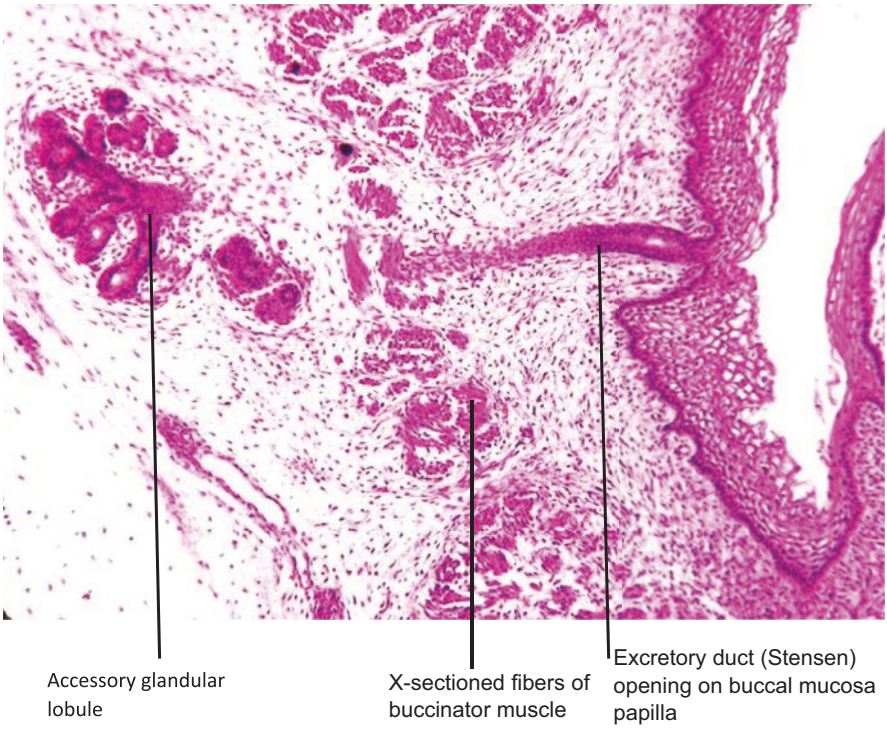

Fig. 1.4 Parotid excretory duct (Stensen) in human fetus (5 months). Coronal section. The duct crosses the buccinator muscle, the fibers of which are seen in this view in cross section. Original magnification 25 × [6]. A small accessory glandular lobule may be associated with the excretory duct

In addition to the poorly defined connective tissue capsule of the parotid, a well-recognized complicating factor in the surgery of the parotid gland is the presence of the five principal branches of the facial nerve (N VII) that run through the parotid space and supply the muscles of facial expression. The variability of the branching pattern and the relationships between the branches [16] may lead to facial nerve palsy during facial surgery.

Vascular and Nerve Supply

The parotid gland lies superficial to the external carotid artery and the external jugular vein and some of their branches. While the facial artery, which branches off the external carotid artery, and the retromandibular vein, which drains into the external jugular vein, are considered the principal vessels that provide the arterial supply and the venous drainage of the gland, these functions may also be carried out opportunistically by other branches of these principal vessels.

The parotid gland receives its afferent nerve supply from the auriculotemporal nerve (V3). This nerve carries the postganglionic parasympathetic (cholinergic) nerve fibers.

The preganglionic parasympathetic (cholinergic) nerve fibers that are destined for the parotid gland accompany the glossopharyngeal nerve (IX) to the otic ganglion where they synapse and travel from there with the auriculotemporal nerve to the parotid.

The preganglionic sympathetic (adrenergic) nerve fibers that are destined for the parotid gland synapse in the superior cervical ganglion and travel from there to their destination in the gland along the vascular coats of the arteries that travel there.

See [17, 18] for detailed studies on anatomical variations of the parotid gland.

Submandibular Gland

The larger and well-defined part of this gland lies in the superficial (close to the skin) submandibular triangle that is formed by the anterior and posterior bellies of the digastric muscle and the inferior border of the mandible. The floor of the triangle is the mylohyoid muscle. The submandibular gland has a distinct connective tissue capsule, which is relatively non-adherent to the surrounding connective tissue, facilitating the removal of the gland if necessary.

The gland is hook-shaped. It curves around the posterior border of the mylohyoid muscle to form the so-called deep process (Figs. 1.5 and 1.6). This is the smaller, more variable part of the gland which lies on the oral side of the mylohyoid muscle. This part of the gland was the earliest to develop. Space restrictions imposed by the surrounding tissues forced the further development of the gland into the

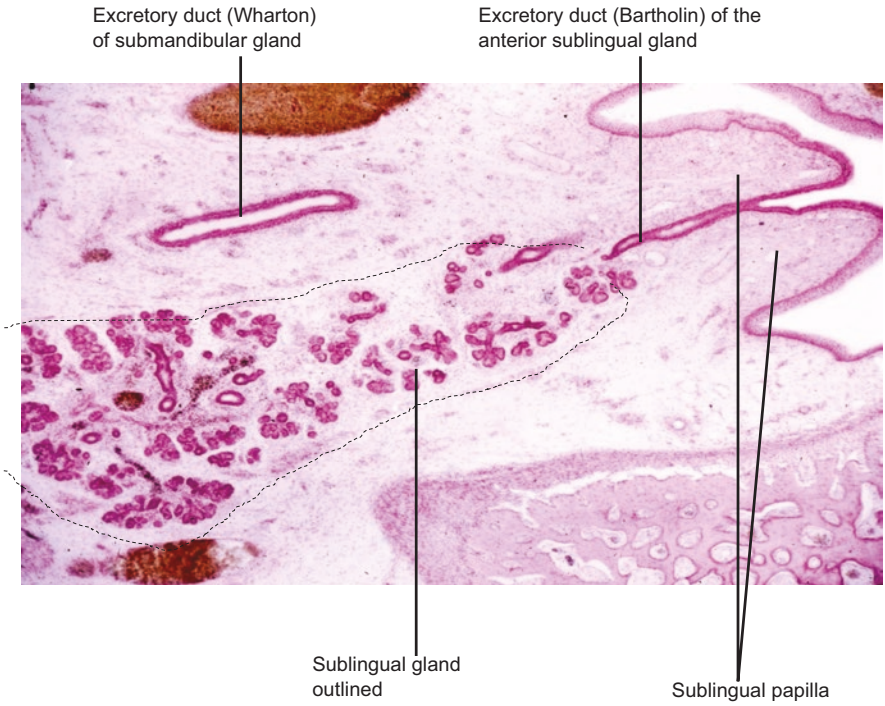

Fig. 1.5 Developing sublingual gland in human fetus (5 months). Sagittal section of the sublingual region. The lingual surface of the developing mandible is shown in the lower right-hand corner. Original magnification 6 ×. Author's slide collection

submandibular triangle. The excretory duct (Wharton) runs anteriorly from the deep process to open on the summit of the sublingual papilla. Along its path, the duct crosses the lingual nerve that runs in a medial direction to innervate the tongue.

Sublingual Gland

The sublingual gland is the smallest of the major salivary glands. It is located on the oral side of the mylohyoid muscle, in the sublingual fossa of the mandible, and immediately below the sublingual mucosa which forms a sublingual fold. As noted before, a distinct anterior major sublingual gland with a well-developed excretory duct (Bartholin) may be present in 65% of the cases. A group of minor sublingual glands is located along the sublingual fold with a variable number [1, 9–20] of small excretory ducts (Rivinus). While they are separate, they are considered part of the total mass of the sublingual gland.

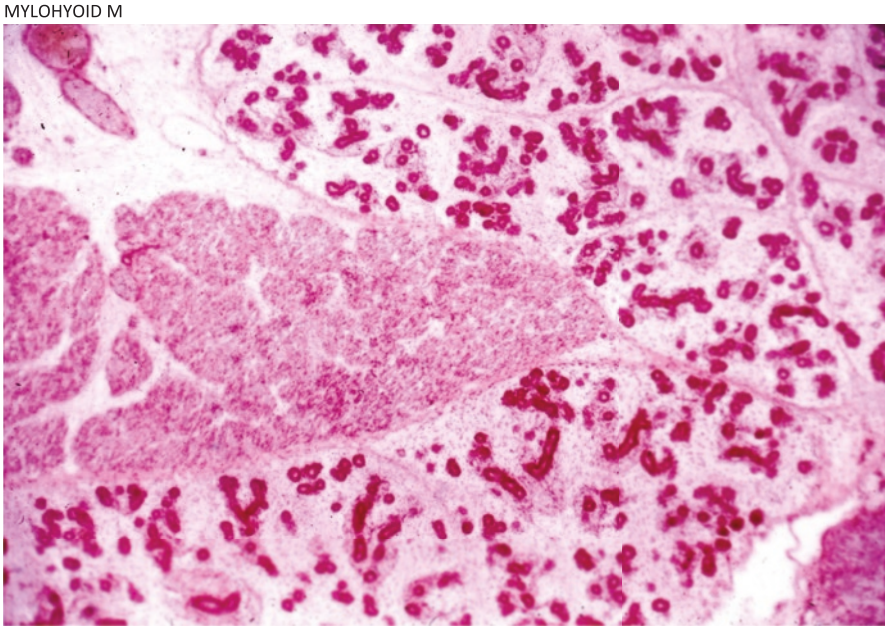

Fig. 1.6 Developing submandibular gland in human fetus (5 months). Sagittal section. Original magnification 6 ×. Author's slide collection. The larger and well-defined part of this gland lies in the superficial submandibular triangle (bottom of this image). The gland is hook-shaped. It curves around the posterior border of the mylohyoid muscle the fibers of which are cross-sectioned in this image

On occasion, portions of the developing sublingual gland may slip between two developmentally distinct parts of the mylohyoid muscle. Both parts initially attach to Meckel's cartilage. During the early fetal period, the anterior part of the attachment is transferred to the developing mandible at the superficial side (skin side) of Meckel's cartilage, while the attachment of the posterior part moves to the mandible at the deep side (oral side) of Meckel's cartilage. The resulting slit-like space between the anterior and posterior muscle components allows the developing sublingual gland to grow from the deep to the superficial side [19, 20] (Fig. 1.7).

Vascular and Nerve Supply

The submandibular and sublingual glands receive their vascular supplies from branches of the facial and lingual arteries.

Their afferent nerve supply is from the lingual nerve (V3). The preganglionic parasympathetic (cholinergic) nerve fibers that are destined for the submandibular and sublingual glands accompany the facial nerve until they are carried by the chorda tympani to the lingual nerve. They synapse in the submandibular ganglion. The postganglionic fibers rejoin the lingual nerve to supply the glands.

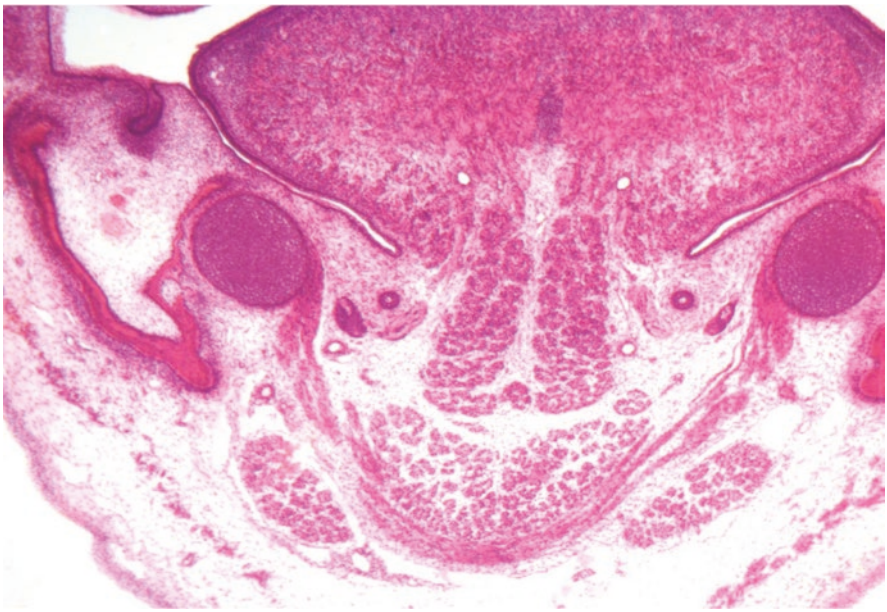

Fig. 1.7 Initial attachment of the mylohyoid muscle to Meckel's cartilage. Human fetus 8 weeks, original magnification 6 ×. Author's slide collection. The attachment of the anterior portion of the muscle will subsequently migrate to the mandible on the superficial (skin) side of the lower jaw, while the attachment of the posterior portion of the muscle will migrate to the mandible on the deep (oral) side of the lower jaw. Developing sublingual glands occasionally slip between the anterior and posterior portions of the mylohyoid muscle from the deep side to the superficial side of the mylohyoid muscle, as described in [19]

The postganglionic sympathetic (adrenergic) nerve fibers reach the glands with the branches of the facial and lingual arteries.

Morphology and Function of the Acino-Ductal Tree of Major Salivary Glands

Saliva is a product that is secreted and modified throughout the length of the acino-ductal system. Saliva is a product that is secreted and modified throughout the length of the acino-ductal system.

With the exception of the excretory ducts, the other ducts and the acini are characterized by simple epithelia. Their epithelial cells are supported by a basal lamina at the interface with the connective tissue stroma; their apical ends face the central lumina of the acini and ducts. All cells are attached apically by tight junctional complexes (terminal bar system), which prevent the salivary product from moving into the intercellular spaces and start digesting the gland itself.

Acini

Acini may be spherical (serous) or sausage-shaped (seromucous). Even in purely seromucous glands, a seromucous acinus frequently has a cap of serous cells *(serous crescent: Gianuzzi; serous demilune: Heidenhain)* that occupies the terminal face of the acinus. The acinar cells form a *simple cuboidal-pyramidal epithelium* that surrounds a narrow lumen. Their apical cytoplasm is filled with secretory granules, whose contents may be discharged into the lumen upon stimulation.

In serous cells, these granules contain *zymogen,* the precursor of a watery enzyme product, composed of α-amylase: an enzyme for digesting starches, histatins, positively charged glycoproteins, proline-rich proteins, and secretory protein. The contents of the zymogen granules are visible in the light microscope. Prior to discharge, the acinar cells look well-filled.

In mucous cells and serous acinar cells of (sero)mucous glands, the granules contain *mucin (MUC5B and MUC7)*, the precursors of a heavy, viscous product, composed of negatively charged, high-molecular-weight sialomucins, which tend to form aggregates and a mucous coat on the oral mucosal surfaces. The mucous coat may serve not only as a protective shield but may also provide key immunoregulatory signals that educate dendritic cells to develop tolerance toward food and commensal antigens, like the function of MUC2 that is found in the GI tract [21].

In addition to the zymogen/mucigen product, salivary glands are the most important source for secretory IgA antibodies in the upper respiratory and digestive tracts.

Secretory IgA coats oral epithelium and limits colonization of micro-organisms, thereby reducing an influx of soluble antigens. It also mediates immune responses such as phagocytosis and antibody-dependent, cell-mediated cytotoxicity through a specific IgA receptor that is expressed by monocytes, eosinophils, neutrophils, and macrophages [22]. Importantly, IgA permits a response to harmless commensal bacteria in the oral cavity by limiting inflammation, thus preventing damage to the epithelial barrier.

The serous acinar cells of all major salivary glands and the von Ebner glands secrete **histatins** in the saliva. Histatins are low-molecular-weight histidine-rich proteins that are bactericidal and fungicidal. They are a major component of the innate host non-immune defense system [23].

Also added to the saliva are several growth factors [24, 25].

Intercalated Ducts

Intercalated ducts are the narrowest of the salivary ducts. They are lined by a single layer of *low cuboidal cells,* whose cytoplasm stains relatively neutral and whose volume is occupied mostly by a nucleus. Like the acinar cells, intercalated duct cells are also involved in the *production of secretory IgA,* which is added to the salivary product. The cells are *mitotically active* and may serve as a source of renewal for adjacent acini (although this point has been contested [26]) and striated ducts. Small

groups of stem cells have been identified in murine intercalated ducts [27]. Certain salivary gland tumors first develop in these ducts.

Myoepithelial cells surround all intercalated ducts, as well as the acini and parts of the striated ducts (in humans only). Myoepithelial cells are dendritic. They have a cell body in which the nucleus is located and several dendritic cell extensions that surround the acino-ductal components. For this reason, they are sometimes called *basket cells*.

The cell extensions contain *myofibrils* and are contractile. Myoepithelial cells have an epithelial origin and are located on the epithelial side of the basal lamina. Myoepithelial cells have dual sympathetic and parasympathetic innervation. Upon stimulation by either, they contract and assist in the discharge and movement of the salivary product. Myoepithelial cells communicate through gap junctions whose gap junctional protein, connexin 43, is different from the proteins, connexin 32/26, which are found in gap junctions between alveolar cells and are more characteristic for secretory and resorptive epithelia, among others. This suggests separate communication compartments: myoepithelial cells communicate with each other and are related to contraction, and the alveolar cells are related to secretion [28, 29].

Striated Ducts

Striated ducts are lined by a simple, (tall) columnar, epithelium. The epithelial cells are *eosinophilic and highly refractile.* In their basal cytoplasm, rows of *mitochondria are aligned parallel to the long axis of the cell, between deep infoldings of the basal cell membrane.* This arrangement gives the impression of a striated basal cytoplasm, which gives this duct its name. The histology of striated ducts resembles that of the distal convoluted tubules of the kidney—for a similar functional reason: the *salivary product is altered by a modification of the electrolytes*: the removal from the saliva of NaCl (essentially without water, thereby making the final saliva hypotonic) and secondarily addition of K-ions and HCO_3 ions.

Salivary fluid secretion in the alveolar cells is driven by an electrolyte co-transport system, which results in a net increase of Cl^- ions as well as water in the initial saliva product. Ion transport is necessary to restore the electrolyte balance. Carbonic anhydrase, an enzyme associated with Cl^- ion transport, is prominently present in striated and excretory ducts. Striated duct cells are also implicated in the transport of secretory IgA and release of growth factors into the saliva [30].

Excretory Ducts

Excretory ducts are lined near the lobules by simple, tall columnar epithelium. The epithelium gradually changes to the pseudostratified epithelium. Near the oral cavity, the lining changes to stratified squamous epithelium [31]. These ducts are by no means passive conduits. They *further modify the salivary product by the following:*

Apocrine secretion from the principal epithelial cells (product unknown).

Secretion products of associated sebaceous glands.

Secretion product (mucins) of goblet cells, which are present in the epithelium [21].

Absorption of Cl^- ions.

Release of secretory IgA into the lumen [32].

Once the salivary product is discharged into the oral cavity, it is *further modified* by growth factors, as well as IgG, all of which are added through the gingival crevice.

Morphology and Function of Minor Salivary Glands

All minor salivary glands are mixed, predominantly seromucous in nature, except for *the purely serous von Ebner* glands, which are associated with the vallate and foliate papillae of the tongue. Minor salivary glands have the following:

- *Mucous acini with serous or seromucous demilunes.*
- *Short, intercalated ducts (frequently only some isolated cells).*
- *Intralobular ducts without striations (frequently only some isolated cells).*
- *Short excretory ducts.*

In contrast to the major glands, which must be stimulated to secrete, the minor glands produce a continuous flow of saliva at a rate of about 0.1 μL/minute/gland. Their product is rich in highly glycosylated mucins (MUC5B and MUC7) for tissue lubrication and bacterial aggregation. Minor salivary glands play a critical role in maintaining oral health by secretion of secretory IgA as well as the production by ductal cells of human β defensins. A few additional proteins have been identified in the proteomes of human minor salivary gland secretions that are not present in the secretions of the major salivary glands. This finding suggests that the minor salivary gland may have specific functions in the oral cavity.

The purely serous Von Ebner glands that are associated with circumvallate and foliate papillae have recently been shown to produce a significant amount of histatins, which may suggest that they have an important role in preventing microbial assaults on the tissues of the posterior region of the tongue [23].

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