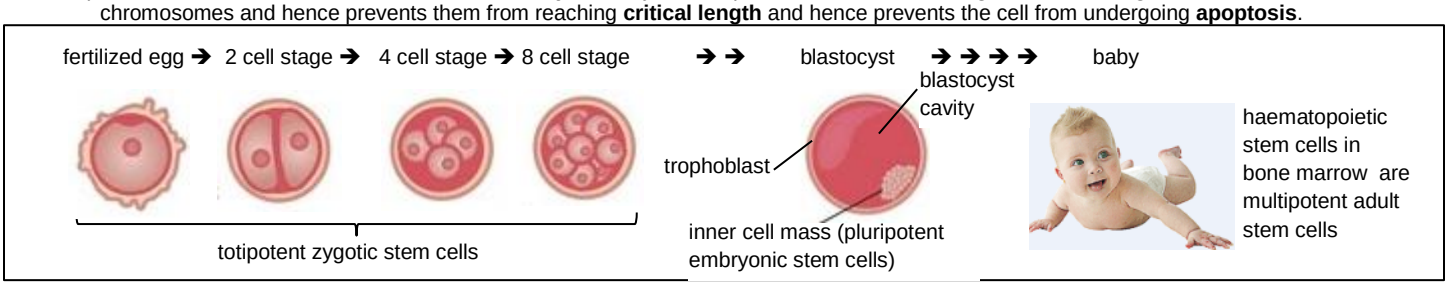
Stems Cells

a) are **unspecialized/undifferentiated** i.e. they do not have any tissue-specific structure for it to perform a particular function
b) are **able to differentiate** to produce specialised cells upon receiving appropriate **molecular signals** (e.g. hormones, growth factors)
c) undergo **extensive proliferation** and **self-renewal** i.e. they can divide many times by mitosis, with the daughter cells possessing the same developmental and replicative potential as the parent cell

d) can undergo
1) symmetrical division ➔ produces 2 **identical** daughter stem cells ➔to **ensure a constant pool of stem cells**
2) asymmetrical division➔produces a) 1 daughter stem cell ➔ to **ensure a constant pool of stem cells**
& b) 1 **progenitor** cell ➔to **replace a population of specialised cells** in a specific tissue that died
➔occurs in the presence of appropriate **molecular signals**

e) can be
1) **totipotent** ➔ can **differentiate into all of the cell types** that make up an **entire** organism **<u>including</u>** the extraembryonic tissue e.g. the **placenta**
➔ e.g. **<u>fertilised egg to 8 cell stage</u>** (These cells are **zygotic** stem cells.)
2) **pluripotent** ➔ can **differentiate into all of the cell types** that make up an organism **<u>except</u>** the extraembryonic tissue such as the **placenta**
➔ e.g. **<u>inner cell mass</u> of blastocyst** (The cells in the inner cell mass are **embryonic** stem cells.)
3) **multipotent** ➔ can develop into only a **limited and related range of cell types** and tissues in an organism
➔ e.g. **<u>haematopoietic stem cells</u>**, which are found in the bone marrow & give rise to all of the cells found in the blood, including red blood cells, white blood cells, and platelets. Haematopoietic stem cells are **adult** stem cells. They are also found in babies.)

Note: 1) Stem cells can differentiate into different cell types due to the presence of molecular signals that cause **differential switching on of genes**.
2) A progenitor cell is an early descendent of a stem cell that can only differentiate. It cannot renew itself. e.g. **lymphoid** progenitor cells gives rise to B cells, T cells and natural killer cells while **myeloid** progenitor cells give rise to red blood cells, monocytes, platelet producing cells, neutrophils, basophils and eosinophils
3) Stems cells can continue to divide **mitotically** as they can express their **telomerase gene** which **lengthens the telomeres** of their chromosomes and hence prevents them from reaching **critical length** and hence prevents the cell from undergoing **apoptosis**.



Discuss the ethical implications of the application of stem cells in research and medical applications and how induced pluripotent stem cells (iPSCs) overcome some of these issues. (procedural details of how iPSCs are formed are not required)

<u>Ethical implications of the use of stem cells in therapy</u>

<u>Argument against using embryonic stem cells</u>	**<u>Argument for using embryonic stem cells</u>**
Some believe that the **embryo** has the **status of a human being** as it has the potential to become one. Embryonic stem cell research is tantamount to murder.	Embryos are **not equivalent to human** life: Embryos are not conscious, cannot feel and cannot survive outside the womb.
Some object to extracting stem cells from an **embryo** to make replacement body cells is treating the embryo as just a **source of spare parts**.	Blastocysts are a **cluster of human cells** that have not differentiated into distinct organ tissue, making cells of the inner cell mass no more "human" than a skin cell. Some believe **life only begins when the heartbeat develops** (during the fifth week of pregnancy) or when the **brain begins developing** (at 54 days after conception).
Claims of the **benefits** of embryonic stem cell research are **over-rated** as there are few (if any) examples of success in medical applications	Embryonic stem cells can **potentially treat** a wide range of diseases as they have the **potential to grow indefinitely** in a laboratory environment and can differentiate into almost all types of bodily tissue.
Adult stem cell treatment is established, have produced some results and there are fewer ethical issues involved. Thus adult stem cell research may be able to **make greater advances** if more money and resources were channeled into it instead of embryonic stem cell research.	It is **unethical not to use established protocols** on **embryonic stem cell research** to further embryonic stem cell research to help relieve human suffering.
Current benign applications may lead to **abuse in the future**. Once human status is denied to embryos, this **precedent** may extend to other categories of human beings such as the **profoundly disabled** or the **elderly infirm**.	There is **legislation** on the period when ES cells can be extracted. eg: Current UK legislation **does not allow use of embryos that are more than 14 days old**. In fact, ES cells are obtained earlier from blastocyst (between 3-8 days after fertilization).
Possibility of **unforeseen consequences** in treated patients such as possible risks of tumor formation, immunological reactions, unexpected behavior of the cells, and unknown long-term health effects.	More than a **third of zygotes do not normally implant** in the uterus. Thus, far more embryos are lost due to chance than are proposed to be used for embryonic stem cell research.
As embryonic stem cell research is **expensive**, funds can be channeled to **treat other more treatable diseases**.	**Surplus embryos** created via ***in vitro*** **fertility treatments** are **destroyed**, or stored long past their viable storage life. These can be used for creating new stem cell lines for research which would otherwise be destroyed.
For **donors** of eggs, embryos or tissues, there are **issues** of **informed consent**, understanding of research aims and privacy.	

Potential solution to overcome some of these issues

Induced pluripotent stem cells (iPSCs)

Induced pluripotent stem cells are pluripotent stem cells that can be generated directly from adult somatic cells (e.g. skin cells) Adult somatic cells are not totipotent, pluripotent or multipotent. The non-pluripotent cell is therefore induced to become pluripotent. The iPSC technology was pioneered by Shinya Yamanaka's lab in 2006 that the introduction of four specific genes encoding transcription factors could 'reprogramme' some specialised cells to become pluripotent so that they lose their specialised functions and behave in virtually the same way as embryonic stem cell.

Advantages of iPSCs	**Possible problems of iPSCs**
• Since iPSCs can be obtained directly from **adult tissues**, it **does not generate or destroy any human embryos.** • Adult tissue (e.g. skin cells) required to make iPSCs can be **easily obtained** from donor **without risk to the donor** • In contrast to ES cells extracted from human embryos, iPSCs derived from a **patient's own cells** would open the possibility of generating lots of patient-specific cells, which will **not be rejected by the immune system** (as it is not a **foreign cell**) upon transplantation. • Hence, there will also be **no need to use immunosuppressant drugs** after transplantation and the problem of looking for a suitable donor for transplantation will also be overcome. • Further, it also allows the generation of **pluripotent stem cell lines** from patients with **inherited diseases**, in order to better **understand why the diseases develop** and use in personalized drug discovery efforts. • An **additional reproductive technology** that may be enabled by iPSCs is the generation of sex cells (sperm and eggs) for treating infertility.	• **Low efficiency**: in general, the conversion to adult somatic cells to iPSCs has been incredibly low. For example, the rate at which somatic cells were reprogrammed into iPSCs in was 0.01–0.1%. • Genetic modification of adult somatic cells to obtain iPSCs **may cause cancer** by overexpression of proto oncogenes or switching off of tumour suppressor genes. • There are **ethical concerns** (e.g. lack of consent, long term unexpected consequences) related to the creation of embryos and children from IPSC-derived sex cells.
Ethical complications are related to the means of obtaining stem cells (e.g. techniques involving the destruction of human embryos), human cloning and the exploitation of embryo and egg donors. The use of iPSCs still appears to overcome many ethical issues and provides viable solutions related to stem cell research.	

Comparison of human embryonic stem cells and human adult stem cells

	Embryonic stem cells	**Adult stem cells**
Differentiation ability	**Pluripotent:** capable of becoming any cell in the human body except extraembryonic tissue e.g. placenta.	**Multipotent:** typically only give rise to the cells of the tissue in which they are found.
Role in body	To develop the embryo into an **entire human**.	To **replace specific cells** in the body which die throughout life due to wear and tear or injury and disease.
Sources	**Unused IVF embryos** which have been donated, or embryos created for the purpose from donated eggs and sperm.	**Bone marrow**, muscles and skin; and from the foetus, umbilical cord, placenta etc.
Advantages in research and therapy development	• Embryonic stem cells make up a significant proportion of a developing embryo and are **easier to isolate** and grow *ex vivo* than adult stem cells • Have a **strong ability to self-renew** in the laboratory and divide more rapidly than adult stem cells, resulting in a **constant supply** of ES cells. • **Pluripotency** means that ES cells have the potential to **produce any cell type** in the body, potentially allowing them to **treat** a **wider range of diseases**.	• If taken from the patient's own body for use in therapies, cells would be genetically identical to that of the patient, **avoiding** the **problem of immune rejection**. • There are **less ethical considerations** compared with using embryonic stem cells.
Disadvantages in research and therapy development	• Genetically different to cells of potential patients, so **immune rejection** could occur. • **Ethical issues** over **embryo destruction**	• They usually only produce a **limited number of different cell types**. • **Conditions supporting self-renewal** in the laboratory have only been **identified for a few tissue stem cell types**, for instance skin and cornea. • Are found in **small numbers** and are **difficult to isolate**. • Adult stem cells with **genetic mutations from the patient's own body** will **not be effective** in treatment of genetic disorders.