Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Mosul
College of Dentistry

Salivary Gland

A Project Submitted to
The College of Dentistry, University of Mosul, Department of in Basic Dental Sciences /Pharmacy Partial Fulfillment for the Bachelor of Dental Surgery

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February /2025

Certification of the Supervisor

I certify that this project entitled " **Salivary Gland** " was prepared by the fifth-year student **Ahmed Abd-Alrazzaq Suwileh** under my supervision at the College of Dentistry/University of Mosul in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

Signature:

Assist.Lec.Dr.Maha Talal

Date: / / 2025

Dedication

This study is wholeheartedly dedicated to my beloved parents, who have been my source of inspiration and gave me strength when I thought of giving up, who continually provide their moral, spiritual, emotional, and financial support.

To my brothers, sisters, friends who shared their words of advice and encouragement to finish this study.

Acknowledgments

I thank God first and foremost for his countless love and support always, I pray that I will live up to be a responsible Doctor.

I would like to express my deep appreciation and indebtedness particularly to my supervisor **Assist.Lec.Dr.Maha Talal**

For her endless support, kind efforts, time, advice and scientific opinions and I'm really proud to be one of her students.

The completion of this project could not have been possible without the participation and assistance of so many people whose names may not all be enumerated. Their contributions are sincerely appreciated and gratefully acknowledged.

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Introduction

The major and minor salivary glands of the head and neck are important structures that contribute to many of the normal physiologic processes of the aerodigestive tract. The major salivary glands are routinely included within the field of view of standard neuroimaging, and although easily identifiable, salivary pathology is relatively rare and often easy to overlook. Knowledge of the normal and abnormal imaging appearance of the salivary glands is critical for forming useful differential diagnoses, as well as initiating proper clinical workup for what are often incidental can affect the salivary glands. **(Dobrosielski-Vergona et al., 2020)**

The major salivary glands are easily identified on routine imaging and contribute to many of the important deep neck spaces of the suprahyoid neck. The minor salivary glands are poorly visualized on routine imaging, but can also give rise to salivary pathology anywhere along the aerodigestive tract. After an extensive review of the radiology, otolaryngology, and pathology literature, we present a comprehensive discussion of salivary gland anatomy, as well as illustrate the broad range of nonneoplastic disease that can be visualized in the salivary glandsThe salivary glands in mammals are exocrine glands that produce saliva through a system of ducts. Humans have three paired major salivary glands (parotid, submandibular, and sublingual), as well as hundreds of minor salivary glands .**(Edgar et al., 2021)**

These Structures secreting fluid to facilitate feeding emerge progressively throughout evolution and can be found in very simple organisms and more complex species. In humans, major and minor salivary glands produce and secrete digestive fluids or protein-rich fluids. The three pairs of major salivary glands are responsible for the production and secretion of saliva in the oral cavity, whose moisturizing effect preserves oral hygiene and allows taste, speech and mastication. **(Amano et al., 2020).**

The parotid gland (PG) is mainly composed of serous acini-secreting αamylase-rich saliva. The sublingualgland (SL) secretes mucous, a viscous solution rich in mucins **(Korsrud et al.,2019).**

The submandibular gland (SMG) is composed by a mixed population of acini with a mucous and serous function. These three major salivary glands account for more than 90% of salivary secretion. Minor salivary glands are distributed throughout the oral cavity, specically in the labial and lingual mucosa, as well as palate and floor of the mouth. Saliva is an essential fluid for oral cavity maintenance and functionality**(Treuting, P.M et al., 2022).**

Digestive enzymes within saliva initiate the digestion process, and at the same time, saliva acts as a lubricant of solid nutrition, thus helping its passage through the esophagus. By moisturizing the tongue and other tissues of the oral cavity, saliva has an essential rolein speech and taste sensitivity **(Matsuo et al., 2020).**

It also balances the pH of the mouth, thus protecting the soft oral tissues and teeth from an extended exposure to an acidic environment. Saliva contains several signalling molecules, such as EGF, FGF, NGF and TGF-α, that are essential for the regeneration of oral and esophageal mucosa. Finally, the antibacterial and antifungal components of the saliva, such as lysozymes, immunoglobulin and lactoferrin, inhibit the progression of bacterial infection and dental caries. **(Kondo and Nakamoto, 2021)**

Aim of the study

is to able the dentist to discover different methods in imaging of salivary glands for better diagnosis the diseases, and neoplasms that effect major and minor salivary gland in oral and maxillofacial region, and show the importance of different imaging modalities in diagnosis of salivary glands' diseases.

Chapter one

Review of literature

1.1 Morphogenesis Of Salivary Gland

Salivary glands originate from an epithelial placode during embryonic development (from E11 to E16 in mice and between the 4th and the 12th embryonic weeks in humans). The initial placode grows and extends into the underlying mesenchyme, acquiring a bud shape. The growing epithelial bud progressively straties with concentric layers each formed by a specialized cell type. During branching morphogenesis, the initial salivary bud divides into additional, independent buds that grow and cleave again, until the formation of an extensive arborization typical for the mature salivary gland **(Jimènez-Rojo *et al*., 2022).**

A portion of the cells forming the outer epithelial layer of the buds differentiates into myoepithelial cells. They will then acquire smooth muscle characteristics and locate in direct contact with the acinar structure to regulate the release of secretion . Inner epithelial cells differentiate further to acquire a distal (tips) or proximal (stalk) identity, which, in turn, evolves into acini or ducts, respectively Both epithelial and mesenchymal cells produce the basement membrane and stromal extracellular matrix. The composition of the extracellular matrix varies from region to region during branching, and bundles of collagen I, IV and bronectin are thought to directly control the maturation process. **(Chatzeli *et al*., 2020).**

1.2 Importance of Salivary Glands

Salivary glands are essential components of the human digestive system, playing a crucial role in maintaining oral health, facilitating digestion, and contributing to speech and taste. These glands produce saliva, a complex fluid that contains various enzymes, electrolytes, and other substances vital for oral and systemic health. Saliva serves multiple functions, including:

- Lubrication: Moistening the oral cavity and food, making it easier to swallow and speak.
- Digestion: Initiating the breakdown of carbohydrates with the enzyme amylase.
- Protection: Neutralizing acids, buffering pH levels, and protecting the teeth from decay.
- Antimicrobial Properties: Containing lysozyme and other antimicrobial agents that help prevent oral infections.The importance of salivary glands is evident in conditions like xerostomia (dry mouth), which can lead to significant oral health issues, including dental caries, periodontal disease, and difficulty in speaking and eating.

1.3 Type of salivary gland

1.3.1 parotid gland

The two parotid glands are major salivary glands wrapped around the mandibular ramus in humans.These are largest of the salivary glands, secreting saliva to facilitate mastication and swallowing, and amylase to begin the digestion of starches**(Nanci A, 2022).**

It is the serous type of gland which secretes alpha-amylase (also known as ptyalin).It enters the oral cavity via the parotid duct. The glands are located posterior to the mandibular ramus and anterior to the mastoid process of the temporal bone. They are clinically relevant in dissections of facial nerve branches while exposing the different lobes, since any iatrogenic lesion will result in either loss of action or strength of muscles involved in facial expressionThey produce 20% of the total salivary content in the oral cavity. Mumps is a viral infection **.(Holmberg and Hoffman, 2023)**

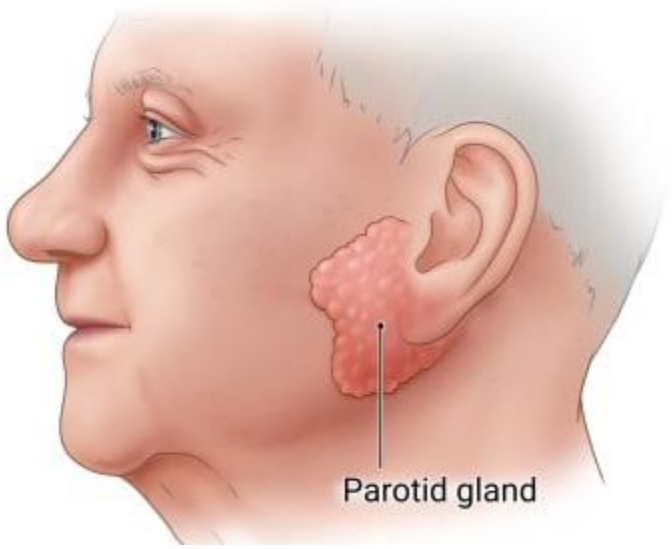

Figure.1 parotid gland

1.3.2 Submandibular salivary gland

The submandibular glands (previously known as submaxillary glands) are a pair of major salivary glands located beneath the lower jaws, superior to the digastric musclesThe secretion produced is a mixture of both serous fluid and mucus, and enters the oral cavity via the submandibular duct or Wharton duct.Around 70% of saliva in the oral cavity is produced by the submandibular glands, though they are much smaller than the parotid glands**(Bialek EJ *et al*., 2020). (Nanci A, 2024).**

This gland can usually be felt via palpation of the neck, as it is in the superficial cervical region and feels like a rounded ball. It is located about two fingers above the Adam's apple (laryngeal prominence) and about two inches apart under the chin.

1.3.3 Sublingual salivary gland

The sublingual glands are a pair of major salivary glands located inferior to the tongue, anterior to the submandibular glands The secretion produced is mainly mucous in nature, but it is categorized as a mixed gland. Unlike the other two major glands, the ductal system of the

sublingual glands does not have intercalated ducts and usually does not have striated ducts, either, so saliva exits directly from 8-20 excretory ducts known as the Rivinus ducts.About 5% of saliva entering the oral cavity comes from these glands**(Bialek EJ et al., 2020). (Nanci A, 2024).**

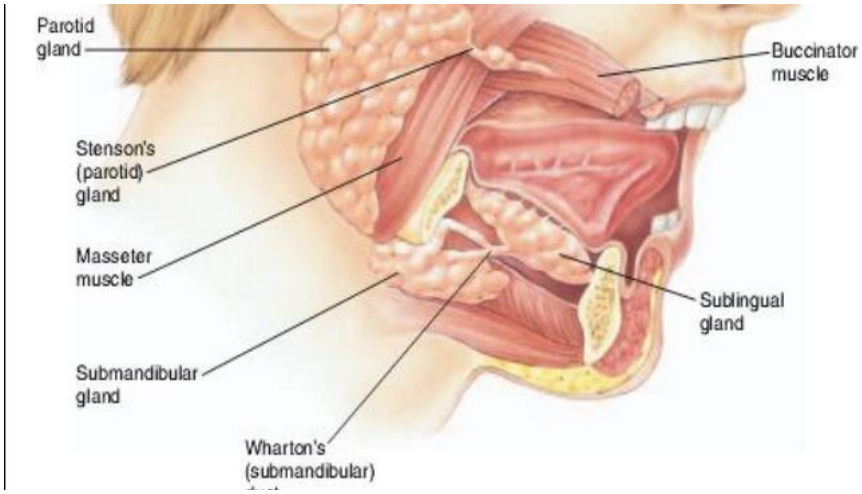

Figure.2 Submandibular Gland And Sublingual Gland

1.3.4 Tubarial salivary gland

The tubarial glands are suggested as a fourth pair of salivary glands situated posteriorly in the nasopharynx and nasal cavity, predominantly with mucous glands, and its ducts opening into the dorsolateral pharyngeal wall. The glands were unknown , when they were discovered by a group of Dutch scientists using with prostatespecific membrane antigen PET-CT. This discovery may explain mouth dryness after radiotherapy despite the avoidance of the three major submandibular salivary gland glands. However, these findings from just one study need to be confirmed On the other hand, an interdisciplinary group of scientists disagree with this new discovery. They believe that an accumulation of minor salivary glands has been described **(Guntinas-Lichius et al., 2020).**

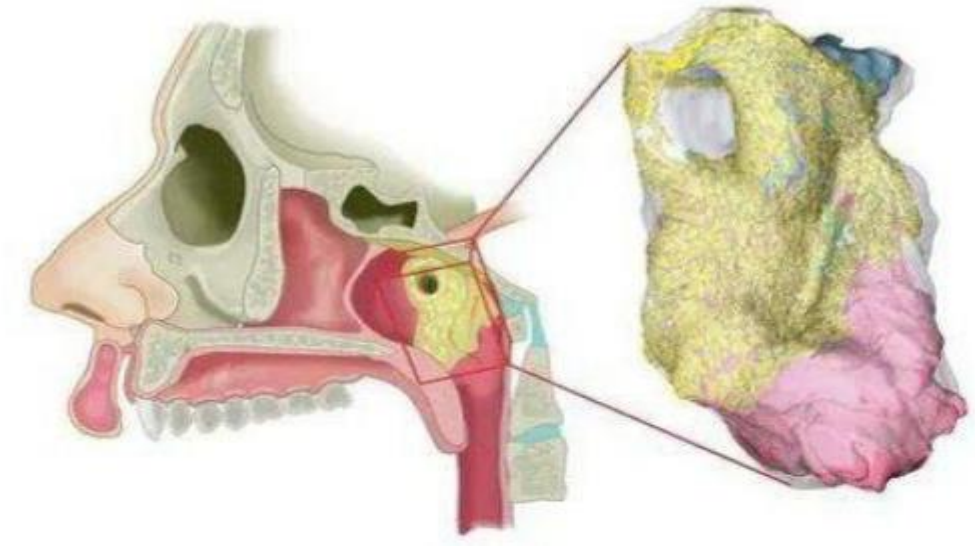

Figure.3 Tubarial Glands

1.4 Chemistry of secretion and function of saliva

Secretion itself is a combination of three events:

- nervous cholinergic stimulation initiates uidltration from blood plasma to the acinar lumen.
- exocytosis of cytoplasmic granuli-containing proteins into the acinar lumen.
- mechanical contraction of the secretory end-pieces mediated by specialized myoepithelial cells **(Cristina et al., 2022).**

1.5 Component and Function of saliva

Saliva is a very dilute fluid, composed of more than 99% water. Saliva is not considered an ultrafiltrate of plasma initially, saliva is isotonic; it is formed in the acini, but it becomes hypotonic when it travels through the duct network.

1)Bicarbonates, phosphates, and urea act to modulate pH and the buffering capacity of saliva.

2)Macromolecule proteins and mucins serve to cleanse, aggregate, and/or attach oral microorganisms and contribute to dental plaque metabolism.

3)Calcium, phosphate, and proteins work together as an antisolubility factor and modulate demineralization and remineralization.

4)Immunoglobulins, proteins, and enzymes provide antibacterial action**(Humphrey et al., 2024).**

1.6 Salivary Gland Disease

1.6.1 Infection

Several viruses and bacteria infect the tissue of salivary glands in a specic manner. Endemic parotitis is due to infection of the mumps virus and lead to PG swelling and systemic symptoms. It is mainly affecting children in pre-scholar age and treatment is primarily symptomatic. The HIV virus can infect the PG and induce the formation of cystic lesions with surgical resection being the most common treatment procedure. Hepatitis C and coxsackievirus are RNA-bound viruses, able to infect salivary glands and damage the host tissue, leading to xerostomia. One of the main routes of viral spreading is the gland secretion itself and thus transmission through saliva exchange is the major infection mode. Bacterial infection is very rare and mainly affects the PG in patients already debilitated by other conditions, such as diabetes, recovery after surgery or immunodeciency.

1.6.2 Primary Sjögren's Syndrome (pSS)

is a systemic autoimmune disease affecting salivary and lacrimal glands. Often accompanying other immune system disorders (such as lupus and rheumatoid arthritis), its main effect is the loss of mucous membrane and moisture-secreting gland cells, resulting in xerostomia and xerophthalmia. Although the pathogenesis of the disease remains largely unknown, the role of the Blymphocytes appears to be essential in the initiation of the disease. Members of the TNF superfamily (such as BAFF/APRIL) are

produced not only by patrolling immune cells but also by the epithelial cells of the salivary glands. Through these pathways, B-cells are activated and start to proliferate in an uncontrolled manner. Their pivotal role includes inltration of the salivary glands to produce an ectopic germinal centre and local secretion of autoantibodies. The centre can grow independently from the surrounding tissue and can evolve in more complex diseases such as non-Hodgkin lymphoma**(Chadburn et al., 2024).**

Figure.4 Primary Sjögren's Syndrome (pSS)

1.6.3 Sialadenitis

is an inflammatory condition of the salivary glands, often caused by bacterial or viral infections

- Symptoms: Pain, swelling, redness, and tenderness in the affected gland, fever, and difficulty swallowing
- Etiology: Common pathogens include Staphylococcus aureus, Streptococcus species, and viruses such as mumps
- Treatment: Antibiotics for bacterial sialadenitis, antiviral medications for viral causes, and supportive care such as hydration and warm compresses **.(Epstein *et al.*,2022).**

Figure.5 Sialadenitis

1.7 Neoplastic Conditions

1.7.1 Benign Tumors

- Pleomorphic Adenoma: The most common benign tumor of the salivary glands, typically occurring in the parotid gland .
- Symptoms: Painless, slowly growing mass in the affected gland .
- Treatment: Surgical excision with careful preservation of the facial nerve **.(Barnes L,*et al.*,2024)**

Warthin's Tumor

A benign tumor that usually affects the parotid gland, more common in males and often associated with smoking .

- Symptoms: Bilateral, painless, mobile masses in the parotid gland .
- Treatment: Surgical excision, with a low recurrence rate **.(Spiro RH.2022)**

Figure.6 Warthin's Tumor

1.7.2 Malignant Tumors

Mucoepidermoid Carcinoma

The most common malignant tumor of the salivary glands, often found in the parotid gland .

- Symptoms: Painful, rapidly growing mass, facial nerve paralysis .

- Treatment: Wide local excision, often combined with radiation therapy **.(Seethala RR, and El-Mofty SK.2021)**

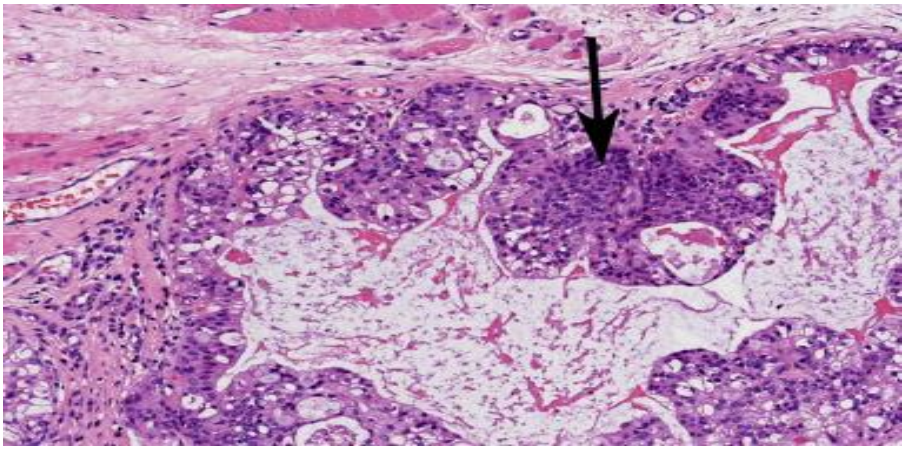

Figure.7 Mucoepidermoid Carcinoma

1.8 Obstructive Conditions

1.8.1 Salivary Duct Stones (Sialolithiasis)

The formation of stones within the salivary ducts, most commonly in the submandibular gland .

- Symptoms: Pain, swelling, and difficulty eating, especially during meals when salivary flow increases .
- Etiology: Dehydration, poor oral hygiene, and certain medications can predispose to stone formation .
- Treatment: Conservative management with hydration and sialogogues, surgical removal of stones, or extracorporeal shock wave lithotripsy **(Moher D,*et al.*,2022).**

Figure.8 Salivary Duct Stones (Sialolithiasis)

1.9 Drug Effects on Salivary Glands

1.9.1 Anticholinergic Drugs

- Mechanis: Anticholinergic drugs block the action of acetylcholine, a neurotransmitter that stimulates salivary secretion .
- Examples: Antihistamines (e.g., diphenhydramine), tricyclic antidepressants (e.g., amitriptyline), and antipsychotics (e.g., clozapine) .
- Effects: Reduced salivary flow leading to xerostomia, increased risk of dental caries, and oral infections **.(Smidt D,*et al.*,2021)**

Figure.9 Clozapine Drug

1.9.2 Chemotherapy and Radiation Therapy

- Mechanism: Both chemotherapy and radiation therapy can damage the salivary gland tissue, reducing its ability to produce saliva .
- Effects: Severe xerostomia, mucositis, and an increased susceptibility to oral infections and dental problems **.(Lynge Pedersen AM,*et al.*,2022)**
- Management: Artificial saliva, saliva stimulants, and meticulous oral hygiene .

1.10 Emerging Therapies

(A) Gene Therapy Potential for treating genetic disorders affecting salivary gland function .

(B) Stem Cell Therapy Regeneration of damaged salivary gland tissue .

(C) Targeted Therapy Development of targeted drugs for specific types of salivary gland cancers **.(Baccaglini I,*et al.*,2023)**

1.11 Preventive Strategies

- Lifestyle Modifications: Smoking cessation, proper hydration, and good oral hygiene
- Vaccination: Prevention of viral infections that can cause sialadenitis .
- Regular Check-ups: Early detection and management of salivary gland disorders **.(Eviö S,*et al.*,2006)**

Chapter Two

2.1 Disscussion

Saliva plays a crucial role in maintaining the health and functioning of the mouth. Its functions include

(1) maintaining a moist oral mucosa,

(2) mucinous content acting as a lubricant in the mouth and oesophagus,

(3) taste recognition by acting as a medium for suspension of tastants,

(4) digestion of starches with the help of amylase,

(5) acid buffering in the mouth and oesophagus mainly by bicarbonate,

(6) protection of teeth from acids by being supersaturated with respect to tooth mineral and by contributing to the acquired enamel pellicle,

(7) modulation of the oral microbiota with the help of anti-bacterial, anti-viral, and anti-fungal components, and

(8) facilitating wound healing in the oral cavity .

Medications may act on the central nervous system and/or at the neuroglandular junction, explaining the pathogenesis of MISDG. The secretory cells are supplied with muscarinic M1 and M3 receptors, α1- and β1-adrenergic receptors, and certain peptidergic receptors that are involved in the initiation of salivary secretion **(Ord RA, Blanchaert RH Jr.2018)**

It is therefore understandable that drugs that have antagonistic actions on the autonomic receptors but that are used to treat dysfunctions in the various effectors of the autonomic nervous system may also affect the functions of salivary glands and thus cause oral dryness. However, in some cases, the cause of oral dryness is not as evident, as with the bisphosphonate alendronate that was reported to reduce the unstimulated secretion of saliva .

The anti-muscarinic drugs are well-known inducers of oral dryness as they prevent parasympathetic (cholinergic) innervation from activating the secretory cells. Surprisingly, The number of patients adversely affected by a specific drug, as well as the severity of the effect of this drug, are usually dose dependent. Figures for these parameters are not presented in the current study. Lack of saliva is often manifested as the sensation of dry mouth (xerostomia). A number of studies have suggested an association between the incidence of xerostomia and the number and dose of medications .

Chapter Three

3.1 Conclusion

The salivary glands play a critical role in maintaining oral health and facilitating digestion. Understanding the anatomy, physiology, and common diseases of these glands is essential for diagnosing and managing related conditions. Additionally, recognizing the impact of various drugs on salivary gland function is crucial for optimizing patient care and minimizing adverse effects. Future research should focus on developing new treatments and preventive strategies to address the challenges posed by salivary gland disorders.

A variety of disease patterns involve the major salivary glands with few characteristic features on imaging. high-resolution ultrasonography should be the first screening imaging tool followed by sialography. The conclusion of this review of literature is to assess different type of imaging modalities for detect various disease and different type of tumors that effect parotid and submandibular salivary gland, and to focus on the important aspect of imaging the salivary gland disorders by selection of appropriate imaging method and accurate interpretation of images will help in correct diagnosis of conditions .

References

1.Nanci A (2022). Ten Cate's Oral Histology: Development, Structure, and Function (ninth ed.). ISBN 978-0-323-48524-1.

2.Brown JE, Drage NA, Escudier MP, et al. Minimally invasive radiologically guided intervention for the treatment of salivary calculi. Cardiovasc Intervent Radiol. 2022;25(5):352-355.

3.Chatzeli, L.; Gaete, M.; Tucker, A.S. Fgf10 and Sox9 are essential for the establishment of distal progenitor cells during mouse salivary gland development. Development 20124, 144, 2294–2305.

4.Holmberg KV, Hoffman MP (2023). "Anatomy, biogenesis and regeneration of salivary glands". Saliva: Secretion and Functions. Monographs in Oral Science. Vol. 24. pp. 1–13. doi:10.1159/000358776. ISBN 978-3-318-02595-8. PMC 4048853. PMID 24862590

5.Dobrosielski-Vergona, K. Biology of the Salivary Glands; CRC Press, Taylor & Francis Group: Abingdon, UK, 2020; ISBN 978-0849388477

6.Amano, O.; Mizobe, K.; Bando, Y.; Sakiyama, K. Anatomy and histology of rodent and human major salivary glands: Overview of the Japan salivary gland society-sponsored workshop. Acta Histochem. Cytochem. 2020, 45, 241–250.

7.Korsrud, F.R.; Brandtzaeg, P. Quantitative immunohistochemistry of immunoglobulin-andJ-chain-producing cells in human parotid and submandibular salivary glands. Immunology 2019, 39, 129–140

8.Jimènez-Rojo, L.; Granchi, Z.; Graf, D.; Mitsiadis, T.A. Stem Cell Fate Determination during Development and Regeneration of Ectodermal Organs. Front. Physiol. 2022, 3, 107.

9.Matsuo, R. Role of saliva in the maintenance of taste sensitivity. Crit. Rev. Oral Biol. Med. 2020, 11, 216–229.

10.Bialek EJ, Jakubowski W, Zajkowski P, Szopinski KT, Osmolski A (2020). "US of the major salivary glands: anatomy and spatial relationships, pathologic conditions, and pitfalls". Radiographics. 26 (3): 745–63. doi:10.1148/rg.263055024. PMID 16702452.

11. Barnes L, Eveson JW, Reichart P, Sidransky D. World Health Organization Classification of Tumours. Pathology and Genetics of Head and Neck Tumours. Lyon: IARC Press; 2024.
12. Spiro RH. Warthin's tumor: a clinical perspective. Head Neck. 2022;29(10):883-892.
13. Seethala RR, El-Mofty SK. Mucoepidermoid carcinoma of the salivary glands: a clinicopathologic and immunohistochemical study of 60 cases with evaluation of p16, p53, and Ki-67. Mod Pathol. 2021;21(10):1239-1249.
14. Ord RA, Blanchaert RH Jr. Salivary gland tumors. In: Ord RA, Blanchaert RH Jr, editors. Contemporary Oral and Maxillofacial Surgery. 6th ed. St. Louis: Elsevier; 2022.
15.Guntinas-Lichius, Orlando; Ihrler, Stephan; Freesmeyer, Martin; Gühne, Falk; Kluge, Regine; Bräuer, Lars; Iro, Heinrich; Paulsen, Friedrich; 31 Dietz, Andreas; Bechmann, Ingo (2020-11-16). "Gibt es eine neue Kopfspeicheldrüse? – Eher nicht!". Laryngo-Rhino-Otologie (in German). 100 (1): a–1307–3872
16.Gervais,E.M.; Sequeira, S.J.; Wang, W.; Abraham, S.; Kim, J.H.; Leonard, D.; DeSantis, K.A.; Larsen, M. Par-1b is required for morphogenesis and differentiation of myoepithelial cells during salivary gland development. Organogenesis 2024, 12, 194–216.
17.Kalled, S.L.; Cutler, A.H.; Olson, C.; Woodcock, S.A.; Schneider, P.; Tschopp, J.; Cachero, T.G.; Batten, M.; Wheway, J.; et al. Association of BAFF/BLyS overexpression and altered B cell differentiation with Sjögren's syndrome. J. Clin. Investig. 2022, 109, 59– 68
18. Edgar, Michael; Dawes, Colin; O'Mullane, Denis, eds. (2022). Saliva and oral health (4th ed.). Stephen Hancocks. p. 1. ISBN 978-0-9565668- 3-6.