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Programme: M.Sc., Biomedical science

Course Title : Stem Cell Biology & Tissue Engineering

Course Code : 18BMS48C14

Unit-I

TOPIC: Introduction to Stem Cell Biology

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STEM CELL

Introduction
Features of stem cells
3 Unique features of stem cells
Distinguishing features of progenetor/precursor cells & Stem cells

classification of stem cell
Embryonic stem cell
Adult stem cell
Induced pluripotent stem cells
Regenerative medicine & cell therapy
Clinical applications

Introduction

- self-renewal
- differentiation.
- Self-renewal is the ability of cells to proliferate.
- blank cell / precursor cell
- building block of the human body

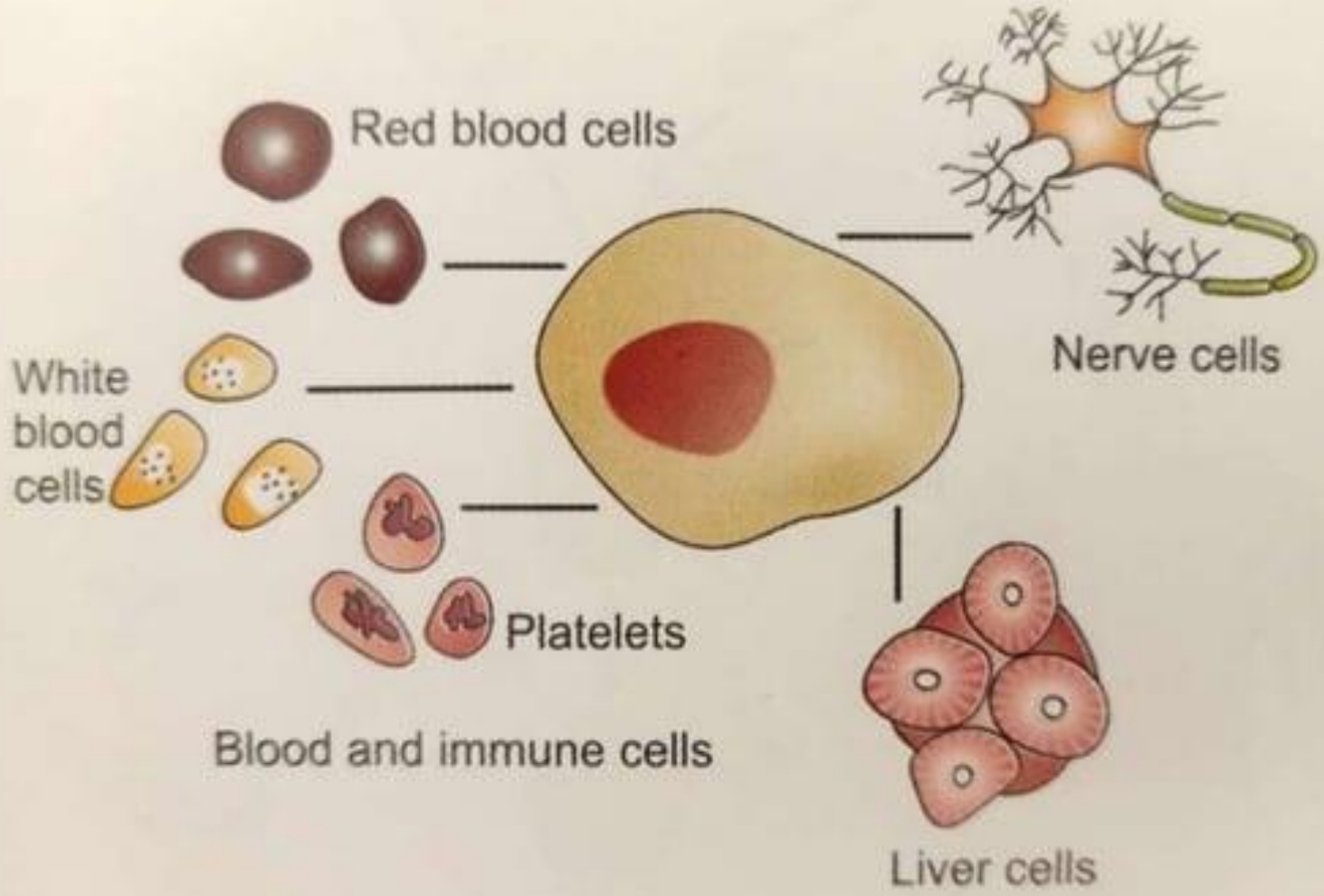


Fig. 1.1: Stem cells can differentiate into many cell types

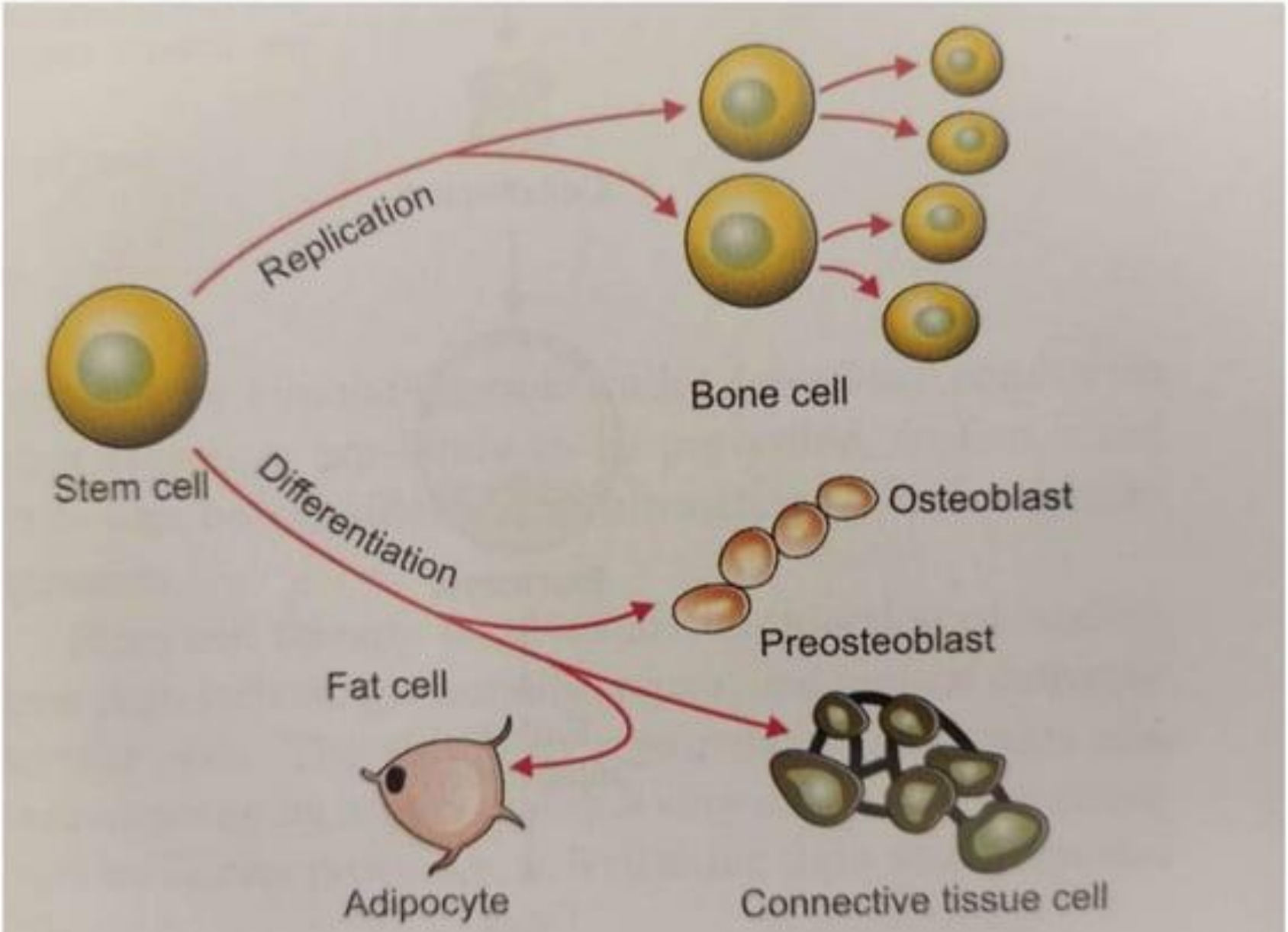


Fig. 1.2: Stem cells

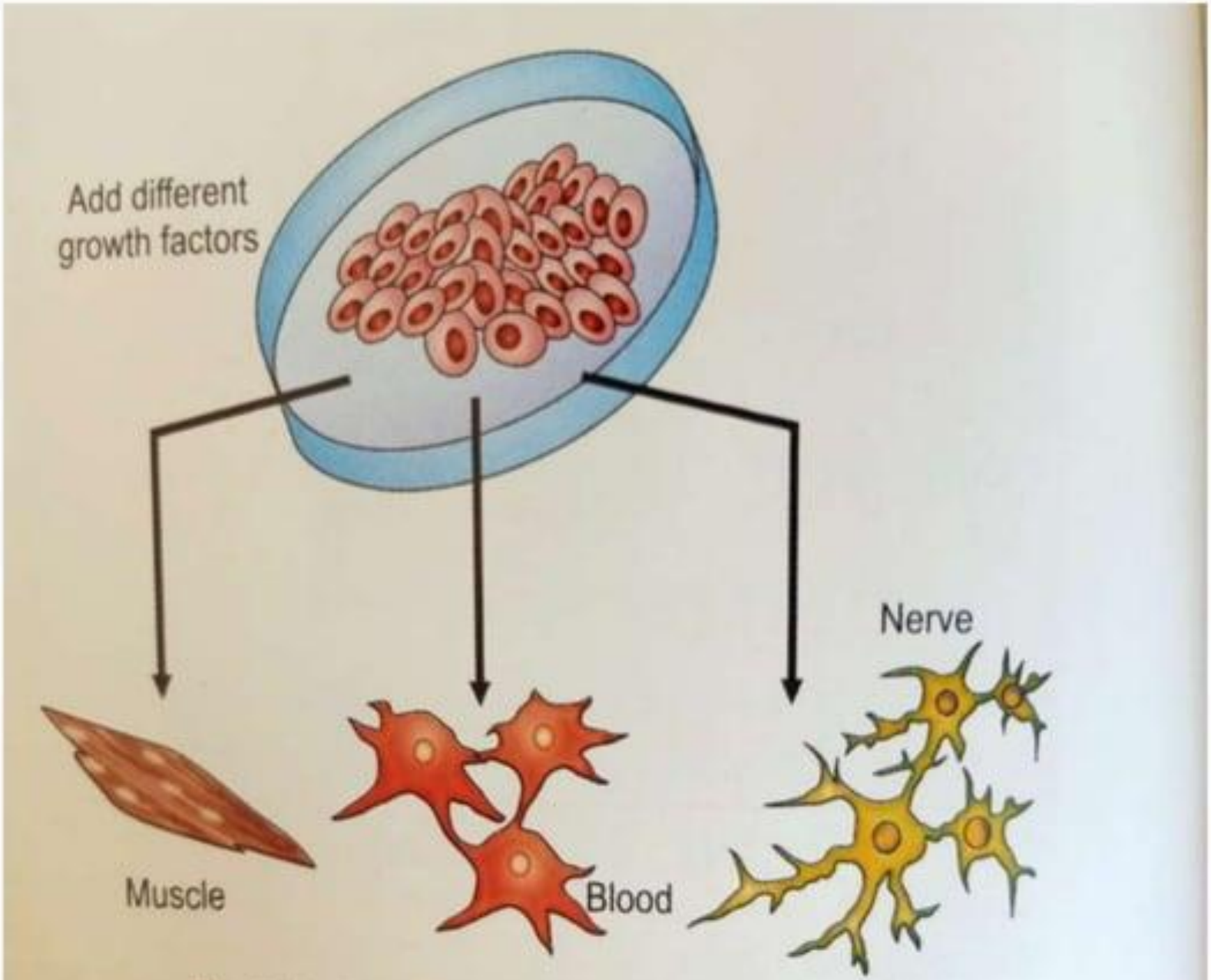


Fig. 2.19: Differentiating the stem cells into the precursor cells for all types

Features of Stem Cells

unique cells.

amazing ability to develop into several distinct cell types

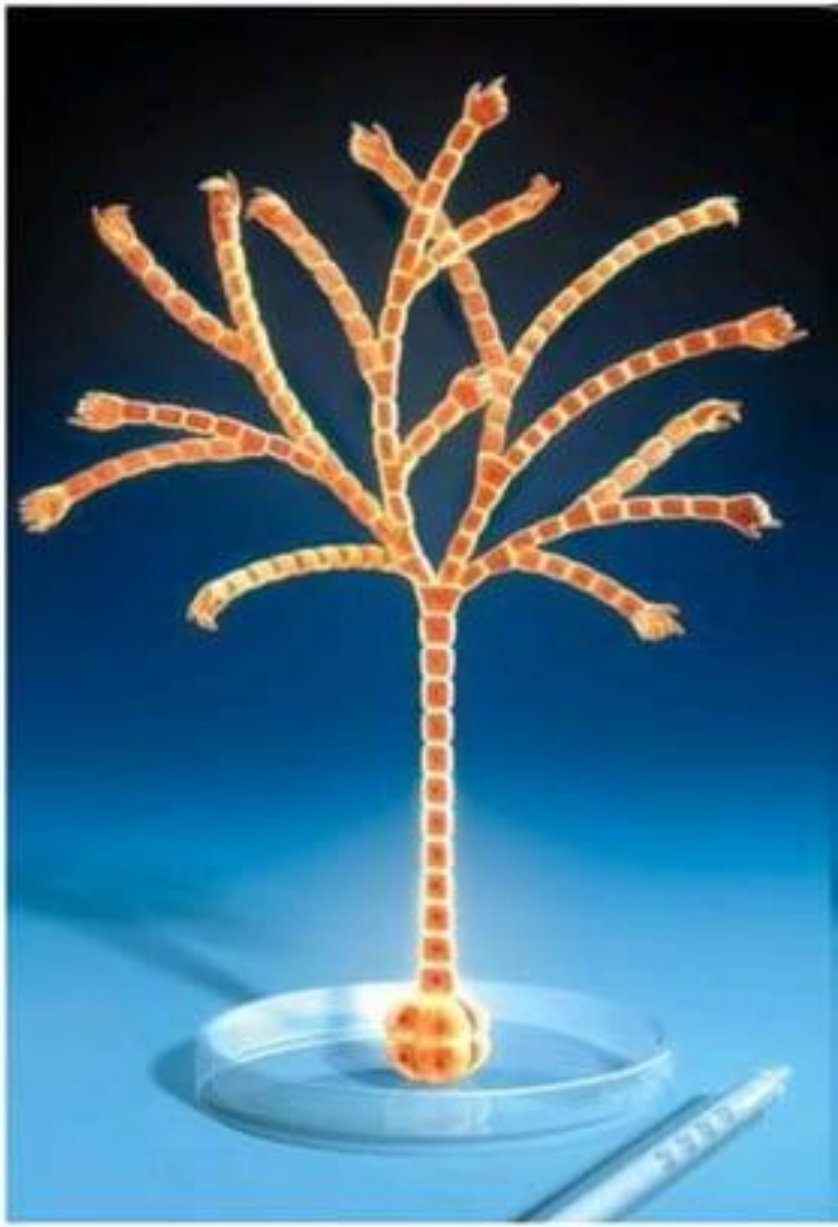
Stem Cells can be used as a repair system for the body.

divide without limit in order to replenish various types of cells.

When a stem cell divides - remain a stem cell or become another type of cell with a more specialized function (i.e. a muscle cell, a red blood cell, a brain cell, etc.).

Three unique properties of stem cells

Stem cells are capable of dividing & renewing themselves for long periods



Three unique properties of stem cells

A stem cell is "uncommitted," until it receives a signal to develop into a specialized cell

Three unique properties of stem cells

Stem cells are unspecialized cells that develop into specialized cells

(make up the different types of tissues in the human body).

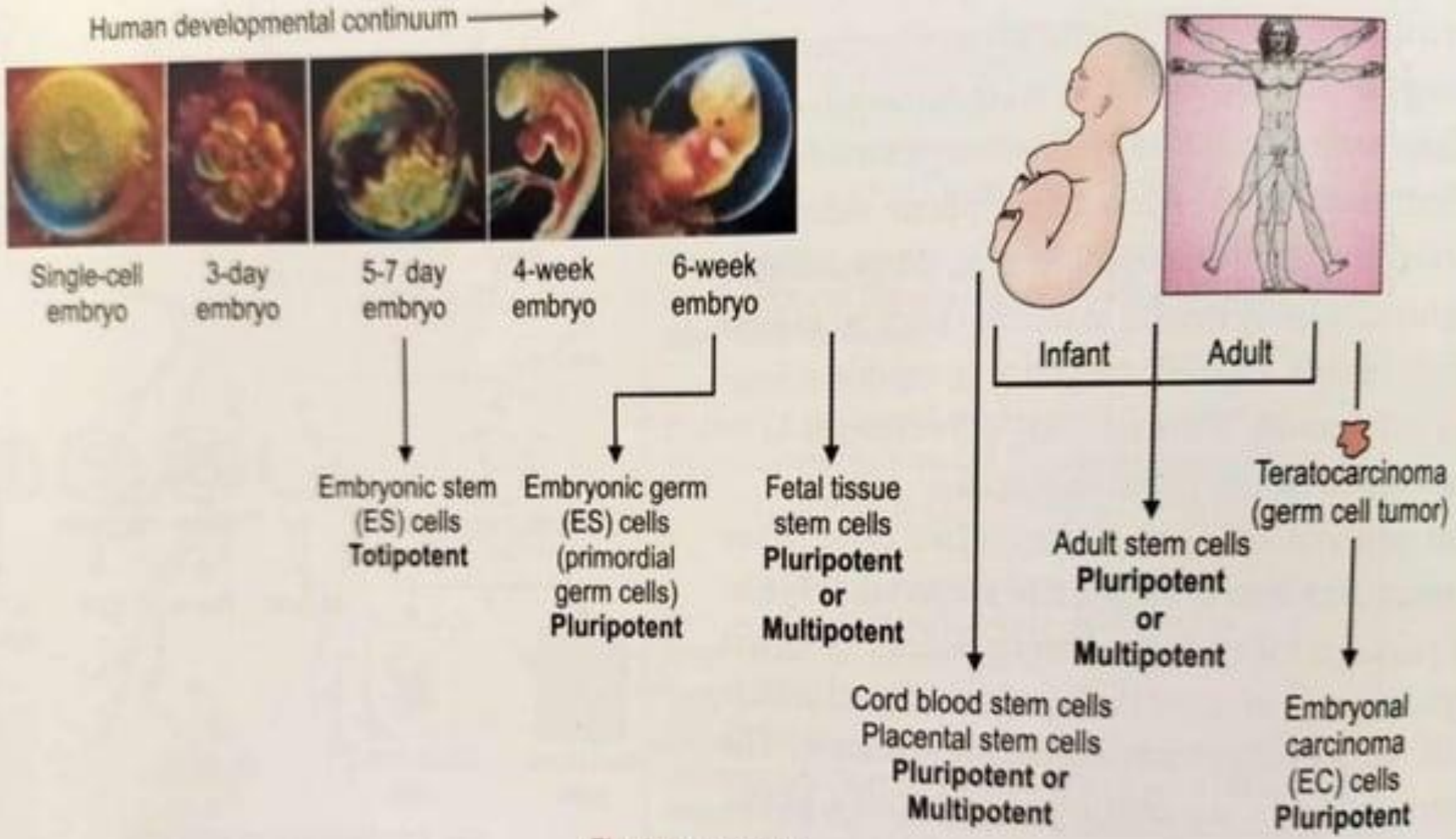


Fig. 2.4: Stem cells

Distinguishing Features of Progenitor / Precursor Cells and Stem Cells

A stem cell is an unspecialized cell that develops into a variety of specialized cell types.

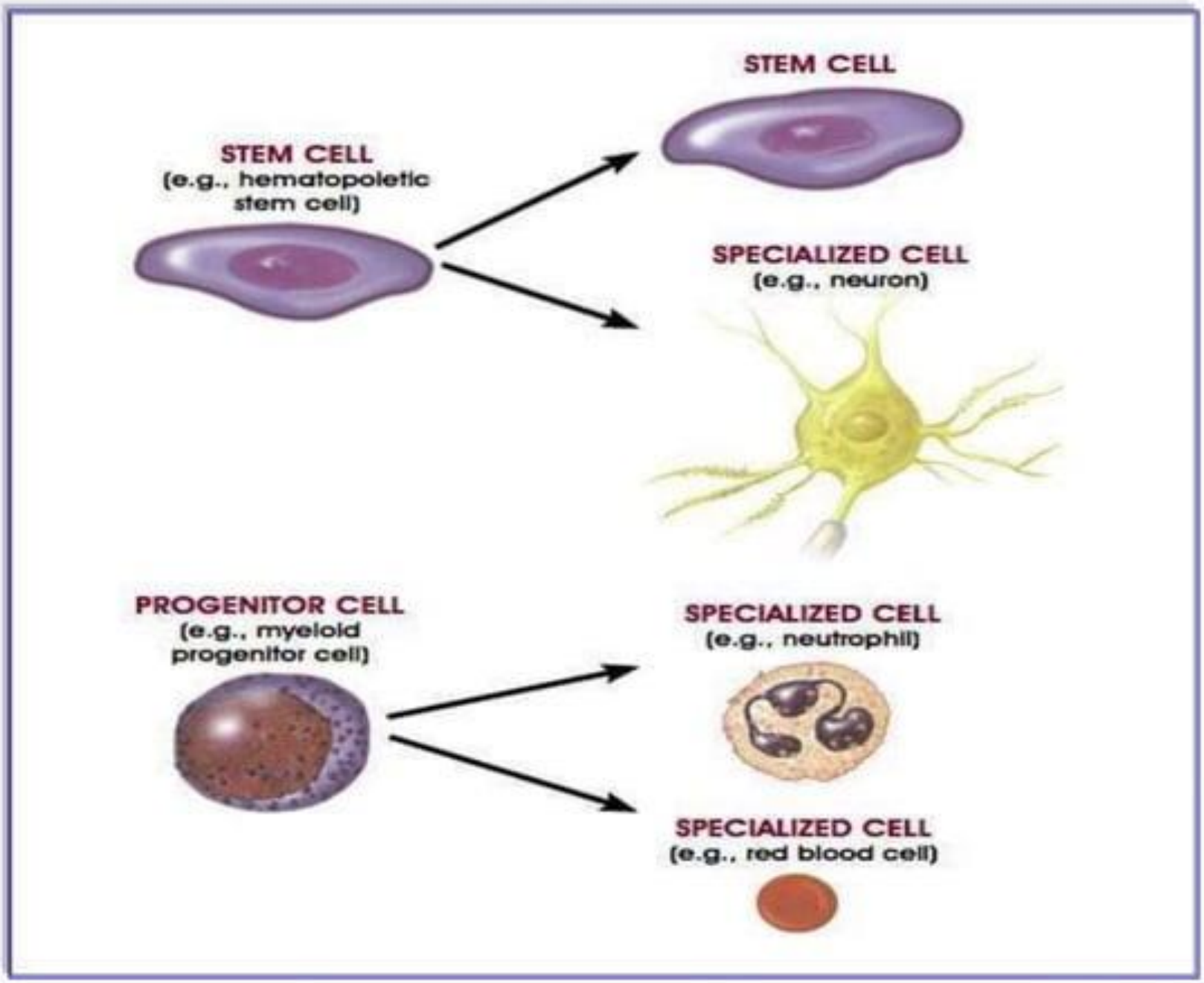
A stem cell divides and gives rise to one additional stem cell and a specialized cell.

Example:
a hematopoietic stem cell produce a second generation stem cell and a neuron.

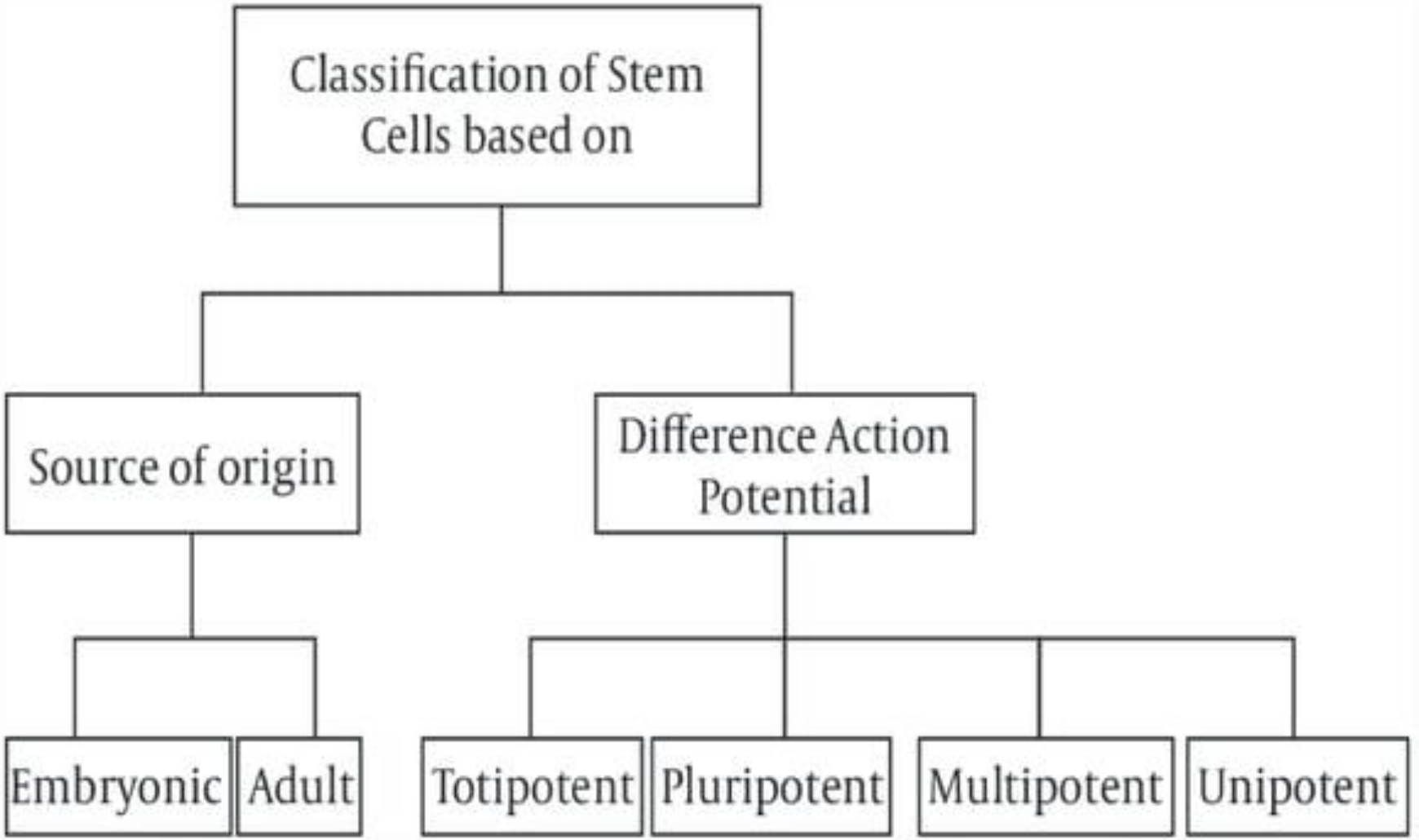
Distinguishing Features of Progenitor /Precursor Cells and Stem Cells(Conti....)

A progenitor cell is unspecialized that is capable of undergoing cell division and yielding two specialized cells.

Example: a myeloid progenitor/precursor cell undergoing cell division to yield two specialized cells (a neutrophil and a red blood cell).


STEM CELL
STEM CELL
(e.g., hematopoietic
stem cell)
SPECIALIZED CELL
(e.g., neuron)
PROGENITOR CELL
(e.g., myeloid
progenitor cell)
SPECIALIZED CELL
(e.g., neutrophil)
SPECIALIZED CELL
(e.g., red blood cell)

classification



The potency of a stem cell is defined by the types of more differentiated cells that the stem cell can make.

Stem cells can be either:

- totipotent,
- pluripotent,
- multipotent, or
- unipotent.

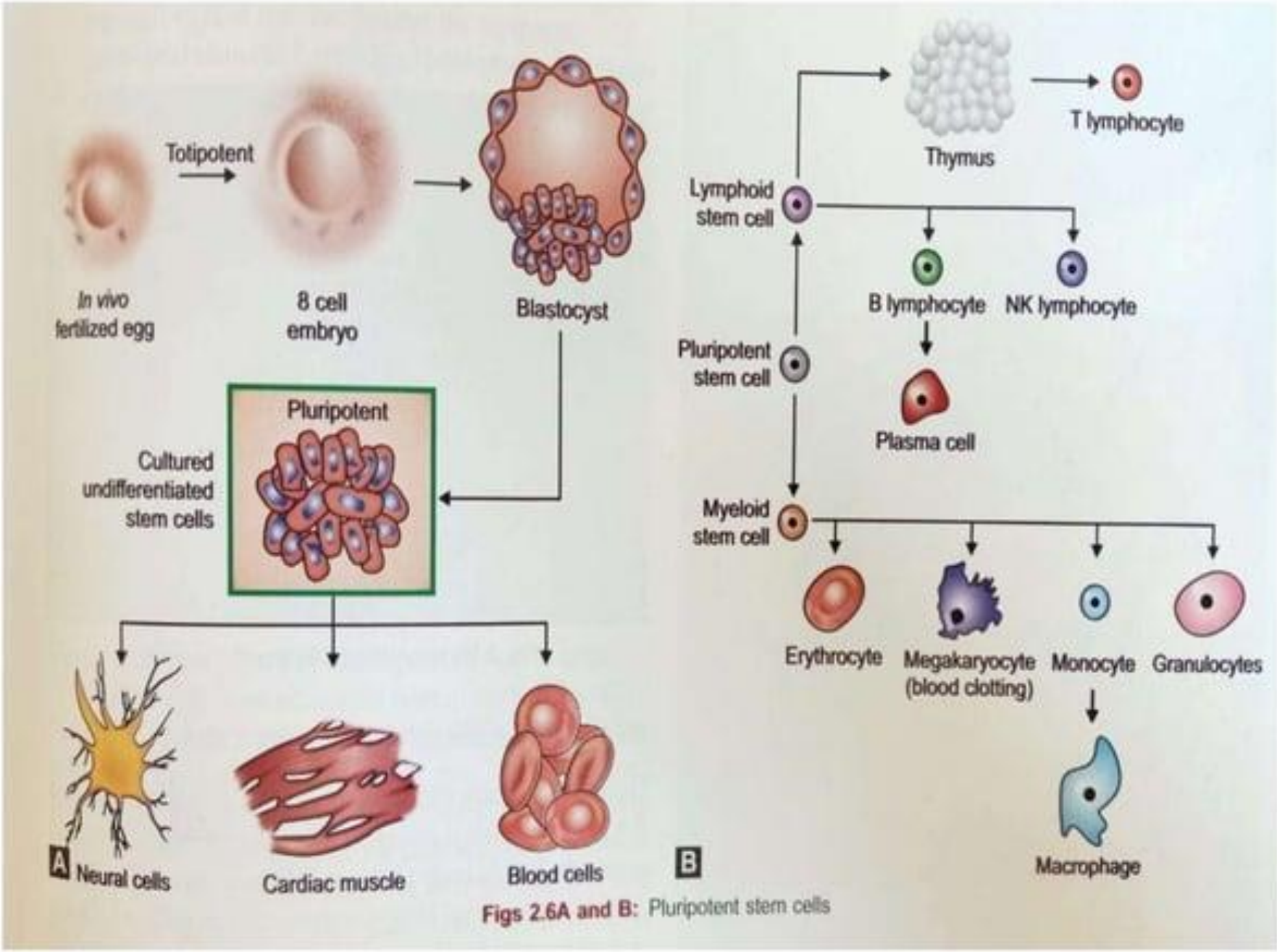
Totipotent stem cells

Totipotent cells have the capability to **produce all cell types** of the developing organism, including both embryonic and extraembryonic (eg, placenta) tissues.

Pluripotent cells

Pluripotent cells can only **make cells of the embryo proper**,

Can make all cells of the embryo (germ cells, cells from any of the germ layers. Therefore, they can make any cell of the body.



Figs 2.6A and B: Pluripotent stem cells

Multipotent cells

Multipotent cells **can only make cells within a given germ layer.**

For example, multipotent stem cells from a mesodermal tissue like the blood can make all the cells of the blood,

but cannot make cells of a different germ layer such as neural cells (ectoderm) or liver cells (endoderm).

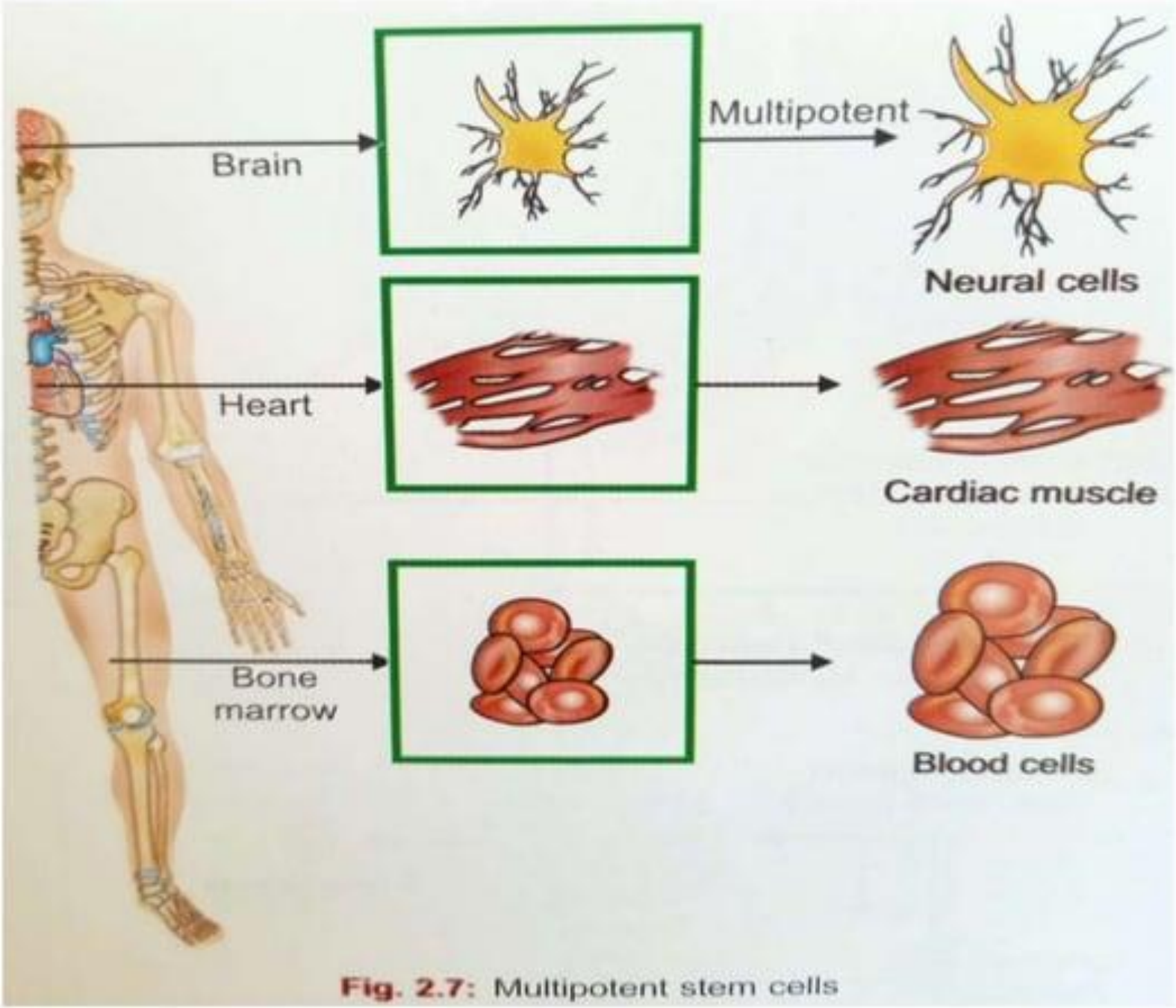


Fig. 2.7: Multipotent stem cells

Unipotent cells

Unipotent cells make cells of a single cell type.

An example is a germ cell stem cell that makes the cells that mature to become egg or sperm, but not other cell types.

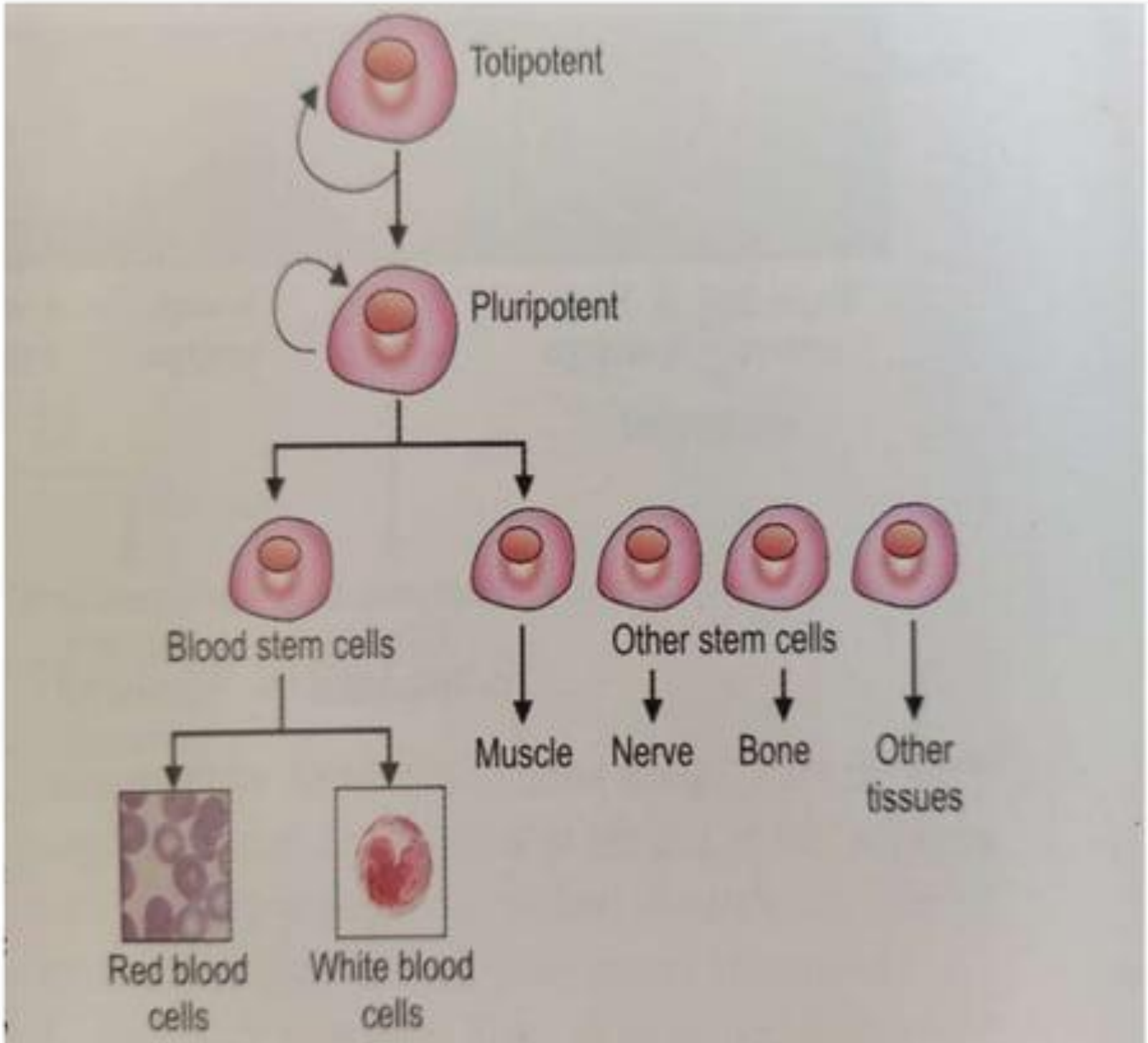


Fig. 2.1: Hierarchy of stem cells

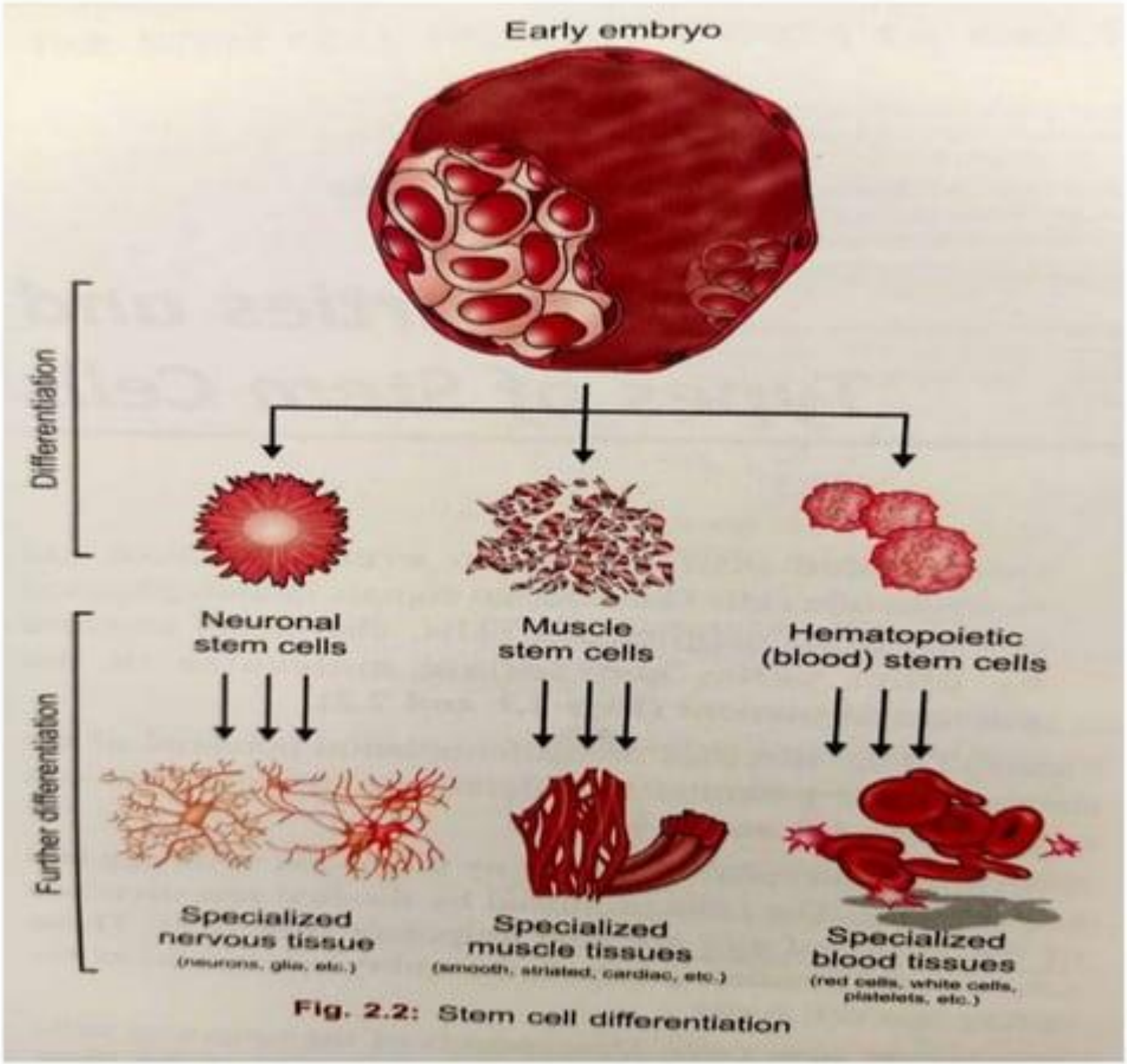


Fig. 2.2: Stem cell differentiation

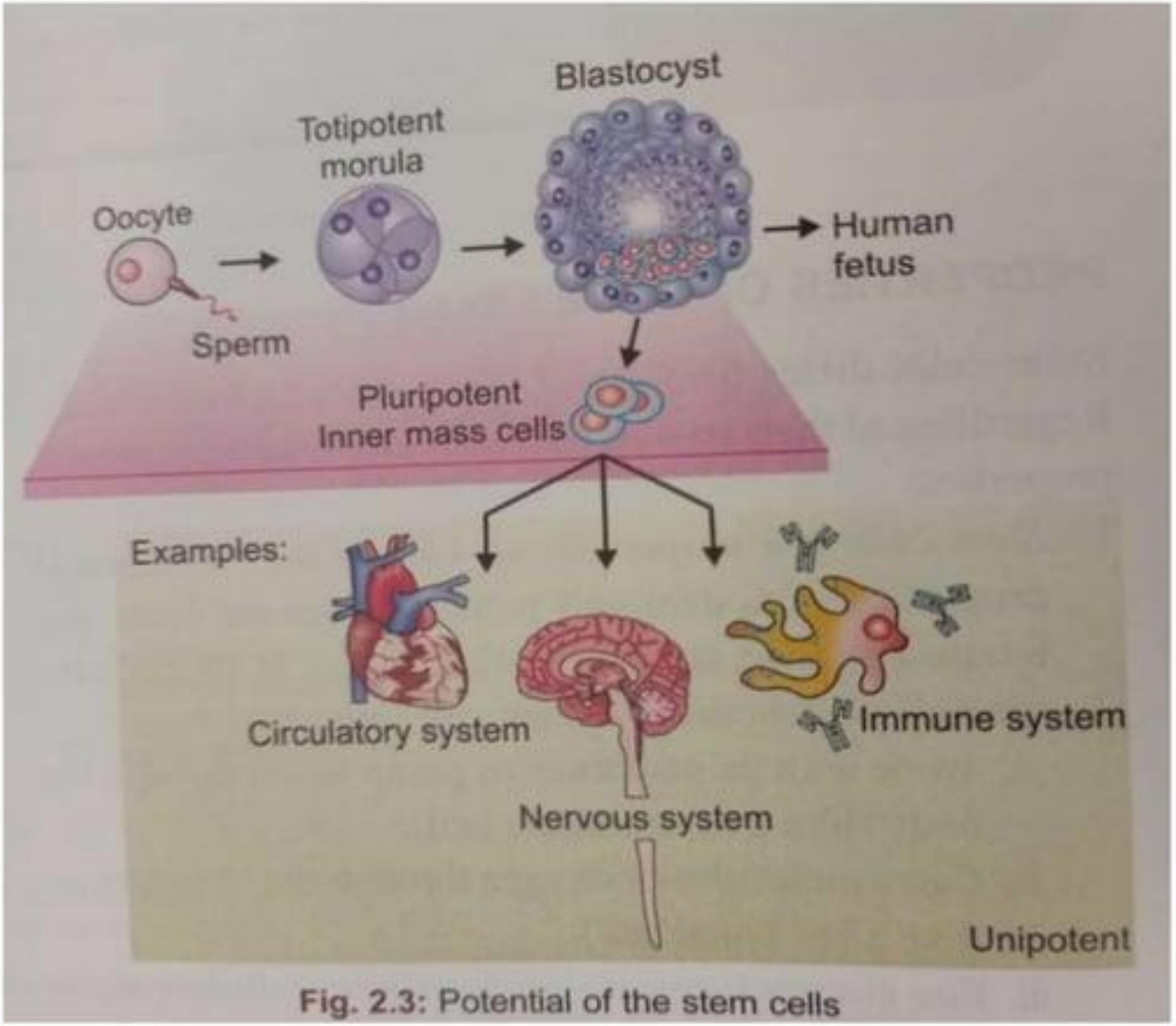
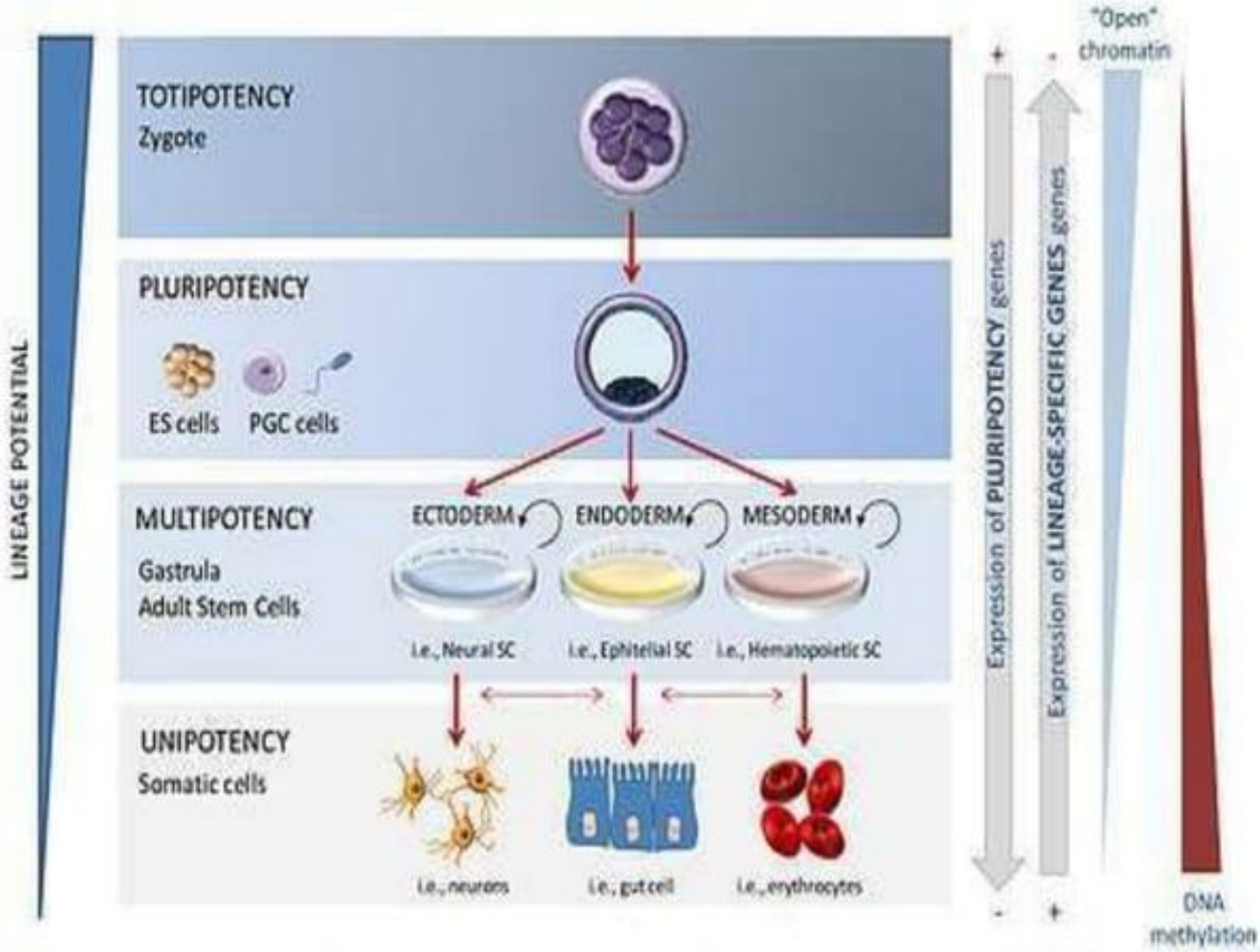
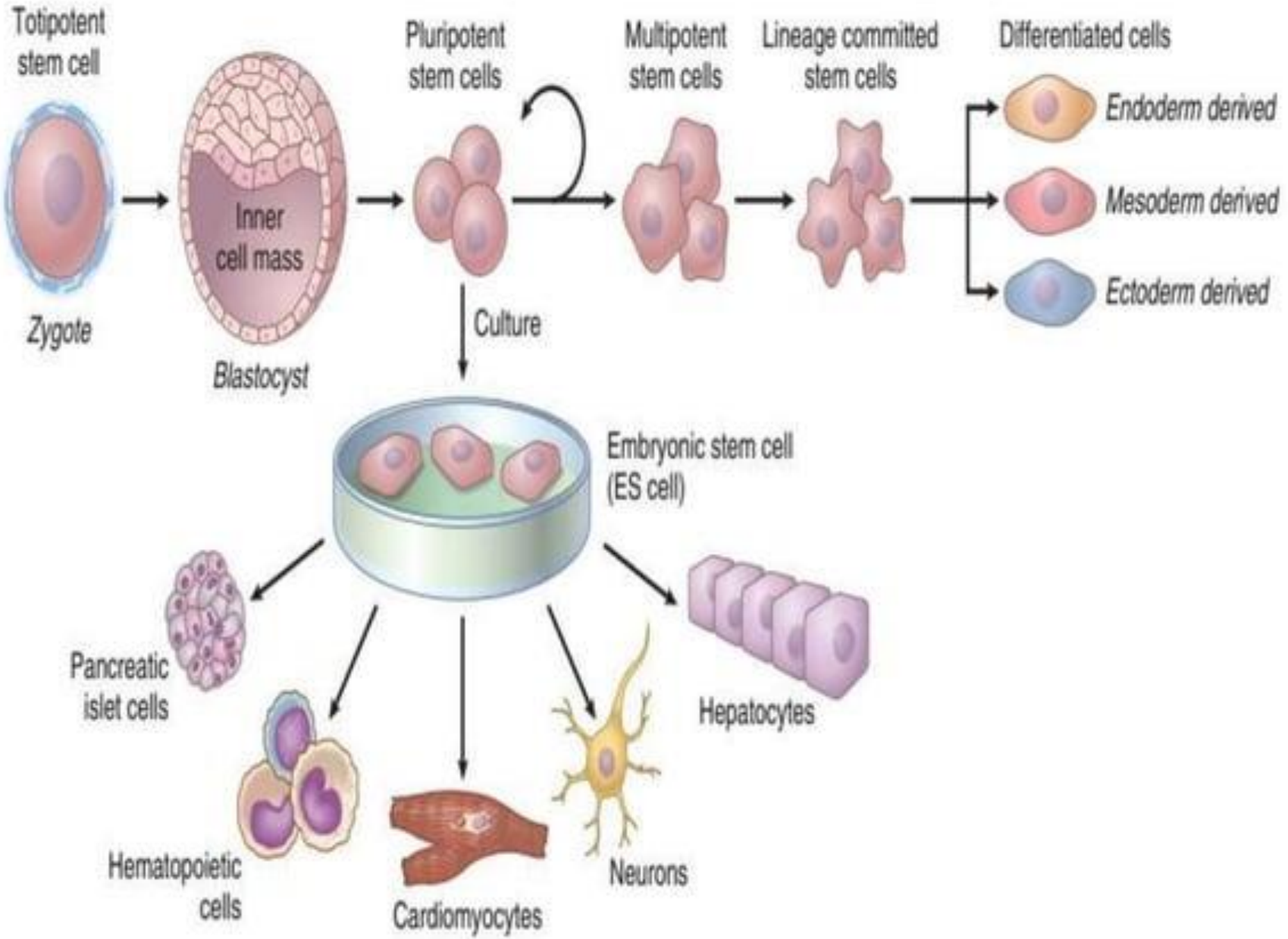


Fig. 2.3: Potential of the stem cells


LINEAGE POTENTIAL
TOTIPOTENCY
Zygote
PLURIPOTENCY
ES cells
PGC cells
MULTIPOTENCY
Gastrula
Adult Stem Cells
ECTODERM
ENDODERM
MESODERM
i.e., Neural SC
i.e., Ephitelial SC
i.e., Hematopoietic SC
UNIPOTENCY
Somatic cells
i.e., neurons
i.e., gut cell
i.e., erythrocytes
Expression of PLURIPOTENCY genes
Expression of LINEAGE-SPECIFIC GENES genes
"Open" chromatin
DNA methylation


Totipotent stem cell
Zygote
Inner cell mass
Blastocyst
Pluripotent stem cells
Culture
Multipotent stem cells
Lineage committed stem cells
Differentiated cells
Endoderm derived
Mesoderm derived
Ectoderm derived
Embryonic stem cell (ES cell)
Pancreatic islet cells
Hematopoietic cells
Cardiomyocytes
Neurons
Hepatocytes

Embryonic stemcells

Embryonic stem cells are MOST UNDIFFIRENTIATED

Derived from the **inner cell mass of a blastocyst**.

LIMITLESS Cell renewal capacity

Can give rise to every cell in the body (Therefore said TOTIPOTENT)

Induced to form specialized cells of all 3 germ cell layers (neuron, cardiac muscle, liver cells, pancreatic islets cells

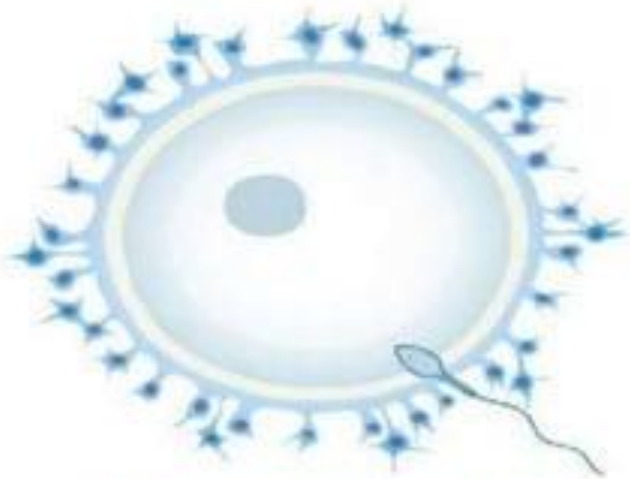
Embryonic stem cells

Human embryos reach the blastocyst stage 4–5 days post fertilization, at which time they consist of 50–150 cells.

Human ES cells measure approximately 14 μm

This would provide a radical new treatment approach to a wide variety of conditions where age, disease, or trauma has led to tissue damage or dysfunction.

Isolating **ES cells**



1 Sperm and egg join

2 Embryo develops for 5-7 days

Blastocyst

3 Remove inner cell mass

4 Grow in dish

5 Change culture conditions to stimulate cells to differentiate into a variety of cell types

Neural cells

Skin cells

Skeletal muscle cells

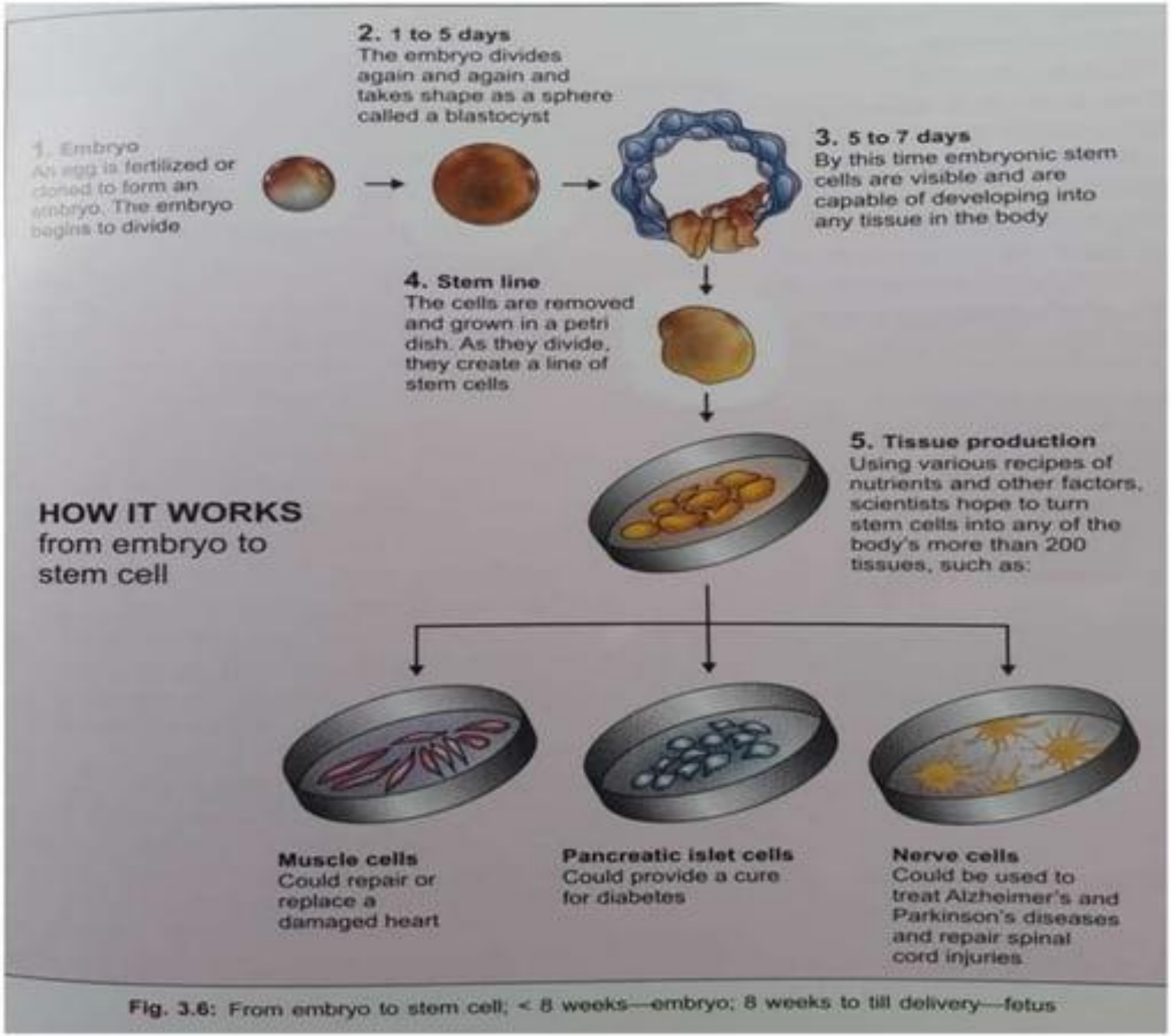


Fig. 3.6: From embryo to stem cell; < 8 weeks—embryo; 8 weeks to till delivery—fetus

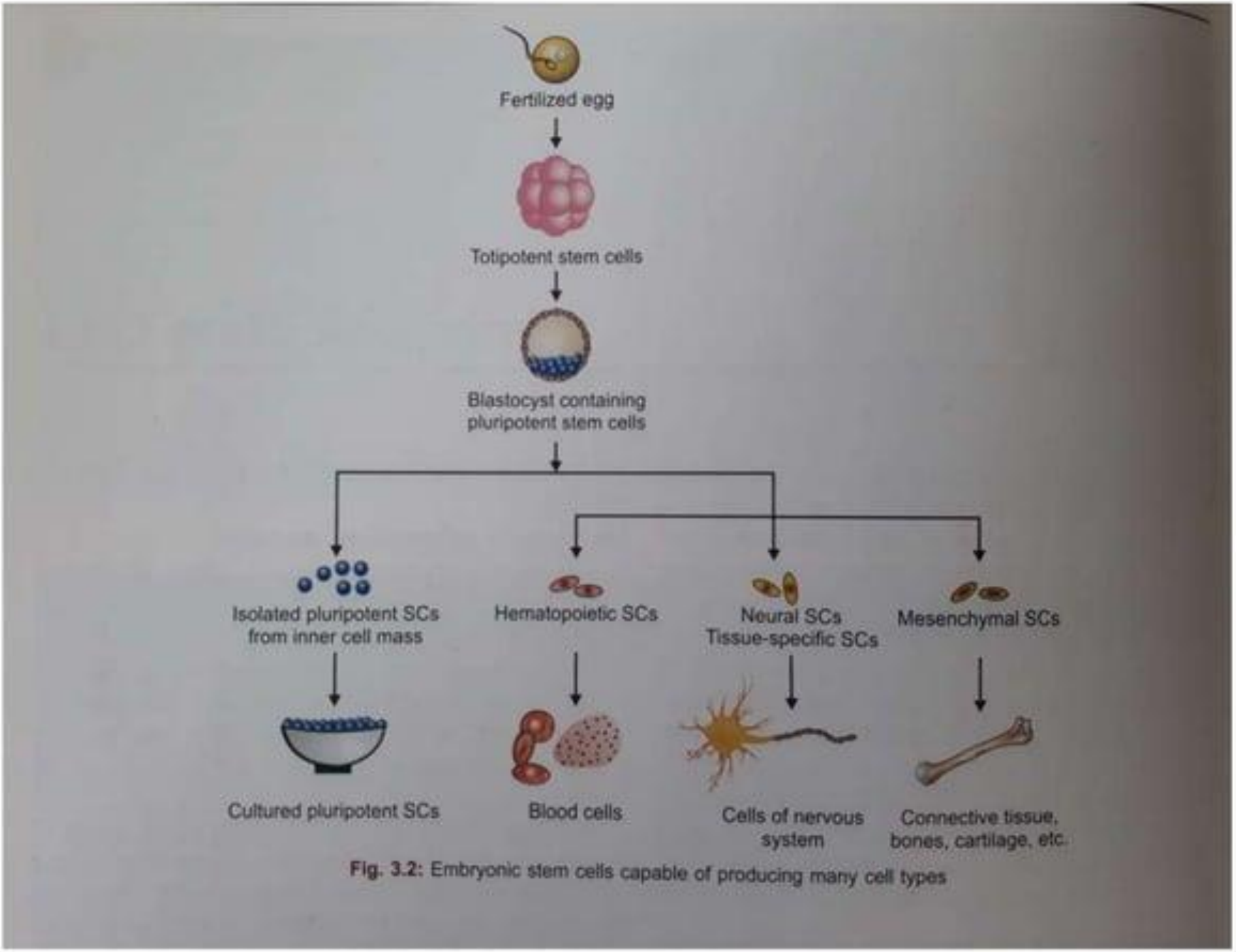


Fig. 3.2: Embryonic stem cells capable of producing many cell types

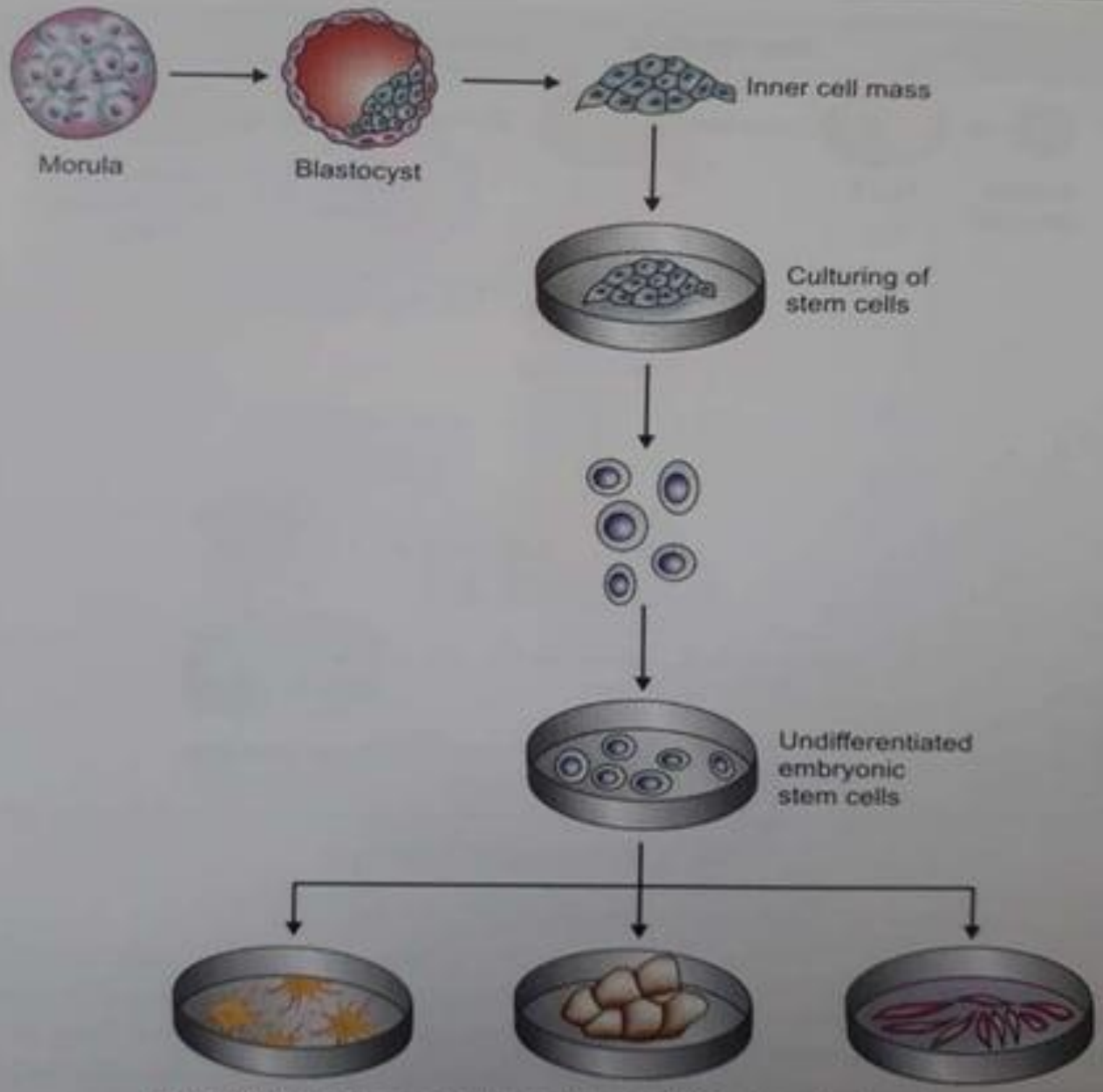


Fig. 3.12: Isolation and culture of human ESCs from blastocyst

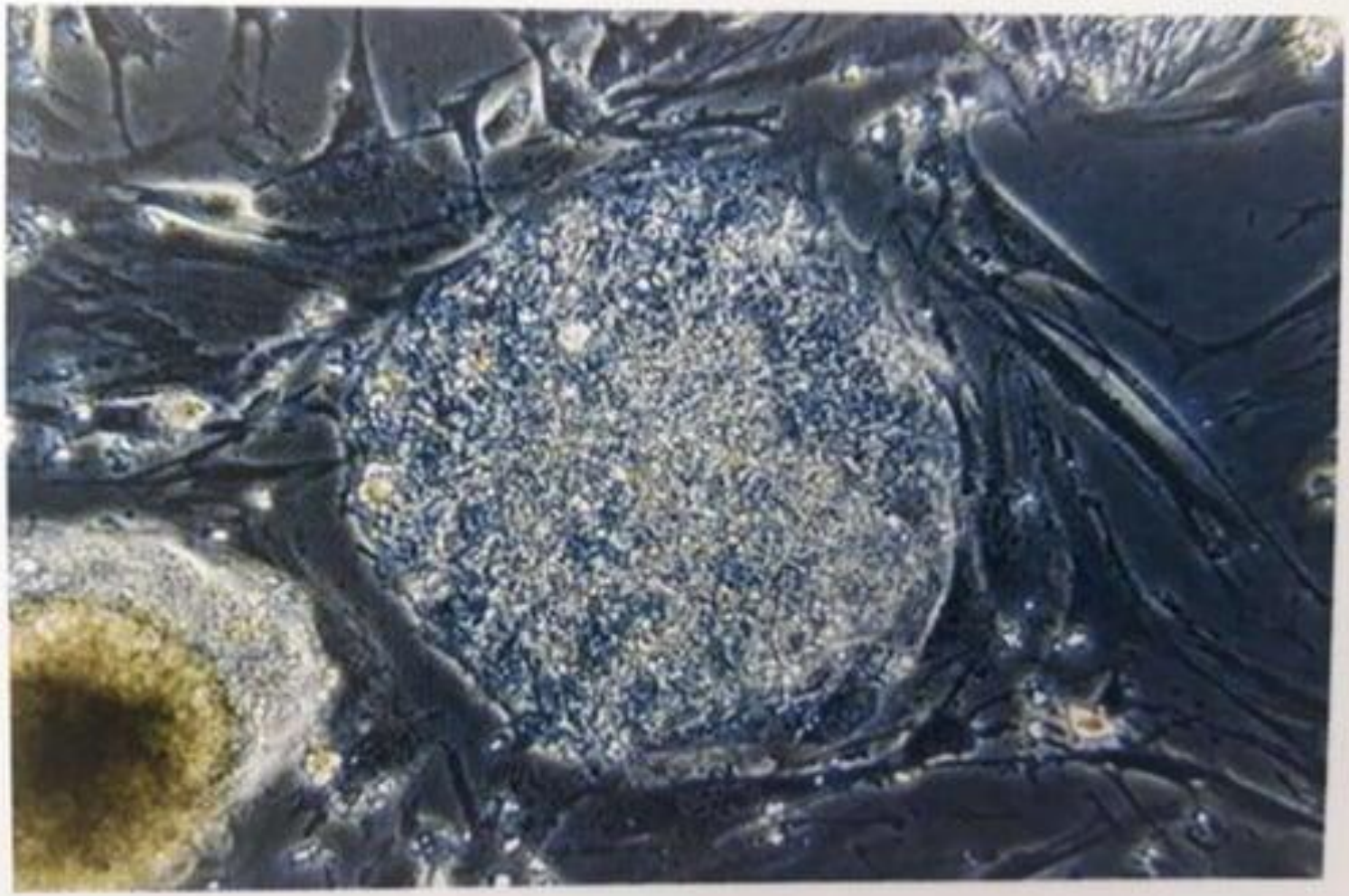


Fig. 3.3: Embryonic stem cells under the microscope

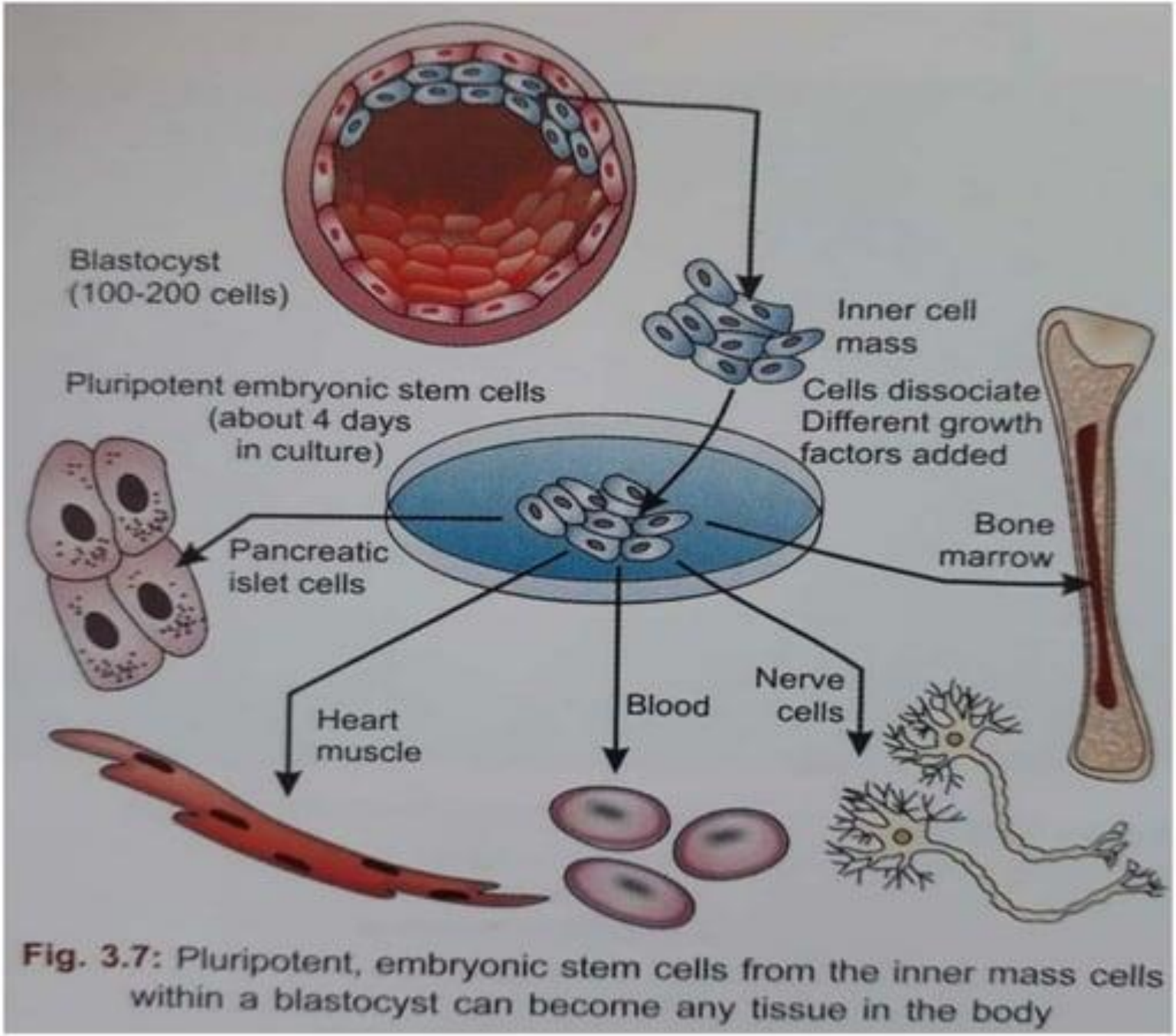


Fig. 3.7: Pluripotent, embryonic stem cells from the inner mass cells within a blastocyst can become any tissue in the body

Advantages of Embryonic Stem Cell

1. **Flexible** - appear to have the potential to make any cell.

2. **Immortal** - one embryonic stem cell line can potentially provide an endless supply of cells with defined characteristics.

3. **Availability** - embryos from *in vitro* fertilization clinics.

Disadvantages of Embryonic stem cell

1. Difficult to differentiate uniformly and homogeneously into a target tissue.

2. Immunogenic - embryonic stem cells from a random embryo donor are likely to be rejected after transplantation

3. Tumorigenic - capable of forming tumors or promoting tumor formation.

4. Destruction of developing human life.

ADULT STEM CELLS

ADULT STEM CELLS

- **Undifferentiated cell**, found among differentiated cells *(Stem cell niches)*.

- The adult stem cell can renew itself and can differentiate to yield some or all of the major specialized cell types of the tissue or organ.

- The primary roles of adult stem cells in a living organism are to **maintain and repair the tissue** in which they are found.

- Scientists also use the term **somatic stem cell** instead of adult stem cell.

Differentiation pathways of adult stem cells

Neural stem cells - in the brain give rise to its three major cell types: nerve cells (neurons) and two categories of non-neuronal cells —astrocytes and oligodendrocytes.

Epithelial stem cells - lining of the digestive tract occur in deep crypts) - give rise to several cell types: absorptive cells, goblet cells, Paneth cells, and enteroendocrine cells.

Skin stem cells - occur in the basal layer of the epidermis and at the base of hair follicles.

The epidermal stem cells - give rise to keratinocytes

The follicular stem cells - can give rise to both the hair follicle and to the epidermis

Advantages of Adult Stem Cell

Adult stem cells from bone marrow and umbilical cords appear to be as flexible as the embryonic type

Somewhat specialized – inducement may be simpler.

Not immunogenic - recipients who receive the products of their own stem cells will not experience immune rejection.

Relative ease of procurement - some adult stem cells are easy to harvest (skin, muscle, marrow, fat)

Non-tumorigenic- tend not to form tumors.

No harm done to the donor.

Disadvantages of Adult stem cells

Limited quantity - can sometimes be difficult to obtain in large numbers.

Finite - may not live as long as embryonic stem cells in culture.

Less flexible - may be more difficult to reprogram to form other tissue types

Why are adult stem cells preferable to embryonic stem cells?

- Adult stem cells are **naturally exist in our bodies**, and provide a **natural repair mechanism** for many tissues.

- They **belong in the microenvironment of an adult body**, while embryonic stem cells belong in the microenvironment of the early embryo, where they tend to cause tumors and immune system reactions.

Induced pluripotent stem cells

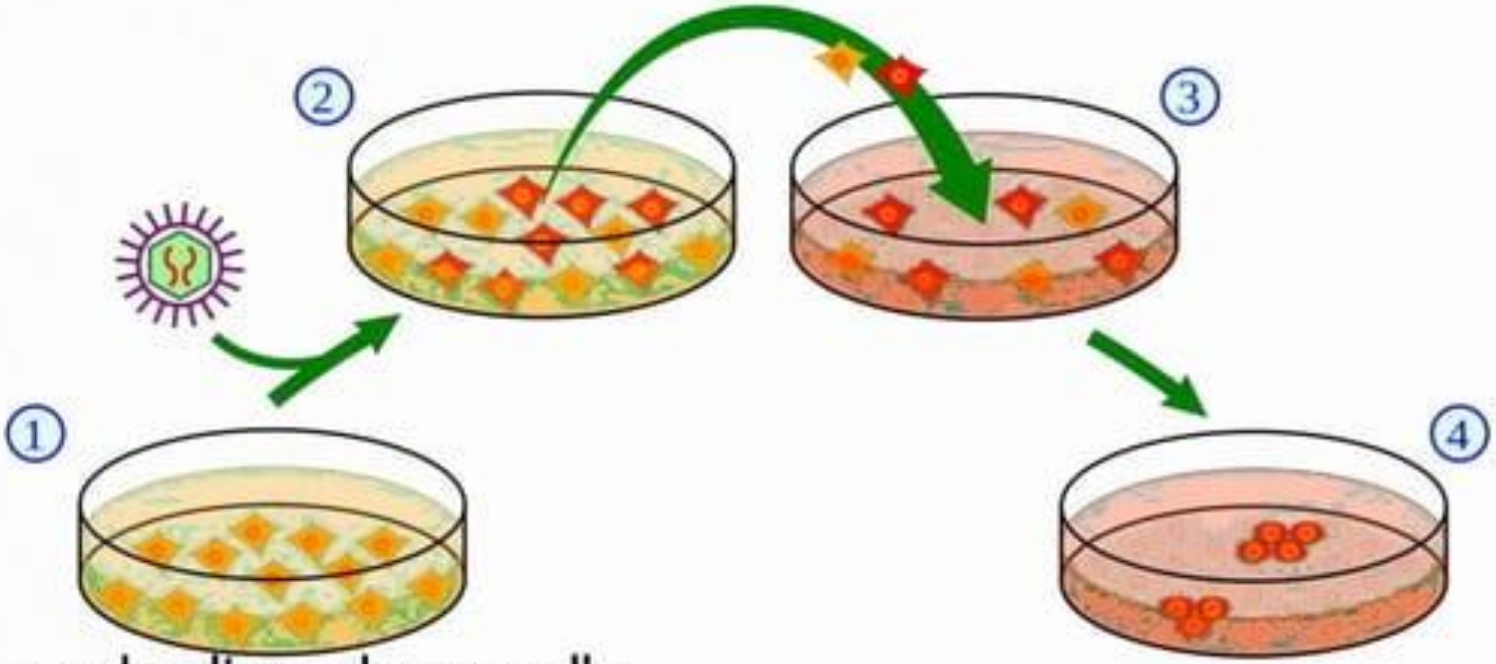
- **Induced pluripotent stem cells (iPSCs)** are **adult cells** that have been **genetically reprogrammed** to an embryonic stem cell–like state.

- Mouse iPSCs were first reported in 2006

- human iPSCs were first reported in late 2007.

- Mouse iPSCs demonstrate important characteristics of pluripotent stem cells, including expressing stem cell markers.

- **Human iPSCs also express stem cell markers and are capable of generating cells characteristic of all three germ layers.**

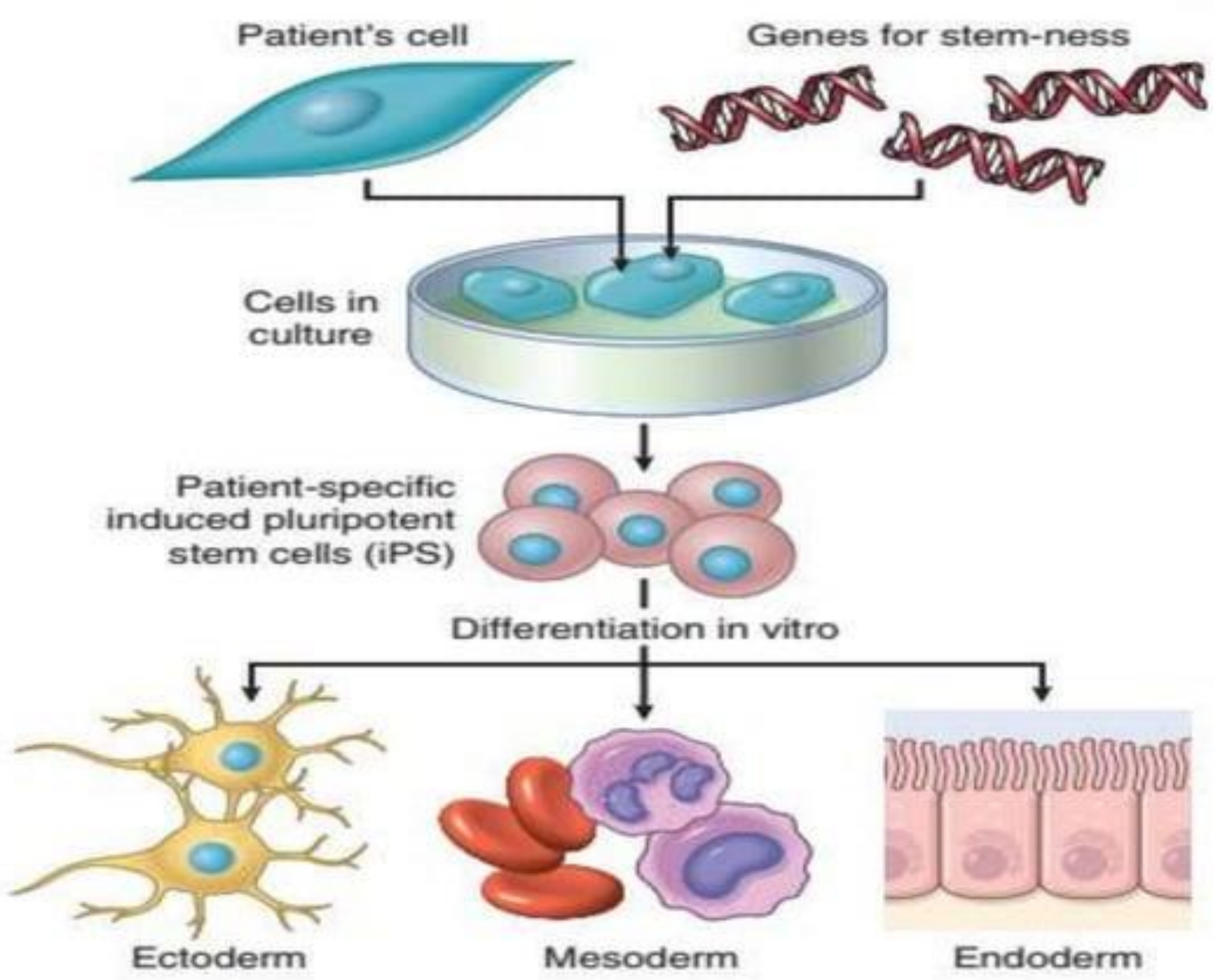


(1)Isolate and culture donor cells.

(2)Transduce stem cell-associated genes into the cells by viral vectors. Red cells indicate the cells expressing the exogenous genes.

(3)Harvest and culture the cells according to ES cell culture.

(4)A small subset of the transfected cells become iPS cells and generate ES-like colonies.


Patient's cell
Genes for stem-ness
Cells in culture
Patient-specific induced pluripotent stem cells (iPS)
Differentiation in vitro
Ectoderm
Mesoderm
Endoderm

Source of Stem cells

- Stem cells may be derived from autologus, allogeneic or xenogenic sources.
- Histocompatability is prerequisite for transplantation of allogeneic stem cells.
- Fatal tissue is the best current tissue source for human neural stem cells, however ethical issues are a major concern.

Potential sources of stem cells

- Fetal tissue that becomes available after an abortion
- Excess embryos from assisted reproductive technologies such as commonly used in fertility clinics

- Embryos created through in vitro fertilization specifically for research purpose

- Other sources of stem cells are those from umbilical cord blood, & bone marrow.

- In addition, neural stem cells, haematopoetic stem cells & mesenchymal stem cells can be harvested from fetal blood and fetal tissue.

Placenta a Source of Stem Cells

Placental stem cells, like umbilical cord blood and bone marrow stem cells, can be used to cure chronic blood-related disorders such as sickle cell disease, Thalasemia, and leukaemia.

Umbilical Cord Blood Stem Cell Transplant

Umbilical cord blood stem cell transplants are **less prone to rejection** than either bone marrow or peripheral blood stem cells.

This is probably because the cells have not yet developed the features that can be recognized and attacked by the recipient's immune system.

Applications

- **Stem cells can be used to study development**
- Stem cells may help us understand how a complex organism develops from a fertilised egg.
- In the laboratory, scientists can follow stem cells as they divide and become increasingly specialized, making skin, bone, brain, and other cell types. Identifying the signals and mechanisms that determine whether a stem cell chooses to carry on replicating itself or differentiate into a specialized cell type, and into which cell type, will help us understand what controls normal development.
- Some of the most serious medical conditions, such as cancer and birth defects, are due to abnormal cell division and differentiation.
- A better understanding of the genetic and molecular controls of these processes may yield information about how such diseases arise and suggest new strategies for therapy. This is an important goal of stem cell research.

Stem cells have the ability to replace damaged cells and treat disease

- treatment of extensive burns,

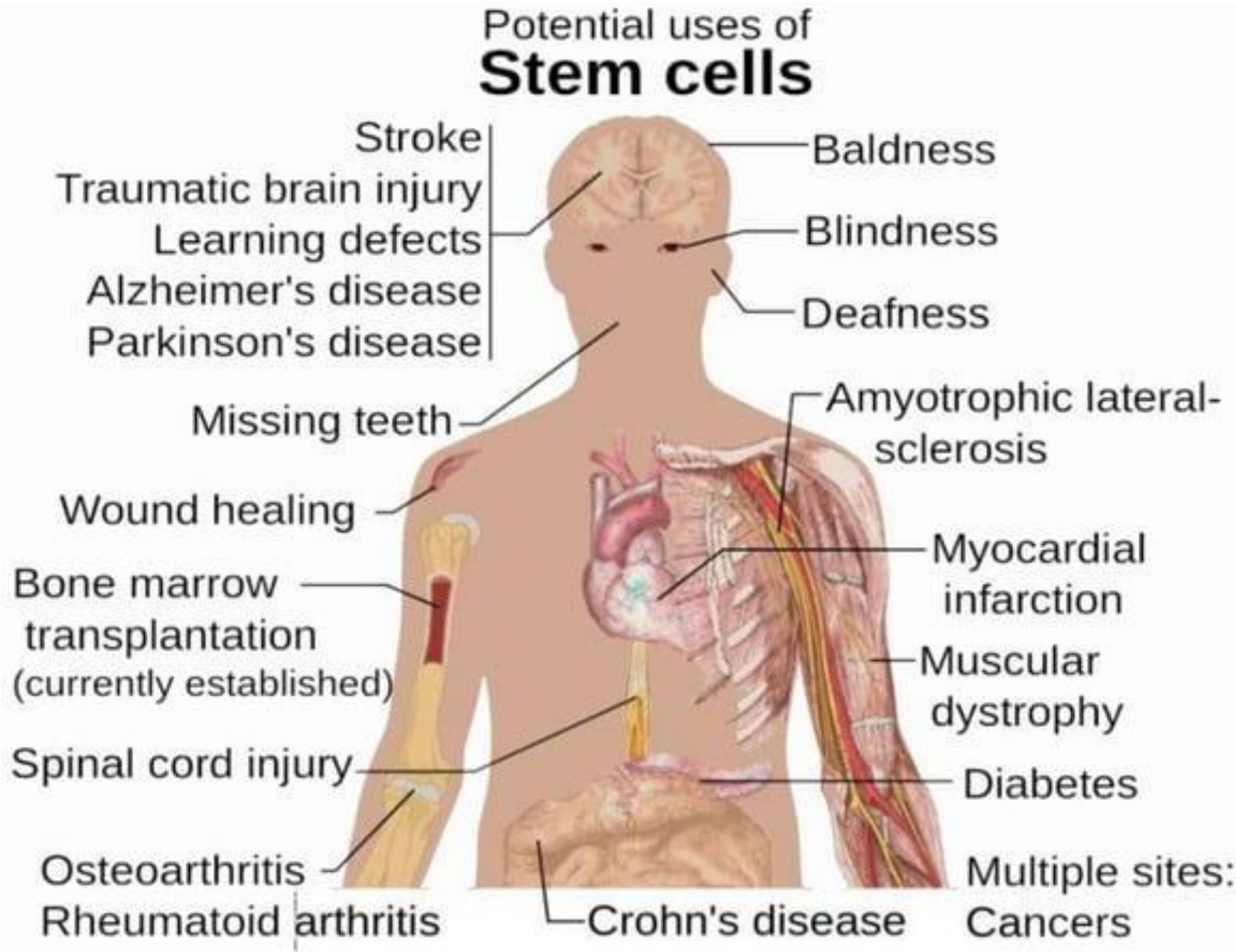
- to restore the blood system in patients with leukaemia and other blood disorders.

- Stem cells may also hold the key to replacing cells lost in many other devastating diseases

- Stem cells, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including Parkinson's, stroke, heart disease and diabetes.

Stem cells could provide a resource for testing new medical treatments

- New medications could be tested for safety on specialized cells.
- Other kinds of cell lines are already used in this way.
- used to screen potential anti-tumour drugs.


Potential uses of
Stem cells
Stroke
Traumatic brain injury
Learning defects
Alzheimer's disease
Parkinson's disease
Missing teeth
Wound healing
Bone marrow transplantation (currently established)
Spinal cord injury
Osteoarthritis
Rheumatoid arthritis
Baldness
Blindness
Deafness
Amyotrophic lateral-sclerosis
Myocardial infarction
Muscular dystrophy
Diabetes
Multiple sites: Cancers
Crohn's disease

POSSIBLE USES OF TISSUE DERIVED FROM STEM CELLS TO TREAT DISEASE

Cell type	Target disease
Neural (nerve) cells	Stroke, Parkinson's disease, Alzheimer's disease, spinal cord injury, multiple sclerosis
Heart muscle cells	Heart attacks, congestive heart failure
Insulin-producing cells	Diabetes
Cartilage cells	Osteoarthritis
Blood cells	Cancer, immunodeficiencies, inherited blood diseases, leukemia
Liver cells	Hepatitis, cirrhosis
Skin cells	Burns, wound healing
Bone cells	Osteoporosis
Retinal (eye) cells	Macular degeneration
Skeletal muscle cells	Muscular dystrophy

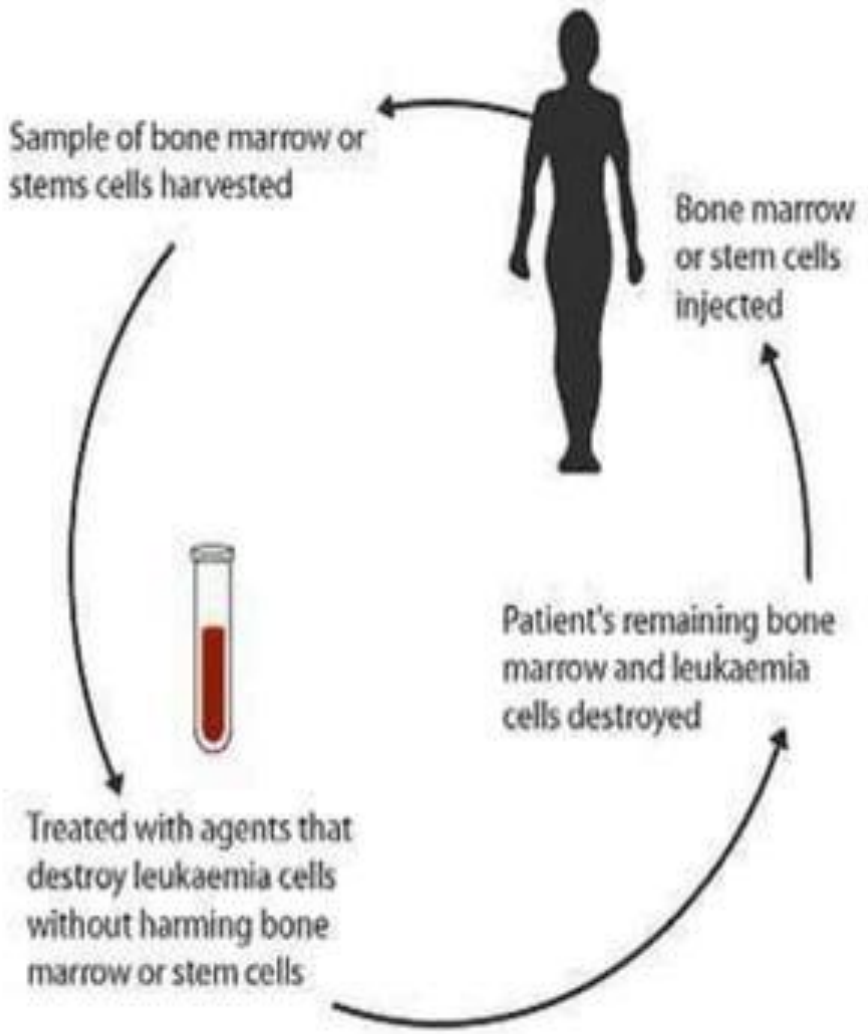
Cell therapy.

- Treatment of neural diseases such as Parkinson's disease, Huntington's disease and Alzheimer's disease.
- Stem cells could be used to repair or replace damaged neurons.
- Repair of damaged organs such as the liver and pancreas.
- Treatments for AIDS.

How Does Cell Therapy Work?

Stem cells can be used to generate healthy and functioning specialized cells, which can then replace diseased or dysfunctional cells.

It is similar to the process of organ transplantation only the treatment consists of **transplanting cells instead of organs**.



How Does Cell TherapyWork?

Bone marrow transplants are an example of cell therapy in which the stem cells in a donor's marrow are used to replace the blood cells of the victims of leukemia.

Cell therapy is also being used in experiments to **graft new skin cells** to treat serious burn victims, and to **grow new corneas** for the sight-impaired.

In all of these uses, the goal is for the healthy cells to become integrated into the body and begin to function like the patient's own cells.

REFERENCE:

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THANK YOU