

# Bacteria and Viruses in Periodontics- A review

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## Abstract:

Periodontal diseases are infectious diseases, but the specific mechanism by which the tooth-supportive tissue is destroyed is not clearly understood. Periodontitis is a multifactorial, chronic disease followed by destruction of encompassing structures of teeth and when left untreated leads to loss of alveolar bone and exfoliation of the involved teeth.

The main etiological factor for development of periodontitis is oral biofilm containing anaerobic microorganisms. Microbiological culture studies have identified more than 1200 bacterial species in the oral cavity. Although the role of bacterial plaque in general seems to be evident, on the contrary the role of virus has been largely unexplored.

Viral infection impairs periodontal defenses, thereby permitting subgingival overgrowth of periodontopathic bacteria. The role of viruses is significant, as they may induce abnormalities in the adhesion, chemotaxis, phagocytosis, and bactericidal activities of polymorphonuclear leukocytes. When associated with one another, viruses and bacteria have stronger periodonto-pathogenic potential than individually. Therefore, it is significant to know all etiologic factors and such an insight would lead to the better treatment of the disease.

**Keywords:** bacteria, viruses, periodontal disease, periodontopathic pathogens

## INTRODUCTION:

The typical sign of periodontal disease is the progressive degeneration of the periodontal complex's soft and hard tissues, which is mediated by the interaction of dysbiotic bacteria communities and aberrant immune responses in the gingival and periodontal tissues.<sup>1</sup> As the local oral microbiota becomes dysbiotic and inflammatory reactions cause tissue degradation, putative periodontal pathogens become more abundant. This results in an ongoing positive feedback loop of proteolysis, inflammation, and enrichment for periodontal pathogens. The development of periodontal disease depends critically on keystone microbial infections and persistent gingival inflammation.<sup>2</sup>

Recent research, however, has highlighted the significance of previously undetected microorganisms, such as different viruses, phages, and bacterial species, in the development of disease.<sup>5</sup> Additionally, recently discovered immunological, genetic, and environmental host variables, including nutrition and lifestyle, have been recognized as additional contributing factors in periodontitis. The recognized story of the development of periodontal disease has been broadened by these elements taken

together. In accordance with this, novel theories about preserving periodontal health and treating illness have been investigated, such as the use of oral probiotics to stop and slow the spread of disease.<sup>6</sup>

It is well known that systemic host pathologies including diabetes and autoimmune diseases play a part in the etiology of periodontal disease. Recent research has also shown that periodontal disease has a reciprocal role in aggravating distal sites of systemic disease states like oral cancer, inflammatory bowel disease, and Alzheimer's disease.<sup>3</sup> These findings emphasize the significance of the oral cavity for overall health. Here, we review historical information on the development of periodontal disease while incorporating cutting-edge research ideas that have expanded our comprehension of periodontal health and illness.<sup>4</sup> We also explore novel possibilities that might develop to fill in large gaps in our fundamental understanding of periodontal disease.

### **The Oral Microbiome: Heroes and Villains**

#### The Good Part:

The oral microbiome is made up of the 700 or more bacterial species that live in the mouth cavity.<sup>1</sup> The oral microbiome is made up of a distinct and varied ecology of microorganisms that interact physically and physiologically. Physio-chemical gradients produce various niches for bacteria with varying metabolic needs as a result of such interactions, which lead to the establishment of complex biofilm communities.<sup>2</sup> A "hedgehog-like" structure with a radial organization best describes the spatial-chemical structure of healthy supragingival plaque, as shown in work by Welch et al.<sup>3</sup> According to this theory, *Corynebacterium* species anchor to early colonizers like *Actinomyces* species and *Streptococcus* species and then radiate outward to form a lengthy, annular structure.

The oxygen- and nutrient-rich periphery is occupied by *Haemophilus*, *Aggregatibacter*, and *Neisseriaceae*, which are joined at the annulus' tip. The biofilm center, where anoxic capnophilic species like *Capnocytophaga*, *Leptotrichia*, and *Fusobacterium* grow along the middle of the annulus, is created by metabolic output from oxidative species at the perimeter. In addition, this study identified 13 genera with at least 3% abundance that made up 85% of all sequencing in supragingival plaque and more than 80% of all subgingival plaque in healthy subjects. This study also discovered startling similarities in the composition of supragingival plaque and subgingival plaque in healthy subjects. Microbial dysbiosis occurs when the intricate ecosystem of the oral biofilm is disturbed.<sup>4</sup>

The etiology of gingivitis and the progression of periodontal disease are both greatly influenced by this change in the dynamics of the microbial community. According to Ebersole et al.<sup>5</sup>, Periodontitis is also characterized by immune dysregulation, inflammation, and increased representation of periodontal pathogens. These factors work in concert to destroy the tooth-supporting structures, such as the periodontal ligament (PDL) and alveolar bone. A growing understanding of the pathophysiology of periodontal disease includes the influence of chronic inflammatory illnesses at locations outside of the mouth cavity on periodontitis and the developing involvement of periodontitis in systemic inflammation.<sup>6</sup>

#### The Bad Part:

The polymicrobial and synergy model, put forth by Lamont and Hajishengallis<sup>4</sup> in 2013, incorporates elements of several hypotheses regarding the etiology of periodontal disease. For instance, studies on the immune network that distinguishes between states of health and disease<sup>7</sup>, the ecological plaque hypothesis put forth by Marsh (1994), the red complex discovered by Socransky et al.<sup>8</sup>, the model

of synergistic interactions between keystone pathogens and commensals<sup>9</sup>, and the model of synergistic interactions between keystone pathogens and commensals.

It is generally acknowledged that a variety of factors, including host immunity, host environmental factors, and keystone periodontal bacteria that are essential to the disease's etiology, contribute to periodontitis. Socransky et al.<sup>8</sup> used checkerboard DNA-DNA hybridization and genomic DNA probes to identify *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* as species that appear together at higher frequency with increasing severity of periodontal disease, thus dubbed the cluster "the red complex" (Socransky et al.<sup>8</sup>). However, outside the red complex, other species linked to periodontitis have emerged over time, such as *Filifactor alocis*, *Porphyromonas*, *Synergistetes*, and *Peptostreptococcaceae*<sup>10,11</sup>, as well as *Actinomyces actinomycetemcomitans* that is associated with aggressive periodontitis.<sup>12</sup>

### **The Oral Virome in Periodontal Disease**

The advancement of periodontal disease and the oral microbiota have been linked mostly through bacterial species-related dysbiosis. However, the oral virome, which is made up of bacteriophages, viruses, and retroviruses, within the oral microbiota, continues to play a very minor role in periodontitis.<sup>11</sup> A number of oral pathologies have been linked to specific viruses, including Epstein-Barr virus, herpes simplex virus, and cytomegalovirus provided a thorough summary of the findings about the role of viruses in the etiology of periodontal disease, including the disease potentiation by viruses through interactions with periodontal pathogens, viral infection of host cells, and viral-mediated biofilm dysbiosis.<sup>13</sup> In contrast, the importance of the oral virome in periodontitis has not yet been thoroughly explained. For 8 weeks, a murine model of periodontal disease was used to study the effects of infection on PDL properties, alveolar bone loss, the host serum immune profile, and the local oral microbiota.<sup>14</sup> The inoculum contained *P. gingivalis*, *F. nucleatum*, *T. denticola*, and *T. forsythia*. Oral swabs were taken before the infection was given (after antibiotic treatment) and at 1, 4, and 8 weeks after the infection to better understand how the oral microbiota changed over time in tandem with the progression of the disease.<sup>15</sup> Metagenomic shotgun sequencing was done on maxillary and mandibular specimens to look at changes in the oral microbiota brought on by the pathogenic inoculum.<sup>14</sup>

Most viruses present in the oral cavity are bacteriophages, many of which belong to the *Caudovirus* families, *Siphoviridae*, *Myoviridae*, and *Podoviridae*.<sup>15</sup> Like bacterial constituents of the oral microbiome, the virome is altered by environmental influences and is highly variable amongst individuals.<sup>12</sup> Moreover, oral viruses have been shown to elicit host immune responses, thus implicating a role for periodontal disease pathogenesis in the crosstalk between host immunity and the oral microbiota.<sup>16</sup>

In a 2014 study, Ly et al.<sup>17</sup> tried to distinguish between the oral microbiome in healthy individuals vs those with periodontitis. 16 patients with mild to severe periodontitis or with periodontally healthy gums had saliva and oral biofilm samples taken. Salivary viromes are grouped in accordance with the presence of periodontal disease. Viromes from participants with severe periodontitis grouped together in supra- and subgingival biofilm samples, which also reflected this.

The most prevalent viruses in saliva at a higher taxonomic level were those from *Firmicutes* and *Proteobacteria*, followed by *Bacteroidetes* and *Actinobacteria*. On the other hand, those connected to *Bacteroidetes* and *Proteobacteria* were more prevalent in biofilm samples. According to several studies, bacteriophages—the most prevalent viruses found in the oral cavity—serve as significant drivers of bacterial diversity in various microbial ecosystems.<sup>18,19</sup>

Therefore, it is crucial to comprehend the oral virome for both its potential direct effects on periodontal disease and its potential role in the disease potentiation caused by bacterial infection.

### **The Necessities in Periodontal Immunity**

A sustained host immunological response is elicited within the periodontium as supra- and subgingival polymicrobial biofilm populations continue to accumulate.<sup>4</sup> If the microbial biofilm is eliminated, the inflammatory process can be stopped, and only the gingival epithelium and connective tissues are affected. However, if biofilm buildup continues and results in involvement of deeper periodontal tissues, such as deepening of the gingival crevice, destruction of the PDL, and loss of alveolar bone, the inflammatory process becomes irreversible.<sup>20</sup> At this point, the disease progresses from gingivitis to periodontitis. The ensuing growth of periodontal pathogens that thrive in inflammatory environments, during which proteinaceous by-products of tissue destruction (such as collagen breakdown products, amino acids, iron, heme, etc.) reinforce pathogen outgrowth, further contributes to this sustained inflammation.<sup>4</sup> The intricacy of the inflammatory cell infiltrate increases with the severity of periodontal disease. The early lesion is characterized by elevated macrophages and T cells, and the later established and advanced lesions are characterized by B cell and plasma cell involvement, according to the Page and Schroeder model.<sup>21</sup> The initial lesion is dominated by neutrophils. Despite the fact that a microbial challenge is required for the development of the illness, host inflammatory involvement is the main catalyst for the loss of periodontal tissue.<sup>6</sup>

### **CONCLUSION**

Cornerstones in the development of periodontal disease include supra- and subgingival biofilm dysbiosis and persistent gingival inflammation.<sup>8</sup> According to several studies<sup>16,17</sup> putative periodontal pathogens are essential for inducing disease and causing host inflammation. They also continue to perpetuate disease by manipulating tissues and subverting the immune system. As a result of their complex interactions with keystone pathogens like *P. gingivalis*, *A. actinomycetemcomitans*, and *T. forsythia*, oral commensal and pathobionts play an essential role in promoting periodontal disease, according to a number of models that have emerged. Furthermore, there is growing interest in the unique relationship between the progression of disease and non-bacterial microorganisms, such as the several viruses and phages that make up the oral microbiota.<sup>14,15</sup> The oral virome is dramatically altered in periodontal disease, as evidenced by observations, and this raises the possibility that some viral species may influence both bacterial and host processes in the course of the disease.<sup>14</sup> There are now additional host environmental factors that can affect microbial dysbiosis and periodontal inflammation in addition to the simple lack of oral hygiene. These additional factors include psychological stress and diet.<sup>16</sup>

Psychological stress and poor diet may promote periodontal disease *via* encouraging host inflammation. However, the stress hormone cortisol was shown to directly affect microbial dysbiosis and pathogen outgrowth *in vitro*, thus demonstrating a direct role for stress in affecting microbial communities. Novel concepts in periodontal immunity have introduced a role of cell senescence in promoting the inflammatory process, as well identifying unique immune responses in the gingiva that are distinct from other barrier sites.<sup>7</sup> The presence of additional chronic inflammatory diseases, such as IBD, cardiovascular diseases, and autoimmune disorders have additionally been recognized as co-morbidities that may promote periodontal disease pathogenesis.<sup>9</sup>

Altogether, these findings excitedly integrate novel concepts into existing models of periodontal disease pathogenesis, further emphasize the role of oral health to systemic health, and continue to advance our knowledge of disease, corresponded by growing ideas for novel treatments.

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