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# Pathophysiology of Stress & Its Impact on Human Health

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**Abstract--** Homeostasis of our body is constantly challenged by internal or external adverse forces known as stressors which have a major impact on human behaviour and both mental and physical health. Chronic stress can cause a variety of symptoms and affect our overall well-being. The impact of stress on the body may not be the same in all people. It may vary depending on factors like the genotype, sex, age, physiological conditions and past experiences of the person. The stress response involves the involvement of both nervous as well as endocrine systems. Most of the effects are due to increased concentrations of corticoids and adrenaline. Stress and its related factors mostly depress immune function and increase sensitivity for several disorders related to different organ systems. This review article focuses on the mechanism of stress and effects of stress on the human physiology.

**Keywords--** Stress, Stressors, HPA axis, Human Physiology, Stress Management.

## I. INTRODUCTION

Today's life style both personal and professional are often challenging and require intense physical and psychological efforts in order to be sustained and maintained the overall stability. Stress is a natural response to a challenging situation that can manifest physically, emotionally, and mentally. Selye (1956) coined the term "stress" to represent the effects of any stimuli that seriously threatens homeostasis. Any physical or psychological stimuli that disrupt homeostasis are called stressors. It is the body's way of preparing to face a threat or pressure and can be caused by various factors such as work, relationships, or financial issues. When an individual is in some unfavourable condition (physical or mental), his/her body tries to maintain the homeostasis and protect itself from such events adopting some 'changes'. Stress is a series of events our body follows to cope with such situations (D. K. Sharma, 2018). While some stress can be beneficial in motivating individuals to perform at their best, prolonged or excessive stress can have detrimental effects on health and well-being. Stress can be positive i.e. 'eustress' such as getting a job promotion or being given greater responsibilities. Stress becomes negative i.e. 'distress' when a person faces continuous challenges without relief or relaxation. Eustress fosters mental acuity and motivation whereas distress is characterized by adverse effects on the body and mind.

Stress has both a physical (objective) and a psychological (subjective) component. Koolhaas and colleagues (2011) described that psychological part depends on the perception of an individual and the way a person can predict a certain stressor and then control it. This process is variable that how promptly and efficiently it is activated promoting adaptation and how fast it is turned off once equilibrium has been recovered (A. Mariotti, 2015). The time period of stress response is characterized by massive neuroendocrine and behavioural changes. But all stimuli that elicit strong neuroendocrine responses are not real stressors, only those that exceed the individual's capacity to change and adapt.

The World Health Organization has defined health as a "complete state of physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 2005). Chronic stress exposure has led to a maladaptive stress response that is associated with a huge range of diseases such as cardiovascular malfunction, cancer sensitivity, obesity, and many others. In recent years, there has been a growing interest in understanding the impact of chronic stress on various physiological systems. Psychological and social factors are thought to influence risk for a range of diseases including heart diseases, high blood pressure, type 2 diabetes, infectious illness, bronchial asthma, and musculoskeletal pain (A. Steptoe & L. Poole, 1998). Studies have shown that prolonged exposure to stress hormones, such as cortisol, can lead to dysregulation of the immune system, increased inflammation, and changes in brain structure and function. Additionally, chronic stress has been associated with an increased risk of developing mental health disorders, such as anxiety and depression (A. Monaj Kumar & R. Baruah, 2020). Understanding the intricate pathways through which stress influences health outcomes is crucial for developing targeted interventions that can help individuals better manage and mitigate the effects of stress on their overall health.

Studying the effects of stress on human physiology and health is crucial in understanding how it impacts various bodily systems and functions. Chronic stress has been linked to a range of health problems, including heart disease, depression, and weakened immune function.

By investigating the mechanisms through which stress affects the body, researchers can develop strategies and interventions to help individuals better cope and minimize the negative consequences of stress on their overall well-being. This knowledge can also contribute to the development of more effective stress management techniques and therapies that can improve quality of life for those struggling with chronic stress.

## II. TYPES OF STRESS

Based on duration, source, and response, stress can be divided into following types -

*2.1 Acute stress:* The short-term stress that typically results from immediate stressors or after experiencing a traumatic event. Acute stress disorder (ASD) was first outlined in 1994 at the diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) as a new diagnosis (M. Fanai et al., 2023). The body's fight-or-flight response leads to temporary physiological changes such as increased heart rate and adrenaline release. The diagnosis is based on history and physical examination and main treatment is psychotherapy.

*2.2 Chronic stress:* This occurs when the stressor persists over an extended period that means the body remains in a constant state of physiological arousal. Prolonged exposure to chronic stress can lead to cumulative physiological and psychological effects, increasing the risk of health problems such as cardiovascular disease, anxiety, and depression. Diseases affected by stress are cardiovascular dysfunctions, diabetes, cancer, autoimmune syndromes and mental illnesses such as depression and anxiety disorders.

*2.3 Episodic stress:* When acute stress starts to become a regular occurrence, it is referred to as episodic stress. This pattern may be characteristic of individuals who lead chaotic or disorganized lifestyles, constantly facing deadlines, commitments, or interpersonal conflicts. The cycle of stress exacerbates health issues and impairs daily functioning. The signs of episodic stress can range from cognitive, emotional, physical and behavioural symptoms.

*2.4 Traumatic stress:* This type results from exposure to traumatic events, such as natural disasters, accidents, or violent acts. Trauma (may be one-time, multiple, or long-lasting repetitive events) affects everyone differently. The impact of trauma can be subtle, insidious, or outright destructive. The trauma may lead to posttraumatic stress disorder (PTSD) which is characterized by symptoms impairing cognition, mood, somatic experience and behaviour (S. K. Mann et al., 2024). PTSD can cause chronic impairments, intrusive memories, avoidance behaviours, and lead to an increased risk of suicide (X. R. Miao et al., 2018).

*2.5 Environmental stress:* Environmental stimuli not only affect human health and well-being solely by physical and direct means but also indirectly have the huge impact on mental health through stress responses (Cohen et al., 1995). In several studies, researchers investigated the role of stress and annoyance in the relationships between environmental factors and health (Dzhambov et al., 2018; Héritier et al., 2014). This type arises from adverse or challenging conditions such as noise, pollution, overcrowding or unsafe living conditions. These stressors can have detrimental effects on physical and mental health, contributing to a sense of discomfort or unease (M. L. Cantuaria et al., 2023).

*2.6 Psychological stress:* The stress stems from cognitive or emotional factors, such as perceived threats, worries, or negative thoughts. Typical stressors include work-related pressures, academic expectations, social comparisons, or self-imposed demands. Psychological stress only becomes pathological when it interferes with a person's health and well-being. Manifestations include anxiety, rumination, or perfectionism.

*2.7 Physiological stress:* The physiological stress refers to the body's response towards the internal or external physical stressors, such as injury, diseased condition, excessive workout, sleep deprivation or nutritional deficiencies that disrupt homeostasis (McEwen, 2006). The physiological response is initiated by the sympathetic nerve system, which releases the stress hormones such as cortisol and adrenaline and human body triggers the "fight or flight" response (G. Karuppaiah et al., 2023).

## III. MECHANISM OF STRESS

Allostasis is more precise biological concepts than the word "stress" to describe adaptation to "stressors". The physiological response of stress response can be two types – one is slow response mediated by the hypothalamic-pituitary-adrenal (HPA) axis and another is fast response mediated by the Sympathetic-Adreno-Medullar (SAM) axis (Marian Joels & Tallie Z Baram, 2009).

The hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system along with the metabolic system and the pro- and anti-inflammatory components of the immune system act together to maintain homeostasis (B. S. McEwen et al., 2015). Due to stress, the hippocampus, amygdala, and prefrontal cortex of brain undergo structural remodelling, which alters behavioural and physiological responses. When hypothalamus of the brain is encountered with a stressor, it performs some specific functions.

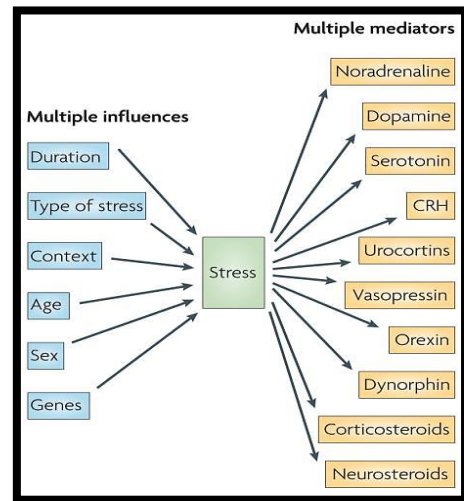
Hypothalamus activates autonomic nervous system (ANS); by releasing Corticotrophin Releasing Hormone (CRH), it stimulates Hypothalamic Pituitary Adrenal (HPA) axis and secretes antidiuretic hormone. Autonomic nervous system consists of sympathetic (arousal) and parasympathetic (relaxed) nervous system. The ANS regulates visceral activities like circulation, digestion, respiration, temperature regulation and some vital organs (D. K. Sharma, 2018).

Scantamburlo et al., (2001) reported that arginine vasopressin modulates the effect of CRH on ACTH secretion. ACTH released from anterior pituitary gland in response to CRH stimulates adrenal cortex to release corticoids (glucocorticoids and mineralocorticoids). Chronic stress regulates the behaviour by altering the body's homeostatic cortisol levels as well as the function of brain-specific genes (R. S. Lee, 2022). The major function of glucocorticoids is to release energy via glycogenolysis & lipolysis, which is required to control the ill effects of stressor. Other functions of corticoids are - increased urea production, appetite suppression, suppression of immune system, exacerbation of gastric irritation, associated feeling of depression and loss of control. These are the common symptoms seen in a person under stress. Mineralocorticoid (aldosterone) promotes retention of Na<sup>+</sup> and elimination of K<sup>+</sup> which increases blood pressure by increasing blood volume. The medulla of the adrenal gland secretes epinephrine and norepinephrine which reinforce the functions of sympathetic nervous system. The release of these hormones acts as a support system to ensure the most efficient means of physical survival.

ADH is synthesised by hypothalamus and released by posterior pituitary. The main function of ADH (vasopressin) is to regulate fluid loss through urinary tract and it has another important role on regulation of blood pressure during stress when the homeostasis of the body is disturbed. Psychological stress increased the systolic and diastolic blood pressure as well as heart rate, also elevated the cortisol and AVP concentration in both plasma and CSF in a stress level-dependent manner (L. L. Bao et al., 2014).

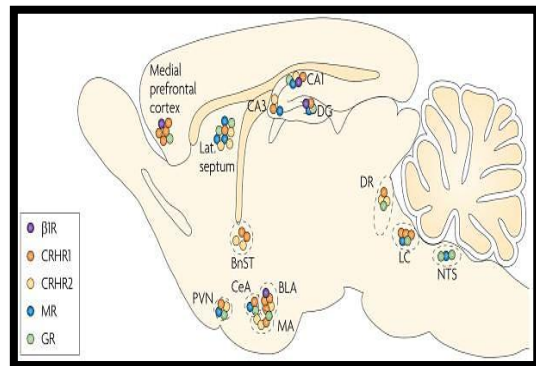
Some other hormones such as Growth Hormone (GH) and thyroid hormones (TSH) also play significant role in stress. Both are released from anterior pituitary gland. GH is a stress hormone and its level can increase up to ten folds due to acute physical stress (S. Ranabir & K. Reetu, 2011). It has been observed that, in human, psychological stimuli increase the concentration of thyroid hormones. Thyroid releases thyroxine and triiodothyronine. The main function of thyroid hormones is to increase overall metabolic rate, heart rate and the sensitivity of some tissues to catecholamines.

This leads to increased cardiac output, skeletal muscle blood flow, sodium retention, reduced intestinal motility etc. (D. Goldstein, 1987).



**Figure 1. Different Stressors Require Different Responses.**

[Picture Courtesy: Marian Joels & Tallie Z Baram (2009) -The neuro-symphony of stress. *Nat Rev Neurosci*;10(6):459-466.]



**Figure 2. Brain Hot Spots of Receptors.**

[Picture Courtesy: Marian Joels & Tallie Z Baram (2009) -The neuro-symphony of stress. *Nat Rev Neurosci*;10(6):459-466.]

Different stress mediator receptors are often expressed in 'hot spots' of the brain, such as the prefrontal cortex, the amygdala, the hippocampus and the neurotransmitter synthesis areas. For example, neurons in the amygdala (which are affected by noradrenaline, dopamine, CRH and corticosteroids) are responsible for sympathetic and neuroendocrine activation and the processing of emotional and contextual aspects of stress.

The quick response triggered by Sympathetic-Adreno-Medullar (SAM) axis activation leads to increased secretion of norepinephrine and epinephrine from the adrenal medulla into the circulation resulting increased level in the brain. The released epinephrine and norepinephrine interact with  $\alpha$ - and  $\beta$ -adrenergic receptors in the central nervous system and on the cell membrane of smooth muscles and other organs all over the body initiating an intracellular cAMP signalling pathway that rapidly activates cellular responses (Brianna Chu et al., 2024).

#### IV. IMPACT OF STRESS ON HUMAN HEALTH

Human body is well equipped to handle minute stresses, but when that stress becomes long-term or chronic, it can have serious effect/effects on human health. Stress generally affects all over the body including cardiovascular, respiratory, endocrine, gastrointestinal, nervous, muscular, and reproductive systems.

##### *4.1 Effect on cardiovascular system*

Acute stress causes an increase in heart rate and stronger contractions of the heart muscle with the stress hormones such as adrenaline, noradrenaline, and cortisol. Chronic stress has been linked to a variety of negative health effects, including an increased risk of cardiovascular disease. Psychological stresses are closely associated with cardiovascular diseases and as a result they are included within the psychosomatic group of diseases (S. Golbidi et al., 2015). Both adrenaline and cortisol (increased during stress) affect heart and blood pressure. More adrenaline initiated high blood pressure which affects the functioning of the heart can produce coronary heart disease, strokes and sudden cardiac arrest (D. K. Sharma, 2018). The work stress increased heart rate as well as an increase in systolic blood pressure level and lower vagal tone (T. G. Vijkotte et al., 2000). Acute emotional stress can also stimulate severe catecholamine release, leading to direct myocyte injury known as myocytolysis which can trigger a heart failure syndrome.

The risk for heart disease associated with stress appears to differ for women, depending on the premenopausal or postmenopausal state. Level of estrogen in premenopausal women appears to help blood vessels respond better during stress. Postmenopausal women lose the level of estrogen and as a result they don't have the protection against heart disease. Women are more prone to develop mental-stress-induced myocardial ischemia (MSIMI) than men as they have greater brain activation patterns for mental stress (M. Y. Henein et al., 2022).

##### *4.2 Effect on immune system*

Different psychiatric illnesses, stress and distress are increasingly reported to be associated with immunosuppression by affecting CNS and neuroendocrine system (D. K. Khansari et al., 1990). The high levels of stress hormones suppress the release of cytokines which regulate both cell-mediated and humoral immune response in the body. When the body is constantly in a state of stress, it can impair the immune system's ability to function properly, leaving individuals more vulnerable to viruses and bacteria. This can lead to frequent colds, flu, and other illnesses, as well as prolonged recovery times. J. Leserman et al., (2000) reported that stress and depression affect the body cortisol level as well as the progression of HIV-1 infection.

##### *4.3 Effect on digestive system*

Stress shows both short-term and long-term effects on the functions of the gastrointestinal tract which include inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), peptic ulcer and gastroesophageal reflux disease (GERD) and other functional gastrointestinal diseases (P. C. Konturek et al., 2012). Several studies reported a negative effect of acute stress on maintenance of blood glucose concentrations in patients with type 1 and type 2 diabetes. So, stress can influence the development of type 2 diabetes indirectly by stimulating obesity and metabolic syndrome (M. L. Marcovecchio & F. Chiarelli, 2012).

##### *4.4 Effect on reproductive system*

Stress can impact negatively on the reproductive function. The reproductive system, both in females and males, is inhibited at all levels by the HPA axis. Along with this, glucocorticoids exert inhibitory effects on GnRH neurons, pituitary gonadotrophs and directly on the gonads. As a result, steroidogenesis is directly inhibited at both the ovaries and testes (C. Tsigos et al., 2000). Negative effects of HPA axis on female reproduction are responsible for various stress conditions such as anxiety, depression, eating disorders etc. (G. Valsamakis, 2019). Katrina Nakamura et al., (2008) reported that maternal perceived stress is claimed as a cause of infertility, miscarriages, late pregnancy complications and/or impaired fetal development.

##### *4.5 Effect on respiratory system*

Acute stress can result in changes in breathing patterns due to airway constriction, leading to shortness of breath and rapid shallow breathing, exacerbating respiratory symptoms. Chronic stress also compromises immune function, increasing susceptibility to respiratory infections and exacerbating conditions such as asthma and chronic obstructive pulmonary disease (B. Chu et al., 2025).

Certain psychiatric disorders, including anxiety disorders particularly panic symptoms and affective disorders are unusually common among asthma patients (P. Lahrer, 2006). Sometimes parent's chronic stress may increase the probability of their children having asthma (Sujaritha et al., 2022).

- Acute stress can cause anxiety, personality changes, sadness, irritability, insomnia, and memory loss, among other mental and emotional issues (K. Vedhara et al., 2003).

## V. STRESS MANAGEMENT

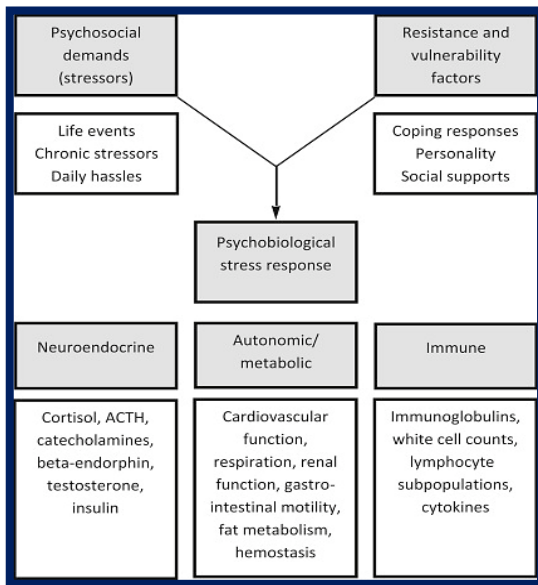
It is important to prioritize self-care practices such as exercise, meditation, and adequate sleep to help manage stress levels. Engaging in activities that bring joy and relaxation can also play a significant role in reducing the negative effects of chronic stress on the body. Additionally, seeking professional help from therapists or counsellors can provide valuable tools and strategies for coping with stress in a healthy way. By taking proactive steps to address chronic stress, individuals can improve their overall health and quality of life.

One way to manage chronic stress is through regular exercise. Physical activity has been shown to reduce levels of stress hormones in the body and promote the release of endorphins, which are natural mood lifters. Exercise can also improve cardiovascular health by strengthening the heart and improving circulation. In addition to exercise, practicing relaxation techniques such as deep breathing, meditation, or yoga can help to calm the mind and reduce stress levels. Seeking support from friends, family, or a therapist can also be beneficial in managing chronic stress and improving overall well-being. By taking proactive steps to address and manage chronic stress, individuals can reduce their risk of cardiovascular disease and improve their overall health and quality of life.

Mindfulness and relaxation techniques can also be beneficial in reducing stress levels. Mindfulness involves focusing on the present moment and being aware of your thoughts and feelings without judgment. This practice can help you stay grounded and prevent your mind from wandering to stressful thoughts. Additionally, seeking support from friends, family, or support groups can provide a sense of community and understanding during difficult times. Prioritizing self-care and seeking professional help when needed are essential steps in managing chronic stress and maintaining a healthy lifestyle.

## VI. CONCLUSION

This is clear that stress can have a significant impact on both our mental and physical health. From increased risk of chronic diseases to impaired cognitive function, the effects of stress on the body are vast and far-reaching.



**Figure 3. Outline of The Major Physiological Elements Of The Psychobiological Stress Response.**

(Picture courtesy: Andrew Steptoe & Lydia Poole, 1998. *Psychophysiological Bases of Disease*. Comprehensive Clinical Psychology, Volume 8, 1998, Pages 39-78).

### 4.6 Other effects

- Acute stress might lead to overeating, consumption of high caloric food, inactivity and shortening sleep (A. J. Tomiyama, 2019).
- P. R. Martin (2016) reported that stress stimulates headaches and the mechanism of the role of stress in the developmental and psychosocial context of headaches. Symptoms of migraine seems to increase in a setting of stress, partially driven by psychiatric comorbidity (A. Stubberud et al., 2021).
- Stress directly boosts glucose levels in persons with type II diabetes. Energy mobilization is a primary result of the fight or flight response. In absolute lack of insulin, stress-induced increases in glucose cannot be metabolized properly. But the effect of stress on type I diabetes is not clear (R. S. Surwit et al., 1992).

However, by recognizing the importance of self-care and seeking help when needed, individuals can take proactive steps towards managing and reducing stress in their lives. It is crucial to prioritize mental health and well-being, as they are essential components of overall health and happiness. Remember, you are not alone in facing these challenges, and there are resources and support systems available to help you on your journey towards better mental and physical health.

Whether it's through therapy, mindfulness practices, exercise, or simply taking time for yourself, finding ways to cope with stress and prioritize self-care is key. By making small changes in our daily routine and seeking help when needed, you can begin to build resilience and better manage the stressors in your life. Remember, self-care is not selfish, it is necessary for your overall well-being. So don't hesitate to reach out for support and make yourself a priority.

It is important to recognize the signs of stress and take proactive steps to address it before it escalates. This may involve setting boundaries, practicing self-care, and engaging in activities that bring joy and relaxation. It is also essential to prioritize self-awareness and listen to our bodies and minds, as they often provide valuable cues about our stress levels. By making stress management a priority in our daily lives, we can cultivate a greater sense of well-being and resilience in the face of adversity.

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