Stem cells are undifferentiated cells that through replications have the capabilities of both self-renewal and differentiation into mature specialized cells. Broadly, there are two types of stem cells, embryonic stem cells and adult stem cells. Embryonic stem cell biology has been associated with ethical controversy and also their growth is difficult to control. Adult stem cells are located in tissues throughout the body and function as a reservoir to replace damaged or aging cells. Embryonic stem cells are by definitions, the master cells capable of differentiating into every type of cells either in-vitro or in-vivo. Several lines of evidence suggests, however, that adult stem cells and even terminally differentiated somatic cells under appropriate micro-environmental cues are able to be reprogrammed and contribute to a much wider spectrum of differentiated progeny than previously anticipated. Hematopoietic Stem Cells (HSCs), for example, from different sources have been shown to cross the tissue boundaries and give rise to the cells of the other germ layers.

In the past few years, the plasticity of adult cells in several post-natal tissues has attracted special attention in regenerative medicine. Stem cell therapies represent a new field of biomedical science which could provide in the future the cure for diseases until now considered incurable. The reconstitution of adult stem cells may be promising source for the regeneration of damaged tissues and for the resolution of organ dysfunction. However, there are two major limitations to the use of such cells:- (i) They are rare and (ii) Only a few types exist that can be isolated without harming the patient.

Due to the inability to efficiently and safely harvest or expand stem cells from most adult organs (e.g. liver, gastrointestinal tract, heart, brain), the majority of human stem cell trials have focused on clinical applications for HSCs, mesenchymal stem cells (MSCs), or both, which can be easily obtained in clinically sufficient numbers from peripheral blood, bone marrow, umbilical cord blood or placenta. HSCs can give rise to muscle, liver cells, astrocytes, etc, especially when co-cultured with the particular tissue progenitor cells and in presence of MSCs.

**Indications for HSC transplantation:**

1. **Malignant conditions:**
   
   A. **Allogeneic Stem Cell Transplantation (SCT):**

   1. **Hematological Malignancies:** CML, AML, ALL, NHL, HD, MDS.
2. Solid Tumors: Renal Cell Carcinoma, etc

B. Autologous Stem Cell Transplantation:

1. Hematological malignancies: AML, NHL, HD, MM
2. Solid Tumors: Neuroblastoma, EWS, RMS, etc

2. Non-Malignant conditions:

1. Hematological: Aplastic Anaemia, Fanconi Anaemia, Thalesemia, Sickle Cell Diseases, Myelofibrosis
2. Non Hematological: Osteopetrosis, Storage diseases (e.g. Gauchers)
3. Immune Disorders: SCID, HLH, etc.

3. Non-Malignant conditions:

1. Autoimmune Disorders: systemic sclerosis, multiple sclerosis, systemic lupus erythromatosis, juvenile idiopathic arthritis.
2. Heart Disease: HSCs expanded ex-vivo (especially after B-catenin treatment) have been found useful in the treatment of ischemic myocardial injury.
3. CNS: HSCs have been used in the treatment of ischemic stroke, spinal cord injury and neurological disease like Parkinson’s disease.
4. Diabetes Mellitus:
5. Gastro-intestinal & liver diseases:
   1. Cirrhosis end stage liver disease
   2. Acute Liver failure

3. Metabolic liver diseases
5. Patients with refractory celiac disease
7. Skin repair & regeneration

4. Generation of normal tissues:
   Potential therapeutic use of ex-vivo produced blood substitutes such as:
   1. RBCs
   2. Platelets

The outcome of HSCTs can be improved by various manipulations.

A. Before HSCT:
   Expansion of HSCs using:
   1. Culture with various cocktails: SCF + TPO + Flt-3l; IL-3 (promotes higher CD133 cell expansion) + IL-6 (maintains immature phenotype); G-CSF / GM-CSF + IL-3 + SCF, etc
   2. cMPL agonist NR-101
   3. Fetal liver stromal cells
   4. MSCs: provide suitable cellular environment for in-vitro expansion of HSC & HPCs from umbilical cord blood.
   5. Valproic acid; T-hoxb4-H, etc

   Expansion should favor cell proliferation over cell differentiation.

B. During HSCT:
   Enhance engraftment by using:
   1. Mesenchymal stem cell infusions
   2. Valproic acid
   3. Double / Triple cord blood transplants

C. After HSCT:
Infusion of:
1. Dendritic Cells
2. T-Regs: for modulation autoimmune disease or for transplant tolerization; derived from CB-HPCs
3. NK-Cells

**Uses of MSCs when used along with HSCs:**

MSCs have low inherent immunogenicity. Sources: Bone marrow; Wharton’s Jelly umbilical cord.
1. Enhancement of hematopoietic engraftment provide the supportive micro-environmental niche for HSC
2. Prevention / suppression of GVHD: MSCs exert an immediate anti-inflammatory & immunomodulatory role; cause induction of transplant tolerance
3. MSCs home to damaged tissue to participate in regenerative process; rebuild diseased tissues along with HSCs
4. Foster engraftment of haploidentical HSCs
5. Cell therapy & tissue engineering

Though HSCs have been used in all the above indications under laboratory condition, in animal studies, or even in humans, there is lot that still needs to be done before HCTs become standard of care.

**Status of HSCT in India:**

A pubmed search for HSCT & India yielded only 87 publications. Though the first Allogenic BMT was done at TMH long back in 1983, in the last 25 years hardly 2000 transplants have been performed in a country of over a billion population. This is compared to nearly 4000 transplants done each year world over. As of now, there are approximately 20 units doing SCT in India, the main among them being CMC, Vellore; TMH, Mumbai & AIIMS, Delhi. Apart from these centers, two other centers which have consistently published are, Stem Cell Biology Laboratory of National Institute of Immunology, Delhi & Dr. H.L. Trivedi Institute of Transplantation Sciences, Ahmedabad. However, most of published work in this field from India is in the preliminary stages and it may take some time before the translational research reaches to the bedside.