

# The Role of the Immunology in Periodontal Disease - Update on Current and Emergent Data

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**Abstract:** Periodontal disease (PD) is a highly complex and multi-factorial disease. The two major factors responsible for initiation and progression of the majority of PD are the composition of the microbes in the subgingival plaque and the host immune response to these organisms. This review summarizes role of immunology and some immunological factors involved in the development and control of PD such as: bacterial complexity of PD and microbial dysbiosis, the participation of inflammatory cells in local inflammation. Despite to the fact of innate and adaptive immune activation, and resultant inflammation, our immune response fails to cure PD. Although several studies have tried to clarify some of the immune mechanisms involved in periodontal disease, role of microbial dysbiosis and immune imbalance in the pathogenesis of disease, more studies must be conducted to understand its development and progression and consequently to discover new alternatives for the prevention and treatment of this severe inflammatory disease.

**Keywords:** Periodontal disease, Immunology, Inflammation, Host-Pathogen interaction, Microbial dysbiosis, Chemotaxis, Complement system

## 1. Introduction

Periodontal diseases are chronic inflammatory Gram-negative anaerobic bacterial infection that affects one or more of the periodontal tissues-alveolar bone, periodontal ligament, cementum, gingiva and bone that supports the teeth. The pathogenesis of this disease is multifactorial but majorly depends on involvement of immunological responses leading to tissue destruction and bone loss. In 1965, Brandtzaeg and Kraus were the first to postulate the autoimmune basis in the pathogenesis of periodontal disease, an increasing number of reports in the past decade have lent support to the concept of an autoimmune component of periodontal disease.<sup>1</sup> Autoimmunity can be delimited as breakdown of mechanism responsible for self-tolerance and initiation of an immunologic response against portions of the self. This chronic inflammatory disease results from the response to bacteria in dental biofilm and may persist confined to the gingival tissues with minimal tissue alterations or this disease may advance to extreme periodontal demolition with the loss of attachment and alveolar bone. Periodontal pathogens generally involved with this type of disease are; *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Tannerella forsythia* and *Treponema denticola*; genetic and environmental factors seem to increase the susceptibility of some individuals in getting this severe inflammatory disease.<sup>2</sup> Periodontal disease occurs due to a combining factors; pathogenic bacteria, high levels of inflammatory cytokines, matrix metalloproteinases (MMPs), prostaglandin E2 (PGE2), low levels of anti-inflammatory cytokines including inter-leukin-10 (IL-10), transforming growth factor (TGF- $\beta$ ) and tissue inhibitors of MMPs (TIMPs). The majority of reports deal with the detection of antibodies to host components, in particular, collagen, although antibodies to DNA and aggregated IgG have also been reported.<sup>3</sup> This review aims to summarize some immune mechanisms and autoimmunity concepts related to periodontal disease.

## 2. Discussion

Periodontal disease is a complex contagious disease whose etiopathogenesis is still a riddle in spite of various progressions made in periodontics. This type of devastating disease is characterised by the loss of the normal supporting tissues of the teeth. The main culprit of this autoimmune disease is connected to the humoral and cellular immune response to antigens of gram-negative anaerobic microorganisms in subgingival dental plaque.<sup>4</sup> This review summarises role of immunology and some immunological factors involved in the development and control of PD, such as: bacterial complexity of PD and microbial dysbiosis, the engagement of inflammatory cells in local inflammation.

**Bacterial Complexity of PD and Microbial Dysbiosis:** Culture established cultivation of organisms of subgingival dental plaque in effected cases of periodontal diseases distinctly suggests the presence of bacteria from “Red Complex” group. The red complex, includes *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Treponema denticola*, and *Tannerella forsythia* (formerly *Bacteroides forsythus*), are acknowledged as the most significant pathogens in adult periodontal disease. According to recent findings these periodontic pathogens have a lot of virulence factors which have the power to alter local inflammatory surroundings making it conducive for endurance of these pathogens resulting in microbial dysbiosis.<sup>5</sup>

**Participation of Immune Cells and Inflammatory Mediators in local Inflammation:** The autoimmune (Innate and Adaptive immunologic) response is reported in PD, with obvious role of varied inflammatory cells, several intermediators like cytokines, chemokines, acute phase mediators, and antibodies. Inflammatory cells like neutrophils predominate in early or active PD, whereas in advanced chronic lesions, monocytes like T cells, B cells, dendritic cells (DC), and macrophages are found. These cells

conglomerates in infectious region and with the assistance of chemical mediators adhere to bacterial sites and release inflammatory cytokines including tumour necrosis factor (TNF)- $\alpha$ , interleukin (IL)-1, IL-6, interferon (IFN)- $\gamma$ , and IL-12, resulting majorly in bone loss. Recently the role of helper T cells (Th 1,2 types) is suggested in progression of PD.<sup>6</sup> The various antibodies found in periodontal disease play different roles like protection, destruction, or inconsequential part in the pathogenesis of the disease. Autoimmune response outcomes in pathologic destruction, as a result of induction of humoral and/or cellular immune activity competent of inducing damage or disease. In PD predominantly, IgG is local antibody to collagen type I (whereas IgM is usually autoimmune antibody in serum). Another antibody having role in periodontal disease is antinuclear cytoplasmic antibodies (ANCA). Combined role of 'super-antigen property' of periodontal pathogens and the production of tumor necrosis factor (TNF- $\alpha$ ) sensitise the PMNs neutrophils which successively could activate the production of ANCA. The ANCA activated neutrophils bear theatrical role in holding up apoptosis, release reactive oxygen radicals, enzymes, and various proinflammatory cytokines, all of which are known to mediate periodontal devastation.<sup>7</sup>

In some respects, etiopathogenesis of PD is apprehended as follows: The intact epithelial barriers may holdup the entrance of periodonto-pathogenic bacteria and their products in oral tissues, asserting the health of periodontium. In the presence of active disease, the epithelial migration results in deep periodontal pocket ensuing bacterial invasion, inflammation and destruction of the connective tissue, with resultant bone loss and possible tooth loss. The epithelium can take part in the infection by signaling added innate and acquired immune responses. The adaptative immune response is aerated when the epithelial barrier, with its antimicrobial peptides and other elements of innate systems, are gapped. Interruption of epithelial barriers grants the entry of bacteria and their products in the tissues host. In response, cells of the innate and adaptive immunity are activated and produce defensins, cytokines and chemokines against inflammatory cells. As a result, loss of periodontal tissues and bone loss occurs.<sup>8</sup> Still etiopathogenesis of periodontal disease remain unresolved, the understanding of role of autoimmunity in periodontics is still quite challenging. Understanding the exact role of autoimmunity can have critical remedial new approaches entailed to treatment of periodontitis either in the form of evolution of a vaccine or some miracle drug. Although a vaccine for PD is captivating, to date, none subsists. Various empirical vaccines or drugs tried are: Resolvin R1 in rabbit prevented periodontitis, C5aR antagonist in mouse limited oral bone loss. Moreover, treatment of mice with all-trans retinoic acid (ATRA), cut down the levels of alveolar bone loss. Additional research and clinical studies are mandatory to render the ability of these treatment approaches to restrain human disease.<sup>9</sup>

### 3. Conclusion

Periodontal disease being a chronic inflammatory disease has a complex etiopathogenesis which needs to be understood much more. There has been more than enough

evidence to quote an autoimmunity aspect to periodontal disease that leads to a general microbial dysbiosis, which could be the primary cause why the initiation and progression of this disease is still unclear. The objective of the review is to highlight this particular aspect of the disease so that further research can be conducted to get a clearer picture of the autoimmune component of this disease and how we can apply it in therapeutics. With advancements in possibly relevant biomarkers at the micro-environmental level, immunological understanding and better targeting of disease therapy based on novel pathogen composition in the approximate future more beneficial control of PD advancement may be on the purview.

### References

- [1] M. G. Newman, H. Takei, P. R. Klokkevold, and F. A. Carranza, *Carranza's Clinical Periodontology*, Elsevier, 10th edition, 2006.
- [2] Socransky SS, Haffajee AD, Cugini MA, Smith C, Kent Jr RL. Microbial complexes in subgingival plaque. *J Clin Periodontol*. 1998; 25:134–44.
- [3] Gemmell 2. E, Seymour GJ. Immunoregulatory control of Th1/Th2 cytokine profiles in periodontal disease. *Periodontol 2000* 2004; 35:21-41.
- [4] Chinen J, Shearer WT. Basic and clinical immunology. *J Allergy Clin Immunol*. 2005; 116:411–418.
- [5] Darveau RP. Periodontitis: a polymicrobial disruption of host homeostasis. *Nat Rev Microbiol*. 2010; 8:481–90.
- [6] Cochran DL. Inflammation and bone loss in periodontal disease. *J Periodontol*. 2008; 79:1569–76.
- [7] J. A. Encinas and V. K. Kuchroo, "Mapping and identification of autoimmunity genes," *Current Opinion in Immunology*, vol. 12, no. 6, pp. 691–697, 2000.
- [8] Seymour GJ, Taylor JJ. Shouts and whispers: An introduction to immunoregulation in periodontal disease. *Periodontol 2000* 2004; 35:9-13.
- [9] Wang L, Wang J, Jin Y, Gao H, Lin X. Oral administration of all-trans retinoic acid suppresses experimental periodontitis by modulating the Th17/Treg imbalance. *J Periodontol* 2014; 85:740-750.