From the Desk of Director Research

Palliative cancer care is the integration of therapies into cancer care addressing the multiple issues that cause suffering for patients and their families and impact their life quality. “Special Feature” of this issue highlights ‘Palliative Care in Cancer’. The Institute is highly obliged to Dr Rajeev Agarwal, Sr Consultant, Sir Ganga Ram Hospital and Dr Priya John, Palliative Care Physician, Shanti Avedna Sadan, for providing “Guest Article” on ‘Hospice Care-Care of the Terminally Ill Cancer Patient’.

‘Endoscopic Ultrasonography’ profiled under “Perspective” is a relatively new endoscopic technique for a variety of diagnostic and cancer staging indications including therapeutic interventions. HPV vaccines have raised enormous hope in the medical community and public for the prevention of cervical cancer. “In Focus” brings to light ‘HPV Vaccination for Control of Cervical Cancer: Indian Scenario’.

A lecture by Dr Zvi Ram, Dept of Neurosurgery, Tel Aviv Medical Center, Israel on ‘Local Therapies for Brain Tumors’ and a CME on ‘Medico-legal Issues in Healthcare’ have been covered under “Activities of RGCI&RC”.

Pfizer Inc. is one of the world’s largest research based pharmaceutical companies. Special thanks to Pfizer Limited for funding this issue of Cancer News. We gratefully acknowledge the contributions made by Medical Director, Clinicians, Scientists and DNB Students of the Institute. Views and suggestions from readers are welcome. Happy Deepawali!

Dr D C Doval
SPECIAL FEATURE

PALLIATIVE CARE IN CANCER

Introduction

Every year, 10 million people worldwide are diagnosed with cancer and 6 million die from the disease. Fifty percent of the world’s new cancer cases occur in the developing countries. In the year 2004, over 20 lakh Indians had cancer. More than 80% were incurable at the time of diagnosis, and required palliative care. By the year 2015, the total projected prevalence of cancer in India would be 25 lakh approximately and nearly 12.5 lakh would require palliative care. Palliative care, being an urgent humanitarian need, has been included under National Cancer Control Plans as a routine part of comprehensive cancer care for all patients. Effective palliative care services are integrated into the existing health system at all levels of care.

Palliative Care

The word ‘palliative’ is derived from ‘Pallium’, a Latin word meaning ‘cloak’ or ‘cover’. Palliative care is the active total care of patients whose disease is not responsive to curative treatment. Control of pain and other symptoms, such as psychological, social and spiritual problems is paramount. Radiotherapy, chemotherapy and surgery have a place in palliative care, provided that the symptomatic benefits of treatment clearly outweigh the disadvantages. Investigative procedures are kept to a minimum. Palliative care:

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten or postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patients’ illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated; and
- enhances the quality of life, and may also positively influence the course of illness.

Palliative care has its origin in the hospice movement. In recent years, palliative care has become established in an increasing number of countries and is now a recognized specialty. Palliative care is holistic care that includes four aspects: ‘knowing’, ‘feeling’, ‘being’ and ‘doing’, all to fulfill the needs of the dying patient. It meets the needs of all the patients requiring relief from pertinent symptoms, and the needs of patients and their families for psycho-social and supportive care especially in patients with advanced stage and with very low chances of cure. Because of the emotional, spiritual, social and economic consequences of cancer and its management, palliative care services addressing the needs of patients and their families from the time of diagnosis, can improve the quality of life and the ability to cope effectively with the impending event.

WHO Definition of Palliative Care: Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems—physical, psycho-social and spiritual problems.

Principles of Palliative Care

The four cardinal principles of palliative care are:

- Non-maleficence (Do no harm)
- Beneficence (Do good)
- Patient autonomy (patient’s right to be informed and involved in decision-making)
- Justice (balancing needs of individuals with that of society)

These four cardinal principles need to be applied against a background of:

- Respect for life,
- Acceptance of the ultimate inevitability of death,
- Potential benefits of treatment as against the potential risks and burdens,
- Striving to preserve life, and
- Individual needs balanced against those of society.

Standards of Palliative Care

Institutions should develop a process ensuring that all patients have access to palliative care services from the initial visit. All cancer patients should be screened for their palliative care needs at the very first visit, at appropriate intervals, and as clinically indicated. Patients and families should be informed that palliative care is an integral part of the comprehensive cancer procedure. It should be delivered based on the clinical practice guidelines. Educational programs should be
provided to all health care professionals and trainees so that they can develop effective palliative care knowledge, skills and attitudes. Skilled palliative care specialists and interdisciplinary palliative care teams should be readily available to provide consultative or direct care to patients/families that request or require their expertise. Medical care contracts should include appropriate reimbursement for palliative care. Clinical health outcomes measurement should include palliative care domains. Quality of palliative care should be monitored by institutional quality improvement programs.

Skills Required for Palliative Care Services

The skills required for palliative care services include:

(i) Communication
(ii) Decision-making
(iii) Management of complications of treatment and the disease
(iv) Management of pain and other symptoms
(v) Psychosocial care for the patient and family
(vi) Spiritual understanding and approaches
(vii) Care of the dying
(viii) Bereavement care

Communicating with patients is a core skill of palliative care medicine. A fundamental goal of palliative care is the relief from pain and other symptoms. Improved treatment of symptoms has been associated with the enhancement of patient and family satisfaction, functional status, quality of life, and other clinical outcomes. Patients who experience spiritual and psychological distress are more likely to express a desire for death than other patients, and their family members are more likely to have an extended or complicated grief and bereavement process and are at high risk for illness and death.

Palliative Cancer Care Continuum

Patients with advanced cancer face difficult decisions regarding their treatment, and many may need to make difficult choices about end-of-life care because although cancer directed therapies are increasingly available, few provide a cure. High quality cancer care includes access to palliative care throughout the cancer care continuum, and increasing evidence suggests that timely enrollment in hospice can increase the quality of life for patients dying from cancer. Therefore, clinicians must learn to identify patients who are hospice eligible and to develop prognostication and communication skills that enable honest provider-patient dialogue about end of life options.

Primary palliative cancer care is typically provided by the palliative care interdisciplinary team, involving physicians, nurses, social workers and counsellors, home health care aides, clergy therapist and trained volunteers. Besides pain and symptom control, they provide spiritual care individualized to meet the particular requirement of patients and their families. These clinicians are skilled in core palliative care competencies, including basic symptom assessment and management, communication and decision-making skills, and knowledge about psycho-social and community services. To provide the secondary level of palliative cancer care, oncologists require more knowledge and skill to manage complex situations and interactions. When the complexity of a patient’s suffering exceeds the experience of the primary cancer care team, consultation with tertiary palliative care experts may be necessary. Services can be provided through in-patient, out-patient and home-based care.

Hospice: Palliative care for terminally ill cancer patients may be delivered by cancer physicians and specialists, specially trained palliative care physicians, through hospital or home care based Hospice Services. Hospice is a philosophy of care. It recognizes death as the final stage of life and seeks to enable patients to continue an alert, pain free life and to manage other symptoms so that their last days may be spent with dignity and quality, surrounded by their loved ones. Hospice affirms life and neither hastens nor postpones death. Hospice care treats the patient rather than the disease; it emphasizes on quality rather than length of life.

Cancer Control Knowledge into Action

The international cancer community has developed several strategies as outlined in the WHO non-communicable disease Action Plan (which includes cancer control) as the World Health Assembly and the UICC World Cancer Declaration, both of which include primary prevention, early diagnosis, treatment, and palliative care.

WHO Guide for Effective Program: Palliative care is a key component of an overall cancer control plan and program. It responds to the needs of advanced cancer patients and their families. Palliative care services should be linked to cancer prevention, early detection and treatment strategies in order to respond to all the cancer priority needs in a community and make the best use of scarce resources. Evidence-based standards of
palliative care services, focusing on improving clinical and organizational knowledge and practice are needed. Simple and low-cost public health models of palliative care can be implemented to reach the majority of the target population, particularly in low-resource settings, where most of the cases are diagnosed in late stages, with integration of palliative care services in the existing health system at all levels of care with special emphasis on community and home-based care. They involve the public and the private sector, and are adapted to the specific cultural, social and economic settings.

**National Cancer Control Program - Task Force Reports for XIth Plan:** Common barriers to access to palliative care are lack of palliative care services in most of the country, lack of awareness among professionals, administrators and the public, lack of facilities for palliative care education in the country, unrealistic narcotic regulations preventing access to opioids for those in pain; and lack of clear guidelines for those wishing to provide palliative care services.

Broad objectives to develop palliative care programs include strategies for:

(i) Formulation of palliative care policy, including involvement of non-govermental organizations
(ii) Development of palliative care delivery services, including manpower
(iii) Improved, safe, availability of opioids for pain relief
(iv) Palliative care education and training of professionals and others, including volunteers
(v) Advocacy, awareness building and community participation

**World Hospice and Palliative Care Day:** To create awareness, World Hospice and Palliative Care Day is celebrated on second Saturday of October every year. It is a unified day of action to celebrate and support hospice and palliative care around the world. Aims of World Hospice and Palliative Care Day are:

(i) To share the vision to increase the availability of hospice and palliative care throughout the world by creating opportunities to speak out about the issues.
(ii) To raise awareness and understanding of the needs – medical, social, practical, spiritual – of people living with a life limiting illness and their families.
(iii) To raise funds to support and develop hospice and palliative care services around the world.

The **theme** for 2010, which will take place on 9th October, is “Sharing the care”. It will highlight the role of individuals, such as community members, family members and health professionals as well as different organizations such as governments, funding organizations, health care centers, NGOs and hospices.

**Indian Association of Palliative Care**

The Indian Association of Palliative Care (IAPC) was formed in 1994 in consultation with World Health Organization and Government of India. It is a forum for activities aimed at the care of people with life limiting illness, such as cancer. Its mission is to promote affordable and quality palliative care across the country through networking, and support to palliative care institutions.

Keeping in mind the barriers to palliative care, IAPC has identified the following objectives for the next five years. These are:

(i) Linking palliative care to the national health policy
(ii) Integrating palliative care into all branches of medicine
(iii) Campaigning for the widespread availability of affordable morphine
(iv) Promoting the inclusion of palliative care in all relevant training programs
(v) Developing awareness of palliative care provision amongst the public

**Summary**

The worldwide need for palliative cancer care to mitigate the sufferings of patients and families living with cancer is greater than ever. It is particularly required in places where a high proportion of patients present advanced stages of the disease with little chance of cure. Ideally, palliative care services should be provided from the time of diagnosis of life threatening illness, adapting to the increasing needs of cancer patients and their families as the disease progresses into the terminal phase. They should also provide support to families in their bereavement. Effective palliative care services are integrated into the existing health system at all levels of care, especially community and home-based care, involving both public and private sector; and adapted to specific cultural, social and economic settings.

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**Philosophy of Palliative Care**

Adding “life to days” and not “days to life”

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(Reviewed by Dr Ashish Goel, Consultant; Dr AK Dewan, Senior Consultant, Dept of Surgical Oncology & Medical Director)
HOSPICE CARE – CARE OF THE TERMINALLY ILL CANCER PATIENT

Introduction

Hospice originates from the Latin word *hospes* which means host. Hospice, in the earliest days, was a concept rooted in the centuries-old idea of offering a place of shelter and rest or “hospitality” to weary and sick travelers on a long journey. In 1967, Dame Cecily Saunders, a medical professional, founded the first modern hospice, St Christopher’s, in London, whose aim was to combine the tradition of compassion that characterised the medieval hospice, with the achievements of modern medicine, in the service of relieving the suffering of terminally ill patients and their families.

Living with cancer is a journey that goes beyond the domains of physical definitions and limitations. It is a journey that the patient does not take alone. The family, friends and the team of health professionals commit to walk alongside. But at the onset of this journey, definitions are required for a better understanding and an acceptance of the road that lies ahead.

Defining cancer is not simple. Textbooks define it as any malignant growth or tumor caused by abnormal and uncontrolled cell division. Once the diagnosis of cancer is made, a series of burning questions are immediately sparked off. How? Why me? Why now? What will happen? What to do now? Where to go? – These are but a few.

Cancer care begins with the oncologist and the aim of treatment options is curative. The palliative care team is involved but their role is minimal at this stage. As the journey unfolds, the interventions of the palliative care team assume a greater significance. These interventions are holistic and are aimed at the quality of life of the patient and their families. The transition from active to palliative care does not happen at a single point of time; it is a process, and its dynamics are different in every patient.

The terminally ill patient is one who has come to that part of the journey where the road ahead is now limited. Technically it means that the patient has a disease which is progressive and is not responsive to curative treatment anymore. For this part of the journey, the health professionals and the family, aim to provide support. The support is to ensure a peaceful, comfortable and dignified end to the journey. For the patient, it has a special meaning because it is rationed and therefore emotionally laden.

Hospice Care

Hospice care is an approach. It is a philosophy of care which can be rendered either in a separate institution, a main hospital, in the community or at home. Hospice care seeks to incorporate all the principles of palliative care which address physical, psycho-social, spiritual and emotional problems. In every hospice there is:

*Ongoing meticulous efforts to control the patient’s symptoms:* The patient’s symptoms are varied and need to be controlled. More importantly, symptoms need to be pre-empted. Pain is one of the main symptoms but other problems like nausea, vomiting, constipation, agitation, breathlessness, anorexia etc are all equally distressing. The physician is required to have a comprehensive knowledge of symptom control and an in-depth understanding of every drug prescribed. The use of controlled drugs like opioids is common in palliative care and only a physician can prescribe it. It is important to keep the drug regime as simple and as effective as possible.

*Maximum regard for the patient and the family in identifying the sources of distress and shaping the treatment program:* Keeping the communication gates open is of paramount importance. In the care of the terminally ill patient, the health care team will discover that not everything that hurts can be treated with analgesics. The understanding of ‘total pain’ by the health care team will lead them to respond better to the physical, emotional and spiritual pain of the patient and their families. Listing not only symptoms but also the fears and concerns of the patient will go a long way in providing holistic care. Thus to shape an adequate treatment program the team must comprise of a doctor, nurses, a social worker, a counselor, a spiritual leader and therapists (physio/occupational/dietitian/pharmacist etc). Community volunteers can also become part of the team and improve its effectiveness.

*Establishing relations of full trust between patient and family and the health care team:* There is no place for dishonesty in palliative care because it destroys trust between the patient and the doctor and the family. The patient is entitled to the truth and including him/her
A commitment to offering a place of security, peace and comfort for the patient and his family: The patient and his family should be made to feel at home. This sense of security is essential. Comfort of the patient cannot be stressed enough. If any intervention is required, like a Foley’s catheter or a Ryle’s tube or even an injection, it is important that the patient is fully agreeable to the procedure. The ethical principles of doing benefit (Beneficence), doing no harm (Non-maleficence), patient consent (Autonomy), and appropriateness of the treatment (Justice) all need to be considered when providing care to the terminally ill.

Support of the patient’s family, emotionally, socially, spiritually and practically: The interdisciplinary team approach gives the edge to providing holistic care. The concerns of the patient and the family can be practically addressed with the help of the social worker. The fears of the patient and the family, however, need to be approached differently. The counsellor and spiritual leader need to be included in this area. The availability of the team defines the success of a palliative care program and is a pre-requisite.

Care of the terminally ill patient is a discipline within medicine which requires the guidance of skilled and experienced health care professionals no less than any other branch of clinical medicine. The interdisciplinary team approach is the strength of this care and must be medically directed and nurse-centred. The use of appropriate drug regimes to alleviate symptoms and the WHO analgesic ladder approach to pain management are the cornerstones of medical care for the terminally ill. All decisions need to be patient and their family centred to provide the dignity and comfort that hospice care boasts of.

Hospice Care in India

Shanti Avedna Sadan. India’s first hospice, started in 1986 at Bombay as Shanti Avedna Ashram for palliative care/continuing care to patients with advanced and terminal cancer. It has two other branches in Delhi and Goa. Hospices as a separate institution are few in India. There are about 7-8 hospices in India. However, hospice care is provided at homes and in main hospitals all over the country. Indian Association of Palliative Care (IAPC), Calicut Medical College, is involved in promoting palliative care all over India. Training programs are conducted across the country by the IAPC, NGOs like Christian Medical Association of India and mainline hospitals, e.g., All India Institute of Medical Sciences (AIIMS), Tata Memorial Hospital, St Johns’ Medical College, Christian Medical College, Vellore. CanSupport in Delhi provides free home care services to patients with advanced cancer. Dean Foundation provides home care in Chennai. Bangalore Baptist Palliative Care Program provides in-patient, out-patient and home care to all requiring palliative care.

In conclusion, hospice care/palliative care needs to become an integral part of academic medicine and health care system as a whole.

Reference
1. Handbook of palliative care in cancer. Alexander Waller, M.D., Nancy L. Caroline, M.D.

(\textit{Dr Priya John, Palliative Care Physician, Shanti Avedna Sadan, New Delhi; Dr Rajeev Agarwal, Sr Consultant, Surgical Oncology & Palliative Care, Sir Ganga Ram Hospital, New Delhi})

Palliative Care Workshop
December 11, 2010
Venue:
Tecnia Institute, Madhuban Chowk, Rohini, Delhi
Target Audience
Cancer survivors, families of patients, volunteers, doctors & nurses in practice of Oncology
Organized by
Rajiv Gandhi Cancer Institute & Research Centre
Chairman, Organizing Committee
Dr A K Dewan, Medical Director
Contact for Details
Dr Rajni Mutneja, Organizing Secretary
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ENDOSCOPIC ULTRASONOGRAPHY

Introduction

Endoscopic ultrasound (EUS) has been in clinical use since early 1990s and has now become firmly as an established valuable tool for a variety of diagnostic and cancer staging indications. The ability to perform ultrasound-guided fine needle puncture has allowed not just tissue sampling with fine needle aspiration (FNA), but also therapeutic fine needle insertion and injection (FNI) to assist in treatment.

Equipment

EUS is carried out using specialised endoscopes called echoendoscopes. Echoendoscopes have an ultrasonic transducer attached to the tip of the endoscope. These endoscopes are typically side-viewing endoscopes, and are of two types: radial and linear. In the radial echoendoscopes the scanning plane is perpendicular to the axis of the endoscope. The images obtained are similar to those seen in CT. For many years, the radial echoendoscopes had a rotating ultrasound transducer driven by a motor. Currently, these endoscopes are electronic and do not have rotating parts, and are less prone to breakdown. There is a small accessory channel that allows for small mucosal biopsies to be performed. In linear echoendoscopes, the scanning plane is parallel to the long axis of the endoscope. The advantage of the linear echoendoscope is that endosonography-guided FNA biopsy can be performed. Linear echoendoscopes show the entire length of the biopsy needle, whereas radial echoendoscopes are only capable of showing a portion of the needle. The echoendoscope is connected to an EUS processor. Miniprobes, also known as ‘catheter probes,’’ are small-diameter (2–2.6 mm) catheters with a mechanical radial ultrasonic probe at the tip.

Indications for EUS

1. Staging of esophageal, pancreatic, gastric, bile duct, papilla of Vater and rectal cancers
2. Evaluation of submucosal lesions
3. Evaluation of extramural impressions
4. Evaluation of pancreatic lesions
5. Evaluation of thickened gastric folds
6. Chronic pancreatitis
7. Evaluation and EUS-guided FNA of lesions adjacent to esophagus, stomach, duodenum, and rectum
8. Detection of CBD stones
9. EUS-guided drainage of pancreatic pseudocysts
10. Celiac plexus block

Role of EUS in Various Clinical Conditions

Lung Cancer

EUS plays an important role in diagnosing and staging of lung lesions. EUS guided FNA of lung masses and mediastinal lymph nodes in detecting nodal involvement.

Mediastinal Masses

EUS-FNA can evaluate and biopsy various types of lesions (masses, lymph nodes, cysts, and abscesses) within the mediastinum. The most common indication for EUS of the posterior mediastinum is abnormal lymph nodes, which can be either benign or malignant. Benign lymph nodes may be reactive in nature or caused by chronic infections, such as sarcoidosis, histoplasmosis, or tuberculosis. The overall accuracy rate for diagnosing posterior mediastinal malignancy with EUS-FNA is around 93%. EUS-FNA has diagnosed malignant lymph nodes related to lymphoma and metastatic disease from primary lung, breast, colon, renal, testicular, laryngeal, pancreas, and esophageal cancer. EUS-FNA has also been used in cases of mediastinal abscesses to obtain material for culture and sensitivity.

Esophageal Cancer

Treatment and prognosis of patients with esophageal cancer is stage dependant. Accurate staging is necessary for selecting appropriate treatment. CT, PET, and EUS are used for staging of esophageal cancer. CT and PET are best used to exclude the presence of distant metastases. If distant metastases are excluded based on these imaging modalities, patients should undergo EUS for definitive T (depth of invasion and size) and N (nodal involvement) staging, and to determine if endoscopic mucosal resection is possible. EUS is the best technique and is superior to CT for locoregional staging of esophageal cancer, specifically with tumor size and invasion (T) and lymph node (N) involvement.

Pancreatic Cancer

EUS is the most sensitive method for the detection of benign and malignant pancreatic tumors. The sensitivity of EUS for the detection of pancreatic tumors ranges from 85% to 100% in different studies. EUS is better than conventional CT. Currently, pancreatic masses
are mostly biopsied by EUS-FNA. The overall sensitivity and specificity of EUS-FNA for the diagnosis of pancreatic tumors is 85% and 98%, respectively. EUS also plays a valuable role in staging of pancreatic tumors. A combination of both multidetector-row CT scan and EUS is probably the most accurate approach for assessing local tumor (T) staging and vascular invasion of pancreatic cancers. Specifically, EUS is best for assessing vascular invasion of the portal vein and splenic vein.

**Pancreatic Cysts**

Pancreatic cysts are now detected frequently because of increased use of CT and MRI. Of these lesions, 80% to 90% are pseudocysts; 10% are cystic neoplasms (serous cystadenoma, mucinous cystadenoma, mucinous cystadenocarcinoma, and intraductal papillary mucinous neoplasia). EUS has the unique ability of providing high-resolution images of the pancreatic cysts and a means of sampling the cyst and its fluid. With EUS-FNA the cystic fluid obtained can be evaluated for malignant cells, mucin stain, amylase, and carcinoembryonic antigen (CEA).

**Chronic Pancreatitis**

The diagnosis of chronic pancreatitis can sometimes be very difficult, especially in early cases of chronic pancreatitis. Different imaging techniques have been used to diagnose this disorder, including CT, MRI, magnetic resonance cholangiopancreatography (MRCP), and endoscopic retrograde cholangiopancreatography (ERCP). These imaging modalities specifically look for changes within the pancreatic parenchyma and ducts consistent with chronic pancreatitis. EUS can evaluate both the changes in the pancreatic parenchyma and the pancreatic duct for the diagnosis of chronic pancreatitis. Smaller cysts, mildly dilated side branches, and calcifications a few millimeters in size can be identified by EUS.

**Submucosal Lesions**

Diagnosis of submucosal lesions of the gastrointestinal tract is one of the main indications for EUS. The prevalence of submucosal lesions at routine endoscopy is 0.36%. EUS is the best modality for precise diagnosis of submucosal lesions. EUS is more accurate in detecting and assessing the size and location of submucosal lesions. EUS is also able to tell from which layer of the gastrointestinal wall the lesion is originating and allows for tissue sampling by FNA. It is more accurate in differentiating between submucosal tumors and extraluminal compression.

**Rectal Cancer**

As with most malignancies, treatment of rectal cancer depends on the stage of the disease. A number of studies have demonstrated that transrectal EUS is superior to CT and MRI for tumor depth and size (T) and nodal (N) staging. The accuracy of transrectal EUS for T staging ranges from 80% to 95%.

**Therapeutic EUS**

EUS is now also being used for therapeutic procedures, such as celiac plexus block, stent placement in pancreatic pseudocysts, or failed common bile duct–pancreatic duct cannulations, and chemotheraphy.

EUS has been used to perform celiac plexus block or neurolysis in patients with chronic pancreatitis and pancreatic cancer. “Celiac plexus block” is the term used when steroid and local anesthetic is injected in the celiac ganglion. In celiac plexus neurolysis, a neurolytic agent, such as alcohol, is injected. Pancreatic pseudocysts can be drained by ultrasound or CT guidance. EUS-guided drainage of pseudocysts is more commonly performed. With EUS-guided drainage, vessels present in the gastric, duodenal, or cyst wall can be visualized and avoided. The cyst wall is punctured with a needle under direct vision, reducing the risk of perforation, with subsequent placement of a pigtail catheter.

EUS has been successfully used to perform cholangiography or pancreatography in patients in whom the bile duct or the pancreatic duct cannot be cannulated during ERCP. EUS-guided injection of various antitumor agents into unresectable pancreatic cancer has been reported in clinical trials. There are case reports describing EUS-guided brachytherapy to malignant perigastric lymph nodes in a patient with recurrent esophageal cancer and EUS-guided injection of 95% ethanol into a gastrointestinal stromal tumor.

**Summary**

The convergence of endoscopy and ultrasound has provided an exciting new technology for the examination of various anatomic structures and associated diseases. EUS provides a safe procedure with excellent diagnostic capabilities based on both images and tissue diagnosis. As EUS use has expanded, there is now the ability to perform specific therapeutic interventions.

(Dr Vikram Sagar, DNB Student; Dr S Avinash Rao, Sr Consultant, Dept of Radiology; Dr A K Khurana, Sr Consultant, Dept of Gastroenterology)
Breakthrough in Cancer Research

Treatment of patients with glioblastoma multiforme (GBM) brain tumor is a major challenge as GBM is extremely difficult to manage. Researchers have made a major breakthrough in how to target and destroy GBM cancer cells without harming healthy cells. The findings allow for new possibilities in cancer research previously not known to be readily feasible. They have created a “designer protein”, a single chain protein that not only targets a specific cell type, but then invades that cell and is drawn directly to a chosen compartment without harming normal neighboring tissues. Researchers hope that it would be possible for them to design the protein in such a way that it recognizes GBM cancer cells and then delivers a drug or some other therapy into those cells in a way that will put those active agents into a specific sub-cellular compartment like the nucleus, destroying only that specific cell. This study is the first to document in a direct way both a single-chain protein that can recognize GBM cancer cells and its journey from attaching to the cell’s surface to reaching the cell’s nuclei.

(Wake Forest University, Aug 2, 2010)

GRB7 Protein in Breast Cancer

Researchers at Oregon Health and Science University (OHSU) have found that levels of growth factor receptor bound protein seven (GRB7) are important on their own as a marker for aggressive breast cancer. Previously, it was understood that patients whose breast cancer tumors tested positive for high levels of the protein human epidermal growth factor receptor-2 (HER-2), tended to have a more aggressive form of the disease than patients whose tumors did not have elevated levels of this protein. However, researchers at OHSU have found that the protein driving this aggressive form of disease is GRB7 rather than HER-2 on its own. The study shows that GRB7 protein levels are important and independent factor in determining a prognosis for breast cancer. The findings could have implications for the types of therapies used. The researchers plan to determine if high levels of the GRB7 protein influence patient response to anti-HER2 (Herceptin) therapy. The research is being advanced to provide cancer patients with personalized treatments that target the specific characteristics of their disease.

(BreakThrough Digest Medical News, July 21, 2010)

Leptin Linked to Colorectal Cancer

According to researchers in Italy, leptin may promote colorectal cancer. Leptin is a fat tissue-derived pleuripotent cytokine that normally increases in obese or overweight individuals. While researchers have known that obesity increases the risk for the development of colon cancer, the underlying molecular mechanisms have remained unclear. A collaborative study of researchers has found that an increase in leptin may promote colorectal neoplasms by activating cancer stem cells, which constitute a small subfraction of tumor cells. Since targeting cancer stem cells may be translationally relevant strategy to improve clinical output, interfering with leptin signaling by targeting leptin receptors might become a novel attractive option for colorectal cancer treatment, particularly in obese patients. Cancer stem cells have been identified in several human malignancies. Researchers would test the effects of leptin antagonist compound on colon cancer stem cells and also study the results of leptin stimulation on cancer stem cells isolated in other cancer tissues.

(Sbarro Health Res Org, July 21, 2010)

New Probe for Cancer Detection

University of California Davis researchers have developed a laser probe for the early detection of oral cancer. A trial with human subjects showed that the device could also be used during surgery to locate the edges of a tumor. The fibre-optic probe stimulates molecules in the patient’s tissues with a laser. Some of these molecules naturally respond by re-emitting fluorescent light. The device rapidly detects and analyzes this light using a process called “time-resolved fluorescence spectroscopy”, which provides information about the types of molecules present. During surgery, blood can distort the intensity of the fluorescence signal but not its duration. By using sensitive measurements of the change in fluorescence over time, surgeons can see the tumor margins even as they are cutting the tissue. Based on the encouraging results in animal tests, the researchers recruited nine human volunteers from among patients who arrived for surgical therapy of the mouth, throat and larynx. They compared readings from spectroscopy with biopsy samples from the same locations and found that the probe could accurately diagnose the cancer in the surgical environment.

(Medical News Today, Aug 6, 2010)
NEW TECHNOLOGIES

DIAGNOSTICS

Detection of Kidney Cancers

The ability to distinguish pre-operatively between aggressive and less aggressive kidney masses is a critical clinical challenge. The PET imaging with 124 I-girentuximab (REDECTANE) antibody, is a cutting edge type of molecular imaging tool for presurgical detection of kidney cancers. The antibody is injected intravenously and in the case of kidney cancer, it provides oncologists with superior imaging, allowing them to distinguish the aggressive renal cell carcinoma (RCC) phenotype from other renal cell subtypes and benign tumors much better than the current tests. The results of multicenter Phase 3 REDECT trial for the presurgical detection of clear cell RCC demonstrated that the use of 124 I-girentuximab with PET/CT imaging can help distinguish clear cell RCC, the predominant variant of kidney cancer, from other types of benign or malignant kidney masses. The technology may also aid in more precise diagnosis of tumor stage, detecting early, otherwise undetectable, metastatic deposits. Such strategies can avoid unnecessary surgeries and guide individualized patient management.

(Science Daily, June 1, 2010)

Early Detection of Cancer

UK researchers have developed a leads to groundbreaking blood test which would aid the detection of cancer as much as five years earlier than current testing methods such as mammography and CT scans. The University of Nottingham spin-out company, Oncimmune Ltd has developed a new technique which replicates the cancer proteins that trigger the body’s response to the disease and robotic technology to measure this response. This new technology (immuno-biomarkers) for early detection of cancer is likely to change the current paradigm of diagnosis and treatment for most solid cancers, such as lung, breast, ovarian, colon and prostate. Based on early work, Oncimmune has successfully transformed this science into a reproducible commercial test. Initially, the test for lung cancer, EarlyCDT-Lung™ would be offered via primary care physicians and pulmonologists in the USA for high risk asymptomatic patients as well as patients who have indeterminate lung nodules, followed by launch in the UK early next year. This test along with other tests in the next few years would lead to a better prognosis for a significant number of cancer sufferers.

(The University of Nottingham, June 2, 2010)

Genetic Test in Lung Cancer

Response Genetics Inc. has developed PCR-based genetic test - ResponseDX™ - to help physicians make more informed therapeutic treatment decisions. ResponseDX: Lung™ genetic test panel detects the presence of EML4-ALK gene variants in lung cancer patients. EML4-ALK fusion genes are present in about four percent of tumors from patients with non-small cell lung cancer. These rearranged genes promote tumor cell growth and predict lack of benefit from therapies that inhibit epidermal growth factor receptor activity. This genetic panel gives physicians even more information to help this unique group of patients with treatment resistant lung cancer. By assessing mutations and expression levels across multiple genes, this test panel may help physicians tailor treatment to their patients, improving outcome to therapy for newly diagnosed lung cancer patients. EML4-ALK test has been accepted and used by the oncology community.

(Response Genetics, Inc, July 4, 2010)

New Blood-Based Screening Test

New version of Septin 9 methylated DNA test is new blood-based colorectal cancer screening method, developed and validated independently by ARUP Laboratories, a leader in innovative laboratory research and development. This test is clinically proven to detect a higher proportion of colorectal cancers than Septin 9 tests developed by other companies. Research has shown that half of the population that should be screened is actually being screened. This blood-based test makes the screening easier and less invasive for patients. The test can be performed without preparation by the patient, without the time commitment of an endoscopy or the need to handle one’s stool as part of a fecal test. Nine out of ten people with previously undetected colorectal cancer, including those with early stage, could be identified with this test. When detected in early stages, survival rates for colorectal cancer exceed 90 percent. This test is designed primarily for patients who cannot or will not undergo the established screening methods; it is not meant to replace colonoscopy.

(ARUP Laboratories, July 22, 2010)
**DRUGS**

**Telatinib**

Telatinib is a highly selective oral small molecule drug that inhibits the VEGFR, PDGFR and KIT receptor tyrosine kinase. It has received orphan drug designation from the US FDA for the treatment of gastric cancer. It would be the first kinase inhibitor approved for patients with this disease and is also a highly promising treatment for other solid tumor types. It is extremely selective, thus eliminating off-target side effects and providing the potential for better efficacy and superior combinability with other anti-cancer agents. Telatinib has demonstrated strong anti-tumor activity in the clinic as a single agent, including objective tumor responses. It has also demonstrated combinability at full dose with several chemotherapy regimens, including capacetabine/cisplatin without apparent additive side effects. Currently, it is in Phase 2 clinical testing in the USA and Europe for the first-line treatment of advanced gastric cancer patients in combination with standard-of-care chemotherapy. Phase 3 study for gastric cancer treatment is expected by the end of 2010, with New Drug Application filing targeted for 2013.

*(ACT Biotech, Inc, June 4, 2010)*

**Trastuzumab-DM1**

Trastuzumab-DM1 (T-DM1) an antibody-drug conjugate also known as an armed antibody, is being studied for advanced HER2-positive breast cancer. T-DM1 attaches trastuzumab and the chemotherapy DM1 together using a stable linker. The antibody binds to the HER2-positive cancer cells, and is thought to block out-of-control signals that make the cancer grow while also calling on the body’s immune system to attack the cells. When T-DM1 is absorbed into those cancer cells, it is designed to destroy them by releasing the DM1. Genentech, a member of the Roche Group, has submitted a biologics license application to the US FDA for T-DM1 in people with advanced HER2-positive breast cancer and who have previously received multiple HER2-targeted medicines and chemotherapies. This submission is based on results of a Phase 2 study, which showed T-DM1 shrank tumors in one-third of women who had received on an average 7 prior medicines for advanced HER2-positive breast cancer. The company has submitted this application to FDA for offering a potential new medicine to people with this type of breast cancer.

*(FierceBiotech, July 7, 2010)*

**TECHNIQUES**

**Innovative Imaging System**

Cancer treatments, including associated surgeries, can damage or destroy the lymphatic system leading to lymphedema. Approximately 30% of breast cancer survivors develop lymphedema. The University of Texas Health Science Center at Houston has developed cutting-edge medical imaging system, which is being studied in US FDA-approved clinical trials. Light-sensitive cameras can view a fluorescent dye as it works its way through the lymphatic system. The fluorescent light emission can be seen through the skin. The use of this system may allow clinicians to diagnose damage to a patient’s lymphatic system well before symptoms develop. As a result, doctors may be able to more accurately determine when to place patients on a different therapeutic regimen in order to avoid some of the more extreme symptoms from lymphedema. In contrast to CT and PET scanners, cameras used in this system are relatively inexpensive and easy to use. The dyes used are non-radioactive and can generate images at micro dosing levels facilitating approval of technology through the regulatory process. UT Health looks forward to working with a commercial partner to get this technology into the clinic.

*(UTHealth, July 16, 2010)*

**Prostate Surgery Without Scar**

Natural Orifice Transluminal Endoscopic Surgery (NOTES) procedure has advanced over the past several years, but it has not been done in prostate cases before, because of the challenge of rejoining or suturing the bladder back to the urethra. Physicians at Mayo Clinic in Arizona have developed specialized techniques and instruments that allow to perform NOTES procedure for treatment of prostate cancer, signaling the next step in evolution of minimally invasive surgery for prostate cancer. To perform NOTES radical prostatectomy, the instruments are inserted through the penis and an innovative technique is used to remove the entire prostate. Surgeons then rejoin the internal tissues via specialized instruments designed to work through the urethra. Patients benefit from the procedure because there are no incisions, little risk of bleeding and are usually able to leave the hospital within 24 hours. The first operated patient had no problems or complications throughout any part of the operation.

*(Mayo Clinic, July 29, 2010)*
Dasatinib for Chronic Myeloid Leukemia

Results from randomized Phase 3 DASISION trial reported at European Hematology Association Congress, showed that BCR-ABL kinase inhibitor dasatinib achieved significantly higher rates of complete cytogenetic response & major molecular response than imatinib as first-line treatment in patients with previously untreated chronic myeloid leukemia (CML). Complete cytogenetic response at 12 months was significantly higher in patients treated with dasatinib (77%) compared to those randomized to imatinib (66%). Patients treated with dasatinib were twice as likely to achieve a major molecular response (46% vs 28%). 30-50% patients with CML treated with imatinib in clinical practice do not achieve a major molecular response, underlining the need for even more effective therapies. Dasatinib as initial therapy may improve long term outcomes in patients with newly diagnosed CML. Good tolerability and once daily dosing with dasatinib would help to optimize long term adherence.

(Medical News Today, June 14, 2010)

Early Breast Cancer

According to a randomized Phase 3 trial, called TARGIT-A, for selected patients with early breast cancer, a single dose of partial breast irradiation delivered at time of breast conservative surgery (BCS) by use of targeted intraoperative radiotherapy should be considered as an alternative to external beam radiotherapy (EBR) delivered over several weeks. Women 45 years or older with invasive breast carcinoma undergoing BCS were enrolled. 1113 patients were randomly allocated to targeted intraoperative radiotherapy and 1119 to EBR. Of 996 patients who received targeted intraoperative therapy, 86% received targeted intraoperative therapy only and 14% received targeted intraoperative plus EBR. 1025 patients in EBR group received the allocated treatment. At 4 years, there were 6 local recurrences in intraoperative radiotherapy group and 5 in EBR group. Frequency of any complications and major toxicity was similar in the groups. Radiotherapy toxicity grade 3 was lower in targeted intraoperative radiotherapy group. Thus, single dose partial breast irradiation is safe for some women with invasive breast cancer.

(Lancet, July 10, 2010)

Gefitinib in Lung Cancer

A Phase 3 study conducted at Miyagi Cancer Center in Myagi, Japan, establishes the clinical benefit of gefitinib (Iressa), an EGFR tyrosine kinase inhibitor as first-line therapy in patients with non-small cell lung cancer (NSCLC) and sensitive EGFR mutations. 230 patients from 43 institution, newly diagnosed with metastatic NSCLC, were enrolled and analysed. Patients who had received gefitinib had significantly higher response rates and longer progression-free survival compared with patients who received carboplatin plus paclitaxel (73.7 percent versus 30.7 percent and 10.8 months versus 5.4 months respectively). At 1 year, 42.1 percent of patients receiving gefitinib had not progressed, compared with 3.2 percent of those receiving chemotherapy. After 2 year, all chemotherapy patients had progressed, while 84 percent of those receiving gefitinib still had not. Patients who completed their first line therapy or whose disease progressed while receiving chemotherapy were allowed to cross over and receive gefitinib. NSCLC is a rapidly progressive disease and this study establishes the clinical benefit of gefitinib as first line therapy.

(NCI Cancer Bulletin, June 29, 2010)

Prostate Cancer

Results from an international Phase 3 trial, known as Intergroup T-94-0110 study showed that adding radiotherapy to hormonal androgen deprivation therapy (ADT) improved survival in locally advanced prostate cancer. It reduced the risk of death from prostate cancer by 43 percent in men with locally advanced disease. Between 1995 and 2005, 1205 men were randomly assigned to receive ADT plus radiation or ADT alone. Most of the men had stage T3/T4 disease. After a median follow up of 6 years, 51 of the 603 men who received the combined modality therapy had died, compared with 89 of the 602 men who received ADT alone. Fewer than 2 percent of patients in either group experienced significant gastrointestinal toxicities. Patients receiving radiation had more low-grade diarrhea and rectal bleeding. The researchers projected that fewer men who received ADT plus radiation would die from their prostate cancer over 10 years than would men who received ADT alone (15 percent vs 23 percent). These results suggest that adding radiation therapy to the treatment plan for these patients could become part of standard therapy.

(NCI, July 8, 2010)
Assessment of Tumor Margins
Breast conservative surgery involves removal of the cancer with a surrounding margin of normal breast tissue. Pathological margin status is an important predictor of local recurrence. To assess surgical margins, intra-operative frozen section and touch prep cytology have not been widely adopted because of the need of a pathologist, prolonged surgical time required for specimen processing, significant technical challenges and limited coverage of the tumor margins. Because of these limitations, re-excision of the tumor site is frequently required. To address the need for robust, reliable and rapid strategies for assessing tumor margins, United States Patent No 7,751039 on optical assay system for intraoperative assessment of tumor margins, assigned to Ramanujam et al on July 6, 2010, includes a biological sample containment and illumination apparatus for holding a biological sample for illumination by a plurality of electromagnetic radiation probes. The apparatus includes a plurality of frame members positioned with respect to each other to form an interior space for receiving a biological sample.

(USPTO, July 6, 2010)

Bladder Cancer Biomarker in Urine
The inventors Goodison Steve (US) et al have been assigned Patent No US2010184049 (A1), entitled “Glycoprotein Profiling of Bladder Cancer” on July 22, 2010. Current methods in the non-invasive detection and surveillance of bladder cancer via urine analysis are a challenge because of the poor sensitivity of voided urine cytology and false positive rates of currently available protein assays. The present invention relates to a method for the diagnosis, prognosis and monitoring of bladder cancer by detecting in a urine sample from a subject at least one biomarker for bladder cancer identified herein, such as alpha-1B-glycoprotein, haptoglobin, serotransferrin, or alpha-1-antitrypsin. The biomarkers may be detected and measured using an agent that detects or binds to the biomarker protein or an agent that detects or binds to encoding nucleic acids, such as antibodies specifically reactive with the biomarker protein or a protein thereof. The invention relates to the kits for carrying out the methods of the invention as well as to a device for the rapid detection of one or more bladder cancer biomarkers in urine and methods for rapidly measuring bladder cancer biomarkers in urine.

(esp@cenet.com, July 22, 2010)

Body’s Own Cells to Fight Cancer
Medistem Panama, licensee of Medistem Inc. announced on July 7, 2010 that Dr Riordan, founder of Medistem Panama has been granted United States Patent No 7,749, 495 covering a new method for treating cancer. The new method involves taking out patient cells, manipulating them and re-introducing them into the body. This procedure, called dendritric cell therapy has demonstrated positive results in patients with metastatic renal cell carcinoma, neuroblastoma, adenocarcinoma, breast cancer, sarcoma and rectal cancer. Dr Riordan has established cancer treatment centres using dendritic cell therapy over a decade ago, yet only this year did the US Food and Drug Administration approve this approach. The CEO of Medistem Inc said that the ground breaking findings that were granted the present patent attest the successful integration of basic research and clinical practice.

(Medistem Inc., July 7, 2010)

VeriStrat® Test for Lung Cancer
Biodesix, Inc, a company developing and commercializing molecular diagnostics for personalized medicine, has been awarded the United States Patent No 7,736, 905 on June 15, 2010. The invention provides coverage of the company’s first product, VeriStrat®, which is used by physicians to enhance clinical decision making and care for patients with advanced lung cancer. VeriStrat® is a non-invasive pretreatment serum test that identifies patients with advanced non small lung cancer (NSCLC) who are likely or not to benefit from targeted therapy with epidermal growth factor receptor inhibitors (EGFRIs). Studies have shown that this test correlates with survival outcomes and is predictive of objective response and disease control in advanced NSCLC patients treated with EGFRIs. Because the test requires a simple blood draw and results are returned within 72 hours, this noninvasive method helps oncologists guide treatment decisions quickly. VeriStrat® has been validated in clinical studies with over 1500 patients and tests are processed in Biodesix CLIA laboratory.

(Biodesix, June 23, 2010)
Octopus Venoms for Designing Drugs

Venoms have long been recognized as a potential and valuable resource for drug development. Researchers have collected venom from octopuses in Antarctica for the first time, significantly advancing the understanding of the properties of venom as a potential resource for drug development. They collected 203 octopuses from Antarctic waters and genetically profiled each specimen to identify the species and collected venom to analyse in the lab. The study provides the first insight into the properties of Antarctic octopuses venom and reveals the existence of four new species. Researchers found that this particular venom harbors a range of toxins, two of which had not previously been described. They discovered new small proteins in the venom with very intriguing activities. Understanding the structure and mode of action of venom found in all octopuses may help design drugs for conditions like pain management, allergies and cancer. The study is funded by the Australian Antarctic Division and according to researchers not only do Antarctic octopuses have the most unique venom out there, but there are a lot more species than originally thought.

(Australia: University of Melbourne, July 28, 2010)

Genetic Basis of Prostate Carcinogenesis

A genome-wide study on Japanese subjects offers a first ever glimpse of the genetic basis for prostate cancer susceptibility in non-European population. Researchers have carried out a genome-wide association study and replication study using 4,584 Japanese men with prostate cancer and 8,801 control subjects. They have identified 5 new genetic variations associated with prostate cancer and revealed differences and similarities between Europeans and Asians in susceptibility to the disease. Out of 31 single nucleotide polymorphisms (SNPs) variations linked to prostate cancer susceptibility in previous studies on European subjects, they confirmed that 19 were also associated with susceptibility in the Japanese population. The remaining 12 SNPs showed no association. A better understanding of such variation promises more accurate risk assessment, improvements in screening protocols and more effective clinical treatment.

(Japan: Nature Genetics, Aug 1, 2010)

Biobank Project

The most comprehensive health study, UK Biobank Project which has so far cost about £65 m, was set up by the Department of Health, Medical Research Council, Scottish Govt. and the Wellcome Trust Charity. It has reached its goal of enrolling 500,000 adults aged 40-69. Volunteers have undergone medical checks, answered health and lifestyle questions and given genetic samples to be stored for decades. Aim of the gene bank is to improve the prevention, diagnosis and treatment of a wide range of conditions such as cancer, heart disease and dementia. Scientists hope to work out why some develop diseases while others do not. Recruitment to the project began three years ago. Volunteers to the project were told that it was not intended to help improve their health, but that of future generations. Much of the interesting research would not be done for at least another decade. In 10 or 20 years time, the researchers would be able to analyse things in the samples that researchers have not even thought about yet. The next generation of scientists would be able to unlock new secrets as to how to prevent the disease.

(UK: UICC News, July 7, 2010)

Parental Cancer

Cancer diagnosis and treatment of parents greatly impacts the lives of their minor children and can pose special challenges for families. For example, survivors caring for young children have often significant concerns about living to see their children’s future and the risk of their children getting cancer. They may also struggle with parenting while dealing with their own health challenges, both during and after cancer treatment. In the first ever published estimate of percentage and number of cancer survivors who live with their minor children, researchers in US have found that millions of cancer survivors are parenting young children, highlighting a group of survivors with very special needs. The analysis revealed that an estimated 18% of newly diagnosed cancer survivors and 14% of all US cancer survivors reside with one or more of their minor children. This represents a population of 1.58 million US survivors living with 2.85 million children. According to the researchers, greater awareness of the number of characteristics of cancer survivors living with minor children may facilitate clinical screening and referral efforts, inform public health planning and stimulate research on these understudied families.

(US: Cancer, June 28, 2010)
HPV VACCINATION FOR CONTROL OF CERVICAL CANCER: INDIAN SCENARIO

Cervical Cancer: Etiological Role of HPV

Carcinoma of cervix has two major forms: the predominant (~90%) squamous cell carcinoma (SCC) that shares similarities with the stratified squamous epithelium, and the less common adenocarcinoma (~10%), which is thought to originate from the columnar epithelium of the endocervix. Cervical cancer is the second most common malignancy among women worldwide after breast cancer, with about 500,000 new cases and 300,000 deaths every year. In India, cervical cancer is the leading cancer among women with an annual incidence of about 132,000 cases and 70-75,000 deaths. India shares about one-fourth of the global cervical cancer burden. In 2008, Harald zur Hausen received the Nobel Prize in Physiology and Medicine for his pioneering work that unequivocally demonstrated a causative role of Human Papillomavirus (HPV) in the development of cervical cancer.

HPV is a double stranded circular, nonenveloped, epitheliotropic DNA virus. With more than 110 different HPV genotypes identified so far, only a subset is associated with carcinoma of cervix and precancerous lesions and have been classified as high-risk types (HR-HPV) (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82), probable high-risk types (PR-HPV) (26, 53, and 66) whereas types associated with benign lesions like Condylomata acuminata and genital warts are classified as low-risk types (LR-HPV) (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, and CP6108). HPV16 and HPV18 are the two most prevalent carcinogenic HPV types responsible for about 70% of cervical SCC and, together with other HR-HPV types, are found in almost all cervical carcinomas whereas the low risk types HPV 6 and 11 are responsible for about 90% of genital warts. The prevalence of HPV type 16 is exclusively high (~90%) while occurrence of HPV type 18 varies from 3-19%.

HPV infection is most often spread through penetrative or non-penetrative vaginal or anal intercourse and most frequently detected in young women. HPV infection is usually transient and resolves spontaneously, however, infection with HR-HPV types, particularly HPV16/18, takes much longer and is considered to be the event responsible for causation of precancerous lesions and their subsequent progression to cancer. A large number of co-factors is known to contribute to high incidence of this disease but most important of these factors are early age of marriage (<18 years), multiple sexual partners, multiple pregnancies, poor genital/sexual hygiene, use of oral contraceptives, and are primarily associated with poor-socio-economic status.

Cervical Cancer Control Strategies

Currently, the best way to prevent cervical cancer is through regular gynecological screening by cytologic Pap test and treatment of precancerous lesions. In US and Europe, Pap test has brought down cervical cancer burden by more than 70%. In India and other developing countries, however, this method has only a limited impact due to the absence of organized early screening program, lack of trained manpower and infrastructure. Recent large epidemiological studies conducted in India also demonstrate a better efficacy of HPV testing. It is ironical that many gynecologists and pathologists in private and public clinics in India are even unaware of HPV. Because of infectious etiology, cervical cancer is considered to be a preventable cancer. With development and successful clinical evaluation of prophylactic HPV vaccines, opportunity to control this cancer by vaccination is being explored. Current options available for HPV vaccination and issues involved with its implementation have been briefly described below.

Prophylactic Vaccines

Gardasil®, a quadrivalent HPV-16/18/6/11 L1 vaccine, is a virus like particle (VLP)-based vaccine that has been developed by Merck & Co. Inc., Pennsylvania, USA. For each HPV VLP, the L1 protein is expressed in a Saccharomyces cerevisiae (Baker’s Yeast). The vaccine consists of purified L1 VLPs of HPV types 6/11/16/18 at 20/40/40/20 Îµg/dose, respectively, formulated on a proprietary alum adjuvant. Gardasil® is available as a 0.5 ml intramuscular injection administered in a three-dose immunization protocol at 0, 2 and 6 months.

Cervarix™ on the other hand, a bivalent HPV-16/18 L1 VLP vaccine has been developed by GlaxoSmithKline Biologicals, Rixensart, Belgium. The L1 protein of each HPV type is expressed by a recombinant baculovirus. Cervarix™ consists of purified...
L1 VLPs of HPV types 16/18 at 20/20 μg/dose, respectively, formulated on a more stock adjuvant ASO4. It is administered as a 0.5 ml intramuscular injection in a three-dose immunization protocol at 0, 1 and 6 months.

Both these vaccines have got approval for clinical use by Drug Controller General of India in 2008 and 2009 for the prevention of cervical cancer and were found to be highly immunogenic and safe against HPV 16 and 18 infections. However, the efficacy is yet to be evaluated in the Indian context. Both the vaccines have some common adverse events such as pain and swelling at injection site, headache, fever and vomiting. However, not much adverse events have been reported in Indian context. Considering an over representation of HPV16, these vaccines are expected to perform better in Indian scenario.

Issues Related with HPV Vaccination

There are a number of limitations and issues associated with the vaccine itself and its implementation in developing countries like India. These are:

1. Prophylactic only and no therapeutic utility.
2. Derived against only a few oncogenic types and expensive which require a substantial reduction in cost to make it affordable to general public.
3. VLPs are not as per Indian variants.
4. Vaccine is anti-HPV but its anti-cervical cancer effects are yet to be proven which will take about 15-20 years.
5. Operational issues as it requires refrigeration and has a multidose schedule.
6. The relationship between antibody titre and extent of protection and whether the antibody titre remains for lifelong or there is a need for booster dose at a regular interval is not clear.
7. Lack of public awareness, social, religious, cultural and ethical issues.
8. By whom to be implemented, a gynecologist or pediatrician or venereal disease specialist, dermatologists or surgeons.

Upcoming Vaccines

**Therapeutic HPV vaccine:** Because of limitations of the current HPV vaccines as mentioned above, necessity of therapeutic vaccines for the treatment of HPV-associated lesions still exists, even after the prophylactic vaccine program are implemented in the world. Development of the HPV therapeutic vaccines are being carried out for the last two decades and these are still under different stages of clinical trials.

**Second-generation vaccines:** The main goal of the second-generation vaccines is to develop vaccines that will be more suitable to resource limited countries, that reduce the cost of production, have a longer shelf-life, single dose delivery, long lasting immunity, do not require refrigeration and incorporate other oncogenic HPVs. Recently, HPV 16 L1 pentameric capsomeres produced in *E. coli* bacteria have been shown to induce neutralizing antibodies in animal model. Capsomeres represent a highly stable alternative to VLPs as it can be easily expressed in *E. coli* and would be cheaper to produce. One of the second-generation vaccines are "Genetic vaccines” or "DNA vaccines”. In the last few years, several DNA vaccines have been developed against a variety of viral, bacterial as well as parasitic infections in animal models, showing long lasting immunity and protection. Since genetic vaccine is a plasmid-based vaccine, it is cost-effective and simple to produce in large quantities. Chimeric vaccines with both prophylactic and therapeutic potential are also being developed and will prove more useful in Indian scenario.

Conclusion

Leading with almost 80% of the global cervical cancer cases, the developing countries are in urgent need of an effective and affordable HPV vaccine. The currently available prophylactic vaccines developed against the most prevalent HPV types 16 &18 in carcinoma of cervix and genital warts are beyond the reach of these countries due to the high cost of these vaccines. Considering the vast diversity in socio-economic status in India, it is expected that the vaccination will soon pick up in well-off families on one to one basis in India. With other competing medical priorities in India the present trends indicate that it is unlikely for HPV vaccination to move into national immunization program, unless the pharmaceutical companies bring the cost down to make it comparable to common childhood vaccines. Reduced costs, simple vaccine regimes, improving coverage of all oncogenic HPV types and strengthening vaccine delivery and monitoring platforms for adolescents should eventually facilitate successful HPV vaccine introduction in India.

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(Ms Shilpi Gupta, Division of Molecular Oncology, Institute of Cytology and Preventive Oncology)
LOCAL THERAPIES FOR BRAIN TUMORS

Dr Zvi Ram, MD Chairman, Department of Neurosurgery, Tel Aviv Medical Center, Israel, visited Rajiv Gandhi Cancer Institute and Research Centre on July 23, 2010 and delivered a lecture on “Local Therapies for Brain Tumors”. It was attended by Director Research, Consultants, DNB students and Research Officers of the Institute.

Malignant brain tumor is in fact a “systemic infiltrative disease”. The conventional treatment for glioblastoma has been maximal safe debulking followed by radiotherapy and concomitant chemotherapy. But despite all the above mentioned measures, the mean survival reported in the literature is approximately 10-14 months. 90% of GBM recur within 2 cm from the original resection site, which makes local therapy an exciting option.

Modest improvements in prognosis have been seen in recent years with the emergence of new local treatments like Diffusion-based delivery (Gliadel) and Convection-Enhanced Delivery. Gliadel wafer therapy has been approved as an adjunctive treatment by US FDA for primary and recurrent glioblastoma.

Gliadel wafer (polifeprosan 20 with carmustine implant) contains a biodegradable polyanhydride copolymer and 7.7 mg of carmustine [BCNU]. Carmustine is a nitrosourea oncolytic agent, which is homogeneously distributed in the copolymer matrix. Gliadel wafers are biodegradable in human brain when implanted into the cavity after tumor resection. BCNU is released via surface erosion. Hydrophobic monomers permit surface erosion for slow release and protect active agent from hydrolysis. 70% BCNU are released by 3-4 weeks. During the biodegradation process, a wafer remnant may be observed in brain imaging scans or at re-operation even though extensive degradation of all components has occurred.

Results of placebo-controlled trial of safety and efficacy of intraoperative controlled delivery by biodegradable polymers of chemotherapy for recurrent gliomas, published in the Journal Lancet, showed survival at 6 months with Gliadel® Polymer 56% and Placebo Polymer 36%. European study of BCNU-Polyanhydride Polymer as the initial treatment of malignant glioma showed that two years after implantation, 31% of patients are alive versus 6% of patients with placebo polymers.

Systemic temozolomide is most effective in regions of tumor that are most vascular, whereas local delivery of carmustine allows direct access of the chemotherapeutic agent independent of vasculature. Gliadel wafer delivery of local BCNU offers a bridge for the nontherapeutic period following surgery, thus allowing continuous adjuvant therapy, beginning immediately following tumor resection.

Gliadel® demonstrates proof of principle that controlled release with polymers directly to the brain is safe and improves survival when combined with radio-chemotherapy. The morbidity associated with Gliadel wafers has been well reported in the literature. Adverse events of concern include seizures, cerebral edema, wound healing abnormalities and intracranial infection.

Dr Ram also highlighted the concept of Convection-Enhanced Delivery (CED) for brain tumor therapy while describing bypassing the Blood Brain Barrier via Intra-Tissue Drug Delivery. He told the right drugs for CED depend on efficacy, toxicity to normal brain, stability in situ and individual distribution characteristics (Infusate!). He mentioned that backflow reduces efficacy of distribution and increases toxicity (spillage of the drug into the subarachnoid space and CSF where it can affect the entire brain surface).

Based on in vitro studies, taxol is a good candidate for CED into brain tumors. Causes of failure include, mechanical/physical issues, placement in cystic/necrotic cavities, penetration into ventricles/cysts/necrosis, backflow (associated with CSF distribution and toxicity), anatomical/structural boundaries (glial scars, tissue conductivity, etc).

To improve CED, research goals are to optimise convection, better distribution enabling better response (optimal infusate), imaging the convective process, simulation of convection (pre-treatment). Future possible applications of CED include neoplastic diseases, degenerative brain diseases (Parkinson’s disease, Alzheimer’s), metabolic and genetic disorders, extracranial indication.

Dr RS Jaggi, Neurosurgeon, conducting the meeting thanked Dr Zvi Ram for the informative presentation.

(Reviewed by Dr R S Jaggi, Consultant, Dept of Neurosurgery)
MEDICO-LEGAL ISSUES IN HEALTH CARE

Medicine today is practiced within an expanding and evolving system of legal rights and obligations, patient protection, healthcare financing regulations and standards of care. Doctors/consultants are at the potential risk of facing criminal/civil suits from any of their patients or their relatives anytime during their professional carrier. To educate the medical fraternity involved in the day-to-day care of the patient and to give them a complete overview about various aspects related to the medico legal issues, a CME on “Medico-Legal Issues in Healthcare” was conducted on August 21, 2010 at Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC). The speakers in the CME included Dr RK Mani, Director-Pulmonology, Critical Care & Sleep Medicine, and Dr P K Kohli, Consultant Surgeon, Artemis Health Institute, Gurgaon, Dr D C Doval, Chief of Medical Oncology & Director (Research), and Advocate Mansi Bajaj, Legal Consultant, RGCI&RC.

Dr Mani delivered a talk on 'Limitation of Life Support- Ethical and Legal Perspectives in India'. He emphasized on the aim to treat and cure critically ill patients but not to prolong death. He said that ethical standards demand that appropriate medical decision be taken even if an enactment of law is awaited. There is complete absence of legal guidelines on most issues related to end-of-life care. The 'Do Not Resuscitate' order is still not a documented legal practice in India. In most cases, it is a verbal communication between the clinician and the patient’s relative or the caregiver. The autonomy of the patient also remains a weak concept. The doctor is best qualified to judge whether the treatment is to be continued or withheld or withdrawn. Patient’s autonomy in making an informed choice of therapy should be accepted. The lecture gave an insight into how to manage critically ill patients and the options available to physicians in such situations.

Dr Kohli delivered a lecture on 'Rights and Responsibilities (of Patients and Doctors)'. Healthcare seekers and healthcare providers should ideally be on the same side, fighting against a common enemy, ie ‘disease’. Honesty, transparency, and sensitivity should be the ‘mantra’ for doctors. Respect, trust and faithful compliance would do the trick for patients. He said that rights and responsibilities go hand in hand. In general, rights of patients are responsibilities of doctors and rights of doctors are responsibilities of patients. Conflicts occur if either or both parties concentrate only on their rights and forget their responsibilities. It's very important for healthcare service providers to make their patients and doctors know about their rights and responsibilities to act more efficiently and to provide better care to patients.

Dr Doval gave an overview on 'Documentation in Medical Practice'. He said that practicing medicine now is hazardous and risky. Moreover, mutual faith has been replaced with mutual suspicion, hence practicing defensive medicine is inevitable. He advised to be careful about documentation which includes consent and informed consent and medical records. Medical record documentation includes patient’s social data, administrative data and clinical data. Medical record is a legal document which is required at each step to prove that the doctor did not intend any harm to the patient. In this information age, scrutiny of all aspects of medical care has become a norm. Professionals should be mindful of this reality and change their practice habits accordingly. He reiterated the importance of documentation in medical field to help healthcare providers to delivers better care to patients and avoid any future litigation in the court of law.

Advocate Mansi Bajaj delivered a lecture on 'Medical Negligence'. She said that medical malpractice law is emerging as a very important area of law. Doctors being sued for negligence on their part was said to be a common occurrence in the western countries. With the era of globalization and increased awareness of the people, it is now becoming common in India. Laws under which the complainant can go to the court include Consumer Protection Act, Civil law, Constitutional Remedy and Criminal law. Patient can approach the court for damages like general damages- pain and suffering, loss of amenity, loss of future earnings, etc.

The CME was well applauded by Dr A K Dewan, Medical Director, Consultants, DNB students and Research Officers of the Institute which enabled them to understand the current medico legal scenario related to the healthcare services.

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Theme: “Malignancies in Childhood”
4th - 6th February 2011
Venue: India Habitat Centre, New Delhi