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DHARAMSHILA HOSPITAL AND RESEARCH CENTRE

(A unit of Dharamshila Cancer Foundation And Research Centre)

Dharamshila Marg, Vasundhara Enclave, Delhi - 110 096 T +91-11-43066666, 22618675

F +91-11-22617770 E contact@dhrc.in W www.dhrc.in

Join us on **facebook** **HELPLINE** +91-8130000120

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Dharamshila Hospital And Research Centre
 Dharamshila Marg, Vasundhara Enclave, Delhi 110096

FACILITIES AVAILABLE

DIAGNOSTIC SERVICES

Radiology and Imaging Services
 - PET CT Scanner with HD Technology
 - Gamma Camera for Nuclear Scans
 - 16 Slice Multi Detector CT Scanner
 - 1.5 Tesla Magnetic Resonance Imaging (MRI)
 - Mammography
 - Ultra Sonography Scans
 - Colour Doppler Vascular & Cardiac Studies
 - CT /USG guided Interventions
 - Image Intensifier - C-Arm
 - Digital Radiography
 - Interventional Radiology

Cardiopulmonary Lab
 - ECG - Holter Test - TMT, PFT
 - Stress/Dobutamine Echo with Colour Doppler

Laboratory Services
 - Histopathology - Haematology
 - Cytopathology - Biochemistry
 - FNAC & Guided FNAC - Clinical pathology
 - Frozen Section - Microbiology
 - Immunohistochemistry
 - Tumour Markers
 - Cytochemistry
 - Serology
 - 24x7 Blood Bank with Apheresis and Blood Components facility

Endoscopic Suite - Full Range of Fibre-optic Endoscopic Procedures

RADIATION ONCOLOGY

- Triple energy Linear Accelerator with Volumetric Arc Therapy (VMAT)
 - IGRT, IMRT, 3D Conformal Treatment
 - Stereotactic Body Radiation Therapy (SBRT)
 - Stereotactic Radio Surgery (SRS) and
 - Stereotactic Radio Therapy (SRT)
 MicroSelection Digital (HDR-V3) Brachytherapy
 Afterloader Intracavitary, Interstitial, Intra luminal and Surface mould
 Treatment Planning Systems
 (Eclipse, CMS Xio, Monaco, ERGO+, Plato Sunrise)

SURGICAL ONCOLOGY

- Head and Neck Cancer Surgery
 - Esophageal Cancer Surgery
 - Breast Cancer Surgery
 - Chest & Thorax Cancer Surgery
 - Gynae Cancer Surgery
 - Gastrointestinal Cancer Surgery
 - Uro oncology surgery
 - Neuro oncology Surgery
 - Bone and Soft Tissue

MEDICAL ONCOLOGY

Chemotherapy Normal & High Dose Including

- Infusional Chemotherapy
 - Targeted Therapy
 - Immunotherapy / Biological Therapy
 - Hormonal Therapy
 - Site Specific Chemotherapy

HAEMATO ONCOLOGY (ADULT & CHILDREN)

State-of-the-art Blood And Marrow Transplant Centre
 - Autologous BMT for Myeloma, Lymphoma, Paediatric tumours, Multiple Sclerosis and Auto-immune disease, not responding to the medical treatment.

- Allogenic BMT for Acute Leukemia, Chronic Leukemia, Lymphoma, Myeloma, Thalassemia, Sickle cell disease, Childhood genetic diseases, Immunodeficiency, Metabolic diseases, Solid tumours and Auto-immune disease not responding to the medical treatment.

- Non-Malignant Hematology services to cater to patients with Thalassemia, Aplastic Anemia and others
 - Excellent Blood bank facilities for Collection, Processing, enumeration and Cryopreservation of stem cells. BMT Labs are equipped with state-of-the-art equipments for Routine and Specialized Tests, HLA Testing, Bacterial and fungal cultures, Flow Cytometry, Conventional and Real Time PCR for viral pathogens, Molecular Biology Lab, Cell Culture Lab and Magnetic separation of cells using MACS technology.

ALLIED SPECIALITIES

Superspecialities
 - Gastroenterology & Gastro-intestinal Surgery
 - Nephrology - Dialysis
 - Neuro Surgery
 - Plastic and Cosmetic Surgery
 - Pulmonology
 - Urology

Specialities

- Dental
 - Ear, Nose and Throat (ENT)
 - General and Laparoscopic Surgery
 - Gynaecology
 - Internal medicine
 - Orthopaedics (Joint Replacements)
 - Rehabilitation & Speech Therapy

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Dear friend,

Wish you a very happy, healthy and prosperous Diwali with a roaring practice, great name and fame for your professional excellence.

This Diwali is very special for Dharamshila Hospital. Dr. Sandeep Chatrath, our new C.E.O. will celebrate the Diwali with 700 members of Dharamshila family. You will be happy to know that Maulana Azad Medical College, International Training Centre has certified Dharamshila Hospital And Research Centre as Satellite Centre / Nodal Centre of MAMC-ITC from 16.07.2013 for AHA Certified BLS and ACLS Certified Courses. Please do send your delegates for the workshop for BLS and ACLS Life Support Provider Course on 6th, 7th and 8th December 2013.

Our Centre of Minimal Invasive Cancer Surgery is now being headed by Dr. (Prof.) Suraj Manjunath, MCh (Gold Medalist) from Kidwai Memorial Institute of Oncology. He also did his Fellowship in GI and Minimal Invasive Oncosurgery from Detroit Medical Centre, Wayne State University. Dr. (Prof.) Manjunath is a recipient of eleven National and International awards and has 28 Scientific Publications in National and International indexed Journals to his credit. He has been deeply involved in professional community services.

Dharamshila Bone Marrow Transplant Centre has started attracting Children and Adults suffering from Malignant and Non-malignance Haematological disorders for Allogenic and Autologous Transplants. Dharamshila BMT Centre is supported by state-of-the-art Labs for routine and specialized tests, Flowcytometry, HLA Testing, Conventional and Real-time PCR for Viral Pathogens, Bacterial and Fungal Cultures, Molecular Biology, Cell Cultures and Magnetic Separation of Cells using MACS Technology.

Dharamshila BMT Lab has facilities for collection, processing, enumeration and cryopreservation of cells at -190°C with Liquid Nitrogen Vapour System and we also have Controlled Rate Freezer.

In our pursuit towards excellence, since 1994, we have been continually adding new techniques, technologies, facilities and services to improve patient care and safety, cut down treatment costs, minimize hospitalization and achieve optimal treatment outcomes. This has helped us to earn the goodwill of our patients and our referral base, who is delighted with our honest policies, transparent billing and highest standards of care. This has been instrumental for our growth and development.

We salute you for your unstinting support.

Thanking you

Dr. S. Khanna - President,
 Dharamshila Cancer Foundation And Research Centre (DCFCR)

WE WELCOME OUR NEW LEADERS



Dr. Sandeep Chatrath (C.E.O.)

M.B.B.S., DHA (Y.M.C.A.)
 MBA (Healthcare Administration) from Faculty of Management Studies, Delhi University
 Lead Assessor for NABH and ISO 9002 / OSHA Quality Healthcare System

Dr. Chatrath has 20 years of rich experience from large NGOS and Corporate Hospitals of India. His core strength areas are Hospital Operation; Strategic Business Development and Planning; Clinical Program Development; Facility and Capital Planning; Leadership and Professional Development; Quality Management and Performance Improvement; Education and Training.



Dr. (Prof.) Suraj Manjunath

Senior Consultant - Surgical Oncology
 MCh (Surgical Oncology) Kidwai Memorial Institute of Oncology, Bangalore, 2003-2006
 MS (General Surgery), Bangalore Medical College, 1999-2002
 MBBS, Bangalore Medical College, 1992-1998
 Fellowship in GI and minimally Invasive Oncology from Detroit Medical Center, Wayne State University, 2011

AWARDS

- Detroit Visiting Fellowship - of Indian Association of Surgical Oncology, 2011
- Gold Medal - Mch (Surgical Oncology) 2006
- Best Paper Award - 'Surgical Society of Bangalore', 2008
- Best Paper Award - 'The Association of Gynaecologic Oncologists of India (AGOICON 2006)', AIIMS, New Delhi, 2006
- Best Poster Award - 'National Update on Gynaecological Oncology', Coimbatore, 2006
- Best Paper Award - 'Surgical Society of Bangalore', 2005
- Best Paper Award - 'Surgical Society of Bangalore', 2004
- Certificate of Honour - 'Academic Society of Bangalore Medical College & Combined Hospitals', 2002
- All India Best Paper Award - 'Association of Surgeons of India - 61st Annual National Conference (ASICON)' - 2001
- All India Best Chapter Paper Award - 'Association of Surgeons of India - 61st Annual National Conference (ASICON)' - 2001
- Best Paper Award - 'Surgical Society of Bangalore', 2001

EDITORIAL AND RESEARCH ACTIVITIES

- Member, Panel of Reviewers, European Journal of Surgical Oncology
- Member Panel of Reviewers, The Open Cancer Journal
- Evaluation of AYUSH QOL-2C as an adjuvant therapy for patients with Breast cancer receiving Chemotherapy.
- AYUSH Govt. of India sponsored trial Co-principal Investigator. "An Observational Longitudinal Prospective Study to Evaluate Molecular Markers of Prognosis, Treatment Response and Disease Outcome in Breast Cancer" - study in association with IPHCR. Ongoing trial.

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India's First NABH Accredited Cancer Hospital | Laboratory Services Accredited by NABL
 ISO 9001:2008 and ISO 14001:2004 Certified by TUV - NORD, Germany

- Contributor to FIGO (International Federation of Gynaecology and Obstetrics) 27th volume of the Annual Report on the Results of Treatment in Gynaecological Cancer, 2006 for
 - Carcinoma of the Vulva
 - Carcinoma of the Corpus Uteri, and
 - Gestational Trophoblastic Neoplasia.
- Reviewer (Sentinel Reader) for Evidence-based Medicine Information System (bmjupdates), Health Information Research Unit, McMaster University, Canada. 2006 onwards

LAPAROSCOPY IN ONCOLOGY – CURRENT TRENDS

Although it is over a hundred years since the initial development of laparoscopy, it is only in the past three decades that there has been a revolution in the field with surgeries like laparoscopic cholecystectomy becoming the gold standard worldwide.

Advantages of laparoscopic surgery are well known, and include dramatically reduced hospital stay, better patient comfort, rapid return to employment, lesser tissue handling and superior cosmesis compared to open surgery. Further, there is better visualization and magnification especially in areas like the pelvis and the thorax which are often difficult to access in open surgery. Systemic immune competence has also been shown to be better preserved after laparoscopic surgery.

The role of laparoscopy for cancer has expanded to include diagnosing, staging, treating, monitoring, and palliating many types of malignancies. Laparoscopic guided biopsy allows the confirmation of malignancy by providing tissue specimens, especially in cases where other means of biopsy are not feasible.

Laparoscopic staging can identify unresectable disease, which often dramatically alters therapy. With increased accuracy in staging, many patients can avoid pain and prolonged hospital stay of a nontherapeutic laparotomy

For resectable disease, a wide range of curative laparoscopic resections have been described. However, it is imperative that the laparoscopic oncosurgeon follows all the principles of surgery for cancer just as in open operations. The principles of laparoscopic onco-resection include

- Maintenance of the integrity of the oncologic resection (e.g., margins of resection, lymph node dissection)
- Demonstration of improved outcome parameters for the resection (e.g., decreased hospital stay, decreased pain, decreased cost, more rapid return to work), and
- Absence of any negative impact on survival (e.g., induction of carcinomatosis or metastasis by laparoscopy, portsite recurrences).



**THORACOSCOPIC
ESOPHAGEAL RESECTION
USING THREE PORTS**

Colorectal cancer is one of the malignancies in which extensive research has been done comparing open versus laparoscopic resection (COST trial, CLASSIC trial, COLOR trial) and it has been shown that there is no compromise in oncologic outcomes with laparoscopic surgery. Other cancers which are amenable to laparoscopic resection include cancers of the esophagus, stomach, small intestine, kidney, adrenal, spleen (hematologic), pancreatic tail, some liver tumors, and gynaecologic cancers.

The role of laparoscopy extends beyond diagnosis and treatment. Many a time, patients with incurable cancers need palliation of their malignancy. A common scenario is gastric outlet obstruction or intestinal obstruction. When the gastric outlet is obstructed by a tumor such as an incurable gastric or pancreatic cancer, a laparoscopic stapled gastrojejunostomy can be performed quickly to provide pain relief and allow resumption of eating. Intestinal stomas can also be created when bowel loops are involved with tumor and intestinal bypass is not feasible.

Laparoscopic surgery is heavily dependent on technology. With rapid evolution in the field of technology, we now have available excellent telescopes and camera systems, high-definition monitors, high end energy sources and tissue sealing devices, and staplers manufactured for laparoscopic use. There are also many opportunities for the interested surgeon to train himself/herself in laparoscopic oncosurgery in India as well as abroad.

With this, it is clear that laparoscopic oncosurgery has proved to be a boon for many patients. With time, more and more patients will be offered this modality of treatment, so that they can also enjoy its potential benefits.

Dr. (Prof.) Suraj Manjunath
Senior Consultant – Surgical Oncology

BASIC LIFE SUPPORT (BLS) AND ADVANCED CARDIAC LIFE SUPPORT PROVIDER (ACLS) COURSE

(American Heart Association Certified)

6th, 7th and 8th December 2013

This course will be conducted by the AHA Certified ACLS Instructors from Dharamshila Hospital And Research Centre, Nodal Centre of prestigious Medical Institute Maulana Azad Medical College, Delhi.

COURSE DETAILS

Dates	Timings	Course	Fees	No. of Seats
6th Dec. 2013	8:00 A.M. – 6:00 P.M.	BLS	Rs. 2,200/-	10
6th, 7th & 8th Dec. 2013	8:00 A.M. – 6:00 P.M.	ACLS	Rs. 7,000/-	24

Venue: Conference Hall, Dharamshila Hospital And Research Centre

Last Date of Registration – 25th November 2013 (Spot Registration is not available)

For more details and to download the registration form, kindly visit our website www.dharamshila.com or contact Dr. Neha Agrawal : +91-9818415651 and 011-43066153

BLOOD AND MARROW TRANSPLANTATION BEYOND BARRIERS

Introduction

Allogeneic Blood and Marrow Transplantation (BMT), which employs the use of hematopoietic progenitor cells (HPC) from a donor to replace the diseased or defective hematopoietic as well as the immune system has evolved radically over the last three decades. The indications for Allo-BMT are no longer limited to end-stage leukemias. This is deemed curative and often the only option for many non-malignant conditions as well. These advances have been possible through better understanding and management of post-transplant complications, both infectious and non-infectious. The key to this success is perhaps related to the optimum selection of donors for Allo-BMT. Human Leukocyte Antigen (HLA) system is pivotal to the outcome of Allo-BMT unlike solid organ transplantation. HLA-matched family member was and still is considered the donor of choice for Allo-BMT for all indications; a paradigm which remains unchanged despite tremendous advancements in this field. Based on mendelian laws of inheritance, the chances of siblings being matched to each other at class I and II HLA locus are only 20-30%. Thus 70-80% of patients eligible for an Allo-BMT would be unlikely to find a donor within the family. Thus the large majority of patients do not find a matched family donor and are candidates for an alternative donor BMT.

Unrelated Donors (UD) as a Source of Cells for Allo-BMT

The options for alternative donor were limited by the initial studies demonstrating the primacy of HLA matching in dictating the outcome of BMT. The chances of finding a HLA match within the extended family is remote and even more so from an unrelated donor. The National Bone Marrow Donor Registry was federally funded in 1986, and in 1987 the first donor match was made. In 1988, the name was changed to the National Marrow Donor Registry (NMDR). The NMDR now includes a network of donor registries in 30 countries. Its database contains more than 5.5 million donors and facilitates an average of 200 transplants each month. Several such registries are operational in all developed countries accounting for over 11 million donors worldwide. At the inception, UDBMT was an extremely high risk procedure with a transplant related mortality (TRM) of nearly 50 % which is now reduced to less than 30%.

Unrelated Cord Blood Transplantation (UCBT)

A decade after the first UDBMT, Gluckman and Broxmeyer carried out the first successful related cord blood transplantation (CBT) in a patient with Fanconi's Anemia. This was a result of several years of research establishing the survival and repopulating potential of cord blood both fresh and frozen. It was established

subsequently that compared to bone marrow, one log less mononuclear cells are sufficient for engraftment in CBT, but this is invariably delayed.

Whilst cord blood provided a unique source of HPC, engraftment was uniformly delayed for neutrophils and more so for platelets. Since the first CBT, more than 20,000 CBTs have been reported worldwide and more than 400,000 cord blood units have been stored in more than 100 cord blood banks. The main practical advantages of using cord blood as an alternative source of stem cells are the relative ease of procurement, the absence of risks for mothers and donors, the reduced likelihood of transmitting infections, particularly CMV and the ability to store fully tested and HLA-typed transplants in the frozen state, available for immediate use.

The donor who is always there- the Haploidentical Family Donor

Based on Mendelian laws of inheritance, HLA alleles are inherited as haplotypes from each parent. Thus, parents are matched atleast one haplotype with the patient. In addition, 90% of the siblings are expected to be matched at one haplotypes. Initial attempts at transplantation with haploidentical donors within the family were met with universal failure as a result of very high incidence of graft rejection or severe GVHD. With the developments in UDBMT and UCBT, this donor source was ignored completely in the mainstream of AlloBMT.

A group of researchers led by Martelli and Reisner, proposed a modality of Haploidentical BMT wherein infusion of very high dose of CD34 + cells depleted of T cells would be infused following intensive myeloablative as well as immunoablative conditioning. It took several years to optimise the procedure and in its final form, CD34 + cells were purified using immunomagnetic methods for positive selection and the final product contains less than 2 x 10⁴ /kg T cells and more than 10 x 10⁶ /kg CD34 cells. Almost all patients achieved engraftment with virtually no GVHD.

NK Cell Alloreactivity

On further exploration, the same group uncovered a unique phenomenon related to superior survival of patients with AML. Pioneering work by Ruggeri et al demonstrated that, in the setting of haploidentical transplantation, NK-cell alloreactivity is key to the antileukemia effect. Those patients who were mismatched at Killer Ig Receptor (KIR) genes of the NK cells with the donor had a significantly superior survival without any increase in GVHD. This was the first time GVHD and GVL could be dissected at a clinical level.

Standard GVHD Prophylaxis

The researchers in China adopted an intensive conditioning schedule with aggressive GVHD prophylaxis along with G-CSF primed marrow or peripheral blood. The results from Peking University were particularly impressive. 100% engraftment was achieved in 250 patients with acute leukemia. In addition, Haploidentical donor graft conferred a survival advantage over matched donors in advanced leukemia due to a superior GVL effect.

Post transplant High Dose Cyclophosphamide

Cyclophosphamide was one of the first drugs used in conditioning for BMT. It was also tried as GVHD prophylaxis in low doses due to its immunosuppressive properties. However this was not found to be effective at the low weekly doses employed in these studies. Although the preclinical data confirmed the efficacy of cyclophosphamide in inducing transplant tolerance at a much higher dose, the clinical studies employed much lower doses due to the concern over its deleterious effect on progenitor cells. The researchers at the Johns Hopkins and others discovered the unique property of primitive HPCs of being resistant to the cytotoxicity of cyclophosphamide by dint of very high expression of aldehyde dehydrogenase which metabolises the drug.

The Indian Scenario

Compared to over 10,000 BMT performed in the USA per year, less than 1000 are performed in India as of 2010 with only 5% being from alternative donors compared to 50% in the USA. There is no public cord blood bank in India and two struggling Unrelated Donor registries. The chance of obtaining a 10/10 HLA match for an Indian donor from European or American registries is only about 10%. Moreover the cost of obtaining a UD graft for an Indian patient is about \$25-30,000. The same is the case with UCBT. Thus most patients eligible for an allogeneic BMT do not receive a transplant in India. One must learn from the outcome of African-Americans undergoing UDBMT. The realistic possibility of obtaining a 10/10 matched unrelated donor from a Caucasian dominated registry is about 6%. Repeated studies have confirmed poorer outcome after UDBMT in this group which is attributable to less engraftment and more GVHD related to less than full match and transplants across ethnic groups. Similar inferior outcomes have been reported following mismatched UCBT in African-Americans.

Problems Thwarting Development of Unrelated Donor Registry (UDR) in India

The absence of a congruous policy and access to healthcare for all it's citizens plague the healthcare system in India. Development of UDR needs education, awareness and motivation amongst the people along with a sense of altruism. Lack of a national policy regarding cancer and thalassemia does not allow further headway regarding more intensive therapy regarding these diseases, such as BMT. Where voluntary blood donation is linked to guaranteed availability of blood products to the donor, volunteer bone marrow donor registry is likely to be a more distant reality. Several attempts have been made by various organisations, but poor recruitment and a faster attrition of donors have hampered the development of a viable registry. In addition, the funding required for infrastructural support and sustenance is a daunting task for charitable organisation.

On the other hand, Public Cord Blood Bank requires a lot more capital investment although there is no risk of attrition. Conservatively, a UDR requires one million donors and a PCBB should have an inventory of at least 20,00 units if more than 50% of patients are to find a suitable alternative donors. Either of these require active BMT programs across the country to sustain such alternate donor banks with over 500 UDBMT and UCBT performed per year. Until that becomes a reality or even without it, the need for Indian patients requiring alternative donor BMT is to develop Haploidentical BMT Programs.

Haploidentical BMT in the Indian context

Although a few of the centres in India are carrying out UDBMT and UCBT, none have developed a Haploidentical BMT program. In view of the above consideration, we developed a Haploidentical BMT program first time in india. In the first phase, we selected only patients with refractory AML. The donor selection was based on the following algorithm : 1) Mother if NK alloreactive donor is not available 2) NIMA mismatched donor if mother is not available as a donor. All patients were transplanted with over 30% marrow blasts and had failed several lines of treatment. The conditioning protocol employed high dose cytosine and an anthracycline for 3 days followed by a regimen similar to Johns Hopkins except low dose Total Body Irradiation (TBI) being replaced by melphalan. High dose cyclophosphamide was employed on days 3 and 4 after infusion of the graft which was mobilized from peripheral blood HPC rather than bone marrow.

All 3 patients engrafted neutrophils and platelets at a median of 14 and 16 days respectively. Donor engraftment above 95% was achieved in all at 30 days. None developed acute GVHD de novo. At a median follow-up of 180 days, all had relapsed. Our study suggested that Haploidentical BMT is feasible in patients with advanced leukemia. The prompt engraftment and lack of GVHD warranted Haploidentical BMT to be employed early in the course of the disease and with more intensive conditioning. The subsequent 8 patients were transplanted with more intensive conditioning with 50% disease free survival at one year.

We extended this program further to patients with Severe Aplastic Anemia (SAA) and thalassemia. 8 patients with Aplastic anemia and one patient with Thalassemia have undergone Haploidentical BMT with 60% survival at one year. Our research on the NK cell alloreactivity in Haploidentical BMT using post-transplant cyclophosphamide has brought to light several key issues related to SAA and its outcome for the first time.

More importantly, in our Haploidentical program with over 25 Haploidentical BMT performed, the cost of such BMT was comparable to that of matched family donors. In our attempt to expand the program to the next level, the newer technologies of selective T cell depletion are going to be introduced, which would be more expensive but expected to be more successful at the same time with lesser complications and virtual elimination of long term immunosuppression and antibiotic usage. UDBMT from western registries is unlikely to be a long term solution due to both the cost involved and a low yield of full HLA matched donors. The same is true for UCBT. Mismatched UDBMT should be discouraged from ethnically disparate registries if we are to learn from the outcome in African-Americans. Similar to other Asian countries such as China and Korea, Haploidentical BMT programs need to be developed in India to cater to the majority of patients requiring a BMT. The challenge in India is not just to develop a Haploidentical BMT program for malignant diseases, but to do the same for nonmalignant diseases which account for half of the transplant indications currently.

Dr. Sarita Jaiswal

Associate Consultant – Haemato-oncology & BMT

Dr. Suparno Chakrabarti

Program Director - Blood and Marrow Transplantation
Senior Consultant & HOD – Haemato-oncology & BMT