

Chapter 10

Systemic Diseases & Periodontal Pathogens

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Introduction

Periodontitis is one of the most common infectious diseases of humans. Periodontitis results from chronic exposure of the periodontium to dental plaque, especially subgingival plaque, which contain mostly gram-negative anaerobic bacteria. The associated tissue destruction results from the various toxic bacterial products and host responses. Considering the chronic nature of the disease, bacterial toxins and the local and systemic host responses involved, it is reasonable to argue that periodontitis may influence systemic health. Observational studies indicate periodontal infection as a risk factor for pre-term low birth weight and systemic conditions like cardiovascular disease.

Over the past 10 years, several studies have been published pointing towards a relationship between periodontal disease and various systemic disorders or diseases. Here we present data from our laboratory, as well as from available literature on the link between peripheral vascular disease (PVD) and *Helicobacter pylori* associated gastritis to oral microbiota.

This paper discusses the biological possibility for a link between periodontal infection and systemic disease. It has become increasingly clear that the oral cavity can act

as the site of origin for dissemination of pathogenic organisms to distant body sites.

Periodontal pathogens in oral cavity, aortic aneurysm and atherosclerotic blood vessels

Epidemiological studies show periodontal patients have a higher risk (odds ratio: 1.5 - 2.0) of fatal cardiovascular diseases (CVD) than periodontally healthy subjects. A positive and significant correlation has been shown between periodontal infections and heart disease including CVD and stroke.

Numerous studies indicate the association between oral bacteria and cardiovascular diseases (Haraszthy *et al* 2000, Okuda *et al* 2001, Stelzel *et al* 2002). Therefore, we undertook the task of detecting periodontopathic bacterial DNA in peripheral vascular diseases and comparing the detection to that of levels in the oral cavity. 32 patients with PVD were selected. Periodontal status of these patients is presented in Figure 1. Informed consent was obtained from each subject. Saliva samples were collected before the surgery and aortic lesions removed by surgeon were examined. Arterial wall samples were homogenized and then the DNA of periodontal pathogens was extracted from the homogenized samples by High Pure PCR Template Preparation Kit® (Roche). The 16S

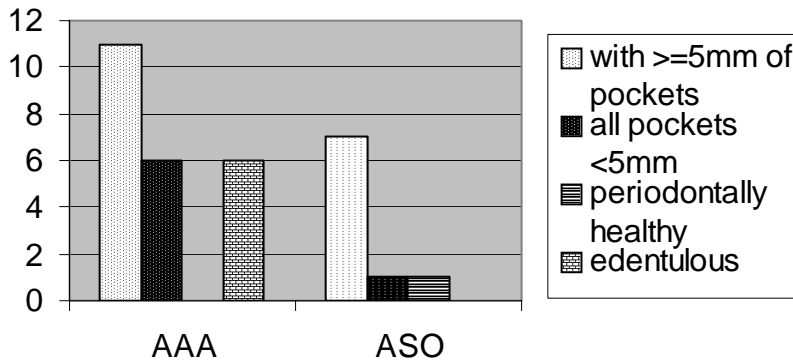


Figure 1. Periodontal status and AAA and ASO patients

<i>P. gingivalis</i> positive	24/32	75.0%
AAA Lesion	17/23	75.0%
Arterial wall	15/21	71.4%
Thrombus	8/9	88.9%
ASO Lesion	7/9	77.8%
<i>T. Denticola</i> positive	20/32	62.5%
<i>P. intermedia</i> positive	11/32	34.4%
<i>C. rectus</i> positive	4/32	12.5%

Figure 2. The detection frequency of periodontopathic bacteria in aortic lesions examined by PCR

rRNA-based PCR detection of periodontal pathogens was performed in abdominal aortic aneurysm (AAA) lesions and arteriosclerosis obliterans (ASO) lesions resected by surgery (Ashimoto *et al* 1996). Our results showed quite high detection rates of periodontal pathogens in the examined AAA and ASO samples (Figure 2). Particularly, *P. gingivalis* was detected in 75.0% of examined aortic lesions by PCR method. Bacterial enzymes, *P. gingivalis* gingipains, can stimulate platelet aggregation and thrombus formation (Lourbakos *et al* 2001). These bacterial

components may feature in the co-aggregation process of atherosclerosis and formation of aortic aneurysm.

According to our data, PVD patients whose saliva was positive for *P. gingivalis* and *T. denticola* showed higher detection rates for these bacteria in the examined aortic lesions, while negative patients showed a lower detection for these bacteria in the lesions. This may be an important finding to indicate the close relationship of periodontal pathogens and cardiovascular diseases.

History of gastritis or peptic ulcer	Subjects	Positives	Rates of positives (%)
With	45	18	40.0
(subjects with <i>H. pylori</i> in stomach or duodenum)	(28)	(13)	(46.4)
Without	12	2	16.7
Total numbers	57	20	35.1

Figure 3. Detection frequencies of *H. pylori* in the oral cavity (nested PCR)

	Subjects	Positives	Rates of positives (%)
Patients with pockets <4 mm	11	1	9.1
Patients with pockets ≤4 mm	17	7	41.1

Figure 4. Prevalence of *H. pylori* in the dental plaque of patients with the bacterium present in stomach or duodenum

Detection of *Helicobacter pylori* in the Oral Cavity of Periodontitis Patients by PCR Method

Helicobacter pylori is a spiral, microaerophilic, Gram-negative, motile bacterium with polar-sheathed flagellae. It has been associated with the development of peptic ulcers and gastric cancer (Henshall & Warren 1984). Although it may be transmitted through the oral cavity, it is unknown whether the oral cavity acts as a permanent reservoir for this bacterium (Bernander *et al* 1993, Banatvala *et al* 1993, Hammar *et al* 1992,

Krajden *et al* 1989, Nguyen *et al* 1993, Shimada *et al* 1994). *H. pylori* infection is more prevalent in developing countries than in developed countries. Its presence is always associated with chronic active gastritis, and eradication of the bacterium is always followed by resolution of gastritis. Nearly all patients with duodenal ulcer disease have *H. pylori* gastritis, and ulcer relapse is exceptional after *H. pylori* eradication. *H. pylori*-infected persons have an increased risk of developing intestinal-type, but not undifferentiated, gastric adenocarcinoma.

In this study we used nested polymerase chain reaction (PCR) to clarify whether the oral cavity acts as a reservoir for *H. pylori* (Mapstone *et al* 1993). The existence of *H. pylori* in the oral cavity was determined by nested PCR in 57 subjects and by culture method in 18 subjects. The presence of periodontopathic bacteria was also determined by 16S rRNA-based PCR method. Although *H. pylori* was rarely detected in the oral cavity by culture technique, it was frequently detected (35.1%) by nested PCR in the oral cavity, especially among periodontitis patients who had the bacterium in the gastrointestinal tract (46.4%) (Figure 3). Among the subjects who harboured *H. pylori* in the stomach or duodenum, 41.2% of patients with periodontal pockets $>$ or $=$ 4 mm and 9.1% of subjects without pockets showed *H. pylori* in dental plaque, although a statistically significant difference was not observed (Figure 4). One patient who had periodontal pockets retained *H. pylori* in the oral cavity even after eradication of the bacterium from the stomach and duodenum. Most (8/10) of the patients who had *H. pylori* in dental plaque harboured *Bacteroides forsythus* in their oral cavities. These results suggest that close attention should be given to periodontitis patients who harbour *H. pylori* in the oral cavity.

Conclusion

These studies add to the existing evidence that periodontal pathogens may contribute to a variety of systemic diseases. Furthermore, we suggest that the oral cavity may act as a reservoir for *H. pylori* infection (Umeda *et al* 2003). At present the major concern in periodontal disease management is to prevent the progression of local tissue destruction. Nevertheless, the above discussion and others of its kind points out the impact of periodontal disease and oral microbiota on systemic

health. Further investigations are needed to clarify the relationship between periodontal disease and systemic diseases. This in turn will determine if periodontal disease management will help prevent systemic conditions like CVD, PVD, gastric carcinoma and pre-term low birth weight infants.

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