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Stress Hormones and Their Impact on Cancer Development and Progression

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Abstract - Psychological stress is an unavoidable element of modern life and has been increasingly recognized as a significant biological factor influencing cancer development and progression. Stress hormones, especially glucocorticoids and catecholamine, are released through activation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic-adrenal-medullary (SAM) system. Under chronic stress, persistent elevation of these hormones can lead to dysregulation of immune function, increased inflammation, impaired DNA repair, and enhanced tumour cell proliferation, angiogenesis, and metastasis. Emerging research in psychoneuroimmunology demonstrates that stress-mediated signaling pathways promote survival of malignant cells and suppress anti-tumour immunity. Although evidence does not confirm stress as the sole cause of cancer, it significantly modifies tumour microenvironment and therapeutic outcomes. This review evaluates the molecular mechanisms through which stress hormones influence oncogenesis and tumour progression, highlights cancer types most affected by stress, and discusses clinical implications including therapeutic strategies targeting stress responses. Understanding these interactions may lead to integrative cancer care approaches that combine psychological therapy, pharmacological inhibitors, and lifestyle interventions to improve patient outcomes.

Keywords - Stress hormones, Cancer progression, Cortisol, Catecholamine's, Tumour microenvironment, Psychoneuroimmunology.

I. Introduction

Cancer is one of the leading causes of global mortality, with approximately 20 million new cases and 9.7 million deaths reported worldwide in 2022 (World Health Organization, 2023). Although genetic mutations play a central role in oncogenesis, environmental and psychosocial factors significantly influence cancer risk and outcomes. Psychological stress has emerged as a major modifier of biological processes that underpin tumour initiation and progression.

Stress arises when individuals perceive a threat beyond their coping capacity, leading to activation of neuroendocrine systems. Acute stress can be adaptive, improving immune surveillance and survival responses. In contrast, chronic stress produces sustained elevation of stress hormones—primarily glucocorticoids (e.g., cortisol) and catecholamine (e.g., adrenaline and noradrenaline)—which adversely affect immune function, metabolism, and cellular homeostasis (Cunningham et al., 2021).

Psychoneuroimmunology research has shown that these hormones alter the body's defense against cancer by promoting DNA damage, suppressing cytotoxic immune cells, inducing angiogenesis, and increasing metastatic potential. Cancer patients frequently experience anxiety, depression, or long-term stress, making this hormonal interaction clinically significant (Lutgendorf & Sood, 2019). Therefore, understanding how stress hormones affect tumour biology is essential for developing more effective and integrative cancer treatment strategies.

This review analyzes the neuroendocrine pathways activated by stress and explores their mechanistic influence on cancer development and progression, along with therapeutic implications.

Stress Hormones: Classification and Functions

Glucocorticoids (Cortisol)

Cortisol is synthesized in the adrenal cortex and regulated by the hypothalamic–pituitary–adrenal (HPA) axis. Its physiological roles include glucose metabolism regulation, immune modulation, and maintaining homeostasis during stress. Chronic cortisol elevation leads to immune suppression, reduced apoptosis of damaged cells, and increased inflammatory cytokines that support tumour growth (Yang et al., 2022).

Catecholamine (Adrenaline and Noradrenaline)

Catecholamine are produced by the adrenal medulla and sympathetic nerve terminals during activation of the sympathetic-adrenal-medullary (SAM) system. They bind to β-adrenergic receptors on tumour and immune cells to enhance proliferation, angiogenesis, invasion, and metastasis (Cole & Sood, 2021).

HPA Axis and Sympathoadrenal System

These two core stress pathways regulate the fight-or-flight response. Under chronic psychological stress:

HPA axis → Persistent cortisol release

SAM system → Continuous catecholamine secretion

Such dysregulation shifts the body from protective to pathogenic mode.

Uncontrolled stress creates a biological environment conducive to cancer development and progression.

Mechanisms Linking Stress Hormones to Cancer

Persistent elevation of stress hormones produces biological changes that favour oncogenesis and tumour progression. Key mechanistic pathways include:

Cancer Types Associated with Stress Hormonal Influence

While stress alone does not directly cause cancer, multiple studies demonstrate that chronic stress hormones significantly influence progression, recurrence, and metastasis in several cancer types.

Breast Cancer

Breast cancer cells highly express β-adrenergic receptors, making them responsive to catecholamine. Chronic stress promotes:

Increased angiogenesis

Greater metastatic spread

Reduced treatment responsiveness

Clinical studies indicate that patients experiencing long-term psychological distress show faster disease progression (Lutgendorf & Sood, 2019).

Ovarian and Cervical Cancer

Catecholamine enhance invasion of ovarian tumour cells by activating pro-metastatic signaling pathways such as STAT3 and MMP-9 (Leng et al., 2021). Stress also disrupts hormonal balance in reproductive tissues, increasing susceptibility to malignant transformation.

Prostate Cancer

Chronic cortisol exposure increases androgen receptor sensitivity and reduces apoptosis in prostate cancer, accelerating tumour growth (Hassan et al., 2020). Stress-related behavioral factors like sleep disruption and smoking further worsen prognosis.

Gastrointestinal Cancers

Colorectal and gastric cancers are influenced by stress-induced inflammation.

These cancers are highly associated with anxiety, lifestyle stress, and depression among patients.

Haematological Cancers

Long-term stress suppresses bone marrow immunity, creating conditions favourable for leukaemia and lymphoma development (Nikolich-Žugich, 2023). Abnormal cortisol levels impair immune cell maturation, promoting malignant transformation.

Psychological Stress and Cancer Progression

Psychological stress significantly influences not only the initiation of cancer but also its clinical course, treatment responsiveness, and patient survival rates. Cancer patients frequently experience anxiety, fear of recurrence, depression, financial strain, and social isolation. These psychological burdens lead to chronic activation of the HPA and SAM systems, promoting biological conditions favourable for tumour progression (Cunningham et al., 2021).

Psychological Counselling

Cognitive Behavioral Therapy (CBT) is frequently recommended for cancer patients.

It: Promotes positive coping strategies

Reduces fear of recurrence

Alleviates depression and emotional distress

CBT has been shown to slow cancer progression indirectly by stabilizing stress hormones (Lutgendorf & Sood, 2019).

Social and Family Support

Social interaction buffers stress responses. Patients with strong support systems:

Better tolerate treatment

Show improved immune markers

Experience lower recurrence rates

Support groups and therapist-led programs enhance emotional well-being, especially among women with breast cancer.

Lifestyle Modifications

Daily routine changes significantly improve hormonal balance:

Lifestyle Component Impact

Physical exercise Reduces cortisol & inflammation
Nutritious diet (antioxidant-rich) Lowers oxidative stress
Adequate sleep Regulates hormonal rhythm
Avoiding smoking & alcohol Limits carcinogenic effects
Thus, integrating healthy habits offers both preventive and supportive care effects.

Holistic Approach in India

Integrative oncology combining Ayurveda, yoga therapy, and counselling is increasingly recognized in Indian cancer care centres. These approaches are patient-friendly and culturally acceptable, supporting physical and emotional healing.

II. Conclusion

Stress hormones like cortisol, adrenaline, and noradrenaline play a critical role in cancer development and progression by affecting DNA stability, immune function, and the tumour microenvironment. Although stress is not a direct cause of cancer, chronic activation of the HPA and SAM systems accelerates tumour growth, angiogenesis, and metastasis, while increasing the risk of poor treatment response.

Evidence strongly supports the integration of psychological care into cancer management. Mind–body interventions, counselling, social support, and healthy lifestyle practices effectively reduce stress hormones and enhance survival quality. Therefore, addressing emotional well-being is a scientifically justified and ethically essential component of comprehensive oncology care.

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