Students in 4th and 5th grade participated in a study of the positive effects of chewing during a comprehension test. They were exposed to short stories and told to learn as much as possible, then were asked to recall and write down what they remembered 5 minutes and 24 hours later. Gum chewing had no effect on their performance at 24 hours but improved recall and better writing ability were noted after the 5-minute delay for patients who chewed gum.

An assessment of cognitive function was done in older adults with normal cognitive status. The mean Mini-Mental State Examination results were compared between a group who wore dentures and one having all natural teeth. A remarkably higher score was found for those having natural teeth than for those with complete dentures.

A study of healthy adult individuals in age-related cognitive decline investigated the number of remaining teeth in relation to the gray matter volume in their brains. Fewer teeth status was related to diminished gray matter around the hippocampus and frontal lobe volume.

Several animal studies have also evaluated mastication's relationship to cognitive function or working memory. Chewing tended to improve the ability to learn and increase the number of dentate gyrus cells in the hippocampus. Difficulty with motor and sensory information processing was noted when multiple teeth were lost.

Stress and Occlusal Disharmony

Stress activates the autonomic and neuroendocrine systems via the HPA axis, thereby releasing hormones and corticosteroids. Mastication alters HPA axis activity and influences the autonomic nervous system. The changes that resulted indicate that mastication can be a stress coping behavior that reduces stress-induced disorders.

Occlusal disharmony and mastication can also be affected. Learning-related c-Fos expression was significantly reduced when reduced mastication resulted from occlusal disharmony. In addition, when occlusal disharmony was corrected, cortisol and corticosterone levels returned to base values. In older adults, working memory function was tested in relation to mandibular displacement. Impaired memory function was noted in elderly patients who had artificially produced occlusal disharmony.

Animal studies have also investigated occlusal disharmony and mastication. One tested animals' ability to run a maze when occlusal disharmony is present. A radical decrease in the density of dendritic spines and pyramidal neurons and an increase in astrocytes and hypertrophy of hippocampal CA1 field were noted and correlated with impaired spatial memory. Overall, it was determined that mastication preserves memory and learning when the occlusion is normal but can adversely affect those functions when there is occlusal disharmony.

Clinical Significance

Mastication has been proved to maintain the peripheral sensory input in general health and increase blood supply to various brain regions. The result is better cognitive function. Further studies are needed to determine what else might be impacted by good masticatory function and normal occlusion compared to their compromised function. It appears that the ability to chew is essential to good cognitive function.

Krishnamoorthy G, Narayana AI, Balkrishanan D: Mastication as a tool to prevent cognitive dysfunctions. *Jap Dent Sci Rev* 54:169-173, 2018

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MICROBIAL ECOLOGY

The oral microbiome

BACKGROUND

Humans have a complex microbiome consisting of usually over 1000 species of bacteria, fungi, archaea, and viruses. The microbiome is formed through a highly selective process that begins at birth and continues throughout an individual's lifetime. The balance between the different types of organisms is established as a result of the interactions of the characteristics of the various habitats in the body and aspects of the individual's lifestyle, including dietary patterns, the frequent consumption of sucrose, smoking, and the use of antimicrobials and vaccines, among others. Recent studies of the nature of the human oral microbiome and its beneficial and detrimental aspects, including factors that can cause imbalance between the organisms dwelling there, have contributed to better understanding of this important topic.

FORMATION AND FUNCTION OF THE ORAL MICROBIOME

The 700 species of bacteria seen in the oral cavity include a core group of species that tend to be present in all humans and others that differ in their presence between persons. The initial colonizers of the oral cavity of newborns come from the birth canal, breast milk, and the mother's mouth. Thus the method of feeding is an important component in determining the infant's oral microbiome. It has been hypothesized that the infant's tolerance of the microbiome of the mother during prenatal development may govern his or her ability to successfully acquire a normal microbiome.

Within the first 6 weeks of life, the structure and function of the infant microbiota expand and diversify. Many different niches are established in the oral cavity based on the pH, oxygen, ligands for bacterial adhesins, and nutrient availability, among other factors, with organisms selecting the areas that most closely fit their requirements. Later changes occur when the teeth erupt, during puberty, and during pregnancy, but generally consist of changing the relative proportion of the oral microbiome members rather than their presence. These changes tend to promote fitness and survival.

In addition to the diverse species, many oral bacteria are present as distinct clones that show fluctuations unrelated to immune responses but rather driven by strain-specific competition. Different people carry different clones. Although they all belong to the same species, clones can differ in their ability to produce acid under low pH conditions and in how they interact with potential adhesin ligands and coaggregation partners.

BENEFICIAL ASPECTS

It's appropriate to consider the host (person) and the microbiome as a superorganism or holobiont because the 2 exist as an integrated organism. Benefits to the host include resistance to infections mediated by inhibition of colonization to pathogenic microorganisms, maturation of innate and adaptive host immune systems, and refining of the body's reaction patterns to achieve a balance between inflammatory and anti-inflammatory responses. The microbiome of the human gut plays a critical role in metabolism, the extraction of energy and nutrients from food, provision of nutrients and growth factors as needed, and regulation of fat storage and hormone levels. Some evidence suggests a link between the gut microbiome and brain development. It's conceivable that many of these effects also apply to the oral microbiome. The beneficial effects between host and microbiome depend on maintaining a balance within the microbiome and between the microbiome and the host.

DYSBIOSIS EFFECTS

Imbalance or dysbiosis is associated with many systemic disorders, including asthma, atopic disorders, inflammatory bowel disease, autoimmune diseases, obesity, metabolic syndrome, colon cancer, peripheral vascular disease, hypertension, aberrant responses to drugs, depression, and autism. Although causal mechanisms have yet to be proven, many of these associations are based on a significantly altered microbiome composition.

The acidogenic and aciduric properties of oral streptococci are highly diverse. Some clones of *Streptococcus mitis* produce as much acid at a pH of 5.5 as the mutans streptococci, but other clones are significantly less acidogenic (Figure 1). Ammonia is released by streptococci during the metabolism of arginine, but others release it

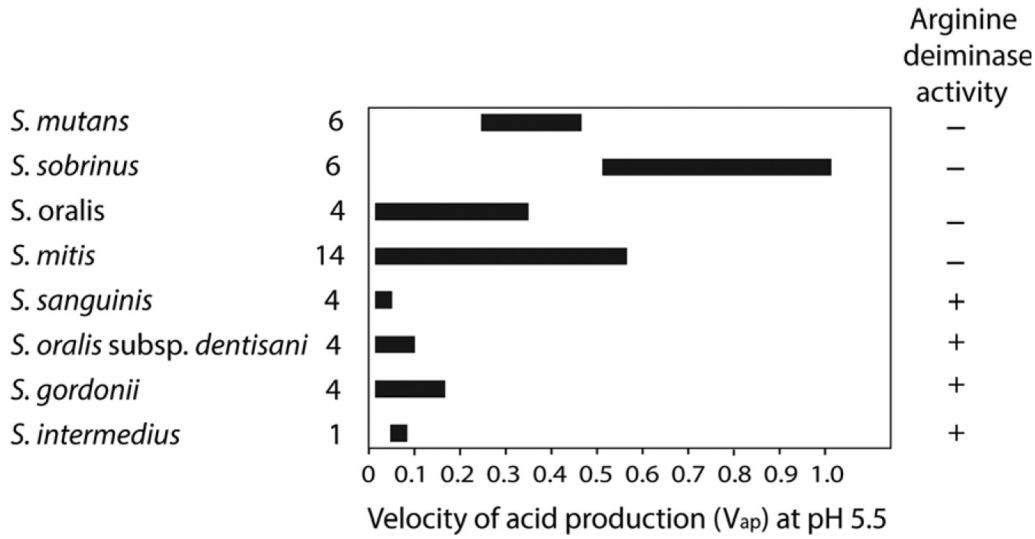

Figure 1. Oral *Streptococcus* species form 2 functionally distinct groups with regard to their velocity of acid production at pH 5.5, defined as the amount of H^+ produced per minute per mg of cells (V_{ap}), and their ability to release ammonia from arginine by arginine deiminase activity. Note the significant differences in acid production among members of the species *Streptococcus mitis* and *Streptococcus oralis.* Adapted from data published previously (27, 45). *Streptococcus oralis* subsp *dentisani* was previously classified as *Streptococcus mitis* biovar 2 and subsequently as *Streptococcus dentisani.* (Courtesy of Kilian M: The oral microbiome – friend or foe? *Eur J Oral Sci* 126:5-12, 2018.)

during urease activity. Other species metabolize lactic acid to weaker acids. All of these diverse activities are present in the oral microbiome of most individuals, but their relative proportions, which determine the final pH and cariogenic potential, depend on environmental pressure on the microorganisms involved.

Inflammatory and anti-inflammatory responses can be induced in host tissues by members of the oral microbiota. Gingivitis studies have shown that short-term cessation of tooth brushing can significantly increase the proportions of gram-negative rods and spirochetes, resulting in gingivitis. Although attachment loss is not caused by gingivitis itself, long-term inflammation can cause the exudation of inflammatory cells and plasma with serum proteins, including those of the immune system. The local inflammatory exudate then stimulates changes in the relative proportions of the microbiota. This alteration in the balance with host tissues permits new dominant bacteria to inactivate immunoglobulins, components of the complement system, and antibacterial peptides, which mouse studies have shown leads to periodontal disease.

Among the factors that can lead to dysbiosis are those related to lifestyle, such as sucrose consumption and smoking; the use of antibiotics and vaccines; host factors; and extra-oral infections. With respect to lifestyle factors, the direct effects of sucrose consumption and smoking on caries and periodontal disease are well documented.

Antibiotics and Vaccines

The widespread use of antibiotics has an unpredictable effect on the microbiome. Evidence suggests that repeated exposure to broad-spectrum antibiotics between birth and age 23 months is associated with early childhood obesity. In adults, consumption of the antibiotic ciprofloxacin is considered to exert limited effects on the microbiome. DNA-based mapping shows this antibiotic causes profound, rapid effects, including the loss of diversity and a shift in the composition of the bacterial members of the microbiome within 3 to 4 days of beginning the drug. A return to the individual's normal state begins within a week of discontinuing a course of treatment, but it's often an incomplete return. Other antibiotics also exert long-lasting negative effects on the fecal microbiome. The salivary microbiome tends to be significantly more robust, but possible effects of antibiotics remain unclear.

When vaccines are given against viral and bacterial pathogens, carrier rates are significantly reduced, resulting in the virtual elimination of the targeted organism. However, recent studies show that oral streptococci express polysaccharide capsules similar or identical to those produced by their pathogenic relative *Streptococcus pneumoniae*. Although *S oralis* subsp *dentisani* strains are considered beneficial in relation to caries, they express capsules identical to those of serotypes of *S pneumoniae*.

It's also possible that selection pressures force bacteria to adapt genetically to new environmental conditions through the accumulation of mutations and the importation of new genes or the loss of superfluous genes. These changes alter the organism's ability to manage and adapt to different environments. Antibiotic resistance is one highly visible genetic adaptation of oral bacteria to selection pressures. It's widespread likely because resistance-relevant mutations have accumulated over time. As a result, some oral bacteria no longer respond to normal treatment.

Host Factors and Extra-oral Infections

Individuals differ in their immunological reaction patterns because of genetic differences, differences in how their immune system developed, and their general condition of health. Temporary or permanent resistance can be suppressed by conditions such as reduced salivary flow; immune system dysfunction caused by infection, cancer, uncontrolled diabetes, or stress; disruption of the local anatomy; or the breakdown of structural barriers. In addition, commensal members of the oral microbiota can become opportunistic pathogens if they are introduced into normally sterile areas of the body. Although oral bacteria do not have properties that allow them to actively invade the bloodstream, inflamed periodontal tissues can facilitate their passive transfer to the circulation and cause bacteremia. Once in the bloodstream, oral bacteria can infect previously damaged heart valves or form thrombi or abscesses in the brain. Certain oral bacteria may also contribute to the pathogenesis of cardiovascular disease.

Clinical Significance

Considering the human body and its microbiome as an integrated superorganism allows the conceptualization of the importance of balance between the host and microbiome to ensure a healthy organism. Humans share many of the same members of the oral microbiome, although each person will also have microorganisms that are peculiar to his or her specific course of development. If the balance in the oral microbiome is disrupted, caries, periodontal disease, or candidiasis can result locally, but the imbalance can also contribute to systemic disorders and be influenced by these disorders. Our best course of action as dental professionals appears to involve selectively favoring the growth of beneficial species and controlling the growth and metabolism of the biofilm so that dysbiosis is less likely to occur.

Kilian M: The oral microbiome – friend or foe? *Eur J Oral Sci* 126:5-12, 2018

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