

# Immunity and Periodontal Disease

Prangya Elina Singh<sup>1</sup>, Manoj Kumar<sup>2</sup>, Rinkee Mohanty<sup>3</sup>,  
Rashmita Nayak<sup>4</sup>, Anurag Satpathy<sup>4</sup>, Gatha Mohanty<sup>5</sup>

<sup>1</sup>Intern, Institute of Dental Sciences, <sup>2</sup>Associate Professor, <sup>3</sup>Professor & Head, <sup>4</sup>Professor, <sup>5</sup>Senior Lecturer,  
Department of Periodontics & Oral Implantology, Institute of Dental Sciences, Siksha "O" Anusandhan Deemed  
to be University, Bhubaneswar, India

## Abstract

Periodontal diseases are the inflammatory disorders mostly include gingivitis and Periodontitis, which further leads to tooth loss. Now-a-days periodontal disorders become the most common disease worldwide. Though it is of microbial origin, the destruction mostly depends upon the host response. This article concentrates on the essentials and importance of immunology in periodontal diseases. Significant aspects like immunity, cell of the immune system, Major histocompatibility complex system and Human leukocyte antigen system, participation of the inflammatory cells in the development of the disease, release of chemokines, cytokines, molecular biology etc.

**Keywords:** *gingivitis, periodontitis, immunity, cells of immune system, host response.*

## Introduction

Periodontal disease is a persistent bacterial infection which mostly attack the gingiva and the nearby tissues that support the tooth to hold in the proper position and in the alveolar bone.<sup>1,2</sup> This inflammatory disease results from the bacterial response in dental plaque or biofilm. The bacteria like *P. Gingivalis*, *A. Actinomycetemocomitans* and *T. Forsythia* involve in this disease and remain confine to the gingival tissue with minimal destruction.<sup>1,2,3</sup> But some genetic, environmental and host response can lead to this alteration in tissue to the level of epithelial attachment loss and tooth loss.<sup>2,3</sup> Only the presence of pathogenic bacteria can't be the cause of periodontitis. The defense mechanism of the host plays an important role by including the release of anti-inflammatory cytokines, providing the more numbers of Neutrophils and building the protective antibodies.<sup>1,2</sup> But, this disease progress rapidly due to other factors which may include high levels of inflammatory mediators like cytokines, matrix metalloproteinase (MMPs), low level of interleukin-10 (IL-10), Transferring growth factor and inhibitors of MMPs in the body as the outcome of the disruption or disturbances in the host defense mechanism to the pathogens.<sup>2,3</sup> These mediators stimulate the resorption of the alveolar bone and extracellular matrix destruction in the gingiva.<sup>2,3</sup> This review article further describe

the immune system briefly and the impact of this in periodontal disease.

**Immunity:** Immunity is the reluctance to accept any foreign antigen by the host and towards the injury caused by microorganisms and their products.<sup>4</sup> Immunity is of two types, one is innate or native and another adaptive or acquired. Innate immunity categorized into species immunity, Racial immunity, Individual immunity. And Acquired immunity classified into Active and Passive. Both active and passive immunity further divided into Natural and Artificial type.<sup>4,5</sup>

**Innate Immunity:** Gives the first line of defense against any kind of infection and microorganisms.<sup>5,6,7</sup> It constitutes of four types of barriers:

**Anatomic:** Include skin which has thinner outer epidermis and thicker inner dermis. And mucosal member which also consists of an outer epithelial and inner connective tissue.<sup>6</sup>

Physiologic barrier: include temperature, ph. and chemical mediators.<sup>6,7</sup>

Phagocytic barriers: contains Neutrophil, macrophages and Nkcells.<sup>6,7</sup>

Inflammatory Barriers

**Acquired Immunity:** Develop in the body by the host after the contact with suitable antigen or after transfer of antibodies or lymphocyte from an immune donor.<sup>5,6,7</sup> The acquired immunity has four characteristics features named as; Antigenic specificity- The capability of recognizing even minute difference between antigens.<sup>6,7</sup> Diversity-entitle immense diversity through antibodies as the immune system has perceived and reacted accordingly.<sup>6,7</sup> Immunological memory-remains through out the life of the individual and a second exposure will be responded.<sup>6,7</sup> Self, non-self-discrimination of molecules.<sup>6,7</sup>

**Cells of immune system:** Lymphoid and myeloid arm of the Hematopoietic system give rise to the principal cells of the immune system. Cells like erythrocyte, phagocytes (Neutrophils and monocyte), eosinophils, platelets, basophils, peripheral dendritic cells, mast cell precursors are derived from myeloid arm in the bone marrow. Peripheral DCs, monocytes and mast cell precursors again get transformed in the tissue.<sup>7,8</sup> Monocyte may change to become a macrophage. Similarly, Natural killer (NK) cells, pre-T cells and B cells are derived from the lymphoid arm in the bone marrow. T cells are found in the thymus; as they are the differentiated form of the Pre-T cells in the thymus. DCs, B cells and antigen presenting cells convert the antigens to T cells in the lymph node and the spleen, which are considered as the secondary lymphoid organs. Final differentiation of T cells and B cells happens in the lymph node and spleen.<sup>7,8</sup>

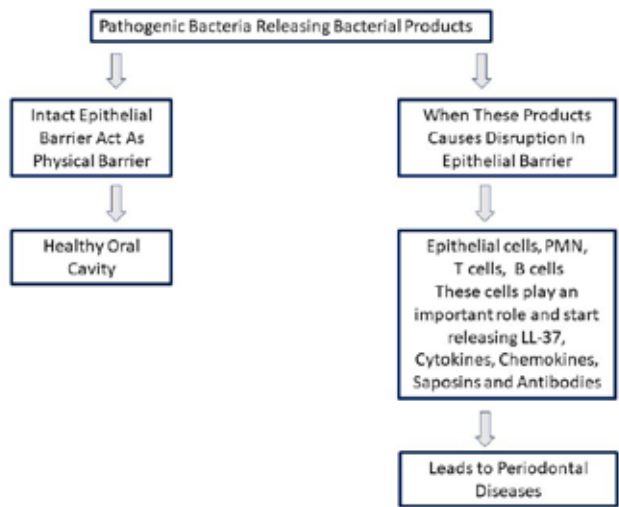
Mast cells are mostly responsible for the immediate hypersensitivity reaction. They remain very close to the blood vessels and consists of cytoplasmic granules filled

up with mediator molecules or effect. Tissue and mucosal mast cells are the two form of mast cells. They vary from each other by their activities, anatomical placements.<sup>7</sup>

Basophils release their cytoplasmic granules which have pharmacologically active components and oppose against the foreign pathogens or microorganisms. They are also associated with allergic response.<sup>3,5,7</sup> Eosinophils have anti-parasitic and bactericidal activities. DCs are found in the basal and supra basal layer of oral mucosa as the cell component of innate immune system. The mechanisms that are lie behind the periodontal diseases by these cells are; conversion or transition of adaptive response, direct relation to the pathogenic signals and ability to impact the other cells of immune response.<sup>3,7</sup>

Macrophages are the quick protective mechanism. Whereas the MHC molecules contain various glycoprotein which recognize the T cells by binding the antigen over it. So, it is also known as “antigen presentation”. Neutrophils act as phagocytic cells and they are in large number.<sup>3,5</sup>

Lymphocytes: There are 3 types of lymphocytes like T cells, Bcells and NK cells based on their functions and surface markers. Interleukin-7(IL-7), the triggering factor for forming these lymphocytes from the bone marrow stem cells. Tcells are the important part of acquired immunity. Some different subsets of T cells are present in periodontal tissue. They directly attack and breakdown the infected cells with the help of active macrophages. B cells manifest the humoral immunity.<sup>5,7</sup> The number of B cells is more than the Tcells. NK cells are the particular type of lymphocyte which don't have class 1 MHC molecules and kill the infected cells.



**Fig. 1. Mechanism involved in the development of periodontal disease.**

**Response of innate immunity in periodontal disease:** Polymorphonuclear leukocyte plays the main role in continuing the healthy status of periodontium.<sup>1,3</sup> Patients with cyclic neutropenia and leukocyte adhesion deficiency disorders are more vulnerable to the gingival infection or early and severe form of the periodontitis.<sup>3</sup> Defects in PMN in molecular basis can result in development of periodontitis. The protective response of PMN against the periodontal pathogens is degraded when they fail to transmigrate into the endothelium, this ultimately increases the inflammatory response.<sup>5,7,9</sup>

Periodontal epithelium acts as a physical barrier towards the infection. The physical barrier is formed by the epithelial cells, as they remain in constant contact with bacterial products.<sup>9</sup> In case of disease formation of deep periodontal pocket, inflammation of connective tissue and bacterial invasion is formed due to the migration of epithelial cell.<sup>10</sup> Epithelial cells counter the pathogens by changing the cell differentiation, by proliferation, by changing their cell signaling events.<sup>10,11</sup> Langerhans cells and dendritic cells have the connection with acquired immunity. Epithelial cells create different types of antimicrobial peptides which have been found throughout the body in human.<sup>12,13</sup> These are also related to saliva or remain in the dentogingival junction.<sup>14,15</sup> When the microbial pathogens attack cell-cell junction, the integrity of the epithelial barrier breaks down.<sup>1,11,12,15</sup> These proteins or peptides have an action against gram+ve, gram-ve, yeast and some viruses. They linked to the anionic microbial surface, then assemblage to form pores or damage the microbial membranes, new evidence shows some has cytoplasmic targets.<sup>15,16,17,18</sup> These peptides complement histatins, lysozyme and salivary immunoglobulins, the antimicrobial factors of saliva having a role in innate host defense responding to an infection.<sup>14,15,17</sup> Some peptides like alpha-defensins and cathelicidin LL37 activate the classical complement pathway and increase the IL-8 production by epithelial cells, which enrich the neutrophil count to the site of infection.<sup>11,17,18</sup> Innate immunity has an ability to admit bacteria as non-self agents because the microorganisms have PAMPs in bacterial wall, which are recognized by pattern recognition receptors on immune cells.<sup>17,18,19</sup>

**Adaptive immune response in periodontal disease:** The adaptive immune response comes into role when the epithelial barrier and its component of innate systems, are ruptured.<sup>12,18,19</sup> The balance between Th1 and Th2, Cytokines regulate the immune response against the infection.<sup>16,19</sup> According to some studies a

decrease in Th1 response and increase Th2 response may develop periodontitis, some also shows the superiority of Th1 response over the Th2 response. Boyel et al advocated that the integrity of tissues in bone depends on the equilibrium between osteoclasts and osteoblasts.<sup>20</sup> During synthesis, osteoblasts express some chemokine receptors. Besides, some important chemokines which take part in recruitment of PMN and different lymphocyte, can be produced by an osteoclast.<sup>18,20</sup>

Chemotaxis of inflammatory cells in bone environment due to the production of chemokine may lead to bone disruption and tissue destruction.<sup>21</sup> Periodontal disease tissue contains both T and B cells.<sup>3</sup> The phagocytic activity of macrophages and neutrophils would increase or intensify when INF-alpha is produced by T cells. B cells are activated by IL-4 production which causes the antibody production.<sup>10,20,22</sup> These antibodies act against specific bacterial antigens like LPS of *A. Actinomycetemcomitans* LPS of *P. Gingivalis*. This antibody response is mostly facilitating the bacterial clearance and stops the progressive nature of disease and provides protection against bacteria.<sup>9,10</sup> Regulatory T cells are the definite subgroup of CD4+ T cells which give response to any kind of infection depending on the cytokine pattern induced.<sup>8,22</sup> According to Cardoso et al, more number of T regulatory cells in gingival tissues with chronic periodontal disease patient provides the idea of involvement of type of cell in periodontal disease. Anyhow, the action of T cells in developing periodontal diseases remains unrevealed.<sup>6,7</sup>

## Conclusion

This review details about the periodontal disease, contribution of pathogenic bacteria with other factors in development of inflammatory reaction. It also emphasizes the immune system of human body and implication of innate and acquired immunity in initiation and progression of various periodontal diseases. Further, there is less evidence about the immune system control of the disease as more studies are going on over this.

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