# Immunology and root resorption: a possible relationship

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**Abstract**

This work studied the relationship of immunology with dental resorptions, specifically the elements of the immunologic system that would directly act in the process which identifies the root of a dental element as something to be destroyed. A literature review was accomplished, from 1989 to 2005, through scientific articles published in the health area. The articles were obtained from databases such as PUBMED and BIREME. The two sets of responses that the immunologic system uses to combat foreign antigens, the innate and adaptive immune responses are approached in this review. Some studies showed the capacity of the immunologic system to interpret fractions of dentinary components as "nonself" structures, establishing the concept of dentinary antigen. Low serum levels of circulating anti-dentin antibodies in the blood of mice and dogs indicate the antibody-antigen interaction when crude extract of circulating dentin runs in their blood, what brought about researches that verified alterations in the levels of IgG and IgM in humans, shimmering the possibility of a serum diagnosis, which would enhance the precocious detection of dental resorptions. We concluded that dentin is not recognized as a self structure in the human immunologic system; probably being interpreted as a foreign antigen.

## INTRODUCTION

Dental resorptions constitute a challenge to dentistry due to their organic complexity. The concern and curiosity on this subject are not recent. The oldest report about resorptions of the dental structures was described by Michael Blum in 1530, probably the first book about the topic. However, the scientific study of root resorptions is considered recent, embracing nearly two decades.

The aim of this study was to accomplish a literature review on which components of the tooth, once exposed, would trigger root resorptions, in search of a better understanding of this process.

## LITERATURE REVIEW

Lymphocytes are the primary cells of the immunologic system, and have developed one of the most sophisticated defense mechanisms in the biological system. The review of Alam and Gorska [1] enlightens that the T lymphocytes play a major role in the organization of the immune response, eliminating intracellular pathogens (virus, and bacteria) through the generation of cytotoxic T lymphocytes. The B lymphocytes protect the organism against extracellular pathogens by the production of antibodies. The natural killer cells (NK) are an important component of the innate immunity. The dendritic B cells begin the immunologic response by presenting antigens to the T lymphocytes. The authors resume that the interaction among the T lymphocytes, B lymphocytes, dendritic cells and the natural killer cells (NK) constitutes the fundamental defensive mechanism of the host.

The mechanism against pathogenic microbes demands different responses depending on the characteristic of the pathogen and on the attacked tissue. Chaplin [2] claimed that the organism of the host has developed innate and adaptive immune mechanisms of defense, being the former unspecific, attacking any nonself structure or antigen, and the latter, on the other hand, extremely specific. Both types of immune response act together in order to eliminate pathogenic antigens through the discrimination of what is self and what is not. The review describes the key-mechanism used by the immunologic system to respond to such antigens.

The role of the IL-1 cytokine family (interleukin-1), which represents a group of proteins that possesses synergic and contrasting biological responses was studied. IL-1 and its precursory forms are strongly involved in the establishment of inflammation and host defense. Within this family of gene products, there is also a naturally occurring antagonistic receiver, IL-1ra, as well as a family of receiving proteins with functions and differential signaling activities. It was

added that the study of such proteins in human diseases, including the allergic ones, has led to a better understanding of the underlying general inflammation associated with these syndromes and has been promoting opportunities to shimmer new forms of interventions to the allergic diseases [3].

Systemic factors, such as the inflammatory chemical mediators produced by asthma are able to reach the periodontal ligament (PDL) and act synergically to increase root resorption. It was objectified to determinate if asthmatic patients exhibited a higher incidence of apical root resorption compared with healthy patients after fixed orthodontic treatment. It was claimed that the displacement of a tooth for an orthodontic load results in the death of many cells in the periodontal ligament area (PDL); the removal of the consequent necrotized tissue is necessary before the dental movement take place. It was concluded that the combinatory analysis of the teeth showed that asthmatic patient showed more statistically significant dental resorptions than non asthmatic patients; however, in spite of the higher incidence of the first group, both groups exhibited similar amounts of resorption degree 2 (moderate) and degree 3 (severe) [4].

Class I MHC molecules (also called the human leukocyte-associated [HLA] antigens) are cell surface glycoproteins that bind peptide fragments of proteins that have been synthesized within the cell. Class II MHC molecules are extracellular glycoproteins that have been ingested by the cell and are proteolytically processed [125].

The antigen presenting cells (APC) are those that express high levels of class II MHC molecules; with internalizing ability to process and expose foreign antigens in the fitting MHC. Therefore, the immune response comes mainly from the action of four cellular types: T cells (fundamental in the elimination of intracellular pathogens such as virus and bacteria) through the generation of cytotoxic T cells. B cells, which defend the organism against extracellular pathogens by the production of antibodies. Natural killer cells (NK), which constitute a subserie of positive cytotoxic lymphocytes CD56, which, in spite of belonging to the innate immunologic system for not presenting surface receptors, are fundamental for the recognition of pathogens, and Dendritic cells (DC), cells, which activate the immunologic response by the exhibition and consequent presentation of foreign antigens to the T cells [1267].

During the dentinogenesis the coronary dentin is protected by the recently-formed enamel as well as the dental external epithelium, stellate reticulum, stratum intermedium and by the ameloblasts. The root dentin is protected by Hertwig's epithelial root sheath, by the intermediate cementum, and, after the fragmentation of the sheath, by the cementoblasts and cementum. Such structures keep the dentin protected against the immunologic system during the development of the natural tolerance, and in case the dentinary proteins are exposed, they may cause an immunologic response against the components of the organism itself, which is known as an auto-immune reaction.

The dentinogenesis involves the synthesis of a collagen-rich extracellular matrix (ECM) and predentin that is converted to dentin when the collagens fibrils become mineralized. It was postulated that extracellular events regulate dentinogenesis. Similarly, osteogenesis involves an initial mineralized osteoid that is progressively mineralized and converted to bone. To understand the process, it was compared ECM proteins in bone with the ones in dentin, focusing on the sialic acid (SA)-rich proteins. It was observed qualitative similarities between the SA-rich proteins, but distinct differences in the amounts of (OPN) and dentin sialoprotein (DSP) were found. OPN, a predominant protein in bone, it was found in much smaller amounts in the dentin. On the other hand, DSP, abundant in dentin ECM, was found sparingly in bone [58].

Another work [9] has claimed that the depression in autoantibody titers to tooth root antigens has been shown to coincide with active root resorption in dogs. The objectives of their study were to develop a quantitative mouse model for root resorption and to determine if a similar drop in tooth root autoantibodies coincided with active root resorption in that species. Uniform areas of necrosis were created in the periodontal ligaments of lower incisors of 36 male Swiss albino mice by inserting a cryoprobe through a skin incision. Contralateral incisors served as controls. At 0, 3, 5, 7, 10, 14, and 21 days; six mice were killed, and blood and incisors were collected. Serum autoantibody titers were determined with an enzyme-linked immune sorbent assay antigen prepared with extract of the roots of the incisors that were harvested in the mice. No root resorption was evident on control teeth. Localized lesions on treated teeth were found to be of significant size between 7 and 14 days ($p < 0.05$), but most of these erupted into the mouth by 21 days. Autoantibody titers were reduced by 3 days, remained depressed until 14 days, and returned to pretreatment levels by 21 days. Furthermore, the mouse, like the dog, harbors a serum autoantibody to tooth root antigens and this is

suppressed during active root resorption.

In a study carried out to examine the response to traumatic root resorption in mice after their hyperimmunization with a crude tooth extract (dentin) [10] , mice were immunized with mouse dentin and controls were sham immunized. All mice were boosted four weeks later with or without mouse dentin as appropriate. All mice were booted again two more times at weekly intervals with mouse dentin and then twice at weekly intervals with rat dentin, in order to increase mouse serum antibody titers to dentin. Mice were killed ten days later, and serum tested for antibody to dentin antigen. Root resorption was observed on the incisors in the sham-immunized mice but not in the dentin-immunized mice. Only the serum antibody titers to dentin from preimmune mice and bleed five were statistically significant. The authors' data indicate that antibodies do not mediate the traumatic root resorption process as originally hypothesized. They suggest that hyperimmunization with dentin may protect against traumatic root resorption.

Some works have featured that replacement dental resorption may be a consequence of trauma and may cause transplant and reimplants to fail [1112] . They demonstrated the participation of the immuno-pathological response in inflammatory dental resorption. They claim that the mechanisms of the two types of dental resorption are different. The aim of their study was to observe the immunol responses of patient who suffered dental trauma with subsequent replacement dental resorption. The result of ELISA demonstrated that serum from patients with replacement root resorption contained larger amounts of IgG and smaller amounts of IgM anti-total human-dentin extract and anti-fractions of extract than did serum from control individuals. Their results signal a hypothesis that dentin is immunogenic and the serological profile of patients with replacement dental resorption may be identified through biochemical analysis of their blood. The authors conclude that this method may allow early diagnosis of the dental resorption before it becomes radiographically visible.

## CONCLUSIONS

After reading and analyzing the results of several articles, and considering the current limitations of the applied methodologies, through this discussion it is concluded that dentin is not recognized as a self structure by the immunologic system, being the component of the tooth which is more likely to trigger root resorptions.

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