



# NewsLetter

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## EDITORIAL

### HEALING BEYOND MEDICINES

The practice of modern medicine treats the body as a biochemical machine and physicians as specialized technicians who can repair the machine. While there have been monumental advances in the medical field as a result of this tradition. It comes at the cost of abandoning healing the ill patient, particularly when physical cure is not possible. In this era of "personalized" medicine, health care has increasingly become depersonalized.

It is estimated that one in four persons have one or more chronic health problems. These numbers will continue to increase as our population ages. With more patients suffering longer with chronic illnesses, it will become more pertinent to revive medicine's goals of healing and relief of suffering.

Undoubtedly there is confusion and skepticism regarding the role of healing in medicine. Medicine offers no definition for healing, nor does it attempt to, as it does so for science. Modern medicine considers healing beyond its domain, leaving the task of healing to alternative medicine. There has been a greater outcry from the public for more holistic and religious approaches to be integrated in conventional medicine.

In 2007 about 38% of U.S. adults (about 2 in 5) used some form of alternative medicine. These numbers can be interpreted as a growing discontent with the technologically-oriented health care system or a search for care not provided by the contemporary clinician.

Curing refers to treating a physical illness, while healing refers to the inner sense of peace and purpose, the patient finds even in the midst of an incurable condition. In 2004 Huber and her colleagues in Europe proposed a newer definition of health "health is the ability to adapt and to self-manage." This recognizes an individual's ability to cope with chronic illness and be healthy even with the presence of ongoing chronic illness or conditions. The spiritual domain is an essential domain in this definition of health. This domain refers to the ability of people to achieve individual fulfillment, meaning, and purpose.

The role of a physician requires shifting from achiever to guider and expert fixer to companion. Authority becomes genuine caring, which makes way for relief of suffering and healing. Modern medicine does not train physicians as healers. Indispensable to the art of healing is narration—listening deeply and with care to the patient's story and accompanying the patient in discovering a new meaning in it.

Medicine these days stakes legitimacy through its scientific approach. Physicians, trained as scientists focus on diagnosis, treatment, and prevention. In doing so, cure and not care, has become the primary outcome. Not every patient can be cured. With growing tide of consumerism physicians have turned into providers, patients into customers, and medicine a byproduct. The result? Health care is like

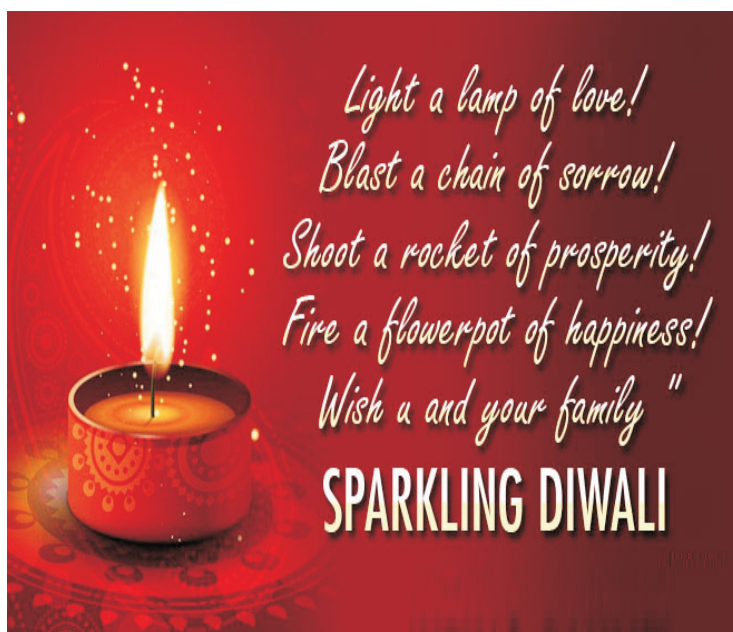
any other industry, where the principle virtue is no longer a virtue. We are removing compassion and empathy for efficiency. Medicine has become a system where parts are interchangeable and any patient can see any physician about any problem at any place at any time. Medicine must heal through our gentlest form of humanness laden with honesty, courage, and presence and not through a blind pursuit of attaining medical perfection. Patients want more from us as healer than a purely physical approach. They want us to share our hearts, souls, minds, and yes, our prayers with theirs in a collaborative process of healing. Healing beyond medicine emphasizes the importance of emotional and psychological wellness on overall health and well being. It focuses on nutrition, exercise and other tools such as quality sleep, emotional issues, reducing stress, prayer and faith, among other things to achieve its goal of wholesome wellness..

Attention all cancer patients!!

Cancer is not a death sentence. No doctor, no nutritionist heals you, your body heals you. No one talks of diet, friends, prayer, faith and love, these are inexpensive. These are free, no one talks of these. You should have that attitude that I am going to beat this anyway. Cancer has given you a chance to reinvent yourself. When we know we have cancer, we start respecting our body. Food, family, friends, meditation, sleep, nourishment, love, hope, forgiveness heal body beyond medicine!!



**Dr. A. K. Dewan**  
Director - Surgical Oncology



## PREDICTIVE IMMUNE BIOMARKERS OF RESPONSE TO IMMUNE CHECK POINT INHIBITORS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)

Head and Neck Squamous Cell Carcinoma (HNSCC) is the 6th most common cancer worldwide and commonly presents with locally advanced disease, which has a recurrence rate of around 50% despite aggressive multi-modality treatment involving surgery, radiotherapy and chemotherapy  $\pm$  EGFR inhibition. Anti- PD1 monoclonal antibodies: pembrolizumab and nivolumab got the FDA approval in 2016 for platinum-refractory recurrent/metastatic (R/M) HNSCC. Although these immune check-point inhibitors (ICI) have demonstrated tangible evidence of survival benefit in these patients, the overall response rate (ORR) ranged from 13 to 18 % and a significant proportion of patients show primary resistance to anti PD-1/PDL-1 agents. In view of potential immune related toxicities of ICI and their considerable cost, there has been a search for a validated predictive biomarker of response to these ICI. Here we discuss the role of following emerging immune biomarkers:

**1) PDL1 expression:** Most of the clinical trials evaluating ICI in R/M HNSCC have suggested an improved response rate in PDL-1 + tumors, however, the reports and data are still contentious. The data from the phase III randomized trials investigating pembrolizumab (KEYNOTE- 040 AND KEYNOTE-048) has demonstrated significant increased survival in PD-L1+ patients. The results from the phase III KEYNOTE-048 study in first line R/M HNSCC revealed that pembrolizumab monotherapy improved OS when compared with the EXTREME regimen in patients whose tumors had PD-L1 tumor proportion score (TPS)  $>1\%$  and combined positive score(CPS)  $>20\%$  .However, in KEYNOTE-040, the correlation with clinical outcome was also strongly positive when using PD-L1 expression in tumor cells only (TPS $>50\%$ ). On contrarily, CHECKMATE-141 failed to show a significant correlation in between PDL-1 expression and tumor response or survival when evaluating nivolumab in R/M HNSCC.

HPV+ Oropharyngeal Squamous Cell Carcinoma (OPSCC), have shown to have less immunosuppressive tumor microenvironment (TME) than HPV negative HNSCC and harbours greater infiltration by TILs, higher proportion of CD8+ T-cells and lower number of Tregs.

Recent trials have shown that HPV + tumors, had increased ORR to Pembrolizumab, Durvalumab while no significant ORR to Atezolizumab and Nivolumab when compared with HPV negative tumors.

**Cd8+ Tumor Infiltrating Lymphocytes (TILs) and Tregs:** Multiple immune cells coexist within the TME, including TILs (CD8+ T cells and Tregs), NK cells, macrophages, APC and myeloid-derived suppressor cells. A recent retrospective study with evaluation of 126 patients diagnosed with R/M HNSCC have shown that increased tumoral infiltration by CD8+ T cells and an increased ratio of CD8+ T cells/Tregs were positively correlated with treatment response to antiPD-1/PDL-1 agents indicating their potential role as predictive biomarkers.

Gene-expression profiling (GEP) signatures that identify tumors with a T-cell-inflamed phenotype have shown promising results in predicting response to anti-PD-1/PD-L1 agents. Despite the prognostic implications and early data suggesting correlation between TILs and response to anti-PD-1/PD-L1 therapy, prospective

validation is needed.

**Tumor Mutation Burden (TMB):** TMB is a quantitative measure of the total number of coding mutations in the tumor genome. TMB has been recently evaluated as a potential biomarker of response to ICI in prospective clinical trials and across many tumor types. Increased TMB and neoantigen load has shown a significant correlation with response to ICI in HPV negative HNSCC, while no such correlation seen in HPV positive patients. Smoking seems to contribute to a more immunosuppressive tumor microenvironment and negatively impact on anti-PD-1/PD-L1 efficacy in HNSCC.

Analyses of clinical trials evaluating pembrolizumab, atezolizumab and nivolumab in metastatic HNSCC have demonstrated not only increased ORR but also improved survival in patients with high TMB. However, the cut-off and measure used to define a high TMB differed between studies, thus precluding direct comparisons. In a retrospective analysis of 126 HNSCC patients treated with anti-PD1/PDL-1 agents, TMB was found to be significantly higher among responders (21.3 versus 8.2 mut/MB,  $P<0.01$ ) and was correlated with increased median OS (20 months if TMB $>10$  mut/MB versus 6 months if TMB $<5$  mut/MB,  $P=0.01$ ) in HPV negative disease.

**HNSCC mutational landscape:** Tumors characterized by mutations affecting DNA damage response, such as those with microsatellite instability high (MSI-H) or mismatch repair deficiency (dMMR), have the highest mutational load. These tumors have been shown to be particularly sensitive to ICI in prospective clinical trials, leading to the FDA approval of pembrolizumab for patients with dMMR or MSI-H tumors, regardless of histology. The incidence of MSI-H tumors among HNSCC has been reported to be around 8%.

**The Microbiota in HNSCC:** Retrospective cohort studies have shown different microbiota composition in the saliva of HNSCC patients compared with healthy controls. Differentially enriched microbiota found in HPV+ and HPV- OPSCC and oral cavity SCC indicates the existence of specific microbiota according to tumor location and HPV status. One study analyzing the oral microbiota present in the saliva of HNSCC patients before and after treatment (including surgery, chemoradiotherapy and ICI) showed an association between specific oral bacteria composition (Fusobacterium and Lactobacillus), down-regulation of immune-signaling pathways and upregulation of oncogenic Wnt/Beta-catenin pathways. Whether the microbiota has a role in predicting response to immunotherapy in HNSCC is yet to be determined.

To conclude, till date there are no validated predictive biomarkers of response that are applicable uniformly to all HNSCC patients, although many candidate biomarkers with promising results are undergoing investigations. Appropriate selection of patients who will benefit from these therapies is crucial.

**Dr. Gurudutt Gupta & Dr. Sunil Pasricha**  
Department of Pathology

## CME - IMA MATHURA



RGCIRC organized a CME in association with IMA Mathura, UP on Saturday, 7<sup>th</sup> September 2019 at Hotel Madhuvan, Krishna Nagar, Mathura, UP. Dr. Leena Dadhwal, Consultant – Surgical Oncology delivered a lecture on Recent Advances in Surgical Management of Breast Cancer and Dr. Sajjan Rajpurohit, Consultant – Medical Oncology spoke on Recent Advances in Systematic Cancer Treatment in the said CME. The CME was very well appreciated by the gathering.

## ANNUAL CONFERENCE OF IMA ROHINI ZONE



RGCIRC participated in Annual Conference of IMA Rohini Zone held on Sunday, 15<sup>th</sup> September 2019 at Hotel Crowne Plaza, Rohini, Delhi. Dr. Sunil K. Khetarpal, Chief of Operations & Medical Superintendent delivered a lecture on Current Healthcare Scenario in India and Dr. Abhishek Bansal, Consultant – Interventional Radiology spoke on Interventional Radiology – Treatment Paradigms to Help Your Patients.

## CONGRATULATIONS TO DR. SUNNY MALIK



Dr. Sunny Malik, Consultant - Department of Anaesthesia and Pain Medicine at Rajiv Gandhi Cancer Institute and Research Centre, Niti Bagh received “Susan Raj Young Pain Physician of the Year 2018 - 19” Award at International Conference on Recent Advances in Pain (2019) for his contribution in the field of pain management of cancer patients and raising public awareness on issues pertaining to pain and palliative care management.

## *Rajiv Gandhi Cancer Institute & Research Centre, Niti Bagh*

### PAIN AND PALLIATIVE CARE: A PILLAR IN CANCER CARE

Pain and palliative care is the need of the hour in cancer treatment because it has been found that pain is the most common symptom for which the patients land up in hospital emergency during the course of cancer treatment. Cancer pain and palliative care experts are trained in dealing with such subset of patients. They are part of multidisciplinary meetings along with oncologists (surgical, medical, radiation), radiologists, pathologists and counseling team for the discussion of treatment plans after a patient gets diagnosed with cancer.

Pain and palliative care services include relief of physical and emotional suffering, strengthening communication process between the patient - physician - pain & palliative care expert, coordinate the continuity of care across healthcare settings - hospital, home, hospice, and end of life care, prescribing opioids as per the WHO analgesic step-ladder, performing minimally invasive interventions in the form of nerve blocks and counsel the patient about alternative treatment therapies in refractory cancer pain.

Cancer pain can be managed successfully utilizing this holistic approach that includes an understanding of the pathophysiology and the type of pain, psychosocial aspects involved, the pharmacology of the pain-relieving drugs and by the use of pain relieving nerve blocks depending on the patient. It has been found that pain and palliative care services if started early in the course of cancer treatment definitely improves the quality of life of the patient.

**Dr. Sunny Malik**  
Consultant - Department of  
Anaesthesia and Pain Medicine



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## CONGRATULATIONS TO DR. MANISH SHARMA



We are pleased to inform that Dr. Manish Sharma, Consultant - Medical Oncology RGCIRC has brought laurels to RGCIRC by being awarded ANBAI DNB superspeciality gold medal award for year 2017. This award is given to a student scoring highest marks in DNB superspeciality exit examination all over India amongst all the superspecialities of Medicine. Earlier, he was also awarded President NBE gold medal award for scoring highest marks in Medical Oncology examination at National Level. We wish him best of luck for his brilliant career ahead.

## CME - NEURO ONCOPATHOLOGY



The Department of Pathology, RGCIRC, Rohini, Delhi, organized its first CME in Neuro Oncopathology on Saturday, 24<sup>th</sup> August 2019. It included didactic lectures by eminent Neuropathologist Dr. Vani Santosh, Professor, NIMHNANS, Bangalore who talked on Adult Gliomas and Embryonal Tumors. The sessions were interactive and lively with enthusiastic delegates discussing their problem areas. Director, Head of the Department and Senior Consultants from RGCIRC e.g. Dr. S. Avinash Rao, Dr. Munish Gairola, Dr. Gurudutt Gupta, Dr. Anila Sharma and Dr. Sunil Pasricha contributed immensely to make the CME an academic feast. The penultimate difficult case discussion by Dr. Vani Santosh and Dr. Garima Durga gripped the audience and were the jewel in the crown of the entire CME. The CME was attended by pathologist from Delhi and nearby states. The department plans to organize similar CME annually.



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