

**THE USE OF STEM CELLS\***  
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**View of the European Board**  
**and College of Obstetrics and Gynaecology**

**1. Definition of stem cells**

Stem cells are cells that can replicate and form one or more differentiated cell types.

1.1. *Progenitor stem cells*; resulting in the differentiation of a single cell type (ex. spermatogonial cells resulting in spermatozoa).

1.2. *Multipotent stem cells*; resulting in several cell types constituting a specific tissue or organ (ex. skin stem cells, haematopoietic stem cells, neural stem cells).

1.3. *Pluripotent stem cells*; resulting in all different cell types in vitro. However, they are not able on their own to form a whole embryo.

Cells isolated from primordial germ cells in the foetus are embryonic germ cells. Cells isolated from the inner cell mass at a blastocyst-stage of the embryo are embryonic stem cells.

1.4. *Totipotent stem cells*; having still the ability to give rise to a whole embryo. In humans this ability is preserved until the 8 cell stage.

Characteristics of the different stem cells.

*Progenitor and multipotent stem cells* are present throughout life. However they are more abundant in the foetus than in the adult (see haematopoietic cells in the cord blood). It is thought that *pluripotent stem cells* are not present after the embryonic stage of development. However it has recently been found that thyroid cells from fetal or embryonic origin were present in the thyroid of a woman with thyroiditis, years after pregnancy.

**2. Source of stem cells**

2.1. Stem cells of adult origin.

Progenitor and multipotent stem cells are present in adults.

Somatic stem cells can generate for example liver, pancreas, bone, cartilage, neural system cells.

Haematopoietic stem cells are present in the blood, originating from the bone marrow after stimulation.

2.2. Stem cells of fetal origin.

– Haematopoietic stem cells are present in umbilical cord blood.

– Multipotent and pluripotent stem cells can be obtained from the fetus after termination of pregnancy.

2.3. Stem cells of embryonic origin.

Pluripotent embryonic stem cells can be obtained from an embryo at the blastocyst stage. The embryo can be produced by in vitro fertilisation or by transfer of an adult nucleus to an enucleated oocyte (somatic cell nuclear transfer).

**3. Human embryonic development**

3.1. At two or three days after fertilisation, an embryo consists of identical cells which are totipotent. That is to say that each could give rise to an embryo on its own producing for example identical twins or quadruplets. They are totally unspecialised and have the capacity to differentiate into any of the cells which will constitute the fetus as well as the placenta and membranes around the fetus.

3.2. At four or five days after fertilisation (morula stage), the embryo is still made up of unspecialised embryonic cells, but these cells can no longer give rise to an embryo on their own.

3.3. At five to seven days after fertilisation (blastocyst stage), a hollow appears in the centre of the morula, and the cells constituting the embryo start to be differentiated into inner and outer cells:

– The *outer cells* will constitute the tissues around the fetus (trophoblast), including the placenta.

– The *inner cells* (20 to 30 cells) will give rise to the fetus itself as well as to some of the surrounding tissues. If these inner cells (embryoblast) are isolated and grown in the presence of certain chemical substances (growth factors), pluripotent embryonic stem cells can be derived. These embryonic stem cells are pluripotent, not totipotent since they can-

\* Uredništvo je od Evropskog odbora i koleđa za opstetriciju i ginekologiju (EBCOG) primilo nacrt dokumenta »The Use of Stem Cells« (Uporaba matičnih stanica), kojeg je sastavila radna grupa u sastavu: prof. F. A. Van Assche, prof. W. Holzgreve, lord N. Patel i prof. S. Mancuso. Dokument će biti raspravljen u Pragu na 17. Europskom kongresu ginekologije i opstetricije. Dokument je od značenja, jer i embrionalne stanice spadaju u matične stanice, s mogućnošću genetskog inženjerstva i terapijske uporabe u budućnosti. O eventualnim promjenama dokumenta ćemo izvijestiti u sljedećem broju časopisa.

not develop into an embryo on their own. If they are transferred to a uterus, they would neither implant nor develop into an embryo.

#### 4. Research on animals

##### 4.1. Embryonic stem cells.

For the last two decades research on embryonic stem cells has been performed in vitro. Embryonic stem cells need differentiation in vitro before they can be used for therapeutic purpose. Some success has been demonstrated in the treatment of traumatic spine injury and myocardial injury.

4.2. Recently it has been shown that so called »adult« stem cells have more malleability than previously believed. Mouse neural stem cells can, in specific conditions of culture, form cells of other organs (blood, muscle, intestine, liver, heart). Moreover marrow stromal cells have been shown to generate astrocytes and myocytes.

#### 5. The therapeutic use of human stem cells

##### 5.1. Neural stem cells.

Clinical trials in patients with Parkinsons disease have been performed. Transplantation of neural cells derived from the human fetus has been used and shows a therapeutic effect. This procedure is still experimental; five to six aborted fetuses are necessary to provide enough neural tissue to treat one patient with Parkinsons disease. Proliferation in culture of these neural cells is necessary to provide a large amount of cells, needed for transplantation.

##### 5.2. Haematopoietic stem cells.

Adult haematopoietic stem cells can be derived from bone marrow of donors, or from the patients themselves (before chemotherapy). They can also be obtained from the peripheral blood, after treatment to induce the passage of stem cells from the bone marrow into the blood circulation.

Haematopoietic stem cells of fetal origin are obtained from the cord blood.

These cells are preserved in cord blood banks.

They are collected immediately after birth of the newborn and before the delivery of the placenta, without interfering with the usual procedure of cord clamping.

Currently an international network of banks for stem cells from cord blood for allogenic transplantations is developed. Also targeted transplantations are performed where cord blood is used for first degree relatives, and even autologous banking is propagated to be used like a special form of »private life« insurance.

##### 5.3. Perspectives for the future.

Production of specific cell lines for therapeutic transplantation is considered as an important step to cure congenital or acquired lesions in human tissues; often referred to as »regenerative medicine«. Results of cell ther-

apy in animals are promising, but as yet not applicable for clinical use.

Embryonic or fetal stem cells are less rejected compared to adult stem cells. Tissues derived from allogenic human stem cells will have the problem of rejection.

This can be avoided by the use of autologous stem cells from adult tissue (or in principle autologous cord blood). It is also possible to create an embryo with genetic characteristics of the receptor, using somatic cell nuclear transfer (therapeutic cloning).

#### 6. Ethical considerations

6.1. The philosophical and religious views on the use of embryonic stem cells in therapeutic research have been well documented in the Unesco document of the Division of Human Sciences, Philosophy and the Ethics of Science and Technology (Bio 7/00/GT – 1/2, April 2001).

6.2. There has been an intense debate about the moral status of the human embryo, which has not lead to a general European consensus. There are two major approaches to formulate the value of human life: first, absolute dignity, respect and protection to all human life; second, relative dignity, respect and protection to human life, differing and depending on the development, environment and interests.

6.3. The human embryo possesses dignity and deserves respect and protection. This respect and protection are not absolute, but gradual, as accepted by a large majority, since it is agreed that spare embryos, not retrieved for reproduction, may be destroyed.

6.4. Human embryonic cells have the potential of treating congenital and acquired diseases in the human (regenerative medicine). Research on human embryonic stem cells may be necessary if this treatment in the human is to succeed.

6.5. Stem cells isolated from the blastocyst no longer by themselves have the ability to develop into a human being. However these cells should be handled respectfully like any human tissue.

6.6. The moral principles that apply to the use of spare embryos resulting from infertility treatments are different from those embryos created specially for research or for therapeutic use by somatic nuclear transfer methodology (therapeutic cloning).

6.7. It is necessary that any research on human embryos, embryonic tissues and human stem cells should be approved by Research Ethics Committees.

#### 7. E.B.C.O.G. recommendation

7.1. The use of adult stem cells should be treated in the same way as any other tissue (organs and blood) donation, based on respect for the integrity of the human body and the free and informed consent of the donor.

7.2. The use of haematopoietic stem cells from the cord blood after birth of the newborn requires informed consent regarding possible uses of cells by the donor (woman or couple).

7.3. The use of fetal stem cells requires free and informed consent from the woman or couple. The conditions of legal abortion should not be changed for the purpose of obtaining fetal tissues. When termination of pregnancy is carried out, the timing and method used might not be influenced by the need to retrieve fetal tissue.

7.4. In some European countries the creation of »spare embryos« is permitted. When decided that spare embryos will be destroyed it is accepted that after thawing further in vitro culture is performed, to produce blastocysts to retrieve embryonic stem cells for research. Free and informed consent from the woman or couple is required when these spare embryos are used for obtaining embryonic stem cells.

7.5. In most European countries the creation of embryos for research is not permitted; it is assumed that

this is in major conflict with the priority of human dignity. If somatic cell nuclear transfer proves effective for »regenerative medicine«, it may be acceptable in the future that embryos are created for this purpose, under strict regulations.

7.6. Reproductive cloning shows severe ethical problems regarding human dignity. Furthermore given the high risk of abnormalities, the scientific objections to human cloning are currently overwhelming. Therefore reproductive cloning in the human should be forbidden.

7.7. Research on stem cells should include research on adult stem cells, embryonic, fetal and cord blood stem cells.

7.8. The use of stem cells needs strict regulations.

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**VIJESTI  
NEWS**

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