

## Current Concept of Autoimmune Disease and Holistic Therapeutic Approach

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### Abstract

Autoimmunity or horror autotoxicus is the body's own immune system is acting against their own cells at certain conditions such as chronic psychological stress considered as a major causative factor recently begin to evolve. Chronic psychological stress releasing neuropeptides such as noradrenaline, cortisol and ACTH induced inflammatory mediators activate NF-kB a key transcription factor involved in chronic inflammation, immunomodulation, cell proliferation, angiogenesis and tissue damage is the main factor involved in autoimmunity. This article briefs about the role of chronic psychological stress in autoimmunity and about natural holistic therapeutic strategies by endorphins.

**Keywords:** Cortisol; ACTH; Noradrenaline; TH1 Cells; TH2 Cells; IL-1; IL-6; TNF- $\alpha$ ; Tregs; NF-KB; STAT3

### Introduction

First, Horror autotoxicus is a horror of self-toxicity coined by bacteriologist and immunologist Paul Ehrlich described the body's innate aversion to immunological self-destruction. Later autoimmunity is the system of immunological responses of an organism against its own healthy cells and tissues. Any disease that results from such an aberrant immune response is termed an autoimmune disease [1,2].

### Role of chronic psychological stress in autoimmunity

Chronic psychological stress, depression, anxiety, induced release of CRH (corticotrophin releasing hormone) from hypothalamus activates HPA-axis through ANS (Autonomic nervous system) mediated release of neuropeptide's such as cortisol, noradrenaline, and ACTH activates inflammatory mediators such as IL-1  $\beta$ , TNF-  $\alpha$ , IL-6, and COX-2, which activates NF-KB and STAT-3 key transcription factors induced expression of inflammatory mediators such as chemokines, cytokines, growth factors, and proteolytic enzymes involved in conversion of Th1 lymphocytic type to Th2 lymphocytic type produce IL-4,IL-5,IL-13 pro-inflammatory cytokines, Th17 cells involved in immune modulation, chronic inflammation and tissue damage. Growth factors such as EGF, FGF, VEGF involved in cell proliferation and angiogenesis. Altered induced Tregs (Regulatory Tcells) formed from TH1 cells through TGF- $\beta$  inflammatory mediator release IL-4, IL-5, IL-10, IL-13, IL-17 pro-inflammatory cytokines involved in immune modulation, otherwise normally involved in self-tolerance and immune modulation. Proteolytic enzymes such as matrix metallo proteases (Mmp's) involved in tissue damage all these changes leads to autoimmune disease [3-11]. During this process all immune cells and other cells are affected, how can in autoimmune diseases, affects the individual cell out of 17 - 18 billion cells in our body as seen in example - Auto antibodies against desmoglein-1,2 in pemphigus vulgaris, BP-120 and 180 in bullous pemphigoid, ANA in SLE and DLE, PCNA-scleroderma, Lichen planus, Psoriasis (Figure 1-3).

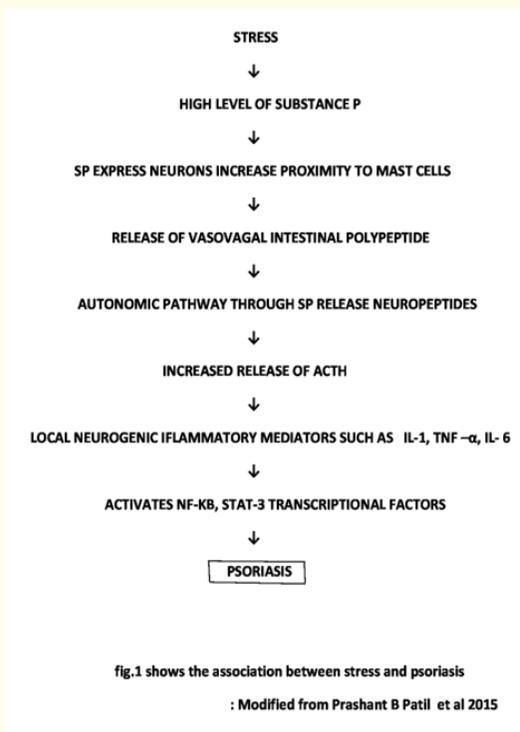


Figure 1: Shows the association between stress and psoriasis. Modified from Prashant B Patil, et al. (2015).

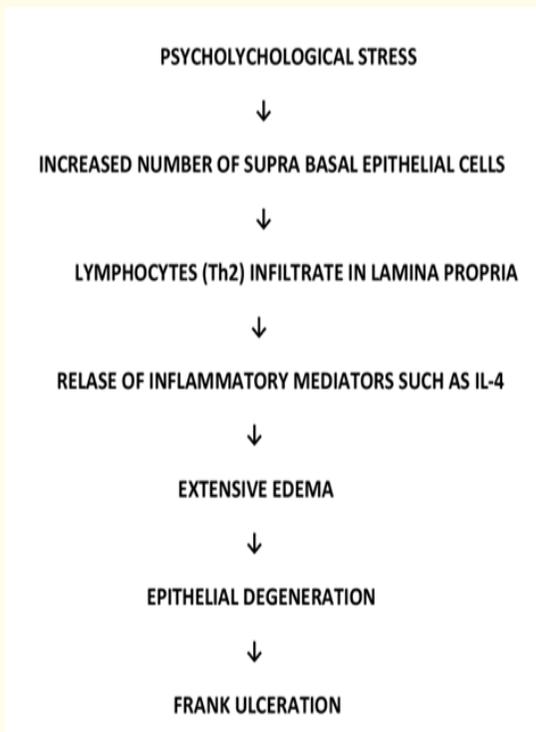
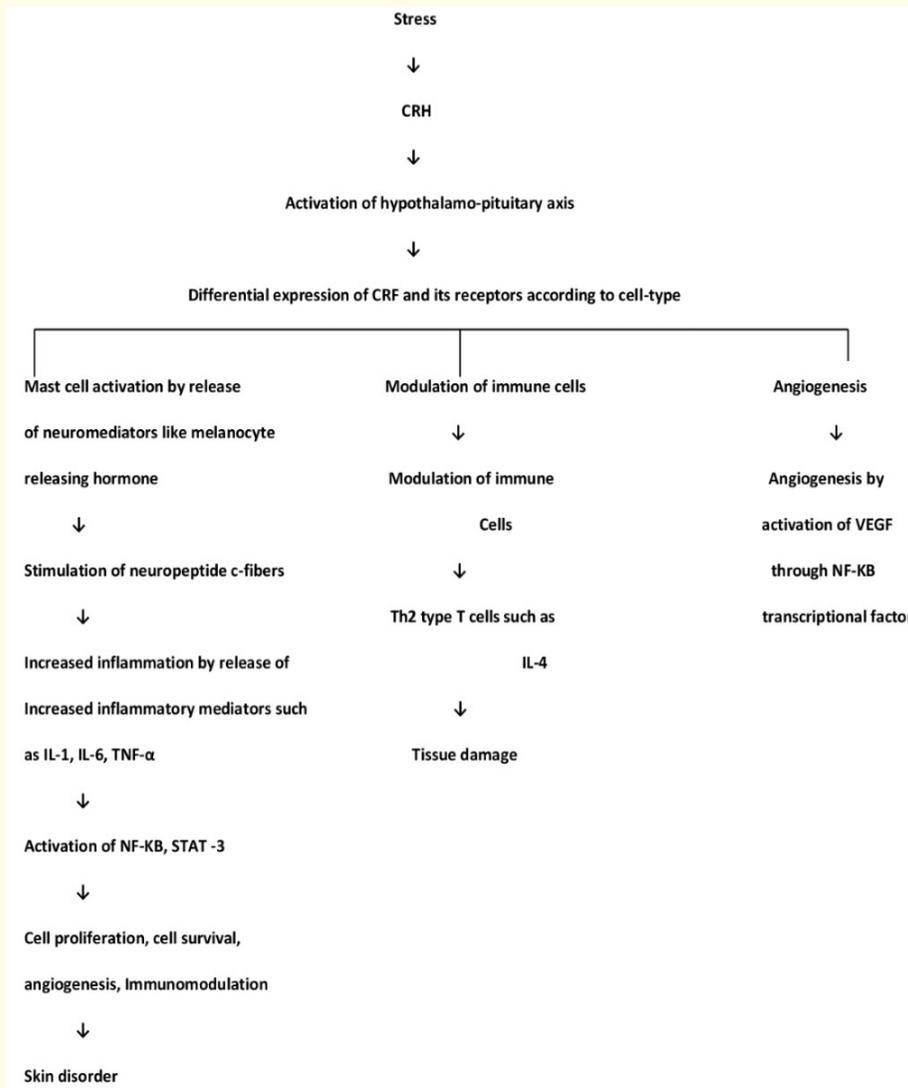


Figure 2: Shows the association between psychological stress and oral ulcers. Modified from Prashant B Patil, et al. (2015).



**Figure 3:** Shows the association between stress and skin disease. Modified from Prashant B Patil, et al. (2015).

Where these autoantibodies do comes from and how it develops autoimmunity against particular individual cell component [7-15].

**Beta-endorphins in treatment of autoimmune disease**

Endorphins are endogenous morphine, neuropeptides produced in the pituitary gland in response to stress and pain. There are three types of endorphins such as beta-endorphins, enkephalins and dynorphins binds to mu, kappa and delta receptors situated on nervous system and immune cells. Beta endorphins are an abundant endorphin, synthesized and stored in the anterior pituitary gland, it is a precursor of POMC (proopiomelanocortin). Most of all immune cells produce endorphins, in inflammatory state recruitment of immune cells by chemokines produce endorphins. In inflammatory site binding of endorphins to the receptors on peripheral nerves inhibits substance p, a neurotransmitter of pain and inflammation, also produce anti-inflammatory cytokines such as IL-10, IL-18 and IFN-γ [16,17].

In the PNS, binding of beta endorphins to the μ(mu) receptors on peripheral nerves results in inhibition of substance p a neurotransmitter of pain and inflammation. In the CNS, binding of beta endorphins to the μ (mu) receptors on central nervous system instead of

inhibiting substance p a neurotransmitter of pain, it inhibits GABA (gamma amino butyric acid) a inhibitory neurotransmitter and activation of dopamine neurotransmitter involved in analgesic activity, euphoric activity, tranquility of mind, cognitive development, and stress buster activity [18,19].

Chronic psychological stress mediated induced release of cortisol, catecholamine's, and ACTH neuropeptides activates inflammatory mediators such as IL-1 $\beta$ , TNF- $\alpha$ , IL-6, COX-2 and decreased expression of IL-2 and IFN- $\gamma$  by activating key transcription factors NF-KB, STAT-3 play an important role in autoimmunity by conversion of TH1 to TH2 lymphocytic type, TH17 cells, involved in chronic inflammation, immune modulation, and tissue damage. Altered Tregs (regulatory T cells) involved immune modulation, otherwise it is involved in self-tolerance and immune homeostasis, growth factors (EGF, FGF, VEGF) involved in cell proliferation and angiogenesis, matrix metallo proteases (mmp's) involved in tissue damage, all these changes leads to autoimmune disease.

Beta endorphins inhibits chronic psychological stress induced sympathetic nervous system activity and activates parasympathetic nervous system of ANS (autonomic nervous system) through inhibition of HPA-axis mediated release of neuropeptides release such as cortisol, noradrenaline and ACTH, which induce inflammatory mediators such as IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and COX-2, activates NF-KB and STAT-3 transcription factors involved in chronic inflammation, immune modulation, cell proliferation, angiogenesis, and tissue damage, all these changes leads to autoimmune disease.

Endorphin receptors are situated on all most all immune cells. Binding of beta endorphins to the  $\mu$  (mu) receptors on immune cells such as NK cells, neutrophils, macrophages, DC's, T cells, and B cells involved in immune stimulatory activity by releasing opsonin, granzyme-B, and antibodies involved in antitumor activity, antibacterial activity, anti-inflammatory activity, and anti-viral activity.

Beta-endorphins delay aging by lengthening telomeres, which otherwise shorten with aging and other mechanism by inhibiting the release of ROS,RNS free radicals from inflammatory cells such as neutrophils, macrophages, and DC's during oxidative stress through NADPH oxidase pathway, free radicals involve in cell aging, genetic mutation and cell death.

Endorphins are produced during yoga, meditation, pranayama, intense physical exercise creates a psychological relaxed state known as "Runners high", acupuncture, love, music therapy, pranic healing, sympathy, empathy [16-20].

Love everybody, hate no body produces endogenous opioid in the brain is the effective treatment, endogenous opioid acts as a pain killer, stress buster and immune modulator. Tranquility of mind can be obtained by yoga and meditation. Practice sympathy and empathy for caring the patient is the ultimate treatment choice in autoimmune disease rather than very often steroid treatment need to be revisited.

### Conclusion

Chronic psychological stress induced release of CRH from hypothalamus activates HPA-axis through ANS release neuropeptides activates inflammatory mediators IL-1 $\beta$ , IL-6, TNF- $\alpha$  and COX-2 mediated activation of NF-KB and STAT-3 key transcription factors activation involved in chronic inflammation, tissue damage, immune modulation leads to autoimmune disease. Endorphins are endogenous morphine, neuropeptides produced in the pituitary gland involved in reduction of psychological stress mediated activation of inflammatory mediators activates NF-KB, STAT-3 involved in immune modulation, chronic inflammation, cell proliferation, angiogenesis, tissue damage all these changes leads to autoimmune diseases. Thorough understanding of endorphins especially beta endorphins, mechanisms of action, duration of action, in natural holistic treatment of autoimmune diseases without adverse effects and inexpensive.

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