

Educational Article

Impact of chronic stress on periodontal health

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Abstract – Introduction: Periodontal diseases are caused by pathogenic microorganisms that induce increases in of local and systemic proinflammatory cytokines, resulting in periodontal damage. The onset and evolution of periodontal diseases are influenced by many local and systemic risk factors. **Educational objective:** In this article, we aim to review the results of the research on the impact of chronic stress on the occurrence, development, and response to periodontal disease treatments and on the pathophysiological mechanisms of periodontal disease. **Conclusion:** Chronic stress has a negative impact on the occurrence, development, and response to the treatment of periodontal disease *via* indirect actions on the periodontium. This can result from behavioral changes caused by stress (poor dental hygiene, smoking, etc.) and a direct neuroimmunoendocrinological action related to the consequences (particularly immunological) of the secretion of certain chemicals (*e.g.*, cortisol) induced by the activation of the hypothalamus and the autonomic nervous system in response to stress. These factors necessitate multidisciplinary management (*e.g.*, physician, oral surgeon, and psychologist) of patients to identify subjects with chronic stress and to employ countermeasures to decrease the impact of stress on the periodontium.

Introduction

Periodontal diseases contribute directly and/or indirectly to systemic infections with bacteria involved in their etiology and pathogenesis [1]. Thus, periodontal diseases are a risk factor for many other conditions such as infectious endocarditis, coronary disease, fatal or nonfatal stroke, premature labor, diabetes, certain pulmonary and sinus diseases [2]. Maintaining good periodontal health is therefore essential for the patient's well-being well beyond the orofacial region. To achieve this goal, it is necessary to understand all the factors that can influence periodontal diseases. The educational objective of this article is to review the results of the research on the impact of chronic stress on the occurrence, development, and response to periodontal disease treatments and on the pathophysiological mechanisms of periodontal disease.

Periodontal diseases

Definition

Periodontal diseases can be defined as multifactorial infectious diseases [2]. They are characterized by symptoms

and clinical signs that may include visible or unsightly inflammation, spontaneous or induced gingival bleeding of varying severity, formation of pockets related to bone attachment losses, and alveolar bone losses, dental mobility and can lead to tooth loss [2].

Epidemiological data in France

The French Union for Oral and Dental Health conducted a multicenter study titled "Periodontal Health and Associated Risk Factors" in 2002–2003 to produce an estimate of the national prevalence of adult periodontal disease in France [3]. This study showed that 16–17 million adults aged 35–64 years in France show clinical signs of periodontitis [3].

Risk factors for the occurrence and/or worsening of periodontal disease

The main etiological factor for the occurrence of periodontal disease is plaque accumulation [4]. Nevertheless, the risk of occurrence and changes in the development, severity, and response to periodontal disease treatments depend on several individual factors. These factors include: bacterial flora, poor oral hygiene, age, sex, diabetes, HIV,

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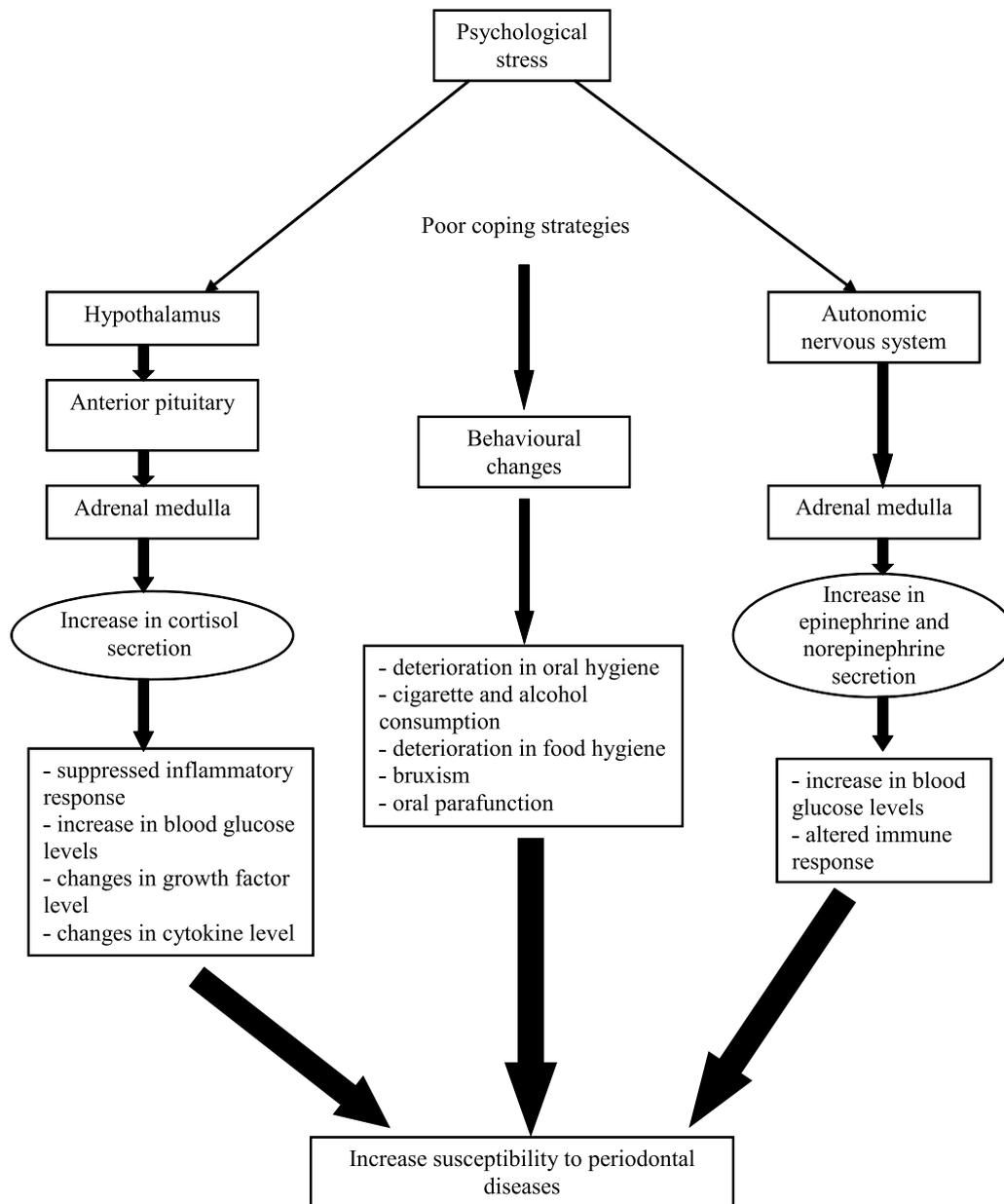


Fig. 1. Biological mechanisms and behaviors linking stress and periodontal disease [31].

pregnancy, menopause, smoking, low socioeconomic status, and local factors (cavities, dental morphology, etc.). Some other general factors are stress, immune deficiency, and nutritional factors, which appear to modulate the body's immune response and determine the level of susceptibility to the disease [5]. The list of these risk factors remains controversial [6].

Stress

Stress is a specific human reaction in response to a trigger, and is characterized by three successive phases: alarm, resistance, and general coping syndrome [7]. The stress response corresponds to the activation of the catabolic mechanisms: activation of the adrenocorticotrophic axis and the sympathetic autonomic nervous system (ANS), and withdrawal of the

parasympathetic ANS. Recovery involves anabolic pathways including sleep and activation of a wave tone. These regulatory pathways allow the human body to react in a coordinated and adjusted manner for reestablishing homeostasis (*eustress*) [8].

The stressor characterizes any situation that activates the pathways of stress, irrespective of its nature, intensity, and duration [7]. It may be external to the subject, imposed by an environmental change, or self-generated by negative influences or thoughts, including anxious thoughts.

Acute stress/chronic stress

Acute stress is the sudden and temporary response of the human body to a stressor which has a defined beginning and end. Exposure to the stressor results in an alarm response that

is characterized by a “fight or flight” reaction [8]. Chronic stress is the response to intermittent and repeated exposure to a stressor over a continuous period [9]. Exposure to chronic stress has biological cost and can lead to neurobioimmune dysfunction (*distress*) [9,10].

Impact of chronic stress on periodontal disease

First link highlighted for necrotizing ulcerative gingivitis (NUG)

Because of its particular nature (sudden onset of acute pain, ease of diagnosis), NUG is the periodontal disease associated with the most studied psychosocial factors. A link was established between NUG and psychogenic factors such as stress, anxiety, and depression in the 1970s [11]. These factors predispose to NUG by promoting bacterial growth and/or decreasing host defenses [12]. This decrease would result in increased levels of corticosteroids and catecholamines *via* ANS. This could decrease gingival microcirculation and salivary flux and improve the nutrition of the *Prevotella intermedia*. Concomitantly, these hormones cause the suppression of leucocyte and lymphocyte functions, which subsequently promote bacterial invasion. It has also been reported that, compared to the patients in the control group, patients with NUG have a reduction of the following:

- chemotaxis of polymorphonuclear leukocytes and phagocytosis [12];
- proliferation of lymphocytes during stimulation by a nonspecific mitogen [13].

Progressive establishment of the link between chronic stress and periodontal diseases in NUG patients

Since 1976, DeMarco has used the term “periodontal emotional stress syndrome” to describe the impact of the stress suffered by the soldiers involved in the Vietnam War on the progression of periodontal disease [13]. It was not until the 1990s when there was any significant research into the relationship between stress and periodontal disease [14]. At first, although the work concluded that there was a link [15], the inconsistency of the results led to doubts over the strength or even the existence of that link [16]. These differences were related to the following:

- the complexity of the individualization of a risk factor, stress, multifactorial etiology for periodontal diseases [17];
- the nonhomogeneity of research protocols that did not use the same criteria to define and measure periodontal disease and stress [17].

Harmonization of the protocols was carried out between the years 2000–2010 with the systematic use of biomarkers to objectify the stress levels of an individual. These biomarkers include: measuring salivary cortisol levels, standardized stress scales and questionnaires, and the community index of periodontal care needs (CIPC) [18]. From there, studies conducted on animals [19–21] and on people, whether it be cohort, cross-sectional, case-control or clinical trials [6,15,28,22] showed a positive

correlation between stress and the occurrence of periodontal disease. According to several recent literature reviews, the evidence is currently sufficient to suggest that stress is a risk factor for the occurrence of periodontal disease in the presence of pathogens as well as the worsening of pre-existing periodontal diseases [8,12,15,17,23–26].

Pathophysiological mechanisms linking chronic stress and periodontal disease

Despite numerous experimental, clinical, and epidemiological studies on the relationship between stress and periodontal disease, the exact mechanisms linking these two phenomena remain largely unknown [22,27–29]. As a first step, these studies have shown the indirect impact of stress on the periodontium through changes in behavior and lifestyle (food and oral hygiene, smoking, parafunctions, etc.) [13]. More recently, the progress of neurology and psychoimmunoenocrinology and the growing interest in the study of stress and its medicopsychosocial consequences have made it possible to demonstrate a direct, biological impact of stress on the periodontium [13,30] (Fig. 1).

Behavioral approach

Neglect of oral hygiene

Oral hygiene depends in part on the mental health of the patient [32]. It has been reported that psychological disorders can lead patients to neglect their oral hygiene resulting in a build-up dental plaque, which can be damaging for periodontal health [33]. Studies have shown that the stress generated by university studies results in a decrease in oral hygiene levels and an increase in crevicular interleukin-1 β levels [34]. The authors conclude that stress is a risk factor for gingival inflammation [34].

Changes to diet

The psychological state of an individual affects the choice, consistency, and quantity of food they consume [35,36]. This may include an increase in the consumption of carbohydrate-rich foods and soft foods, which do not require as much chewing. This type of diet can result in plaque accumulation [35]. Overconsumption of high-fat foods induced by stress can lead to increased cortisol production and thus immunosuppression [35,37]. Any changes to diet can cause stress and can be a risk factor for periodontal disease [25,35].

Smoking

Of all the oral habits that can be picked up because of stress, smoking is the one which has the most damaging effect on the periodontium [32,38] since:

- the frequency of periodontal disease is 7–8 times greater for smokers than for nonsmokers [39];
- the severity of periodontal disease is higher among smokers (depth of periodontal pockets, periodontium, and bone attachment losses) [40];

- smokers respond less favorably to periodontal treatments whether they be nonsurgical, surgical, and/or medically [39,40].

The presence of nicotine in the blood also results in [32] the following:

- vasoconstriction because of the release of adrenaline and noradrenaline. This vasoconstriction blocks nutrients from reaching periodontal tissues;
- *in vitro* suppression in antibody response;
- inhibition of the neutrophil oral function.

Oral habits and parafunctions

Psychological disorders associated with stress can be expressed at the level of the oral sphere by the introduction of certain rare behaviors, which may include thumb-sucking and infantile swallowing. More frequently occurring behaviors include biting the tongue, lips, cheeks, or objects (pen, etc.). Nail-biting, object sucking, and tongue pressure on the teeth can also occur. [32]. These actions, when repeated, can lead to dental migration and occlusal trauma that can cause or aggravate periodontal disease [32].

Bruxism

Bruxism can be defined, from a phenomenological point of view, as repetitive, involuntary, and unconscious masticatory movements and grinding (and/or tightening) of teeth, with no functional purpose, and is associated with an abnormal tooth position and jaw muscle discomfort [41]. Many studies have shown that bruxism patients exhibit particular psychological traits, such as stress, anxiety, manic depressive symptoms, and mood disorders [41]. The researchers suggested that bruxism could be considered a marker for chronic stress [41]. Although the impact of bruxism on periodontal health has no consensus [41], it seems to be an aggravating factor for advanced periodontitis [42] even if it has little or no influence on a healthy periodontium or early-stage periodontitis [43].

Biological approach

Exposure to chronic stress will lead to biological mechanisms that will result in a decrease in the patient's immune response and chronic inflammation [44]. These mechanisms are based on complex interactions between immunology, psychology, neurology, and endocrinology [44] (Fig. 1). The set of mechanisms induced by the stress reactions should be considered for understanding the impact of chronic stress on periodontal health.

Decreased host resistance

Corticotropic mechanisms. As a physiological response to stress, the hypothalamic-pituitary-adrenal axis is activated, resulting in the secretion of corticotropin-releasing hormone and vasopressin by the hypothalamus, which act on the

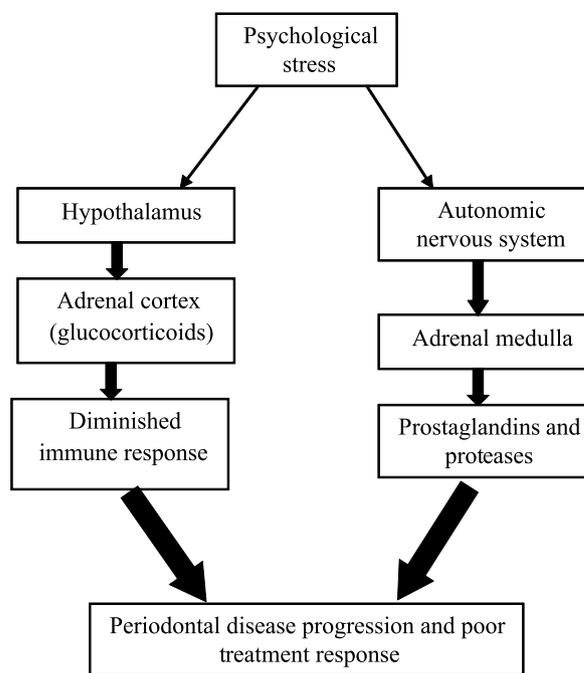


Fig. 2. Mechanisms linking maladaptive stress coping and progression of periodontal diseases and/or poor response to treatments [54].

pituitary gland. In response, the pituitary gland secretes pituitary corticotrophic hormones to act on the adrenal cortex and increase the production and release of cortisol and glucocorticoid hormones, which are necessary for a long-term stress response [45]. Glucocorticoids induce a decrease in immunocompetence by modifying the behavior of lymphocytes, macrophages, and monocytes. These changes, when they occur over a long period, contribute to the risk of cardiovascular disease, diabetes mellitus, rheumatoid arthritis, and other diseases [32,33,46-48].

This decrease in immunocompetence occurs because of the following [32]:

- changes to the inflammatory response;
- inhibition of IgA, IgG, and neutrophil function that leads to an increase in bacterial colonization of the biofilm and a decrease in the ability to prevent connective tissue invasion;
- changes to the initial cytokine profile in place of interleukin-1 and TNF α ;
- elevated blood glucose levels;
- a change in the rates of certain growth factors.

Therefore, periods of chronic cortisol elevation and the immune dysfunction they induce, lead to the deregulation of the inflammatory inhibitory abilities of cortisol, promoting chronic inflammatory damage within the periodontium [32,49].

Vegetative mechanisms (SNAS)

ANS stimulation when exposed to stress results in the release of catecholamines by the adrenal gland (adrenaline/noradrenaline), Chromogranin A (CgA), and various

neuropeptides, such as substance P, by sensitive nerve fibers [50]. The production of epinephrine and norepinephrine results in elevated blood glucose levels and alterations in the immune response that increase susceptibility to periodontal disease [32,47]. Catecholamines regulate the immune response by stimulating the activity and spread of the immune cells whereas CgA has an antimicrobial effect [51]. ANS also acts on the salivary glands during periods of stress by secreting enzymes such as salivary alpha-amylase (sAA) that acts by neutralizing and preventing pathogens from entering the body *via* mucous membranes and inhibiting adhesion and bacterial growth in the oral cavity [52].

Modification of the salivary flux and composition

Psychological stress leads to a transient decrease in salivary flux that promotes plaque and calculus formation, which results in periodontal disease [52]. Stress also generates a change in salivary composition [52]. The biological properties of some of its components (catecholamines, cortisol, IgA, CgA) influence the genesis and development of periodontal diseases [53].

Blood flow to the gingiva

The smooth muscle tone of the blood vessels can be altered as a result of the patient's perceived stress *via* ANS [32]. Prolonged and continuous exposure to stress may result in the constriction of blood vessels and lead to a decrease in oxygen and nutrient intake at the tissue level [8,32].

Impact of stress on the development and severity of periodontitis (Fig. 2)

The immune cell response plays a crucial role in the healing of periodontal tissues, both by preventing infection of the injured site and by preparing and regulating the repair mechanisms [37]. Some cytokines, interleukins (IL-1 β , IL-6, IL-8) and TNF- α are involved in the production of phagocytic cells, which are needed to repair the injured site and to regulate the production of fibroblasts and epithelial cells [37]. In the case of a normal healing process, the production of cytokines, interleukins (IL-1 β , IL-6, IL-8), and TNF- α decreased significantly. In a stressed subject with periodontitis, the production rate is high, resulting in an increase in the severity of periodontal damage [19]. Stress can also burden some aspects of the immune response such as mitogen stimulation, antibody and cytokine production, and NK cell activity [54]. By deregulating the inflammatory and immune response, stress can alter the tissue-healing process and promote the development of some oral pathologies such as periodontitis [55].

Studies have also shown that some hormones released under stress cause a proliferation of certain bacteria such as *Fusobacterium nucleate*, therefore aggravating the severity of periodontal damage [56].

The periodontal repair process is also regulated by multiple growth factors, including the bFGF (basic fibroblast growth factor), which is the key factor in the regeneration of the periodontal ligament [57]. bFGF has multiple effects on cell proliferation, differentiation, and angiogenesis [58]. Animal studies have shown a link between stress, decreased bFGF, and the severity of periodontal disease [19]. Rats with artificially created periodontitis show a greater bone and attachment loss when subjected to stress [20]. For some authors, the greater severity of periodontal disease in stressed rats also results from stress-induced tissue hypoxia (hypoxia assessed by hypoxia-inducible factor-1 (HIF-1) levels) [59].

Individuals with an inadequate stress response also have a decreased response to nonsurgical periodontal treatments than other patients and therefore more severe periodontal diseases [55]. The 5-year clinical and microbiological follow-up of patients treated for early-stage periodontitis showed that periodontal disease evolves more rapidly in stressed patients [22]. For Lu *et al.* [60], this rapid evolution is because of the stimulation of the stress-induced ANS stimulation, which results in the release of neurotransmitters (catecholamine neurotransmitter, epinephrine). These neurotransmitters are capable of binding to α 1-adrenergic (α 1-AR) receptors present on the surface of periodontal cells, thus decreasing their biological activity and causing a massive release of inflammatory factors [60].

Conclusion

Psychological stress is a risk factor for periodontal disease. Stress can also increase the severity of periodontal disease and decrease the effectiveness of treatments. When only the indirect action of stress on the periodontium was known (appearance of risk behaviors for periodontal-induced stress: smoking, poor food and oral hygiene), care of patients could be limited to educating patients about the consequences of these behaviors. Now, advances in biomedical research show that stress also has a direct effect on the periodontium by the implementation of neuro-immunoendocrinological mechanisms. These results suggest the multidisciplinary management (physician, dentist, psychologist) of patients to identify subjects with chronic stress and to put in place countermeasures to decrease the deleterious effect stress has on the periodontium.

Conflicts of interest: The authors declare that they have no conflicts of interest in relation to this article.

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