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內文：

Introduction

- ✧ Salivary fluid consists of approximately 99% water, electrolytes (sodium, potassium, calcium, chloride, magnesium, bicarbonate, phosphate), proteins (represented by enzymes, immunoglobulins and other antimicrobial factors), mucosal glycoproteins (traces of albumin and some polypeptides and oligopeptides), glucose and nitrogenous products (urea and ammonia).
- ✧ Saliva refers to the mixture of fluids from the salivary glands, the gingival fold, oral mucosa transudate, mucous of the nasal cavity and pharynx, non-adherent oral bacterial, food remainders, desquamated epithelial and blood cells, as well as traces of medications or chemical products
- ✧ At rest, there is a small, continuous salivary flow (SF), denominated basal unstimulated secretion; stimulated saliva is produced by mechanical, gustatory, olfactory, or pharmacological stimulus, contributing to 80% to 90% of daily salivary production.
- ✧ The SF index classifies stimulated and unstimulated saliva flow as normal, low, or very low (hyposalivation). A healthy person's mean daily saliva production ranges from 1 to 1.5L. In adults, normal total stimulated SF ranges from 1 to 3 mL/min, low ranges from 0.7 to 1.0 mL/min, hyposalivation is less than 0.7 mL/min. The normal unstimulated SF ranges from 0.25 to 0.35 mL/min, low ranges from 0.1 to 0.25 mL/min, hyposalivation is less than 0.1 mL/min.
- ✧ At present, saliva represents an increasingly useful auxiliary means of diagnosis. Such as sialometry and sialochemistry can diagnose systemic illnesses, monitoring general health, and as an indicator of risk for diseases. However, since several factors can influence salivary secretion and composition, the aim of this literature review was to investigate the composition and functions of saliva as well as describe the factors that influence SF and its biochemical composition.

Saliva Functions and Composition

Taste

- ✧ The SF initially formed inside the acini is isotonic with plasma, as it runs through the ducts, it becomes hypotonic. The hypotonicity of saliva and its capacity to provide the dissolution of substances allows the gustatory buds to perceive different flavors.

Protection and Lubrication

- ✧ Saliva forms a seromucosal covering that lubricates and protects the oral tissues against irritating

agents, due to mucins responsible for lubrication, protection against dehydration, and maintenance of salivary viscoelasticity.

- ✧ They also selectively modulate the adhesion of microorganisms to the oral tissue surfaces (control of bacterial and fungal colonization).They protect tissues against proteolytic attacks by microorganisms. Mastication, speech, and deglutition are aided by the lubricant effects.

Dilution and Cleaning

- ✧ Sugars are present in total stimulated and unstimulated saliva at a mean concentration of 0.5 to 1 mg/100mL.High concentrations of sugar in saliva mainly occur after the intake of food and drink. There is a correlation between the glucose concentration in the blood and salivary fluid, particularly in diabetics, but this is not always significant.
- ✧ Its fluid consistency provides mechanical cleansing of the residues present in the mouth such as nonadherent bacteria and cellular and food debris. SF tends to eliminate excess carbohydrates, limiting the availability of sugars to the biofilm microorganisms. The greater the SF, the greater the cleaning and diluting capacity.

Buffer Capacity

- ✧ Saliva behaves as a buffer system to protect the mouth:
  1. It prevents colonization by potentially pathogenic microorganisms by denying them optimization
  2. Saliva buffers (neutralizes) and cleans the acids produced by acidogenicmicroorganisms, preventing enamel demineralization

  biofilm thickness, and the number of bacteria determines the efficacy of salivary buffers.
- ✧ Negatively loaded residues on the salivary proteins work as buffers. Sialin, a salivary peptide, increasing the biofilm pH after exposure to fermentable carbohydrates.
- ✧ Urea is another buffer which causes a rapid increase in biofilm pH by releasing ammonia and carbon dioxide when hydrolyzed by bacterial ureases. Children with chronic renal insufficiency present with less caries due to the increased levels of salivary urea.
- ✧ Ammonia is an important factor in the initiation of gingivitis because it may increase the permeability of the sulcular epithelium to other toxic or antigenic substances in addition to the formation of dental calculus.
- ✧ The carbonic acid-bicarbonate system is the most important buffer in stimulated saliva, while in unstimulated saliva it serves as the phosphate buffer system.

Integrity of Tooth Enamel

- ✧ Saliva maintains the physical-chemical integrity of tooth enamel by modulating remineralization and demineralization. The main factors controlling the stability of enamel hydroxyapatite are the concentrations of calcium, phosphate, and fluoride and the salivary pH.
- ✧ The high concentrations of calcium and phosphate in saliva guarantee ionic exchanges directed towards the tooth surfaces that begin with tooth eruption resulting in post-eruptive maturation. Remineralization of a carious tooth mainly due to the availability of calcium and phosphate ions

in saliva.

- ✧ The concentration of salivary calcium varies with the SF and is not affected by diet, diseases such as cystic fibrosis and some medications such as pilocarpine cause an increase in calcium levels.
- ✧ Inorganic orthophosphate found in saliva consists of phosphoric acid (H3PO4) and primary ($H2PO4^-$), secondary ($HPO4^{2-}$), and tertiary ($PO4^{3-}$) inorganic phosphate ions. As the flow increases, the total concentration of inorganic phosphate diminishes. The most important function is to maintain the dental structure, another function is its buffer capacity, only in unstimulated SF.
- ✧ Fluoride concentration in saliva depends on the fluoride in the environment, especially in drinking water. Other sources such as dentifrices and products used in caries prevention. Fluoride ions diminish the solubility of dental hydroxyapatite during a drop in biofilm pH, making it more resistant to demineralization. Fluoride also reduces the production of acids in biofilm
- ✧ Normal salivary pH is from 6 to 7 and varies in accordance with the SF, from 5.3 (low flow) to 7.8 (peak flow). There are various sources of hydrogen ions in oral fluids: secretion by the salivary glands, production by the oral microbiota, or acquisition through food. These ions influence the equilibrium of calcium phosphates in the enamel. The higher the concentration of hydrogen ions, the lower the pH.

Digestion

- ✧ Saliva is responsible for the initial digestion of starch, favoring the formation of the food bolus, by the digestive enzyme α-amylase, divides the starch into maltose, maltotriose, and dextrins.
- ✧ This enzyme is contributing 40% to 50% of the total salivary protein produced by the glands. 80% of this enzyme is synthesized in the parotids and the remainder in the submandibular glands. Its action is inactivated in the acid portions of the gastrointestinal tract and is limited to the mouth.

Tissue Repair

When saliva is experimentally mixed with blood, the coagulation time can be greatly accelerated, clinically the bleeding time of oral tissue is shorter than other tissues. Experimental studies in mice have shown wound contraction is increased in the presence of saliva due to the epidermal growth factor produced by the submandibular glands.

Antibacterial Properties and Participation in Film and Calculus Formation

- ✧ Saliva contains immunologic and non-immunologic proteins with antibacterial properties. In addition, some proteins are necessary for inhibiting the spontaneous precipitation of calcium and phosphate ions in the salivary glands and in their secretions.
- ✧ Secretory immunoglobulin A (IgA) is the largest immunologic component of saliva. It can neutralize viruses, bacteria, and enzyme toxins, serves as an antibody for bacterial antigens and inhibiting bacterial adherence to oral tissues. Others such as IgG and IgM, occur in less quantity and probably originate from gingival fluid.
- ✧ The non-immunologic salivary protein components, such as enzymes (lysozyme, lactoferrin, and

peroxidase), mucin glycoproteins, agglutinins, histatins, proline-rich proteins, statherins, and cystatins.

- ✧ Lysozyme can hydrolyze the cellular wall of some bacteria. Gram-negative bacteria are more resistant to this enzyme due to the protective function of their external lipopolysaccharide layer.
- ✧ Lactoferrin causes bactericidal or bacteriostatic effects on microorganisms requiring iron for their survival such as the *Streptococcus mutans* group.
- ✧ Peroxidase or sialoperoxidase offers antimicrobial activity.
- ✧ The proline-rich proteins and statherins inhibit the spontaneous precipitation of calcium phosphate salts and the growth of hydroxyapatite crystals on the tooth surface, preventing the formation of salivary and dental calculus.
- ✧ The cystatins are related to film formation and to hydroxyapatite crystal equilibrium.
- ✧ The histatins have antimicrobial activity against *Streptococcus mutans* and inhibit hemoagglutination of the *Porphyromonas gingivallis*. They neutralize the lipopolysaccharides of the Gram-negative bacteria and are potent inhibitors of *Candida albicans* growth and development.
- ✧ Salivary agglutinin frequently associated with other salivary proteins and secretory IgA, is one of the main salivary components responsible for bacteria agglutination.

Factors Influencing Salivary Flow and Composition

SF and its composition vary greatly among individuals and in the same individual under different circumstances

Individual Hydration

The degree of individual hydration is the most important factor that interferes in salivary secretion. When the body water content is reduced by 8%, SF virtually diminishes to zero. During dehydration, the salivary glands cease secretion to conserve water

Body Posture, Lighting, and Smoking

- ✧ Patients kept standing up or lying down present higher and lower SF than seated patients.
- ✧ 30% to 40% decrease of SF in people that are blindfolded or in the dark. However, the flow is not less in blind people.
- ✧ Olfactive stimulation and smoking cause a temporary increase in unstimulated SF. Men that smoke present higher stimulated SF than non-smoking men. The tobacco increases glandular excretion, and nicotine causes morphologic and functional alterations in the salivary glands

The Circadian and Circannual Cycle

- ✧ SF attains its peak at the end of the afternoon but goes down to almost zero during sleep. Salivary composition is related to the circadian cycle, ex: proteins attain its peak at the end of the afternoon, while the peak of sodium and chloride occur at the beginning of the morning.
- ✧ In the summer lower volumes of salivary flows from the parotid gland, while in the winter there are peak volumes of secretion.

Medications

✧ Drugs with anticholinergic action (antidepressants, anxiolytics, antipsychotics, antihistaminics, and antihypertensives), may cause reduction in SF and alter its composition

Thinking of Food and Visual Stimulation

✧ Thinking of food or looking at food is weak salivation stimuli in humans. Some researchers observed a small increase in SF in visual stimuli, while others observed no effect.

Regular Stimulation of Salivary Flow

✧ Regular stimulation of SF with the use of chewing gum leads to an increase in stimulated SF.

Size of Salivary Glands and Body Weight

✧ Stimulated SF is directly related to the size of the salivary gland, contrary to unstimulated SF. Unstimulated SF appears to be independent of body weight.

Salivary Flow Index

✧ The main factor affecting salivary composition is the flow index. As the SF increases, the concentrations of total protein, sodium, calcium, chloride, and bicarbonate as well as the pH increases, whereas the inorganic phosphate and magnesium diminish.

✧ Mechanical or chemical stimulus is associated with increased salivary secretion. Acid substances are considered potent gustatory stimuli.

Contributions of Different Salivary Glands

✧ The percentage of contribution by the glands during unstimulated SF is as follows:

• 20% by the parotid glands
• 65%-70% submandibular glands
• 7% to 8% sublingual glands
• <10% by the minor salivary glands

When SF is stimulated, there is an alteration with the parotids contributing over 50% of the total salivary secretion.

✧ Serous secretions, produced mainly by the parotids, are rich in ions and enzymes. Mucous secretions are rich in mucins (glycoproteins), produced mainly by the smaller glands. In the mixed glands (submandibular and sublingual glands), the salivary content depends on the proportion between the serous and mucous cells

Physical Exercise

✧ During physical activities sympathetic stimulation appears to diminish or inhibit salivary secretion. In addition to the determined intensity of the exercise, there is a rise in salivary levels of α-amilase and electrolytes (especially Na+).

Alcohol

✧ The intake of ethanol causes a reduction of stimulated SF. This diminishment results from the altered release of total proteins and amylase as well as in diminished release of electrolytes.

Systemic Diseases and Nutrition

✧ In some chronic diseases such as: pancreatitis, diabetes mellitus, renal insufficiency, anorexia,

bulimia, and celiac disease, the amylase level is high. Depression is accompanied by diminished salivary proteins. Nutritional deficiencies may influence salivary function and composition.

Fasting and Nausea

✧ Short-term fasting reduces SF but does not lead to hyposalivation, and the flow is restored to normal values immediately after the fasting period ends. Saliva secretion increases before and during vomiting

Age

✧ With advancing age the salivary glands is gradually replaced by adipose and fibrovascular tissue, and the volume of the acini is reduced. However, functional studies among healthy individuals indicate aging does not necessarily lead to diminished glandular capacity to produce saliva

✧ Navazesh et al. found the unstimulated SF is lower in healthy patients between the ages of 65 and 83 years, in comparison with patients between the ages of 18 and 35 years. However, the stimulated SF was higher in the elderly.

✧ Percival et al. also found the unstimulated SF is related to age, reduced in healthy elderly persons aged 80 years or older. However, no age-related reductions in stimulated SF. The reduction in unstimulated SF could contribute to the appearance of diseases in the oral mucosa.

✧ Lima et al. demonstrated elderly persons presented a very low daily saliva production, but this appears to be more related to systemic diseases and the use of medications than to aging.

Gender

✧ Two theories about the differences in salivary secretion between men and women: 1. Women present smaller salivary glands and 2. The female hormonal pattern may diminish salivary secretion. However, menopause and hormone replacement therapy are not associated with salivary dysfunction of the parotid.

Conclusion

Since several factors can influence salivary secretion and composition, a strictly standardized collection must be made so the sialometry and/or sialochemistry are able to reflect the real functioning of the salivary glands and serve as efficient means for monitoring health.

Clinical Significance

Since many oral and systemic conditions manifest themselves as changes in the flow and composition of saliva the dental practitioner is advised to remain up-to-date with the current literature on the subject.

題號	**題目**
1	以下何者不是造成 xerostomia 的原因? (A) Medication (B) Impaired fluid intake (C) Sjögren syndrome (D) Age
答案(D)	出處：Neville, Oral & Maxillofacial Pathology (2nd edition), P.398,Box 11-1

題號	題目
2	以下何種藥物不會造成 xerostomia? (A) Antihistamines (B) Antipsychotics (C) Anticholinergics (D) NSAIDs
答案(D)	出處：Neville, Oral & Maxillofacial Pathology (2nd edition), P.399,Table 11-1