Editorial

Shakuntala Chhabra

In this era of glittering technology, attempts continue for quality life for everyone, so research goes on, for preventing and curing cancers. This dreaded disease, which at one time meant call of death, has yielded to advances in screening, diagnosis as well as in multimodal management strategies. But there are increasing cancer deaths also, resulting from the overall increase in ageing populations, improved diagnosis, better reporting, and probably greater incidence because of increase in carcinogenic exposures. Since the introduction of multidisciplinary approach to cancer care, there is evidence of decrease in mortality rates and increased survival rates for many cancers. Over all treatment of cancers has undergone revolutionary alterations due to better underlying processes understanding and developments. End point of treatments is also becoming biologic (the monitoring through sera), with other noninvasive modes. If achievements of past are the prologue to possible innovations in future, the vision has to be for continued research in the fields of prevention, diagnostics, cure with emerging concepts in etiology, therapy and rehabilitation. Cancer is a multistage disease. The carcinogenesis is sometimes slow, sometimes fast. Viewed through a molecular biologic window; the activation or suppression of intrinsic cellular oncogenes leads to dysregulation of the cell cycle, proliferation, or differentiation through gene expression. Series of genetic alterations occurring within a cell through process of promotion and progression, lead to cancer. Delineating the genetic mechanisms of carcinogenesis may provide the key to early detection and may yield genetic approaches for prevention of malignant transformation. Other concepts involve the developments in the imaging techniques.

Cancer can be cured by surgery, radiation, hormones, chemotherapy, targeted therapy, including immunotherapy such as monoclonal antibodies and so on.

Choice of therapy depends on the location, grade, stage, of the cancer, and also the general state of the patient. There have been advances in each modality of cancer therapy for Quality Life (QL). Advances in surgery with better anesthesia, antibiotics, and blood replacement products, etc are focusing on refinements. Organ structure preservation has been emphasized. Surgery eliminates the cancer but it may not always be possible. At diagnosis, if cancer is metastasized to other sites of body, complete surgical excision becomes impossible.

Entire removal of cancer without damage to the other sites of the body (*i.e.*, attaining cure with near-zero adverse effects) is the ideal target of the treatment. Sometimes it can be achieved by surgery, but cancer with the propensity to invade adjacent organs or spread to distant sites, often limits this.

Moreover, for removal of the primary tumor, surgery is usually necessary to determine extent of the illness, whether it has metastasized to regional lymph nodes. Stage is the biggest determinant of prognosis needed for adjuvant therapy. Casually, palliative surgery is essential to control symptoms.

Surgery while takes out the cancer, organ elimination is a reality. Surgery can be used as the only modality and can also be performed either after or before other forms of treatment. Radiotherapy affects gonads, uterus, cervix, vagina. It can be given prior to surgery, after surgery or with chemotherpay or as the only therapeutic.

The aim of radiation is to destroy as many cancer cells as possible, limiting harm to healthy tissue. Therefore, it is given in many parts, allowing healthy tissues to recover between fractions. A radiation dose to each site depends upon number of factors, including the radio sensitivity of each cancer type and although there are tissues and organs nearby that might be damaged by radiations.

Degree of damage depends on dose, irradiation field, modality and age at exposure. Preventive modalities need to be utilized wherever possible. The dramatic advances in the field of radiation allows better treatment planning with standardization, simulation, radio sensitization *etc*. Chemotherapy is a double aged sword, while it can destroy the disease completely, vital organ damage and gonadotoxic effects are realities. Effects depend on chemotherapeutic agent's type, doses, age of the patient and organ reserve. Most chemotherapeutic agents target all quickly dividing cells are not definite to cancer cells, though some degree of specificity could come from the inability of many cancer cells to repair DNA damage. Hence, chemotherapy has the potential to damage healthy tissue, particularly those with extraordinary replacement rate (*e.g.* intestinal lining). Cells regularly overhaul themselves after chemotherapy.

Chemotherapy before surgery, neoadjuvant therapy, may provide better results of surgery. Since some medications work better together than unaided, two or more drugs are often given at the same time as a combination therapy. Cancer chemotherapy is getting better with development of new chemotherapeutic drugs with better safety profile. Newer modalities and alternative therapies are being researched keeping long term health in mind. Earlier sequences in therapy were like a relay race, with the surgeon passing the baton to the radiation oncologist, then on to the chemotherapist however the multidisciplinary approach to cancer has come as a boon to cancer care. The preplanning of protocols with integrated approach has been the major shift. The search goes on for the bullets that would blast the cancerous organs. Late effects in survivors have become of increasing concern as the mission has to be quality life. Well-coordinated and synchronized attacks are being attempted by conservative

modalities modified to prevent the need for aggressive, often mutilating surgery with a more conservative approach like trachelectomy or nerve sparing radical hysterectomy in cervical cancer.

Number of new cancer treatments are also under development. There is overall increase in the survival rates and a decrease in mortality rates. In addition, the use of a single modality is found to be sufficient in quite a number of cases. Follow up, monitoring is important. Currently, attempts are to try and prevent cancers, and if they occur, diagnose early and cure by comprehensive care.

Consequently cure with non-negligible opposing effects may be recognized as a practical aim in some cases. Also curative intent, practical goals of therapy can also comprise suppression of the cancer to a subclinical state, keeping quality life with palliative care without curative committed for advanced-stage metastatic cancers.

With better understanding of the disease and treatment processes, management strategies are being modified for improving effectiveness, precision, survivability, and quality life. Clinical trials involve many treatment modalities as new approaches, new drugs, radiation therapy, surgery, new combinations of treatments, or new approaches (*e.g.* gene therapy).

Immunotherapy, therapeutic plans to make the patient's own immune system to fight the cancer is another modality. Growth of some cancers can be reserved by blocking or providing specific hormones. Blocking or removing testosterone or estrogen is often an significant additional treatment. Management of hormone agonists, such as progestogens might be therapeutically helpful in endometrial cancer. Angiogenesis inhibitors stop the extensive development of blood vessels (angiogenesis) that tumors need for survival.

Occurrence of gynaecological cancers in young women is a reality. Another harsh truth is the impact of gynaecological cancers on reproductive health. QL including reproductive health is a complex issue especially because this is affected by therapies also.

Though the control of the signs is not typically supposed to be as the end point of cancer therapy, This is a significant determinant of the quality of cancer patients, which plays an important role in the patient's decision to undergo a particular treatment. The treatment of ovarian cancers needs to be individualized. Majority of elderly patients are able to bear the standard treatment for ovarian cancer, early surgical cytoreduction followed by platinum and taxane chemotherapy.

The aggressiveness of surgical management in some patients is an ethical dilemma and is an ongoing debate, as surgeons have apprehended increase in postoperative morbidity and mortality. Due to the apprehension and inhibition on the part of treating team the elderly patients with OC often receive suboptimal therapy. Hence there is need for standardization of cancer surgery despite the difficulties, in view of heterogeneity of the group. Fallopian Tube cancer is rare and there are no large, prospective clinical trials exclusively evaluating its treatment. Available guidelines recommend strategies similar to management for epithelial ovarian cancers (EOC). Treatment depends on stage of disease and performance status of patients. In early disease comprehensive staging is recommended while in advanced stage debulking with the aim to achieve optimal cyto-reduction should be done.

Fertility preservative surgery is a choice for selected women. When diagnosed, more than 70% of cases of endometrial cancer are stage I, with a reported 5-year survival rate of 90%.

Standard surgical method for comprehensive surgical staging should be minimally invasive surgery. For stage I or stage II endometrial cancers, adjuvant radiation does not affect overall survival, but reduces local recurrence rate. Chemotherapy improves outcomes for patients with advanced endometrial cancer. Cervical cancer needs to be treated in individualized way depending on age of patient and stage of cancer. Conservative modalities as well as extensive surgery are available options.. Chemotherapy improves results of therapy, surgical as well as radiation in cervical cancer. Since vaginal cancer is rare, strong evidence based recommendations are lacking. Radiotherapy is the primary modality for vaginal cancer. Though radical surgery may give good results in selected early stage cancer. Patients who have undergone treatment for cancer 5 of cervix or vulva need to be followed up for vaginal cancer. Advanced-stage vaginal cancer is primarily managed with definitive radiation therapy with stage specific survival rates.

Treatment of patients with vulvar cancer is thought-provoking. Indication for adjuvant treatment has to be balanced with psychosocial aspects to treat patients adequately. Clinical management is thus highly dependent on the tumor stage. The therapy mostly focuses on surgery with resection of the main tumor and staging of the groin lymph nodes.

Sentinel node barrier is considered a positive alternative for patients with clinically node negative groins. The increasing complexity of gynaecologic cancers therapy requires team approach. The goal is maintaing QL when survival is not possible. The goal of care of gynaecological cancers is to reduce morbidity and mortality. The focus is turning to the ultimate aim of prevention. The link between identification of etiologic factors and possibilities for prevention is essential. Combined efforts in research and development of laboratory, clinical and epidemiological aspects of gynaecological cancers are needed to realize these propositions. More is known about the causes unified theory of how all risk factors may operate through a final common pathway. A woman's milieu may prove to be favourable to modification at a practical level. Pain management can improve QL at any stage of cancer. Variety of modalities to treat and control pain is available. Hospice care at home in advanced cases with

poor long term prognosis is an option. Complementary and Alternative Medicines (CAM) though not a part of conventional medicine, are used specially in situations of lack of awareness or when conventional therapies are not helping. There is place for relevant research, may be reverse pharmacology also. Quality life must be incorporated into plans as early as possible in all cases of gynaecological cancers.

The special issue has the upto date information available about the treatment of most of the gynaecologic cancers. We hope that readers will be benefited reading this issue, and that it provides meaningful information which will result in the improved care of gynaecological cancer patients.

Shakuntala Chhabra
(*Guest Editor*)
Reviews on Recent Clinical Trials
Director Professor, OBGY, CEO,
Aakanksha Shishu Kalyan Kendra,
OSD, Melghat Project, MGIMS,
Sevagram, Wardha, Maharashtra,
India 442102