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SUPPLEMENT

Functional foods/ingredients and periodontal diseases

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Periodontal diseases are a collection of inflammatory processes that affect the periodontium, that is, the teeth supporting tissues. Gingivitis (infected red swollen and easily bleeding gums) is a mild reversible form of periodontal disease. Almost 100% of the population suffers from time to time from gingivitis. Gingivitis can develop into periodontitis, which is a chronic inflammatory disease of the supporting tissues of the teeth [34]. In conjunction with red, swollen gums that easily bleed as a result of the disease, teeth may show exposed root surfaces and often dental radiographs reveal periodontal (alveolar) bone loss around the teeth due to the inflammation process; teeth will become mobile and migrate and will eventually exfoliate.

Patients with periodontitis may have bad breath, suffer from important subjective and objective esthetic problems and experience problems with chewing due to tooth mobility and loss of teeth. Dental professionals provide labor-intensive treatment to periodontitis patients, including periodontal surgery.

Like gingivitis, also periodontitis has a relative high prevalence in the population. About 10% of the total adult population and about 30% of individuals over the age of 50 years have been estimated to suffer from severe periodontitis [9]. Chronic, adult form of periodontitis progresses at a relative slow rate and is diagnosed during middle age. However, in some individuals, the disease manifests itself at adolescent or post-adolescent age in a rapidly progressive manner, and this form of disease is diagnosed as early onset periodontitis or aggressive periodontitis [42].

Periodontitis may be considered as a model for the other inflammatory diseases, with a pathogenesis that is multifactorial, involving complex interactions between multiple genetic traits, infectious agents and lifestyle factors such as diet and smoking.

Several lines of data suggest that periodontitis may be associated with systemic diseases. For example, periodontitis has been associated with increased risk for cardiovascular diseases (for a recent review see [46]), possibly through the elevation of the acute-phase reactant C-reactive protein or other systemic markers of inflammation [24]. Oral bacteria may play an important role in the systemic reactions to periodontitis. There are strong indications that the inflamed and ulcerated subgingival pocket epithelium forms an easy port of entry for oral bacteria. Short moments of bacteremia occur most likely several times a day. Like any other inflammatory condition, untreated chronic periodontitis may pose a risk for the overall health of the subject [23].

The etiology of periodontitis is multifactorial, involving the following.

1. Microbial factors

Many oral bacteria are able to colonize the subgingival pocket, that is, the area directly around the teeth below the gum line. These bacteria form dental plaque, which is attached to the surfaces of the teeth. It is recognized that in the subgingival pocket, bacteria are organized in a complex microbial biofilm. This biofilm consists mainly of Gram-negative strict anaerobic bacteria [11]. Of the several hundreds of oral bacterial species, a limited number of species is recognized as periodontal pathogens and have

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been identified as important markers of progressive disease. These include: *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Tannerella forsythia, Treponema denticola, Prevotella intermedia* and *Fusobacterium nucleatum* [45]. It has been proposed that the bacteria in the subgingival biofilm are organized in complexes and interplay with various species associated with periodontitis [39].

It is important to note that not the same periodontal pathogens and not all the periodontal pathogens are infecting all patients with periodontitis. The microbiological factors of periodontitis differ considerably among different patients, which make periodontitis polymicrobial.

2. Genetic factors

It is recognized that siblings of patients with early onset aggressive periodontitis also suffer from periodontitis [7]. Evidence for genetic susceptibility for chronic adult periodontitis is deduced from family studies and studies in twins [43]. From the twin studies, it has been estimated that 38–82% of population variance in periodontal disease expression may be attributed to genetic factors [31]. Further chronic adult periodontitis was estimated to have 50% heritability, which was unaltered following adjustments for lifestyle variables including smoking [30].

In the last years, the search for genetic markers and candidate disease-modifying genes in periodontitis has received great attention. Especially, genetic variation (single nucleotide polymorphisms = SNPs) of genes encoding for host defense system molecules has been targeted [23]. Parallel to other complex inflammatory diseases, periodontitis is a polygenic disorder. Possible modifying disease genes have been identified in the interleukin (*IL*) -1 gene cluster [16, 19, 20] and *Fc* gamma receptor loci [25, 28, 47]. Moreover, there is growing evidence that SNPs in the *IL-10*, vitamin-D, *CD14* and Toll-like receptor (*TLR*) genes may be associated with periodontitis [3, 12, 13, 20, 35, 40].

3. Lifestyle factors

Smoking is currently accepted as the most significant lifestyle factor in periodontitis [22]. Smokers are more susceptible to periodontitis, suffer from a more progressive disease and have more severe periodontal breakdown than non-smoker patients. Smoking has also been shown to be a predictor for the recurrence of periodontitis [26]. Moreover, smoking periodontitis patients show a less favorable response to non-surgical and surgical periodontal treatments.

The exact role of smoking in periodontitis is still unknown. Smoking and non-smoking periodontitis patients have been suggested to differ in their subgingival microflora [44]; however, others studies did not report this relation [5]. In smokers, the host resistance and immunological functions may be hampered, for example, by reduced phagocytosis, altered T-cell function, lack of immunoglobulin production and reduced local blood supply in comparison with non-smoker periodontitis patients [6, 14, 26].

4. Topical effects of "Ingredients"

Other factors that have been proposed as environmental risk factors for periodontitis include diet and stress [2, 8]. A recent review by Schifferle [36] makes clear that good nutrition (proteins, carbohydrates, lipids, vitamins and (trace) minerals) is essential for general health, and therefore, a nutritional adequate diet is also helpful in preventing periodontal problems. And although there is a wealth of information on the relationship between vitamin/mineral deficiency and periodontitis, it was nevertheless concluded that there is insufficient evidence to justify treatment with supplementation in adequately nourished individuals. Also, no "topical" effects were described.

In a recent review on the relationship between diet-derived antioxidants and the control/prevention of periodontal disease, a similar conclusion was drawn: although antioxidants are important in the control/prevention of periodontal diseases, the effects are systemical, via modulation of the host's inflammatory response [10].

The effects of tea (derived ingredients) on periodontal health have also received a lot of attention in the last years. Very recently, it was shown that production of a chemokine ligand (CXCL10), which plays an important role in the development of the diseases, was inhibited by the green tea-derived polyphenols, catechins [15]. Green tea catechin also inhibits lipopolysaccharide-induced bone resorption in vivo [32]. A recent clinical study on green tea (polyphenols; [18]), where the epidemiologic relationship between the intake of green tea and periodontal disease was investigated by following periodontal parameters in 940 Japanese men, showed that there was a modest inverse association between the intake of green tea and periodontal disease. Studies that could reveal whether the effects of polyphenols are topical or systemic are scarce. Two studies on local (oral) applications of polyphenols [17, 21] have to conclude that green tea catechins and polyphenols might have a positive influence on the inflammatory reaction of periodontal structures, but larger scale studies would be necessary to determine the efficacy and oral health benefits of oral administration.

Topical effects of polyphenols (like those derived from cranberries) have been shown to have an inhibitory effect on periodontal pathogenic bacteria in vitro. These effects have recently been reviewed by Bodet et al. [4] and Petti and Scully [33] who list inhibitory effects of cranberry fractions on biofilm formation, and adherence of *P.*

gingivalis and *F. nucleatum*, and proteolytic activities (*P. gingivalis*) and coaggregation of periodontal pathogens. Also wine catechins were shown to have a strong antimicrobial activity against *P. gingivalis* and *P. intermedia*. This indicates that the plant-derived polyphenols could serve as topical bioactive molecules for the prevention and/or treatment of oral diseases.

Some promising "topical effects" can be concluded from several studies on the application of probiotics for the management of periodontal diseases: It was shown that colonization of *Lactobacillus reuteri* in the oral cavity leads to decreased gum bleeding and reduced gingivitis [18], and also effects of this bacterium on inflammatory mediators were reported [41]. Improvement of periodontal health was also reported after colonization of *Lactobacillus salivarius* [37], possibly via reduction/replacement of pathogenic bacteria [27]. Several in vitro studies on possible positive effects of probiotic bacteria in relation to periodontal diseases have been recently reviewed by Meurman and Stamatova [29], who recommended more investigations before conclusions could be drawn.

There are several publications on the positive effects of dairy products [1, 38], but it is not at all clear whether these effects are topical or systemical.

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