Saliva, a thick, colorless, fluid that is constantly present in the humans mouth. It is composed of water, mucus, proteins, mineral salts, and amylase. As saliva circulates in the mouth cavity it picks up food debris, bacterial cells, and white blood cells. Three major pairs of salivary glands and many smaller glands scattered in the surface tissue of the cheeks, lips, tongue, and palate contribute to the total amount of saliva. Small amounts of saliva are continually being secreted into the mouth, but the presence of food, or even the mere smell or thought of it, will rapidly increase saliva flow.

The functions of saliva are numerous. Primarily, it lubricates and moistens the inside of the mouth to help with speech and to change food into a liquid or semisolid mass that can be tasted and swallowed more easily. Saliva helps to control the body’s water balance; if water is lacking, the salivary glands become dehydrated, leaving the mouth dry, which causes a sensation of thirst and stimulates the need to drink. Saliva reduces tooth decay and infection by removing food debris, dead cells, bacteria, and white blood cells. It also contains small amounts of the digestive enzyme amylase, which chemically breaks down carbohydrates into simpler compounds. (2).

Saliva physiology

Saliva is a complex liquid consisting of secretions from the major and minor salivary glands. As estimated there are 450-750 minor accessory salivary glands, situated on tongue, buccal mucosa and palate except the anterior part of the hard palate and gums (2,3,4). Saliva has hundreds of components that may serve to detect systemic diseases or as evidence of exposure to various harmful substances, as well as providing biomarkers of health and disease status. The average daily volume of saliva production is 500-1000 ml. Submandibular glands produce 70% of the overall volume, the parotid glands 25%, and the sublingual glands about 5% (5). The greatest volume of saliva is produced before, during and after meals, reaching its maximum peak at around 12 a.m. and falls considerably at night, while sleeping. Several physiological and pathological conditions can modify saliva production quantitatively, e.g. smell and taste stimulation, chewing, psychological and hormonal status, drugs, age, hereditary, oral hygiene and physical exercise (3,6,7,8,9). Saliva is sterile when it leaves the salivary glands.

Saliva is interstitial fluid from blood capillaries which enters via the salivary gland ducts where it is modified from isotonic into hypotonic fluid (2, 5, 9). Every type of salivary gland produces a typical secretion. The parotid glands produce serous fluids, the submandibular glands a sero-mucous secretion, and the sublingual glands secrete mucous saliva. The minor glands produce a viscous secret (4). About 99% of saliva is water and the other
1% is a complex of organic and inorganic molecules. Saliva has three major functions: digestion, protection and lubrication.

**Saliva pH**

Microorganisms generally cannot tolerate extreme pH values. In the oral cavity, the pH is maintained near neutrality by the buffering activity of saliva (6.7 to 7.3). The saliva eliminates metabolized carbohydrates and acids produced by bacteria. Bicarbonate is the major salivary buffering system of saliva, but peptides, proteins, and phosphates are also involved. Increases in pH also result from bacteria that metabolize sialine and urea into ammonia. Acids that are produced by the microbial metabolism of carbohydrates may accumulate in dental plaque because of the slow diffusion of saliva through dental plaque. Following sugar intake, the pH of dental plaque may decrease to below 5.0. The pH is an important parameter in oral microbial ecology (14, 15, 19).

**Oxidation-reduction potential and anaerobiosis**

Many enzymatic reactions are oxidation-reduction reactions in which one compound is oxidized and another compound is reduced. The proportion of oxidized to reduced components constitutes the oxidation-reduction potential or redox potential (Eh). Anaerobic bacteria need a reducing environment (negative Eh) for growth, while aerobic bacteria need an oxidizing environment (positive Eh). The mouth is characterized by a wide range of oxidation-reduction potentials, allowing the growth of aerobic, facultative anaerobic, and anaerobic bacteria (49).

In general, the dorsum of the tongue and the buccal and palatal mucosa are aerobic environments with positive Eh, thus better supporting the growth of facultative anaerobic bacteria. The gingival crevice and the approximal surfaces of the teeth (surfaces between teeth) possess the lowest Eh and the highest concentration of obligately anaerobic bacteria. The Eh values vary between 1158 to 1542 mV in saliva but may reach 2300 mV in gingival crevices (495). The Eh also varies during plaque formation, changing from positive values (1294 mV) on clean tooth surfaces to negative values (2141 mV) after 7 days (22). The fall in Eh during plaque formation is the result of oxygen consumption by facultative anaerobic bacteria as well as a reduction in the ability of oxygen to diffuse through the plaque. This explains in part the increased in number of obligately anaerobic bacteria during plaque formation.

**Saliva and diets**

In the oral cavity, microorganisms living in the supragingival environment have access to nutrients from both endogenous (saliva) and exogenous (diet) origin. Saliva is an important source of nutrients and can sustain normal growth of microorganisms in the absence of exogenous nutrients (16, 45). Saliva contains water, carbohydrates, glycoproteins, proteins, amino acids, gases, and several ions including sodium, potassium, calcium, chloride, bicarbonate, and phosphate. Among exogenous dietary components, carbohydrates and proteins have the greatest influence on the composition of the oral microbiota (12, 34, 45). The gingival crevice is not exposed to dietary components and saliva, and its principal source of nutrients is the gingival crevicular fluid. The crevicular fluid originates from plasma and is an excellent source of nutrients for fastidious microorganisms. It contains growth factors such as hemin and vitamin K required by some grame negative rods associated with adult periodontitis.
Some microorganisms cooperate for the degradation of nutrients. Some bacteria also use nutrients and other substances produced by other microorganisms.

**Saliva defense mechanisms**

The continuous flow of saliva increased by the muscular activity of the lips and tongue removes a large number of bacteria from teeth and mucosal surfaces. Saliva also contains several specific and nonspecific defense factors. SIgA is the principal specific defense factor of saliva. The nonspecific defense factors include mucins, nonimmune salivary glycoproteins, lactoferrin, lysozyme, peroxidase, histatins, and cystatins. Mucins are high-molecular-weight glycoproteins produced by submandibular, sublingual, and numerous minor salivary glands. Saliva contains two forms of mucins, MG1 and MG2. The MG1 mucin, which has a molecular mass greater than 1,000 kDa, is involved mainly in tissue coating; MG2, which has a molecular mass of 125 kDa, affects the aggregation and adherence of streptococci. In the oral cavity, mucins provide a protective coating for both soft and hard tissues. The mucins form a viscous slime layer on oral mucosa that traps microorganisms and antigens, limiting their penetration into the tissues (466, 467). Harmful microorganisms are thus eliminated by the continuous renewal of the mucous layer combined with the washing action of salivary flow.

Saliva also possesses defense factors with direct antimicrobial activity in vitro. A group of salivary proteins, lysozyme, lactoferrin, and peroxidase, act in conjunction with other components of saliva to limit the growth of bacteria or kill them directly. Lysozyme is a small cationic protein that is present in all major body fluids; it is secreted by intercalated duct cells. Lysozyme can lyse some bacterial species by hydrolyzing glycosidic linkages in the cell wall peptide glycan. It may also cause lysis of bacterial cells by interacting with monovalent anions, such as thiocyanate, perchlorate, iodide, bromide, bicarbonate, nitrate, and fluoride, and with proteases found in saliva. The combination leads to destabilization of the cell membrane probably by activation and deregulation of endogenous bacterial autolysins (31, 40). Also, lysozyme can aggregate oral bacterial cells and inhibit their colonization on mucosal surfaces and teeth (41).

**Lactoferrin** is an iron-binding glycoprotein produced by intercalated duct cells. It inhibits microbial growth, probably by sequestering iron in the environment. In addition, iron-free lactoferrin (apo lactoferrin) possesses a direct, iron-independent bactericidal effect against various oral bacterial strains (10, 11).

**Salivary peroxidase** is an enzyme secreted by salivary gland acinar cells. It is part of an antimicrobial system that involves the oxidation of salivary thiocyanate to hypothyocyanite and hypothiocyanous acid by hydrogen peroxide, generated by oral bacteria. These oxidizing agents react with sulfhydryl groups of the enzymes involved in glycolysis and sugar transport (48). Salivary peroxidase removes toxic hydrogen peroxide produced by oral microorganisms and can reduce acid production in dental plaque (17).

**Histatins (histidine-rich peptides** are a family of small basic peptides (3 to 5 kDa), with a high content of histidine, that are produced by acinar cells (51). They inhibit the development of some yeasts from the non infective to the infective form (343), aggregate oral streptococci, and inhibit the growth of some bacteria. (39).

**Cystatins** are a family of cysteine-containing phosphoproteins that are secreted by acinar cells (20, 58). These proteins are also present in plasma and may reach the oral cavity via the gingival crevicular fluid (20).
Cystatins act mainly as thio protease inhibitors and can inhibit proteases produced by suspected Periodontal pathogens.

However, saliva does not gain access to the gingival crevice, and this area of the oral cavity is almost essentially controlled by the antimicrobial factors of plasma.

**Cellular and humoral components of blood** can reach the gingival crevice of the oral cavity by the flow of gingival fluid through the junctional epithelium. Even in the healthy state, there is a continuous flow of small quantities of fluid and leukocytes from the gingival capillaries through the crevicular epithelium into the gingival crevice. This flow increases greatly with inflammation induced by plaque accumulation (29). The continuous flow of gingival fluid from the crevice to the oral cavity removes non adherent bacterial cells.

**The leukocytes in gingival crevicular fluid** are composed of 90% polymorphonuclear leukocytes (PMNs) and 10% mononuclear cells. Among the mononuclear cells, 60% are B lymphocytes, 20 to 30% are T lymphocytes, and 10 to 15% are macrophages. About 80% of PMNs are viable and functional within the crevice. The cells are capable of phagocytosis and of killing microorganisms (59).

**Lysozyme and peroxidase** that are released from the lysosome of PMNs during phagocytosis might also control microbial growth in the gingival crevice. Components of the complement cascade are present in the gingival crevicular fluid. In subjects with healthy gingivae, C3 and C4 components of complement can be detected. During gingival inflammation, C3a, C3b, and C5a appear, suggesting that complement activation may have occurred in vivo. Complement factors may initiate bacterial cell lysis or enhance phagocytosis of microorganisms (29, 43).

**The IgG, IgM, and IgA antibodies**, are found in plasma and crevicular fluid even in healthy individuals (18, 23, 30, 35, 44). These antibodies may influence the oral microbiota by interfering with adherence or by inhibiting bacterial metabolism (29, 44). Furthermore, the IgG antibodies may enhance phagocytosis and killing of oral microorganisms through activation of complement or opsonization (9, 29, 33, 42). The immune response itself may contribute significantly to the periodontal destruction, sometimes even more than the pathogens.

**Hormonal changes.** Puberty and pregnancy are accompanied by increased levels of steroid hormones in plasma and subsequently in the crevicular fluid and saliva (52, 54). Also, pregnancy and puberty are associated with an increase in gingival inflammation which is accompanied by an increase in gingival exudates (50). The exacerbations in gingival inflammation might be due to hormone-induced alterations in the microbiota of the gingival crevice (21, 27, 50). Microorganisms in the sub gingival area that use hormones as growth factors may be favored during the period of hormone increase associated with puberty and pregnancy (28). Increase in the subgingival microbiota of pregnant woman, corresponding to an increased level of estrogens and progesterone in plasma. Also, progesterone or estradiol can substitute for vitamin K as an essential growth factor for some microbes was reported (28).

**Oral mucosal surface receptors**

Microorganisms must first adhere to teeth or to mucosal surfaces for providing resistance to the flow of saliva. Adherence is mediated by adhesins on the microbial surface and by receptors on the oral surface. These adhesins are found as cell wall components or are associated with cell structures, such as fimbriae, fibrils or capsules. The receptors may be salivary components (mucins, glycoproteins, amylase, lysozyme, IgA, IgG, proline-rich proteins, and statherins) or bacterial components (glucosyltransferases and glucans) that are bound to oral surfaces (53, 56, 57). The adherence may result from nonspecific physico chemical interactions between the bacteria and the oral surfaces. However, these interactions cannot alone explain the selective attachment of bacteria to
various oral surfaces. It is believed that another mechanism accounts for this selective colonization, perhaps involving specific or stereo chemical interactions between bacterial adhesins and host receptors. It is probable that the bacteria first adhere by nonspecific interactions which are followed by stronger stereochemical interactions (57).

The stereochemical interactions involved in bacterial adhesion in the oral cavity are analogous to the interactions between antigen and antibody or between an enzyme and its substrate. Another adherence strategy involves a lectin-like bacterial protein with the complementary carbohydrate receptor located on glycoproteins (37). Bacteria may also colonize host surfaces by adhering to other bacteria, and several examples of coaggregation between human oral bacterial species have been demonstrated in vitro. Many of these interactions appear to be mediated by a lectin from one cell type that interacts with a complementary carbohydrate receptor from the other cell type (24,25,26). Coaggregation may be important in the development of dental plaque because it allows the colonization of bacteria that are not able to adhere directly to the acquired pellicle. (38). Another example of coaggregation is the synthesis of extracellular polysaccharides from sucrose by mutans streptococci. The glucosyl transferases that are bound to the surface of mutans streptococci synthesize glucans in the presence of sucrose. Thus, the polymers are cell associated and can bind to the tooth surface or to other bacteria via other glucosyl transferases or via independent glucan-binding components. These polysaccharides consolidate bacterial attachment to teeth and contribute to an increased stability of the plaque matrix. (55).

CONCLUSION

Saliva is an important body fluid for detecting the physiological and pathological situations of the human body. Saliva is a complex and dynamic biological fluid containing wide range of compounds. The biochemical and physical chemical properties of these salivary components and their interaction function in the oral cavity. In the last few years scientific interest has been raised to saliva not only for the various compounds, e.g., drugs, pollutants, hormones into saliva, but also the well-documented relation of saliva with bacterial, viral and systemic diseases.

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