

Stress and Cancer: Why Stress Reduction is Essential an Overview

Kshama Vairagi^{1*} Dr. Sujata Gupta Kedar²

¹Research Counsellor at Tata Memorial Hospital, University-Pebble Hills University

²Head & Associate Prof at Dept. Of human Development-Bangalore

Abstract – Mediation members effectively diminished articulation of genius incendiary and metastasis-related qualities and expanded articulation of interferon-related qualities when contrasted with controls. Interferons are proteins that enable correspondence between cells to trigger the defensive barriers of the insusceptible framework against infections, microbes, and most vital, tumor cells. As such, serious personality body, push diminishment practices can change our bodies, directly down to our cell and hereditary reactions. The impact of psychosocial factors on the advancement and movement of malignancy has been a longstanding theory since old circumstances. Truth be told, epidemiological and clinical investigations in the course of recent years have given solid proof to joins between incessant anxiety, sorrow and social segregation and tumor movement. By differentiate, there is just restricted confirmation for the part of these behavioral factors in disease start. Late cell and sub-atomic investigations have recognized particular flagging pathways that effect malignancy development and metastasis.

Keywords: Stress, Cancer, Stress Reduction.

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INTRODUCTION

The significant reason for death from malignancy is metastasis that is impervious to traditional treatment (Fidler, 2007). Essential neoplasms are organically heterogeneous and the procedure of metastasis comprises of a progression of consecutive and specific advances that couple of cells can effectively entire. The result of growth metastasis relies upon various cooperations between metastatic cells and homeostatic components that are remarkable to a given organ miniaturized scale condition (Fidler, 2002). Hence, the treatment of metastasis ought to be focused on against disease cells, as well as against the host factors that add to and bolster the dynamic development and survival of metastatic malignancy cells. Clinical and epidemiological examinations in the course of the most recent 30 years have distinguished psychosocial factors including stress, endless sorrow and absence of social help as hazard factors for tumor movement (Spiegel and Giese-Davis, 2003. Bukberg, et. al., 1984. Spiegel D., 1994. Chida, et. al., 2008). Though prove for the part of psychosocial factors in growth start is constrained and some-what opposing (Duijts, et. al., 2003. Lillberg, et. al., 2003. Geyer, 1991. Michael, et. al., 2009), bolster is more grounded for joins between mental factors, for example, stress, sadness and social disconnection and sickness movement (Steel, et. al., 2007, Satin, 2009). Chronicity of negative effect, as showed by discouraged state of

mind or sadness, seems to have more grounded associations with results than do unpleasant occasions, recommending that managed actuation of negative full of feeling pathways may give the most grounded connects to disease movement (Everson, et. al., 1996. Stommel, et. al., 2002. Watson, et. al., 1999. Buccheri, 1998). Arbitrators of stress, for example, social help, have been much of the time contemplated as for disease results. Social help alludes to a person's apparent fulfillment with social connections and is thought to assume a noteworthy part in buffering mental and natural anxiety reactions (Cohen and Willis, 1985).

The greater part of us naturally perceive the connection amongst push and the invulnerable framework. How often in your life have you contracted an icy or other viral disease soon after times of high-stretch? Presently, envision what your body experiences when presented to worry over years. Generous confirmation proposes that presentation to long stretches of stress builds rates of tumor advancement and development. How is this conceivable, you inquire?

New research indicates that stress can cause permanent changes to our genes. One hypothesis of how stress impacts on cancer development or growth

is that these genetic changes could develop in key control points in the cancer process.

Another hypothesis involves the connection between the brain, the peripheral nervous system and the body (called "psychoneuroimmunology.")

Stress and cancer development:

Scientists (psychoneuroimmunologists), believe that this is the end result of our chronically stressed-out brains sending stimulatory signals to our adrenal glands to produce stress hormones (like cortisol and epinephrine.) Long-term exposure of our cells to these hormones causes:

- Stress hormones increase the production of free radicals→DNA damage and impaired immune function
- Stress hormones increase inflammation through the production of inflammatory proteins (cytokines) →impair immune function and promote cancer growth
- Stress hormones directly impair immune cell function
- Stress hormones reduce the ability of abnormal cells to undergo apoptosis (cell death) and DNA repair, important self-regulating anticancer mechanisms
- Stress hormones stimulate the production of IGF-1 (insulin-like growth factor-1), VEGF (vascular endothelial growth factor) and other growth factors that can promote tumor cell growth

The resistant reconnaissance hypothesis (or, immunosurveillance hypothesis) proposes that at any one time inside a person, there are various cells (precancerous and harmful) that can possibly turn into a tumor if not identified and crushed by the insusceptible framework. Luckily, within the sight of a solid insusceptible framework, invulnerable cells (i.e. white platelets, characteristic executioner cells, macrophages) ensure us by distinguishing and take out these precancerous and growth cells when they recognized. Our safe framework is likewise continually shielding us from infections that can cause tumor (i.e. Epstein-Barr infection, human papilloma infection, hepatitis C infection, hepatitis B infection, human herpes infection 8 and human T-cell leukemia infection.) If our invulnerable framework is debilitated or smothered, precancerous and disease cells and tumor causing infections can wreak destruction and in the end prompt the advancement of uncontrolled malignancy cell development.

Serious anxiety, for example, happens in people determined to have post-horrendous anxiety issue (PTSD), seems to prompt perpetual changes to

qualities (DNA) that control resistant capacity. In a study(published in May 2010, in the Proceedings of the National Academy of Sciences) agents have found that people with PTSD have 6-7 fold the number of changes to qualities that control insusceptible capacity contrasted with people without PTSD. Despite the fact that the exact mechanism(s) to clarify how these hereditary changes happen is(are) not yet known, we now have information that demonstrate that PTSD can for all time change one's DNA, diminishing the capacity of their invulnerable framework.

Did you realize that having a determination of cancer can prompt post-horrible anxiety issue or cause a significant number of similar side effects that are experienced by those with this condition? There are numerous people who grow intense enthusiastic and mental reactions to their tumor determination, side effects and treatment that they can create extreme anxiety disorders. In a study (distributed in May 2010, in Pediatrics) specialists found that in a populace of more than 6,500 grown-ups, who were survivors of adolescence tumors, there was high-rate who announced signs and indications steady with a conclusion of post-awful anxiety issue (PTSD). The creators contrasted the tumor survivors with those of their unaffected kin, and noticed that the survivors had a 4-overlap higher danger of having PTSD.

Additionally confounding this photo, it is very much perceived that anxiety is related with different high-hazard practices that may expand the danger of creating growth (i.e. smoking and inordinate liquor utilize, less than stellar eating routine, absence of activity, stoutness, and so forth.) Sleep is regularly influenced as an outcome of stress, and rising information correlatedisturbed circadian rhythms with expanded occurrence of specific tumors. Modified circadian (rest wake cycle) rhythms have been appeared to influence the neurohormal hub, and therefore adjust the control of the insusceptible framework. The pineal hormone melatonin has been connected to various instruments credited to resistant improvement (i.e. expanded T and B cell insusceptibility, expanded monocyte movement, expanded NK cell action, expanded discharge of cytokines), diminishment of oxidative anxiety (free radicals), tumor cell apoptosis (cell passing/suicide) and decrease of vein development in tumors.

Stress and Cancer Progression:

Once a tumor has developed, stress may modulate neuroendocrine pathways and affect numerous mechanisms that potentially lead to the progression of cancer:

- Stress hormone stimulation of beta-adrenergic receptors (present on all cells) increases tumor growth rates

- Stress hormones increase tumor cell invasiveness and metastatic activity
- Stress hormones increase tumor blood vessel growth
- Stress hormones suppress natural killer (NK) cell activity (immune suppression)
- Stress hormones reduce the cancer-killing effects of chemotherapy on tumor cell apoptosis (cell death/suicide)

Stress may be present from diagnosis to the survivorship period, and can be associated with behavioral comorbidities and diminished quality of life (i.e. depression, fatigue, sleep disturbances, and cognitive dysfunction.) Medical complications or side effects of cancer and treatment can further exacerbate these symptoms.

Multiple studies demonstrate that chronic stress increases the rate of tumor metastases in animals with cancer. For example, norepinephrine (stress hormone) has been shown to increase the migration of breast, prostate, and colon carcinoma cells (in-vitro) and increase the incidence of prostate carcinoma lymph node metastases (in-vivo.) This phenomenon seems likely to be related to the chronic stimulation of beta-adrenergic receptors (stress hormone receptor):

- In a study (published in *Cancer Research*, September 2010), investigators from UCLA examined the effects of chronic stress in mice injected with breast cancer cells. The mice were subjected to a chronic stress model by being confined to a small cage for 2-hours each day for 20-days. During this time, they underwent injection of fluorescent-labeled breast cancer cells and then observed for metastatic spread. They compared the results to a control group of mice that were not subjected to chronic stress. The results were significantly different. The stressed mice had a 30-fold increase in the development of metastases compared to the non-stressed mice. The authors found, in the stressed mice, that cells in their immune system (i.e. macrophages) were genetically altered by the activity of stress hormones in such a way that increased the ability of the injected cancer cells to gain access to the blood system and thereby spread around the body.
- Interestingly, the researchers also tested the effects of a stress hormone blocking medication ("beta-blocker", propranolol) on the stressed mice. What they found was incredible...propranolol completely blocked the effects of stress hormones on causing the

rapid progression of cancer metastases! As propranolol is an inexpensive and widely available blood pressure medication, the authors have suggested that it may have a future role in helping to reduce the risk of cancer progression.

- Similar findings have also been reported by other groups.

Stress reduces the effectiveness of cancer drugs.

In a 2013 study, researchers discovered that mice implanted with **prostate cancer** cells and treated with a prostate cancer drug (ZSTK474) had much slower tumor growth when the mice were kept calm compared with a group of mice who were placed under stress. It appeared that in the stressed mice, the cancer cells didn't die and the drug did not slow tumor growth. In a second experiment, mice genetically modified to develop prostate cancer were used. When these mice were repeatedly stressed, the size of prostate tumors increased. When the mice were treated with a commonly used prostate cancer drug (bicalutamide), their prostate tumors decreased in size. However, if mice were subjected to repeated stress, the prostate tumors didn't respond as well to the drug.

Stress is often associated with sleeping disturbances.

Increasingly, data suggest a link between disruptions in the circadian (sleep-wake) rhythm and cancer:

- direct effects of altered hormone levels on tumor cells
- effects on tumor versus host metabolism
- neuroimmune effects resulting in cell mediated immune suppression
- increase cortisol release and expression of pro-inflammatory cytokines (i.e. IL-6, tumor growth factor-alpha), which can stimulate tumor development and progression

By reducing stress, sleep disturbances should improve and these cancer promoting effects will be diminished. (Read more about this on my blog entry on this subject.)

Why is stress reduction so important?

The resistant reconnaissance hypothesis (or, immunosurveillance hypothesis) hypothesizes that at any one time inside a person, there are various cells (precancerous and threatening) that can possibly turn into a tumor if not recognized and devastated by the safe framework. Luckily, within the sight of a sound

invulnerable framework, insusceptible cells (i.e. white platelets, normal executioner cells, macrophages) secure us by distinguishing and dispose of these precancerous and growth cells when they recognized. Our resistant framework is additionally always shielding us from infections that can cause malignancy (i.e. Epstein-Barr infection, human papilloma infection, hepatitis C infection, hepatitis B infection, human herpes infection 8 and human T-cell leukemia infection.) If our insusceptible framework is debilitated or stifled, precancerous and disease cells and tumor causing infections can wreak devastation and in the end prompt the advancement of uncontrolled malignancy cell development.

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radicals), tumor cell apoptosis (cell passing/suicide) and diminishment of vein development in tumors.

Stress reduction may improve cancer survival rates:

The effects of long-term exposure of stress hormones on our cells has not been definitely linked to the development or progression of cancer, but the evidence supporting this potential association is very compelling. It seems highly unlikely that chronic stress exacerbates nearly every other disease except for cancer.

An important meta-analysis (published in 1998, in Nature Reviews Clinical Oncology), of 165 studies on the topic of stress and cancer statistics (incidence & outcomes), reported that stress was associated with higher cancer incidence in initially healthy populations (6-21% higher) and higher cancer mortality (29-133% higher). The following study is one of the strongest pieces of evidence ever reported on the positive impact of stress reduction on cancer progression and recurrence:

- In a study (published in June 2010, in Clinical Cancer Research), investigators update the results of a fascinating experiment in which 227 breast cancer patients were randomly assigned to two groups: group 1 (received psychological interventions such as relaxation training and advice on minimizing stress in 39 therapy hours, over 12 months), group 2 (received no psychological interventions). The patients have been followed for over 11 years since their initial enrollment. Patients were reassessed every four months during year one, every six months during years two to five, and annually thereafter. In their initial publication, the authors previously reported that patients in the intervention group had a 45% reduced risk of breast cancer recurrence, improvements in multiple immune function measurements, and improvements in various quality of life outcomes.
- In this paper, the authors analyzed the patients who recurred in both groups. Incredibly, they found that those in the intervention group had a 59% reduced risk of death from breast cancer!!

The results of this important study suggest that a relatively short and inexpensive psychosocial stress reduction program may be effective in improving the survival of breast cancer patients.

The authors hypothesize that the mechanism for this improvement in survival and reduction in recurrence

is due to the positive effects of stress reduction on the immune system.

To satisfy the skeptics out there, I want to emphasize (dare I say 'stress') the point that the direct association between chronic stress, the immune system and cancer has not been definitively established, but increasingly the evidence seems to support this.

While the concept of stress is universal and readily understood, it is often a challenge to operationalize it for research. Perhaps one of the reasons for why linkages between cancer and psychological stress is not well-defined is due to the lack of clear understanding on what constitutes stress, and how stress is measured and defined. Stress is not a distinct state of mind, but is in fact a combination of various psychological components (i.e. depression, anxiety, frustration, fear, hopelessness, etc.) resulting from exposure to adversity, cognitive appraisal, behavioral characteristics and coping style, personality, social support, and emotional responses. Each of these components may be activated by different emotional or physical experiences and can involve different neural pathways, ultimately leading to complex downstream physiological effects.

Stress reduction improves quality of life:

Regardless of whether stress reduction techniques are able to improve cancer outcomes, there is no doubt that they can greatly improve quality of life. Stress reduction techniques can involve any of variety of effective options, such as: massage therapy, meditation, guided imagery, yoga, cognitive based therapies, prayer, walking on the beach, and many others. Here are three studies looking at just one of these stress reducing modalities, yoga:

- A recent study reported that breast cancer survivors who practiced yoga for 3-months had a significant reduction in cancer related fatigue and improved vigor. This reduction in fatigue is thought to be due to yoga's effects on the immune and neuroendocrine systems (likely through increased physical activity and stress reduction).
- A short, 4-week yoga course has also been reported to improve sleep quality and fatigue after cancer treatment.
- An 8-week yoga course was reported to reduce salivary cortisol (stress hormone) levels, improve emotional well-being and reduce fatigue after cancer treatment.

CONCLUSION

In modern lifestyle societies, chronic stress has been associated with the pathogenesis of many diseases, including cancer. Chronic stress results in the activation of specific signaling pathways in cancer cells and the tumor microenvironment, leading to tumor growth and progression.

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Corresponding Author

Kshama Vairagi*

Research Counsellor at Tata Memorial Hospital,
University-Pebble Hills University

madhuri.teenu@gmail.com