

## **IMPACT OF ADRENAL HORMONES ON PERIODONTAL HEALTH**

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### **ABSTRACT**

Periodontitis is a multifactorial disease with microbial dental plaque as the initiator of periodontal disease. However, the manifestation and progression of the disease is influenced by a wide variety of determinants and factors. The strongest type of causal relationship is the association of systemic and periodontal disease. Adrenal hormones are specific regulatory molecules that have potent effects on the major determinants of the development and the integrity of the skeleton and oral cavity including periodontal tissues. It is clear that periodontal manifestations occur when an imbalance of these adrenal hormones take place. This review focuses on the effects of adrenal hormones on the periodontium and the goal was to inform and update practitioners' knowledge about the impact of these hormones on periodontal status.

**Keywords:** Hormones, Chemical messenger, Periodontium, Periodontal disease, Adrenal hormones

### **INTRODUCTION**

Periodontitis is a multifactorial disease with microbial dental plaque as the initiator of periodontal disease. However, the manifestation and progression of the disease is influenced by a wide variety of determinants and factors. The strongest type of causal relationship is the association of systemic and periodontal disease. The periodontium involves complex multifactorial relationships, in which the endocrine system also plays an important role for the homeostasis.<sup>1</sup>Hormones are specific regulatory molecules that have potent effects on the major determinants of the development and the integrity of the skeleton and oral cavity including periodontal tissues.<sup>2</sup>The term “endocrine” implies that in response to specific stimuli, the products of those glands are released into the bloodstream.<sup>3</sup> The hormones then are carried via the blood to their target cells. Some hormones have only a few specific target cells, whereas other hormones affect numerous cell types throughout the body. The target

cells for each hormone are characterized by the presence of certain docking molecules (i.e., receptors) for the hormone that are located either on the cell surface or inside the cell. The importance of hormones for the homeostasis of the human body is underscored by the fact that these chemical messengers affect every tissue of the body, including the periodontium, during the life of the individual. The adrenal gland is located on top of each kidney. Like many glands, the adrenal glands work hand-in-hand with the hypothalamus and pituitary gland. The adrenal glands make and release corticosteroid hormones and epinephrine that maintain blood pressure and regulate metabolism.<sup>2</sup>

Hormones play an important role in maintaining a balance of periodontal health hence the aim of this review article is to compile all the available literature with respect to role of adrenal hormones on periodontal health.

### DEFINITIONS AND CHARACTERISTICS OF HORMONES

According to American Academy of Periodontology, hormones is defined as the chemical messenger that are secreted into the blood stream by specialized cell capable of synthesizing and secreting them in response to specific signals.<sup>4</sup>

The term “hormone” was first used by *Starling* and *Bayliss* in 1905 for secretin, a polypeptide formed in the upperregions of the small intestine, because it *stimulates* the secretory activity of the pancreas.<sup>5</sup> (In the classic experimentcarried out by *Bayliss* and *Starling* on the dog, the production of digestive juice by the pancreas was stimulated when the mucous membrane of a section of the small intestine (jejunum) that is connected to the rest of the body only by blood vessels was wetted with dilute hydrochloric acid.<sup>6</sup> There chief characteristics are:

- Hormones act as messengers carrying information to the organs.
- They are produced either in organs having this as their specific function, which are called endocrine glands (*e. g.* adrenals, thyroid, gonads, pituitary gland), or in tissues whose primary functions are entirely different.
- Those produced in endocrine glands are called glandular hormones, while those formed in other tissues are called tissue hormones (*e. g.* secretin formed in the intestine, or histamine in the lungs, liver, and skin).

- Unlike the products of other glands (*e. g.* salivary, digestive, and sweat glands), hormones are released into the blood stream, a process that is known as “internal (endocrine) secretion”.

## CLASSIFICATION OF HORMONES

The chemical structure of a hormone determines its solubility within the polar aqueous environments of the extracellular fluid and intracellular fluid and in the nonpolar environment of the lipid bilayers of cell plasma membranes and nuclear membranes. Hormones can be classified into three broad categories according to their chemical structure

- a) Steroid hormones,<sup>7</sup>
- b) Protein and peptide hormones,<sup>8</sup>
- c) Hormones derived from single amino acids.<sup>9</sup>

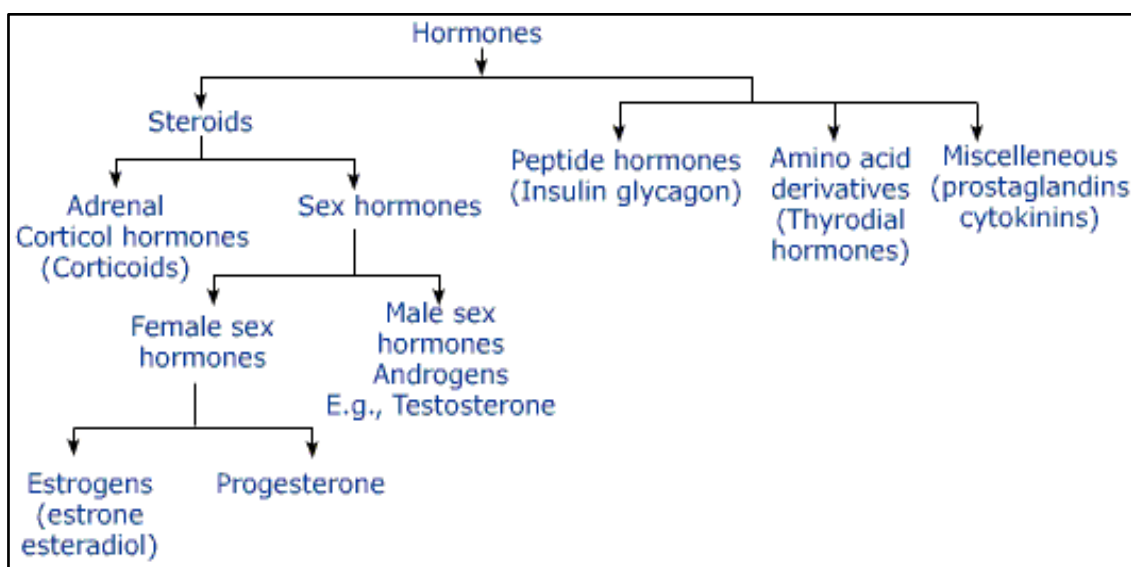


Figure 1: Classification of Hormones

## MECHANISM OF HORMONAL ACTION<sup>9</sup>

The mechanism of hormone action is grouped into two classes:

- Fixed membrane receptor mechanism
- Mobile receptor mechanism

### Fixed Membrane Receptor Mechanism

- This type of mechanism is shown by the water-soluble hormones that are amines or proteins in composition such as the growth hormone, oxytocin, ADH, etc.

- These hormones can't pass through the lipid membrane. They have their target receptor on the cell membrane to which the hormone binds.
- When the hormone binds on the specific target receptor, the enzyme adenyl cyclase in the cell membrane is activated. This helps in the production of cyclic AMP (cAMP).
- cAMP acts as the secondary messenger. It diffuses through the cell membrane and activates several enzymatic reactions to cause biochemical changes.
- The target cell responds to these changes and cAMP is deactivated by the enzyme phosphodiesterase.

### Mobile Receptor Mechanism

- This type of mechanism is shown by lipid soluble hormones such as fatty acids and steroids that can easily pass through the plasma membrane.
- They possess intracellular receptors. The hormones bind to the target receptor that activates the enzymatic activity of the cell to bring about biochemical changes.
- Transcription of DNA is initiated by the hormone-receptor complex.
- The mRNA is translated into protein. This protein causes biochemical changes inside the cell.

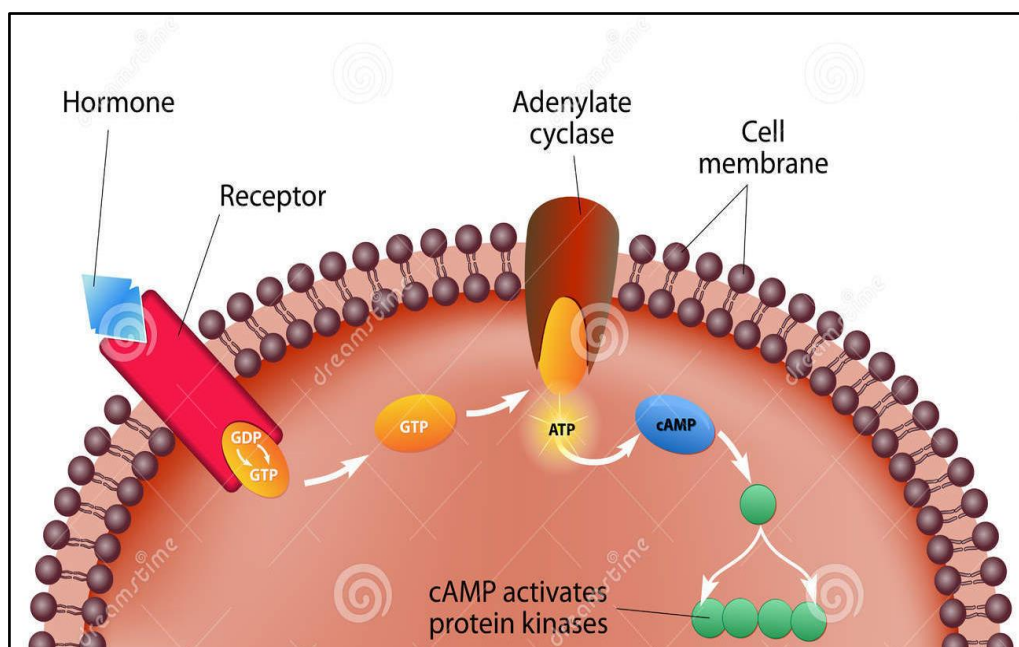


Figure 2: Mechanism of action of hormones.

## EFFECT OF ADRENAL HORMONES ON THE PERIODONTIUM

The hormones produced by the adrenal cortex include mineralocorticoid hormones (e.g. aldosterone), glucocorticoid hormones (e.g. cortisol) and gonadal hormones (e.g. dehydroepiandrosterone). Aldosterone is primarily involved with regulation of extracellular volume and control of potassium homeostasis and it has also been implicated in enhanced cardiac muscle contraction, increased vascular resistance and decreased fibrinolysis.<sup>10</sup> Cortisol affects numerous physiological processes (e.g. metabolism, inflammation, growth and levels of awareness) and the optimal functioning of body systems requires the circulating cortisol levels be maintained within a relatively narrow range.<sup>149</sup> Dehydroepiandrosterone and androstenedione are weak androgens that can be converted to more potent androgenic or estrogenic hormones by peripheral tissues.

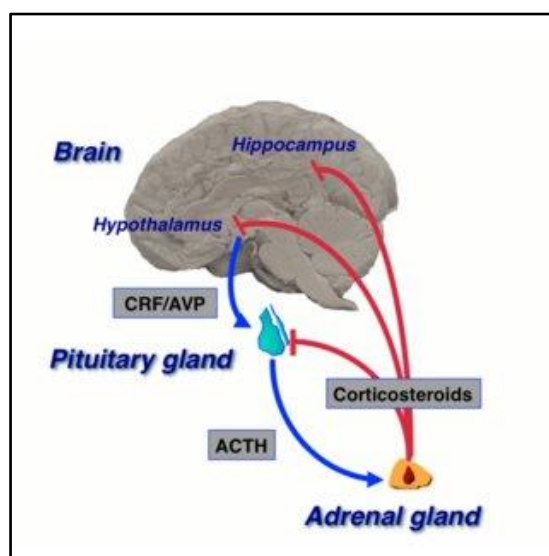


Figure 3: Stimulation of adrenal hormones

The hormones produced by the adrenal medulla are primarily catecholamines (e.g. epinephrine and norepinephrine). Catecholamine secretion is increased by adrenocorticotropic hormone and glucocorticoids but can also be affected by sympathetic nerve stimulation, hypoglycemia, hypoxia, hypercapnia, acidosis, hemorrhage, glucagon, histamine and angiotensin II.<sup>150</sup> Catecholamines have diverse effects throughout the body but generally their release has been associated with the flight or fight response.

On the periodontium, of all the adrenal hormones, cortisol, by far, has been implicated most for its effects on the periodontium. A few, relatively small, descriptive clinical studies have

attempted to demonstrate an association between elevated cortisol levels and periodontitis; however, the data are not convincing regarding a causal relationship. Furthermore, it is interesting to note that the putative effects of cortisol have not come from evaluating changes in the periodontium during disease states, such as Cushing's disease (excess cortisol) or Addison's disease (deficiency of cortisol) but from the effects that this hormone may produce as a result of stress. It is well known that there are many different physiological and psychological components of stress which cause the release of a myriad of endogenous signals, including cortisol, which may affect periodontal tissues.<sup>11</sup> As a result, the direct or pleiotropic role of cortisol in the pathogenesis of periodontal diseases remains to be elucidated.

### **BIOLOGIC RESPONSE TO STRESS**

The physiologic stress response is an evolutionarily conserved biologic mechanism that connects an organism to the surrounding environment. Stressor cues can take on both physical and/or psychologic forms in modern times. Physical cues that activate stress include associations with trauma, infection, or tumour. Psychologic or emotional cues include life events, such as financial deficits, caregiving, or the loss of a spouse; or ongoing disorders such as post-traumatic stress disorder or depression.<sup>12</sup>

### **IMPACT OF STRESS ON DEVELOPMENT AND SEVERITY OF PERIODONTITIS**

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.<sup>14</sup> Some cytokines, interleukins (IL-1b, IL-6, IL-8) and TNF-a 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. In the case of a normal healing process, the production of cytokines, interleukins (IL-1b, IL-6, IL-8), and TNF-a decreased significantly. In a stressed subject with periodontitis, the production rate is high, resulting in an increase in the severity of periodontal damage. Stress can also burden some aspects of the immune response such as mitogen stimulation, antibody and cytokine production, and NK cell activity. 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. Studies have also shown that some hormones released under stress cause a proliferation of

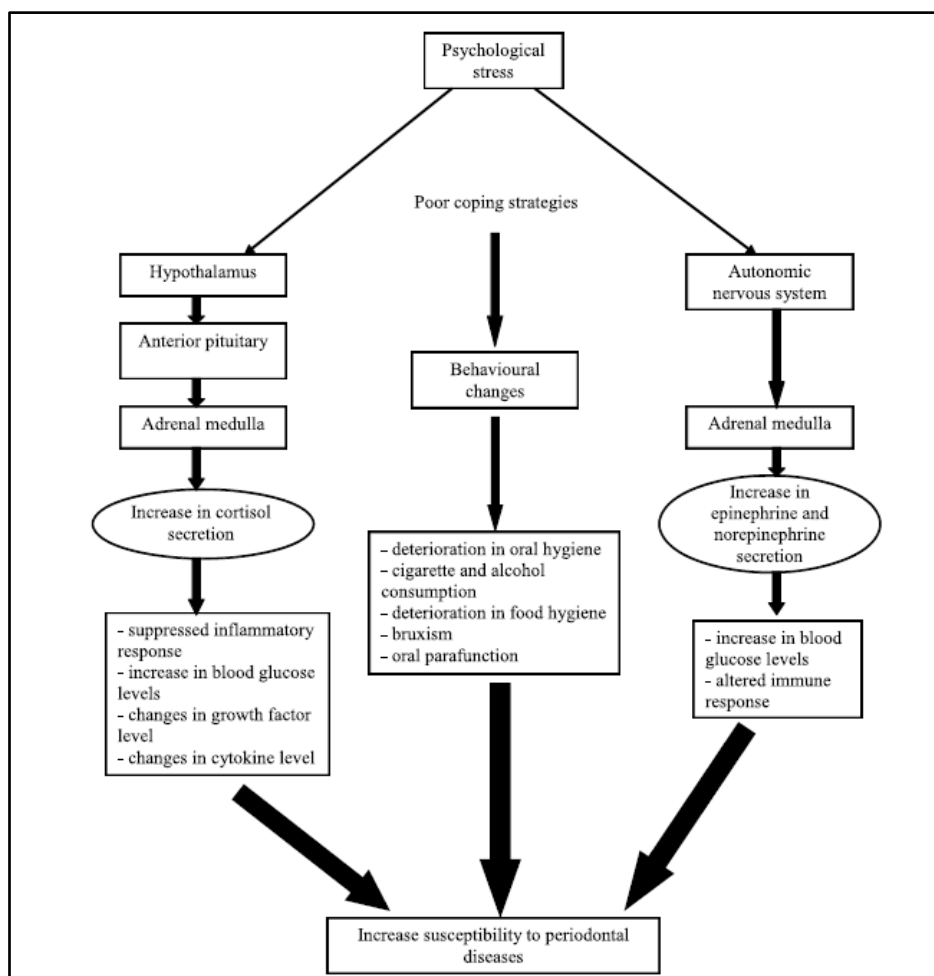


Figure 4: Biological mechanism and behaviour linking stress and periodontal disease<sup>13</sup>

certain bacteria such as *Fusobacterium nucleate*, therefore aggravating the severity of periodontal damage.<sup>15</sup>

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. bFGF has multiple effects on cell proliferation, differentiation, and angiogenesis.<sup>16</sup> Animal studies have shown a link between stress, decreased bFGF, and the severity of periodontal disease.

Individuals with an inadequate stress response also have a decreased response to nonsurgical periodontal treatments than other patients and therefore more severe periodontal diseases.<sup>14</sup> The 5-year clinical and microbiological follow-up of patients treated for early-stage periodontitis showed that periodontal disease evolves more rapidly in stressed patient.

## CONCLUSION

The periodontium is an interesting model for the manifestations of hormone-mediated actions on connective tissue and bone, owing to its communication with the oral cavity and vulnerability to inflammatory challenges. Circulating levels of hormones associated with pregnancy, stress, usage of medications associated with gingival overgrowth, glucocorticoids and insulin deficiency, can affect the presentation and progression of inflammatory periodontal diseases. These changes are more significant in the presence of plaque associated gingival inflammation, due to alteration of the immune response, interaction with cytokines and cellular responses associated with wound healing.

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