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Review Article

REVIEW ON STEM CELL THERAPY

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ABSTRACT

Stem cells are biological cells found in mammalian organisms that have the capacity to convert into any type of cells. They are capable of dividing and renewing themselves for long periods. They are unspecialized. They can give rise to specialized cell types. Stem cells are further categorised as adult stem cells and embryonic stem cells. The main aim of stem cell therapy is to cure diseases and disorders that have no treatment. Stem cell therapy is emerging as a potentially revolutionary new way to treat disease and injury, with wide-ranging medical benefits. It aims to repair damaged and diseased body-parts with healthy new cells provided by stem cell transplants. Preclinical and clinical research has recently tremendously improved stem cell therapy, being a promising treatment option for various diseases in which current medical therapies fail to cure, prevent progression or relieve symptoms. However, Stem cell research presents many ethical and scientific questions as well as future challenges. Nevertheless, stem cell therapy, a prologue to an era of medical discovery of cell-based therapies that will one day restore function to those whose lives are now challenged every day, is still at the beginning of the road. This review summarizes general aspects as well as current and future perspectives of stem cell therapy.

KEYWORDS: *Stem cell, Stem cell therapy, Adult stem cells, Embryonic stem cells.*

INTRODUCTION

Stem cells are undifferentiated self-replicating cells found in multicellular organisms. They have the ability to proliferate or regenerate the damaged tissues. Regeneration means that these cells have the ability of asymmetric division by which one of the resulting cells remains as stem cell while another cell, which is called daughter cell, becomes more specialised cells with a more specific function such as formation of new blood cells, brain cells, heart muscle cells or bone cells. No other cells in the body have the ability to generate new cells. Stem cells are unspecialised that is they does not have any tissue specific structures that allow them to perform specialised functions [1]. They may remain inactive for a long time till they enter cell division again. They serve as a repair machine for the body. Stem cells have two properties:

- Capable of dividing and renewing themselves
- Give rise to specialised tissues

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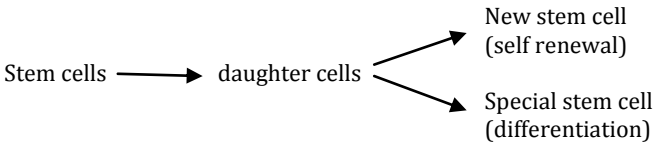
In a human body stem cells are present throughout their life from the time when embryo develops and these stem cells are used whenever the body needs them for regeneration processes for replacing dead cells.

Stem cells can be developed in laboratory for therapeutic and research purposes. Stem cell therapy can be used for tissue regeneration such as in conditions of burns or injuries of skin by grafting this tissue onto the damaged skin and new skin will grow back. The effects of newly developed drugs can be tested on tissues grown from stem cells in laboratory instead of testing them directly on human volunteers.



History:

The origin of stem cell research lies in a desire to understand how tissues are maintained in adult life, rather than how different cell types arise in the embryo. In 1878 attempts were made to fertilize mammalian eggs outside the body. In 1959 First animals were developed by in-vitro fertilization (IVF). In 1968 the first bone marrow transplant (adult stem cells) was successfully used in treatment of SCID. In 1968 the first human egg is fertilized in vitro. In 1978 the first IVF baby is born. In 1981 Mouse Embroyonic stem cells are derived from

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the inner cell mass of blastocysts. In 1984-88 Embryonal Carcinoma (EC) cells are developed. When exposed to retinoic acid these cells differentiate into neuron-like cells and other cell types. In 1994 Human blastocysts are generated and the inner cell mass is maintained in culture. ES like cells form in the center and retain stem cell like morphology. In 1998, James Thompson (University of Wisconsin - Madison) isolated cells from the inner cell mass of early embryos, and developed the first embryonic stem cell lines. In 2001 Human embryonic stem cell lines are shared and new lines are derived, more research groups are focusing attention on the differentiation of cells in vitro [3]. In 2004 election, California had a Stem Cell Research Funding authorization initiative on the ballot that won by a 60% to 40% margin. It established the "California Institute for Regenerative Medicine" to regulate stem cell research and research facilities. In early 2007, researchers led by Dr. Anthony Atala claimed that a new type of stem cell had been isolated in amniotic fluid. In 2008 NAS Release New Guidelines for stem cell research. In 2011 researchers uncovered the mechanism governing the Pluripotent Stem Cell Metabolism. The first human stemcells were extracted from primordial gonodal tissue which was taken from a non-living fetus [4].

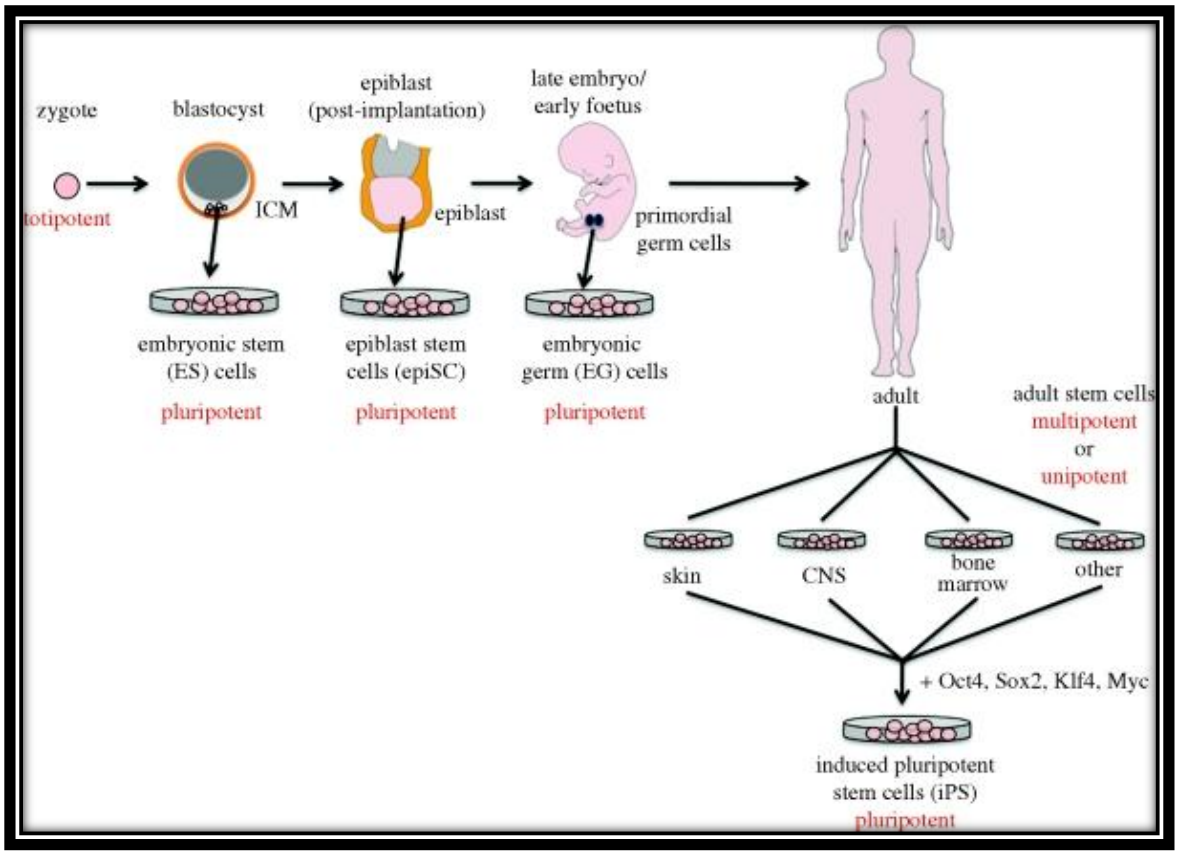

Fig. 1: Origin of stem cells

Cells are described as pluripotent_if they can form all the cell types of the adult organism. If, in addition, they can form the extraembryonic tissues of the embryo, they are described as totipotent. Multipotent stem cells have the ability to form all the differentiated cell types of a given tissue. In some cases, a tissue contains only one differentiated lineage and the stem cells that maintain the lineage are described as unipotent.

SOURCES OF STEM CELLS:

Stem cells originate from two main sources:

1. Adult body tissues
2. Embryo

Table No. 1: Sources of Stem cells

ADULT STEM CELLS	EMBRYONIC STEM CELLS
• Also called tissue-specific or somatic stem cells • Adult stem cells exist throughout the body from the time an embryo develops • An adult stem cell is an undifferentiated cell found among differentiated cells in a tissue or organ, can renew itself and can differentiate to yield the major specialized cell types of the tissue or organ. • The cells are in a non-specific state, but they are more specialized than embryonic stem cells These are of two types:	• Embryonic stem cells (ES cells or ESCs) as the inner cell mass of a blastocyst, an early-stage pre-implantation embryo. • Embryonic stem cells can differentiate into more cell types than adult stem cells. 1.**Mesenchymal stem cells (MSCs):** MSCs come from the connective tissue or stroma that surrounds the body's organs and other tissues [11-15]. 2.**Induced pluripotent stem cells (IPS):** Induced pluripotent stem cells (also known as iPS cells

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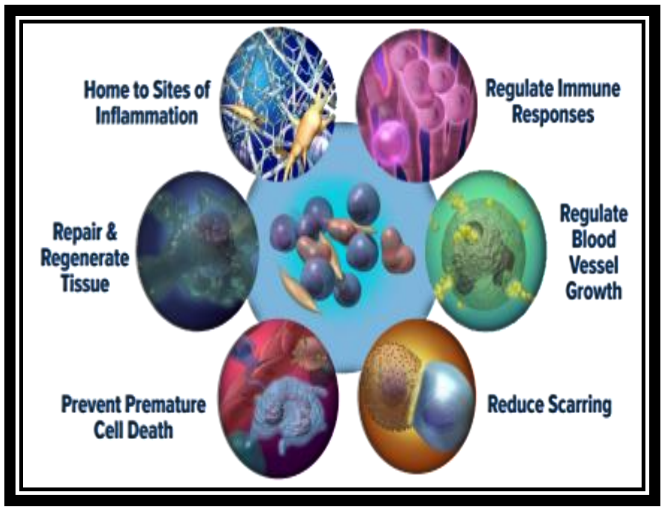
1. **Hematopoietic stem cell:**
   HSCs are found in the bone marrow of adults, especially in the pelvis, femur, and sternum. They are also found in umbilical cord blood and, in small numbers, in peripheral blood [2].
2. **Bone marrow stromal cells:**

The bone marrow stroma containes cells with a stem-cell-like character that allows them to differentiate into bone, cartilage, adipocytes, fibrous connective tissues and hematopoietic supporting tissues.

MECHANISM:



1. Your own adult stem cells can facilitate the growth of new blood vessels, a process known as angiogenesis, which leads to improved blood flow in tissue.
2. These cells also provide an anti-inflammatory effect which aids in healing.
3. They encourage repair of damaged tissue and regeneration of new, healthy tissue.
4. Adult stem cells also aid in reducing the size of any scar tissue, such as that which forms after a heart attack, wounds, or injury to a joint
5. The unique combination of stem and regenerative cells present in adipose (fat) has demonstrated remarkable effectiveness in halting destructive immune response.
6. Last but not least, your own fat-derived stem cells can prevent premature cell death.

Diseases and conditions have been treated with adult stem cells:

- **Cancers**
- **Auto-Immune Diseases**
- **Cardiovascular Diseases**
- **Ocular:**

Corneal regeneration
Macular Degeneration

- **Neural Degenerative Diseases and Injuries:**

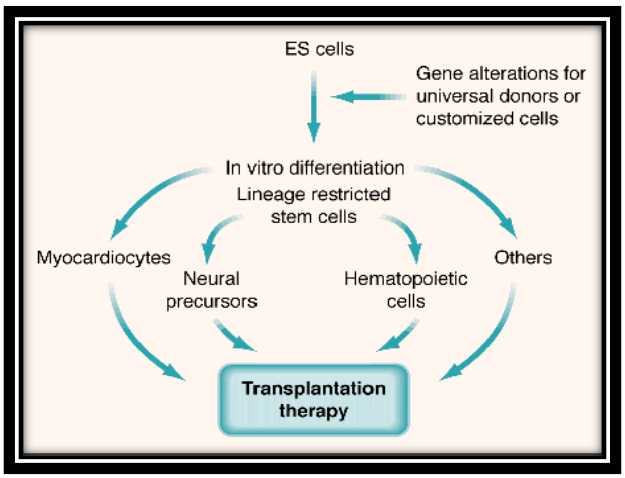
Parkinson's Disease
Spinal Cord Injury
Stroke Damage

- **Anemias and Other Blood Conditions**
- **Wounds and Injuries:**

Limb Gangrene
Surface Wound Healing
Jawbone Replacement
Skull Bone Repair

or iPSCs) are a type of pluripotent stem cell that can be generated directly from adult cells.

MECHANISM:



1. Self-renewal is the process by which stem cells divide to make more stem cells, perpetuating the stem cell pool throughout life.
2. Self-renewal is division with maintenance of the undifferentiated state. This requires cell cycle control and often maintenance of multipotency or pluripotency, depending on the stem cell. Self-renewal programs involve networks that balance proto-oncogenes (promoting self-renewal), gate-keeping tumor suppressors (limiting self-renewal), and care-taking tumor suppressors (maintaining genomic integrity).
3. These cell-intrinsic mechanisms are regulated by cell-extrinsic signals from the niche, the microenvironment that maintains stem cells and regulates their function in tissues.
4. In response to changing tissue demands, stem cells undergo changes in cell cycle status and developmental potential over time, requiring different self-renewal programs at different stages of life.
5. Reduced stem cell function and tissue regenerative capacity during aging are caused by changes in self-renewal programs that augment tumor suppression

Diseases and conditions have been treated with embriyonic stem cells:

- traumatic spinal cord injury
- stroke
- severe burns
- rheumatoid arthritis
- heart disease
- hearing loss
- retinal disease
- Huntington's disease
- Parkinson's disease

COLLECTION:

- The embryonic stem cells are removed from the embryos in vitro by adopting a technique called in vitro fertilization (IVF).

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- **Other Metabolic Disorders:**

Hurler's Syndrome
Osteogenesis Imperfecta
Krabbe Leukodystrophy
Osteopetrosis
Cerebral X-Linked Adrenoleukodystrophy

- **Liver Disease**

COLLECTION:

- The collection of stem cells from bone marrow requires a surgical procedure in which the donor is given anesthesia first and a needle is inserted into the bone marrow at a specific site to collect the stem cells [6-9].
- Collection of adult stem cells from blood is done by collecting the blood intravenously from one hand and passing it through a processor which separates the stem cells from the blood.
- Once the stem cells are separated, the blood is sent back to the body.
- In this method the sperm is inserted into the egg under controlled laboratory conditions. The use of in vitro embryos for harvesting stem cells is a very accurate procedure which is done only by obtaining permission from the couple whose egg and sperm are used in developing the embryo.
- The umbilical cord blood is a rich source of stem cells. In order to collect the cord blood for stem cells, the cord between the placenta and the baby is clamped and a trained person collects the blood from the umbilical cord by using a needle.
- The collected blood is transferred to the sample vial and sent for storage. Sterile conditions are maintained during the process of collection to avoid contamination of the sample.

After collecting the stem cells they are tested for any infectious diseases and contaminations. After successful positive results they are processed and they undergo different levels of quality assessment to ensure the feasibility and purity of stem cells.

Preservation of Stem Cells:

The samples of stem cells are mixed with solution called cryogenic (Cryogen is the solution which can maintain cell viability under cold state) [9]. Then they are transferred to big cryogenic containers that contain liquid nitrogen has temperature about – 150^{o} C to maintain cryogenic conditions below.

Problems of Stem Cells Preservation:

1. There is no standard procedure for preserving stem cells
2. DMSO is associated with adverse effects, hence, it is not approved for human infusion
3. Presently storage of stem cells requires equipment and intensive monitoring. New techniques for its storage are necessary.

Applications of Stem Cell Therapy:

1. Transplants with stem cells are already helping people with diseases such as lymphoma.
2. First, with the right stimulation, many stem cells can take on the role of any type of cell, and they can regenerate damaged tissue, under the right conditions.
3. This potential could save lives or repair wounds and tissue damage in people after an illness or injury. Scientists see many possible uses for stem cells.
4. By using IPS cells to create heart cells and other cells, pharmaceutical companies can also test their new drugs' effectiveness and uncover potential side effects, as well as develop personalised medicines.
5. Clinical studies over the last 10 years suggest that stem cell transplantation also has potential as therapy for neurodegenerative diseases. Clinical trials have involved grafting brain tissue from aborted foetuses into patients with Parkinson's disease and Hunting-ton's disease.
6. Allo-geneic stem cell transplantation is now a common procedure for the treatment of bone marrow failure and haematological malignancies, such as leukaemia.

Future Clinical Applications of Stem Cell Research:

- ✓ Stem cell treatments for conditions with no known cure
- ✓ Stem cell treatment for macular degeneration
- ✓ Stem cells lower the cost of therapy by eliminating continuous use of drugs
- ✓ Stem cells overcome tissue and organ donor shortages
- ✓ They replace invasive surgeries
- ✓ Mesenchymal stem cells (MSCS) can home into sites of injury, synthesize and secrete a variety of macromolecules to exert paracrine effects, and influence their local microenvironment. MSCS can also take up exogenous dna and keep introduced genes, an attribute that may allow the use of the cells in the therapeutic delivery of molecules to target regions of the bodys
- ✓ Almost every day there are reports in the media of new stem cell therapies. There is no doubt that stem cells have the potential to treat many human afflictions, including ageing, cancer, diabetes, blindness and neurodegeneration.
- ✓ An alternative strategy to stem cell transplantation is to stimulate a patient's endogenous stem cells to divide or differentiate, as happens naturally during skin wound healing. It has recently been shown that pancreatic exocrine cells in adult mice can be reprogrammed to become functional, insulin-producing beta cells by expression of transcription factors that regulate pancreatic development. The idea of repairing tissue through a process of cellular reprogramming in situ is an attractive paradigm to be explored further.

Problems of Stem Cell Therapy:

- Stem cells have the potential to divide many times and differentiate into many cell types. Paradoxically because of these abilities stem cells also have the potential to form tumors.
- While collecting adult stem cells the cells that are damaged or that contain altered gene may be collected.
- Embryonic stem cells might also trigger an immune response in which the recipients body attacks the stem cells as foreign invaders, or the stem cells might simply fail to function normally with unknown consequences.

Controversy:

- There has been some controversy about stem cell research. This mainly relates to work on embryonic stem cells.

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- The argument against using embryonic stem cells is that it destroys a human blastocyst, and the fertilized egg cannot develop into a person [4, 5].
- Nowadays, researchers are looking for ways to create or use stem cells that do not involve embryos.
- Mixing humans and animals: Stem cell research often involves inserting human cells into animals, such as mice or rats. Some people argue that this could create an organism that is part human.
- In some countries, it is illegal to produce embryonic stem cell lines. In the United States, scientists can create or work with embryonic stem cell lines, but it is illegal to use federal funds to research stem cell lines that were created after August 2001.

Stem cell therapy and FDA regulation:

- ✓ Some people are already offering "stem-cells therapies" for a range of purposes, such as anti-aging treatments.
- ✓ However, most of these uses do not have approval from the U.S. Food and Drug Administration (FDA). Some of them may be illegal, and some can be dangerous.
- ✓ Anyone who is considering stem-cell treatment should check with the provider or with the FDA that the product has approval, and that it was made in a way that meets with FDA standards for safety and effectiveness.

CONCLUSION

Stem cells are a boon to medical therapy and research. This technology has revolutionized the laboratory cell biology and will provide much improved cell culture models for discovery and development of drugs, and fundamental studies of the genetic basis of disease. Clinical trials can be conducted on stem cells rather than conducting on humans. They can be used to repair body. A useful analogy is to imagine your stem cells as a team of repairmen in your newly constructed mansion. When the mansion is new and the repairmen are young, they can fix everything perfectly. But as the repairman age and reduce in number, your mansion eventually goes into disrepair and eventually crumbles.

REFERENCES:

1. Sachin Kumar, NP. Singh et al. Stem cells: A new paradigm. Ind J Hum Genet **2006**;12
2. FM. Watt & RR. Driskell. Review. The therapeutic potential of stem cells
3. Ramachandran RP, Yelledahalli LU. Exploring the Recent Advances in Stem Cell Research. J Stem Cell Res Ther **2011**;1:113. doi:10.4172/2157-7633.1000113
4. Anon, Human embryo research/fetal experimentation, focus on the family policy statement dated **1997** december 15.
5. NBAC. Research Involving Human Biological Meterials. Ethical Issues and Policy Guidance. **1999**;1:72.
6. Hewitt R and Watson P. Defining biobank. Biopreserv Biobank **2013**;11:309-315.
7. Jacob Hanna and Allison Hubel* Preservation of stem cells
8. Sputtek A, Sputtek R. Cryopreservation in Transfusion Medicine and Hematology. In: Fuller BJ, Lane N, Benson E, eds. Life in the Frozen State. Boca Raton, FL: CRC Press **2004**;483-504.
9. Berz D, McCormack EM, Winer ES, Colvin GA, Quesenberry PJ. Cryopreservation of hematopoietic stem cells. Am J Hematol **2007**;82:463-72.
10. Chandross KJ, Mezey E. Plasticity of adult bone marrow stem cells. Mattson MP and Van Zant G editors. JAI Press: Greenwich, CT; **2001**.
11. Slack JM. Stem cells in epithelial tissues. Sci **2000**;287: 1431-3.
12. Bain G, Kitchens D, Yao M, Huettner JE, Gottlieb DI. Embryonic stem cells express neuronal properties. Dev Biol **1995**;168:342-57.
13. Odorico JS, Kaufman DS, Thomson JA. Multilineage differentiation from human embryonic stem cell lines. Stem Cells **2001**;19:193-204.
14. Potocnik AJ, Nielsen PJ, Eichmann K. In vitrogeneration of lymphoid precursors from embryonic stem cells. EMBO J **1994**;13:5274-83.
15. Stem cell therapy in India. Available from: http://www.tour2india4health.com/Stem-Cell-Therapy-in-India.html. Accessed September 20, 2017.
16. Tappenden P, Saccardi R, Confavreux C, et al. Autologous haematopoietic stem cell transplantation for secondary progressive multiple sclerosis: an exploratory cost-effectiveness analysis. Bone Marrow Transplant **2010**;45(6):1014–1021.
17. Arruda LC, de Azevedo JT, de Oliveira GL, et al. Immunological correlates of favorable long-term clinical outcome in multiple sclerosis patients after autologous hematopoietic stem cell transplantation. Clin Immunol **2016**;169:47–57.

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