



CMA - 4

Psycho - Spiritual Oncology

Dr. Varsha Sagdeo

Professor & Head, Dept., of Surgery
Govt. Medical College, Nagpur

Dr. Varsha Sagdeo, Presently Professor, head dept. of Surgery, Government Medical College and Hospital, Nagpur. She has done Ms in General Surgery and also Specialised in D.N.B. Pediatric Surgery. With teaching experience over 28 Years, she has presented 50 research papers in national & international Conferences and over 15 Publications in various journals. She has been the Guide & Supervisor for thirty research projects for the Post Graduate students thesis in general Surgery. She is also the Coordinator, executive member, and governing Council member for different Association of Surgeons of India. She is also the recipient of different awards and honours including CVP GOLD Medal; for Best research article of Indian Journal of Surgery 1989, O.P. Taneja Gold Medal; for best research article in Urology in Indian Journal of surgery 1992; Behrampur oration Award by Orrisa State Chapter etc.,

It's no surprise that being diagnosed with cancer is stressful. A more interesting problem for many researchers is whether heightened stress can increase a person's susceptibility to cancer or worsen the prognosis of a person with cancer.

There have been many studies that have shown that your health is greatly affected by how you react to stressful events in life-setbacks or deadlines at work, conflicts and losses at home. Most people with healthy immune systems take their resistance to disease for granted, but the most common cause of a weakened immunity in healthy individuals are stress and aging.

The notion that stress exerts its adverse effects upon our health has entered popular culture in an all-pervasive way. Terms like 'stressed out', 'chill-out', 'freak-out', 'burn-out', 'adrenaline buzz', 'flight-or-fight', testify to the widespread general knowledge that the direct or indirect effects of stress can cause heart attacks, exacerbate pre-existing health complaints (arthritis, allergies, headaches) lead to depression or even be a factor in the onset and/or the outcome of cancer.

It was known to our fore fathers that a definite link exists between psychosocial stress & cancer. Galen, the famed Greek physician of the 2nd Century AD attributed cancer to a melancholy disposition. A century ago the physician, Sir James Paget wrote: 'The cases are so frequent in which deep anxiety, deferred hope and disappointment are quickly followed by the growth and increase of cancer that we can hardly doubt that mental depression is a weighty additive to the other influences favoring the development of the cancerous constitution'. Sir Heneage Ogilvie, a British surgeon, in his book, No Miracles Among Friends says: 'The instances when the first recognizable onset of cancer has followed almost immediately on some disaster, a



bereavement, the breakup of a relationship, a financial crisis, or an accident, are so numerous that they suggest that some controlling force that has hitherto kept this outbreak of cell communism in check has been removed'. J. I. Rodale, a lifetime student and author on the subject of health, collated so much material linking state of mind with cancer that he wrote a book on the subject called Happy People Rarely Get Cancer.

Dr. Lawrence Le Shan, an experimental psychologist and research specialist, noticed this link among his patients over twenty years ago. He made a preliminary test to confirm for himself the link of emotional disturbance with cancer which involved 28 subjects, 15 patients with cancer, eight patients with no cancer and five free of disease. Considering emotional factors only, he correctly selected 14 out of 15 cancer patients, having cancer. The factors he considered were: loss of a crucial relationship and loss of purpose for living, the inability to express hostility, and emotional tension over the death of a parent, not necessarily recently. In 22 years of continued research, the syndrome of despair, the bleak hopelessness of ever achieving any meaning, zest or validity in life, he found to be the predominant factor. Seventy-six percent of all cancer patients studied, Dr Le Shan said, had this syndrome as against 10% of non-cancer patients.

However in last few decades science has become more proof & statistic oriented, and in this process mind was separated from body, without realizing that it is the mind-body complex, which responds together to any situation within or outside in the surrounding.

To study the link between stress and tumor lots of animal studies were initiated, Studies in animals--mostly rats--have slowly built the case for the link between stress and the progression of cancerous tumors. Chronic and acute stressors, including surgery and social disruptions, appear to promote tumor growth. But the studies are difficult to do, say researchers, and the variables that seem to affect cancer in animals are many. Even harder is research with humans. The interactions of the many systems that affect cancer--from the immune system to the endocrine system--along with environmental factors that are impossible to control for, make sorting out the role of stress extremely difficult. In addition, researchers can't expose people to tumor cells as they do with animals. Instead, they either have to work retrospectively--interviewing people with cancer about their stress levels prior to diagnosis--or follow large numbers of people for many years until some develop cancer. To study the link between stress and tumor growth in animals, researchers expose the animals to stress, then inject them with tumor cells (or vice versa) and monitor tumor growth. In such studies, researchers find a clear connection between stress and tumor growth, but it's not as simple as: More stress equals a bigger tumor. Instead, it depends on the type and timing of the stressful experiences.

'These things are not simple,' says Emory University psychologist Jay Weiss, PhD. 'That's why the results aren't just simple and straightforward. Instead you get these interesting and



unexpected courses of tumor development.' Once researchers establish a connection between stress and cancer in animals, the next question centers on what mechanism links stress to tumor development.

The strides made within an incredibly short time by researchers elucidating the mechanisms of psycho-neuro-endocrino-immunology have succeeded in placing psychological approaches to stress management at the forefront of cancer treatment. Ader and others have fleshed out many details of how immune cells - B-cells, T-cells, natural killer cells, macrophages - communicate with the brain.^{1-2,3}

How the brain/mind/emotions communicate with the immune system is one of the hottest areas in scientific research today. Most of us are familiar with one communication mechanism which is via the endocrine system, in particular the hormone pathway from the hypothalamus (corticotrophin-releasing hormone, CRH) to the pituitary gland (adreno-cortico trophic hormone) to the adrenal medulla (HPA axis) Where, upon interactions with T- and natural killer cells, adrenaline, growth and sex hormones act upon a complex network of genes and alter immune function.^{4,5}

The other mind-immune system communication link, which was only recently discovered during the 1980s, is via nerve fibers interlaced between T cells, lymphocytes and macrophages which are linked to ganglia (nerve bundles) which are then connected to the spinal cord and thence to the brain.²⁶ These nerve pathways form an integral part of the sympathetic/parasympathetic nervous system, which, through neurotransmitters such as noradrenalin, can bind to immune cell receptors which in turn can modulate immune function . Not only is the complexity of the mind-immune communications networks enormous; the effect of one particular chemical, say, nitric oxide, may exert contradictory effects upon different components of the immune system - slow down T-cell division (immune suppression) and kill bacteria and inhibit tumour growth (immune enhancement). Furthermore, the very same stress which may affect one person negatively may actually enervate or motivate another person. There thus remain a myriad of unanswered questions in this exciting area of research.

Now, scientists also report that psychological stress may exact its toll, at least in part, by affecting molecules believed to play a key role in cellular aging and, possibly, disease development. In the study, published in the November 30 issue of Proceedings of the National Academy of Sciences, the University of California - San Francisco-led team determined that chronic stress, and the perception of life stress, each had a significant impact on three biological factors -- the length of telomeres, the activity of telomerase, and levels of oxidative stress -- in immune system cells known as peripheral blood mononucleocytes, in healthy premenopausal women.



Telomeres are DNA-protein complexes that cap the ends of chromosomes and promote genetic stability. Each time a cell divides, a portion of telomeric DNA dwindles away, and after many rounds of cell division, so much telomeric DNA has diminished that the aged cell stops dividing. Thus, telomeres play a critical role in determining the number of times a cell divides, its health, and its life span. These factors, in turn, affect the health of the tissues that cells form. Telomerase is an enzyme that replenishes a portion of telomeres with each round of cell division, and protects telomeres. Oxidative stress, which causes DNA damage, has been shown to hasten the shortening of telomeres in cell culture.

The results of the study -- which involved 58 women, ages 20-50, all of whom were biological mothers either of a chronically ill child (39 women, so-called 'caregivers') or a healthy child (19 women, or 'controls') -- were dramatic.

As expected, most women who cared for a chronically ill child reported that they were more stressed than women in the control group, though, as a group, their biological markers were not different from those of the controls. However, in one of the study's key findings, the duration of care giving -- after controlling for the age of the women -- proved critical: The more years of care giving, the shorter the length of the telomeres, the lower the telomerase activity, and the greater the oxidative stress.

Moreover, the perception of being stressed correlated in both the caregiver and control groups with the biological markers. In fact, in the most stunning result, the telomeres of women with the highest perceived psychological stress -- across both groups -- had undergone the equivalent of approximately 10 years of additional aging, compared with the women across both groups who had the lowest perception of being stressed. The highest-stress group also had significantly decreased telomerase activity and higher oxidative stress than the lowest-stress group. Oxidative stress is one of the most important factors believed to be responsible for cancer.

'The results were striking,' says co-author Elizabeth Blackburn, PhD, Morris Herzstein Professor of Biology and Physiology in the Department of Biochemistry and Biophysics at UCSF. 'This is the first evidence that chronic psychological stress--and how a person perceives stress -- may damp down telomerase and have a significant impact on the length of telomeres, suggesting that stress may modulate the rate of cellular aging.'

'Numerous studies have solidly demonstrated a link between chronic psychological stress and indices of impaired health, including cardiovascular disease and weakened immune function,' says lead author Elissa Epel, PhD, UCSF assistant professor of psychiatry. 'The new findings suggest a cellular mechanism for how chronic stress may cause premature onset of disease. Anecdotal evidence and scientific evidence has have suggested that chronic stress



can take years off your life; the implications of this study are that this is true at the cellular level. Chronic stress appears to have the potential to shorten the life of cells, at least immune cells. 'While it is not yet clear how psychological stress impacts telomeres, the team suspects stress hormones may play a role.

The psychological and the hormonal response to a specific emotional stressor (a video film on treatment of infertility, pregnancy, and delivery) were investigated in 30 women and the responses were correlated with their trait anxiety level. The experiment included a resting period before and after the stressor. The psychological response, i.e., the change in state anxiety, was in phase with the stressor and varied with the trait anxiety level. The endocrinological response, i.e., the time courses of prolactin, cortisol, and testosterone, was not in phase but varied with the trait anxiety level. Stress increases prolactin secretion. And excessive prolactin can enhance breast cancer, brain tumors and leukemia. Oxytocin regulates prolactin secretion. The effect of a specific emotional stressor on prolactin, cortisol, and testosterone concentrations in women varies with their trait anxiety.

Breast cancer patients who feel high levels of stress concerning their diagnosis and treatment show evidence of a weakened immune system compared to patients experiencing less stress, a new preliminary study shows. Researchers found that the highly stressed women had lower levels of natural killer cells than women who reported less stress. Natural killer cells are one vital weapon making up the immune system. 'Natural killer cells have an extremely important function with regard to cancer because they are capable of detecting and killing cancer cells,' said Barbara Andersen, leader of the research team and professor of psychology and obstetrics and gynecology at Ohio State University.

'These results, although preliminary, suggest that psychological stress may play a role in how the immune system responds to cancer.' Researchers want to examine whether psychological interventions can reduce stress in these cancer patients, improve immune function, and possibly even extend patient survival.

Psycho biologist Shamgar Ben-Eliyahu, PhD, of Tel Aviv University in Israel, has been working for the past decade on the link between stress, tumor development and natural killer (NK) cells. Of all the immune system cells, NK cells have shown the strongest links to fighting certain forms of the disease, specifically preventing metastasis and destroying small metastases.

Ben-Eliyahu and his colleagues have found that stress--including forced swim, surgery and social confrontation decreases NK-cell activity in rats for as little as an hour and as long as a day or two. In addition, these types of stresses also cause a two-to five-fold increase in certain types of tumors, as well as promote tumor metastasis, the researchers find.



Recently Emory's Weiss found evidence that b-lymphocytes are involved in fighting tumor cells in the lungs of rats (Cancer Research, Vol. 99, p. 1080-1089). This finding is exciting because b-lymphocytes are the immune cells that are most influenced by stress, Weiss's research suggests that b-cells can work on tumor cells in ways other than through their antibody system, which normally takes several days to kick in. Instead, he and his colleagues found, these b-cells begin working just hours after tumor cells are injected into the animals. One possible explanation is that the b-cells begin to produce a substance called interleukin 12, which is known to activate NK cells. This implies that stress-induced reductions in b-cells may influence cancer by interrupting the production of interleukin 12

Janet Keicolt-Glaser, PhD, and her husband, virologist Ron Glaser, PhD, which found that stress, impedes cells' ability to repair DNA damage. Failure to repair DNA damage is one of the first stages of cancer development, many theories say.

In addition to the research at the psycho-social level, there is now a greatly burgeoning body of published evidence which documents at the biochemical and even molecular level, how and to what extent; states of mind such as anxiety, depression and anger affect the functioning of immune cells - T-cells, B-cells, natural killer cells, and macrophages. Evidence showing that support networks act to buffer the physiological effects of stress,⁶ that bereavement affects plasma levels of cortisol and the activity of natural killer cells,⁷ that the stress of examinations reduces natural killer cell activity,⁸ and that the stress hormone prolactin accelerates the progression of prostate cancer.⁹ These studies are merely the tip of the iceberg of the extensive body of published research which has begun to document how our mind and our emotions affect our immune system our health and even our mortality.

The strides made within an incredibly short time by researchers elucidating the mechanisms of psycho-neuro-endocrino - immunology have succeeded in placing psychospiritual approaches to stress management at the forefront of cancer treatment

It has been documented in many researches that meditation reduces the stress & its all effects. It also increases natural killer cell count. It restores H.P.A. Axis diurnal rhythm. It has been recorded that the Psycho spiritual interventions reduce side effects of cyto- toxic therapy. It has been reported that it increases disease free survival.

References

1. Spiegel D. Living Beyond Limits: New Hope and Help for Facing Life-Threatening Illness. Vermillion. 1993.
2. Ader R., ed. Psychoneuroimmunology. Academic Press. 1981.



3. Ader R, Felten DL and Cohen. Interactions between the brain and the immune system. Annual Review of Pharmacology and Toxicology. 30: 561-602. 1990.
4. Madden KS, Felten SY, Felten DL, Felten PR et al. Sympathetic neural modulation of the immune system. 1. Depression of T cell immunity in vivo and vitro following chemical sympathectomy. Brain, Behavior, and Immunity. 3: 72-89. 1989.
5. Rose RM. Overview of endocrinology of stress. In Neuroendocrinology and Psychiatric disorder. Eds Brown GM et al. Raven Press. 1984.
6. Levine S, Coe C and Weiner SG. Psychoneuroendocrinology of stress: A psychobiological perspective. In Psychoendocrinology. Eds. Brush FR and Levine S. Academic Press. 1989.
7. Irwin M, Daniels M, Risch SC, Bloom E and Weiner H. Plasma cortisol and natural killer cell activity during bereavement. Biological Psychiatry. 24: 173-78. 1988.
8. Kiecolt-Glaser JK, Glaser R et al. Modulation of cellular immunity in medical students. Journal of Behavioral Medicine. 9: 5-21. 1986.
9. Webber MM. Prolactin in the etiology and progression of human prostate carcinoma. Proceedings of AACR. 27: 222. 1986.
10. G. Randolph Schrodtt, Jr; and Sandra E Sephton Psychological aspects of breast cancer Cancer of the Breast 956-966 2002

