2016

Periodontitis and the link with heart disease: can common oral bacteria be eliminated to prevent heart disease?

Caron, Nicole Rose

http://hdl.handle.net/2144/19203

Boston University
PERIODONTITIS AND THE LINK WITH HEART DISEASE: CAN COMMON ORAL BACTERIA BE ELIMINATED TO PREVENT HEART DISEASE?

by

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B.S., Emmanuel College, 2014

Submitted in partial fulfillment of the requirements for the degree of Master of Science

2016
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NICOLE CARON

ABSTRACT

The importance of oral health on systemic health is a highly researched area of study in recent years. There has been a shift in dental visits from acute emergencies to ongoing preventative care due to the knowledge connecting oral and systemic health. One of the commonly researched connections is the link between periodontal disease and heart disease. Periodontal disease is defined as inflammation of the gum tissue, resulting in periodontal pockets that can lead to infection, bone loss and even loss of the tooth. Cardiovascular disease, or heart disease, is a term that encompasses many different conditions of the heart, including heart failure, myocardial infarction, atherosclerosis and angina. There is constant research to better understand the relationship between the two diseases, as well as any causality that may exist. Recent studies have been able to link the diseases, but no causal link has been found. The role of the bacteria involved in both diseases has recently been considered to see if these organisms are related to a potential causal link.

Two particular bacteria that are known to be involved with periodontal disease are Porphyromona gingivalis and Treponema denticola. These bacteria are present when a patient develops periodontal disease, but they are not usually present in a healthy individual. Additionally, the bacteria that make up the
contents of plaque found in the heart have been studied to see if there are any similarities with oral microbes. It has been found that oral bacteria can be present in arterial plaque samples. This research may allow a better understanding of how and why heart disease occurs and potentially serve as a way to treat heart disease accompanied by periodontal disease, if a causal relationship is elucidated.

Heart disease is usually a devastating disease, sometimes resulting in the death of the patient. If more patients attend the dentist as a preventative measure, the risk of periodontal disease and associated pathologies may be reduced. Additionally, those that have already developed periodontal disease can work with a dental professional to reverse the disease. It is known that the bacteria in the mouth can enter the bloodstream upon infection, so patients with suspected periodontitis should be treated to avoid the bacteria from entering the blood and affecting other organs such as the heart.

An examination of the bacteria commonly found in the oral cavity at times of periodontal disease may lead to a better understanding of how and why these bacteria invade the bloodstream. It would be beneficial to compare the microbiota of both the plaque in the mouth and the plaque in a vessel supplying the heart in a patient suffers from heart disease. This understanding may lead to therapeutic interventions that aid in the prevention of bacteria traveling in the bloodstream.

For many Americans, oral health care was believed to end at home by brushing and flossing. However, it is important to see a dental professional to
avoid any possible complications that may not be apparent to the untrained eye. A simple dental cleaning may be important to detect the start of periodontal disease, and treatment can be initiated to end the potential spread of bacteria. It is important to maintain positive oral health in order to maintain overall systemic health, including the avoidance of heart disease.
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LIST OF ABBREVIATIONS

ADA .................................................................American Dental Association
AHA ..............................................................American Heart Association
CHD .................................................................Coronary heart disease
CVD .................................................................Cardiovascular disease
LDL .................................................................Low-density lipoprotein
LPS .................................................................Lipopolysaccharide
NHLBI ..........................................................National Heart, Lung, and Blood Institute
NIDCR .........................................................National Institute of Dental and Craniofacial Research
P. gingivalis .................................................. Porphyromonas gingivalis
T. denticola ..................................................... Treponema denticola
INTRODUCTION

For many Americans, brushing their teeth once or twice daily and flossing regularly are adequate to maintain a healthy smile. In fact, according to a study as part of the Gallup-Healthways Well-Being Index, only about 64.7% of adults went to a dentist in 2013. Many patients are unaware of the importance of visiting a dentist and the systemic health consequences. In the past, the dentist was visited when there was a problem. However in recent years, there has been a push to visit the dentist to prevent the possibility of dental and periodontal emergencies. Additionally, according to the American Dental Association (ADA, n.d.), people with a high risk of periodontitis should visit the dentist more frequently, and low-risk patients should still plan to visit the dentist regularly to prevent any unwanted oral health problem (Bushak, 2014). Annual dental visits are important to not only to protect a patient’s teeth, but also to maintain systemic health due to recent findings.

In recent years, the importance of positive oral health has been shown to help maintain positive systemic health. Research has shown that gum disease may be linked to diseases such as heart disease or diabetes (Beck et al., 1996; Chistiakov et al., 2016). Studies indicate that individuals with gum disease, or periodontitis, tend to experience heart disease or diabetes more often than those without periodontitis. This connection, however, does not consider any other factors, such as smoking, that could contribute to both periodontitis and heart disease (ADA, n.d.). The connection between heart disease and periodontitis is a
field of research that is actively being explored to gain insight on the importance of oral health to maintain systemic health.

According to a recent study completed by Jeffcoat et al., (2014) the researchers explored whether or not periodontal treatment had an effect on systemic health issues based on the cost of treatment. In this study, it was concluded that simple treatment of periodontal disease may improve health in systemic conditions. This finding will encourage further research in the association between periodontitis and conditions such as heart disease (Jeffcoat et al., 2014). Three of the most understood and researched conditions known to be affected by periodontitis include heart disease, diabetes, and preterm delivery in females (Michalowicz, 2006; Taylor, 2008).

Periodontitis and heart disease are frequently studied to determine if a correlation between the two diseases exist, as there are similar risks for the diseases. A study completed in 2013 hoped to find a causative relationship between these diseases by examining particular bacteria found in periodontitis and the effects on atherosclerosis. It is believed that the particular bacteria examined were able to enter the blood stream from the gums and may have promoted the formation of plaque in the aorta. Additionally, the mice used in this study will be a helpful model in the future to continue experimentation (Rivera et al., 2013). Finding a causal connection between heart disease and periodontal disease is a goal for current research.
In addition to the association between heart disease and periodontal disease, there is also considerable research documenting a connection between diabetes and periodontitis. According to a 2008 review, diabetes has a negative effect on periodontal health, causing periodontitis. The information gathered through this review showed that periodontal disease likely had harmful effects on diabetes. The goal of future research is to uncover whether or not diabetes can be managed by controlling periodontal disease (Taylor & Borgnakke, 2008). Because many Americans develop diabetes, connecting periodontitis and diabetes may help lessen the prevalence of the disease or help to reduce the association if periodontitis is treated appropriately.

Like heart disease and diabetes, another common risk factor of periodontal disease is preterm birth. In one study of pregnant women, the treatment of periodontal disease was found to be safe to perform and did not affect the rate of preterm birth (Michalowicz et al., 2006). However, a more recent study completed in 2016 showed that periodontitis was found to be associated with preeclampsia, a condition that results in high blood pressure and swelling for the mother. This study claims that periodontitis is not associated with unprompted preterm births (Soucy-Giguere et al., 2016). There are many risk factors associated with periodontitis that go beyond the mouth and likely affect systemic health.

It is now known that the effects of periodontitis go far beyond the mouth. Because of this, it is important for the patient to regularly visit the dentist to avoid
any future risks, such as heart disease, diabetes, or preterm birth. The connection between oral health and heart disease has been avidly studied but additional research is needed. CVD is the leading cause of death throughout the world. It is estimated that in 2012, about 3 of every 10 deaths was related to heart disease (World Health Organization, n.d.). Because of the effects of this serious disease, it is important to eliminate the risks as much as possible.

**Periodontitis**

Gum disease, or periodontitis is a common oral health problem among adults in the United States. Gum disease occurs when bacteria build up and form plaque on the teeth. If the plaque is not properly removed, it will harden and form tartar, which can only be removed by a dental professional. Initially, the bacteria will cause gingivitis, which is an inflammation of the gums; this can usually be reversed if positive oral habits are initiated. However, if gingivitis is not properly cared for, periodontitis can occur (Figure 1). In this case, pockets form between the teeth, causing the gums to move away from the teeth. The plaque on the teeth is able to grow below the gums, and the body begins to fight the infection. Because the bacteria are now surrounding the bone, the body will attack the bone and tissue supporting the teeth, which can cause the teeth to be removed (National Institute of Dental and Craniofacial Research (NIDCR), n.d.). It is very important to maintain good oral health to prevent tooth loss, as well as potentially life-threatening health concerns.
Figure 1. Progression of periodontal disease. Top left: an image of a healthy mouth with normal, healthy gums. Top right: an image of gingivitis, which causes mild inflammation of the gum tissue. Bottom left: an image of a person with moderate periodontitis. This patient is experiencing inflammation and recession of the gums, as well as decay of the teeth, especially at the gum line. There is also likely bone loss. Bottom right: an image of severe periodontitis. This patient has inflammation, as well as great recession of the gums. There is also a great amount of decay and likely bone loss. This patient is at risk of edentulism if periodontitis is not properly treated (The Smile Consultants, n.d.)
Ideally, at a dental visit, a patient will have healthy gums and teeth. However, when there are signs of periodontal disease, the dental professional will check for periodontal pocket depth as well as the presence of plaque and tartar or bone recession. In a patient with healthy gums, the gum tissue is firm and there is no bone or ligament loss. When a patient develops gingivitis, there is slight inflammation of the gums, and a pocket can be detected using a probe. In serious cases when a patient develops deep and infected periodontal pockets, as well as bone and ligament loss, a dental professional must treat the area (Figure 2). An efficient and traditional way to treat periodontal disease without surgery is by scaling and root planing, along with compliance of the patient to participate in good oral hygiene. This technique has been used to treat periodontal disease for over 50 years. More recent technological advancements in the field have allowed for better treatment when combined with scaling and root planing (Zaugg et al., 2014). If the patient has progressed beyond healthy gums to gingivitis or periodontitis, a dental profession will have to treat the area, likely by scaling a root planing.
Figure 2. Diagram of the process of periodontitis. In a healthy mouth, the gums are firm, and there are no underlying issues with the tooth structure or bone. If the tooth is healthy, there is no loss of bone or the periodontal ligament. When a patient develops gingivitis, there is an indication of swollen gums, as well as the start of periodontal pockets. These pockets are detected using a probe, an instrument the dental professional will use to measure the depth of the pocket present. The most severe form of the inflammation is periodontitis. This occurs when the pocket is deep and infected, and plaque and tartar are present. At this stage of the disease, there is also loss of the bone and ligament, which can result in the loss of one or multiple teeth (Periodontal disease, (n.d.)).
There are certain types of bacteria normally inhabiting the gingival sulcus, the area between the tooth and the gingiva. These bacteria include streptococci, and *Neisseria* species, for example. The bacteria normally found here can be anaerobic. Once plaque begins to form, more bacteria, such as actinomycetes and *Veillonella* species are able to adhere (Table 1). There are over 500 species of bacteria found in dental plaques, and the type of bacteria depends on factors such as oxygen supply, pH, diet, and oral health. Factors such as poor oral hygiene or smoking, as well as other negative behaviors can lead to gingivitis, and these factors can lead to a different population of bacteria (Chistiakov et al., 2016). Thus, while bacteria normally exist in the oral cavity, however, poor oral health can lead to changes in the types of bacteria present and some may be harmful.
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**Table 1. Bacteria commonly present in dental plaque.** Many types of bacteria exist in the oral cavity, including both Gram-negative and Gram-positive bacteria of different sizes and shapes. Although some bacteria are normally found in the oral cavity, some bacteria are an indication of disease (Lockhart, Bolger, et al., 2012).
Gingivitis is the beginning of periodontal disease, and at this time, the amount of bacteria increases in this setting (Chistiakov et al., 2016). The pathogens found at this time mainly include *Porphyromonas gingivalis* as well as other Gram-negative bacteria. The bacterial attack also induces inflammation by attracting pro-inflammatory immune cells. This inflammation, along with the dental plaque causing a deeper sulcus and bacterial destruction, results in a periodontal pocket. This further induces inflammation and bacterial invasion, and gingivitis will progress to periodontitis. Periodontal disease results in multiplication of dental plaques leading to bone loss and eventual tooth loss. The periodontal pocket will discharge gingival crevicular fluid, which contains many products, including inflammatory mediators and enzymes. Periodontitis often leads to bleeding of the gums, which allows the fluid and the bacteria to enter the bloodstream (Chistiakov, 2016). Periodontal disease has many types of bacteria involved. Although some bacteria are normally found in the oral cavity, there are some dangerous Gram-negative bacteria that can lead to serious oral health defects as well as systemic health issues.

**Coronary Heart Disease**

Coronary heart disease (CHD) results from disease of the blood vessels in the heart that leads to a heart attack. A heart attack occurs when an artery becomes blocked and cannot deliver nutrients to the heart (National Heart, Lung, and Blood Disease (NHLBI) What is Heart Disease?"(n.d.)). This blockage is
often caused when plaque builds up in the artery walls leading to narrow arteries and eventually a blockage in a process referred to as atherosclerosis (NHLBI “What is Cardiovascular Disease?”, n.d.). Heart disease can lead to heart failure or even death, indicating the importance of proper diagnosis and treatment.

Some of the controllable risk factors of CHD include high cholesterol, elevated blood pressure, diabetes, being overweight, smoking, unhealthy diet, and stress. A healthy lifestyle can help control the risks of heart disease to lower the chance of suffering from a myocardial event ((NHLBI “What Are CHD Risk Factors?”, n.d.). Some of these risk factors, such as smoking and diabetes, are also shared with periodontal disease. This helps explains why periodontitis and heart disease may occur at the same time, and further evidence suggests that there may be an additional association between these two diseases, such as the bacteria present in the plaque formation. The best ways to lower the risk of heart disease and potentially periodontal disease are to stop smoking, control body weight and blood pressure, and implement a workout regimen (American Heart Association (AHA), 2013).

A common predictor for heart disease is chest pain, often referred to as angina. If the symptoms of angina are recognized and treated early, the patient will likely lower the risk for developing heart disease. When plaque develops in the arteries, the heart muscles are weakened due to a lack of oxygen (Figure 3). It is important for patients to understand the symptoms of angina, as treating the
start of CVD could save the person’s life. Additionally, these symptoms differ in men and women, which can make the symptoms more difficult to detect and diagnose. Men more often experience obstructive coronary artery disease, whereas women often develop microvascular disease, which occur within the arteries branching from the coronary arteries (AHA, “Angina in Women Can Be Different Than Men”). It is important to understand if angina is occurring in order to help prevent future heart disease.
Figure 3. Development of heart disease due to plaque. In heart disease, plaque will build up on the arterial walls, which obstructs the flow of oxygen and blood. Without both oxygen and blood, the heart will begin to die because it is no longer receiving essential nutrients. If the heart tissue continues to die, heart failure can occur and cause death (Adam Images, n.d.).
Periodontitis and Coronary Heart Disease

Patients with periodontitis are more likely to develop heart disease due to two paths. One explanation is that the bacteria involved in periodontitis are able to release toxins that can travel throughout the body to help form plaque in the heart. Another explanation is that inflammation occurs due to the bacteria affecting the liver and causing release of proteins. This release of proteins could lead to inflammation of blood vessels, leading to heart disease, such as heart attack, or a stroke (Colgate Oral Care, 2013). Studies have reported that in patients with periodontal disease, heart disease is the most common situation to occur (Beck et al., 1996). Both possibilities lead to serious systemic health issues, such as heart disease, and it is therefore important to control.

In addition, patients with heart disease are also at risk of developing endocarditis, which is usually a bacterial infection of the heart valves. Because of this, antibiotics are usually given to people at risk because of valvular disease before any dental procedure is performed (Colgate Oral Care, 2013). There are many risks associated with heart disease. Because the connection between oral health and systemic health has been shown in recent years, it is important to maintain positive oral health to maintain systemic health.

A review study completed in 2008 compared studies conducted in Brazil to determine a causal relationship between heart disease and periodontal disease (Weidlich et al, 2008). The study determined that more research should be completed in order to find a causal relationship, as opposed to an association,
which is consistent with many studies on this topic. Although this particular review focuses only on the Brazilian population, any information gathered can be used to better understand the association with all populations. The review showed that the studies that have been conducted focus on an association, rather than a cause for the relationship. A comparison of three studies shows the results of these findings (Table 2). Recent studies have shown that there is an association between periodontal disease and heart disease, but many studies are trying to find a causal relationship to better understand how to protect people with both diseases (Weidlich et al, 2008).
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Table 2. A Comparison of Studies Evaluating the Association of CVD and Periodontal Disease. Three studies are compared to determine any differences in the outcomes of periodontal disease and heart disease that are indicative of a causal relationship. The three studies compare Brazilian populations, and all three studies found an association between periodontal disease and the type of heart disease that was examined in each particular study (Weidlich et al, 2008).
Bacteria Involved in Periodontitis

There are many types of bacteria involved in periodontitis, and these bacteria form a buildup, or plaque, on the teeth, which can eventually get below the gums if not properly treated. The bacteria within the plaque produce many compounds including H$_2$S, NH$_3$, endotoxins, enzymes, and antigens. These compounds are known to produce an inflammatory response. Gingivitis, the beginning stages of gum inflammation, and localized juvenile periodontitis, which is plaque accumulation on certain teeth during puberty, also result in plaque accumulation. However, these diseases are often characterized by different bacteria in comparison to bacteria causing adult periodontitis. *P. gingivalis*, an anaerobe, and spirochetes often associated with the disease. A particular spirochete, *T. denticola*, is also often associated with periodontal disease (Loesche, et al., 1996). The common types of bacteria associated with periodontal disease are identified, which helps to understand if these bacteria originate in the mouth and then travel systemically.

Furthermore, a study conducted at Cornell University in 2010 showed that bacteria commonly found in arterial plaque are also found in plaques located in the mouth, as well as other parts of the body including the blood. In this study, the common bacteria found were bacteria such as *Veillonella* and *Streptococcus* species (Ramanujan, 2010). This research further draws a connection between periodontitis and heart disease. However, two extremely common bacteria found to be involved with periodontitis include *T. denticola* and *P. gingivalis*. Further
research is necessary to make a connection between these types of bacteria and heart disease, as these are the prevalent forms of bacteria.

Porphyromonas gingivalis

*P. gingivalis* is one type of bacteria commonly associated with periodontal disease. It is Gram-negative and anaerobic, and it can be found in healthy patients at low levels, but it tends to accumulate on the teeth in a person with periodontal disease. In patients with periodontitis, pockets can form, and within these pocket is crevicular fluid, which promotes inflammation and serves as necessary nutrients for the bacteria (Figure 4) (Hussain et al., 2015). This fluid greatly increases when there is inflammation of the gum tissue, and complement components are present within this fluid. *P. gingivalis* is able to avoid being killed due to its use of the complement system, with additional support from gingipains, cysteine proteases produced by *P. gingivalis* that can cleave complement components. This type of bacteria is able to induce inflammation through its involvement with the complement system. Additional research has shown that there are periodontal bacteria, such as *P. gingivalis*, present in the plaque found in atherosclerosis, and there may be a way for the bacteria to enter the bloodstream (Hussain et al., 2015).
Figure 4. Periodontal pocket compared to healthy gums. A periodontal pocket is greater than 4mm deep, compared to healthy gums, with a superficial pocket of 1-2mm. Healthy gums will not bleed when probed, whereas there will be a great amount of blood during probing of a periodontal pocket (USTIINY Dental Institute, n.d.).
Once *P. gingivalis*, along with other bacteria involved in periodontitis, enter the bloodstream, it is believed that these bacteria interact with various immune and non-immune cells with different effects on the cell population. When periodontal disease begins to get more aggressive and destroys the gingiva, the periodontal bacteria is able to enter the bloodstream to affect various cell types with varying effects. The bacteremia caused by periodontitis affects many cells of the body, including B cells, T cells, dendritic cells, neutrophils, platelets, macrophages, monocytes, smooth muscle cells and endothelial cells (Figure 5). The resulting effect on these cells can be devastating, and a common effect on most of the cells is increased inflammation. Due to extensive research on animal models and patients with periodontal disease, *P. gingivalis* is used as a model organism for periodontitis (Chistiakov et al., 2016).
When periodontal disease progresses, the bacteria spreads and can enter the bloodstream. This invasion results in various affects on cells of the body including B cells, T cells, dendritic cells, neutrophils, platelets, macrophages, monocytes, smooth muscle cells and endothelial cells (Chistiakov et al., 2016).

**Figure 5. Cells affected by periodontal disease.**
**Treponema denticola**

*T. denticola* is a Gram-negative spirochetal bacteria commonly associated with periodontitis. This type of bacteria can be cultured, allowing it to be studied and altered genetically. An analysis completed by Shvartsbeyn et al. showed that *T. denticola* likely remains involved in periodontal disease, and it does not go into systemic infections (Seshadri et al., 2004). The study shows the importance of *T. denticola* in periodontal disease.

*T. denticola* causes periodontal damage, especially when it is paired with other Gram-negative anaerobes, such as *P. gingivalis*. *T. denticola* and the proteases that it is able to make are often found in cases of periodontal disease, indicating the role of this bacteria in inflammation (Sela, 2001). *T. denticola* is often found involved with inflammation during periodontal disease, and by identifying this bacteria and understanding its role in periodontitis, it will hopefully be possible for researchers to better understand the development of periodontal disease and the connection or causal link with heart disease.

The role of *T. denticola* in periodontal disease is still being researched to understand its function in the development of periodontal disease. *P. gingivalis* is known to act as an inducer of the production of endothelial cells, whereas *T. denticola* does not seem to have any effect (Chistiakov et al., 2016). Understanding the role of *T. denticola*, along with the role of other bacteria involved in the development of periodontal disease, will allow researchers to gain
more knowledge about the topic, and hopefully find a way to prevent heart
disease by treating periodontal disease.

**Ways to Prevent Periodontitis**

There are many recommended ways to lower the risk of gum disease,
which may also prevent heart disease and decrease the effect if a patient suffers
from one of these diseases. The best ways to prevent include brushing and
flossing, maintaining a healthy diet, avoiding tobacco, and visiting the dentist
regularly (Delta Dental, n.d.). Preventing periodontitis may be able to help
prevent heart disease if the bacteria associated have a causal relationship. It is
important to avoid periodontitis for both oral and systemic health.

Heart disease often has devastating results, and by finding a causal link
between heart disease and periodontitis, researchers may be able to find a way
to prevent heart disease by treating periodontal disease. This paper will
investigate *Treponema denticola* and *Porphyromonas gingivalis*, two types of
bacteria often found in dental plaque, and the connection these bacteria have to
heart disease. The goal is to investigate whether or not the elimination of these
bacteria could lead to a decrease in the association between heart disease and
oral health.
PUBLISHED STUDIES

The link between heart disease and periodontal disease has been studied extensively attempting to elucidate the underlying correlation between the two diseases as no known connection due to common risk factors has been identified. The common bacteria involved with periodontal disease, *P. gingivalis* and *T. denticola*, likely play a role in the development of heart disease in patients with periodontitis. The aim of the research is to better understand the role of the bacteria that are primarily present in oral disease and their connection to heart disease.

**Periodontal Disease and Heart Disease**

In order to connect periodontal disease and heart disease, research has tried to identify possible associations to determine a causal association in addition to common risk factors. DeStefano et al. examined the relationship between heart disease and periodontitis by completing a prospective cohort study. The results found that patients with periodontal disease had an increased rate of 25% of developing heart disease than those with no or very little periodontal disease (1993). Poor oral hygiene also increased the risk of developing heart disease. This study, published in 1993, was unclear whether the diseases have a causal association or if poor oral health is an indication of poor hygiene in general, leading to overall poor systemic health. This study
required more research, and in recent years, more studies have been completed to understand the relationship between oral health and heart disease.

A study completed in 2015 investigates the relationship between the two diseases by examining over 15,000 individuals with varying degrees of periodontitis and heart disease. The study found that the more teeth an individual had, the more likely he or she was to have lower glucose levels, low low-density lipoprotein (LDL), cholesterol, blood pressure. In addition, those with gum bleeding generally had LDL levels and higher systolic blood pressure (Vedin et al., 2015). This study reinforced that there is an association between periodontitis and heart disease, but it remains hopeful that future studies will elaborate on the causal effects of the diseases.

An additional study summarized associations between cardiovascular disease (CVD) and periodontal disease. A common risk factor for CVD includes infections, with periodontal disease being a leading contributor (Demmer & Desvarieux, 2006). In the past, it has been difficult to interpret the association due to unclear findings about the topic. The bacteria involved in periodontal plaque formation can be quantitatively measured to better understand the main bacteria involved in periodontal disease, and this data can be compared with results found from data collected about heart plaques. Of the bacteria identified, two of the main four bacteria were \textit{P. gingivalis} and \textit{T. denticola}. It was suggested that the bacteria involved in periodontal disease have a positive correlation with the presence of coronary heart disease. This study provides
evidence of a link between periodontitis and CVD. Based on the findings, periodontal treatment will not necessarily prevent CVD. However, a person needs good oral health in order to be healthy (Demmer & Desvarieux, 2006). The findings continue to show the importance of the relationship between oral and systemic health.

In a study completed by Persson et al., subjects with acute myocardial infarction (AMI) were studied to understand the relationship between chronic periodontal disease and CVD. In the study, researchers identified 160 individuals, 80 patients with AMI and 80 control patients, and completed a dental examination to identify periodontitis based on certain criteria. The study shows that those with more bone loss around the teeth, which is indicative of periodontal disease, may be at risk in the future for AMI (Persson et al., 2003). This study shows the continued understanding of a link between periodontal disease and heart conditions.

Patients with periodontitis and those with heart disease have similar characteristics. A proposed mechanism suggests that hyper-inflammatory macrophages can lead to predisposition to atherosclerosis or periodontal disease. Once a patient develops periodontal disease, he or she can experience exposure to lipopolysaccharide (LPS) as well as many pro-inflammatory mediators. These consequences can lead to vascular issues of many body tissues, and eventually can lead to heart disease Persson et al., 2003. Therefore,
a connection between the periodontal and heart diseases is made (Figure 6).

This connection is useful to help treat and potentially diagnose the two diseases.
Figure 6. A proposed relationship between periodontitis and heart disease.
This figure shows a hypothetical model for the relationship between periodontal disease and several heart diseases, including atherosclerosis, coronary heart disease and stroke. This model suggests that there is likely a genetic or environmental trigger that results in hyper-inflammatory macrophages. This inflammatory response may lead to atherosclerosis or periodontal disease (Beck et al., 1996).
A study completed by Beck et al. further supported their hypothesis with an assessment of the association between heart disease and oral health (1996). In this study, the poor oral conditions occurred before the heart disease occurrence. The research concluded that oral health disease are associated with heart disease, and periodontal disease may be more strongly associated with fatal CHD; however, the fatal CHD category did not include AMI or angina. Additionally, bone loss due to periodontal disease was most commonly associated with heart disease. Some other variables researched were amount of plaque, missing teeth, and gingivitis. Yet, none of these factors had significance when finding an association with heart disease. This study introduces the idea that periodontal disease may be a risk factor for developing heart disease, including CHD, fatal CHD, and stroke (Beck et al., 1996). This research demonstrates the possibility of periodontal disease as a risk factor for heart disease.

The relationship between periodontal disease and coronary heart disease is studied over the world in an attempt to find a connection. Research completed by Hansen et al. (2016), which used a nationwide cohort study, showed that patients with periodontal disease were more likely to be at risk for heart disease. The study collected data for 15 years using over 17,000 patients with periodontal disease that was diagnosed at a hospital. These patients also had increased co-morbidity by virtue of being smokers, having diabetes mellitus, having hypertension, and being of low socioeconomic status. All of these factors serve
as a danger for both CVD and periodontal disease. This study introduces direct and indirect methods for the connection between periodontal disease and heart disease. The direct method is that the bacteria directly attack arterial walls, leading to atherosclerosis. The indirect method indicates that systemic inflammation may occur due to an infection originating in the oral cavity. The inflammatory response in the oral cavity may lead to atherosclerosis (Hansen et al., 2016). This nationwide cohort study continued to explore the connection between periodontal disease and heart disease.

Another study published in 2002 from Chile, compared patients in four different hospitals with certain heart diseases, such as acute myocardial infarction, unstable angina or angina pectoris, with a control group consisting of patients that had surgery for gall bladder stones or abdominal hernia. This study found that there are several possible explanations for the association between heart disease and periodontitis. The first idea is that monocytes may be overactive when excited by production of LPS found from Gram-negative bacteria. The overactivation may lead to a production of high amounts of cytokines. The second mechanism is that certain bacteria in the oral cavity may increase damage of the endothelial tissue and increase aggregation of platelets. The third possibility is that periodontitis increases the amounts of leucocytes and fibrinogen. This results in increased blood viscosity, which affects the flow of blood (Lopez et al., 2002).
Although it has still not been determined if the relationship between periodontitis and CVD is causal or associated, the results from this study indicate that the findings are useful regardless of the results of future studies. If future studies find the relationship to be causal, then the treatment of periodontal disease should decrease the quantity of heart disease. However, there may be other factors in the relationship that are not causal, but rather may have to with socioeconomic factors, prompting more research to find a cause for the association (Lopez et al., 2002).

Through the findings of various studies, it can be understood that there is an apparent relationship between periodontal disease and CVD. The association, however, is not necessarily a causative relationship. Further research hopes to identify a causal relationship, if possible, to see if one of the diseases causes the other or if the two diseases simply occur due to common risks. In addition, patients with valvular heart disease are more at risk for developing endocarditis, a bacterial infection of the lining of the heart. Further research will identify the relationship between periodontal disease and the development of endocarditis.

**Poor Oral Hygiene and Endocarditis**

Endocarditis is a bacterial infection of the heart valves, and bacteria found on the teeth can cause the infection. In a study completed by Lockhart et al. (2009), the aim was to identify whether or not poor oral health plays a role in the development of bacteremia (Lockhart, Brennan, et al., 2009). To find a potential
association, there were 194 individuals in the study that either was placed in a tooth brushing group or a placebo control group receiving a single tooth extraction. The individuals were evaluated to determine the level of oral health. The study showed that those with poor oral hygiene were more likely to develop an association with bacteremia, potentially leading to endocarditis, after brushing their teeth. Therefore, if patients with poor oral hygiene improve oral habits, there may be a smaller risk of heart disease by decreasing the risk of endocarditis (Lockhart, Brennen et al., 2009). An association between oral health and the development of endocarditis is known, and by improving oral health, it may be possible to decrease the risk of periodontal disease.

Because infective endocarditis commonly leads to death, it is important to understand how it occurs and how to avoid future infections. A study researched by Reis et al. investigated the frequency of endocarditis after a root canal preparation in patients that had teeth with dead roots and periodontitis (2016). The results of this study showed bacteria present in the root canal samples, but there was no bacteremia present in the participants of the study. Additionally, the amount of bacteria present was similar in both those taking prophylactic antibiotics and those that did not. This study demonstrates that the prevalence of bacteremia, potentially leading to endocarditis, is low during endodontic procedures and this may be the best way to remove infected teeth to avoid endocarditis (Reis et al., 2016).
The effects of Periodontal Disease on Young Cardiac Patients

In addition to adults, children with heart disease are at risk when considering dental health. In a study completed by Nosrati et al., the researchers demonstrated that children with congenital cardiovascular disease were more likely to develop periodontal disease (2012). Because of this finding, these children have a higher risk of developing more complications, and their oral health should be monitored closely to avoid endocarditis in the future. Figure 7 shows a chart of the results obtained during this study. The children with heart disease had a much higher modified gingival index and modified plaque index than those children without heart disease. It was also found that these children were more likely to be encouraged to visit a dental professional, however, these children still had more inflammation and poor oral hygiene compared to the systemically healthy children (Nosrati et al., 2012).
Figure 7. Amount of gingivitis and plaque determined for the groups researched. The control group, represented by the blue column, is much lower for gingival index (GI) and plaque index (PI), than the yellow column, which represents the subjects with congenital cardiovascular disease (Nosrati et al., 2012).
In order to properly evaluate these children, the amount of gingivitis and plaque was visually examined on control patients, and the results were compared to patients with congenital cardiovascular disease. The results of these examinations can be seen in Figure 8. Those children with heart disease had more obvious signs of gingivitis, as well as a greater amount of plaque, visualized with disclosure solution. These results reinforce the understanding that patients, including children, with heart disease are more likely to have oral health issues despite visiting a dental professional. Thus, these patients must be monitored closely to ensure that more serious systemic health issues, such as endocarditis, do not occur (Nosrati et al., 2012).
Figure 8. Gingivitis and plaque measurements in control group and group with congenital cardiovascular disease. Image 2 shows the measure of gingivitis on a control patient. Image 3 shows the measurement of gingivitis on a patient with heart disease. When compared, the test patient has more visible signs of periodontal disease, indicated by the red and inflamed gum tissue. Image 4 shows the plaque measurement, determined using disclosure solution. Image 5 also uses disclosure solution on a patient with heart disease. The results are visually available to determine that patients with heart disease have a greater plaque index (Nosrati et al., 2012).
The studies completed on the connection between oral health and heart disease strengthen the connection between the two diseases. Studies have shown that there is a link between periodontal disease and CVD, but the detection of a causal link is still being investigated. This information will be valuable for understanding, treating and eliminating both periodontal disease and heart disease (Dhadse et al., 2010). The link between cardiovascular disease and periodontal disease is important to understand in order to prevent death.
DISCUSSION

The relationship between periodontal disease and heart disease has been studied for many years, but more research regarding the connection between the causal relationship and the role of bacteria is needed. By continuing research and better understanding the role of bacteria, there may be a way to limit the progression of heart disease that occurs in this way.

Overall, studies regarding periodontal disease and heart disease tend to have opposing views, making it difficult to draw conclusions. There is an apparent link between the two, but it is difficult to identify a causal relationship. In the future, periodontal disease should be treated before it begins to lead to any potential issues (Zaugg et al., 2014). It has been found in research studies that bacteria can enter the blood stream through the gums, especially when compromised with periodontal disease. When bacteria are able to travel through the blood, they can cause diseases and health issues, including the build up of plaque in the arteries to cause heart disease (Chest Wall and Spine Deformity Study Group (n.d.)) (Figure 9). The connection between periodontal disease and heart disease needs to be further understood by examining the role of bacteria involved to better understand the causal relationship between the two diseases. Additionally, more information regarding why only specific bacteria cling to arterial walls to cause disease should be researched.
Figure 9. Infected Gums and Heart Disease. When bacteria accumulates on the teeth, plaque forms on the teeth, and periodontal disease causes pockets. The bacteria are then able to get into the pockets and enter the bloodstream, infecting the body and potentially leading to systemic health effects. The diseases that can occur are listed (Chest Wall and Spine Deformity Study Group (n.d.)).
Much of the research on the topic hopes to explore a common cause or a causative link between periodontal disease and heart disease. However, there is not much research on the role of oral bacteria in the development of heart disease. Likewise, the research does not focus in on whether or not heart disease causes or predisposes an individual to develop periodontal disease. If this is explored further, it may be possible to investigate the inter-relationship between heart disease and periodontal disease, which in turn may lead to the development of other complications, such as endocarditis.

A patient with poor oral health may indicate that they also have poor overall health due to lack of health maintenance. This, however, is not always true, as healthy people with limited oral health problems will suffer from heart disease. Poor oral health often leads to more problems in the oral cavity if they are not treated. The result can be caries, which if left untreated can lead to loss of the tooth as well as periodontitis. These dental concerns cause bacteria in the blood, possible weight change, and inflammation. These factors, along with common risk factors, such as smoking and diabetes, can lead to heart disease (Colgate Professional (n.d.)) (Figure 10). This risk of heart disease and potentially disease progression and death can be reduced if periodontal disease is prevented.
Figure 10. Dental Exposures can lead to Cardiovascular Disease. Poor oral health can lead to further oral complications eventually leading to tooth decay and loss due to periodontal disease. These dental conditions can cause bacteremia, weight changes, and inflammation or vascular problems. These results and other common risk factors can lead to CVD, and eventually death (Colgate Professional (n.d.)).
Finding a connection between the two beyond common risks, such as smoking, may help with more successful therapeutic interventions for heart disease. If the connection involves bacteria, it would be beneficial to explore whether certain people are more prone to developing infection due to certain bacteria in the oral cavity compared with other people. Additionally, it would be beneficial to understand whether or not heart disease can cause periodontal disease by exploring patients with heart disease and following any oral changes.

FUTURE DIRECTIONS

The bacteria associated with heart disease and endocarditis is, in part, contributed to oral bacteria. The link between CVD and oral health, however, requires more research to specifically understand the role of bacteria. Further research must be completed to determine if the relationship is causal, and research should also continue to investigate if eliminating bacteria from periodontal disease through scaling and root planing will be beneficial to eliminate heart disease. Inflammation has a role in both CVD and periodontal disease and is therefore is believed to tie the two diseases together. In addition to heart disease, periodontal disease is thought to be connected with other systemic health issues, such as diabetes and preterm births (Omni Dental Group (n.d.)). A depiction of this relationship explains how periodontal disease and CVD are related (Figure 11).
Figure 11. The Effects of Periodontal Disease on the Body. Periodontal disease is related to CVD, and thought to be linked together by inflammation, which occurs in both diseases. In periodontal disease, dental plaque forms on the teeth, and this is composed of different types of bacteria. This oral disease has potential to cause heart disease, as well as diabetes, preterm birth, and possibly joint complications (Omni Dental Group (n.d.)).
Although some research has explored the bacteria composing the arterial plaque causing heart disease, it would be beneficial to further understand how the plaque within the heart is formed. In the future, the bacteria found within the plaque of heart disease patients should be collected and compared to the bacteria within the oral cavity. By comparing these two specimens in the individual patient, researchers will know better if there is a connection in each specific person. If the bacteria compared is the same, further research may be able to investigate why this bacteria forms, and also if the bacteria can be eliminated. Additionally, it would be interesting to understand the longevity of the bacteria. For example, if a patient is diagnosed with periodontal disease and it is treated immediately, it would be beneficial to know if that person is more likely to develop heart disease. This research could also be explored in the other direction, such that if a patient has heart disease, it would be valuable to know if that person will develop periodontal disease in the future.

Probiotics and Bacteria Involved

Periodontal disease causes a disturbance of the bacteria that normally inhabit the oral cavity. Probiotics are drugs that alter the normal population of bacteria to benefit the patient. Research has shown that probiotics that alter the oral cavity may lower the risk of developing heart disease, as determined in a rat study. These probiotic also have no identified negative effects on the rodent model (Terai et al., 2015). The development of probiotics to benefit the oral cavity
will be useful to potentially help limit heart disease by altering the oral microbiota before it develops into harmful bacteria that can lead to heart disease in the future.

The role of bacteria involved in periodontal disease is an important aspect of research, as these bacteria may be involved in certain cases of heart disease. By understanding this connection and treating periodontal disease, a patient will likely be at lower risk for heart disease. This is important because of the high mortality rate associated with heart disease; if it can be avoided with simple periodontal treatment, measures should be taken to ensure it is provided to all patients regardless of social and/or economic status.

Periodontal disease goes beyond the mouth when its relationship to systemic issues is explored. Understanding the importance of oral hygiene is essential in maintaining overall systemic health. As this paper demonstrates, there is a relationship between periodontal disease and CVD, and the determination behind a causal relationship is constantly explored. The role of bacteria in this link is an important aspect that has been researched in recent years. More research must be completed to understand if the role of bacteria makes a causal connection between periodontitis and heart disease. Common oral bacteria that are usually associated with periodontal disease have been identified in patients with heart disease. By exploring this relationship further to understand the underlying pathology may leader to reduction of heart disease and improved quality of life.
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