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Consensus Report

Advances in the pathogenesis of periodontitiss

Group B consensus report of the fifth European workshop in periodontology

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Are Gingivitis and Periodontitis a Continuum of the Same Inflammatory Disease?

Not all patients with gingivitis will go on to develop periodontitis. Gingivitis and periodontitis are a continuum of the same inflammatory disease.

Chronic inflammatory periodontal disease encompasses gingivitis and periodontitis as tangible clinical forms. They differ in histological appearance, in that periodontitis has large proportions of plasma cells and B lymphocytes. The weight of the evidence indicates that prevention of gingival inflammation prevents periodontitis.

The primary etiology of both gingivitis and periodontitis is the subgingival microbial biofilm. Currently oral plaque biofilm disruption is the most effective way to treat and prevent both conditions.

What is the Role of the Host in the Pathogenesis of the Chronic Inflammatory Periodontal Diseases?

The persistent challenge from the biofilm results in chronic inflammation, the function of which is to protect the host and limit the effect of the biofilm. As part of this process some tissue destruction occurs. The extent and severity of damage varies among individuals and over time and may involve attachment loss. This variation in disease expression is the result of the interaction of host genetic, environmental and microbial factors.

Cellular and molecular components involved in the destruction of periodontal tissues are predominantly host derived. Modifying the host response can reduce this tissue destruction.

Can Susceptible Individuals be Identified on the Basis of Genetic Tests?

While it is clear that genetic and environmental factors modify risk for chronic inflammatory periodontal disease we are still some way from screening for disease susceptible individuals using genetic tests.

Do Genetic Variations Alter the Host Response?

Evidence exists that some genetic polymorphisms are associated with alterations in host response such as expression of receptors and secretion of cytokines. There is no evidence for a direct interaction between genetic polymorphisms and inflammatory responses in the periodontal tissues.

Is Therapeutic Modulation of the Host Response useful in the Management of Chronic Inflammatory Periodontal Disease?

There is evidence that adjunctive 20 mg sub-antimicrobial dose doxycycline, taken twice daily over 9 months, is beneficial in the treatment of chronic periodontitis over 12 months. This therapy is the only adjunctive host modulation therapeutic currently approved for periodontal treatment in several countries. Further evidence suggests that in a high risk population (smokers) additional benefits may accrue, although randomized controlled trials are needed to confirm this observation.

The use of some adjunctive host modulation therapies is not without risk, NSAID drugs, including the coxib class of COX-2 inhibitors have significant side effects which preclude their use in periodontal therapy.

The use of bisphosphonates for osteoporosis is widespread and may impact on periodontal therapy. However, the data are conflicting regarding its use as an adjunct to periodontal therapy.

Which Subjects would Particularly Benefit from Host Modulation Therapy (HMT)?

Conventional periodontal therapy is effective in the management of most

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cases of periodontitis. However, there are sub-optimally responding subjects and identifiable high-risk groups where adjunctive HMT may have utility. Further research is required to test the efficacy, cost effectiveness and cost utility of HMT in these groups.

It will be necessary in future to test these added benefit assumptions in clinical trials of adjunctive host modulation in high-risk groups.

Generation of Inflammatory Stimuli: How Bacteria Set up Inflammation in the Gingiva (Madianos et al. 2005)

(1) Bacterial components/virulence factors may be involved in modulating inflammatory responses and include: lipopolysaccharides (LPS), peptidoglycans, lipotechoic acids, fimbriae, proteases, heat-shock proteins, formyl-methionyl-peptides and toxins.
(2) Potential host cell receptors involved in recognizing bacterial components and initiating signaling pathways that lead to inflammatory responses include: Toll-like receptors (TLRs), CD14, Nod proteins and G-protein-coupled receptors, including formyl methionyl peptide receptors and protease-activated receptors.
(3) Of the above bacterial and host molecules, evidence from experimental animal studies implicate LPS, fimbriae, proteases, TLRs and CD14 in periodontal tissue or alveolar bone destruction. However, evidence verifying the involvement of any of the above molecules in periodontal tissue destruction in humans does not exist.

Genetics of Inflammation (Shapira et al. 2005)

(1) Genetic as well as environmental factors influence the inflammatory process.
(2) Genetic factors are likely to be important determinants of risk for the periodontal diseases.
(3) Periodontal diseases are polygenic rather than monogenic.
(4) A large number of 'inflammation' associated single nucleotide polymorphisms (SNPs) have been investigated, including SNPs related to cytokines and receptors. Although many SNPs have been shown to modify function, none as yet have been convincingly associated with parameters of gingival inflammation.
(5) Current information from population genetic studies on periodontal diseases has neither diagnostic nor prognostic utility at an individual or site level.

Aspects of the Adaptive Host Response in Periodontitis (Berglundh & Donati 2005)

(1) Lesions in aggressive and chronic forms of periodontitis exhibit similar cellular composition. Differences in disease severity may be reflected in increased plasma cell and B cell densities.
(2) B cells serve as an important antigen-presenting cell in periodontitis.
(3) The periodontitis lesion expresses a unique T cell receptor gene repertoire that differs from that in blood, suggesting oligoclonality of the T cells within the lesion.
(4) While many studies have attempted to determine the domination of either Th1 or Th2 related cytokines, it is likely that the balance of Th1 and Th2 cytokines is important in disease expression. The relative dominance of B cells and plasma cells in periodontitis lesions cannot entirely be explained by enhanced Th2 functions but may be due to an imbalance between Th1 and Th2 cells.
(5) Autoimmune reactions are evident in periodontitis; however, their role needs clarification.

Therapeutic Modulation of the Host Response in the Management of Periodontal Diseases (Salvi & Lang 2005)

Modulation of various aspects of the host response may provide useful preventive and therapeutic approaches.

(1) MMP inhibitors reduce periodontal tissue destruction and alveolar bone loss in animal experimental periodontitis models. In humans, sub-antimicrobial dose doxycycline as an adjunct to conventional periodontal therapy provides improvements in probing pocket depth and clinical attachment levels.
(2) Adjunctive NSAIDs have been shown to reduce alveolar bone loss associated with periodontitis in animal and humans. The use of NSAIDs, especially selective COX-2 inhibitors, have considerable and prohibitive side effects.
(3) The use of bisphosphonates to prevent bone loss associated with experimental periodontitis or muco-periosteal flap elevation has been documented at the animal level. In addition, preliminary human studies are conflicting with respect to the efficacy of bisphosphonates as adjunct to periodontal therapy.
(4) Lipoxins prevented gingival inflammation and bone loss in animal experimental periodontitis.
(5) Modulation of host cytokine receptors (IL-1ra, TNF-aR1, TNF-aR2), soluble cytokines (rhIL-11) and soluble receptors for advanced glycation end-products reduce periodontal attachment and bone loss in animal experimental periodontitis.
(6) The use of pharmacological inhibitors of nitric oxide and poly-ADP-ribose polymerase synthases reduce periodontal attachment and bone loss in animal experimental periodontitis.

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