



# “Regenerative Medicine Through Stem Cell: A Systematic Review”

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## ABSTRACT:

In this article, we have discussed about stem cell therapy to prevent or treat diseases, with the only FDA approved treatment being haemopoietic stem cell transplantation. This transplantation can take the form of bone marrow or peripheral blood stem cell transplantation, or derive cells from umbilical cord blood.

On going research aims to explore diverse sources of stem cells and apply stem cell therapy to neurodegenerative diseases, diabetes and heart diseases. However, stem cell therapy has sparked controversy due to advancements like isolating and culturing embryonic stem cells, creating stem cells by somatic cell nuclear transfer and generating induced pluripotent stem cells.

Stem cells possess the unique ability to transform into specialized cell types characterized by two key properties i.e. Self-renewal and differentiation into adult cells. There are two primary categories of stem cells:

- pluripotent cells: capable of developing into any adult cell types.
- multipotent cells limited to differentiating into specific cell population.

This discussion explores stem cell sources, characteristics, differentiation potential and therapeutic applications. While stem cells hold immense promise for tissue regeneration and repair, further research is essential to understand their biology, manipulation and safety to unlock their full therapeutic potential.

## KEY WORDS:

Stem cell therapy, Types of stem cell therapy, recent advancements.

## INTRODUCTION:

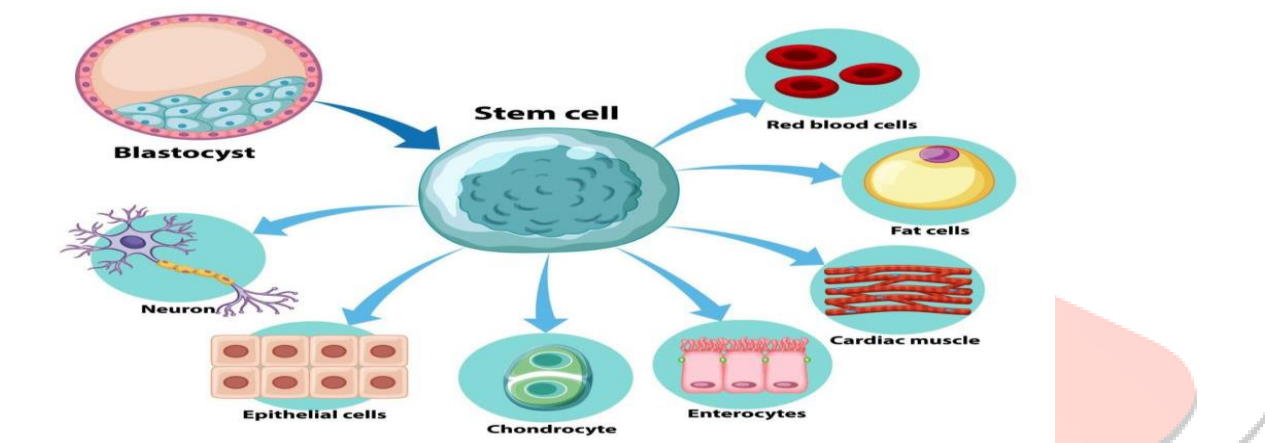
Stem cell therapy owes its origin to the ground breaking work of mid-20<sup>th</sup> century's pioneers. Geroge Mathé's landmark 1956 bone marrow transplant marked the first successful application followed by the decades of transformative contributions from the estimated scientist. Geroge Mathé's life saving treatment of five radiation exposed workers at Vinča Nuclear Institute in Yugoslavia marked the beginning of stem cells advancement. Later, researchers made significant breakthroughs:

- Ernest McCulloch and James Till (1960s): Identified hematopoietic stem cells (HSCs) crucial for blood formation.
- Martin Evans and Matthew Kaufman (1981): Discovered embryonic stem cells.
- James Thomson (1998): Isolated human embryonic stem cells.
- Shinya Yamanaka (2006): Developed induced pluripotent stem cells.

Stem cell therapy primarily focuses on treating blood cancers and some degenerative condition. The key applications of stem cell therapy are hematopoietic stem cell transplantation (HSCT), skin grafts, limbal stem cell deficiency. However, the emerging applications of stem cell therapy are neurodegenerative diseases, diabetes, cardiovascular diseases, spinal cord injuries, and autoimmune diseases.

## WHAT ARE STEM CELLS?

Stem cells are defined as the unique cells with the ability to develop into various types of cells into body. They play important role in growth, development, regenerate and tissue repair.



The human body comprises various cells, lungs, liver, kidney and more. These cells perform unique function such as blood cell facilitating circulation, muscle cell enabling movement, nerve cells transmitting signals. However, there is a special category of cells called stem cells which do not have a predefined role. Instead, they divide and grow in numbers, produce new stem cells, replace damage or missing cells.

Stem cells serve as the body's cellular reservoir maintaining balance and ensuring:

- Liver cells, kidney cells, and other organ cells are replenished.
- Blood cells and muscle cells are produced.
- Tissue repair and regeneration occur

In addition, stem cells are vital for body's functioning, adapting to needs and maintaining cellular equilibrium.

Stem cells possess distinct properties essential for their role in development, tissue repair, and therapeutic applications. The key properties include:

- 1) Self- Renewal: stem cells divide and maintain their population indefinitely.
- 2) Potency: stem cells ability to differentiate into specialized cell types categorized in different types.
- 3) Asymmetrical division: Producing one stem cell daughter and another differentiated cell maintaining population balance.
- 4) Clonogenicity: Forming colonies from single cells demonstrating proliferation and self-renewal.
- 5) Differentiation potential: Responding to environmental signals to differentiate into specific cell types.
- 6) Regenerative capacity: Replacing damaged or lost cells for healing and tissue regeneration.
- 7) Micro environment sensitivity: Behavior influenced by surrounding niche, regulating self-renewal and differentiation.

These properties enable themselves to maintain cellular balance, support tissue repair and regeneration, and offer therapeutic potential.

## **TYPES OF STEM CELLS:**

Stem cells are classified on the two bases:

### **A. Based on the Potency**

- Totipotent
- Pluripotent
- Multipotent
- Oligopotent
- Unipotent

### **B. Based on the Origin.**

- Adult body tissue
- Embryos

### **A. Based on the potency:**

#### **TOTIPOTENT:**

Totipotent cells possess the unique ability to differentiate into any cell type within the body including somatic cells (e.g. skin, muscle, nerve cells), Germ cells (e.g. egg, sperm cells), Extra-embryonic cells (e.g. placental cells).

A prime example of a totipotent cell is the zygote or fertilized egg which has the potential to develop into a fully formed Organism.

#### **PLURIPOTENT:**

Pluripotent stem cells can become almost any cell type in the body except placental tissues. There are two subtypes-

- Embryonic stem cells (ESC)- They are derived from blastocysts they can develop into all cell types
- Induced pluripotent stem cells (iPSC)- Adult cells reprogrammed to an embryonic like state retaining ability to differentiate.

#### **MULTIPOTENT:**

Multipotent stem cells can become multiple cells types within a specific lineage, but with limitations.

For example: Hematopoietic stem cells (bone marrow) develop into various blood cells, Mesenchymal stem cells form bone, cartilage, and fat tissues.

#### **OLIGOPOTENT:**

Oligopotent stem cells possess the ability to differentiate into a restricted number of closely related cell types.

The notable example is myeloid stem cells which give rise to specific blood cell types including White blood cells (WBC), red blood cells (RBC), platelets.

**UNIPOTENT:**

Unipotent stem cells have the most limited differentiation potential producing only one specific cell.

Muscle stem cells generate muscle tissue, skin stem cell only produce skin cells.

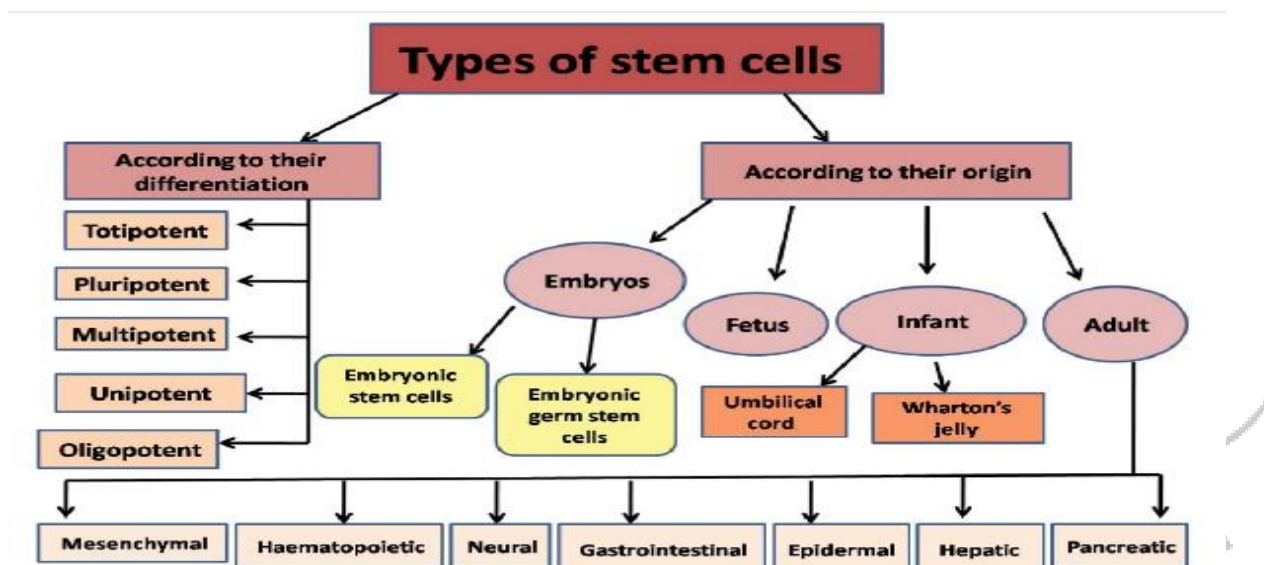
**B. Based on the origin:****ADULT STEM CELL:**

They are also known as somatic stem cells and found in specific tissue. Adult stem cells maintain and repair tissues throughout life.

For example, Hematopoietic stem cells (Blood).

**EMBRYONIC STEM CELL:**

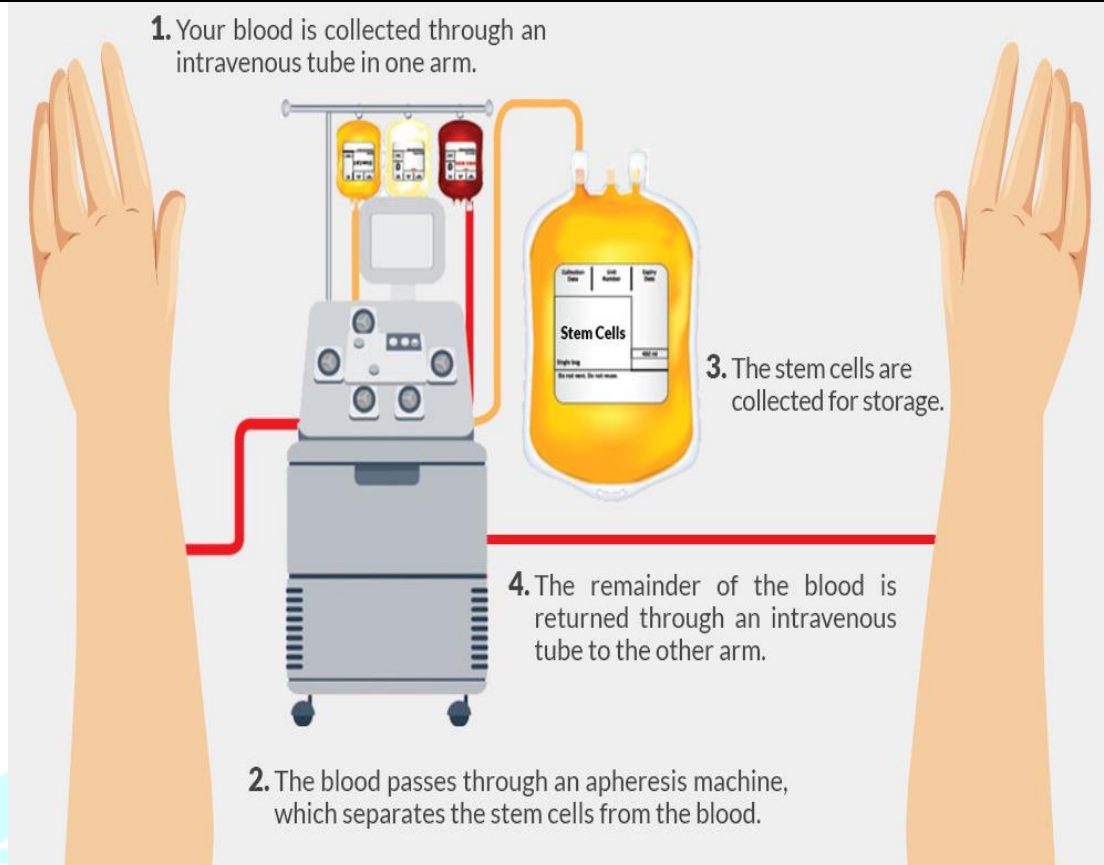
They are originated from inner cell mass of blastocyst. It is also known as pluripotent stem cell.

**STEM CELL HARVEST:**

The process of obtaining stem cell by various methods tailored to specific sources like bone marrow, blood, adipose tissue, umbilical cord or other tissues is known as stem cell harvest or stem cell collection. Following are some techniques used for stem cell harvest:

**1. Peripheral blood stem cell harvesting (Apheresis):**

- Preparation: G-CSF injection is given to mobilize stem cells.
- Procedure: Blood drawn, processed and returned through arms.
- Duration: 2 Hours, potentially multiple sessions.



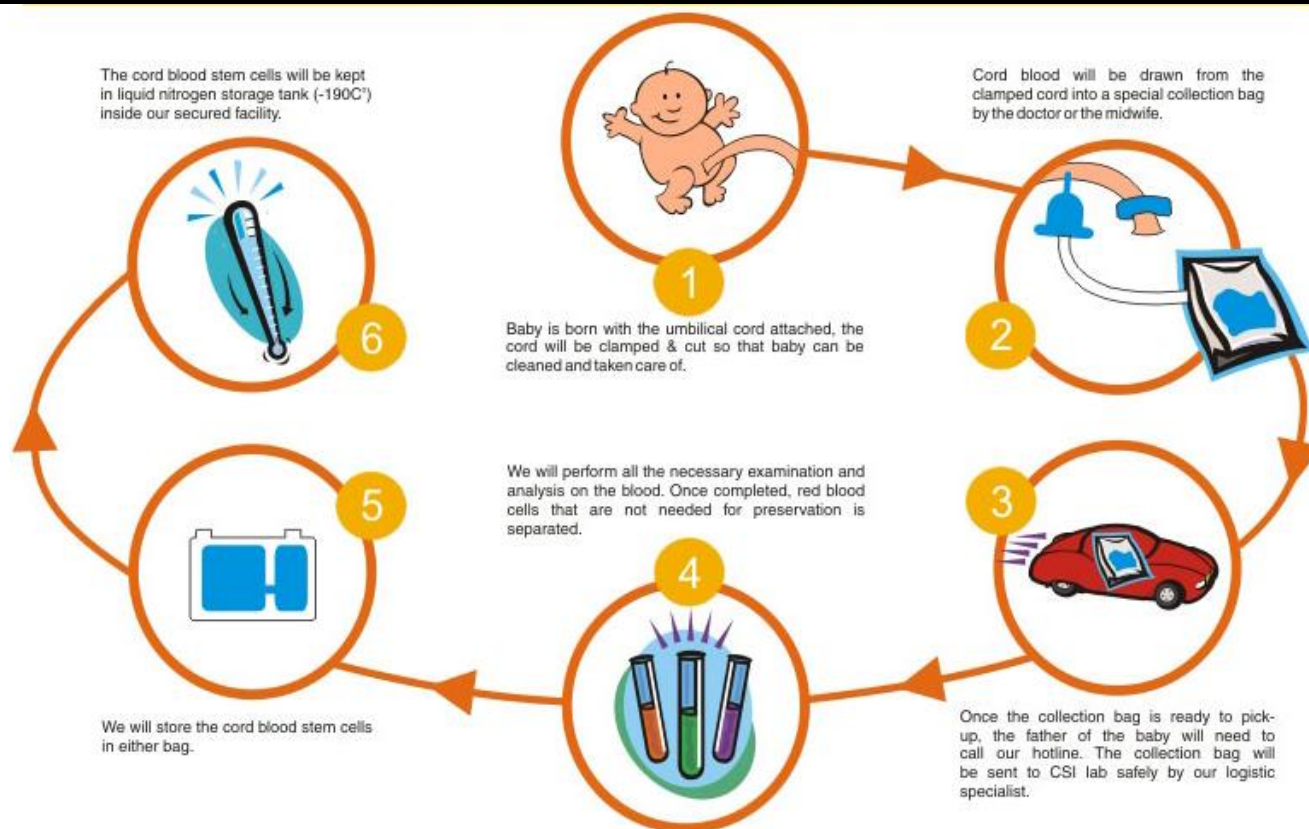
## 2. Bone marrow Harvest:

- Preparation: General anesthesia is administered to patient.
- Procedure: Needle insertion into hip bone is done for extraction of bone marrow.
- Duration: 2 hours required and multiple punctures are done to collect sufficient stem cells from bone marrow.



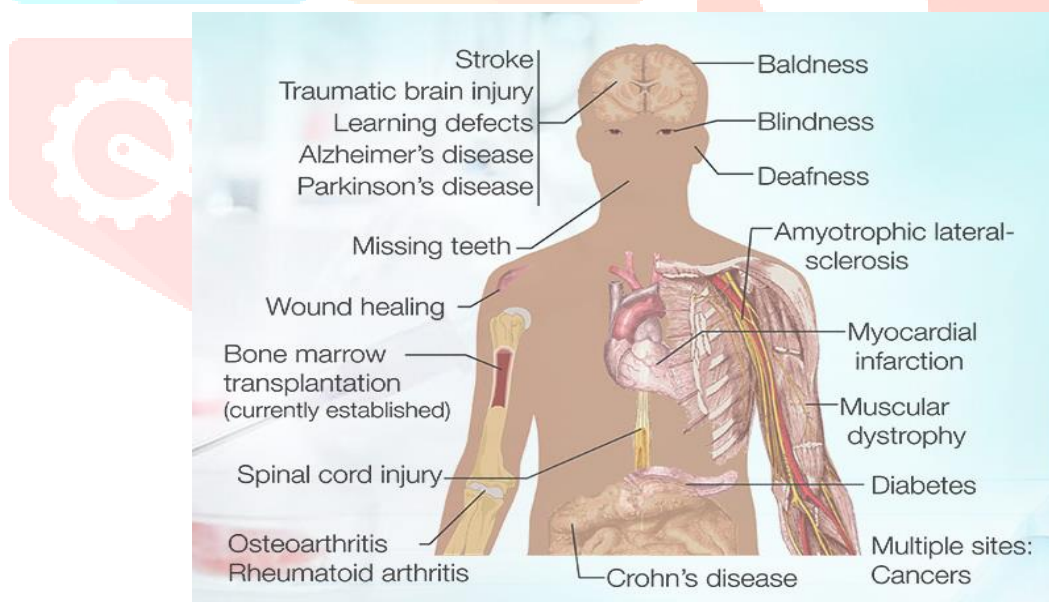
## 3. Umbilical cord blood collection:

- Timing: Immediately at post-childbirth.
- Procedure: blood collection from placenta and umbilical cord.
- Benefits: Non-invasive, painless procedure for mother and child both.



## HOW DOES IT WORK?

First to know how does it works we need to know what are its potential uses:



The image referred above are the potential uses or areas covered by stem cell therapy. By use of stem cell therapy, we can cure or prevent further progression of diseases and aim for a better life of patient.

Mechanism of stem cell therapy in regenerative medicine. Stem cell therapy exploits the unique characteristics of stem cells to treat diseases by following mechanisms:

### 1. Regeneration and repair:

- Stem cells self-renew and differentiate into specialized cells replacing the damaged cells.
- For instance, heart disease- stem cells become heart muscle cells repairing damaged heart tissues.
- Stem cell facilitate tissue repair via multiple mechanism:

- Anti-inflammatory action: Stem cell mitigate inflammation and create a healing environment which helps in recovery.
- Targeted migration: Stem cells migrate to site of injury and recruit endothelial progenitor cells or immune cells.
- Tissue remodeling: Stem cell encourages functional tissue regeneration over scar formation.
- Apoptosis inhibition: Stem cells prevent programmed cell death and enhances tissue viability.
- Differentiation: stem cells become specific cell types for tissue repair (osteogenic, chondrogenic, myogenic)

## 2.Cell specialization:

- In vitro manipulation of stem cells ensures targeted specialization for effective tissue regeneration.
- Mechanism of stem cell specialization:
  - Lineage commitment: Stem cells progress through stages becoming more specialized. Pluripotency  $\Rightarrow$  Multipotency  $\Rightarrow$  Unipotency (restricted potential).
  - Transcriptional regulation: Gene expression shifts as stem cell differentiate. Specific genes are activated or silenced for neurons, cardiomyocytes etc.
  - Epigenetic modification: DNA or histone changes stabilize specialized cells. controlling gene accessibility.

## 3.Immune Modulation:

- Stem cells regulate immune responses benefiting autoimmune diseases and reducing inflammation.
- Mechanism of immune modulation:
  - Interaction with immune cells: stem cells communicate with macrophages T cells and dendritic cells. Altering immune cell behavior for tolerance or activation.
    - Regulatory T cells (Tregs): promote differentiation and expansion.
    - Macrophages polarization: anti-inflammatory M2 phenotype.
  - Selection of soluble factors: Cytokines, growth factors and extracellular vesicles modulate immune responses.
    - Immunosuppressive molecules: transforming growth factor beta (TGF- $\beta$ ), interleukin-10 (IL-10), prostaglandin E2(PGE2) inhibit T cell activation.
    - Antimicrobial peptides: combat infection and reduces hypercytokinemia.
  - Modulation of inflammatory responses: Transition from pro inflammatory to reparative state. Stem cells migrate to affected areas modulate local inflammation. Immune environment “resets” and benefits chronic inflammation or autoimmunity condition.

Here are some applications of stem cells in disease treatment:

- Neurological disorders: stem cells replace damaged neurons:
  - spinal cord injuries
  - Alzheimer’s disease
  - Parkinson’s disease.
- Cardiovascular diseases: stem cells facilitate heart tissue repair and regeneration after myocardial infarction heart failure.
- Diabetes mellitus: stem cells regenerate pancreatic beta cells for type 1 and type 2 diabetes mellitus.
- Oncology: stem cells transplants restore hematopoiesis after chemotherapy for hematological malignancies (Leukemia).
- Musculoskeletal disorders: stem cells promote cartilage repair and reduce inflammation in arthritis joint disorders.

## RISK AND COMPLICATIONS:

Stem cell therapy has potential risks and complication affecting patient outcomes. Understanding these risks is crucial.

- Common risks:
  - Grafts vs host disease (GvHD): Donor immune cell attack recipient tissues.
  - Infections: Increased risk due to chemotherapy and transplant.
  - Reduced blood cell count: Anemia, thrombocytopenia, leukopenia.
  - Chemotherapy side effects: Nausea, vomiting, hair loss, infertility.
  - Organ damage: Liver, kidney, lung, or heart damage.
  - Thromboembolism: Blood clots, pulmonary embolism.
- Specific complications:
  - Autologous Transplant: Bleeding, Anemia.
  - Allogeneic transplant: GvHD, graft failure, donor-recipient mismatch.

## CONCLUSION:

Stem cell therapy has significant potential in the regenerative medicines but further research is necessary to validate its effectiveness. Outgoing studies should focus on:

- Clarifying mechanism of action
- Refining clinical protocols
- Resolving ethical concerns

As the fields evolve it may lead to revolutionary therapy that accelerate healing improve recovery rates benefit patients with various disease and injuries.

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