

## STRESS AND PERIODONTAL DISEASE

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Stress is an association of physiological and psychological reactions of a person confronted to a change of situation he cannot face. The relationship between stress and any disease is explained by hormonal modifications and behavioural changes induced by the stress. Research has suggested that stress and depression are two factors that play a role in the development and progression of periodontal disease. It is not clear, however, whether these factors lead to periodontal disease through physiological or behavioural changes, or by some combination of the two. The purpose of the present review article is to explore the associations between psychological factors, psycho immunologic variables, behaviour, and clinical measures of periodontal disease.

**KEY WORDS:** Psychosocial factors, Depression , Life events, Glucocorticoids

**INTRODUCTION**

Stress, a term continually being redefined in the scientific study of disease and illness, is nevertheless a confirmed and important factor in the aetiology and maintenance of many inflammatory diseases, including periodontal disease<sup>1</sup>. Psychological stress, if sustained over an extended period of time can have deleterious effects on the body, which represents an important example of mind body interaction. Role of stress on systemic health has been known for decades. Similarly, the role of psychological factors in periodontal disease has a significant history<sup>2</sup>.

The term stress has a precise physiological definition. It is a state of physiological or psychosocial strain caused by adverse stimuli, physical, mental or emotional, internal or external that tends to disturb the functioning of an organism and which an organism naturally desires to avoid. Thus "stress" can be viewed as process with both psychological and physiological components<sup>2</sup>.

Sydenham suggested that stress is a pathological state which represents the disease of adaptation. It is a failure of adaptive processes to restore well being. Cannon elaborated stress as how fight or flight mechanisms represents adaptive efforts by the body to re-establish haemostasis. He described stress as a dynamic internal physiological

equilibrium which the body tries to maintain along both physical and emotional dimensions.

Selye was largely responsible for giving the term "stress" its current saliency in relation to the contest between health and disease. He elaborated 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 disease of adaptation and eventually disease of exhaustion and death. He defined forces that have the potential to challenge the adaptive capacity of the organism as "Stressor"<sup>1</sup>.

Stressor is stimulus, situation or circumstance with the potential to induce stress reactions.<sup>2</sup> Stressor could be physical or mental (e.g. emotional) . Selye recognized that stressor acting to produce changes in the body could be positive (e.g. exciting, pleasurable), leading to a response state known as "eustress", or stressor could be negative, threatening homeostasis with pain, discomfort and physical pathology which is known as "distress"<sup>1</sup>.

A subject exhibits stress response or not depends upon the factors, including coping behaviours, genetic predisposition, concomitant stressors, level of social support and their lifestyle factors . Potential effects of stress response that may be observed or

even measured, includes anxiety, depression, impaired cognition, and altered self esteem<sup>2</sup>.

### **Molecular and Endocrine Mechanisms of the Stress Response**

Stress can result in the degeneration of the immune system, mediated primarily through the hypothalamic – pituitary – adrenal and sympathetic adrenal medullary axis. The stress-induced responses are transmitted to the hypothalamic/pituitary/adrenal (HPA) axis to promote the release of corticotrophic-releasing hormone (CRH) from the hypothalamus and glucocorticoids from the adrenal cortex).

Stress perceived by the brain stimulates the hypothalamus to produce CRH, which is released into the hypophyseal portal system, activating the pituitary gland to release adrenocorticotrophic hormone (ACTH), which in turn induces release of corticosteroids from the adrenal cortex.

Glucocorticoids, including cortisol, exert major suppressive effects through highly specific mechanisms at multiple levels. For example, in vivo glucocorticoids reduce the number of circulating lymphocytes, monocytes, and eosinophils. They also inhibit the accumulation of eosinophils, macrophages, and neutrophils at inflammatory sites. At the molecular level, glucocorticoids profoundly inhibit important functions of inflammatory cells including macrophages, neutrophils, eosinophils, and mast cells in functions such as chemotaxis, secretion, and degranulation.

Glucocorticoids also inhibit the cascade of the immune response by inhibiting macrophage-antigen presentation, lymphocyte proliferation, and lymphocyte differentiation to effector cell types such as helper lymphocytes, cytotoxic lymphocytes, natural killer cells, and antibody-forming B cells. Corticosteroids also inhibit production of cytokines including IL-1, IL-2, IL-3, and IL-6, tumor necrosis factor, interferon gamma, and granulocyte and monocyte colony stimulating factors. Glucocorticoids inhibit arachidonic acid-derived proinflammatory mediators such as prostaglandins and leukotrienes. Glucocorticoids also induce endogenous anti-inflammatory proteins and lipocortins, which have the capability of inhibiting phospholipase A2, thereby inhibiting generation of eicosanoids. Hence, the stress-related stimulation of the HPA axis with the production of

glucocorticoids such as cortisol has major suppressive actions on immune and inflammatory responses. This represents the major effector arm of the CNS-hormonal axis. There is also an afferent or feedback arm consisting of stimulation of the HPA axis by cytokines.

Glucocorticosteroids, including cortisol, then depresses immunity including secretory IgA, IgG, and neutrophil functions, all of which may be important in protection against infection by periodontal organisms. Secretory IgA antibodies may protect by reducing initial colonization of periodontal pathogens. IgG antibodies may exert protection by opsonizing periodontal organisms for phagocytosis and killing by neutrophils. This then gives rise to increased susceptibility, which leads to the establishment of periodontal infection which, in turn, results in destructive periodontitis. Periodontitis is brought about by tissue-destroying factors such as IL-1 and matrix metalloproteinases activated by the periodontal pathogens, as well as by the direct effects of pathogenic bacteria<sup>3</sup>.

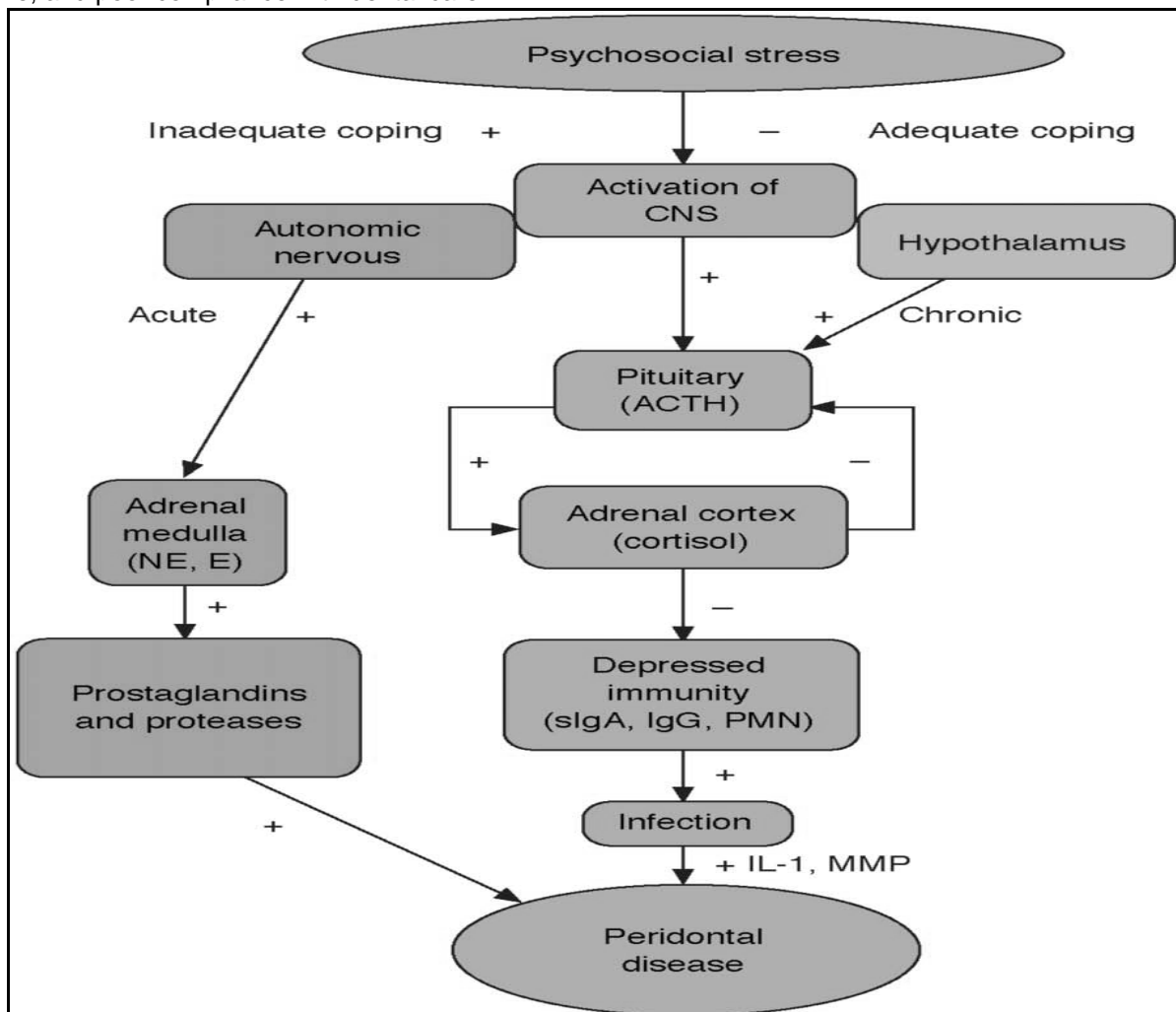
The second major pathway to be activated is the sympathetic nervous system. Stress induced activation of the hypothalamic nervous system results in the release of highly active hormone such as catecholamines. These catecholamines released during stress, contributes to the development of hyperglycemia by directly stimulating glucose production and interfering with the tissue disposal of glucose.

Catecholamines are known to alter the blood flow. Peripheral vasoconstriction may affect important oxygen – dependent healing mechanisms, such as angiogenesis, collagen synthesis and epithelialization. The release of Catecholamines results in hormonal secretion of norepinephrine from the adrenal medulla, which results in a range of effects that may act to modulate immune responses. Increased sympathetic stimulation can also act to decrease salivary secretions typically experienced as anxiety induced dry mouth. Stress that is associated with immune challenge has been called immune stress or inflammatory stress<sup>2</sup>.

### **Mental Stress Response Leading to Behavioural Changes**

It is hypothesized that the main effects of stress occur through behavioural changes which affect at-

risk health behaviours such as smoking, poor oral hygiene, and poor compliance with dental care.



Fig; 1 - Physiological model of effects of stress on periodontal diseases

There is also a possibility that stress leads to other behavioural changes such as overeating, especially a high-fat diet, which then can lead to immunosuppression through increased cortisol production<sup>3,4</sup>.

There are certainly much other possible behaviour that could be affected by stress and inadequate coping and distress, such as depression, which would have significant effects on periodontal disease. **Crouchy R** et al studied the relationship between life events and periodontitis and found that both negative life events leading to oral health risk behaviours such as poor oral hygiene and smoking as important determinants of periodontitis.

#### Social psychology and stress response

Clinical observations and epidemiological studies indicate that there is a relationship between experiences of negative life events and the development and progression of periodontal disease (Monteiro da Silva et al 1996, Moss et al . 1996, Genco et al 1998). It has been experimentally supported that a misguided brain –neuro endocrine –immune regulation of the dental plaque-induced inflammatory response, explains the relationship<sup>5</sup>.

Social factors affect the functioning of the immune system and provides important insight into the roles of psychosocial factors in periodontal diseases Kaplan proposed a model which outlines the direct and indirect effects of four mutually important components: dystrophic responses, behaviours affecting immunosuppression, adverse life experiences and vulnerability. Dystrophia is

measured in terms of unhappiness, depressive effect, hostility and loneliness. There is reduced and altered immunological functions in depressed, anxious and bereaved groups.

The effect of adverse life circumstances is supported by a large body of research. Stressful life circumstances and life change events, such as bereavement or divorce, academic stress or change in employment status, affects levels and activity of killer cells and suppressor- cytotoxic T cells.

The health impact of psychosocial risk factors seems to hinge on chronic stress. Chronic stress imposes the allostatic load and leads to malfunction of some biological functions. As stress affects many physiological systems essential for health maintenance including cardiovascular and immune system, it appears as a kind of general vulnerability factor, making us less able to withstand whatever the environment throws at us. Periodontal health is dependent upon the interaction of extensive risk factors with systemic neuroendocrinal immunological mechanisms, for example smokers are up to 10 times more likely to develop periodontal diseases than non smokers . A potential mechanism is that smoking exacerbates periodontal diseases by altering immune response to periodontal pathogens. Smoking is strongly influenced by the social factors during the life course. Low parental social factors have been related to teenage smoking. Early school leaving, poor educational performances and those experiencing family conflicts are more likely to become teenage smokers.<sup>6</sup>

### **Stress and Systemic inflammatory disorders**

The body of evidence on the relationship of stress to disease activity appears to be greatest for rheumatoid arthritis<sup>1</sup>. Minor daily stressors have been linked to exacerbations of the disease. The relationships among environmental stressors, psychological state, physiological aspects of stress response and disease outcomes in rheumatoid arthritis are complex. Different types of stressors affect disease outcomes differently.

The term inflammatory bowel disease encompasses both Crohn's disease and chronic ulcerative colitis. The available research on inflammatory bowel disease may be directly relevant to periodontal diseases, due to the fact that both disorders affect mucosal tissues<sup>1</sup>.

### **Stress and periodontal diseases**

For the most part, the literature relating stress to periodontal diseases focuses on psychological stressors and their influences on susceptibility to gingival infections or the inflammatory aspects of periodontal diseases. Breivik et al. have stated that "The issue facing us is no longer whether the psyche influences immune cell activities - but rather how this may influence the development of chronic infections such as gingivitis and periodontitis".

The most well documented association between stress and periodontal disease is acute forms of necrotizing gingivitis and periodontitis. Risk factors for these conditions include smoking, poor oral hygiene, stress and immunosuppressive states. An increased incidence of this condition has been well documented in military personnel during stressful activities and in students during examination periods.

Stress has long been recognized as one of the contributing factors for necrotizing ulcerative gingivitis. Although stress is not an easily measured factor, corticosteroid levels in urine can be measured and were found to be high in acute necrotizing ulcerative gingivitis patients.<sup>7</sup>

In a review of psychosocial factors in inflammatory periodontal disease reported in 1995 , Monteiro da silva et al distinguished between acute necrotizing ulcerative gingivitis and adult periodontitis, concluding that the evidence is strong for stress as a predisposing factor to acute necrotising ulcerative gingivitis, while the evidence for psychosocial factors as etiological agents in periodontitis is not as substantative. However in the intervening years studies have provided evidence stating the relationship between phychosocial stressors and periodontal diseases<sup>8</sup>.

Moss et al in their study found that psychologically depressed human subjects who smoked and had high titre of IgG against Tannerella Forsythia were found to have more severe and extensive chronic periodontitis. The authors explained this by the negative influence of depression on the immune system. Depression may reduce patient's willingness to perform physical activities leading them to give less attention to their mouth or depression may cause chemical changes in mouth secretions which in turn increases calculus formation<sup>9</sup>.

Persons under stress and suffering from depression are more likely to have refractory periodontitis. **Axtelius** and co-workers conducted a prospective study on the impact of psychological conditions in response to periodontal therapy. The authors reported that response to the therapy was lower in subjects with psychosocial strain and a more passive – dependent personality<sup>10</sup>. In another study of chronic periodontitis patients it was found that those resistant to therapy were more stressed than those who responded to therapy. Depression whether defined as a trait, a symptom or as a diagnostic disorder is overrepresented among smokers. (Hall et al 1993).

**Nicolau B.** et al in their two phase study in Brazil found that there is an association between socioeconomic and psychological conditions experienced in early life and life course and gingival bleeding. According to them adverse family and socioeconomic environment reduces the chances of having good individual social resources which in turn leads to poor oral health behaviours and low immune responses, increasing the chances of having high levels of gingival bleeding<sup>11</sup>.

#### Stress and wound healing

Chronic stress has a negative impact on wound healing. Longer duration of wound healing, altered cytokine profiles and increased circulating cortisol are usually the consistent findings<sup>2</sup>.

#### CONCLUSION

Studies to date strongly suggest that stress, distress, and inadequate coping are important risk indicators for periodontal disease. Furthermore, it is likely that systemic diseases associated with periodontal disease such as diabetes, cardiovascular disease, preterm delivery, and osteoporosis may share psychosocial stress as a common risk factor. These early beginnings will require extensive study to fully understand the molecular and cellular basis of the role of stress, and in turn these studies may lead to effective intervention strategies that minimize or negate stress as a contributing factor to periodontal diseases.

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