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Alternatives to cloning

New research into stem cells poses a challenge to the needs of therapeutic cloning

The British government backs research in stem cells on human fetuses >

This week, the British government resolved to grant its consent to the use of human fetuses in research associated with the so-called stem cells. Should controlling these cells prove to be successful, it is likely that a considerable number of hitherto incurable illnesses can be cured.

Research into embryonic stem cells paves the way for the cloning of human beings >

The British government's decision has been anticipated for quite some time and it has given rise to a vehement debate. This is chiefly due to the fact that one of the ways in which stem cells that are to be used in research and applying treatment can be procured is to clone human beings with the aid of very same technique that created Dolly, the renowned sheep.

Research can provide alternatives to cloning >

Newer research indicates, however, that it might very well be possible to obtain the benefits of treatment with stem cells without having to resort to cloning human beings.

This issue of "From the Board to the Parliament" casts light on the use of stem cells and on the British government's decision and sets forth alternatives to cloning as a way of generating stem cells

During this coming autumn, the Danish Board of Technology is going to be holding a hearing for the Parliament's Research Committee on therapeutic cloning.
This topic has taken on a considerable degree of importance, ever since the British government resolved last week to give its consent to the use of human fetuses in stem cell research.
Cloning is a process where an embryo is created whose genes are identical with a living (or, for that matter, a deceased) person. It now appears plausible that this can be done with human beings through the aid of the technique known as somatic cell-nucleus transfer. This is one of the techniques employed in creating the cloned sheep named Dolly.
In therapeutic cloning, the embryo is not given the chance to develop for more than - approximately - five days. At no time does this embryo come into any contact with a womb, inside of which it otherwise might have been capable of evolving into a child with all potentials for surviving.
After five days time, the embryo consists among other things of stem cells, (please see the box on the next page). These cells are then "harvested", whereupon they can be used in the treatment of illnesses or for research.

Stem cells are extremely serviceable in the treatment of illnesses, especially because they have the special capacity to evolve into a great many other kinds of cells - of which there are 216 different types - in the human body. For this reason, they can be used for repairing organs and tissues that have been destroyed as a result of illness or injuries.
Already today, stem cells are being used in the treatment of several forms of leukemia and other kinds of cancer. The possibilities for treatment span

from the support of the immune defense system to the **cultivation** and implantation of entire organs.

It is far from being so that cloning is the sole source of stem cells. Adult human beings also have stem cells inside their bodies. However, these cells are not as serviceable as are embryo stem cells for purposes of research and treatment: working with them is more difficult and they cannot evolve into as many different types of cells (please see the box on this page). For these reasons, many scientists are of the opinion that it might be useful to allow therapeutic cloning, with research and treatment in view.

Newer findings, however, have now challenged the general view that stem cells taken from adults are not as serviceable as embryo stem cells are.
Should this branch of research prove to bear fruit, cloning might then prove to be unnecessary.

Treatment with stem cells

Today, stem cells taken from adults are being used as a standard treatment in several types of cancer. The primary focus is on the treatment of leukemia, but stem cells are also being used in treating breast cancer, ovarian cancer and **mylomatosis** (cancer of the bone marrow), which have up until the present day been extremely difficult to treat.
Another area where positive results are turning up - and even more are anticipated - is in the treatment of the autoimmune diseases - for example, arthritis. Up until the present day, these diseases are often treated by suppressing the immune defense system, with a number of concomitant and sometimes unpleasant side effects. In Switzerland and in some other European countries, there have been some positive results with "resetting" or doing away entirely with the patient's own immune system and re-establishing it with stem cells that have been taken from the patient him/herself and **cultivated** in the laboratory.
Research into whether diabetes can be treated in this way - in the earliest stages of the disease - is also underway.

The outlook for treatment with stem cells is getting more and more optimistic. If we can propel specialized cells to come forth from stem cells in the laboratories, perhaps we can create insulin-producing cells for diabetic patients, liver cells for persons suffering disorders of the liver, brain cells for those suffering a cerebral hemorrhage, and so forth. In the long-term perspective there also seems to be the possibility of allowing entirely new organs to grow forth from stem cell cultures.

What is true of all kinds of treatment with stem cells is that it is advantageous if the stem cells are genetically identical with the patient's cells. In this way, the risk of having the new cells rejected by the

Stem cells

The human body consists of 216 different types of cells. An inseminated egg has the potential to evolve into all cell types, as well as the cells that form the placenta inside the uterus during pregnancy. It can be said that the egg is **totipotent**.
The egg divides itself: first into two, then four and then eight cells, each of which is **totipotent**.. It is only after the third division that the first specialization of the cells occurs. Now, one part of the cells will come to constitute the placenta, while the rest of the cells will come to constitute the embryo. The cells comprising the embryo have the potential to form all 216 types of cells found in the human body, but they cannot form placenta cells. Therefore, they cannot, in and of themselves, evolve into an embryo capable of surviving. These cells are called **pluripotent**.
During the development of the fetus, some of the cells maintain their capacity for forming other kinds of cells. Even in the bodies of adult human beings, a number of the body's cells are stem cells. But eventually, as the stem cells mature, they come to be more specialized. Blood stem cells can evolve into all kinds of blood cells. Nerve stem cells into all kinds of nerve cells, and so forth. These stem cells are called **multipotent**.

Studies of animals indicate that there are two main types of pluripotent stem cells.
Embryonic stem cells can be found in embryos for up to (approximately) five days after insemination. At that time, the egg has evolved into a sphere of anywhere from 50 to 100 cells, a so-called **blastocyst**. Inside this sphere there is a nucleus of around 20 **pluripotent** embryonic stem cells.
Embryonic gametes can be harvested up until the time that the fetus is about six weeks old. They exist in close proximity to the cells that will subsequently develop into either eggs or sperm.
Multipotent stem cells can be found in embryos, in children and in adults. Newer research with mice indicates that **multipotent** stem cells can successfully be "reprogrammed" so that they can evolve into a different type of cell.

There are thus several sources of stem cells:
- Inseminated eggs in the early embryonic stage, left over after fertility treatment
- Embryos that have been created with the very same technique that created the cloned sheep, Dolly
- Blood from the umbilical cord
- Gametes from aborted fetuses
- Certain tissue types from adult people. For example, blood, skin and bone marrow
- In time, it might prove possible to "re-program" ordinary cells so that they will behave in the manner of stem cells. But this is still in the realm of hypothesis

Source: Stem Cell Therapy: the ethical issues. Nuffield Council on Bioethics, April 2000. Stem Cell Research: Medical Progress with Responsibility. ***(United Kingdom****) Department of Health, August 2000.*

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patient's immune system and the risk that the new cells will begin to 'attack' the body are lessened.

Stem cells with the same genetic profile as the patient can be obtained in three ways:
- It is possible, as is already the practice, to use stem cells from the patient's own body, such as blood cells and cells from the bone marrow. However, these cells can only be used in a limited number of treatments today, largely because they are specialized for developing into one certain group of cell-types, such as blood cells. Newer research, however, suggests that it might be possible to "re-program" blood cells so that they will behave in the manner of nerve cells, and vice-versa (see the section on "Research into Stem Cells").
- We can make use of stem cells taken from the blood of the umbilical cord if this blood has been frozen immediately after birth. It is likely to assume that these cells have in fact been affected by limitations comparable to what we see in stem cells taken from adults. But there is some degree of hope that it will be easier to 're-program' these kinds of cells.
- A cloning can be carried out by inserting a cell nucleus taken from a patient into an egg which is given the chance to evolve for a few days into the **blastocyst** stage (please see the box on the previous page and the illustration above). This is what is known as therapeutic cloning.

As a rule of thumb, the earlier on in their development the stem cells are, the easier it is to cultivate and work with them.

Research into Stem Cells

In recent years, great strides have been made in research involving stem cells. But there are still many things we do not understand about why stem cells behave as they do and about how they can eventually be controlled.
During these years, research involving stem cells has predominantly been carried out with experimentation conducted on animals. But there will come a time when it might prove necessary to use more human stem cells in the research.

For research purposes, there is access to obtaining stem cells from the following sources:
- Fertilized eggs in the very early embryonic stage, which have been left over from fertility treatments
- Blood from the umbilical cord
- Gametes from aborted fetuses
- Certain tissue types taken from adult persons, such as blood, skin and bone marrow
- Cloned embryos which have been created by means of the same technique that brought the cloned sheep, Dolly, into existence

What also holds true here is that stem cells from the early-developed embryos are generally easier to work with than stem cells derived from later stages of embryonic development and from adults.

However, experiments made on mice indicate that we ought to revise the traditional view that stem cells become less serviceable the more they mature. In one experiment, the results of which were published last year, inside mice's brains, blood stem cells were successfully developed into nerve cells. Shortly prior to this, the converse took place. Nerve stem cells were evolved into blood cells inside mice who had been deprived of the full functions of their immune systems.

There are several plausible explanations for these results. It might be so that it will prove possible to "re-program" stem cells so that they will behave in the manner of other types of cells, when there is a need for this.
It is also possible that the stem cells that were used in the experiment (which were taken from adult mice and not from mice embryos) were, in reality, less mature than people previously assumed them to be. That they were closer to being **pluripotent** than **omnipotent** (please see the box on the previous page).

If either of these explanations proves correct, this will fuel a sense of optimism about obtaining beneficial effects from embryonic stem cells without actually having to employ embryos and without having to resort to therapeutic cloning.

The situation in the United Kingdom

All use of human embryos for medicinal or research purposes in the United Kingdom is regulated by a special advisory agency, the Human Fertilisation and Embryology Authority (HFEA) which was set up as a stipulation of the Human Fertilisation and Embryology Act (HFA) of 1990.
Treatment with stem cells has not progressed beyond the experimental phase.
According to the provisions of the HFA, it is only permissible to use human embryos in research in the event that it proves utterly impossible to carry out the research project without such use *and* if the aim of the project can be said to be one of these five:
- making improvements in treating childlessness
- augmenting our knowledge about hereditary diseases
- augmenting our knowledge about the reasons for involuntary abortions
- bringing about more effective contraception
- developing methods for identifying chromosome defects in embryos

Should it be anticipated that some new aim can play a part in augmenting our knowledge about the formation and the development of embryos, increase our knowledge about disease or make it pos-

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sible to use such knowledge in a better way, the British Minister of Health is empowered to extend this list.

Up until the present time it has been forbidden to carry out research into the treatment of non-hereditary diseases using stem cells from embryos - not even with stem cells from extra eggs left over from fertility treatments or with stem cells that have been produced by cloning.
The cloning of human beings with the SCT method is permissible according to the provisions of the HFA, should the experiment serve one of the aforementioned purposes. But as of yet, no applications have been made to the HFEA for obtaining the agency's approval for cloning.
Cloning with the aim of creating a living clone is strictly prohibited.

In June 1999, the British government commissioned an expert panel, headed up by the English Chief Medical Officer, Professor Liam Donaldson, to investigate the question of whether it ought to be allowed to make use of human embryos in other instances than those circumscribed by the five approved areas of research.
The report from the expert panel was ready **this** June. The British government has used this past summer to consider its stance on the issue.
On August 16, the British government announced that it intends to support the conclusions drawn up by the group of experts. However, the government will put the question of whether the recommendations should be followed to a vote in the British Parliament.
What the panel of experts recommends is that use of human embryos ought to be permitted in connection with carrying out research into stem cell treatment. As has already been mentioned, cloning carried out in connection with research is already permitted, in principle. If the expert group's recommendations are to be followed, this entails that it will become legal to clone human beings for purposes of researching stem cells.
It is the opinion of the expert group, however, that cloning should only be carried out when all other possibilities have been exhausted.
It ought to be mentioned as well that the British expert group appraises that cloning is going to be a transitional phenomenon which will be curtailed as soon as we learn enough about ordinary cells to "reprogram" them to behave in the manner of stem cells.
In the report, it says that cloning and the use of human embryos can be "justified" as "transitional research".

Danish law

In Denmark, the use of fetuses for carrying out research and for therapeutic cloning is regulated by the "Act concerning artificial fertilization in connection with medical treatment, diagnostic procedure and research, etc."
According to the provisions of this act, experiments may only be carried out on eggs or gametes that are going to be used for fertilization if such experiments have the purpose of:
- improving the techniques of artificial insemination
- improving the methods of ascertaining "serious hereditary illnesses or detecting some essential physical abnormality".

The Minister of Health has the authority to determine whether an egg that is left over from an at-

The English expert group's recommendations:
1. Research involving embryos (regardless of whether they are created within an in vitro insemination or as a result of the replacement of cell nuclei) with the purpose of augmenting the understanding of diseases and suffering experienced by people and cell-based treatments ought to be permitted, with all due consideration paid to the Human Fertilisation and Embryology Act.
2. Before permission is granted to research that involves embryos created by replacing cell nuclei, the Human Fertilisation and Embryology Authority must be certain that there are no other ways of attaining the desired experimental results.
3. Persons whose eggs or sperm cells are to be used in the creation of embryos for purposes of research are compelled to grant their express acceptance that the embryos which are being created may be used in carrying out research aimed at obtaining stem cells.
4. Research implemented with the aid of the replacement of cell nuclei inside of human eggs, which is intended to further our understanding of and develop further the treatment for mitochondria illnesses, ought to be permitted with all due consideration paid to Human Fertilisation and Embryology Act.
5. Research into human stem cells ought to be monitored in such a way that it will be possible to evaluate whether the research is yielding the anticipated beneficial results and so that it will be possible to spot problems which eventually might arise.
6. The combining of adult (somatic) human cells and eggs from animals must not be permitted.
7. The transfer into any woman's uterus of an embryo created through the replacement of the cell nucleus (so-called "reproductive cloning") ought to remain a criminal act.
8. It is important to keep an eye on the need for legislation that deals with the use of embryonic cells that are going to be used in treatment.
9. The research councils ought to be encouraged to set up programs for stem cell research and ought to be encouraged to take stock of whether it is possible to create stem cell collections for purposes of making research.

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tempt at artificial fertilization may be used as a source for stem cells. Eggs may not be sold or carried out of the country.

Experiments that involve the use of eggs are subject to the standard approval procedures in the scientific ethics' committees.

According to Danish law, it is illegal to carry out a cloning for purposes of treatment. Nor is it legal to do research on methods that might make cloning possible.
It is similarly illegal to attempt to create any actually living clone of another person in Denmark.

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The latest five issues of "From the Board to the Parliament" are entitled:

139: Uncertain gains for net-municipalities
138: The nation would do well to stake its bets on urban ecology
137: Sshhh ... you're making a racket! - on the Technology Board's project about noise
136: Gene-spliced foodstuffs
135: Xenotransplantation

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