



Saliva: A Biological Fluid and Its Focal Role in Clinical Prosthodontics

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ABSTRACT:

Saliva is a complicated fluid made up of glandular discharges from the salivary canal. The tissues of the oral cavity are in constant contact with saliva. This biological fluid aids in lubrication and digestion. The environment of the oral cavity to a large degree is created and regulated by saliva. The aberrant function and secretion of saliva can readily be used to diagnose any ailment or disease's symptoms. Thus, it's critical to understand salivary gland secretion and function. This article's goal is to explore the elements, their roles, how they affect diagnosis, and the implications for prosthodontics.

INTRODUCTION:

The bodily fluid that is least understood and valued is saliva. It is a complicated fluid made up of glandular discharges from the salivary canal.

Saliva is always in contact with the tissues inside the oral cavity. This secretion is crucial and one of the most significant factors affecting the preservation of oral equilibrium. Nonetheless, this modest secretion is essential to the health of our oral tissues, allowing for articulation, digestion, and swallowing.[1]

Changes in quantity and quality of saliva can have a negative impact on dental health and can cause an array of concerns. Therefore, it is imperative that dentists have a fundamental knowledge of saliva and the glandular role that it serves. This article emphasizes the composition function, dysfunctions and its significance in clinical removable prosthodontics.

SALIVA FORMATION AND ITS SECRETION

Only 10% of the secretion is produced by the 200–400 tiny salivary glands throughout the oral mucosa, excluding the gums and the anterior portion of the hard palate. Three pairs of salivary glands—parotid, submandibular, and sublingual—among the major glands are responsible for 90% of saliva production.[2]

These glands can also be classified in terms of the type of secretion produced as serous, mucus, and mixed. The amount of saliva secreted by the major and minor glands is referred to as whole saliva.

Minor salivary glands contribute significantly to the lubrication of the oral mucosa because of their high protein content. Unlike some other minor salivary glands which are composed exclusively of mucous cells, parotid glands are serous and produce water like secretions. Submandibular and sublingual glands are



mixed. Acinar cells are responsible for the production of the primary saliva. The ductal cells are responsible for further modifications of saliva until it is secreted in the mouth.

On the whole, saliva is a clear, slightly acidic mucinous-serous secretion composed of various electrolytes, small organic substances, proteins, peptides, and polynucleotides.[3]

The normal daily production of saliva varies between 0.5 and 1.5 liters.

Salivary flow is measured from the individual glands as gustatory and resting secretions. [4] Unstimulated saliva (resting flow - NO external stimulus) and stimulated saliva (external stimuli) are the two categories used to describe this saliva flow. Stimulated saliva flow can occur in response to various stimuli such as gustation (taste), tactile, olfaction (smell), mechanical and pharmacological response.

About 0.3–0.4 ml of unstimulated saliva are produced every minute. This rate rises to approximately 0.4 – 0.5ml / min when eating, chewing, and other stimulating activities occur, and drops to 0.1 ml / min

when sleeping. This amply illustrates that salivary secretion rates adhere to a biological rhythm or pattern. [5]

Serous glands, of which the parotid glands are a subtype, account for up to 20% of the total unstimulated salivary volume. [3,6] Mixed serous and mucous glands comprise the submandibular and sublingual glands. Of the entire unstimulated salivary volume, the submandibular and sublingual glands account for 60% and 5%, respectively. A component of serous gland secretions is ptyalin, an enzyme that aids in digestion. Lubrication is aided by the combined secretions of mucous and serous glands. This total regulation of salivary secretion or flow takes place through the sympathetic and parasympathetic branches of the autonomic nervous system. [7]

Saliva is isotonic to plasma when it forms in the gland, but it turns hypotonic when it passes through the ducts.

SALIVA AND ITS CONSTITUENTS

Saliva constitutes of 99.5% of water and 0.5% of solid constituents containing a variety of

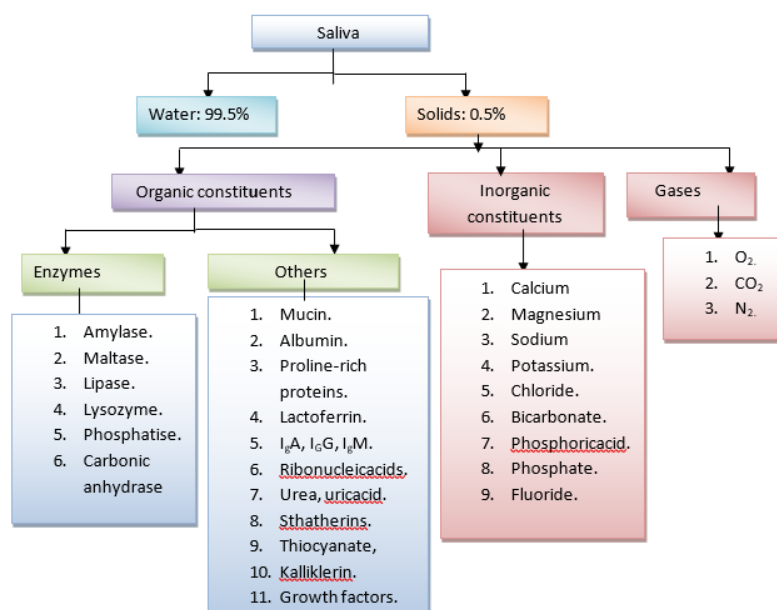


Figure 1: Saliva and its constituents.



electrolytes, digestive enzymes, immunoglobulins, antimicrobial factors, mucosal glycoproteins sugars such as glucose. The exact role of individual salivary constituents is not known. [8-10]

Saliva's composition and secretion rates vary according to various stimuli and from person to person. Given that saliva has buffer mechanisms that keep the acid-base balance in check, its pH ranges from 6.7 to 7.4, which is extremely close to neutral.

As a key salivary buffer, bicarbonate functions. While saliva that has been stimulated can have a pH of 8, the buffers keep saliva at resting at 5.7 and 6.2. [11] For example, consuming dry food causes an increase in watery serous secretions, and the amount can double when pharmaceutical medicines are administered. [12] Salivary concentration increases in conjunction with increased salivary flow and decreases with decreased salivary flow rates, leading to low pH and buffering capability. [10]

FUNCTIONS:

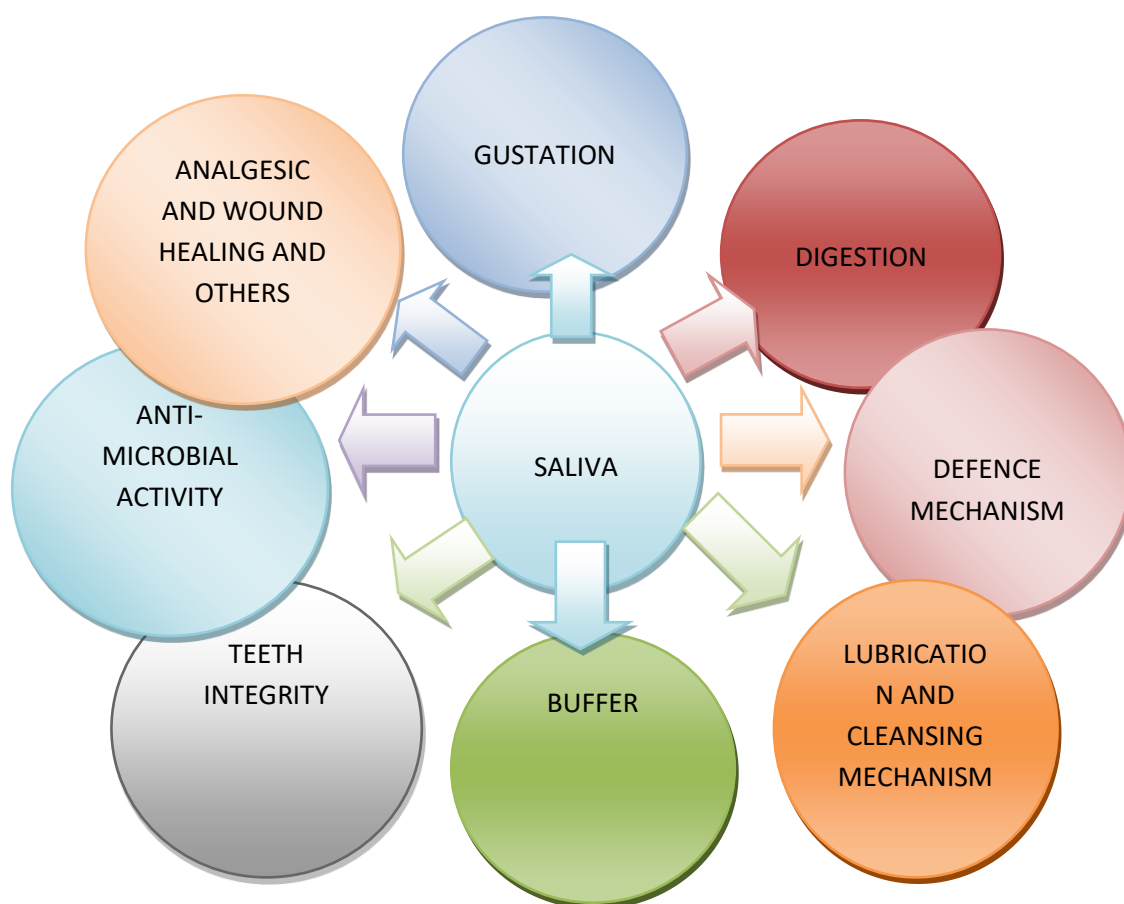


Figure 2 : Functions of Saliva

The defence of the intraoral structures against damage from a variety of pathogenic microorganisms and mechanical or chemical irritants is greatly aided by saliva.

Gustation (or) Taste sensation:

Different flavours can be perceived by the gustatory buds due to saliva's hypotonicity and ability to dissolve things. The development and maturity of gustatory buds appear to require the salivary protein gustin. [3]

Digestion:



The first digestion of a meal bolus is carried out by saliva. The presence of the digestive enzyme α -amylase/ptyalin is primarily responsible for digestion; it gets activated by Cl^- anions present in saliva. [13] Its role is to separate the starch into its constituent maltose, maltotriose, and dextrans. [14]

Defence mechanism:

The mucous membrane surface of the mouth is shielded by salivary mucins (MUC) from irritants and poisons found in food and stimulants. The mouth is protected by these compounds through a variety of methods influenced by distinct polymer architectures, as demonstrated by recent investigations. Initially, mucus might alter the position and retention of salivary proteins, enhancing the mouth's defenses.

Furthermore, MUC7 and MUC5B may interact with oral cavity microbes to lower their pathogenicity and/or accelerate their evacuation [15].

The healing of mucous membrane wounds and abrasions is aided by elements like neutral pH and the presence of Ca^{2+} and Mg^{2+} ions.

Lubrication and cleansing mechanism:

These mucins aid in lubrication that assist in deglutition, mastication and articulation. Through the formation of a protective protein coating known as pellicle, saliva helps remove bacteria, food particles, and hazardous byproducts of bacterial metabolism from the oral cavity and tooth surfaces. [11,16]

Buffering mechanism:

The three buffer systems—phosphate, protein, and bicarbonate—found in saliva aid in preserving the mouth's pH range of 6.0 to 7.5.

Bicarbonate buffer is the most contributing of the three buffer systems. It is the crucial buffer for saliva that is stimulated, whereas the phosphate buffer system is for saliva that is not stimulated. The buffering mechanism functions assertively by denying the ideal environmental conditions to potentially harmful microbes, thus preventing their entry.

It is important to note that Sialin, a peptide found in saliva, plays a crucial role in promoting oral health by increasing the pH of the biofilm after exposure to fermentable carbohydrates. Another salivary buffer called urea, when digested by bacterial ureases, releases carbon dioxide and ammonia, which accelerates the growth of biofilm. [16]

Integrity of tooth:

By regulating demineralization and remineralization processes, saliva plays a critical role in preserving the physical-chemical integrity of dental enamel.

Under normal physiologic conditions the saliva is oversaturated with calcium hydroxyapatite, which prevents dental demineralization

Submandibular salivary gland secretions, for example, have roughly 50% more calcium than parotid gland secretions. [17]

Thus, it has been hypothesized that the differences may account, in part, for the caries resistance of the mandibular incisors.

Fluoride anions present in saliva aid in preserving tooth integrity through their anti-cariogenic properties. [13]

Antimicrobial activity:

Saliva consists of specific and non specific defensive factors. Specific defensive factors include immunoglobulins: IgA (affecting phagocytosis of streptococci by leukocytes), IgG (together with IgA slow down the formation of tartar), and IgM (partially produced by the parotid, their presence indicates the existence of acute inflammation).

In the group of nonspecific defensive factors, we can distinguish enzymes and bactericidal substances, such as lysozyme, lactoferrin, histatins, mucins, and salivary peroxidase. [18]

lactoferrin is believed to have antibacterial, antifungal, and antiviral properties. Salivary peroxidase has antibacterial properties, where as



histatins have been associated with antibacterial and antifungal properties.

The iodine ions play an important role in defence mechanism mainly due to the presence of peroxidases.

Analgesic and Wound healing capacity:

Saliva consists of opiorphins. These opiorphins are peptides with analgesic effect that prolongs the effect of enkephalins - natural analgesics secreted by the brain when pain is perceived. However the duration of action of enkephalins is limited because they are rapidly enzymatically degraded. Opiorphins inhibit the activity of these enkephalin-degrading enzymes and there by prolong the analgesic effect of enkephalins. [19]

Slivary gland is known to be a natural reservoir of growth factor several growth factors such as Epidermal growth factor (EGF) and nerve growth factor (NGF) More recently, transforming growth factor-alpha (TGF-ct), insulin, insulin-like growth factors I and II (IGF-I, IGFII), transforming factor-beta (TGF-6), and basic fibroblast growth factor (bFGF) have been detected.[20]

bFGF has proliferation-promoting effects on various types of cells and influences cell migration, differentiation, tissue regeneration, and neovascularisation.[21]

From its multipotentiality, bFGF is known as a key factor in tissue regeneration. [22,23]

Thus saliva aids in pain management and wound healing.

Others:

In addition to these proteins with specific functions, other enzymes could serve as indicators in diagnosis, such as pseudo cholinesterase for mental disorders (Giddon and Lisanti, 1962).

Saliva contains other organic components, such as glucose, urea, cortisol, sex hormones and blood group substances, which have also been utilized in saliva as screening/diagnostic tools.

In patients with diabetes and chronic kidney disease there is increase in the salivary glucose and salivary urea can be seen pre dialysis test.

In addition, saliva as a “body mirror” can reflect the physiological and pathological state of the oral cavity. Therefore, it serves as a diagnostic and monitoring tool in many fields of science, such as medicine, dentistry, and pharmacotherapy .[24]

SALIVA DYSFUNCTION

Dysfunction results from any alteration in either amount or quality. Both a decrease (hypofunction) and an increase (hyperfunction) in salivary production are considered forms of dysfunction.

Hypo salivation:

Studies have shown that complaints of oral dryness are not a reliable indicator of salivary gland performance. Some patients may have a significant decrease in salivary output and experience no discomfort, and some may not perceive decreased salivary output until the flow rate has decreased by 50%. [25]

Ship et al proposed that the normal range of salivary flow varies for each individual. [26]

Numerous variables contribute to hypo salivation. They include localised, systemic factors, iatrogenic, pharmacological factors and others

Localised factors:

Salivary gland disease (sialadenitis, sialolithiasis) or salivary gland destruction associated with head and neck irradiation for the treatment of carcinomas.

Systemic factors:

autoimmune diseases such as Sjogren’s syndrome, AIDS, systemic lupus erythematosus, rheumatoid arthritis, scleroderma;

hormonal disorders such as uncontrolled diabetes, thyroid dysfunction;



neurological disorders such as Parkinson's, Bell's palsy, cerebral palsy; and psychogenic illness such as anxiety, stress and depression, in these conditions the saliva cortisol level increases as a response of adrenal cortex to the stress.

Iatrogenic factors:

Salivary gland damage is irreversible and results from radiation exposure above 50 Gy and accidental surgical trauma to the underlying glands. [27]

Salivary glands are most radiosensitive, as they have a low mitotic index that usually reflects radioresistance. [6]

Radiation damage may be due to damage to the blood supply (endarteritis), interference with nerve transmission, or destruction of the gland itself.

Pharmacological factors:

Xerostomia, or hypofunction of the salivary glands, is one of the side effects of over 400 drugs. [28]

Older people seem to have more severe side effects, which could be related to slower metabolism, delayed drug clearance.

Drugs that affect gland function include:

- 1.) Anticholinergic and antiparkinsonian agents,
- 2.) Antidepressants,
- 3.) Systemic antihistamines,
- 4.) Antipsychotic drugs,
- 5.) Antihypertensive medications,
- 6.) Central nervous system stimulants and sedatives.

Due to altered sensory function or mucosal and overall body dehydration from increased urine output, analgesics and diuretics can create the sensation of dry mouth.[29]

According to multiple research, people on medication for more than two years and those with at least one systemic condition had considerably reduced salivary flow rates. [30]

Management of Hyposalivation Or Xerostomia:

When it comes to treating xerostomia/drymouth/hyposalivation, *prosthodontists* tend to be the primary healthcare providers. Comprehensive patient education is the first step in the dental therapy of these individuals. Patients must be counselled to apply topical fluoride, arrange regular recalls, and practice immaculate hygiene.

Individuals who have trouble chewing should be reminded that salivation is triggered by mechanical stimulation of the tongue and oral mucosa as well as periodontal mechanoreceptors.

Gum and candies without added sugar are strongly advised in such cases.

Avoid diets that cause dehydration or that irritate the tissues; these include foods high in citrus and alcohol and its derivatives. [31]

In certain cases, preferable individuals may be prescribed medication that stimulates the salivary glands

Cholinergic agonists like Cevimeline and Pilocarpine trigger muscarinic receptors in salivary tissue that is still functional, causing the production of water, salts, and other substances.

[32]

People who wear dentures should undergo frequent oral examinations to identify and treat potential mucosal ulcerations and denture stomatitis.

In case of presence of oral candidiasis :

Topical: Nystatin 15 g, Ketoconazole 2% cream 5 g, Clotrimazole 1% cream 15 g.

Systemic: Ketoconazole 200 mg , Fluconazole 100 mg.

Oral suspension: Amphotericin-B 25 mg/mL, Clotrimazole 10 mg/mL oral, Nystatin 100,000 units/ml.

Mouthgels, oral sprays, and artificial saliva or salivary substitutes can all help relieve the symptoms of dry mouth.



Salivary substitutes aid in inhibiting bacterial colonization. These substitutes consists of carboxy methyl cellulose, parabens, and sugar-free flavoring agents (sorbitol or xylitol).

The saliva substitutes must be as close as possible to the natural saliva in terms of composition as well as in biophysical properties.

Hypersalivation (Ptyalism Or Sialorrhea):

Sialorrhea, also known as hypersalivation or ptyalism, is excessive salivation associated with neurological disorders (**Cerebral palsy and Parkinson's disease**) or localized anatomical abnormalities in the oral cavity.[33]

ETIOLOGY OF SIALORRHEA:

Systemic causes

1. Neuromuscular/sensory dysfunction—cerebral palsy, Parkinson's disease, mental retardation, motor neuron disease (ALS), pseudobulbar/bulbar palsy, stroke.
2. Medication side effects—antipsychotics (clozapine), tranquilizers, anticonvulsants, anticholinesterases, lithium.
3. Toxin exposure—mercury vapor, pesticides, snake poisoning, mushrooms
4. Infection—rabies.
5. Gastric—gastroesophageal reflux.

Local causes:

1. Infection—dental caries, oral cavity infection, tonsillitis, peritonsillar abscess.
2. Anatomic—macroglossia, nasal blockage, oral incompetence,

Physiological causes:

1. Pregnancy

Management of Sialorrhea:

The goal of the treatment for sialorrhea is a reduction in excessive salivary flow, while maintaining a moist and healthy oral cavity.

Treatment of sialorrhea is best accomplished with a multidisciplinary team approach.

The two main approaches are: Non – Invasive and Invasive approach.

1. Noninvasive techniques that include positioning, oral facial facilitation, speech therapy, biofeedback, positive and negative reinforcement, pharmaceutical therapy, oral prosthetic devices, and botulinum toxin.
2. Invasive techniques that include radiation and surgery

Pharmaceutical therapy and other invasive therapies should be taken into consideration if sialorrhea still has an adverse effect on the patient's health and quality of life despite these conservative methods.

Anticholinergic medications, such as benztropine, scopolamine, and tropicamide, are used in oral therapy for sialorrhea. These medications function by inhibiting acetylcholine, which in turn reduces salivary secretion via the parasympathetic autonomic nervous system. [34]

Anticholinergics are contraindicated in patients with glaucoma, obstructive uropathy, gastrointestinal motility disorders, and myasthenia gravis.

For elderly individuals who cannot take medicine or surgery, radiation therapy to the salivary glands is a helpful approach. The primary concern is that radiation can cause cancer, however, this is not as concerning for older or disabled individuals as it occurs 10–15 years after treatment [35].

IMPLICATIONS IN PROSTHODONTICS:

In dentate individuals, saliva is essential for preserving the general health of the oral cavity. Edentulous individuals

For those individuals the quantity and quality of saliva is more important. Saliva quality and quantity are of greater importance to those people. In addition to being crucial for the fabrication of a full denture, optimal salivary flow, quantity, and quality are also necessary for the denture's retention, stability, and support.

Saliva plays an important role as a physical agent in the retention of complete dentures.

The physical factors consist of: Adhesion, Cohesion, Surface tension, Capillary attraction and Atmospheric



pressure. [36]

Adhesion:

It is the physical molecular attraction of unlike surfaces in close contact. It acts when saliva wets and sticks to the basal surfaces of dentures and at the same time to the mucous membrane of the basal seat. Effectiveness of adhesion depends upon close adaptation of denture base to the supporting tissues and fluidity of saliva.

The effectiveness of adhesion depends on close adaptation of the denture base to the supporting tissue and is also directly proportional to the area covered by the denture. [36]

Cohesion: It is the molecular attraction between two similar surfaces or between two like molecules in close contact. It occurs in the layer of saliva between the denture base and mucosa. [36]

Interfacial surface tension:

The phenomenon of surface tension is the force that maintains the surface continuity of a fluid. This results from an imbalance in cohesive forces present at the surface of the layer or column of the fluid. All denture base materials have higher surface tension than oral mucosa, but once coated by salivary pellicle, their surface tension is reduced, which promotes maximizing the surface area between saliva and base. The thin fluid film between the denture base and the mucosa of the basal seat therefore furnishes a retentive force by virtue of the tendency of the saliva to maximize its contact with both surfaces. [36,37]

Capillarity:

Capillary attraction or capillarity is the force that causes the surface of liquid to become elevated or depressed when it is in contact with a solid. When the adaptation of denture base to mucosa on which it rests is sufficiently close, the space filled with a thin film of saliva acts like a capillary tube and helps retain the denture. [38]

Atmospheric pressure:

Atmospheric pressure is an emergency retentive force which comes into play when the denture is being

pulled away from the basal seat and the negative pressure created between the denture and the basal seat helps in retention. Even if the other retentive forces are being over powered the atmospheric pressure may be able to keep the denture in position. [36,37]

SIGNIFICANCE IN PROSTHODONTICS:

Saliva as a physiological factor of retention affects the effectiveness of physical forces. The higher the viscosity occurring to the mucoid content, the lower the flow and greater is the fixation. Hence the mucous saliva provides better cohesion than serous saliva. But the presence of thick ropy mucous saliva may compromise denture retention by creating negative pressure in the area anterior to the posterior palatal seal area causes dislodgement of denture. [39]

Individuals with systemic disorders experience significant difficulties wearing dentures because of insufficient salivary flow and xerostomia. In these partially or fully edentulous patients, there is an increase in susceptibility to mucosal ulcerations and fungal infections due to decreased salivary flow. Due to reduced salivary flow, there is no lubrication or cleansing action of saliva, which causes frictional effects on the mucosa, and dentures will cause high irritation to the mucosa.

These patients must be made aware of dental conditions such as denture stomatitis and oral candidiasis, and they must be thoroughly educated about the importance of well-fitting dentures and reduced usage of dentures when there is decreased salivary flow. It is necessary to counsel and educate them on the significance of artificial substitutes, including pilocarpine medications, salivary substitutes, sugar-free gums like xylitol, fake saliva gel, and salivary substitute mouthwash. Artificial saliva can be sprayed all day on the prosthetic surface and mouth mucosa.

An alternative to the artificial substitutes is prostheses with incorporated chambers to serve as artificial saliva reservoirs. [40-42]



Salivary secretion increases on wearing a new denture. Patients often experience extreme discomfort as a result of their excessive salivation. The patient has to be informed by the dentist that because dentures are perceived as foreign things, they cause the salivary gland to produce extra saliva. The patient may complain of floating dentures if the flow is too high. Reassure the patient that this excessive salivary flow is a typical response that will eventually subside.

To remove excess saliva, the patient must perform deglutition. Spitting should also be avoided as it might cause the dentures to become dislodged.

ROLE OF PROSTHODONTIST:

The prosthodontist or practitioner must have sound knowledge of the salivary glands, their secretion, and their application in clinical prosthodontics. Dentists must be aware of the sequelae of reduced or increased salivary secretion to be prompt in diagnosing and modifying treatment modalities.

If saliva is found to be an issue, the cause must to be investigated and need to be resolved with the appropriate treatment. The mucosal tissues of these patients are thin and fragile due to a lack of saliva. In such conditions, while recording preliminary or primary impressions, rigid impression materials such as impression compounds, ZoE paste, and heavybody elastomers must be avoided. The mucocompressive technique is avoided as it compresses and peels the tissues.

In such patients, mucostatic impression technique is preferred, and impression materials such as hydrocolloids are used preferably.

Excessive salivation, particularly by the submaxillary and sublingual glands presents a problem in impression making. Suitable antisialagogues can be administered prior to impression making.

Excessive secretion of mucous from the palatal glands may distort the impression material in the posterior two thirds of the palate. To counteract this problem, the palate may be massaged to encourage the glands to empty, the mouth may be irrigated with astringent and the palate may be wiped with gauze.

CONCLUSION:

Despite being the biological fluid that is most often overlooked, novel findings have made this biological fluid very pivotal due to its ease of availability and its essentially non-invasive diagnostic use. It will be beneficial in anticipating and diagnosing the disease as well as establishing the treatment appropriately to provide a favorable prognosis; thus, the prosthodontist or dentist must be able to recognize any notable change in normalcy that has to be diagnosed and treated swiftly.

REFERENCES:

1. A.V. Nieuw Amerongen and E. C. I. Veerman, "Saliva—the defender of the oral cavity," *Oral Diseases*, vol. 8, no. 1, pp. 12–22, 2002.
2. E. Kaufman and I. B. Lamster, "The diagnostic applications of saliva—a review," *Critical Reviews in Oral Biology & Medicine*, vol. 13, no. 2, pp. 197–212, 2002.
3. Humphrey SP, Williamson RT. A review of saliva: normal composition, flow and function. *J Prosthet Dent* 2001; 85:162-9.
4. Mandel ID, Wotman S. The salivary secretions in health and disease. *Oral Sci Rev* 1976;8:25-47.
5. Dawes C. Physiological factors affecting salivary flow rate, oral sugar clearance, and the sensation of dry mouth in man. *J Dent Res* 1987;66: 648-53 (diaz article)
6. Sreebny LM. Saliva in health and disease: an appraisal and update. *Int Dent J* 2000;50:140-61.
7. Baum BJ. Neurotransmitter control of secretion. *J Dent Res* 1987;66:628- 32.
8. Saliva: its role in health and disease. Working Group 10 of the Commission on Oral Health, Research and Epidemiology (CORE). *Int Dent J* 1992;42:287-304
9. Tenovuo J. Antimicrobial function of human saliva—how important is it for oral health? *Acta Odontol Scand* 1998;56:250-6.
10. Dowd FJ. Saliva and dental caries. *Dent Clin North Am* 1999;43:579-97.
11. F. Garcia-Godoy and M. J. Hicks, "Maintaining the integrity of the enamel surface: the role of dental biofilm, saliva and preventive agents in



- enamel demineralization and remineralization,” *Te Journal of the American Dental Association*, vol. 139, supplement 5, pp. 25S–34S, 2008.
12. J. K. M. Aps and L. C. Martens, “Review: the physiology of saliva and transfer of drugs into saliva,” *Forensic Science International*, vol. 150, no. 2-3, pp. 119–131, 2005.
 13. P. Denny, F. K. Hagen, M. Hardt et al., “The proteomes of human parotid and submandibular/sublingual gland salivas collected as the ductal secretions,” *Journal of Proteome Research*, vol. 7, no. 5, pp. 1994–2006, 2008.
 14. Almeida P, *Saliva Composition and functions: a comprehensive review*, 2008.
 15. E. S. Frenkel and K. Ribbeck, “Salivary mucins in host defense and disease prevention,” *Journal of Oral Microbiology*, vol. 7, no. 1, Article ID 29759, 10 pages, 2015
 16. Amerongen AV, Veerman EC. *Saliva: the defender of the oral cavity*. *Oral Dis* 2002; 8:12-22.
 17. Edgar WM, O’Mullane DM. *Saliva and oral health*. 2nd ed. London: British Dental Association; 1986. p. 39.
 18. S. Chiappin, G. Antonelli, R. Gatti, and E. F. de Palo, “Saliva specimen: a new laboratory tool for diagnostic and basic investigation,” *Clinica Chimica Acta*, vol. 383, no. 1-2, pp. 30–40, 2007.
 19. Wisner A, Dufour E, Messaoudi M et al. Human Opiorphin a natural antinociceptive modulator of opioid - dependent pathways. *Proc Nat Acad Sci* 2006;103:17979-17983.
 20. Zelles T, Purushotham KR, Macauley SP, Oxford GE, Humphreys-Beher MG (1995). Saliva and growth factors: the fountain of youth resides in us all. / *Dent Res* 74:1826-1832.
 21. Hoppenreijns VPT, Pels E, Vrensen GFJM, Treffers WF (1994). Basic fibroblast growth factor stimulates corneal endothelial cell growth and endothelial wound healing of human corneas. *Invest Ophthalmol Vis Sci* 35:931-94
 22. Gospodarowicz D, Neufeld G, Schweigerer L (1986). Fibroblast growth factor. *Mol Cell Endocrinol* 46:187-204.
 23. Kagami, H., Hiramatsu, Y., Hishida, S., Okazaki, Y., Horie, K., Oda, Y., & Ueda, M. (2000). *Salivary Growth Factors in Health and Disease. Advances in Dental Research*, 14(1), 99–102.
 24. W. V. Giannobile, J. T. McDevitt, R. S. Niedbala, and D. Malamud, “Translational and clinical applications of salivary diagnostics,” *Advances in Dental Research*, vol. 23, no. 4, pp. 375–380, 2011.
 25. Dawes C. Physiological factors affecting salivary flow rate, oral sugar clearance, and the sensation of dry mouth in man. *J Dent Res* 1987;66: 648-53.
 26. Ship JA, Fox PC, Baum BJ. How much saliva is enough? ‘Normal’ function defined. *J Am Dent Assoc* 1991;122:63-9
 27. Fox PC. Acquired salivary dysfunction. *Drugs and radiation. Ann N Y Acad Sci* 1998;842:132-7.
 28. Sreebny LM, Schwartz SS. *A reference guide to drugs and dry mouth—2nd edition*. *Gerodontology* 1997;14:33-47.
 29. Narhi TO. Prevalence of subjective feelings of dry mouth in the elderly. *J Dent Res* 1994;73:20-5.
 30. Navazesh M, Brightman VJ, Pogoda JM. Relationship of medical status, medications, and salivary flow rates in adults of different ages. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;81:172-6.
 31. Atkinson JC, Fox PC. Salivary gland dysfunction. *Clin Geriatr Med* 1992; 8:499-511.
 32. Al-Hashimi I. The management of Sjogren’s syndrome in dental practice. *J Am Dent Assoc* 2001;132:1409-17
 33. Vashishta R, Nguyen SA, White DR, Gillespie MB. Botulinum toxin for the treatment of sialorrhea: A meta-analysis. *Otolaryngology and Head and Neck Surgery*. 2013;148(2):191-196
 34. Lakraj AA, Moghimi N, Jabbari B. Sialorrhea: Anatomy, pathophysiology and treatment with emphasis on the role of botulinum toxins. *Toxins*. 2013;5(5):1010-1031
 35. Hockstein NG, Samadi DS, Gendron K, Handler SD. Sialorrhea: A management challenge.



- American Family Physician. 2004;69(11):2628-2634
36. Jacobson TE, Krol AJ. A Contemporary review of the factors involved in complete denture retention, stability and support, part Iretention. *J Prosthet Dent* 1983; 49:5-15.
 37. O'Dell NL. Anatomy and Physiology. In, Heartwell CM, Rahn AO (ed). *Textbook of complete dentures*. 5th edition. India, Harcourt, 2003; 36-39.
 38. Shay K. The retention of complete dentures. In, Zarb GA, Bolender CL (ed). *Prosthodontic treatment for edentulous patients*. 12th edition. St. Louis, Mosby, 2004; 437-48.
 39. Blahova Zora and Rolf Walstrom, 1971. Physical factors in retention of complete dentures. *J. Prosthet Dent*, 25: 230-5.
 40. Vergo TJ Jr, Kadish SP. Dentures as artificial saliva reservoirs in the irradiated edentulous cancer patient with xerostomia: a pilot study. *Oral Surg Oral Med Oral Pathol* 1981;51:229-33. 72.
 41. Toljanic JA, Schweiger JW. Fabrication of an artificial saliva reservoir denture system for xerostomia management. *Quintessence Dent Technol* 1985;9:355-8. 73.
 42. Vissink A, Huisman MC, Gravenmade EJ. Construction of an artificial saliva reservoir in an existing maxillary denture. *J Prosthet Dent* 1986;56: 70-4