Bleeding gums and systemic disease: are we ignoring an important link?

A short review of the literature: with guidelines from the European Federation of Periodontology, April 2013

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For a number of years, an association between oral health and systemic disease has been recognised and there is considerable epidemiological evidence to link them. The extent and severity of periodontal disease may put patients at significant risk for a variety of systemic conditions.

It appears that the inflammatory component of periodontal disease does have potential systemic effects and an association with cardiovascular diseases, poor glycaemic control in diabetics and low birth weight pre-term babies.

There are a number of mechanisms that have been put forward to explain this and evidence to support an association, but not yet attributable disease. The relationship is not linear but complex.⁽¹⁾

PERIODONTAL DISEASE – WHAT IS IT?

Periodontal disease (gingivitis and periodontitis) is a destructive disease of the gingivae and supporting tissues of the teeth, as a result of the inflammatory response to a microbial biofilm (or dental plaque).

Gingivitis is defined as inflammation of the marginal gingival tissues due to the accumulation of the biofilm and is

characterised by swelling, redness and bleeding of the tissues. The periodontal ligament and alveolar bone are not affected.

Periodontitis is caused by the biofilm that induces inflammation, which results in the destruction of the periodontal ligament, loss of crestal alveolar bone and apical migration of the epithelial attachment (junctional epithelium), which is also called 'loss of attachment' (see figure 1).

Teeth can become loose and mobile and eventually require extraction, or fall out, as a result of periodontitis.

Pathogenic bacteria, which cause periodontitis, are found within the biofilm and the progression and severity of the disease will depend on the host response and associated risk factors. The progression of the disease, therefore, requires a susceptible host and this is not easy to predict. The bacteria within the biofilm induce cells to produce inflammatory mediators at the gingival level. The bacteria and inflammatory mediators may enter the blood and have a measurable impact on systemic inflammation. The epidemiological evidence that supports the link between periodontitis to the progression of systemic diseases is associated with both bacteraemia and elevated markers of systemic inflammation.

Figure 1 Loss of attachment

The risk factors, which will affect the host response and, therefore, the progression of periodontitis, are:

- diabetes
- genetic: eg Down's syndrome (believed to be due to impaired neutrophil function), Pailon-Lefevre syndrome
- smoking: nicotine is implicated in the reduced functional ability of many aspects of the immune response. Healing is also affected
- hormonal changes (puberty, pregnancy)
- immunocompromise either from disease (eg HIV or neutropaenia) or medication
- psychosocial (stress): possibly as a result of behavioural changes, such as increased smoking and poor oral hygiene
- systemic medication that can cause gingival overgrowth: this will not affect the host response, but may inhibit plaque control, eg calcium channel blockers, phenytoin, and cyclosporin

Prevention of the disease requires removal of the biofilm by tooth-brushing, if present at the gingival margin, but will require removal by a dental healthcare worker if more subgingival, within a periodontal pocket.

The treatment of periodontal disease is to reduce the inflammatory component in the gingival and periodontal tissues. Resolution of the inflammation is seen clinically as a reduction of bleeding on probing, reduction in the pocket depth and change in gingival contour. By doing this, it is hoped that the dentition is preserved and there is prevention of further attachment loss.

THE ASSOCIATION BETWEEN PERIODONTAL DISEASE AND SYSTEMIC DISEASE

The evidence from research and epidemiological studies, collected over more than 15 years appears to show an association between periodontal diseases and certain systemic conditions, including diabetes, cardiovascular diseases and pre-term low birth weight.

Diabetes

Diabetes is recognised as a risk factor making patients more susceptible to periodontal disease. There is now increasing evidence that the diabetes-periodontal relationship might be bi-directional, that is, patients with diabetes show an increased susceptibility to periodontal disease and treatment of underlying periodontal disease may improve diabetic glycaemic control. Severe periodontitis is associated with increased HbA1C in individuals with or without diabetes

There is a direct and dose-dependent relationship between periodontitis severity and diabetes complications. Evidence is starting to support an increased risk for diabetes onset in patients with severe periodontitis, mainly for Type 2 diabetes. Diabetes Type 2 is preceded by systemic inflammation, leading to reduced pancreatic β -cell function, apoptosis and insulin resistance. Increasing evidence supports elevated systemic inflammation (acute-phase and oxidative stress biomarkers) resulting from the entry of periodontal organisms and their virulence factors into the circulation, providing biological plausibility for the effects of periodontitis on diabetes.⁽¹⁾

Atherosclerotic cardiovascular disease (ACVD)

A transient bacteremia can be caused after chewing, brushing, flossing or scaling of teeth. If periodontitis is present, then within a periodontal pocket there will be a mixed infection of anaerobic gram negative bacteria, which will increase as the pocket deepens. There is an association between the prevalence of a bacteremia and plaque/ gingival indices. The chronic oral infection of periodontitis leads to entry of bacteria (or their products into the blood stream). The bacteria activate the host inflammatory response by multiple mechanisms.

An hypothesis in cardiology is that chronic infections may contribute to atherogenesis. This has been confirmed by studies showing that subjects exposed to chronic infections have two to three times higher odds of having carotid atherosclerosis.

In 1989, a group of cardiologists in Finland looked into the relationship between oral health and myocardial infarction. Since then there has been a debate with regard to the existence and nature of an association between periodontal disease and atherosclerotic cardiovascular disease.

The debate has centred on whether the association is:

1. Real or due to confounding, eg by cigarette smoking, a common risk factor for both; or
2. Causal in nature, ie periodontitis contributes to the causal path leading to atherosclerosis and/or cardiovascular events.⁽²⁾

Three mechanisms have been suggested:⁽³⁾

- inflammatory cytokines and mediators such as IL-1, IL-6, TNF α , released at the diseased periodontal site, translocating to distant sites via the circulation, inducing changes in the vascular epithelium initiating atheroma formation
- bacteria and/or their products (lipopolysaccharide, lipoteic acid, toxins) via the systemic circulation, directly affecting coronary artery endothelial cells inducing atherosclerosis
- bacteria and their products indirectly accelerating atherosclerosis by inducing the production of inflammatory mediators, primarily in the liver, including C reactive protein CRP fibrinogen and IL-6

However, after many reports there is still a debate about whether the associations are causal or not. Both periodontitis and ACVD are longterm chronic conditions and most clinical trials have not had longterm follow up greater than 12 months. Both have multifactorial aetiology and share a common inflammatory nature and this would indicate that control/removal of local gingival infection might not be sufficient in producing a sustained benefit.

Larger scale studies of longer duration in different populations are required.

Maternal periodontitis and pre-term low birth weight

Adverse pregnancy outcomes are the most common cause of death in babies. Several epidemiological studies have shown a significant association between chronic periodontitis and prematurity and low birth weight. Low birth weight is defined as less than 2,500g at birth. A baby can have a low birth weight either as a direct result of pre-term labour, or as a

consequence of intra-uterine growth restriction, leaving the child small for gestational age. Pre-term birth is defined by the World Health Organisation as delivery of an infant before 37 completed weeks of gestation.

On a worldwide scale, the prevalence of pre-term births varies from 6% to 15% of all deliveries, depending on the demographic and geographical features of the population studied.

Known risk factors are cigarette smoking, maternal alcohol consumption, previous low birth weight infant, psychological anxiety/stress, low socioeconomic status and education, poor maternal nutrition and maternal illness. Adverse pregnancy outcomes are generally associated with elevated local and systemic inflammatory mediators and intrauterine infections. Current evidence suggests that adverse outcomes primarily originate from ascending infections from the vagina or cervix or from haematogenous spread from known or unknown non-genital sources. Maternal periodontitis represents one potential source of micro-organisms, known to routinely enter the circulation and could have potential to influence the health of the foetal maternal unit. However, there does not appear to be evidence that non-surgical periodontal therapy does improve pre-term birth outcomes.⁽¹⁾

OTHER SYSTEMIC DISEASE

Studies have also looked at the associations between periodontitis and other systemic diseases. These have included respiratory disease, chronic kidney disease, rheumatoid arthritis, cognitive impairment, obesity, metabolic syndrome and cancer. There is still insufficient evidence to link these. There is evidence that improved oral hygiene can reduce pneumonia in a variety of at-risk populations. Periodontitis has been identified as a possible risk factor for oro-digestive and pancreatic cancer. However, smoking and socioeconomic status affect both periodontitis and cancer and, therefore, this complicates investigation into any association.

The *Journal of Clinical Periodontology* has a special issue entitled 'Periodontitis and Systemic Disease'. This came about as a result of the 9th European workshop between the European Federation of Periodontology (EFP) and the American Academy of Periodontology. They met to reach a consensus

and to establish, sort and clarify the evidence and interrelation between oral health and general health: the epidemiological association, risk factors and pathogenic mechanisms and greater health implications. Much of the information in this article has been taken from this.

This year, the EFP has started an ongoing media campaign to try to raise awareness about periodontal disease and general health for dental professionals.

Dental healthcare workers may routinely screen a large number of the population and will be the first to see patients with periodontal disease and can advise and commence treatment that may allow primary prevention a chance to work and possibly prevent more serious disease. The EFP have provided guidelines for dental and medical health care workers that can be found on their website. General recommendations from their manifesto are included on the next page.

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EFP GUIDELINES from the MANIFESTO

Given the current evidence, it is timely to provide the following guidelines for periodontal care in diabetes patients for medical and dental professionals and recommendations for patients/the public

- Patients with diabetes should be told that periodontal disease risk is increased by poorly controlled diabetes. They should also be advised that if they suffer from periodontal disease, their glycaemic control may be more difficult to manage, and they are at higher risk for diabetic complications such as cardiovascular and kidney disease.
- As part of their initial evaluation, patients with type 1, type 2 and gestational diabetes (GDM) should receive a thorough oral examination, which includes a comprehensive periodontal examination.
- For all newly diagnosed type 1 and type 2 diabetes patients, subsequent periodontal examinations should occur (as directed by the dental professionals) as part of the ongoing management of their diabetes. Even if no periodontitis is diagnosed initially, annual periodontal review is recommended.
- Diabetes patients presenting with any overt signs and symptoms of periodontitis, including loose teeth not associated with trauma – spacing or spreading of the teeth – and/or gingival abscesses or gingival suppuration, require prompt periodontal evaluation.
- Patients with diabetes who have extensive tooth loss should be encouraged to pursue dental rehabilitation to restore adequate mastication for proper nutrition. Oral health education should be provided to all patients with diabetes.
- For children and adolescents diagnosed with diabetes, annual oral screening is recommended from the age of 6–7 years by referral to a dental professional. Patients with diabetes should be advised that other oral conditions such as dry mouth and burning mouth may occur; and if so, they should seek advice from their dental practitioner. Also, patients with diabetes are at increased risk of oral fungal infections and experience poorer wound healing than those who do not have diabetes.
- Patients who present without a diabetes diagnosis, but with obvious risk factors for type 2 diabetes and signs of periodontitis should be informed about their risk for having diabetes, assessed using a chairside HbA1C test, and/or referred to a physician for appropriate laboratory-based diagnostic testing and follow-up care.

Clear recommendations can be made

- Practitioners should be aware of the emerging and strengthening evidence that periodontitis is a risk factor for developing atherosclerotic cardiovascular disease, advising patients of the risk of periodontal inflammation to general as well as oral health.
- Based on the weight of evidence, periodontitis patients with other risk factors for atherosclerotic cardiovascular disease, such as hypertension, overweight/obesity, smoking, etc. who have not seen a physician within the last year, should be referred for medical examination.
- Modifiable lifestyle associated risk factors for periodontitis (and atherosclerotic cardiovascular disease) should be addressed in the dental surgery/office and within the context of comprehensive periodontal therapy, ie smoking cessation programs and advice on lifestyle modifications (diet and exercise). This may be better achieved in collaboration with appropriate specialists and may bring health gains beyond the oral cavity.
- Treatment of periodontitis in patients with a history of cardiovascular events needs to follow American Heart Association (AHA) guidelines for elective procedures.
- Pregnancy is a time of profound physiological change. These can affect the oral health of the expectant mother as a result of the increase in gingival blood supply and a tendency towards gingival swelling and periodontitis. At the same time, research evidence shows that we need to be mindful of the potential impact of poor periodontal health on the overall health of the mother and developing foetus. So, whilst periodontitis does not currently appear to be a true risk factor for adverse pregnancy outcomes in most populations, it may be in some specific groups, and for these reasons special attention should be given to a woman's periodontal health prior to (if possible) and throughout pregnancy.

Based upon data from five randomised controlled trials (four hospital-based and one in an elderly care home), the following is recommended

- Care home staff responsible for elderly and/or frail patients should be trained in the provision of basic oral hygiene for those patients incapable of self care, and in implementing twice daily oral hygiene in those capable for self care.
- Hospital staff within acute care environments should be trained in the use of antiseptic and manual methods of reducing the oral microbial load in ventilated patients.