

# The Oral Microbiome & Systemic Disease



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**Disclaimer:** Participants must always be aware of the hazards of using limited knowledge in integrating new techniques or procedures into their practice. Only sound evidence-based dentistry should be used in patient therapy.

## Conflict of Interest Disclosure Statement

- The authors report no conflicts of interest associated with this course.

## Introduction – Oral Microbiome

The Oral Microbiome & Systemic Disease will provide an overview of the oral microbiome and its relationship to various systemic diseases, such as diabetes, hypertension, cardiovascular disease and stroke. Techniques for disease prevention and treatment will also be considered.

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## Overview

The purpose of the course is to discuss the relationship between the oral microbiome and systemic disease. First, the role of the oral microbiome will be explained in both oral and systemic homeostasis. Next, items that influence the oral microbiome will be discussed, along with systemic diseases that may be correlated to oral disease states. Finally, methods for microbiome analysis, available interventions, and future directions will be explored.

## Learning Objectives

**Upon completion of this course, the dental professional should be able to:**

- Describe the characteristics of the oral microbiome.
- Discuss the difference between the role of the oral microbiome in oral and systemic homeostasis.
- List the positive and negative influences that are exerted on the oral microbiome.
- Discuss four diseases that may be correlated to disease in the oral cavity.
- Explain diagnostic methods that are available for microbiome analysis.
- Differentiate between the interventions that are available for prevention and treatment.

## Glossary

**commensal organism** – Commensal bacteria are part of the normal flora in the mouth. Commensal organisms live in a relationship in which one organism derives food, or other benefits, from another organism without hurting or helping it.<sup>1</sup>

**dysbiosis** – Dysbiosis refers to microbial imbalance, which can occur in several different ways. For example, dysbiosis can occur when beneficial organisms are lost, when potentially harmful microorganisms increase, or when there is an overall loss of microbial diversity.<sup>2</sup>

**gene expression profiling** – The measurement of the activity (expression) of thousands of genes at once in order to create a global picture of cellular function. For instance, the profiles can be helpful for distinguishing between cells that are actively dividing or for showing how cells react to a certain treatment.<sup>3</sup>

**genome** – A genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism.<sup>4</sup>

**microbiome** – The microbiome is defined as the collective genomes of the microbes (composed of bacteria, bacteriophage, fungi, protozoa and viruses) that live inside and on the human body.<sup>5</sup>

**prebiotics** – Prebiotics are specialized plant fibers. They act like fertilizers that stimulate the growth of healthy bacteria in the gut.<sup>6,7</sup> Prebiotics are found in many fruits and vegetables, especially those that contain complex carbohydrates, such as fiber and resistant starch.<sup>6</sup>

**precision medicine** – Precision medicine is an approach for disease treatment and prevention that considers genes, environment, and lifestyle for each person. Precision medicine will enable doctors and researchers to determine more accurate prevention and treatment strategies for specific diseases in specific groups of people.<sup>8</sup>

**probiotics** – Probiotics contain live organisms (usually specific strains of bacteria) that directly add to the population of healthy microbes in the

gut. Probiotics can be taken via supplements and food, such as yogurt. Yogurt is made by fermenting milk with different bacteria. Other bacteria-fermented foods, such as sauerkraut, kombucha and kimchi, are also good sources of probiotics.<sup>6</sup>

**symbiosis** – The interaction between two (or more) different organisms living in close proximity, typically to the advantage of both.

## Introduction

The Human Microbiome Project, which was begun by the US National Institutes of Health in 2007, and completed in 2016, was intended to characterize human microbes and their potential to affect health and disease. These efforts are now helping scientists and clinicians better understand how the human microbiome interacts with the human immune system to either protect or harm the host. One of the major outcomes of this project was the creation of organ-specific data banks, such as the metagenomics of the human intestinal tract, which has the highest number of species, as

well as the human oral microbiome database (HOMD), which has the second highest number of microbial species.<sup>9</sup> To date, the bank has documented 770+ species while Park et al. have sequenced more than 1,000 species<sup>10</sup> and more than 1,200 to 1,500 are suspected.<sup>11</sup>

The vast majority of the organisms were not cultured in a lab but were identified through sophisticated genome sequencing technology instead. It is the combination of pathogens, commensals and their associated genomes (genetic material) that make up the oral microbiome. Typically, in a state of health, microbes exist in a symbiotic state, however if this homeostatic balance is disrupted, then a state of dysbiosis occurs. For example, figure 1 provides a visual representation of the microbiome of a periodontal pocket in health and disease.<sup>12</sup>

### But is it really that simple?

The oral cavity is a multifaceted environment, and this is reflected in the complexity of the microbiome. The composition of

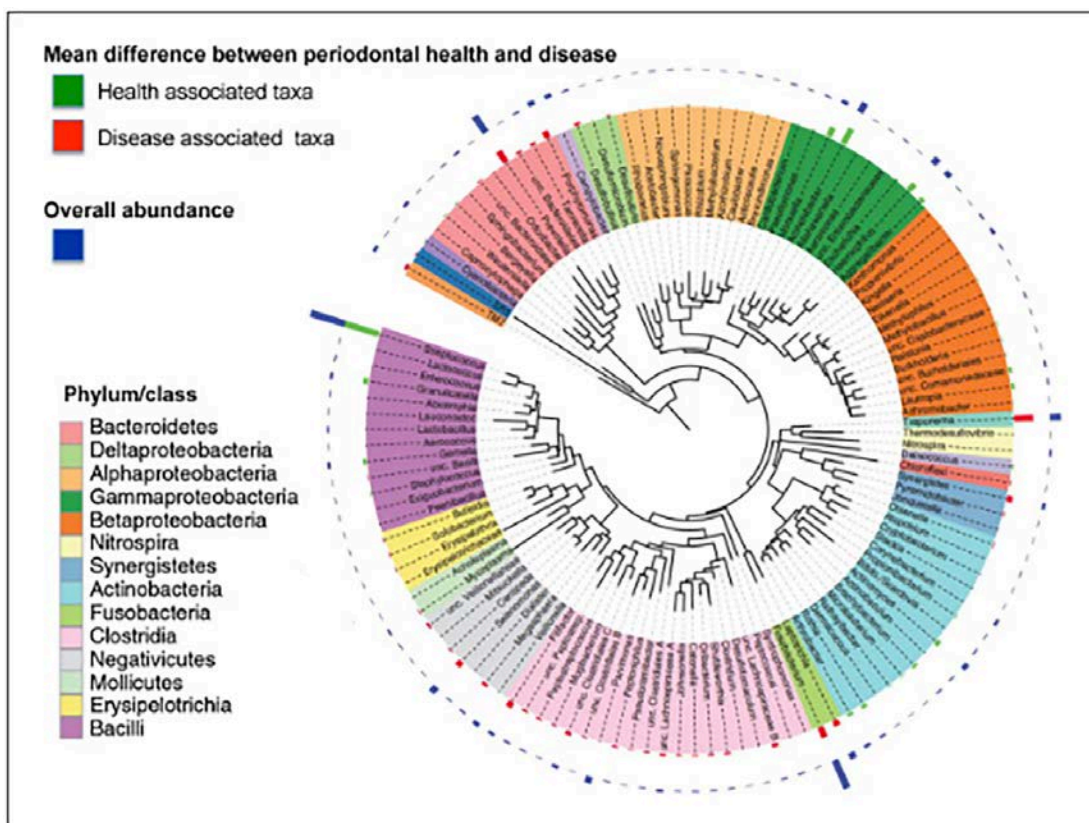


Figure 1. Microbiome of Periodontal Pocket in Health and Disease.<sup>12</sup>

the microbiome varies by location in the oral cavity<sup>13</sup> and that must be taken into consideration when seeking to ascribe some systemic correlation. For example, microbial diversity is different in the floor of the mouth compared to the attached gingiva, and the

supragingival microbiome is different from the subgingival microbiome (Figure 2).<sup>14</sup> Also, there are a variety of factors, such as the time of day and maturity level of plaque, as well as certain foods, drugs and oral care products that can have a profound effect on the oral microbiome.

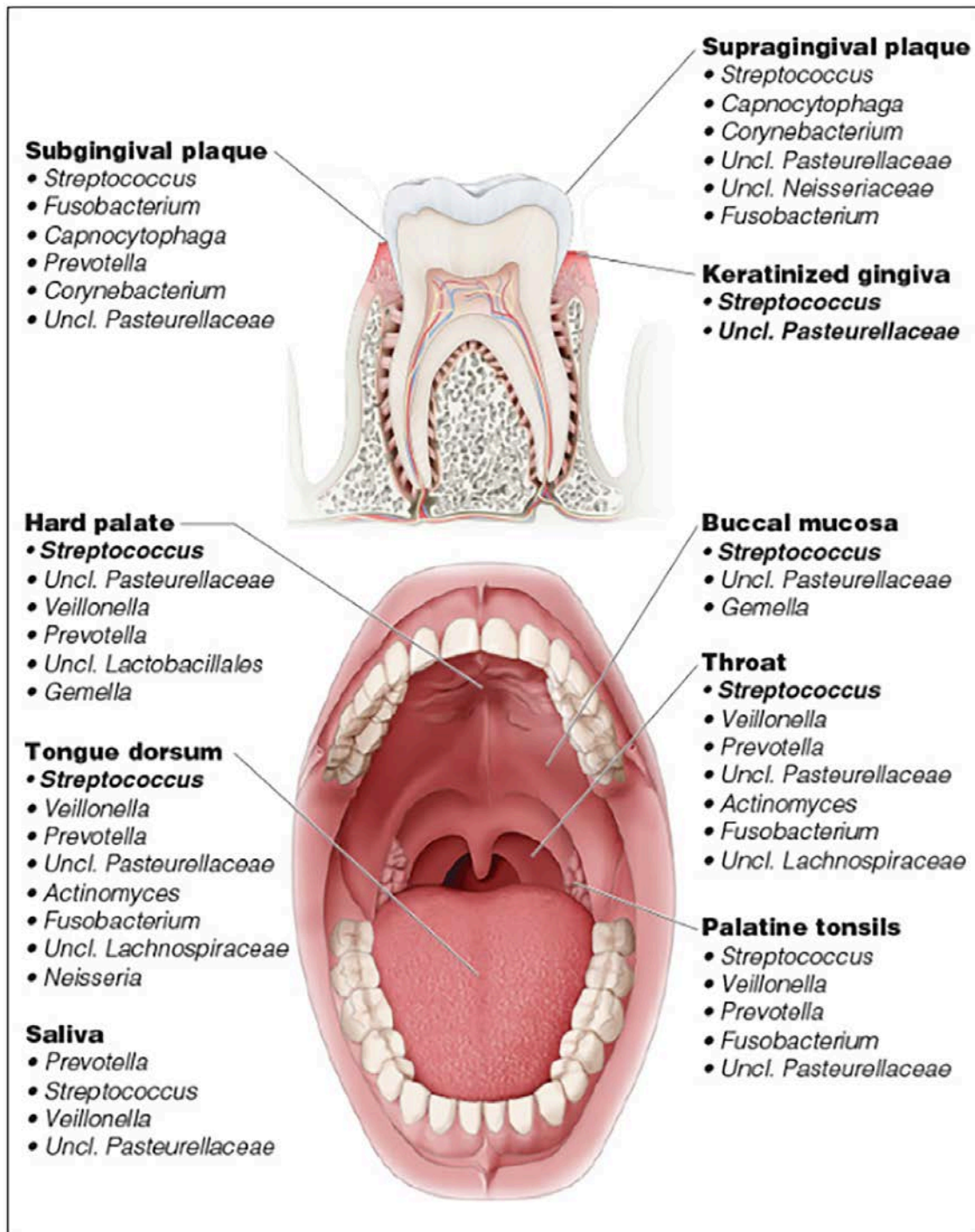


Figure 2. Microbial Diversity in the Oral Cavity.<sup>15</sup>

## Why does it matter?

Recently, there has been increased attention on the role of the gut microbiome and how that influences obesity, diabetes and even depression.<sup>16,17</sup> There is a huge industry that is centered around the identification of microbes within the gut microbiome and the development of interventional therapies as a result. Yet it is easy to forget that the oral cavity is connected to the gut and is the first exposure of the GI tract. Even more importantly, dental professionals are the experts in the oral cavity and should be aware of more than *Streptococcus mutans* and *Porphyromonas gingivalis* and their role on caries and periodontal disease, respectively. In the following sections, we will explore how certain disturbances in the oral microbiome may influence the following systemic diseases:

1. Diabetes
2. Heart disease
3. Hypertension
4. Stroke

Before doing so, it is important to distinguish between correlation and causation. Correlation refers to a negative or positive association with a systemic illness depending on the presence or absence of certain bacterial species in the microbiome. Basically, correlation is a statistical measure of the linkage between two variables, which can range from a weak to strong correlation. Conversely, if a certain bacterial species causes a particular systemic illness, the etiology of the illness is definitively being attributed to an organism and this requires necessary prospective, randomized data. To date, the current scientific data does not support such a causal association for the systemic health conditions we will evaluate. As systemic illnesses are generally multifactorial in nature, we must always be careful in making statements alluding to causality. Two conditions can be associated without a causative link. These conditions may both have similar risk factors, they may be comorbid with a third condition, or there may be population variables that influence both.

## Role of the Oral Microbiome

### Oral Homeostasis

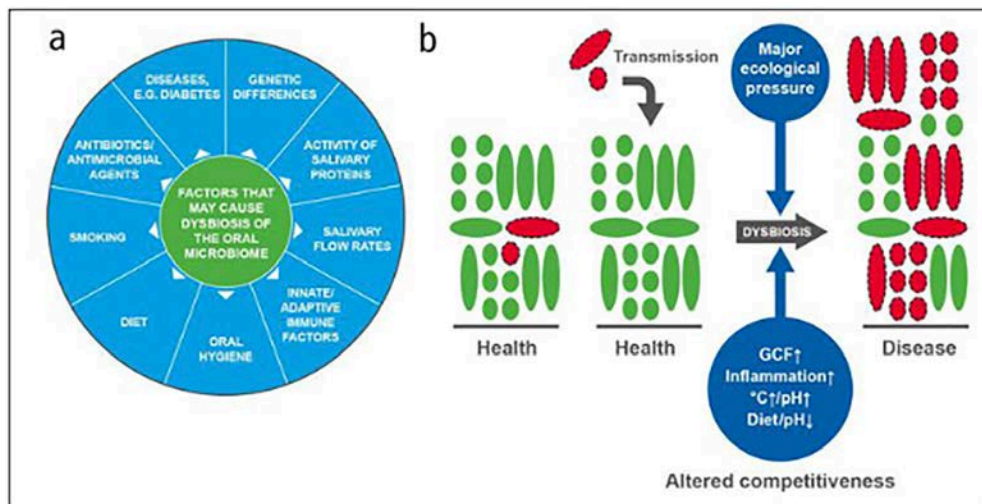
Many may think that all bacteria and microbes are bad, however nothing could be further from

the truth. There are thousands of microbes that are a necessary part of our body's functioning, such as the digestive system as well as the body's normal defense system, many of which produce antibacterial substances (bacteriocins) that serve to eliminate the pathogenic bacteria and work to restore homeostasis.<sup>18</sup> When the body (including the mouth) is in a state of health, there is a balance of microbial species that live in a state of symbiosis, or harmony. While the makeup of the oral microbiome can be very dynamic in a healthy mouth, oral homeostasis can be easily maintained in generally healthy individuals with the right habits.<sup>14</sup>

It is also important for the teeth and associated tissues to be bathed in saliva. Saliva and gingival crevicular fluid (GCF) contain proteins and other substances important for immune regulation, lubrication and maintenance of the oral flora.<sup>19</sup> Some of the substances include immunoglobulin A, lactoferrin and lysozyme which can directly or indirectly regulate the microbiome. While the mechanisms are not fully elucidated, it is well known that the resident flora can have pro and anti-inflammatory functions that work together to maintain oral homeostasis.<sup>20</sup>

For example, oral health is associated with low diversity of bacteria as opposed to greater diversity and richness in a disease state such as periodontal disease. In a healthy mouth, there is a delicate balance between indigenous commensals and putative pathogens that prevent disease from being initiated. The host produces several enzymes (mentioned above) and immunoglobulins (antibodies) that all serve to maintain symbiosis. However, in a case where there are environmental changes in diet (i.e., increase in refined carbohydrates), one may find that there is an increase in pathogens (e.g., *Streptococcus mutans* in caries). If there is no appropriate oral hygiene intervention by the host, over time one can have a shift in bacterial community that leads to dysbiosis and an accompanying disease state (Figure 3).

It is equally as important for the oral microbiome to assist in maintaining oral homeostasis as disturbances to the oral flora can have consequences for oral and systemic disease. Disturbances in the balance of oral flora



**Figure 3.** Shift from Symbiosis to Dysbiosis.<sup>21</sup>

are referred to as dysbiosis. Primary colonizers like gram positive bacteria (e.g., Streptococci species) make up a predominant part of the oral flora and serve as important barriers and first line defense against pathogens (e.g., anaerobic gram-negative bacteria such as *Porphyromonas gingivalis*).<sup>22,23</sup> Generally, the normal flora (i.e., a consortium of beneficial bacteria) in any body site acts like a barrier to the pathogens that seek to invade and disrupt the oral cavity in an attempt to cause disease (e.g., gingivitis, periodontitis and oral Candida infections).<sup>24</sup>

### Systemic Homeostasis

There is a common saying that “a chain is only as strong as its weakest link.” The same concept applies to oral health and how it affects the rest of the body, especially if there is dysbiosis within the oral microbiome. Considering basic anatomy of the body will aid in understanding this relationship. The oral cavity, which is the beginning of the digestive tract, communicates with the sinuses, respiratory tract and digestive tract. It makes sense that the oral cavity would have an effect on multiple systems if compromised. It has taken a long time to recognize that dysbiosis of the oral cavity has an effect beyond the usual suspects of gingivitis, caries and periodontal disease.

However, the advent of molecular techniques, such as 16s ribosomal RNA gene profiling, that identify oral bacterial genetic material have provided insight into correlations with

systemic illnesses, such as diabetes, Alzheimer’s disease, cardiovascular disease and rheumatoid arthritis.<sup>25</sup> While some isolated studies indicate improvement in inflammatory markers and HbA1C levels when periodontal treatment is rendered, there is still not a burden of evidence to conclusively state that oral disease treatment can have a significant effect on systemic health. Much of the evidence is anecdotal, however, anything one can do to improve a patient’s health is worth it. These interventions may provide a more cost-effective way to address or perhaps even prevent some of the costlier chronic diseases.<sup>26</sup>

For example, there are some types of bacteria that convert the nitrates found in food into nitrites.<sup>27</sup> The nitrites are swallowed and converted to nitric oxide, which in turn regulates blood pressure.<sup>27</sup> Imagine if these bacteria in the oral microbiome were lost through poor oral health practices or substances that are ingested. The result would be an increase in blood pressure, which could exacerbate the condition in a patient who is predisposed to hypertension. Hypertension is a universal concern, as approximately half of the American population has some form of cardiovascular disease involving chronic hypertension.<sup>28</sup> This is just one example of how the oral microbiome can influence systemic health and affect systemic homeostasis. However, when reading the following sections, it is helpful to remember that correlation, rather than causation, is typically being discussed.

## Systemic Diseases Correlated with Oral Disease

Two of the most common oral diseases are caries and periodontal disease.<sup>29</sup> Different bacterial profiles have been observed depending on the age of the patient (i.e., child, adult or elderly) or type of decay (severe early childhood caries, root caries, etc.). While caries can be directly affected by shifts in the type and amount of bacteria present in supragingival plaque, periodontal disease is more closely associated with subgingival plaque.<sup>29</sup> Periodontal disease can be considered a “polymicrobial inflammatory disorder of the periodontium.”<sup>30</sup> The disease creates destruction in the gingival attachment, alveolar bone and teeth as a result of proteolytic enzymes released by microbes. The primary pathogens involved in periodontal disease are *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia*, *F. nucleatum*, *T. forsythia*, *E. corrodens*, *T. denticola* and *F. alocis* (Figure 4).<sup>30</sup> These organisms have the dubious distinction of colonizing subgingivally, which allows more direct access to the systemic circulation by travelling through the ulcerated epithelium of the periodontal pocket.

Studies have shown that many oral and systemic diseases may be linked to the oral microbiome.<sup>2</sup> Numerous proposed linkages between oral and systemic diseases are currently being investigated. In fact, a recent systematic mapping of trial registers identified 57 systemic conditions currently being investigated for oral linkages.<sup>32</sup> There are four systemic diseases that have been studied for a number of years that have been found to have good evidence for associations with periodontal inflammation: diabetes,<sup>24</sup> cardiovascular disease,<sup>44-46</sup> hypertension,<sup>33,34</sup> and stroke.<sup>35</sup> As a result of these identified linkages, the World Health Organization has recognized the importance of oral health in their efforts to prevent chronic disease.<sup>36</sup> Dental professionals who are well informed of the relationship between oral and systemic health will be able to provide optimal care for their patients.

### Diabetes

Diabetes mellitus refers to metabolic disorders that interfere with the regulation of glucose. This can occur through insufficient production of insulin by the pancreas or when glucose-dependent cells become resistant to insulin.<sup>37</sup>

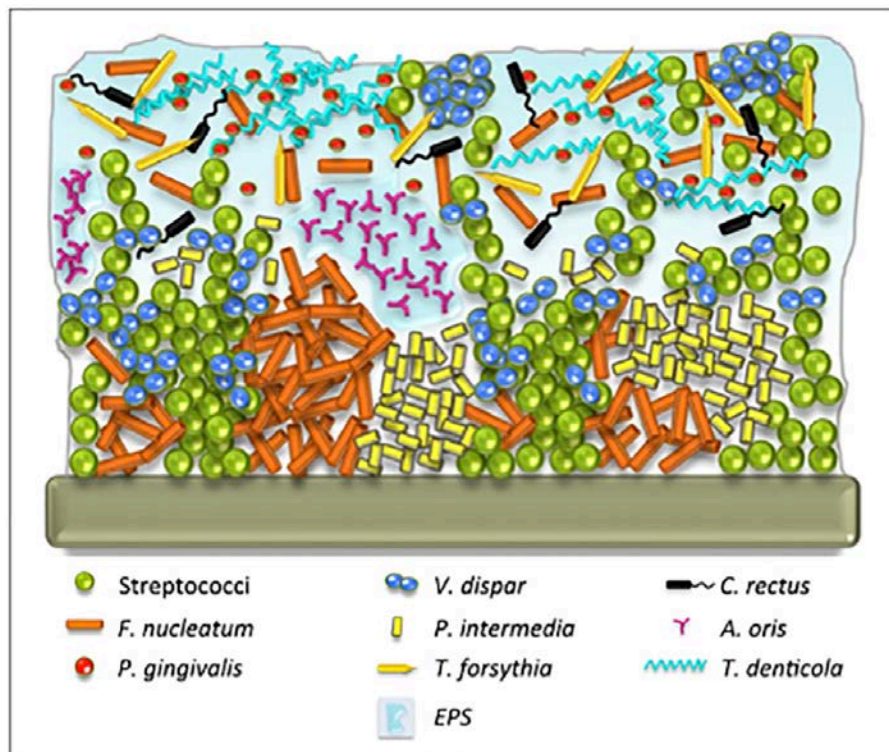


Figure 4. Example of Biofilm in Periodontal Disease.<sup>31</sup>

**Table 1. Microbiota Present in Oral Diseases.**<sup>2,16-18</sup>

<b>Caries</b>	<i>Streptococcus mutans, Lactobacillus sp</i>
<b>Oral Cancer</b>	<i>Peptostreptococcus stomatis, Streptococcus salivarius, Streptococcus gordonii, Gemella haemolysans, Gemella morbillorum, Johnsonella ignava, and Streptococcus parasanguinis</i>
<b>Gingivitis</b>	<i>Leptotrichia, Selenomonas, Streptococcus, Veillonella, Prevotella, Lautropia, and Haemophilus</i>
<b>Periodontal Disease</b>	<i>A. actinomycetemcomitans, P. gingivalis, F. alocis, P. intermedia, F. nucleatum, T. forsythia, E. corrodens, and T. denticola</i>

As the number of Americans diagnosed with diabetes approaches 10% of the population and many more remain undiagnosed,<sup>38</sup> it will be even more important for dental professionals to recognize the screening opportunities that exist within the dental office. For instance, capillary glucose can be measured in the dental office without requiring a finger prick.<sup>39</sup> It is also possible to utilize other diabetic screening tools in addition to a chairside HbA1c screening that assess the patient's history of conditions, such as hypertension and dyslipidemia, as well as an evaluation of periodontal condition and/or missing teeth as an indicator of dysglycemia.<sup>39</sup>

Diabetes and periodontitis are two chronic conditions that have been considered to be linked biologically.<sup>40</sup> It has been established that diabetic patients are at greater risk for developing periodontal disease<sup>29</sup> and that type 2 diabetics have higher prevalence of the disease.<sup>41</sup> In addition, poor glycemic control is often related to more severe periodontal conditions.<sup>41</sup> This could be due to the chronic inflammatory-immune response that accompanies a hyperglycemic environment. Excessive systemic inflammatory mediators travel to the periodontium, which can result in attachment loss, pocket formation and destruction of alveolar bone.<sup>30</sup> Diabetic patients with active periodontal disease may have more difficulty controlling it due to increased inflammation and insulin resistance along with

reduced ability to regulate glucose.<sup>42</sup> There is also a strong microbial component that makes management more difficult.<sup>29</sup> For instance, a study that utilized 16S rRNA gene sequencing noted significant differences between subgingival microbiota in patients with Type 2 diabetes and those without diabetes.<sup>29</sup>

It is thought that periodontal patients who adhere to a strict maintenance program are better able to manage their blood glucose levels and A1c readings. However, research results are mixed. According to a multicenter, randomized controlled trial conducted in 2016, periodontal therapy had no effect on hemoglobin A1c (HbA1c) or other measures indicating glycemic control in diabetic patients.<sup>41</sup> The potential benefit of periodontal therapy is the reduction of local and systemic inflammation, which aids in glycemic control and helps reduce the risk and impact of the disease.<sup>37</sup> Specifically, periodontal therapy helps inhibit the secretion of lipopolysaccharides (LPS) from pathogens, such as porphyromonas gingivalis, which improves the ability of certain cytokine proteins to regulate insulin activity.<sup>30</sup> This suggests that the management of oral disease can positively affect diabetes and vice versa. Additionally, it is worth noting that when diabetic patients receive periodontal treatment and are well-maintained, there is a significant reduction in medical costs and number of hospitalizations observed.<sup>26</sup>



## Cardiovascular Disease

Cardiovascular disease encompasses a variety of conditions, that range from acute to chronic. According to the World Health Organization, cardiovascular diseases are a group of disorders that affect the heart and blood vessels (Table 2).<sup>64</sup> The conditions that fall under the umbrella of cardiovascular disease include, but are not limited to, heart disease, heart attack, stroke, heart failure, arrhythmia, and problems with the heart valves.<sup>43</sup>

Some systematic reviews have established that a relationship exists between periodontitis and cardiovascular disease,<sup>44-46</sup> while others refute this association.<sup>47</sup> One proposed mechanism for this relationship is that periodontal pathogens may be associated with cardiovascular complications, such as increased lipid accumulation and platelet aggregation.<sup>30</sup> For instance, *P. gingivalis* and *S. sanguis* can increase platelet aggregation and gather to form arterial plaque. Atherosclerosis is a progressive disease marked by fibrous elements and lipids accumulating in the large arteries.<sup>40</sup> Interestingly, *A. actinomycetemcomitans* has been located within atherosclerotic plaque.<sup>30</sup> Other oral microbiota, such as *Streptococcus*, *P. gingivalis*, *F. nucleatum*, *T. forsythia*, and *Neisseria*,

have also been detected in atherosclerotic plaque.<sup>39</sup>

It is likely that the pathogens enter the circulatory system via the oral mucosa and move to the arteries where LPS are secreted along with inflammatory mediators that result in atherothrombogenesis.<sup>30</sup> This supports the infection hypothesis of cardiovascular disease, where bacteria invade the bloodstream, enter the endothelium and cause endothelial dysfunction, inflammation and atherosclerosis.<sup>29</sup> Periodontal patients who suffer from cardiovascular disease should be made aware of the potential risk factors associated between the two conditions. However, caution should be used during such discussions as no causal relationship has yet been established.

## Hypertension

Hypertension, or high blood pressure, is highly prevalent amongst world populations and is a major contributor to premature death and disability.<sup>48</sup> According to the World Health Organization, 1.13 billion people are affected by elevated blood pressure worldwide.<sup>49</sup> This number may be even higher when considering the updated American College of Cardiology/ American Heart Association (ACC/AHA)

**Table 2. Cardiovascular Diseases.**<sup>64</sup>

<b>Coronary Heart Disease</b>	Disease affects blood vessels that supply heart muscles
<b>Cerebrovascular Disease</b>	Disease of blood vessels supplying brain
<b>Peripheral Arterial Disease</b>	Disease of blood vessels supplying arms & legs
<b>Rheumatic Heart Disease</b>	Damage to heart valves and muscle due to rheumatic fever, caused by streptococcal bacteria
<b>Congenital Heart Disease</b>	Malformation of heart structure, present at birth
<b>Deep Vein Thrombosis and Pulmonary Embolism</b>	Blood clots in leg veins, which can become dislodged and travel to the heart and lungs

Guidelines for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults.<sup>50</sup> The new ACC/AHA guidelines categorize Stage 1 hypertension at 130/80 mm Hg, rather than 140/90 mm Hg.

Several studies have indicated that periodontal disease and hypertension are related, but differences in population characteristics, diagnostic criteria and risk factors make it difficult to determine exactly how they are related.<sup>51</sup> According to a retrospective study evaluating dental records of 90 patients that underwent periodontal therapy, a possible relationship between periodontal disease and hypertension was reported.<sup>52</sup> A systematic review and meta-analysis found that periodontal diseases, especially severe periodontitis, were associated with a higher risk of hypertension.<sup>51</sup> In a study by Lira-Junior and colleagues, it was noted that patients with hypertension demonstrated significantly higher counts of *P. melaninogenica*.<sup>34</sup> Patients with hypertension and generalized bone loss had higher counts of *S. mitis* in their saliva.<sup>34</sup> However, the medical conditions were disclosed through self-report, rather than a clinical examination and results should be considered accordingly.

In a study involving Japanese university students, periodontal disease was shown to be a risk factor for hypertension.<sup>48</sup> Specific clinical factors, such as clinical attachment level and the number of missing teeth, were associated with increased systolic blood pressure in postmenopausal women who were not currently being treated for hypertension.<sup>53</sup> The findings suggested that the cumulative effects of oral disease may be related to blood pressure control.<sup>53</sup> However, it could also indicate that positive and negative habits accumulate over time. Thus, patients who floss most likely also exhibit other healthy behaviors, such as exercising and eating healthy food.

### Stroke

Cerebrovascular accident (CVA), commonly referred to as a stroke, occurs when brain cells die due to a lack of oxygen resulting from an artery in the brain becoming blocked (ischemic stroke) and/or rupturing (hemorrhagic stroke).<sup>34</sup>

Of the two, ischemic strokes are the more common.<sup>54</sup> The common risk factors include hypertension, diabetes, smoking, obesity and drug use.<sup>55</sup> In a Japanese study conducted in 2016, researchers found that there was an increase (26%) of collagen binding protein, cnm- positive *Streptococcus mutans* in those with hemorrhagic stroke as compared to 6% in ischemic stroke.<sup>56</sup> In a more recent study, there was a correlation between C-reactive protein and moderate-severe periodontitis and ischemic stroke.<sup>57</sup> There has even been an association between *S. mutans* and several types of cerebrovascular events, such as hemorrhage and aneurysms.<sup>58</sup>

The evidence for a causal or correlative relationship between oral bacteria and stroke is still emerging and does not appear to be as strong. However, because strokes represent vascular injury it can be postulated that inflammatory conditions, such as periodontitis, can have an impact on vascular integrity due to hypertension and atherosclerosis of weakened vessels.<sup>35</sup> Research is currently being undertaken to fully understand the role oral bacteria plays in cerebrovascular events, such as strokes, which are known to have multifactorial causes. It can be inferred that periodontitis may be a risk factor for strokes when combined with other more well described risk factors.

### Diagnostic Methods for Microbiome Analysis

Ribosomal RNA gene profiling has been one of the major reasons scientists have been able to identify components of the oral microbiome. For years, study of the microbiome was limited to organisms that could be grown or cultured in a lab. This was a significant drawback, because if an organism could not be grown, it could not be studied in order to determine what impact it has on oral health. The use of ribosomal RNA gene profiling has not only demonstrated that there are numerous organisms that make up the oral microbiome, but it has also enabled greater understanding of the profile of genetic material. In 2010, the Human Oral Microbiome database was launched. Basically, the database contains a library of genetic material that can be matched to existing or known profiles. As

molecular techniques have improved, there are now less costly and faster methods to sequence and identify components of the oral microbiome. Next generation sequencing (NGS) has allowed scientists to perform analysis more efficiently with less cost, thus moving potential understanding along much faster. These techniques have prompted the discovery of over 770 different taxa of microbes to date and have helped house genetic material in a database that can be used to study the oral microbiome more closely.

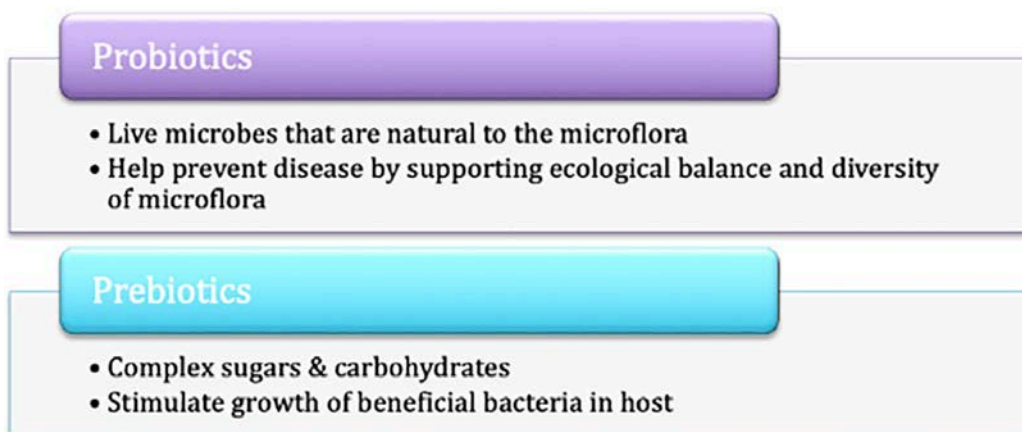
## Current Interventions

### Prevention

If at all possible, it is beneficial to maintain health and prevent disease in the oral cavity before it begins. It has been suggested that the use of probiotics, or live microbes that are natural to the microflora, can help prevent disease by introducing beneficial bacteria that support “ecological balance” or increase the biodiversity of the microflora.<sup>7,30</sup> For instance, people with high levels of *Capnocytophaga ochracea* had lower amounts of *P. gingivalis* and vice versa. Therefore, a patient with elevated levels of *P. gingivalis* may be given *C. ochracea* as a preventive measure before periodontal disease begins.<sup>30</sup> Prebiotics, on the other hand, are complex sugars intended to stimulate additional growth of beneficial bacteria within the host (Figure 5). It is important to note that the effects of probiotics on the host are not well established as many of the studies have been conducted *in vitro*.<sup>30</sup> Thus, caution in recommending their use is advised.

Saliva is another important component in disease prevention. Saliva contains nutrients and antibodies, which act as a very important protective factor for the oral cavity by helping to maintain homeostasis and providing protection from disease.<sup>30</sup> In healthy environments, microorganisms can prevent disease from progressing in the following ways: 1) preventing adherence of pathogens by occupying their preferred site, 2) actively blocking pathogens from adhering, 3) decreasing the pathogen’s ability to multiply, and 4) diminishing the virulence of the pathogen.<sup>30</sup> However, when an ecological shift occurs due to poor oral hygiene, genetics, and/or a compromised immune system, it is possible for the disease process to begin. Therefore, maintaining good oral hygiene is critical, because it is one of the few things patients can control when it comes to disease prevention. Ultimately, the only way to maintain a healthy microbiome is through good oral hygiene and an immune system that is functioning properly.<sup>30</sup>

When considering ways to support the immune system and defend against disease, there are positive benefits to maintaining a healthy body weight. Factors that accompany obesity, such as oxidative stress and inflammation, increase risk factors for disease.<sup>59</sup> Research evaluating the relationship between periodontal disease and obesity suggests that individuals with a BMI > 30 are at three times greater risk of developing periodontitis.<sup>60</sup> Interestingly, patients who received gastric bypass surgery demonstrated a reduction



**Figure 5.** Comparison of Probiotics and Prebiotics.<sup>7,30</sup>

in periodontopathogenic bacteria and select inflammatory biomarkers; however, periodontal conditions did not improve after significant weight loss.<sup>61</sup> This suggests that weight loss alone may not be sufficient for helping improve periodontal status. However, due to the risks associated with obesity and periodontal disease, dental professionals can utilize nonsurgical periodontal therapy and antimicrobials to help control oral pathogens.<sup>59</sup>

### Treatment

The goal of periodontal treatment is to control biofilm and prevent pathogenic bacteria from spreading within the oral cavity<sup>30</sup> and into other body systems. Manual periodontal treatments can be supplemented with local or systemic antibiotics in order to target pathogens in the oral cavity as well as systemically.<sup>30</sup> Systemic drugs however should be used as a last resort and only if other treatments have not been successful, given recent concerns with antibiotic resistance. If possible, genomic analysis of the individual patient's oral microbiome would provide valuable information enabling the clinician to prescribe the appropriate drug that would specifically target the pathogens present.<sup>30</sup> Use of salivary microorganisms could also be beneficial in the future for diagnosing diseases, such as periodontal disease, oral squamous cell carcinoma, and pancreatic cancer because the bacterial composition differs from that of healthy individuals.<sup>29</sup>

Periodontal treatment along with lifestyle modification can be very beneficial when working toward a healthier oral environment. For instance, smoking can negatively affect the composition of subgingival microorganisms, which can increase the risk for developing periodontal disease. In addition, smoking can impact the "symbiotic and commensalistic relationships" between subgingival microbes. However, it is encouraging to note that tobacco cessation can result in a decrease of pathogenic bacteria and an increase in beneficial bacteria, such as *Veillonella parvula*.<sup>29</sup> Therefore, any information that dental professionals can provide patients regarding tobacco cessation will be greatly appreciated. In addition, referrals to local providers who specialize in the subject can be very helpful for patients looking for counseling and guidance in the process.

In the future, BALOs, or *Bdellovibrio*-and-like organisms, which act as predators that target and kill anaerobic, Gram-negative bacteria may be helpful for treating periodontal disease. Since predator-prey interactions are highly strain specific, it would be imperative to identify which bacteria are present before utilizing BALOs.<sup>30</sup> However, there is a drawback, because they have only been studied in laboratory settings, rather than clinical settings. Unfortunately, when tested in a laboratory setting, BALOs had difficulty functioning in anaerobic environments, which would make it impossible to prey on the anaerobic bacteria that reside deep within periodontal pockets.<sup>30</sup> Perhaps future scientific advancements will enable BALOs to target periodontal bacteria in a live patient.

### Summary

As a result of the previous discussion, it is clear that the oral microbiome is both complex and very important in regard to oral and systemic health. There has been a lot of attention focused on gut health, probiotics and the gut microbiome. Because of this, the public may be more receptive to improving oral and systemic health with interventions that influence the oral microbiome. As the oral microbiome and its interactions are more fully elucidated, more interventions will emerge as a potential remedy for oral disease. For instance, toothpastes are being designed with ingredients, such as zinc and arginine, to kill bacteria while fortifying the soft tissue.<sup>62</sup> It is important for dental professionals to stay up to date on the research in order to be informed and better able to answer patient questions that arise.

Due to the new information on metagenomics and the Human Microbiome, it is likely that Precision Medicine will become more common when treating patients. According to the Precision Medicine Initiative, precision medicine is defined as "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment and lifestyle for each person."<sup>8</sup> This type of approach can be helpful for considering the differences between individuals when planning treatment, rather than looking at what might work for the

average person.<sup>61</sup> This type of personalized care can also be seen in the concept of P4 medicine, which is named for the following four attributes: predictive, preventive, personalized, and participatory.<sup>62</sup> This type of medicine uses a combination of biology and technology to analyze data for clinical practice, which will enable practitioners to demystify disease and

focus on wellness for individuals.<sup>63</sup> This type of practice will be very beneficial in dentistry as well. In closing, as research on the human oral microbiome and subsequent interventions continue to develop, it is exciting to consider the possible applications for advancing oral health care.

## Course Test Preview

To receive Continuing Education credit for this course, you must complete the online test. Please go to: [www.dentalcare.com/en-us/professional-education/ce-courses/ce561/test](http://www.dentalcare.com/en-us/professional-education/ce-courses/ce561/test)

- 1. Which of the following are components of the oral microbiome?**
  - A. Pathogens
  - B. Commensal organisms
  - C. Genomes
  - D. All of the above.
- 2. Microbial content varies throughout different locations within the mouth. The supragingival microbiome and subgingival microbiomes are identical.**
  - A. The first statement is false. The second statement is true.
  - B. The first statement is true. The second statement is false.
  - C. Both statements are true.
  - D. Both statements are false.
- 3. It is more challenging to establish a correlation between oral and systemic diseases than it is to establish causation.**
  - A. True
  - B. False
- 4. What is the meaning of oral dysbiosis?**
  - A. Disturbances in the oral flora that negatively affect oral homeostasis.
  - B. Activities that occur within the oral flora that positively affect oral homeostasis.
  - C. Occurs when good and bad bacteria are balanced within the oral microbiome.
  - D. None of the above.
- 5. Which of the following statements is true regarding the association between diabetes and periodontal disease?**
  - A. Type 1 diabetics have a higher prevalence of periodontal disease.
  - B. Having diabetes can decrease the risk of developing periodontal disease.
  - C. There is not an established relationship between periodontal disease and diabetes.
  - D. Periodontal disease may interfere with glucose regulation in diabetic patients.
- 6. All of the following oral bacteria have been detected in atherosclerotic plaque, except one. Which one is the exception?**
  - A. *T. forsythia*
  - B. *S. mutans*
  - C. *A. actinomycetemcomitans*
  - D. *P. gingivalis*
  - E. *Neisseria*
- 7. According to Gordon and colleagues, there were two clinical factors that were positively associated with increased systolic blood pressure in postmenopausal women who were not currently being treated for hypertension. Which clinical factors were they?**
  - A. Mobility
  - B. Clinical attachment level
  - C. Number of missing teeth
  - D. A and B
  - E. B and C

8. **Which type of stroke is the most common?**
- A. Hemorrhagic
  - B. Ischemic
  - C. Rupturing
  - D. Hypertensive
9. **What technique has allowed scientists to perform genomic analysis more efficiently and cost effectively than initial endeavors?**
- A. Polymerase Chain Reaction
  - B. Next generation sequencing
  - C. Shot gun sequencing
  - D. 18s RNA sequencing
10. **Which statement is correct regarding probiotics and prebiotics?**
- A. Probiotics are complex sugars that stimulate growth of beneficial bacteria.
  - B. Prebiotics are live microbes that are natural to the microflora.
  - C. Probiotics are live microbes and prebiotics are complex sugars.
  - D. Prebiotics are simple sugars that stimulate the growth of beneficial bacteria.
11. **Maintaining good oral hygiene is critical, because it is one of the few factors patients can control when it comes to disease prevention.**
- A. True
  - B. False
12. **Why are *Bdellovibrio*-and-like organisms (BALOs) unable to be used for treatment of periodontal disease?**
- A. They target Gram-positive bacteria.
  - B. They have been used successfully in clinical studies.
  - C. They have shown limitations functioning in anaerobic environments.
  - D. They directly target aerobic bacteria.

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### Additional Resources

- [FightGumDisease.com. Gum Disease & Your Whole Body Health](#). Accessed June 18, 2019.
- [FightGumDisease.com. Gum Disease & Diabetes: A Two Way Street](#). Accessed June 18, 2019.
- [CDC. Heart Disease and Stroke Map Widget](#). Accessed June 18, 2019.

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