

## Effects of Stress over Periodontium

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### ABSTRACT

Stress is defined as a total transaction from demand to resolution in response to an environmental encounter that requires appraisal, coping and adaptation by the individual. Coping is the response of the individual to stress relationship of sound mind in maintaining healthy body, which has been recognized from most of the history recorded.

Psychological stress can down regulate the cellular immune response. Communication between the central nervous system and the immune system occurs via a complex network of bidirectional signals linking the nervous, endocrine, and immune systems. Stress disrupts the homeostasis of this network, which in turn, alters immune function. Direct association between periodontal disease and stress remains to be proven, which is partly due to lack of an adequate animal models and difficulty to quantifying the amount and duration of stress and also there are many factors influencing the incidence and severity of periodontal disease. Periodontitis is a chronic inflammatory disease, characterized by gingival bleeding, periodontal pocket formation, connective tissue destruction and alveolar bone loss. Oral bacterial pathogens are responsible for the initiation and progression of periodontitis. Abnormal host responses like elevating the pro-inflammatory cytokines by pathogenic bacteria also play a crucial role in the progression of periodontitis. Periodontal diseases are common chronic inflammatory diseases caused by pathogenic microorganisms which induce elevations of pro-inflammatory cytokines resulting in tissue destruction. Evolution of periodontal diseases is influenced by many local or systemic risk factors. Stress has been suggested as one of them and may negatively influence the outcome of periodontal treatment. The aim of this review is to provide

the relationship between stress and periodontium.

**Keywords:** Inflammatory disease, Periodontitis, Pathogenic microorganism, Stress

### INTRODUCTION

Stress is defined as a total transaction from demand to resolution in response to an environmental encounter that requires appraisal, coping and adaptation by the individual. Coping is the response of the individual to stress relationship of sound mind in maintaining healthy body, which has been recognized from most of the history recorded i.e. from the time of ancient Romans, Greeks and Chinese.<sup>1</sup> Seyle defined Stress as a 'Response state of the organism to forces acting simultaneously on the body which if excessive, that is straining the capacity of adaptive process beyond their limits, leads to a disease of exhaustion and death'.

Stressors are those forces that have the potential to challenge the adaptive capacity of the organism. The group of stressors could be either mental/ psychosocial/ physical. These stressors either lead to eustress/distress, which is body's adaptive to restore homeostasis.

Stress is an equated response to constant adverse stimuli. At one point or another, everybody suffers from stress. Stress is compatible with good health, being necessary to cope with the challenges of everyday life. Problems start when the stress response is inappropriate to the intensity of the challenge. Psychological stress can down regulate the cellular immune response. Communication between the

central nervous system and the immune system occurs via a complex network of bidirectional signals linking the nervous, endocrine, and immune systems. Stress disrupts the homeostasis of this network, which in turn, alters immune function. Direct association between periodontal disease and stress remains to be proven, which is partly due to lack of an adequate animal models and difficulty to quantifying the amount and duration of stress and also there are many factors influencing the incidence and severity of periodontal disease.

Periodontitis is a chronic inflammatory disease, characterized by gingival bleeding, periodontal pocket formation, connective tissue destruction and alveolar bone loss. Oral bacterial pathogens are responsible for the initiation and progression of periodontitis. Abnormal host responses like elevating the pro-inflammatory cytokines by pathogenic bacteria also play a crucial role in the progression of periodontitis.<sup>2</sup>

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Stress is defined as a state of physiological or psychological strain caused by adverse stimuli, physical, mental, or emotional, internal or external, that tend to disturb the functioning of an organism and which the organism naturally desires to avoid. The term stress is used loosely, in layman terms, to describe adverse emotions or reactions to unpleasant experiences. It is also used, in a somewhat circular way, to describe experiences that may provoke these emotions.

### **RISK FACTORS OF STRESS**

As with many other chronic infections, the onset and progression of periodontal disease is largely programmed

by the influence of certain local and systemic risk factors that have a dramatic effect on the resistance of the host to pathogenic bacteria. In periodontal disease, we call these pathogenic bacteria “periodontal pathogens” and the factors that increase the risk for periodontal disease (risk factors) include diabetes, smoking, and a genetic variable called the interleukin-1 polymorphism (IL-1 genotype).

Diabetic patients with poor metabolic control of glycated hemoglobin have a much greater risk for progressive bone loss compared to well-controlled patients, with an odds ratio of 11.4 to 2.2, respectively. The IL-1 genotype is a specific genetic marker that identifies patients who have increased risk of developing severe periodontal disease.<sup>3</sup>

Smokers are 4 times more likely to have periodontitis than nonsmokers. Nonsmokers or former light smokers (< 5pk/yr) genotype-positive individuals are more than 3 times more likely to have moderate-to-severe periodontal disease than individuals who are genotype negative. Patients who are both genotype positive and also smoke may be 7.7 times more likely to have tooth loss than nonsmokers who are genotype negative.<sup>1</sup>

A risk factor is established by longitudinal studies that confirm an association between the factor and the outcome of interest. The association is consistent with the current understanding of the disease process. Furthermore, the association must still remain after controlling for other risk factors and background characteristics. Risk indicators differ from risk factors in so much as the association between the exposure event and the outcome of interest has not yet been demonstrated by longitudinal studies.<sup>4,5</sup>

However, stress, like other risk indicators of periodontal disease (i.e., osteoporosis, HIV, immunocompromised conditions) are commonly accepted (putative) as variables that influence the onset, progression, and severity of periodontal disease. Longitudinal studies are

still needed to support stress as a bonafide risk factor, the role of psychosocial stress in the etiology of periodontal disease.

## **STRESS AND PERIODONTAL DISEASE**

Breivik et al. have stated that ‘The issue facing us is no longer whether the psyche influences immune cell activities, but rather how influence the development of chronic infections such as gingivitis and periodontitis.

Genco et al. offered a schematic model which demonstrates the potential role that psychosocial stressors may play in initiating a cascade of events in corticotrophin releasing hormone/hypothalamic – pituitary – adrenal axis, the autonomic nervous system and the central nervous system, the physiologic consequences of which depress immunity, enhancing likelihood of infection and, specifically, periodontal disease. They also proposed that at-risk health behaviors such as poor oral hygiene and smoking might influence periodontal disease directly.<sup>6,7</sup>

Psychosocial stressors include negative and dysphonic conditions such as pain, bleeding, unpleasant tastes and odors emanating from the mouth and unsightly appearance of the teeth and surrounding hard and soft supporting structures. While gingivitis and periodontal disease in their most common and early forms are typically not painful, symptoms that emerge eventually are known to include fluctuating exacerbations of acute pain that can be very intense or mildly annoying; at later stage, exacerbations of more advanced inflammatory disease are known to include periodontal swelling, abscess formation with pathogenic exudates and intense pain. Other signs and symptoms, such as mobility of teeth and the perceived threat of losing one’s teeth in early adulthood are also often

worrisome, hence serving as potentially powerful negative emotional stressors.

Moreover, treatment of periodontal disease is associated with pain and discomfort, as well as being time consuming and often expensive. All these factors can understandably be viewed as important psychosocial stressors that may induce stress system responses that are further deleterious to periodontal health. Alternatively, these signs and symptoms may trigger sufficient motivation to institute healthy behaviors in an attempt to become more comfortable, halt or reverse the ravages of periodontal disease, and perhaps prevent further hard and soft tissue destruction and/or loss.

The relationship between stress and periodontal disease frequently do not consider how stress, through its effects on the course of diabetes and smoking behavior, may influence, in turn, periodontal disease. The presence of environmental stressors may exacerbate the maladaptive behaviors associated with loss of diabetic control and influence smoking as well. In addition, both smoking and diabetes act as physical stressors capable of activating the stress – immune system. The consequences of behavioral pathogens, extending from neglect of oral hygiene to dietary inadequacies, poor sleep patterns, use of tobacco products and other substance abuse constitute an important class of psychosocial stressors that contribute to the ‘vicious cycle’ of increasingly severe forms of advanced periodontal inflammation and disease. The less common forms of periodontal disease – aggressive periodontitis, periodontal disease associated with diabetes – similarly are associated with a myriad of intra- and interpersonal stressors that are significant risk factors for exacerbating the underlying periodontal disease condition.<sup>8</sup>

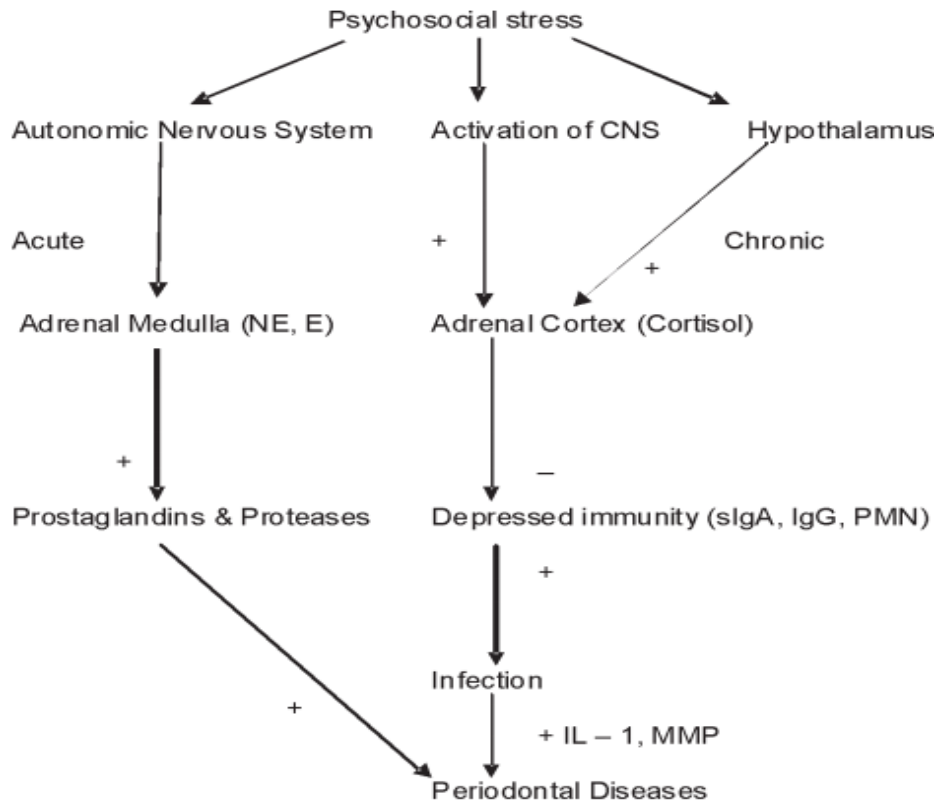


FIGURE 1 - PSYCHOSOCIAL STRESS AND PERIODONTAL DISEASE

It has been suspected that periodontal status is related to alterations in the concentration of adrenal corticoids and by altering the response of oral tissues to bacterial toxins and other hormones involved in the general adaptation syndrome. Some model have been put forth which demonstrates the potential role, that psychosocial stressors may play role in initiating a cascade of events in the corticotrophin releasing hormone/HPA axis, the autonomic nervous system and the central nervous system, the physiological consequences of which are to depress immunity, enhancing the likelihood of infection and specifically, periodontal disease.<sup>9</sup>

Proper oral hygiene is partially dependent on the mental health status of the patient. It has been reported that psychological disturbances can lead patients to neglect oral hygiene and that the resultant accumulation of plaque is detrimental to the periodontal tissue. Academic stress was reported as a risk factor for gingival inflammation with

increasing crevicular interleukin- $\beta$  levels and a diminution of quality of oral hygiene.

Emotional conditions are thought to modify dietary intake, thus indirectly affecting periodontal status. Psychological factors affect the choice of foods, the physical consistency of the diet, and the quantities of food eaten. This can involve, for instance, the consumption of excessive quantities of refined carbohydrates and softer diets requiring less vigorous mastication and therefore predisposing to plaque accumulation at the approximal risk site. It is hypothesized that stress leads to other behavioral changes such as overeating, especially a high-fat diet, which then can lead to immunosuppression through increased cortisol production.

### GINGIVAL CIRCULATION

The tonus of the smooth muscle of blood vessels may be altered by the emotions by way of the autonomic nervous system. Furthermore, in long or continued emotions, a constant constriction of blood

vessels could alter the supply of oxygen and nutrients to the gingival tissues.

### STRESS AND AGGRESSIVE PERIODONTITIS

Page et al (1983) described aggressive periodontitis as a particular disease, where he established the interconnection existing between aggressive periodontitis, psycho-social factors and loss of appetite.

Monteiro da Silva et al (1996) said that people with aggressive periodontitis were more depressed and socially isolated people than people with chronic periodontitis. These studies show the interconnection that exists between aggressive periodontitis and psychosocial stress.<sup>10</sup>

### STRESS AND SYSTEMIC INFLAMMATORY DISEASE

A number of chronic recurrent conditions, in addition to periodontal disease, are characterized by a fluctuating course, with ongoing disease punctuated by

bouts of greater severity. It is well-established that cardiovascular disease, diabetes mellitus, preterm delivery, osteoporosis, rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus etc., are related to stress either as a physiological response to stress or as a behavioral response. It may be that stress is a significant common risk factor for diabetes mellitus, cardiovascular disease, preterm delivery, and osteoporosis, as well as periodontal disease.<sup>11,12</sup> Alternately or simultaneously, stress that is modified by perceptions in coping can give rise to at-risk health behaviors, which then could affect the chronic diseases.

The body of evidence on the relationship of stress to disease activity appears to be greatest for rheumatoid arthritis; however, because of the types of inflammatory tissues affected, information on inflammatory bowel disease may be particularly pertinent to periodontal disease.

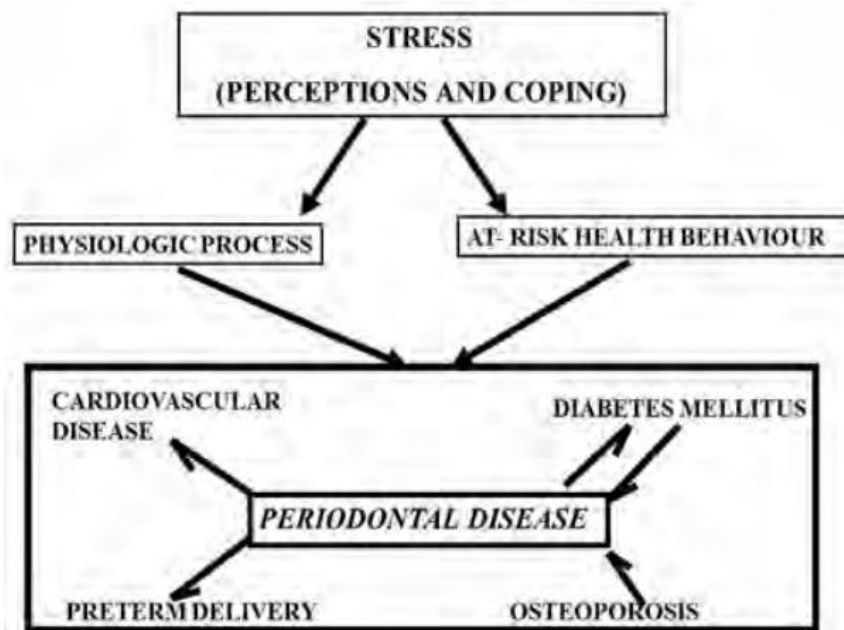


FIGURE 2 - PERCEPTION AND COPING OF STRESS

### STRESS AND WOUND HEALING

Patients with maladaptive coping strategies have more advanced disease and poor response to non-surgical treatment, whereas positive correlation was observed

in reduction of dental plaque and gingival bleeding in patients having an active coping.

Furthermore, the cellular immune response plays a vital role in wound healing. It not only protects the wound site from infection, but also prepares the wound for

healing and regulates its repair. Cytokines such as IL-1, IL-8, and TNF are extremely important in recruiting phagocytic cells to clear away the damaged tissue and to regulate the building by fibroblasts and epithelial cells. A decrease in expression in any of these cytokines could theoretically impair wound healing. Stress could suppress certain aspects of the cellular immune response such as mitogen stimulation, antibody and cytokine production, and NK cell activity. Furthermore, since stress deregulates inflammatory and immune response, stress can alter the course of oral wound healing and affect the management of other oral diseases, e.g., periodontitis.<sup>8</sup> Stress releases highly active hormones like

catecholamine, which results in altered blood flow, peripheral vasoconstriction may affect oxygen dependant healing mechanism which impairs wound healing.

The impact of stress on periodontal wound healing may be influenced by factors as follows: Health-impairing behaviors, such as poor oral hygiene and factors that have pathophysiologic effects, such as altered cytokine profiles. Health-impairing behaviors include neglecting oral hygiene practices increased consumption of cigarettes and alcohol, and disturbed sleeping patterns. Other behaviors potentially harmful to the periodontium are bruxing, anxiety-induced forgetfulness, and difficulty concentrating.

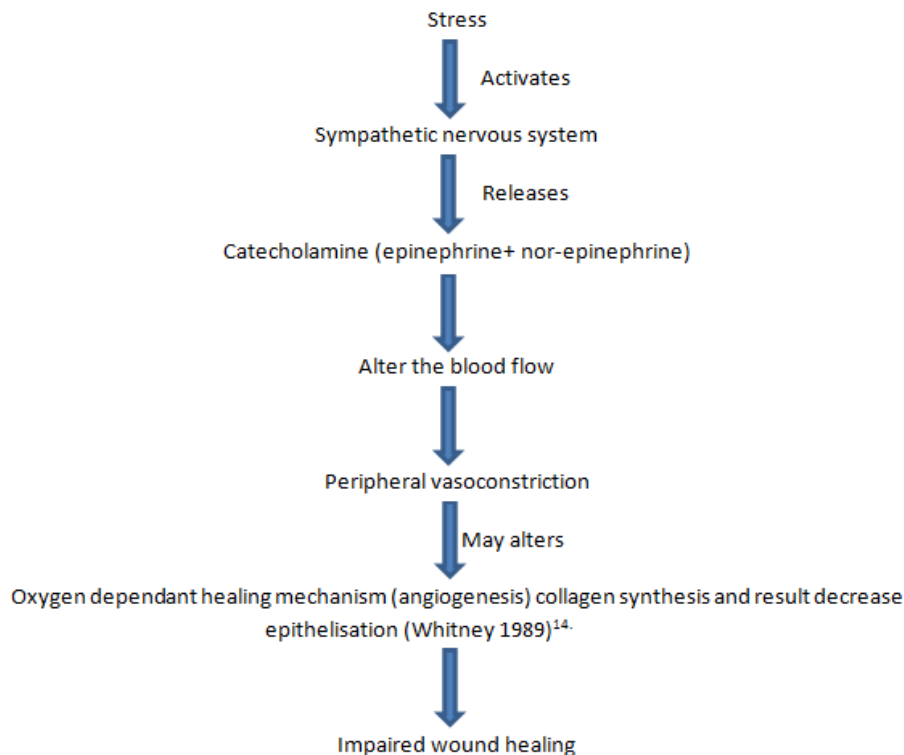


FIGURE 3 – EFFECT OF STRESS ON WOUND HEALING

Depression has consistently been associated with smoking although depression is not synonymous with stress; it has been used in various studies as an indicator of the level of stress. Usually this takes the form of questions on standardized questionnaires, regarding feelings of sadness, hopelessness, and depression.<sup>13</sup>

This provides a strong link between depression and periodontal disease, as smoking is a well-established risk factor for periodontal disease. In addition, smoking has been shown to impair collagen synthesis and increase matrix metalloproteinase-8 levels in blister wounds, compared with nonsmoking controls. Smoking and diabetes, both known risk factors, act as

physical stressors capable of activating the stress-immune system. Stress management has even been shown to be a novel means of improving glycemic control in type 2 diabetes.

Negishi and colleagues examined the effect of lifestyle on periodontal disease status in 57 diabetic Japanese subjects. Data were collected, including clinical measures of periodontal status, diabetic status, lifestyle habits, and behavioral factors. Factors that were found to correlate with poorer periodontal status were glycosylated hemoglobin (>9%), drinking habit, and irascible behavior. It was concluded that lifestyle and psychosocial stress may affect the periodontal status of diabetic patients. Various studies have established a link between stressful life events and poor oral hygiene. In a series of studies on a population of medical students undergoing academic stress, Deinzer and co-workers reported increased dental plaque accumulation and gingival inflammation compared with control students not taking examinations.

Disturbed sleep patterns, as a result of stress, could result in a reduction of

growth hormone, which may act to down-regulate the tissue repair response. This, in addition to poor nutritional intake because of unhealthy eating habits, and excessive alcohol and cigarette consumption, could further impair tissue wound healing. Therefore, it is possible that correlations between stress and an impaired healing response could be secondary to stress-induced changes in health behaviors, which themselves act to down-regulate an individual's immune response. Ebrecht et al. inflicted standardized 4 mm punch biopsy wounds in 24 nonsmoking males. Psychological status was assessed (using questionnaires) on perceived stress, health behaviors, and personality factors. Saliva was collected to determine cortisol levels, and wound healing was assessed using high-resolution ultrasound scanning at 7, 14, and 21 days post-biopsy. The results indicated that wound healing was negatively correlated with perceived stress and positively correlated with perceived optimism. Another finding was that the cortisol response on the morning of the biopsy was negatively correlated with the speed of wound healing.<sup>14</sup>

TABLE 1 – MECHANISMS BY WHICH STRESS MAY AFFECT PERIODONTAL WOUND HEALING

Health-impairing behaviors	Pathophysiological effects
Poor oral hygiene	Higher glucocorticoid levels (cortisol) and higher catecholamine levels (epinephrine and norepinephrine), which may lead to any or all of the following: Hyperglycemia, which may impair neutrophil function and impair the initial phase of wound healing Reduced levels of growth hormone, which may down-regulate the tissue repair response Altered cytokine profiles, which may affect recruitment of cells important to wound remodeling, such as macrophages and fibroblasts Reduced tissue matrix metalloproteinase levels, leading to impaired tissue turnover and reduced wound remodeling Decreased natural killer cell levels, reducing the host ability to mount an appropriate immune response to periodontal pathogens Altered Th1/Th2 ratio, leading to an increased susceptibility to periodontal disease
Increased consumption of cigarettes	
Increased alcohol consumption	
Forgetfulness and difficulty concentrating	
Disturbed sleeping patterns	
Poor nutritional intake	

**ROLE OF OXIDATIVE STRESS IN PERIODONTITIS**

Oxidative stress is defined as an imbalance between oxidants and antioxidants in favor of the oxidants, leading to a disruption of redox signaling and control and/or molecular damage. Oxidative stress is a key driver of chronic inflammation and as a result has a central role in the pathogenesis of a wide range of chronic inflammatory diseases<sup>11</sup> (e.g. type 2 diabetes, cardiovascular disease and metabolic syndrome), indeed it has been proposed as a common link between periodontitis and systemic disease.

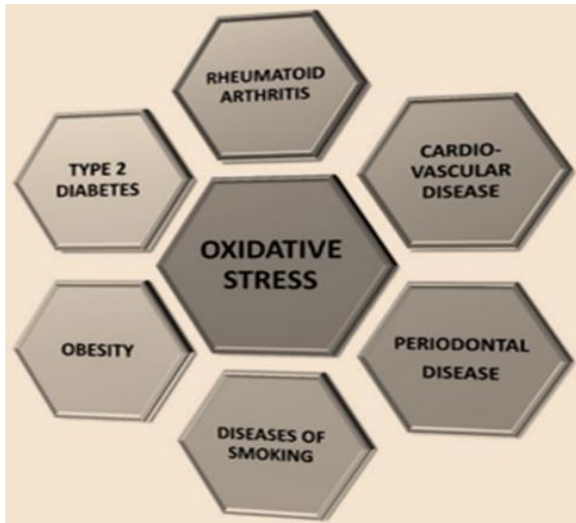


FIGURE 4 - OXIDATIVE STRESS AND CHRONIC INFLAMMATORY DISEASES

In health a fine balance exists between, one the hand oxidants and on the other antioxidants which are found in all tissues of the body. If this fine balance is disturbed by excess production of oxidants and/or depletion of local antioxidants the resulting oxidant excess causes oxidative stress and is associated with the local tissue damage seen in periodontitis.

Oxidative stress was recently defined as “an imbalance between oxidants & antioxidants in favor of the oxidants, leading to a disruption of redox signaling & control and/or molecular damage.<sup>15</sup>

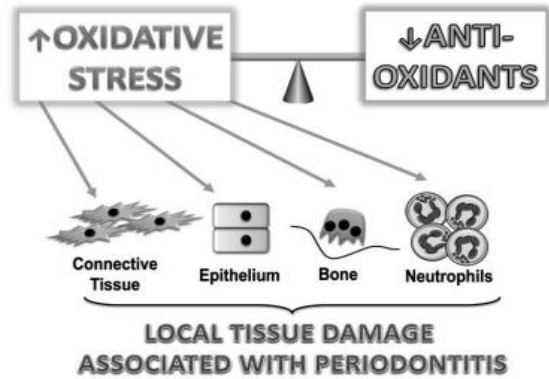


FIGURE 5 – OXIDATIVE STRESS AND ANTI-OXIDANTS

It can cause direct tissue damage by altering molecules, such as proteins, lipids and DNA, thus damaging cells directly, or by activating redox-sensitive transcription factors within the cell that leads to downstream gene expression changes and production of pro-inflammatory molecules. These cytokines or chemical messengers can further enhance and propagate the inflammatory response adding to local levels of oxidative stress. In susceptible patients, where the body’s inflammation resolving mechanisms fail to work efficiently, a vicious cycle is established and results in a transition from acute to chronic inflammatory lesions as found in periodontitis.

Increased levels of oxidative stress can result from cellular metabolism mainly due to electron leakage from mitochondria or via the host’s response to a range of stressful stimuli e.g. periodontal pathogenic bacteria such as *Porphyromonas gingivalis*, one of a number of bacteria strongly associated with periodontitis.<sup>16</sup>

**STRESS AND THE MICROBIOLOGY OF PERIODONTAL DISEASE**

Deinzer R (2004) recognized that microorganisms possess the ability to recognize hormones within the host and utilize them to adapt to their surroundings. This supports the supposition that psychological stress may favor the development of many bacterial infections. Stress may have microbial compositions in the sub gingival niches. In vitro investigations were done to determine



whether noradrenalin (nor epinephrine), and adrenaline (epinephrine), which are released during human stress responses, act as environmental cues to alter the growth of 43 microorganisms found within sub gingival microbial complexes. The 20 species within the subgingival biofilm significantly grew from inoculation with noradrenalin, and 27 species significantly grew when adrenaline was introduced. There was also a difference in the growth response within bacterial species and within and between microbial complexes.<sup>17,18</sup>

It was concluded that this variation may influence the in vivo composition of the subgingival biofilm in response to stress-induced changes in local catecholamine levels and play a significant role in the etiology and pathogenesis of periodontal diseases. Ramifications of these findings are of great significance because *P. gingivalis* is the most often cited periodontal pathogen implicated in the link between periodontal disease and cardiovascular disease.<sup>19, 20</sup>

### MANAGEMENT OF STRESS

- Careful history needs to be taken for checking any underlying stress/psychological disorder
- Patient should be referred to a psychiatrist before commencing of the dental treatment

Basics approaches of dealing with stress

- Removal/alteration of the source of stress
- Learning to change way of perceiving stressful events
- Reducing the effect of stress on the body
- Learning alternative ways of coping
- proactive coping: dealing with stress in advance.
- Breathing exercises
- Drug therapy- antidepressants and benzodiazepines
- Supportive psychotherapy

Coping against stress is the effort to try to reduce, control or tolerate the state of stress. It needs adjustment, adaptation and confrontation strategies. These coping

strategies may be used in generalized stressful situations.

Individuals use coping measures to reduce its intensity or to overcome stress altogether. A successful coping is when the subject has the feeling to face the stress and able to control the given situation. An unsuccessful coping is when the subject is submerged by stressor agents and is in the reaction of stress.<sup>21-23</sup>

### THE INTERNATIONAL STRESS PREVENTION CENTRE

The International Stress Prevention Centre (CSPC or Community Stress Prevention Centre) was established in 1981 Kiryat Shmona, Israel. CSPC is the oldest organization in Israel that deals with the treatment and prevention of psycho trauma. It is a registered NGO which promotes stress and crisis management on National, Organizational, Community and individual levels worldwide.<sup>24</sup>

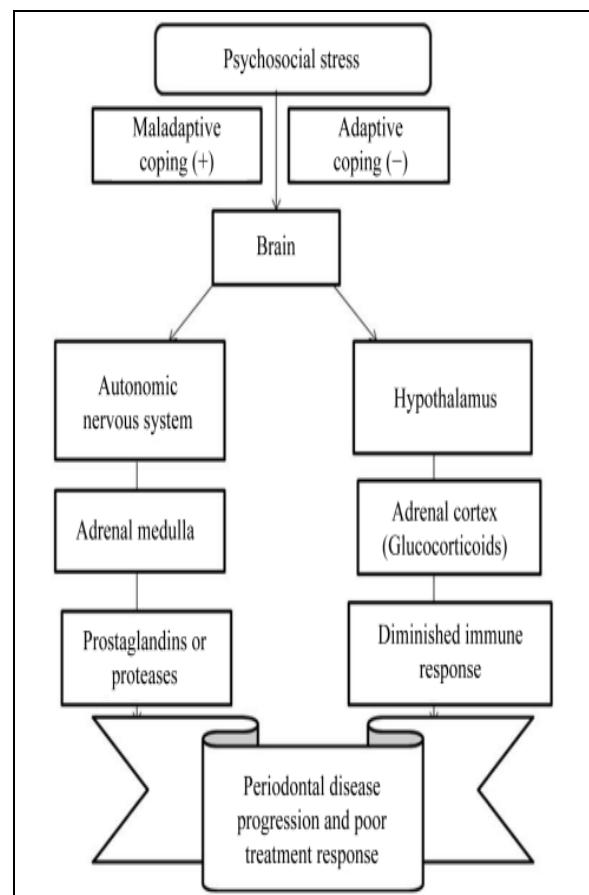


FIGURE 6 - STRESS LEADING TO POOR TREATMENT RESPONSE

## STRESS REDUCTION PROTOCOL

The stress reduction protocol includes two series of procedures that when used either individually or collectively, act to minimize stress to the patient during treatment and thereby decrease the degree of risk presented to the patient.

1) Stress reduction protocol for normal, healthy anxious patients. ASA (American society of anesthesiologist) I.

2) Stress reduction protocol for medical risk patient (ASA II, III, and IV).

Stress Reduction Protocol in Dental Office Includes:

1) Recognition of medical risk and anxiety.

2) Medical consultation.

3) Premedication (Anti-anxiety or sedative-hypnotic drugs given one night before the appointment or one hour before appointment).

4) Appointment scheduling.

5) Minimized waiting time to reduce anxiety.

6) Vital signs monitoring: BP, heart rate, rhythm and respiratory rate

7) Psycho sedation.<sup>25,26</sup>

## STRESS REDUCTION BY THE PATIENT INCLUDES

There are several ways of coping with stress. Some techniques of time management may help a person to control stress. The Journal of the Canadian Medical Association have recently dubbed "Destressitizers" as any process by which an individual can relieve stress.

1) Regular exercise helps to burn off and use up the stress hormones and neurochemicals.

2) The benefits of meditation and other relaxation techniques for 20 to 30 minute sessions a day can have lasting beneficial effects on reducing the stress levels.

3) Elimination of drug use and not more than moderate alcohol use are key to the successful management of stress.

4) Strengthen your relationships by building a strong support network which works as greatest protection against stress. Spend time with the people you love and don't let

your responsibilities keep you from having a social life.

5) Learn better ways to manage time. Think about which things are most important, and do those first.

6) Find better ways to cope. Look at how you have been dealing with stress. Be honest about what works and what does not. Think about other things that might work better.

7) Take good care of yourself. Get plenty of rest. Eat well. Don't smoke.

8) Try out new ways of thinking. When you find yourself starting to worry, try to stop the thoughts. Work on letting go of things you cannot change. Learn to say "No".

9) Speak up. Not being able to talk about your needs and concerns creates stress and can make negative feelings worse. Assertive communication can help you express how you feel in a thoughtful, tactful way.

10) Ask for help. People who have a strong network of family and friends manage stress better.<sup>25,26</sup>

## CONCLUSION

It is now well-established that psychological stress can down-regulate the cellular immune response. Communication between the central nervous system and the immune system occurs through a complex network of bidirectional signals linking the nervous, endocrine, and immune systems. Stress disrupts the homeostasis which in turn, alters immune function. Direct association between periodontal disease and stress remains to be proven, which is partly due to lack of an adequate animal models and difficulty to quantifying the amount and duration of stress. Furthermore, multiple variables affect the severity of periodontal disease and there is uncertainty about the individual's onset of periodontal disease.

Moreover, it is not possible to separate the effects of physical stress from emotional stress in these animal studies. Furthermore, it is likely that systemic diseases associated with periodontal disease such as diabetes, cardiovascular disease etc.,

may share psychosocial stress as common risk factor.

The available scientific evidence thus, does not definitively support a casual relationship between psychosocial factors and inflammatory periodontal diseases. The information reviewed above nevertheless does indicate the possible influence of psychosocial factors in the etiology of inflammatory periodontal diseases though at the moment, the more suggestive evidence relates to ANUG. These studies indicate that psychosocial stress represents a risk indicator for periodontal disease. Consequently, it is noteworthy that the practitioner is aware of these factors and taken them into consideration.

The clinical management of inflammatory periodontal diseases might benefit from an exploration of these relationships, principally when disease severity cannot be explained by established etiological factors and when there is no response to periodontal treatment or when there is a sudden, marked and in explicable increase in the rate of periodontal destruction.

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