Salivary glands

Physiology

Salivary glands secrete saliva of which the functions are:

- Lubrication
- Digestion
- Antibacterial
- Antiviral
- Act as a buffer
- Teeth protection
- Tissue coating
- Mineralisation

Salivary glands are divided into major and minor glands. Major salivary glands in the Head and Neck are the parotid, submandibular and sublingual glands, found bilaterally. Minor salivary glands are scattered through the mucosal lining of the upper airways and is most commonly found on the hard and soft palate, followed by the buccal mucosa, retro-molar trigone, and lips. The parotid glands are serous, submandibular gland mixed, and sublingual and minor salivary glands mucous in nature respectively. The parotid produces roughly 0.7 ml/min/gland of saliva and the submandibular 0.6 ml/min/gland respectively.

Various diseases affect the salivary glands and only some of the more common diseases are discussed.

Salivary gland pathologies

Inflammatory	Acute	Bacterial	Sialadenitis	Common
				Neonatal
				Recurrent parotitis of childhood
			Abscess	
			Lymphadenitis	
		Viral	Mumps	
			HIV	
			Other	
	Chronic	Obstructive	Sialectasis	
			Sialolithiasis	
			Mucocele or cyst	Acquired
				Retention cyst
		Granulomatous	TB / NTB	
			Actinomycosis	
			Cat-scratch	
			Sarcoid	
			Toxoplasmosis	
			Fungi	
		Necrotising sialometaplasia		
Neoplastic	Tissue type	Epithelial (majority)	Benign	Pleomorphic adenoma
				Warthin's tumour
				Others
			Malignant	SCC
				Adenoid cystic
				Mucoepidermoid carcinoma

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				Acinic cell carcinoma
				Adenocarcinoma
				Salivary ductal carcinoma
				Others
		Mesenchymal (more common in children)	Benign	Myomas
			Malignant	Sarcomas
		Haematolymphoid (more common in HIV positive)	Lymphoma	
			Lymphangioma	
			Vascular malformations	
Auto-immune	Sjogren's disease			
	Benign lymphoepithelial cysts			
Trauma	Penetrating			
	Blunt			
	Radiation			
Congenital	Branchial cleft and pouch	First	Work's type I and II	
		Second	In tail	
	Dermoid cyst			
	Ductal cyst			
	Agenesis			
Pseudohypertrophy	Masseter hypertrophy			
	Old age			
	Mass in parapharyngeal space			
	Teeth pathology			
Metabolic diseases	Obesity			
	Diabetes			
	Thyroid			
	Cushing's disease			
	Bulimia			
	Uraemia			
Drugs	Isoprenaline			
	Thio-uracil			
Allergies				

Acute sialadenitis

Acute bacterial sialadenitis

Acute bacterial sialadenitis occurs most commonly in the parotid gland. It typically occurs in the setting of elderly, sick patients, post-operative, and dehydration. It is mostly an ascending bacterial infection due to *Staph Aureus, Streptococcus, Haemophiles Influenza, Pepto streptococci, Bacteroides,* and *Fusobacterium species*. It is acutely painful and even more so when eating. The parotid gland is enlarged with skin signs of inflammation such as erythema and warm to touch. Bimanual examination reveals puss draining from Stenson's duct in up to 75% of patients. Bilateral involvement occurs in 25%. Usually and ultrasound is needed to confirm or exclude abscess formation. Treatment consists of pain relief, rehydration, antibiotics, local applications of heat, massage, aspiration, and draining of an abscess if present.

Acute viral sialadenitis

Mumps

Mumps is a n acute non-suppurative parotitis caused by *paramyxovirus and other viruses*. More than 85% are younger than 15 years of age. There is no natural reservoir, and infection spreads with new cases. Incubation period is 2-3 weeks which allows for this, and the infection period is considered to be 2 days before to 5 days after the onset of parotitis.

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There is typically a viral prodrome which is followed by parotitis, otalgia, dysphagia, and rarely trismus. The parotitis starts unilaterally but will affect the other parotid gland in 75% of causes within 5 days. The swelling usually peaks at day 1 – 3. The diagnosis can be made with a PCR on fluids or IgM on serum. Treatment consists of rest, oral hygiene, and rehydration. Complications, although rare, can include deafness, orchitis, meningitis, pancreatitis, and nephritis.

There is a vaccine for mumps, and the disease was basically eradicated in the USA. However, since 2006 there has been a steady decrease in vaccine uptake with a coinciding rinse in the number of mumps cases. A useful link from the CDC is: Mumps.

Chronic sialadenitis

Chronic sialadenitis follows an inciting incident, usually after acute sialadenitis, and leads to sialolithiasis and sialectasis. It occurs most commonly in the parotid glands and presents with episodic pain usually with eating and inflammation. Upon examination little saliva can be milked from the gland. If conservative measures fail, surgery is indicated to remove the gland. Complication of chronic sialadenitis includes lymphoepithelial lesions (formally Mikulicz disease), Kuttner's tumours, and duct carcinoma.

Sialolithiasis

Stones are far more common in the submandibular glands compared to the others. The reasons include:

- High mucin content
- Alkaline pH
- Higher concentration of calcium and phosphate
- Long length of duct
- Dependant position of duct and that it needs to pump against gravitation

Once stones start forming, it leads to duct destruction (sialectasis), which in itself leads to a higher incidence of sialadenitis. This leads to a self-perpetuating cycle of repeated stones and infection, and then chronic sialadenitis.

Stones can be managed with:

- Non-surgical interventions
    - Sialagogues
    - Heat applications
    - Massaging of the gland
    - Rehydration
    - Antibiotics
- Surgery
    - Removal of stone
    - Removal of gland
    - Lithotripsy
    - Sialoendoscopy

HIV associated salivary gland diseases

Parotid pathology is common in the HIV positive patient. The most common diseases includes:

- Bilateral enlargement especially early in the disease
- Xerostomia

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- Benign lymphoepithelial cysts
- Lymphomas
- Kaposi sarcomas

Benign lymphoepithelial cyst (BLEC) associated with HIV can be difficult to distinguish from other cystic lesions of which some will be neoplasms. In general, HIV associated BLEC will be bilateral, multiple, and show response on ARV medications. BLEC can also be manage with sclerotherapy, such as 90% alcohol.

Salivary gland tumours

Major salivary gland tumours are rare and account for 3-10% of head and neck tumours. Minor salivary gland tumours (MSGT) are even more uncommon and only comprise 9-23% of all salivary gland tumours. According to Globocan 2020 data, which reports on estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, salivary glands tumours were responsible for 55 583 out of 19.3 million cancers (0.3%) (Global Cancer Observatory). This places them at 28th out of 36 tumours included in the report. Put into perspective, the incidence is very similar to anal carcinomas, but vastly smaller than female breast and lung carcinomas which have more than 2.2 million cases per year respectively. According to Stats South Africa 135 males and 117 females had salivary gland tumours in 2019.

Broadly speaking, salivary gland tumours are divided into epithelial, mesenchymal, and haematolymphoid tumours. The most common being epithelial tumours (>80%). Currently the 5th edition of the World Health Organization classification of salivary gland tumours is used. It includes newly established pathological entities due to the diverse nature of salivary gland tumours. Furthermore, it states that molecular testing of salivary gland tumours for differential diagnostic accuracy and appropriate clinical management is becoming routine.

Classic teaching stipulates that the chance of a salivary gland tumour being malignant increases from major to minor salivary glands. Dictums such as 80% of salivary gland tumours occur in the parotid glands, 80% of parotid gland tumours are benign, and 80% of benign parotid gland tumours are pleomorphic adenomas are commonly taught. The inverse is taught with regards to MSGT, with malignancy rates varying from 50-80%. Two leading textbooks report the malignant incidence as follows:

Table 1. Incidence of salivary gland tumours being malignant.

	Scott Brown*	**Cummings****
Gland	**Malignant**	**Malignant**
Parotid	15-32%	25%
Submandibular	41-45%	43%
Sublingual	70-90%	
Minor salivary glands	80%	85%

* van der Poorten V, Bradley P. Scott-Brown's Otorhinolaryngology and Head and Neck Surgery. Eight. Vol. 3. Boca Raton; 2018.

** Flint PW, Francis HW, Haughey BH, Lesperance MM, Lund VJ, Robbins KT, et al., editors. Cummings otolaryngology: head and neck surgery. Seventh edition. Philadelphia, PA: Elsevier; 2021

However, our data and published articles from South Africa and other countries does not support above mentioned dictums. In general, it clearly confirms that in countries with increased sun exposure, the most common malignant parotid tumours are metastatic squamous cell carcinomas from skin primaries. Furthermore, it is interesting to note that the studies from Cape Town and Australia both had a very high prevalence of metastatic melanomas. Another difference is the incidence of malignancy which were 8.95% in the Nottingham study from the UK (1), 27% in the Cape Town study (2), 28.73% in our study, and a staggering 43% in the Australian study (3). Other important findings in the Australian study were increasing age ($p < .001$), fewer parotidectomies for inflammatory lesions ($p < .001$), reduced incidence of mucoepidermoid carcinoma ($p =$

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.048), increasing incidence of parotidectomy for cutaneous malignancies ($p < .001$), and reduced facial nerve sacrifice ($p = .034$). Over the four studies, the prevalence of mucoepidermoid carcinomas decreased from 28.57% in the Nottingham study, to 16.85% in Cape Town, 13.46% for our study, and 4.54% in the Australian study. A possible explanation for the reduced incidence of mucoepidermoid carcinomas is improved immunohistochemistry and that a sizeable portion of these were reclassified as salivary duct carcinoma or poorly differentiated metastatic squamous cell carcinoma. However, once skin metastases such as squamous cell carcinomas and melanomas are excluded, it was the most common primary epithelial malignancy in all four studies. Our study also has a more than double the prevalence of carcinoma ex pleomorphic adenomas (11.54%) compared to the next highest of 5.19% (Nottingham study).

With regards to MSGT we did not see the high malignant incidence that is frequently reported in the literature. Benign and malignant minor salivary gland tumours' incidence was almost equal at 46.46% and 53.54% respectively. Pleomorphic adenomas remain the most common minor salivary gland tumour (38.38% of all tumours and 82.61% of benign MSGT) and occurs most commonly in the palate. In general, most minor salivary gland tumours and benign salivary gland tumours occurred in the palate. We did show an unusually high incidence of polymorphous (low-grade) adenocarcinoma which was also the most common malignant minor salivary gland tumour. Interestingly, this was reported in another study from South Africa. Primary sites other than palate and lips should raise the suspicion of malignant minor salivary gland tumour.

In general, the following symptoms and signs will point to a malignant tumour:

- Fast growth
- Pain
- Nerve involvement
- Lymphadenopathy
- Infiltration of skin, muscles, bone

It is best to refer patients to an ENT specialist if you suspect the patient having a salivary gland neoplasia.

A retrospective descriptive study by us, and all pooled data from South Africa showed the following. Our study showed that 55.25% of all tumours occurred in the parotid gland, 14.19% in the submandibular gland, and 30.56% in the minor salivary glands. The incidence of benign tumours was 71.02% in the parotid, 78.95% in the submandibular gland, and 46.46% in minor salivary gland. Pleomorphic adenomas were the most common tumour, accounting for 53.60%, 78.95%, and 38.38% of all parotid, submandibular, and minor salivary gland tumours respectively. All tumours occurred more commonly in females and in general, benign tumours occurred statistically significantly earlier compared to malignant tumours. Warthin's tumour was the second most common parotid tumour (18.75%) followed by squamous cell carcinoma (5.68%). Our series demonstrated a high incidence of polymorphous adenocarcinomas (15.15%) in minor salivary gland tumours followed by acinic cell carcinomas (14.14%)

Our results combined with published studies from South Africa showed that 68.49% of all salivary gland tumours are benign and 31.51% malignant. The distribution between salivary glands showed that 58.49% occurred in the parotid gland, 19.95% in the submandibular gland and 21.56% in minor salivary glands. In parotid gland tumours (n=583) 71.18% were benign and 28.82% malignant, for submandibular glands (n=125) 79.2% were benign and 20.8% malignant, and minor salivary glands (n=1037) 62.2% were benign and 38.8% malignant. In this study, no cases of sublingual gland tumours were found.

Among parotid gland tumours, 50.43% were pleomorphic adenomas, 8.92% Warthin's tumours, 5.66% mucoepidermoid carcinomas, 4.29% squamous cell carcinomas, and 3.60% acinic cell carcinomas. Seventy-five percent of all submandibular tumours were pleomorphic adenomas. Of the minor salivary gland tumours,

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48.31% where pleomorphic adenomas, 11.09% adenoid cystic carcinomas, 8.29% mucoepidermoid carcinomas, and 7.52% polymorphous adenocarcinomas.

It is clear from the data that salivary gland tumours (SGT) in SA does not follow the 80% rule especially with regards to the incidence of pleomorphic adenomas in parotid glands (only 50% in SA) and the incidence of malignant MSGT (only 40% in SA). Consolidating all the data from SA, it showed that 70% of all SGT are benign and 30% malignant. 60% of tumours occurred in the parotid gland, 20% in the SMG and 20% in MSG. The proportion of benign versus malignant for parotid glands were 70% versus 30%, for SMG 80% versus 20%, and for MSG 60% versus 40% respectively.

Special investigations

Various special investigations can be conducted, of which the most important are:

- Radiology
    - Sialography
    - CT
    - MRI (Preferred to CT for imaging the salivary glands)
    - Ultrasound
- Histology / Cytology
    - FNAC
    - Core needle biopsies
- Sialoendoscopy

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