

Episode #47 – Do Periodontal Diseases have an Autoimmune Component? October 22, 2021

Overview of periodontal diseases

Periodontal diseases are inflammatory diseases that affect the hard and soft supporting structures of the teeth. They can be broadly categorized into gingival diseases and diseases affecting the periodontal attachment (cementum, periodontal ligament, alveolar bone), such as periodontitis. [1] [2]

Gingival diseases can be categorized into dental plaque biofilm-induced gingivitis and non-dental plaque-induced gingival diseases. Dental plaque biofilm-induced gingivitis is one of the most common human inflammatory diseases.[1] It is characterized by various clinical signs and symptoms, such as edema and erythema of the gingiva and bleeding and discomfort on gentle probing (e.g. ~0.25 N of force).[2] Local predisposing factors (e.g., plaque retention factors, quantity and quality of saliva) and systemic modifying factors (e.g., smoking, diabetes, severe vitamin C deficiency, elevated sex steroid hormones, blood malignancies) can affect its extent, severity, and progression. [2]

Non-dental plaque-induced gingival diseases are less common. They include several conditions that are not caused by plaque and usually do not resolve after plaque removal. However, the severity of the clinical signs and symptoms often depends on plaque accumulation and subsequent gingival inflammation. These gingival diseases may be manifestations of a systemic condition (e.g., neoplasms, autoimmune diseases, systemic infections) or may be localized to the oral cavity (e.g., traumatic lesions from mechanical, chemical, or thermal insults). [2] [3]

Periodontitis is a multifactorial inflammatory disease of the periodontal tissues associated with dysbiotic dental plaque biofilms and host immune response resulting in progressive destruction of the supporting structures of the teeth (i.e., clinical attachment loss[3] and alveolar bone loss). It is characterized by periodontal pocket formation and/or gingival recession and gingival bleeding. [4] [5] [6] [7]

Based on pathophysiology, there are 3 forms of periodontitis:

- Necrotizing periodontitis – Typical features of necrotizing periodontitis include papilla necrosis, bleeding, and pain. Several predisposing risk factors are involved with the

[1] Refer to Episode #44 for information on inflammation.
[2] Refer to Episode #20 for information on periodontal probing.
[3] Refer to Episode #20 for information on clinical attachment loss (CAL).

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development of necrotizing periodontitis including a compromised host immune response, malnutrition, psychological stress, insufficient sleep, inadequate oral hygiene, tobacco use, and alcohol consumption. [4] [8]

- Periodontitis as a direct manifestation of systemic diseases – Examples of systemic diseases include diseases associated with immune disorders (e.g., leukocyte adhesion deficiency syndromes,[4] Chediak-Higashi syndrome[5]), diseases affecting the connective tissues (e.g., systemic lupus erythematosus [SLE][6]), metabolic and endocrine disorders (e.g., glycogen storage disease,[7] hypophosphatasia,[8] diabetes, osteoporosis), acquired immunodeficiency diseases (e.g., acquired neutropenia,[9] HIV infection), inflammatory diseases (e.g., inflammatory bowel disease, arthritis), and certain neoplasms. [7] [9]

- Periodontitis – This single category of periodontitis is further characterized based on a multi-dimensional staging and grading system. Primary goals of staging are to classify the severity and extent of damaged tissue attributed to periodontitis and to assess the complexity of controlling the disease as well as managing the long-term function and esthetics of the remaining dentition. Primary goals of grading are to appraise future disease progression risk and response to standard periodontal therapy. This will help to determine the frequency and intensity of therapy and future monitoring. Also, it is to estimate the impact of periodontitis on systemic disease, and vice versa, to guide general health monitoring and interprofessional collaboration with other healthcare professionals for health management. [4] [6]

Overview of autoimmune disorders[10]

Autoimmune disorders are a type of immune system disorder that occurs when the immune system mistakenly targets healthy cells as foreign pathogens or faulty cells (i.e., the immune system cannot distinguish self from nonself). The exact cause of autoimmune disorders is unknown.

Symptoms of autoimmune disorders depend on the type of disorder and the part of the body affected. An autoimmune disorder may affect one or more organ or tissue types.

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[4] Leukocyte adhesion deficiency (LAD) is characterized by recurrent, life-threatening infections and poor wound healing from surgery or trauma. Individuals with this condition are predisposed to periodontal disease. LAD is caused by a mutation in the gene *ITGB2*.

[5] Chédiak-Higashi syndrome (CHS), also called Begnez-Cesar's Syndrome and several other names, is characterized by reduced pigment in the skin and eyes, immune deficiency with an increased susceptibility to infections, and a tendency to bruise and bleed easily.

[6] Systemic lupus erythematosus (SLE), also referred to as lupus, is an autoimmune disorder that can affect joints and many organs (e.g., skin, heart, lungs, kidneys, nervous system).

[7] Glycogen storage diseases are a group of disorders in which stored glycogen cannot be metabolized into glucose to supply energy and to maintain steady blood glucose levels for the body.

[8] Hypophosphatasia (HPP) is a rare genetic disorder characterized by impaired mineralization of bones and teeth. Defective mineralization results in bones that are soft and prone to fracture and deformity. Defective mineralization of teeth can lead to tooth loss.

[9] Neutropenia is a decrease in circulating neutrophils in the blood increasing risk of serious infection. Major causes of acquired neutropenia are infection, drugs (through direct toxicity or immune effects), and autoimmunity.

[10] Refer to Episode #44 & #45 for more information on the immune system and autoimmune disorders.

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Areas often affected by autoimmune disorders include blood vessels, skin, erythrocytes, connective tissues, joints, muscles, and endocrine glands (e.g., thyroid, pancreas).

There are more than one hundred autoimmune diseases, including type 1 diabetes mellitus, rheumatoid arthritis (RA), Graves' disease,[11] Hashimoto's thyroiditis,[12] SLE, pemphigus,[13] and Sjögren's syndrome. An individual may have more than one autoimmune disorder at the same time. [10] [11] [12] [13]

Triggers of autoimmune disorders may include:

- Altered tissues (e.g., by viruses, drugs, sunlight, radiation) are viewed as autoantigens[14] (foreign substances) to the immune system resulting in the production of autoantibodies.[15]
- Cross-reactivity[16] occurs when antibodies to a foreign antigen attack the body's own tissues because they appear structurally or biologically similar to the foreign antigen. For example, antibodies to group A *Streptococcus*[17] may cross-react with an antigen in heart muscle leading to rheumatic fever.
- A body substance normally confined to a specific area is released into the bloodstream causing an autoimmune reaction. For example, eye trauma can cause release of eyeball fluid into the bloodstream triggering the immune system to identifying the fluid as foreign resulting in an attack on the eye causing sympathetic ophthalmia.[18] [10] [11]

It is usually unknown why something triggers an autoimmune disorder in one individual and not another. However, genetic factors maybe involved. Specifically, some individuals have genes that slightly increase their susceptibility to developing an autoimmune disorder, rather than the disorder itself being inherited. [10] [14]

Autoimmune disorders and periodontal diseases

Both periodontal diseases and autoimmune disorders are chronic inflammatory diseases. The pathogenesis of periodontal diseases is influenced by host immunity and greatly influenced by genetic and environmental factors. The host immune response

[11] Graves' disease is an autoimmune disorder that leads to generalized overactivity of the entire thyroid gland (hyperthyroidism).
[12] Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis, is a chronic autoimmune disorder of the thyroid with lymphocytic infiltration, often leading to hypothyroidism.
[13] Refer to Episode #30 for information on pemphigus.
[14] Autoantigens are endogenous (self) antigens, that despite being a normal tissue constituent, are targeted by the immune system (e.g., in autoimmune disease).
[15] Autoantibodies are antibodies made against the body's own tissues or organs (i.e., the immune system fails to distinguish self from nonself). Some autoimmune diseases are caused by autoantibodies.
[16] Cross-reactivity occurs when the immune system identifies proteins in one substance (e.g., latex) and the proteins in another (e.g., kiwi, banana, avocado) as being similar, which results in an immune response to the structurally similar or biologically related substances.
[17] Group A *Streptococcus* can cause a range of diseases including strep throat, scarlet fever, impetigo, cellulitis, toxic shock syndrome, and necrotizing fasciitis. [42]
[18] Sympathetic ophthalmia is inflammation of the uveal tract (uveitis) that occurs in one eye after injury or surgery to the other eye. The uveal tract consists of the iris, ciliary body, and the choroid of the eye.

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during periodontitis involves the innate[19] and adaptive immune systems[20] leading to chronic inflammation and progressive destruction of alveolar bone and periodontal soft tissue. Studies have shown an association between periodontitis and autoimmune disorders, including RA, type 1 diabetes mellitus, inflammatory bowel disease, and SLE. [15] [16] [17] [18]

An autoimmune disorder is a malfunction of the immune system resulting in the production of antibodies to an endogenous antigen (autoantigen) causing the body to attack its own tissues. Autoimmunity is initiated by a combination of genetic predisposition and environmental triggers. Autoimmune diseases can impact the oral cavity directly and indirectly. For example, Sjögren's syndrome is a result of autoimmune destruction of exocrine glandular epithelium, primarily the salivary and lacrimal glands causing xerostomia and dry eyes, respectively. The lack of saliva flow causes increased plaque accumulation and risk of gingivitis, periodontitis, caries, candidiasis, angular cheilitis, and mucositis. Type 1 diabetes mellitus results from autoimmune destruction of the beta cells in the pancreas causing little to no insulin production. Diabetes mellitus is a risk factor for periodontal diseases and associated with significantly higher prevalence and severity of periodontitis. [7] [10] [19] [20]

Comparing autoimmune disorders & periodontal diseases

	Autoimmune disorders	**Periodontal diseases**
Chronic inflammatory condition	Chronic multifactorial inflammatory disease	Chronic multifactorial inflammatory disease
Local vs. systemic inflammation	Autoimmune diseases can be classified as systemic (e.g., RA, SLE) or organ-specific (e.g., thyroid gland in Graves disease, pancreatic beta cells in type 1 diabetes) depending on the location of the autoimmune attack. With systemic autoimmune diseases, the autoantigens are found in almost any type cell in the body. With organ-specific autoimmune diseases a particular organ or tissue is targeted by the immune system. [21]	Localized inflammation of the periodontium. Local inflammatory processes can also become systemic, which in turn affect organs such as the heart.[21] [22] Periodontitis shows evidence of systemic inflammation with elevated C-reactive protein levels in both acute and chronic cases. [23]
Host immune response	Host immune system mistakenly targets healthy cells as foreign pathogens or faulty cells. Dysregulated immune responses resulting in excessive and uncontrolled tissue inflammation. [24]	Host immune response targets supporting structures of the teeth. Diseased periodontal pockets contain significant levels of inflammatory mediators, including tumor necrosis factor alpha (TNF-α), interleukin-1 (IL)-1, IL-2, and IL-8, and

[19] Refer to Episode #6 for information on periodontal disease and the innate immune response.
[20] Refer to Episode #45 for information on the innate and adaptive (acquired) immune system.
[21] Refer to Episode #37 for information on periodontitis & cardiovascular diseases.

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	Autoimmune disorders	Periodontal diseases
		prostaglandins,[22] which can be released into the circulation from the diseased periodontium and can contribute to systemic inflammation. [25]
Tissue destruction	Tissues affected depends on type of immune disorder.	Hard and soft tissues of the periodontium impacted.
Periods of exacerbation and remission	The diseases may have flare-ups and periods of remission where symptoms improve or disappear. [26]	Periodontitis is episodic in nature with bursts of disease activity. [22]
Involvement of pathogens	Emerging evidence demonstrates infections either precede or coincide with disease onset, e.g., Epstein-Barr virus, coxsackievirus. [27] One theory postulates some microorganisms (e.g., bacteria or viruses) may trigger changes that impact the immune system. [13] For example, *Porphyromonas gingivalis* may play a modulating factor in inflammatory rheumatic disorders such as RA, ankylosing spondylitis, and SLE. [28]	Destructive periodontal pathogens include *Treponema denticola, Porphyromonas gingivalis*, *Prevotella nigrescens, Prevotella intermedia*, *Prevotella melaninogenica, Tannerella forsythia, Aggregatibacter Actinomycetemcomitans* [29] [30] Epstein-Barr virus-1 (EBV-1), human cytomegalovirus (HCMV) may act synergistically with bacteria in periodontitis pathogenesis. *Candida* species may also be implicated. [30]
Microbial dysbiosis	Alterations to gut microbiota can cause immune dysregulation possibly increasing risk of autoimmune diseases both within and outside the gut. [31]	Dysbiotic microbial communities in the oral cavity can lead to periodontitis. [32]
Genetic predisposition	Genetics may play a role increasing an individual's susceptibility to an autoimmune disorder (the disease itself is not inherited). In susceptible individuals, a trigger, such as a viral infection or tissue damage, may cause the disorder to develop. [10]	Genetics may play a role in the onset of periodontal disease. [33]
Common risk factors	May include poor diet, smoking, and stress.	Poor diet, smoking, and stress can exacerbate periodontal diseases.
Oral health impact	Autoimmune diseases can impact the oral cavity directly and indirectly, e.g., Sjögren's syndrome causes saliva gland destruction decreasing saliva flow and increasing caries and periodontal disease risk. [20] [34] Diabetes can impact extent and severity of periodontal disease. [35]	Periodontitis leads to connective tissue and collagen loss in the gingiva, periodontal ligament destruction, and alveolar bone resorption causing tooth mobility and loss. [22]

[22] Prostaglandins are hormone-like substances involved in numerous body functions, e.g., modulation of inflammation, smooth muscle contraction and relaxation, blood vessel dilation and constriction, and blood pressure control.

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Autoimmunity in periodontal disease

Brandtzaeg and Kraus (1965) first theorized an autoimmune basis for the pathogenesis of periodontitis. They described the presence of anti-collagen antibodies produced by plasma cells[23] in periodontal tissues of individuals with periodontitis. [15] Since then, much research has investigated the concept of periodontal diseases possessing an autoimmune component, based on its destructive consequences to alveolar bone. For example, both human and animal studies have documented the role of autoimmunity in periodontal disease. The majority of research dealt with the detection of antibodies to host components, especially collagen. [22] [23]

For instance, a pilot study by Koutouzis et al. (2009) reported elevated levels of serum autoreactivity (e.g., to type 1 collagen[24]) in individuals with periodontitis noting serum autoreactivity levels were greater in individuals with more severe periodontitis. The study found healthy individuals did not demonstrate any reactivity. The authors concluded autoimmunity is involved in periodontal disease progression but the extent of the autoreactivity may differ based on the stage of the periodontal disease. [24]

Several other mechanisms have been proposed to explain autoimmune responses in periodontal disease as outlined below.

Autoimmunity normal component of chronic inflammation

Gemmell et al. (2007) hypothesized autoimmunity is an important and normal part of chronic inflammation since it helps the removal of collagen by enhancing fibroblast phagocytosis of protease-digested collagen fragments as well as the removal of destroyed or dying cells. Specifically, during chronic inflammation there is simultaneous tissue destruction and repair. As tissue is destroyed, (i.e., the collagen is broken down into amino acids by various proteases), it must be removed and the amino acids must be made available for reuse by fibroblasts. The production of anti-collagen antibodies could then opsonize[25] the broken-down collagen fragments and enhance their phagocytosis by fibroblasts, hence facilitating the 're-cycling' process. This scenario suggests the role of autoimmunity and the controlling mechanisms are an essential part of homeostasis. Control of this process by regulatory T cells then becomes fundamental and if there is a disturbance in this homeostatic mechanism excessive tissue destruction could result. [25]

Immunoglobulin A (IgA) expression[26]

In several autoimmune diseases, an increase in autoantibody is associated with an increase in molecules involved in antigen presentation (specifically IgA antigen),

[23] Plasma cells, also called plasmacytes, are a type of leukocyte (white blood cell). Plasma cells develop from B cells that have been activated.

[24] Type 1 collagen is the most common collagen accounting for about 90% of total collagen in the body. It is prevalent in tissue, such as skin, tendon, bone, ligaments, dentin, and interstitial tissues.

[25] Opsonize makes a foreign pathogen more susceptible to phagocytosis by tagging it with opsonins for elimination by phagocytes. Examples of opsonins are antibody molecules such as the IgM.

[26] Immunoglobulins (Ig), also called antibodies, are proteins produced by B cells that tightly bind to the antigen of an invader, tagging the invader for attack or directly neutralizing it. The human body produces thousands of different antibodies, each specific to a given antigen. There are 5 classes of antibodies: IgM, IgG, IgA, IgE, and IgD.

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especially on cells which do not normally express these molecules. These cells are not normally involved in antigen presentation. However, when they do, it may lead to autoantigen presentation to the immune system and autoantibody production. [22]

Altered T helper and T suppressor cell function implicated
Research has shown reduction in T cell[27] population of lymphocytes from individuals with periodontal disease led to an increase in the B cell component of the spontaneous proliferation of lymphoblasts (immature leukocytes). This suggests T suppressor activity would increase in individuals with periodontal disease. [22]

Viral and bacterial infection and the immune system
Viral and bacterial infections may play a role as an exogenous factor triggering an autoimmune response. [22]

Predisposing genetic factors
Several studies have reported an association between a high incidence of selected histocompatibility complex antigens[28] and certain autoimmune diseases, for example, RA and SLE. This could be an underlying predisposing factor for the development of autoimmune disease. [22]

Role of antibodies
Perhaps the most pertinent aspect of the antibodies detected in periodontal disease is their role. Pathologic changes appear to occur in those circumstances where the otherwise physiologic autoimmune response leads to the initiation of further humoral and/or cellular immune[29] activity capable of causing tissue damage or disease. [22]

Antineutrophil cytoplasmic autoantibodies (ANCA)
ANCAs represent a heterogeneous group of antibodies that target antigens present in granules of polymorphonuclear leukocytes (PMNs). Some ANCA-associated diseases coexist with periodontitis, such as RA and SLE. More research is required to determine the link between these diseases and their disease processes.

Exposure to periodontal pathogens, along with a genetic susceptibility, could trigger ANCA by two different mechanisms. The production of TNF-*α* would sensitize or prime the neutrophils to express its granule contained enzymes, which in turn could trigger the production of ANCA. In addition, periodontal pathogens are known to possess a

[27] T cells consist of 3 main types helper T cells, suppressor T cells, and killer T cells. Helper T cells help with an immune response by various means, e.g., communicating with other cells, stimulating B cells to produce more antibodies, and attracting more T cells or phagocytes. Suppressor T cells shut off the immune response when it is no longer required. Killer T cells kill infected or malignant cells.
[28] Human leukocyte antigens (HLA), also called human lymphocyte antigens or major histocompatibility complex (MHC), are a group of identification molecules located on the surface of all cells. They are in a combination that is almost unique for each person, thereby enabling the body to distinguish self from nonself.
[29] Refer to Episode #45 for more information on humoral and cell-mediated immunity.

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"superantigen"[30] property, which can also result in the activation of neutrophils. The activated neutrophils release reactive oxygen radicals, enzymes, and various proinflammatory cytokines,[31] all of which can mediate periodontal destruction. ANCA activated neutrophils can also delay apoptosis[32] prolonging neutrophil activity and thereby increasing tissue destruction. Delayed apoptosis has been reported in periodontal disease. In addition, ANCA is known to have a direct toxic effect on the cells bearing antigens such as endothelial cells, which can result in increased endothelial permeability, a common feature in inflammation. However, further research is required to determine the exact role of ANCA in periodontal disease pathogenesis. [22]

Role of natural killer T cells in autoimmunity

A relationship between natural killer cell[33] activity deficiency and autoimmune diseases has been cited in mice research. This impairment could be involved in the pathogenesis of periodontal disease. The results, however, did show an increase of natural killer T cells in periodontitis, suggesting a functional role for these cells. Due to, their ability to secrete rapid amounts of cytokines, they may influence the T helper cytokine response. The role of autoimmunity in chronic inflammation is still unclear. It is possible autoimmunity is a feature of all chronic inflammation. [22]

Role of autoreactive B cells in autoimmunity of periodontal disease

Activated B cells transform into antibody producing plasma cells. Possibly, immunoglobulins produced by plasma cells directed at subgingival plaque may also be autoantibodies towards host cells. It was observed that the gingival lesions contained a large number of cells that produce antibodies directed to type I collagen. [22]

Oral microbiome dysbiosis[34]

The dysregulation of the oral microbiome[35] may lead to local and systemic autoimmune responses mediated by different mechanisms such as:

Autoantigen overproduction – Autoantigen overproduction may occur when enzymes produced by microorganisms break the extracellular matrix of periodontal tissues (e.g., fibrinogen, type I collagen) creating "remnant epitopes"[36] that act as autoantigens.

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[30] Superantigens are a class of antigens produced by some pathogen viruses and bacteria that cause excessive immune system activation, e.g., non-specific activation of T-cells resulting in polyclonal T cell activation and massive cytokine release.

[31] Cytokines are immune system messengers. Leukocytes and other immune system cells produce cytokines when an antigen is detected. There are many types of cytokines with various roles, such as chemokines, interferons (IFNs), interleukins (ILs), lymphokines, and tumor necrosis factor (TNF).

[32] Apoptosis is a programmed cell death where the cell actively destroys itself to maintain the balance of cell multiplication. It has an important role in maintaining the health of the body by eliminating old, unnecessary, and unhealthy cells.

[33] Natural killer T cells are a type of T cell that has certain features of natural killer cells. They can kill invading microorganisms (e.g., bacteria, viruses) by releasing cytokines and can kill certain cells (e.g., cancer cells) either directly or by causing other immune cells to destroy them.

[34] Dysbiosis is change in the characteristic microorganism communities of a particular microenvironment.

[35] Refer to Episode #32 for information on the oral microbiome.

[36] Epitope is the molecular region on the surface of an antigen where the complementary antibody attaches itself in an immune response.

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Alternatively, enzymatic modification of antigens (e.g., by citrullination[37]) causes the production of autoantibodies. [23]

Microbial translocation – Oral bacteria, their products, or products of immune activation against them, can migrate through the bloodstream to different organs leading to an altered local inflammatory response and the production of autoantibodies. Bacteremia leading to microbial translocation is a possible mechanism where microorganisms from the oral cavity can not only pass into the blood but also reach the intestine and induce multiple immune responses. Increased intestinal permeability where microorganisms or their metabolites reach the circulation has been confirmed as a crucial mechanism in multiple autoimmune diseases.

Thus, the translocation of periodontopathogens and their metabolites to distal sites could be involved in systemic autoimmune responses by causing microflora dysbiosis in other organs resulting in activation of autoimmunity mechanisms. Further research is required to determine the processes by which the occurrence of oral pathogens in remote sites cause dysbiosis in other organs, which subsequently dysregulate the systemic immune response in individuals susceptible to autoimmunity. [23]

Molecular mimicry[38] – Molecular mimicry occurs when a self-antigen is so similar to a microorganism's antigen that antibodies against that antigen cross-react and bind to the autoantigen. This is one of the established links helping to explain the generation of autoimmune processes mediated by infections, but is also a possible mechanism of how microorganisms evade the immune response. The presence of periodontal disease has proven to be a source of antigens both locally and systemically. Molecular mimicry may be one of the mechanisms by which it participates as a chronic infection in local and remote autoimmunity. [23]

Cytokines hyperproduction – The hyperproduction of proinflammatory cytokines activated by commensal microorganisms, specifically IL-12, can increase the response of T cells to self-antigens. IL-12 has a dual role in periodontal disease. In gingival fluid, gingival tissue, and serum, IL-12 has been associated with severe periodontal destruction. Also, the polymorphism[39] of the IL-12 gene is associated with increased susceptibility to develop periodontitis. Studies of IL-12 deficient mice with *P. gingivalis*-induced periodontitis showed less bone resorption thus supporting the involvement of IL-12 in bone destruction of periodontitis. Conversely, IL-12 induces the expression of

[37] Citrullination or deimination is the conversion of the amino acid arginine in a protein into the amino acid citrulline. The immune system can attack citrullinated proteins, leading to autoimmune diseases such as RA with its resultant inflammation and joint destruction.
[38] Molecular mimicry has been implicated as a mechanism by which microbes can induce autoimmunity. An example is rheumatic fever, in which antigenic cross-reactivity between cardiac tissue and streptococcal polysaccharides is believed to induce an autoimmune reaction targeting heart valves.
[39] Polymorphism involves one of two or more variants of a particular DNA sequence. It is a place in the DNA sequence where there is variation, and the less common variant is present in at least 1% or greater in the population being tested. Genetic polymorphism is a difference in DNA sequence among individuals, groups, or populations.

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immunosuppressive molecules, such as human leukocyte antigen[40] through an IFN-γ–dependent pathway. IL-12-induced immunomodulation may be an important mechanism that helps regulate the host's immune response and maintain tissue homeostasis during periodontal inflammation. These findings suggest a negative and positive influence of IL-12 on periodontal disease. However, it is unknown how dysbiosis of the periodontal microbiota can guide IL-12 function towards a proinflammatory or protective role. Understanding the microbiota's role in this mechanism could be used to regulate or control the progression of periodontal disease. [23]

Take home messages

- Periodontitis is a chronic multifactorial inflammatory disease. Although dysbiotic plaque biofilm must be present for periodontal disease to occur, a susceptible host is also required, which is determined by genetic, environmental, and acquired factors. One such factor, autoimmunity, may play a role in the onset and progression of periodontitis.
- Further clinical trials are required to understand the role of autoimmunity in periodontal disease, which may lead to new therapeutic modalities for the treatment and prevention of periodontal diseases.
- Similarities exist between periodontal diseases and autoimmune disorders. Autoimmune disorders impact the oral cavity both directly and indirectly and are increasing in prevalence. [35] Therefore, oral health professionals need to be aware of how autoimmune disease impacts the oral cavity to provide client education, comprehensive treatment planning, and referral to other healthcare professionals as required. Further research is necessary to increase the understanding of the relationship between oral health and autoimmune disease to enhance client care.

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[40] Human leukocyte antigen (HLA), also called major histocompatibility complex (MHC) or human lymphocyte antigen, are a group of identification molecules located on the surface of all cells. They are in a combination that is almost unique for each individual, thereby enabling the body to distinguish self from nonself.

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