



CNCI Bulletin

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CHITTARANJAN NATIONAL CANCER INSTITUTE (KOLKATA)
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DIRECTOR'S MESSAGE

Dr. Jayanta Chakrabarti

Director,

Everyone Deserves Access to Cancer Care

World Cancer Day was first celebrated on February 4, 2000, at the World Summit against Cancer for the New Millennium in Paris. The main purpose of this day is to raise awareness about cancer. People are much more aware now. The number of cancer patients is increasing in our country. In 2018, the number of cancer cases in our country was 11 lakh 60 thousand, and by the end of 2020, it has increased to 13 lakh 90 thousand. The study was conducted jointly by the Indian Council of Medical Research (ICMR) and the National Centre for Disease Informatics and Research (NCDRI), Bengaluru. The number of cancer patients in India will reach 15 lakh 70 thousand by 2025.

The Union for International Cancer Control (UICC) focuses on a single agenda under 'close the care gap: Everyone deserves access to cancer care, "campaign. According to UICC, the agenda for 2024 is 'Together, we challenge those in power.' According to the World Health Organization, cancer is the second leading cause of death globally. The cancer burden continues to grow globally. However, survival rates are improving with the help of advanced diagnosis and treatment. Lung, prostate, colorectal, stomach and liver cancers are the most common types of cancer in men, while breast, colorectal, lung, cervical and thyroid cancers are the most common among women, mentions the WHO website. Tobacco use alone accounts for around one-third of deaths from cancer. Other risk factors include high body mass index, alcohol consumption, family history, some health conditions, environment, and infections by certain viruses and more. Although many forms of cancer are not preventable, some people will be diagnosed with cancer even if they lead a healthy lifestyle. Cancer risk can be lowered in a number of ways. Vaccination against Human Papilloma Virus (HPV) and regular screenings and early detection are two main key factors that help improve survival rates.



From Editors Desk



Dr. Suparna Mazumder,

Dear readers,

A new year has begun and on 4th February the world comes together to observe World Cancer Day. We are continuing the theme of Close the Care gap this year too. Our goal is to reduce the global cancer burden, a more equitable distribution of health care and a more collective effort to prevent and control this disease with increased awareness about its causes, effects and treatment opportunities.

The etiopathogenesis of cancer is still not well understood. However, here is a list of probable etiological factors linked to cancer.

FOOD for THOUGHT

Dietary factors linked to increased Cancer risk :

(Colon/Stomach/Esophagus/Breast/Endometrium/Lung)

- ↑Dietary fat/Obesity. ● ↑Red meat. ● ↓Green Veg/Fruit. ● ↓Dietary fiber.
- Contaminants (eg fungal contamination/pesticides). ● Additives (eg preservatives)

Dietary factors linked to decreased Cancer risk:

Diet rich in oleic, olive and fish oil, calcium, Vit A, Vit E&Vit C and Dietary fibers.

A few simple dietary changes depending on locoregional availability may help us to overcome the challenge ahead of us.

Probable Factors & their percentage (in USA)

Factor	Percentage
Diet	35
Tobacco	30
Virus	5
Genetic predisposition	5
Occupational hazards	4
Alcohol	3
Radiation	3
Medications	2
Pollution	2
Unknown	11

And finally I end on a word of positivity :

"Setting goals is the first step in turning the invisible into the visible".

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Let's All Move Forward in the Fight Against Cancer



Prof. Dr. Sankar Sengupta
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The relationship between cancer and microbiology has not been known for a long time. Previously, it was believed that cancer was hereditary, but later it was discovered that not all cancers are hereditary. Frances Peyton Rous, a virologist at the Rockefeller Institute for Medical Research, first observed in 1911 that viruses can create cancerous tumors in many cases. For this discovery, he was awarded the Nobel Prize in 1966. It is now well established that various microorganisms play a significant role in the development of cancer. Unknown microorganisms play an important role in tumorigenesis. In 2002, HPV accounted for the largest global cancer burden, making up 5.2% of infection-associated cancer. Besides viruses, various microorganisms are responsible for different types of cancer, including Helicobacter pylori bacteria for gastric cancer, as well as bladder and gallbladder cancer caused by helminths. Bacteria primarily cause cancer in two ways. Firstly, they induce chronic inflammation, which damages tissues and leads to carcinogenesis, where normal cells transform into cancer cells. For example, when hepatitis C virus infects the liver, it increases the rate of reactive oxygen species (ROS) and cell death signalling mutations, leading to liver scarring, which can progress to cancer. Epstein-Barr virus (EBV) infection can lead to Burkitt lymphoma, Hodgkin and non-Hodgkin lymphoma, and gastric cancer. AIDS, caused by the human papillomavirus (HIV), is responsible for Kaposi's sarcoma, non-Hodgkin and Hodgkin lymphomas, as well as cancers of the anus, liver, mouth, throat, and lungs. Additionally, human papillomavirus (HPV) has 12 strains that cause cervical, anal, penile, vaginal, and vulvar cancers. The HPV vaccine is a key weapon against this virus. The vaccine is provided at the Chittaranjan National Cancer Institute (CNCI).

I urge every child to receive this vaccine to prevent cancer. Additionally, everyone should follow cancer screening guidelines and undergo regular screenings to prevent cancer. Throughout the year, awareness camps are organized in every district by the initiative of the CNCI. Alongside girls, young boys are also being vaccinated against HPV because the virus spreads primarily through sexual contact. By providing vaccines free of charge, the spread of the disease has been largely contained in many areas. It is hoped that the World Health Organization's goal of a cancer-free world through cancer control services will soon be successful. Stay cancer-free, stay healthy. This is our earnest request on International Women's Day.

The Future of Biomedical Research in India



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India ranks high in the world for both scientific publications as well as for the number of PhD, but our lower ranks in patent filings and innovation are a matter of concern. For the research findings to be translated into innovation, there are many stumbling blocks in terms of funding and incoherent research ecosystem. Few of biomedical research generated in India are from peer-reviewed major journals and generally with least societal impact for translation from bench to bedside. According to a study by NITI Aayog and the Institute of Competitiveness, India's R&D expenditure is one of the lowest in the world. Even in the BRICS group, India's Gross Domestic Expenditure on Research and Development (GERD) is at the bottom. In 2022, India spent 0.65% of GDP on R&D, which is much lower than the world average of 1.8%. Since most of the research funding is provided by the government, challenges include inconsistent funding, multilayered hierarchical administrative approval and expenditure system, ill-defined biomedical problem definition and lack of academia-industry-clinician connect, hampering ultimate goals. Due to low transparency in funding mechanism, India's biomedical research funding sometimes don't reflect its actual health and allied biomedical challenges. Further, from 'publish or perish' culture, the world is rapidly moving

towards a 'patent, publish and prosper' culture where India has to quickly secure its seat. Unlike other countries with demonstrated technological advancements, Indian biomedical and pharma industries barely showed perseverance to develop own intellectual property portfolio through investment in R&D, rather preferred incorporation of foreign technologies. The amount spent on importing technology in terms of royalty and technology licensing fees is rising. Unless India rushes to conduct research in frontier areas in biomedical research to promote development of indigenous technology, we will miss the technology bus and continue to remain huge market space for western multinationals. As part of the 2030 Agenda for Sustainable Development, heads of state and government committed to develop ambitious national responses, by 2030, to reduce by one third premature mortality from NCDs through prevention and treatment (SDG target 3.4). Further, as per the National Health Policy 2017 of India, 25% reduction in premature mortality from cancer was proposed by 2025. But according to recent ICMR- NCDIR study, Cancer cases in India projected to rise from 14.6 lakh in 2022 to 15.7 lakh in 2025, and real incidence is likely to be 1.5 to 3 times higher than the reported cases. So, clearly the unmet needs have been realized but the implementation is yet to be reached.

A robust indigenous R&D environment is essential for attracting domestic and overseas investment, enabling the country to excel in cutting-edge technologies and promoting overall socio-economic development. It is well understood that competitive economy is led by knowledge generation, scientific innovation and self-reliance in science and technology (S&T) and 2023 has seen some crucial steps forward in this matter.

In 2023, India's G20 Presidency has seen science-specific work streams like Science 20 (S20), the

Research and Innovation Initiative Gathering (RIIG), and the Chief Science Advisors' Roundtable (CSAR). A series of crucial S20 meetings were organized with the theme "Disruptive Science for Innovative and Sustainable Development" that lead to the S20 Summit in Coimbatore followed by conferences on 'Universal Holistic Health' in Lakshadweep. Further, the main theme of RIIG was "Research and Innovation for an Equitable Society" where important role which science, technology and research play in supporting a more circular and sustainable bio-economy as also the need for innovation, were recognized. Distinctly, the CSAR, a new initiative under the Indian presidency and led by the Office of the Principal Scientific Advisor to the Government of India, focuses on addressing larger structural and policy issues impacting the science ecosystems of countries, like 'Access to Scholarly Scientific Knowledge', 'Diversity, Equity, Inclusion and Accessibility (DEIA) in Science and Technology', and 'Institutional Mechanism for the Global Science and Technology Policy Dialogue'. Similarly, the Health Working Group under the Sherpa track has identified key priorities that include preventing health emergencies, improving preparedness and response strategies, tackling antimicrobial resistance, and promoting the One Health framework.

Anusandhan National Research Foundation (ANRF), approved by the Cabinet recently and implemented by government is seen as a critical step in India's efforts to streamline its research needs and implementation process in 2023. This is in line with the newly implemented National education policy (NEP) where research and development has been given a primal importance in higher education. ANRF proposes a robust ecosystem for scientific research and merging of multiple bodies of fundings. The two main objectives of the NRF are to boost private sector contribution to research in India and ensure that a greater portion

of the funds towards State Universities and colleges. Funds for NRF will be sourced from various avenues, including contributions from industry, philanthropic foundations, international organizations, and other stakeholders. A novel Public Private Partnership (PPP) entity has been proposed for the foundation which emphasizes industry-led initiatives with government support. Only 28% of the proposed five-year allocation of Rs 50,000 crores for R&D through the NRF will be coming from the government. The private sector will finance the remaining 72% through a yet to-be-identified process. Importantly, the proposed structure seeks to establish a more robust intellectual property mechanisms and technology translation by simplifying and streamlining the Indian Patent Act of 1970 so that actionable outcomes may be resulted from biomedical research.

In 2023, The Capacity Building Commission (CBC) has been set up to create a pipeline of skilled researchers, scientists, and professionals, a workforce that can drive the creation of new technologies, products and solutions that address local and global challenges. Building scientific capacity can fuel development of industries, startups, businesses and overall economic growth and employment opportunities.

Although progress has been made, it is crucial to bridge the gap between scientific recommendations and policy implementation. It is apprehended that extensive dependence of ANRF on the private sector may lead to biased or inclined research funding and lobbying of research areas, which may not be in the best interest of equity in R&D being proposed. Still the change in biomedical research ecosystem is well welcomed by scientific communities hoping for a more meaningful contribution to Indian questions, development of transparent research funding and innovation pipelines.

Cancer Stem Cells: The Disrupter of Life Rhythm



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In the vast and intricate kingdom of the human body, where cells harmoniously dance to the rhythm of life, a sinister force named cancer silently emerges, disrupting this once peaceful dance. This disruption is not just a mere disturbance; it is a malevolent transformation of a subset of cells, leading them astray from their intended roles. These cells, now known as cancer stem cells, hold within them the seeds of chaos, possessing unique abilities to orchestrate destruction.

To truly understand this tale, one must first grasp the essence of stem cells. Stem cells, the architects of life, possess the remarkable capability to perpetuate themselves through self-renewal while also giving birth to mature cells specific to particular tissues. While they are a rarity in most tissues, their significance cannot be understated. Their elusive nature demands careful identification and purification for scientific scrutiny. Historically, the quest to pinpoint these somatic stem cells has been akin to finding a needle in a haystack, yet a few notable successes stand out. Bone marrow, previously regarded within the confines of haematopoiesis, has emerged as a potential reservoir for cells

capable of diversifying into non-haematopoietic tissues. Such discoveries hint at the profound plasticity within HSCs, challenging prior assumptions and beckoning researchers to delve deeper into their untapped potential.

However, as the scientific community unravel the mysteries of stem cells, another compelling narrative unfolds: the intricate relationship between stem cells and cancer biology. Three pivotal aspects dominate this discourse. Firstly, a striking resemblance emerges between the mechanisms governing the self-renewal of normal stem cells and those navigating cancer cells, hinting at shared pathways of regulation. Secondly, the tantalizing possibility that tumour cells might trace their origins back to normal stem cells raises questions about the roots of malignancy. Lastly and perhaps most ominously, is the concept of 'cancer stem cells.' In this intricate web of cellular interactions, the haematopoietic system serves as a focal point. Its well-characterized nature and the presence of cancers like leukaemia's offer invaluable insights.

CSCs and conventional stem cells exhibit a considerable degree of overlap in the repertoire of transcription factors and signaling pathways they employ. This molecular similarity poses a formidable obstacle to the precise discrimination and isolation of CSCs from their non-cancerous counterparts. In maximum cases, the resistance is associated with the presence of aggressive cancer cell population that develops chemo resistance and is thus responsible for unsuccessful therapies leading to decreased survival rates even after treatment. Chemotherapy targets highly proliferative cells through DNA damage, its action is limited when it is applied to slow and non-

dividing cancer cells such as CSCs. It resists the effect of a wide range of drugs such as doxorubicin, cisplatin, paclitaxel, etoposide, methotrexate and others. Therefore, following chemotherapy, which destroys the bulk of the tumour (Barbato et al. 2019), CSCs can re-initiate tumorigenic and metastatic processes. CSCs escape therapy through another charismatic figure named transporter, ABC transporters acts as master keys, allowing them to traverse barriers and smuggle unconventional cargo. For example, the ABCC1 (ATP-binding cassette transporter C1) transporter also known as MRP1 (Multi Drug Resistance Protein 1), expressed by CSCs in glioblastoma effluxes a variety of therapeutic compounds including methotrexate, edatrexate, ZD1694, idarubicin, etoposide, paclitaxel, irinotecan, hydroxyflutamide and others.

These rebellious entities (CSCs) also possess a unique ability- the power to resist the natural order of cellular life, apoptosis, the programmed cell death essential to maintain cell death for maintaining balance and health (Dragu et al. 2020). CSCs have also been shown to express higher levels of apoptotic inhibitors. The cellular Fas-associated death domain-like IL-1 β -converting enzyme (FLICE)-inhibitory protein (c-FLIP) is highly expressed in leukaemia stem cells, breast and glioblastoma CSCs. C-FLIP staves off apoptosis by preventing the formation of DISC (death-inducing signaling complex) and consequent activation of the caspase cascade via its interaction with FADD (Fas-associated death domain), caspase-8 or 10 and DR5 (Death receptor 5). CSCs also eludes the immune system, evoking a tale of evasion and subversion. Picture the immune system as a vigilant army, with the soldiers patrolling the bloodstream and tissues, ever



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watchful for signs of trouble. The CSCs, however, adapt at camouflage, mimicked normal cells, evading detection and slipping through the checkpoints and fooled the immune sentinels that were meant to identify and eliminate intruders. However, initial dedicated preclinical studies are supporting the potential targeting of CSCs by cellular immunotherapies, indirect evidence from clinical studies may be derived and new studies are ongoing. Cellular immunotherapies, especially those strategies encircling the genetic redirection with chimeric antigen receptors (CAR), hold admissible promise in several tumor settings and might in theory provide opportunities for selective elimination of CSC subsets. Immunotherapy strategies based on NK and CIK cells have the advantage over other types of autologous T cell therapies, including CAR T cells, of an intrinsic tumor-killing ability by recognizing HLA-independent inducible stress ligands. These properties extend their therapeutic value to numerous types of solid tumours (Galassi et al 2021.). Applying CARs or antibodies to NK and CIK cells, could hopefully add specificity to their tumor killing abilities.

Systemic Treatment with Radiation Therapy: Is it a MYTH?



Dr Koustav Mazumder

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An eighteen-year-old female patient came to my OPD at Chittaranjan National Cancer Institute, Kolkata (CNCI) around 12 months ago with a history of swelling at the left leg for last 6 months. According to the previous medical records, she went to a hospital in South India, where she was diagnosed with osteosarcoma (A cancer arise from bone) and underwent amputation of her left leg at the same hospital.

We advised her to have a whole-body PET CT scan and detected multiple lung metastases, which means the disease has already spread to the lung. She underwent palliative chemotherapy for 3 cycles, and response assessment showed that the lung metastasis decreased in size. After the 4th cycle, she was diagnosed with febrile neutropenia, a dreaded complication post-chemotherapy where various infections loomed large due to low wbc count. She survived the episode, and on the next cycle, she was given chemotherapy after a proper dose reduction. But she again suffered from the same complication and managed to recover from it after 1 month of admission at CNCI.

The tumor board has decided to

keep her on follow-up and to do investigations periodically. She underwent a PETCT scan, which showed that cancer increased at the lung, a new appearance of cancer at the operated site, and a single lesion at the spleen. In view of the poor general condition and previous history of severe reactions to chemotherapy, the CNCI sarcoma Tumor Board had decided to ablate the splenic lesion with a technique called Stereotactic Body Radiotherapy (SBRT). SBRT is high-dose radiotherapy that is normally delivered to any small tumor to destroy it completely. After proper pneumococcal vaccination, SBRT was delivered to the splenic lesion. It was a 14-day treatment where a total of 7 fractions of radiation were delivered on alternate days. The patient tolerated the radiation well and kept up with regular follow-up.

After 3 months of SBRT treatment, she was again advised for a whole-body PETCT scan. Interestingly, we didn't find any tumors in the whole body. At present, the patient is doing well and is on regular follow-up at our sarcoma clinic.

Why is this so Astonishing?

Radiotherapy is regarded as a localized treatment where we expect any effect or side effect to occur locally. E.g., if we give radiation to the spleen, then any effect or side effect is normally confined to the spleen only. But in this patient, we gave radiation to the spleen, but effects occurred at the lung and the primary tumor site (at the leg), both distant from the spleen. This event is called the ABSCOPAL effect.

The abscopal effect is a phenomenon in radiation therapy where localized treatment, such as radiation targeted at a specific tumor site,

leads to systemic anti-tumor effects in distant, non-irradiated areas. In other words, radiation delivered to one part of the body not only affects the targeted tumor but also attacks cancer cells in other parts of the body.

The term "abscopal" is derived from the words "ab" (away from) and "Scopus" (target). The concept of the abscopal effect in the context of radiotherapy has been recognized for several decades, but its understanding and appreciation have evolved over time. The term "abscopal" was first coined by Dr. R.H. Mole in an article published in 1953. The 1970s and 1980s brought a deeper understanding of the immune system, and researchers started to link the abscopal effect to immune-mediated responses. It became apparent that radiation could stimulate an immune response against cancer cells beyond the irradiated area.

The mechanism underlying the abscopal effect involves the immune system. Radiation can cause cell death in the irradiated area, releasing tumor-associated antigens. This may activate the immune system, specifically T cells, to recognize and attack cancer cells throughout the body, even in non-irradiated

areas. The abscopal effect is more likely to occur when the immune system is sufficiently activated and there is a favorable tumor micro environment for immune response.

Although the abscopal effect is a fascinating concept, it is relatively rare and not consistently observed in all patients undergoing radiation therapy. Researchers are actively investigating ways to enhance the likelihood of triggering the abscopal effect, such as combining radiation therapy with immunotherapy or other immune-boosting strategies.

Our patient, who is only 18 years old, was unfortunately diagnosed with metastatic cancer and could not tolerate chemotherapy. For this patient, the decision to undergo splenic radiotherapy was really a blessing, and I would like

To thank our team of doctors treating sarcoma at CNCI: Dr. Chandani Mallik (Medical Oncologist), Dr. Souradeep Gupta (Surgical Oncologist-Breast and Soft Tissue), and Dr. Amitabh Ray (Incharge, Radiation Oncology, CNCI, Newtown Campus) for their constant support in treating the patient.



Microbes and Cancer: What We Know So Far



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Cancer is one of the most prevalent diseases, representing the second leading cause of death worldwide, apart from this, it is associated with relevant social and economic burdens. Cancer is considered not one disease but several diseases. Cancer is also a multifactorial disease, resulting from a combination of genetic and environmental factors, which also contributes to tumour heterogeneity. Infections induced by certain viruses, bacteria or fungi constitute risk factors for cancer development. Globally, 15% of cancers are a result of infection with oncogenic pathogens and, in some cases, co-infection with different agents is known to increase the risk of cancer development. Thus, the study of the mechanisms of infection-mediated cancer is of particular interest, aimed at both preventing cancer and improving current treatments. The main agents in terms of cancer burden are: *Helicobacter pylori* (5%), human papilloma viruses (HPV) (5%), hepatitis B (HBV) and C viruses (HCV), (5%), Epstein-Barr virus (EBV) (1%), and human immunodeficiency virus (HIV) plus human herpes virus (HSV) (1%). Cancer associated viruses can be acquired in utero, during infancy, early childhood, or adolescence, but these agents have long latency periods before inducing carcinogenesis. On the other hand, the susceptibility to infectious

disease is higher in cancer patients. Chemotherapy is one of the most effective treatments for metastatic cancers. Cancer therapy can change the host microbiota, increasing the susceptibility to infection, due to immunosuppression, and may increase the risk for cancer development. Finally, tumour microbiome has been associated with resistance to chemotherapy.

The human organism contains more than 100 trillion microorganisms and these organisms play a significant role in human health and disease. Nevertheless, only 10 species were identified by the International Agency for Cancer Research (IARC) as carcinogenic agents to humans. These pathogenic microorganisms infect a great percentage of humans. However, most of these individuals do not develop cancer, since both the host characteristics and the microbial genotypes influence the susceptibility to develop cancer. Human microbiome disruption is associated with different types of cancer, including gastric, colorectal, pancreatic and breast cancer.

Viral Infections:

Human oncogenic viruses can drive carcinogenesis by integrating oncogenes into the host genome, according to recent publications, oncogenic viruses are responsible for nearly 12% of human cancers and are important factors in the activation of oncogenesis. DNA from certain oncogenic viruses can be integrated into the host genome, leading to the production of viral oncoproteins, which can subsequently inactivate tumour suppressor genes or activate oncogenes.

EBV was the first human virus directly implicated in carcinogenesis, and accounts for 1.8% of all cancer-related deaths worldwide. EBV is linked to several well-recognized malignancies, such as Burkitt's lymphoma and nasopharyngeal carcinoma. According to the World Health Organization (WHO), around 5%

of cancers are instigated by HPV infections. HPV infection is a global public health problem with great rates of transmission from mother to child, and it is highly associated with cervical, vaginal, vulvar, anal, rectal, penile, and oropharyngeal cancers. HPV infection is the most common sexually transmitted disease in the United States and Europe, with HPV16 and HPV18 being the higher-risk HPV types.

Both HBV and HCV are transmitted through exposure to body fluids of infected individuals. HBV infection is considered a global public health problem, due to the high rates of transmission from mother to child. Chronic HBV infection is associated with hepatocellular cancer (HCC). It has been described that 4% of untreated patients with HBV infection develop HCC. About 80% of the HCC cases are linked to chronic infections with either HBV or HCV, and both viruses have been classified by the IARC as human carcinogens. It is estimated that HBV and HCV cause 50-55% and 25-30% of all HCC, respectively. However, the mechanisms of carcinogenesis and/or cancer progression remain to be fully elucidated for both viruses.

Human immunodeficiency virus (HIV) infection is linked with acquired immune deficiency syndrome (AIDS). Kaposi sarcoma (KS) is the most frequent neoplasm among patients living with HIV infection. Additionally, the risk of anal, liver, lung, oropharyngeal cancers, and NHL and Hodgkin's lymphoma (HL) is remarkably higher in HIV-infected patients compared to the general population.

Bacterial Infections:

H. pylori infects more than 50% of the world's population, rendering it the most frequent infection in the world. It is the most central factor of gastric cancer (GC) risk; due to its characteristics, *H. pylori* can adapt to the extreme acidic conditions of the stomach, to establish infection and disturb host mucosa homeostasis, resulting in

gastric pathogenesis and ultimately cancer.

Fungal Infections:

Several publications link the presence of fungal infections with a higher risk of developing cancer. Some strains of filamentous fungi, including *Aspergillus flavus*, *Aspergillus parasiticus* and *Aspergillus nomius*, produce aflatoxins able to induce liver cancer. Other studies indicate that yeast infections are also associated with a higher risk of cancer and can promote cancer progression; such is the case of opportunistic *Candida albicans* infections. Specifically, the role of *Candida* infections has been demonstrated in lung cancer and it has been documented as a risk factor for development of oral carcinoma.

Helminth Infections:

Helminths include free-living and parasitic Platyhelminthes and Nematoda, which infect millions of people worldwide. Some Platyhelminth species of blood (*Schistosoma haematobium*, *Schistosoma japonicum*, and *Schistosoma mansoni*) and liver (*Clonorchis sinensis* and *Opisthorchis viverrini*) flukes are known to be involved in human cancers.

Overall, it seems to be clear that microbial communities that colonize the human body play a crucial role in health and disease. In healthy conditions, microbes are allies and live in dynamic equilibrium with the host. However, in disease conditions, a microbial imbalance is created and they may become faux, having the capacity to sustain disease, including cancer. Thus, "fine tuning" the human microbiome, taking advantage of the relationship with the microorganisms that colonize our body, would likely be a strategy in fighting disease in a more effective way. To master this approach, further investment in research directed to the different aspects of our interaction with the microbes is mandatory.

Indications for Platelet Transfusion Therapy



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Platelet transfusions are a commonly used medical therapy to prevent bleeding (prophylactic use), or to treat patients who are actively bleeding (therapeutic use). The most frequent use of prophylactic platelet transfusions occurs in patients with chemotherapy induced thrombocytopenia. A large proportion of platelet transfusions are administered prophylactically to reduce the risk for spontaneous haemorrhage in patients receiving chemotherapy or HSCT.

Considerable advances have been made in platelet transfusion therapy in the last 40 years, some areas continue to provoke debate, especially concerning the use of prophylactic platelet transfusions for the prevention of thrombocytopenic bleeding. Platelets are a crucial component for maintaining vascular integrity. Thrombocytopenia (low circulating platelets) can lead to bleeding symptoms like bruising, petechial, nose bleeding, bleeding gums, intracranial haemorrhage, and death. Maximum platelet life span is of 10.5 days and about 18% of the normal rate of platelet turnover is required to maintain vascular integrity. There is evidence to suggest that patients require only 7.1×10^9 platelets/l per day to maintain haemostasis. Association for Advancement of Blood and Biotherapies (AABB) has developed guidelines on the appropriate use of platelet transfusion in adult patients. There are many published platelet transfusion guidelines; however, they are not consistently being followed, lack recommendations on some clinical scenarios, or differ in the platelet threshold recommendations in some clinical settings. Platelet transfusion guidelines from different medical societies concur with strongly

recommending prophylactic platelet transfusion in the setting of severe hypo proliferative thrombocytopenia ($10,000/\text{mL}$) following chemotherapy or allogeneic bone marrow transplant. Platelet transfusion decisions, whether for prophylactic or therapeutic indications, should be weighed against the risks of transfusion side effects, refractoriness, contraindications in some clinical settings, and platelet product availability.

The dose of platelets transfused was originally based upon the perceived need to raise the patient's platelet count above a certain 'safe' threshold. Advances in understanding the mechanism of bleeding in thrombocytopenic patients have occurred. Because of the high cost, short shelf life, and higher risk for transfusion complications such as bacterial contamination, transfusion-related acute lung injury (TRALI), allergic transfusion reactions, and febrile nonhemolytic transfusion reactions, interest in reducing platelet transfusions has evolved in recent years.

Platelet transfusions are divided into Therapeutic and prophylactic. Therapeutic platelet transfusions are administered to arrest active bleeds. Currently, platelet count less than $10 \times 10^9/\text{L}$ is considered to be the trigger for prophylactic platelet transfusion by Association for Advancement of Blood and Biotherapies www.transmedcon2023.com 64 (AABB). They recommended platelets for the prevention of spontaneous bleeding in hospitalized patients with therapy induced hypo proliferative thrombocytopenia at a threshold of $10 \times 10^9/\text{L}$. Randomized controlled trials have determined that prophylactic platelet transfusions for the prevention of bleeding in chemotherapy and hematopoietic stem cell transplant patients are superior to a therapeutic approach. While in other patient groups like those in critical care who require prophylactic platelet transfusions, the optimal platelet transfusion management may differ depending upon the underlying clinical diagnosis. Platelet transfusions can have adverse effects and have cost and resource implications for health services, so unnecessary transfusions should be avoided.

The findings of the review led to the following main conclusions: Overall, a standard transfusion trigger of $10 \times 10^9/\text{L}$ appears to be as effective as a higher transfusion trigger of 20×10^9

$/\text{L}$ or $30 \times 10^9/\text{L}$ at preventing clinically significant bleeding (4). Authors found low to moderate grade evidence that a therapeutic only platelet transfusion policy is associated with increased risk of bleeding when compared with a prophylactic platelet transfusion policy in hematology patients who are thrombocytopenic due to myelosuppressive chemotherapy or HSCT.

(6) In case of thrombocytopenia wherein the platelets are not able to complete all the complex metabolic steps necessary for activation, granular release and aggregation may have increased chances of bleeding. In these circumstances, the decision whether to transfuse should be based on clinical status rather than on platelet counts.

Thrombotic thrombocytopenic purpura (TTP) has traditionally been regarded as a contraindication for platelet transfusion. Platelet transfusion is usually avoided in Heparin-induced thrombocytopenia (HIT). The transfusion of platelets in stable, non-bleeding patients with Idiopathic autoimmune thrombocytopenia (ITP) offers no benefits as the platelets are rapidly cleared by circulating antibodies.

Monitoring of the effectiveness of platelet transfusion is required to decide ongoing requirements in a given clinical condition and to identify causes of inadequate response. As some patients may have inadequate post-transfusion response and develop platelet refractoriness. Platelet refractoriness can cause significant issues in multiply transfused patients. The causes of platelet refractoriness are often multifactorial and can be grouped into non-immune and immune causes. Approximately two-thirds of refractory episodes are due to non-immune causes

which include fever, sepsis, DIC, medications etc. Approximately one-third of refractory episodes are due to immune causes. Immune causes include human leucocyte antigen (HLA) alloimmunization and/or human platelet antigen (HPA) alloimmunization due to prior exposure from pregnancy, transfusion or transplantation. Other causes include ABO incompatibility, platelet autoantibodies (e.g. autoantibody to platelet glycoprotein) and drug-related platelet antibodies. In cases of non-immune platelet refractoriness, the underlying illness must be treated. In cases of immune-mediated refractoriness, there are several strategies to consider when selecting platelets for these patients: provision of human leukocyte antigen (HLA)-matched platelets or HLA "compatible" (antigen-negative) platelets; platelets selected by crossmatch tests; and methods to reduce alloimmunization. For the treatment of immune refractoriness, an observational study identified that of the two main ways to treat, the provision of human leukocyte antigen-matched or cross-matched platelets, neither appears to be as effective as previously believed.

(7) The goal of platelet transfusions is to prevent severe and life-threatening bleeding in patients with thrombocytopenia. Platelet transfusion therapy has significantly decreased the morbidity and mortality in thrombocytopenic patients. The optimum therapeutic dose and triggers have been constantly evolving, as they are largely influenced by the cost and availability of a particular product. This aim needs to be balanced against the risks associated with platelet transfusions as well as the challenge of maintaining an adequate supply.

Indications for platelet transfusion (2)

Recommendation	Platelet count	Grade
Prophylactic	$<10,000$	Strong recommendation;
Moderate quality evidence	$<20,000$	Weak recommendation;
Elective central venous catheter placement		
Low quality evidence	$<50,000$	Weak recommendation;
Elective diagnostic lumbar puncture		Low quality evidence
Major elective non-neuraxial surgery	$<50,000$	Weak recommendation;
		Low quality evidence
Surgeries involving the central nervous system	$<80,000-1,00,000$	Low quality evidence

RRR of Oral Cancer surgery



Dr Shubhabrata Ghosh

Oral and Maxillofacial Surgeon
Department of Dentistry
and Dental Rehabilitation

(R e s e c t i o n ... R e c o n s t r u c t i o n ... R E H A B I L I T A T I O N)

You had cancer and you are alive!!! Isn't it enough?!!!"

-Is it? Is it enough.... Just to live??

Is being "disease free" the maximum we can offer our patients?

Cancers of the oral cavity and their surgeries affect the face, its esthetics and impedes all the functions involved like talking, eating, chewing, swallowing, leaving the patient struggling to perform the very basic daily chores.

This shifts our focus to another very important aspect in treating oral cancers, post treatment "Quality of Life".

To ensure an improved quality of life we have to resect adequately, reconstruct optimally and most important, plan the rehabilitation judiciously!

The central tenet of cancer rehabilitation is to help cancer patients and survivors regain and improve their physical, psychosocial and vocational

functioning with the limitations imposed by the disease and its treatment.

But, this is not the work of the surgeon alone. It needs specialists from various specialties to coordinate and work in harmony to plan and execute a proper rehabilitation. Specialists like dental oncologist, speech and swallow therapist, nutritionist, physiotherapist, psychiatrist all are corner stones of rehabilitation and they must be on the same page as the resection and reconstruction team right from the time when the treatment is planned.

Post-operative nutrition is very essential for recovery. "EATING", might sound to be a very simple activity, but to ensure a cancer patient eats properly the whole rehabilitation team needs to toil! The first step to eat is to open the mouth... and there comes the first challenge! Plastic surgeons are of the opinion that post reconstruction, a microstomia is always better than a macrostomia because of the better competence; but what about trismus?!! So many patients with good reconstructions end up having severe trismus because of post surgical and radiation induced fibrosis. It's the duty of the Physiotherapist and the Dental oncologist to start aggressive mouth opening exercises as early as possible for better results. It can be done by simple passive means like performing ice-cream stick exercises or by using active methods like using the Heister's mouth gag or by using sophisticated mouth opening appliances like the Orabite.

The next task is to make sure the food is chewed properly; and there comes the importance of the dentition! Inadequate chewing can lead to improper digestion and intum malabsorption. It is the duty of the dental oncologist to

make sure the patient has sufficient teeth in good condition for mastication. To achieve this, post operative removable or fixed prostheses can also be planned. If dental implants are being planned they have to be placed in the operation theatre during surgery so that there is good implant stability by the time adjuvant radiation is started.

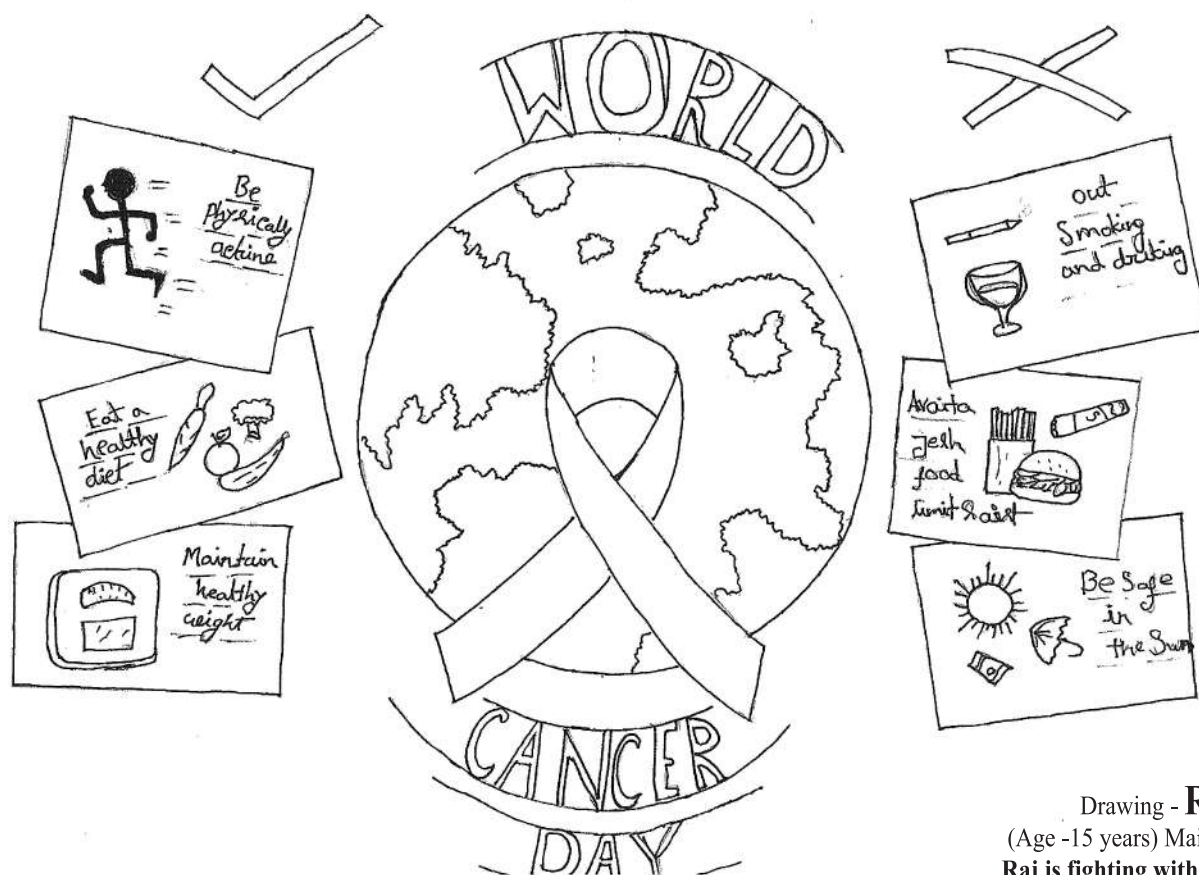
A completely different challenge arises for the dental oncologist when a part of the jaw is resected and the reconstruction if done, only replaces the soft tissue deficit. We all know, the maxilla is fixed to the cranium while mandible is the mobile jaw which moves around a bicondylar synovial joint. In case of hemi or segmental mandibulectomy defects, with time the remaining part of the mandible starts drifting to the opposite side by muscle pull which results in a scissor bite (failure of intercuspation of teeth). In these situations, even if there is sufficient dentition there will be no occlusion rendering the dentition useless as the patient can't chew!! In these situations a "Guide flange" used in initial stages of post operative rehabilitation does wonders and prohibits the swinging of the mandible. In case of maxilla, when a part of it is resected, it has to be replaced by hard or soft tissue. If not, a prosthesis (fixed or removable) is needed to stop nasal regurgitation of food and for better mastication.

Swallowing is a very complex procedure and involves various parts of the oral cavity like the tongue, hard and soft palate, oropharynx etc. In tongue cancer patients, even if the plastic surgeon manages to reconstruct the tongue to its near normal volume or shape, the biggest drawback it has is the lack of sensation! Deglutition is a complex neuro-muscular synchronised

activity which can't be induced unless there is sensation in the tongue!! Here, the swallow specialist steps in and teaches and helps the patient to adapt new maneuvers to swallow the bolus. It's important to mention here that the team ensures that there is enough saliva for bolus formation in post radiotherapy patients, which can be achieved by sialogogues or even artificial saliva.

Speech is another very important function of the oral cavity and surgical impairment of the tongue or palate affects it. For proper pronunciation of words, the tongue tip has to be functioning properly. In cases where tongue tip is preserved but its mobility is affected due to surgery, the speech therapist needs to step in and help the patient adapt. For patients whose tongue tip is reconstructed by flaps, the speech therapist needs to train to speak with the desensate soft tissue replacing the tongue tip. When the patient undergoes near total or total glossectomy, the challenge is far more complicated, as the reconstruction focuses on the bulk in the posterior one third of the tongue for swallowing. Here, the dental oncologist fabricates a tongue prosthesis and works in pair with the speech therapists to improve the patient's speech.

To conclude, in the 21st century when healthcare is improving in leaps and bounds, its insufficient only to ensure a disease free life to oral cancer patients. It becomes our duty to rehabilitate the patient and give a good quality of life to these disease free years he is leading. The first step here is to recognize and acknowledge the need for rehabilitation in oral cancer patients and work as a team so that we can RESECT adequately, RECONSTRUCT optimally and REHABILITATE appropriately...



Drawing - **Raj Dutta**
(Age -15 years) Mairapara, Andal,
Raj is fighting with Blood cancer

Palliative Care intended to Improves Quality of Life of Patients

Dr. Debasish Jatua,

MBBS,CCPPM,NFPM, FPM, CMO, Department of Anesthesiology,
Co-Principal Investigator of HBCR, CNCI & PBCR, Kolkata

Palliative care is a philosophy of Care which enables a caregiver to think of a person suffering with life-limiting chronic disease as a human being first than just only a patient.

The goal of Palliative Care is to neither hasten nor delay the death of a person but to improve the Quality of Life of a person during the course of a life-limiting chronic disease through control of Pain & other controllable symptoms associated with the illness on the basis of four Ethical pillars consisting of

Beneficence

Non-Maleficence

Autonomy & Justice

Which are omnipresent during taking any medical decisions & dispensing opioids.

Beneficence means that all medical practitioners have a moral duty to promote the course of action that they believe is in the best interests of the patient.

While Non-maleficence is the obligation of a physician not to harm

the patient to do No harm. Let us take a situation for further introspection. It is often seen in Palliative care outpatients that cancer patient come with severe constipation after ingesting the combination drug of Tramadol Paracetamol which they buy from any Medicine shop to control their unbearable pain at night.

In this scenario the best interest for sufferer is that the Constipation be relieved which itself will reduce the Pain while any drug which not cause constipation like NSAID & Paracetamol be prescribed along with a H2 receptor antagonist thus practising the principle of Beneficence.

While Removing Tramadol (less strong Opioid) which was causing the constipation by enacting a vicious cycle of pain obligated the Physician in removing the harmful vicious distressing cycle thus practising the principle of Non-maleficence.

Autonomy means that a patient has the ultimate decision making

responsibility for their own treatment because patients have the right to choose what happens to their body. A medical practitioner cannot impose treatment on a patient unless patient is deemed unable to make autonomous decisions.

While Justice is the principle that when weighing up of something; to think whether it's compatible with law, the patient's rights, and if it's fair and balanced to treat all people equally and equitably. Let us take another situation for discussion. An unmarried female patient who recently lost her job due to fun gating Cabreast; on Tramadol 200 mg/day & Lactulose syrup with moderate pain was admitted from emergency. She was prescribed Morphine 60mg/day because Equivalent dose of 200mg of Tramadol is (200/5) i.e. 40mg Morphine, so to control moderate pain half of her equivalent present dose (20mg) of Morphine i.e. (40/2) was increased along with cheaper & stimulant laxative Bisacodyl, antibiotics & referred to

Hospice which she refused.

In this scenario Hospice care was preferred by the physician to incorporate palliative medicine & nursing care together to heal her physical wound while her psychosocio-spiritual distress would have been tackled by a multi professional team of psychologist, social worker & volunteer caregivers thus providing Holistic Care thus providing her fair & balanced mode of management hence emphasising the principle of Justice.

While Since the patient decided against getting admitted in Hospice & preferred to stay in the Hospital, here her decision-making responsibility regarding what happens to her body was acknowledged by the Doctor thus practising the principle of Autonomy. Following the above mentioned medical ethics & putting them in real life practise as elaborated earlier is the key in improving the Quality of Life thus providing optimum patient care in the field of Palliative Medicine

One-Day Symposium

Emerging areas of cancer therapy and management of drug resistance



One-day symposium on "Emerging areas of cancer therapies and management of drug resistance" was organized by Chittaranjan National Cancer Institute (CNCI) in association with the Indian Association for Cancer Research (IACR)-West Bengal (WB) Chapter on 29th November, 2023 at CNCI. The program was inaugurated with the warm welcome address of the Director, CNCI and President of IACR-WB Chapter, Dr. Jayanta Chakrabarti. The symposium included two back to back technical sessions with clinical and research

perspectives. The clinical session was chaired by the IACR-WB Chapter President, Dr. Jayanta Chakrabarti. The eminent radiation oncologist and Joint Secretary, IACR-WB Chapter, Dr. Amitabh Ray, CNCI delivered an informative deliberation on "Radiobiology of Stereotactic Ablative Radiotherapy". This was followed by an insightful lecture of the surgical oncologist, Dr. Souradip Gupta, CNCI on "The Recent Advances in Surgery in Breast Cancer with the Importance of Intermediate Reconstruction of Breast following Mastectomy". The basic and translational research session was chaired by the Joint Secretary, IACR-WB Chapter, Prof. Anupam Basu, The University of Burdwan. Renowned dignitaries included Vice President, IACR-WB Chapter, Prof. Urmi Chatterjee, University of Calcutta who enlightened the audience with a fantastic deliberation on "Therapeutic bottlenecks: Overcoming with Nano formulated and Repurposed drugs". The symposium was further enriched by the invited lecture of Prof. Kartiki. V. Desai, NIBMG on "Unravelling

Transcription Networks Involved in Endocrine Therapy Resistance". The interest, significance and success of the themes discussed were evident from the fact that over 150 participants from multiple universities and institutes took part in the symposium. The program was a perfect platform for fostering professional collaborations and the exchange of insightful knowledge. The impressive and magmatic knowledge shared by the erudite

faculties enriched the students and delegates with new prospects which may be employed in cancer research and treatment. The program was concluded by a vote of thanks from the Secretary, IACR-WB Chapter, Dr. Dona Sinha, CNCI. The symposium was followed by a joint meeting of the Advisory Board and the Executive Committee of the IACR-WB Chapter with all members for smooth operation of the future endeavors.



CNCI NEWS

Ms Salini Das, SRF-CSIR received 1st prize under the category of "Best Young Scientist Paper Award" at the 46th Annual Meeting of Environmental Mutagen Society of India (EMSI) and International Conference on "Environmental Mutagenesis: Impact on Biodiversity and Human Health in a Changing World" organized by Department of Zoology, Central University of Kerala from 29-31 January 2024 under Section: Mutation Research - Genetics Toxicology and Environmental Mutagenesis. She is working under supervision of Dr. Sutapa Mukherjee, Senior Scientific Officer, Head, Department of Environmental Carcinogenesis & Toxicology Title of Oral

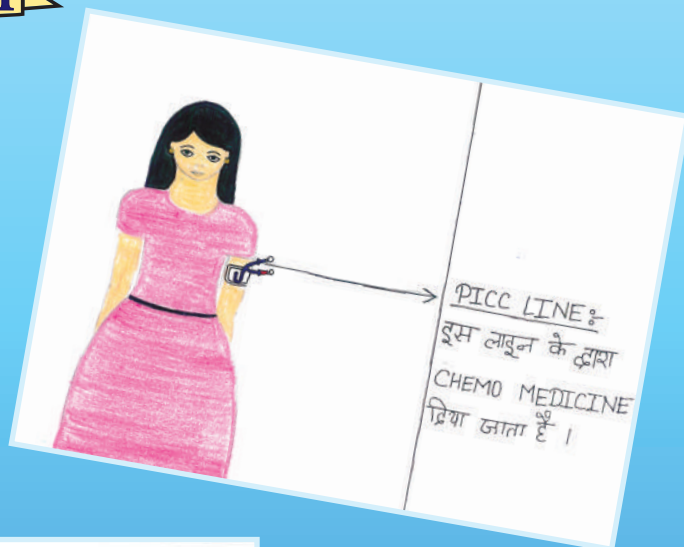
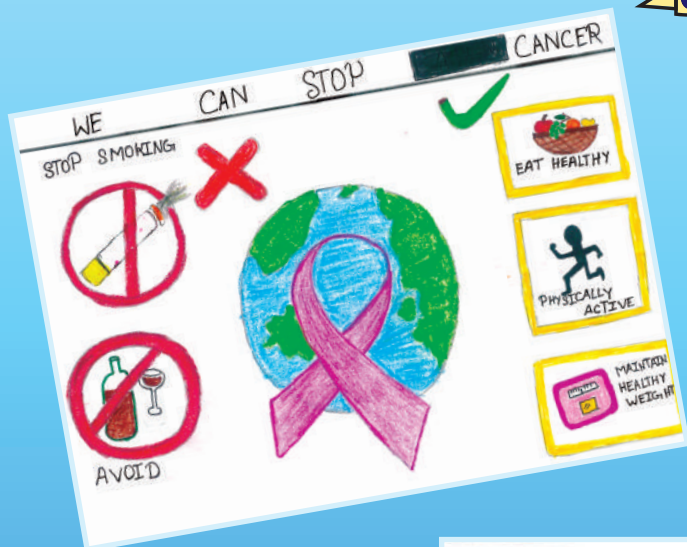


Presentation: Expressional Ratio of Human GADD45? and Aurora Kinase A in Indian Cervical Cancer Patient Cohort: Implications in Predicting Radio therapeutic Success.

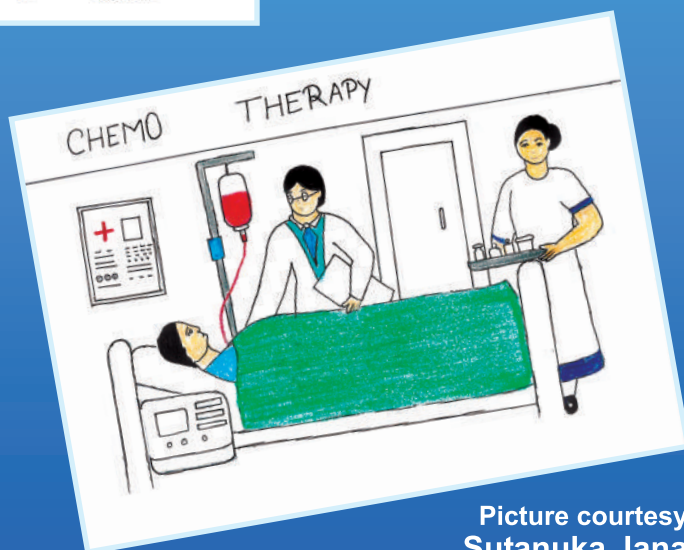
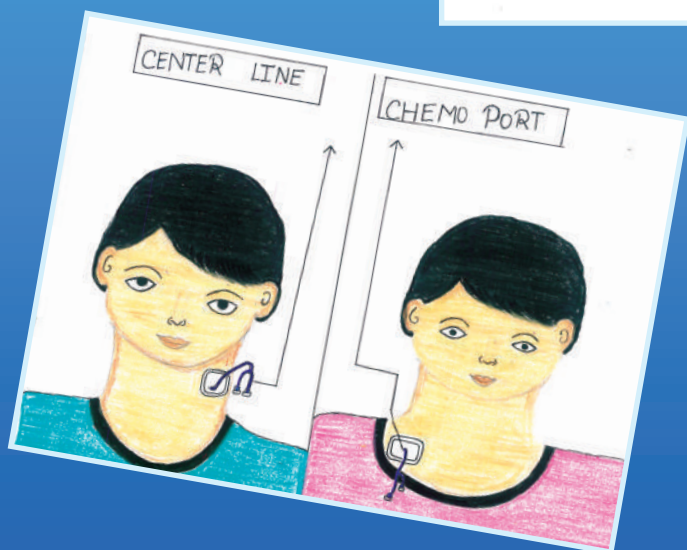
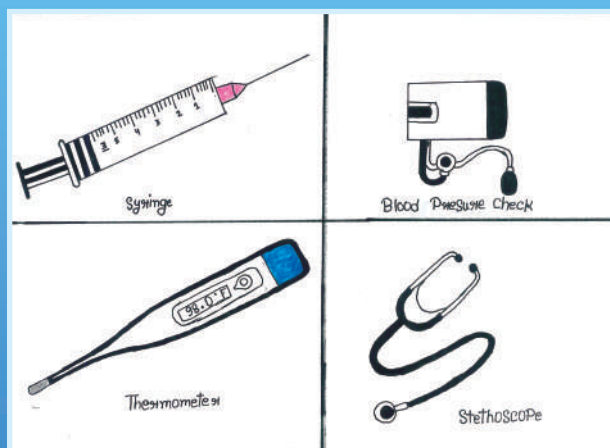
Ms. Anurima Samanta working under the supervision of Dr. Dona Sinha won the Rajanikant Shiva Prasad Baxi Young Scientist Award for poster presentation at the 43rd annual

conference of The Indian Association for Cancer Research at IISER Pune during 19-22 Jan 2024. The title of her work was "Association of DeltaNp63 with EMT, cancer stemness and chemo resistance in smokeless tobacco addicted oral squamous cell carcinoma patients".

Ms. Sukanya Ghosh working under the supervision of Dr. Dona Sinha won the award for poster presentation at the 43rd annual conference of The Indian Association for Cancer Research at IISER Pune during 19-22 Jan 2024. The title of her work was "Influence of Particulate Matter_{2.5} on pro-oncogenic signalling in rural and urban populations".



Drawing -
Sruti Kumari Pandit
(Age -12 years)
Kanaipur, Harisava, Hooghly
Sruti Kumari is fighting
with Cancer



Picture courtesy
Sutanuka Jana

CHITTARANJAN NATIONAL CANCER INSTITUTE (KOLKATA)

(An Autonomous Body under Government of India, Ministry of Health & Family Welfare)

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