

# **Oral Medicine**

## **Salivary gland diseases I**

**Lecture 17**

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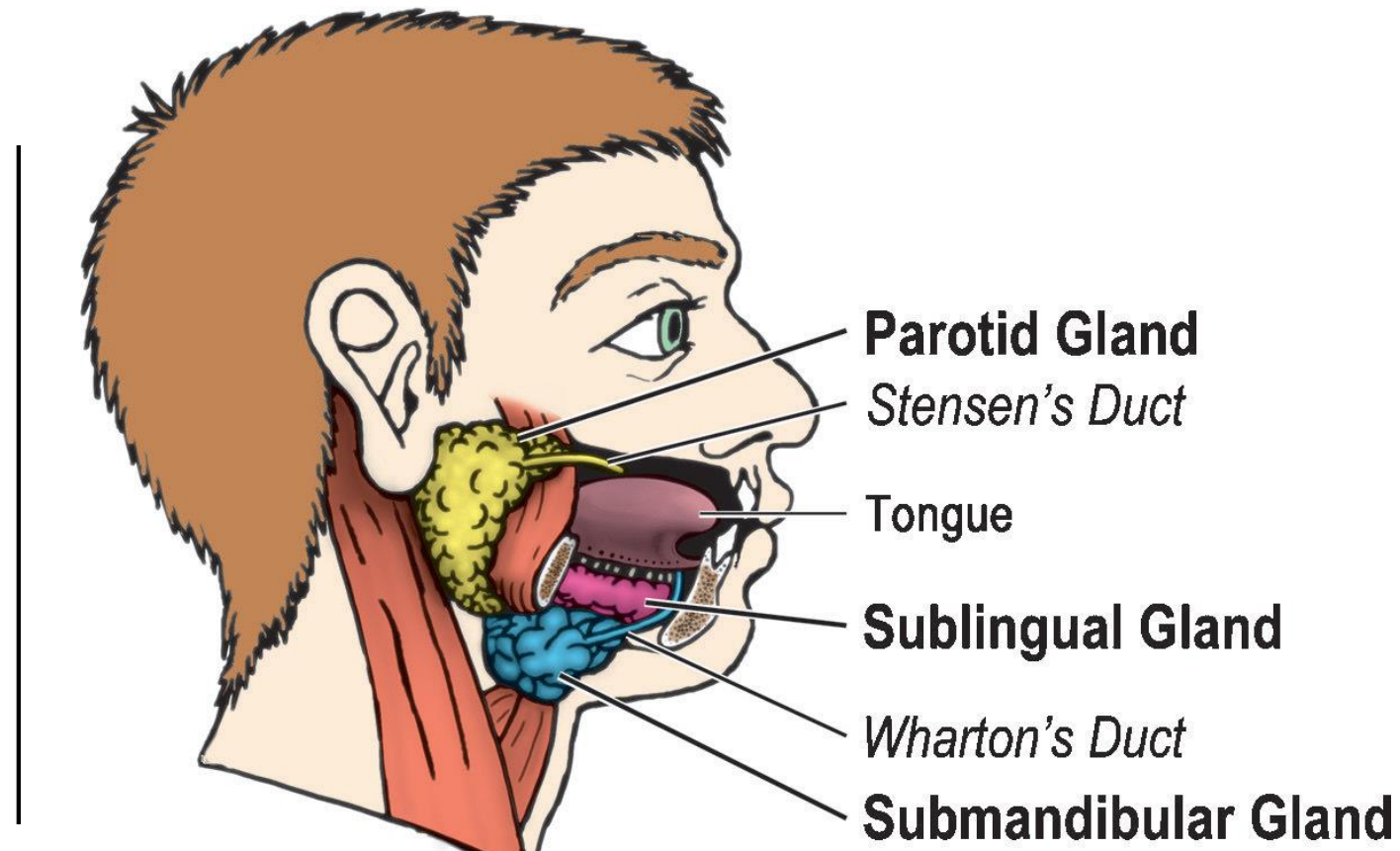
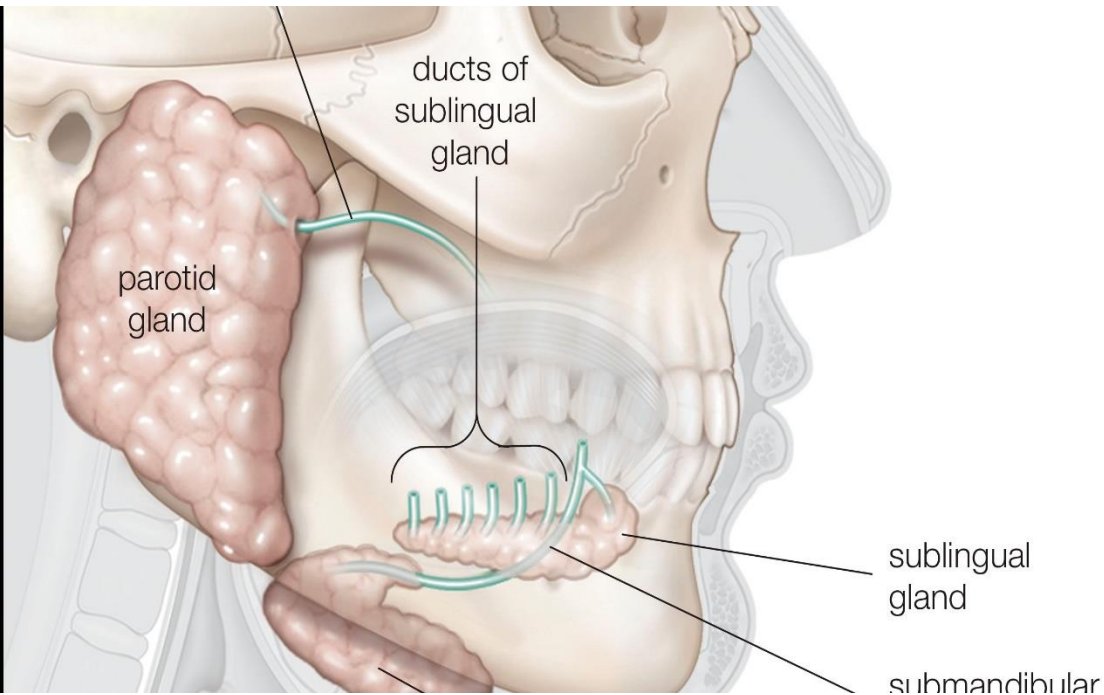
The salivary glands are exocrine glands, whose secretion flow into the oral cavity.

There are 3 pairs of large glands located extra orally known as major SG and numerous small glands widely distributed in the mucosa and submucosa of oral cavity known as minor SG.

The Major groups of salivary glands which are consisting of three major glands:

The parotid, submandibular and sublingual glands.

The parotid and submandibular glands drain into the mouth in a single long duct, while sublingual glands drain via many small ducts.



The major salivary glands can also be classified based on the dominant saliva producing acinar cell type: serous, mucous, or a mix of serous and mucous cells.

Serous cells produce a more watery, enzyme-rich saliva.

Mucous cells secrete a more viscous fluid with plentiful salivary glycoproteins known as mucins.

The parotid gland is composed primarily of serous cells. submandibular gland are a mix of mucous and serous types, while the sublingual and minor salivary glands are of the mucous type.

There are also between 600 and 1000 minor salivary glands named for the sites which they occupy (i.e., labial, buccal, lingual, palatal, retromolar area).

In addition, there are three sets of minor salivary glands of the tongue:

1. The glands of Weber, found along the border of the lateral tongue
2. The glands of von Ebner, surrounding the circumvallate papillae
3. The glands of Blandin and Nuhn, also known as the anterior lingual glands, found in the anterior ventral tongue.

Parotid saliva is secreted through Stensen's ducts, the orifices of which are visible on the buccal mucosa in the vicinity of the maxillary first or second molar.

Submandibular gland saliva is secreted through the submandibular duct (Wharton's duct), which drains saliva from each submandibular gland and exits at the sublingual caruncles on either side of the lingual frenulum.

The sublingual glands are drained by 8-20 excretory ducts called the ducts of Rivinus. The largest of all, the sublingual duct (of Bartholin) joins the submandibular duct to drain through the sublingual caruncle.

The sublingual caruncle is a small papilla near the midline of the floor of the mouth on each side of the lingual frenum.

Most of the remaining small sublingual ducts open separately into the mouth on an elevated crest of mucous membrane.



**Whole saliva:** is a hypotonic fluid relative to blood plasma and is composed of secretions from the major and minor salivary glands. It is composed of greater than 99% water and less than 1% proteins and salts. WS ma also contain variable amounts of gingival crevicular fluid, microorganisms, food debris, exfoliated mucosal cells, and mucus.

## **Salivary gland dysfunction**

Is commonly used to indicate decreased salivary flow or another quantifiable alteration in salivary performance.

**Xerostomia** is the most common presentation of salivary gland disease, which is a subjective complaint of dry mouth.

**Hyposalivation** refers to a quantified reduced salivary flow rate and may or may not be accompanied by xerostomia.

Similarly, xerostomia may or may not be associated with hyposalivation and can be a result of, e.g a change in salivary composition to a greater mucous content.

### **Hypersalivation (ptyalism)**

Refers to an increase in production of saliva and/or a decrease in oral clearance of saliva.

## **Causes of salivary gland hypofunction include:-**

1. Medications: xerogenic medications (including many antidepressants, anticholinergics, antispasmodics, antihistamines, antihypertensives, sedatives, diuretics, and bronchodilators)
2. Other agents (e.g., caffeine, alcohol, cigarette smoking)
3. Irradiation to the head and neck (i.e., external and internal beam radiation therapy)
4. Systemic disease (e.g., diabetes mellitus)
5. Psychological conditions (e.g., depression)
6. Malnutrition (e.g., bulimia, dehydration)
7. Autoimmune disease (e.g., Sjogren Syndrome)
8. Salivary gland masses.
9. Psychological conditions (e.g., depression, anxiety),

# Salivary gland Hypofunction Disorders

- Autoimmune:- Chronic graft-versus-host disease, Sjogren's syndrome
- Developmental :- Salivary gland aplasia
- Iatrogenic:- External beam radiation, Internal beam radiation
- Postsurgical :- (adenectomy, ductal ligation), Botox injection
- Inflammatory:- IgG4 - related disease (Mikulicz's disease)
- Infectious:- Viral infections {CMV, HIV, hepatitis C}
- Granulomatous: - Tuberculosis
- Medication-associated
- Neoplastic :- Benign and malignant salivary gland tumors
- Non-neoplastic :- Sialolithiasis
- Systemic conditions:- Anorexia nervosa, diabetes mellitus, chronic alcoholism, sarcoidosis

# Symptoms of Salivary Gland Dysfunction

1. Decreased fluid in the oral cavity and this may have an effect on mucosal hydration and oral functions.
2. Patients may complain of dryness of all the oral mucosal surfaces, including the lips and throat, and difficulty chewing, swallowing, and speaking.
3. Other associated complaints may include oral pain, an oral burning sensation, chronic sore throat and pain with swallowing.
4. The mucosa may be sensitive to spicy or coarse foods, limiting the patient's enjoyment of meals, which may compromise nutrition.
5. The need to sip liquids to swallow food, or difficulties in swallowing dry food have all been highly correlated with measurable decreases in secretory capacity.



# **Diagnosis of Salivary gland disorders**

## **- Past and Present Medical History**

Collection of the past and present medical history may reveal medical conditions or medications known to be associated with salivary gland dysfunction leading to a direct diagnosis (e.g., a patient who has received radiotherapy for a head and neck malignancy or an individual taking a tricyclic antidepressant).

More than 400 drugs with xerogenic potential have been identified including antidepressants, anticholinergics, antispasmodics, antihistamines, antihypertensives, sedatives, and bronchodilators and therefore a complete history of all medications being taken (including over-the-counter medications, supplements, and herbal preparations) is critical.

A thorough history is essential. If the past and present medical history reveals medical conditions like a patient who has received radiotherapy for a head and the neck malignancy.

If the patient's report of eye, throat, nasal, skin, or vaginal dryness, in addition to xerostomia, may be a significant indication of a systemic condition, such as SS.

# Clinical Examination

Extra and intra oral examination:-

Signs of salivary gland hypofunction may affect several areas of the oral cavity and mouth.

1. The lips are often dry with cracking, peeling, and atrophy.
2. The buccal mucosa may be pale and corrugated.
3. The dorsal tongue may appear smooth due to a loss of papillation and erythematous or may appear fissured.
4. Candidiasis
5. Viscous or scant secretions.
6. A cloudy exudates may be a sign of bacterial infection. The exudates should be cultured if it does not appear clear, particularly in the case of an enlarged gland.
7. Enlargement of salivary gland, that can be associated with a variety of inflammatory, infectious, or neoplastic and other conditions.
8. Function of the facial nerve when evaluating parotid tumors.
9. Tumors of the minor salivary glands are usually smooth masses located on the hard or soft palate.
10. Ulceration of the overlying mucosa should raise suspicion of malignancy.

# Investigation methods that used in determining the lesions of the salivary gland:

**1. Sialometry:** measure the amount of saliva produced in a certain time.

**2. Sialochemistry:** measure the composition of the saliva (electrolytes & enzymes), ex. Salivary amylase.

**3. Salivary Gland Imaging:-**

**a- Plain film radiography**

lateral oblique and anteroposterior (AP) projections are used to visualize the parotid glands.

A standard occlusal film can be placed intraorally to visualize a stone close to the gland orifice.

It is useful particularly for the visualization of radiopaque sialoliths and the evaluation of bony destruction associated with malignant neoplasms and it can provide a background for interpretation of the sialogram.

**b- Sialography:-** is the radiographic visualization of the parotid and submandibular salivary glands and ducts following retrograde instillation of soluble contrast material into the Stensen's or Wharton's ducts .

The ducts of the sublingual glands are too small for reliable injection of contrast medium. It provides the clearest visualization of the branching ducts and acinar end pieces.

It is the recommended method for evaluating intrinsic and acquired abnormalities of the ductal system:-

1. Ductal stricture
2. Obstruction
3. Dilatation
4. Ruptures
5. Identifying and localizing sialoliths

**The contraindications to sialography are:-**

- 1- Active infection
- 2- Allergy to contrast media



Oil-and water-based contrast media are available, (both containing iodine and therefore contraindicated in patients with iodine sensitivity).

Radiographic views for sialography include panoramic, lateral oblique, AP.

Following the sialographic procedure, the patient should be instructed to massage the gland and/or to suck on lemon drops to promote the flow of saliva and contrast material out of the gland.

After approximately one hour. If a substantial amount of contrast material remains in the salivary gland, follow-up visits should be scheduled until the contrast material elutes or is fully resorbed.

Incomplete clearing can be due to:-

- 1- Obstruction of salivary outflow
- 2- Extraductal or extravasated contrast medium
- 3- Collection of contrast material in abscess cavities
- 4- Impaired secretory function

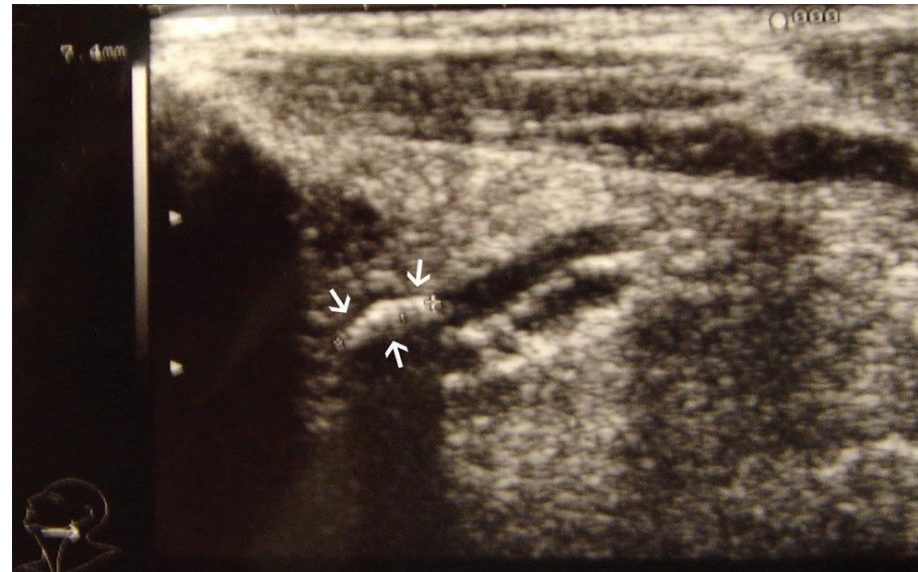
Sialography performed during active infection may lead to :-

1. Further irritate and potentially rupture the already inflamed gland.
2. The injection of contrast material might force bacteria throughout the ductal structure & worsen an infection.

## c- ULTRASONOGRAPHY (US)

### Advantages:

1. Initial evaluation of the salivary glands, especially in children and pregnant women
2. Evaluating for suspected sialolithiasis and salivary gland abscesses.
3. Differentiating between intra-and extraglandular masses
4. Used to distinguish focal from diffuse disease
5. Assess adjacent vascular structures and vascularity
6. Distinguish solid from cystic lesions
7. Guide fine needle aspiration biopsy (FNAB)
8. Perform nodal staging.
9. It can correctly differentiate malignant lesions from benign in 90% of cases



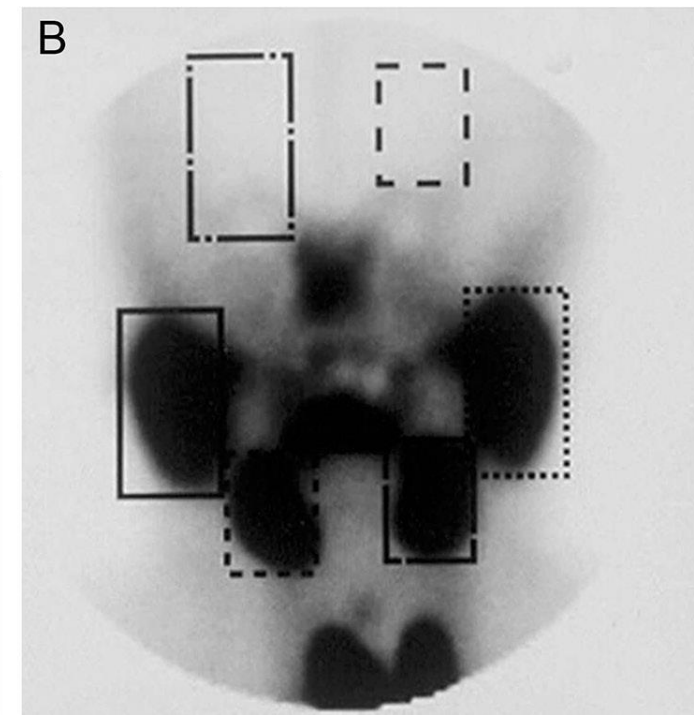
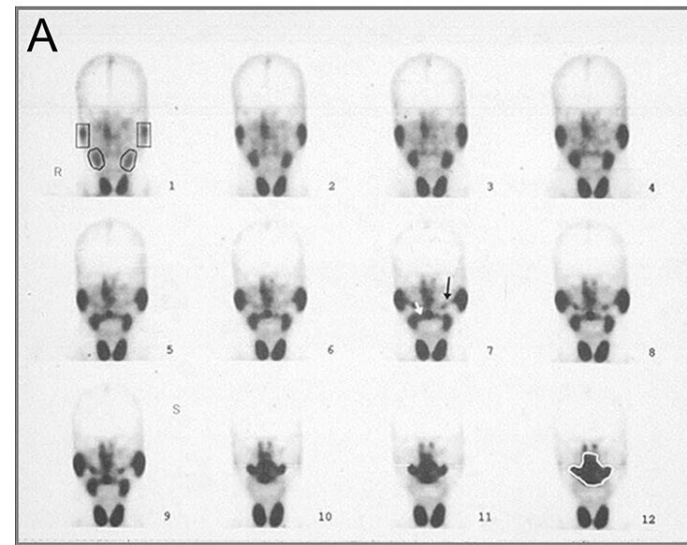
## d- Radionuclide Salivary Imaging

Scintigraphy with radioisotope technetium (Tc) 99m pertechnetate: is a dynamic and minimally invasive diagnostic test to assess salivary gland function and to determine abnormalities in gland up take and excretion.

It is taken up by the salivary glands (following intravenous injection), transported through the glands, and then secreted into the oral cavity.

Only the parotid and submandibular glands are visualized distinctly, as well as the thyroid gland. It has been used to aid in the diagnosis of:-

- 1- Ductal obstruction,
- 2- Sialolithiasis,
- 3- Gland aplasia,
- 4- Bell 's palsy,
- 5- Sjogren's syndrome.



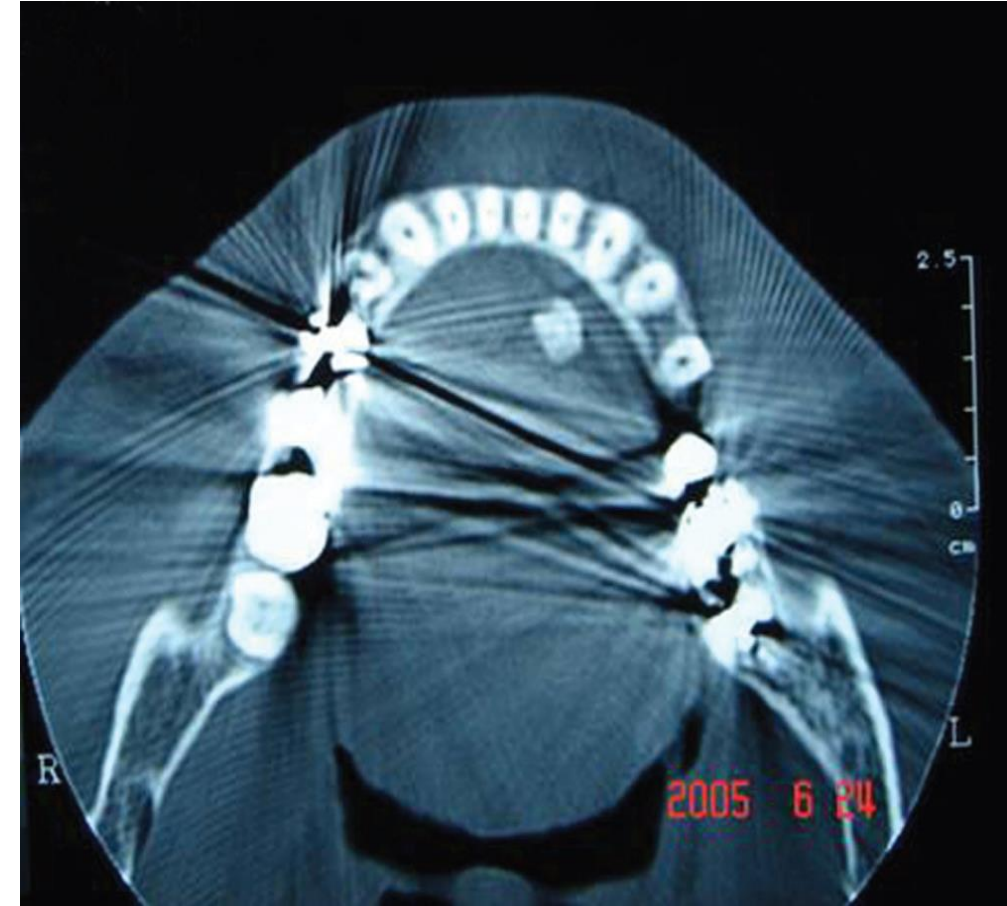
## e- CT and MRI

CT provides :

- Definition of cystic walls, making it possible to distinguish fluid-filled masses from abscess.
- For visualizing masses that are poorly defined on MRI.
- For patients who are unable to lie still long enough for adequate MRI (pediatric, geriatric, claustrophobic, and mentally or physically challenged patients).
- For patients for whom MRI is contraindicated.

The disadvantage of CT include:-

Radiation exposure, administration of iodine-containing contrast media for enhancement, and potential scatter from dental restoration.



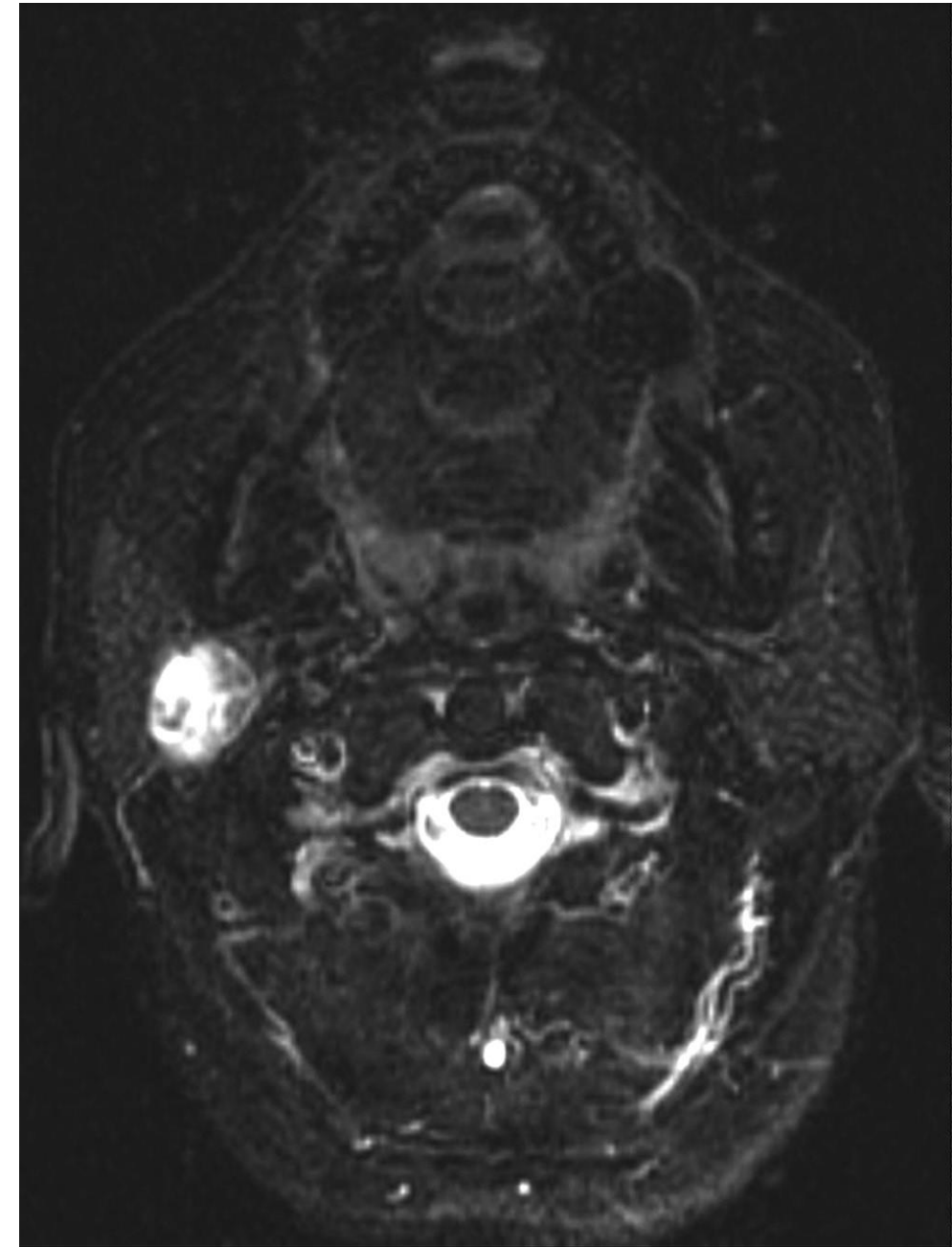


MRI provides images for:

Evaluation salivary gland pathology, adjacent structure, and proximity to the facial nerve.

MRI is contraindicated for:

1. Patients with pacemakers or implants such as aneurysmal bone clips. If the implant contains magnetic metal, an MRI can not be performed; however, dental implants are not magnetic and so are not contraindicated.
2. Patients who have difficulty maintaining a still position.
3. Patients with claustrophobia.



## **f- Cone Beam CT**

Cone beam CT (CBCT) is increasingly being employed in dento-maxillofacial imaging since it provides high spatial resolution of osseous structures at a lower dose of radiation than conventional CT.

Using a cone-shaped x-ray beam and two-dimensional detectors, the CBCT scanner collects volume data by means of a single rotation taking 9 – 40 seconds.

CBCT sialography provides several advantages over conventional sialography including:-

- 1- Three-dimensional reconstruction
- 2- Allowing for manipulation of image rotation
- 3- Slice thickness
- 4- Generation of various cross-sectional slices.

Overall, CBCT sialography appears to offer an improvement in imaging of salivary gland ductal system over conventional sialography.

#### **4. Salivary gland biopsy**

The labial minor salivary glands are most commonly biopsied since they provide the most accessible source of tissue, especially where SS is suspected.

#### **5. Serological Evaluation**

As in sjogren syndrome: antinuclear antibodies, rheumatoid factor and estimation of immunoglobuline ex. IgG.

Autoantibodies are present in the majority of SS cases:-

Elevated immunoglobulins (particularly IgG), Rheumatoid factor (RF), antinuclear antibodies (ANAs), and anti-SSA/Ro and anti-SSB/La are strongly indicative of SS.

The most proposed classification criteria for SS by the American College of Rheumatology (ACR) requires at least two of three criteria for case definition; one of which is a positive serum anti-SSA/Ro and/or anti-SSB/La or positive RF and ANA.

# SPECIFIC DISEASES AND DISORDERS OF THE SALIVARY GLANDS

## Developmental Abnormalities

- **Complete absence (aplasia or agenesis)** of salivary gland which is rare, although it may occur together with other developmental defects
- **Accessory ducts** are common and do not require treatment aberrant salivary glands are salivary tissues that develop at unusual anatomic sites.
- **Ectopic salivary glands** have been reported in a variety of locations, including the middle-ear, external auditory canal, neck, posterior mandible, anterior mandible, pituitary gland, and cerebellopontine angle. These are usually incidental findings and do not require intervention.
- **The Stafne bone defect (SBD; also known as Stafne bone cyst):-**  
Is an asymptomatic depression of the lingual surface of the mandible often associated with ectopic salivary gland tissue. However, it is not a true cyst as there is no epithelial lining. The most common location of the SBD is in the region of the third molar inferior to the mandibular canal

## **Diverticula**

Is a pouch or sac protruding from the wall of a duct. Diverticula in the ducts of the major salivary glands often lead to pooling of saliva and recurrent sialadenitis.

Diagnosis by sialography. Patients with diverticula are encouraged to regularly milk the involved salivary gland and to promote salivary flow through the duct.

## **Darier's Disease**

Salivary duct abnormalities have been reported in Darier's disease (also known as dyskeratosis follicularis).

Sialography of parotid glands in this condition revealed duct dilation, with periodic stricture affecting the main ducts.

Symptoms of occasional obstructive sialadenitis have been reported.

# **Sialolithiasis (Salivary Stones)**

Sialoliths (also termed salivary calculi or salivary stones) are typically calcified organic masses that form within the secretory system of the major salivary glands.

The etiologic factors favoring salivary stone formation may be classified into two groups:

## **1- Factors favoring saliva retention**

Irregularities in the duct system, local inflammation, dehydration, medications such as anticholinergics and diuretics

## **2-Saliva composition**

Calcium saturation, deficit of crystallization inhibitors such as phytate, Bacterial infection also promotes sialolith formation due to an associated increase in salivary pH favoring calcium phosphat supersaturation.

Salivary stones occur most commonly in the submandibular glands (80%–90%), followed by the parotid (5%–15%) and sublingual (2%–5%) and only very rarely occur in the minor salivary glands.

The higher rate of sialolith formation in the submandibular gland is due to:

1. The torturous course of Wharton's duct,
2. The higher calcium and phosphate levels of the secretion contained within
3. The dependent position of the submandibular glands that leaves them prone to stasis
4. The increased mucoid nature of the secretion.

## **Clinical Presentation**

Patients with sialoliths most commonly present with a history of acute, colicky pain and intermittent swelling of the affected major salivary gland during meals.

The degree of symptoms is dependent on the extent of salivary duct obstruction and the presence of secondary infection.

Salivary gland swelling will be evident upon eating since the stone completely or partially blocks the flow of saliva resulting in salivary pooling within the gland ductal system.

Since the glands are encapsulated and there is little space for expansion, enlargement causes pain. Swelling will subside when salivary stimulation ceases and output decreases.

Stasis of saliva may lead to infection, fibrosis and gland atrophy.

If there is concurrent infection, there may be expressible suppurative or non suppurative drainage and erythema or warmth in the overlying skin.

**Complications from sialoliths include:-**

- Acute sialadenitis,
- Ductal stricture,
- Ductal dilatation,
- Fistula and a sinus tract,
- Ulceration in the tissue covering the stone in chronic cases.





## Diagnosis

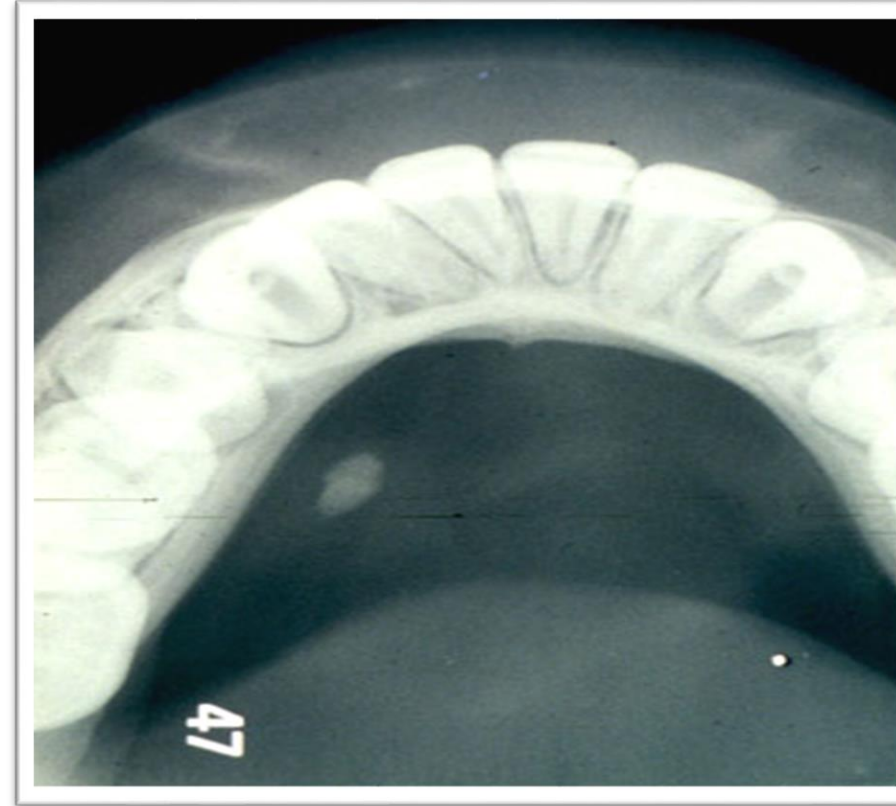
Plain film radiographs are helpful to visualize sialoliths; this is most useful in cases of suspected submandibular sialolithiasis, where an occlusal radiograph taken at 90 ° from the floor of the mouth is recommended.

However, other calcified entities such as phleboliths (stones that lie within a blood vessel), calcified cervical lymphadenopathy, and arterial atherosclerosis of the lingual artery can also appear on these films.

Stones in the parotid gland can be more difficult to visualize for several reasons.

Due to the Superimposition of other anatomic structures, sialoliths may be obscured and therefore the choice of radiographic views is important.

An AP view of the face or an occlusal film placed intraorally adjacent to the duct may be useful in these cases.



Contrast sialography using iodinated contrast media may be used to visualize the parotid and submandibular ductal systems.

Sialography can also aid in differentiating calcified phleboliths from sialoliths since the former lie within a blood vessel, whereas the latter occur within the ductal structure.

Limitations of this modality include the use of ionizing radiation, dependence on successful ductal cannulation, pain during and after the procedure and potential allergy to the contrast medium. The use of contrast sialography is also contraindicated in the presence of acute sialadenitis.



Ultrasound (US) is widely used as a first-line imaging modality to assess the presence of salivary gland calculi.

Transoral sonography using an intraoral approach has been employed as an imaging modality in suspected sialolithiasis. US is non-invasive, less costly than other imaging, and may be able to visualize radiolucent calculi.

## **Treatment**

- During the acute phase of sialolithiasis, therapy is primarily supportive.
- Standard treatment during this phase often involves the use of analgesics, hydration, antibiotics, and antipyretics, as necessary.
- Use Sialogogues (is a drug or substance that increases the flow rate of saliva e.g, pilocarpine, and cevimeline ), massage and heat applied to the affected area may also be beneficial.
- Stones at or near the orifice of the duct can often be removed trans-orally by milking the gland, but deeper stones require intervention with conventional surgery or sialendoscopy placed to maintain patency of the duct.
- Extracorporeal shock wave lithotripsy (ESWL) also allows for fragmentation of large sialoliths of any size or location.

# **Extravasation and Retention (Mucoceles and Ranulas)**

## **Mucocele**

Is a clinical term that describes swelling caused by the accumulation of saliva at the site of a traumatized or obstructed minor salivary gland duct.

Mucoceles can be classified histologically as extravasation types or retention types.

The extravasation mucocele does not have an epithelial lining or a distinct border.

The formation of an extravasation mucocele is believed to be the result of trauma to a minor salivary gland excretory duct. Laceration of the duct results in pooling of saliva in the adjacent submucosal tissue and consequent swelling.

The retention type mucocele is caused by obstruction of a minor salivary gland duct often by sialolith, periductal scarring or tumor.

The blockage of salivary flow results in the accumulation of saliva and dilation of the duct.

## Clinical Presentation

Mucoceleles often present as discrete, painless, smooth-surfaced, fluctuant swellings that can range from a few millimeters to a few centimeters in diameter.

Superficial lesions frequently have a characteristic blue hue. Deeper lesions can be more diffuse, covered by normal-appearing mucosa without the distinctive blue color.

The lesions vary in size over time; superficial mucoceleles are frequently traumatized, causing them to drain and deflate. Mucoceleles that continue to be traumatized are most likely to recur and may develop surface Ulceration.

Extravasation mucoceleles most frequently occur on the lower lip, where trauma is common.

The buccal mucosa, tongue, floor of the mouth, and retromolar region are other areas may be found. It most commonly seen in children and teenagers.



# Treatment

Conventional definitive surgical treatment of mucoceles involves removal of the entire lesion along with the feeder salivary glands and duct. Incomplete removal of the mucocele may result in recurrence.

Surgical management can be challenging since it can cause trauma to adjacent minor salivary glands and lead to the development of a new mucocele.

Alternative treatments that have been explored with varying degrees of success include electrosurgery, cryosurgery using liquid nitrogen, laser surgery and micromarsupialization, intralesional injections of corticosteroids, and sclerotherapy.

## Ranula

A form of mucocele located in the floor of the mouth is known as a *ranula*. named due to its resemblance to the underbelly of a frog (Latin *rāna* = frog).

Ranulas are believed to arise from the sublingual gland. The possible causes include:-

- 1- Mechanical trauma to its ducts of Rivinus, resulting in extravasation of saliva.
- 2- An obstructed salivary duct or a ductal aneurysm.

The predilection of ranulas in the sublingual glands has been thought to be due to the gland's continuous salivary secretion that precludes effective sealing of the mucous extravasation via fibrosis, in contrast to salivary secretion in the parotid and submandibular glands, which is dependent on gustatory stimulation.

In addition, particular anatomic variations of the ductal system of the sublingual gland may contribute to the formation of ranulas.

Ranulas are most common in the second decade of life and in females.

Oral ranula remains confined to the sublingual space.

A congenital predisposition toward development of ranulas has been suggested, particularly in those of Asian descent.

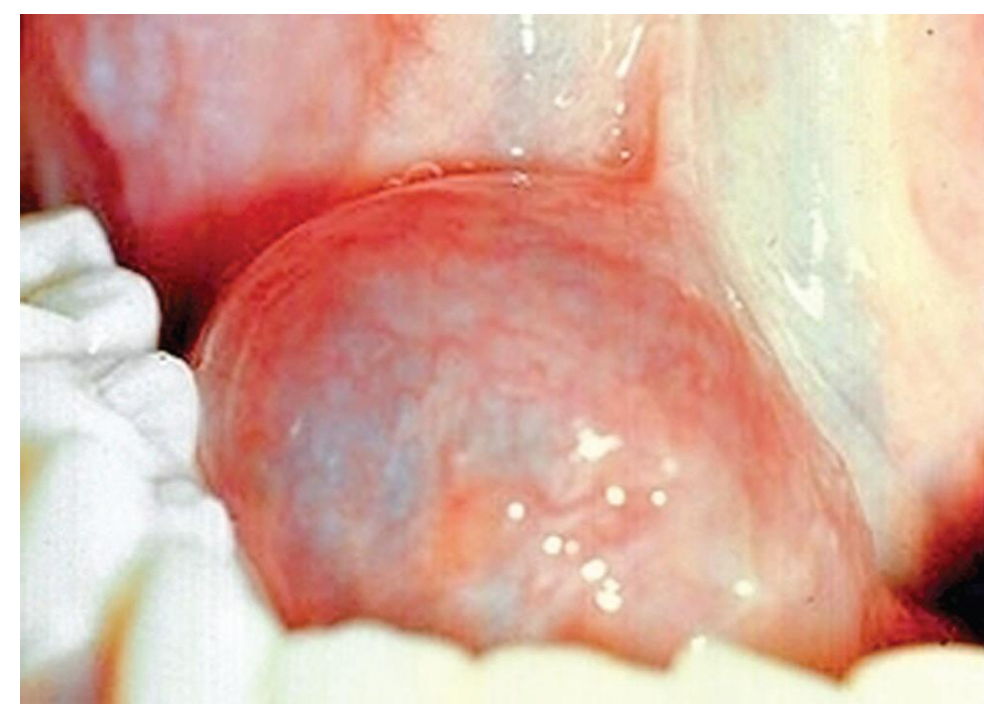
## Clinical Presentation

The most common presentation of the “oral” ranula is a painless, slow-growing, fluctuant, movable mass located in the floor of the mouth.

Usually, the lesion forms to one side of the lingual frenulum; however, if the lesion extends deep into the soft tissue, it can cross the midline.

As observed with mucoceles, superficial ranulas can have a typical bluish hue, but when the lesion is deeply seated, the overlying mucosa may have a normal appearance.

The size of the lesions can vary, and larger lesions can cause deviation of the tongue.





## **Diagnosis**

Imaging to diagnose an oral ranula may not be necessary due to its characteristic clinical appearance, but to rule out other cystic lesions (e.g., thyroglossal duct cyst & epidermoid cyst)

FNA, ultrasound, CT with contrast, and MRI have been used.

Ultrasound has been recommended for oral ranulas.

## **Treatment**

The most predictable method of eradicating both oral and plunging ranulas is to remove the associated sublingual gland because this will almost certainly eliminate recurrences.

Sublingual gland adenectomy combined with intraoral excision of the ranula is suggested for the simple ranula, other procedures used for the treatment of ranulas have included simple excision, marsupialization, injection of the sclerosing agent, silver nitrate, and botulinum toxin (BoNT) all with varying rates of success.

## **Postsurgical complications include:-**

Lesion recurrence, sensory deficits of the tongue, and damage to Wharton's duct.

Frequency of recurrence is related to the surgical technique selected and has been reported as 67% with marsupialization, 58% with excision alone, and 1% with sublingual gland Excision.