CLONING-STATEMENT FROM THE DANISH COUNCIL OF ETHICS

Introduction to the Danish Council of Ethics' Position

Cloning is asexual reproduction. That means that an individual can be created without the involvement of any egg and sperm cells. Cloning generates a copy of the cloned organism's genes-unlike sexual reproduction, in which the offspring takes one half of its genes from the egg cell and the other half from the sperm cell.

The cloning debate arouses intense emotions, which presumably has to do with the fact that cloning strikes at something altogether fundamental, the creation of life. Of course, it can be claimed that people have always been involved in the creation of life when they have children. In recent years, parenting has also taken place with the aid of assisted reproduction, imitating nature's way of uniting eggs and sperm cells. The latest development is that life can be initiated by means of a so-called somatic cell nuclear transfer from a cell that could never evolve into a new individual of its own accord. The next step may be that researchers come by knowledge that will enable them to make changes to the future individual through genetic engineering. Thus, for the first time, people may be faced with the option of being directly capable of influencing their own evolution.

The possibility of cloning gave rise directly to worldwide, yet not undisputed agreement that human cloning should under no circumstances be allowed. However, it turns out that the knowledge about cell specialization to which cloning research has given rise can also be used in other contexts. Other applications of cloning techniques–especially so-called therapeutic cloning–have been suggested, and opinions have now been voiced recommending this use of cloning. Most recently, on 23 january 2001, the British House of Lords finally passed a draft bill to permit some research into human stem cells taken from an embryo —embryonic stem cells— the creation of such stem cells being feasible with the aid of the somatic cell nuclear transfer cloning technique.

The ethical dilemmas associated with permitting stem cell research are essentially linked to embryonic stem cells. On the one hand, the embryo could develop into a child, were it to be implanted in a uterus and otherwise enjoy the right conditions. On the other hand, there is foreseeably great therapeutic potential in exploring stem cells and, more particularly, in embryonic stem cells created by cloning techniques. For some, the ethical misgivings attaching to the use of embryos, formed for example by clo-

ning, are offset by the great benefits the technique may bring with it. For others, despite the objective involved, such use of human embryos would be emblematic of overstepping ethical boundaries in a way that is unacceptable. But if equally suitable stem cells can be acquired by some other means, that would alter the balance for many people and the Council of Ethics has therefore chosen also to include some reference to alternative sources of stem cells that can be used for research and therapeutic purposes.

In this outline, the Council of Ethics takes a stance on whether the use of cloning should be permitted in Denmark to create offspring, and whether the production of embryonic stem cells by cloning techniques should be allowed, or whether embryonic stem cells should even be used for the purpose of research and possibly treatment at all.

The report discusses the concepts and subsequently reviews the Council's ethical deliberations and position. The legal aspects of the topic are dealt with in an appendix.

What is Cloning?

The term cloning is currently used not just of creating a genetically (almost) identical copy of a pre-existing individual. It transpires that the knowledge about cell specialization to which research into cloning has given rise can also be used in other contexts. Two applications of cloning are outlined below: reproductive and therapeutic cloning.[1]

Reproductive Cloning (Cloning to Create Identical Individuals)

Cloning that produces one or more individuals by asexual reproduction can take place in different ways (see fact boxes):

Cloning by embryo splitting. The fertilized egg is divided into two or more early on in the development. Nature itself does this too, including when an embryo divides in the womb to become identical twins (see fact box 1).

Cloning by somatic cell nuclear transfer. This is not just a matter of developing an individual without using the fusion of an egg and sperm cell; here an individual is produced without there being a mother (apart from the surrogate mother) and a father. (See fact box 2).

Dolly the sheep has come to represent the paragon of cloning by somatic cell nuclear transfer. Dolly is a so-called *somatic clone*, having been cloned from a somatic cell from an adult sheep-a body cell as opposed to a germ cell. In Dolly's case it was a cell from an adult sheep's udder. That is to say that a cell that has already specialized into, say, an udder cell, a skin cell or a liver cell can be reprogrammed by the mature egg cell to start dividing and form all of the sheep's tissues and organs, and even a

[1] Attention is drawn to the fact that cloning is also used to denote merely the formation of a cell clone, *i. e.* a collection of identically shaped cells. Technically speaking, therefore, stem cell propagation is cloning, but this is not the sense in which cloning raises ethical considerations.

fully developed offspring. It is a pioneering new realization which has assumed revolutionary importance for scientists' understanding of biology. It was well known that every single cell in the body, apart from the germlines, contains the individual's collective genetic material (the genome), but not that an entirely new and hence genetically identical individual could be formed on that basis. Once this had been proved, all the biology textbooks had to be rewritten as they contained the received line of wisdom to date: that the specialization of cells into particular functions was irrevocable once it had happened.

Some Practical and Technical Difficulties

If it is wished to use cloning techniques to create a genetically identical copy of a human being, the issue of safety comes into play, because there is no experience of what will happen to the cloned individuals in the long term. In a short time-frame, for instance, cows that are pregnant with a cloned fetus (embryonic cloning) turn out to have a slightly extended gestation period and a marked increase in calving problems. In addition, the emerging calves present increased birth weight and mortality.

Cloning by somatic cells appears to present even more difficulties. To produce Dolly, for example, it took just under 300 attempts before succeeding in finally obtaining a vigorous lamb–as well as considerably more deformed and stillborn animals. Currently, only 0.1-1.0% of all eggs that receive transplanted cell nuclei from adult mammals result in the birth of a live animal. Most nuclear transplantees are either incapable of dividing or else develop abnormally.

Therapeutic Cloning (Cloning to Produce Stem Cells)

Research into tissue and organ engineering is based on the hope of being able to reprogramme so-called stem cells into precisely the type of cell needed, for example brain cells in order to be able to treat a patient with Alzheimer's disease. It can be said that the purpose of using stem cells is to develop reserve or repair tissue.

Stem cells are found in the early phases of the fertilized egg, *i. e.* in the embryo. They are therefore called *embryonic stem cells* (see fact box 3). Up to four days after fertilization, the embryo consists of identical cells, which can develop into all types of cells during fetal development, including fetal membranes, placenta, umbilical cord etcetera and are therefore so-called *totipotent*. On about the sixth day the embryo divides into an outer and an inner layer of cells (the blastocyst stage). The outer cell layer forms the tissue around the fetus (fetal membranes etcetera). The inner cells will mainly form the actual fetus. The cells from here are also stem cells and can become all types of tissue in the actual fetus, but cannot develop into the surrounding tissue. These stem cells are called *pluripotent* embryonic stem cells. It is these stem cells that may possibly be usable in treating disease.

One of the methods for gaining access to this type of stem cell is to per-

form the first part of the process that created Dolly, *i. e.* create an embryo from an already specialized cell by somatic cell nuclear transfer. The embryonic stem cells created in this manner can therefore be referred to as cloned stem cells and form the basis of the concept of *therapeutic cloning*.

The idea is to "regenerate" a cell from the body —preferably from the actual patient destined to receive the repair tissue— into embryonic stem cells. For if it were possible to cultivate human tissues and organs on the basis of one cell taken from the sick person, it might be possible to overcome one of the great problems of transplantation from other people: rejection of foreign tissue. First and foremost, therefore, therapeutic cloning is viewed in a "transplantation perspective", namely as an alternative to harvesting fully developed cells or organs from living or dead donors with all the attendant problems: lack of organs, compatibility, voluntariness, trade in organs and so on.

Initially, attempts are being made to control the differentiation of embryonic stem cells in a culture for the purpose of producing specialized cells that could be transferred to the patient to repair damage to a particular organ. This might, for example, be nerve cells for treating Parkinson's disease, kidney cells for treating renal failure or heart muscle cells for treating cardiac failure. The cells will not be rejected by the body if they are cloned from the actual patient and are thus genetically compatible with the patient on whom they are used.

In the same way, looking even further into the future, one option is the ability to cultivate whole organs, but this involves considerable technical difficulties. The future scenario may look like this, for instance:

When the person starts to fall ill, *e. g.* with incipient heart failure, it is envisaged taking a single cell from that person and cloning it, by placing it in an egg cell emptied of its nucleus. The pluripotent stem cells obtainable in this way are then cultured. Once a sufficient number of cells has been acquired, the right differentiation factors are added to make the cells begin developing into heart muscle cells. These precursors to heart muscle cells are then transferred to a heart-shaped mould made of a biodegradable material such as the material from which degradable surgical suture is made. The cells continue growing and gradually replace the mould, and by adding other differentiation factors-and perhaps starting to stimulate the newly formed heart electrically-it is ultimately hoped to get a beating heart ready for transplanting.

While this is still a possible futuristic scenario, artificial skin, cartilage and blood vessels can already be cultured in a similar fashion now. Thus, artificial ears and noses have been cultivated by culturing cartilage cells on ear and nose-shaped moulds.

There are numerous problems that still need to be solved before it is possible to cultivate hearts and other organs, two of which will be highlighted here:

Firstly, we still lack knowledge about differentiation factors. Some, though far from all, are known, and there are therefore limits to how precisely the differentiation process can be controlled.

Secondly, some organs have a relatively complicated three-dimensional structure, with many different cell types needing to be positioned correctly in relation to one another for the organ to be able to perform its function. In the kidney, for example, there are two tubular systems, each complex–one for blood and one for urine; if they are not "properly aligned" relative to each other, the kidney will not function. In order to make a kidney, therefore, it is not enough to be able to cultivate all the different kinds of cell that form part of the kidney; you need to be able to arrange them in the correct position relative to one another as well.

Stem Cells Can Also be Obtained in Other Ways

Embryonic stem cells can be obtained from embryos or from aborted fetuses, as described below. But using any form of embryonic stem cell gives rise to an ethical dilemma, *i. e.* whether mankind is being violated by using the human embryo for research or therapeutic purposes in order to relieve severe disease. This dilemma could be circumvented if it were possible to access and use stem cells which are not embryonic. Several options are being researched here. It is generally true that not much is yet known about the potential of the various stem cells.

In addition to embryonic stem cells formed by somatic cell nuclear transfer, there are different sources for creating both embryonic and other stem cells:

— Embryonic stem cells from *in vitro* fertilized (IVF) eggs.

— Embryonic germ cells from aborted fetuses.

— Stem cells from adults.

— Stem cells from cord blood.

— Somatic cells reprogrammed without the use of cell nuclear transfer.

Embryonic Stem Cells from IVF eggs

Pluripotent embryonic stem cells, which are taken from the embryo after 5-7 days of cell division are also available through the common process of fusing an egg and a sperm cell in a test tube (assisted reproduction–IVF). If a woman being treated for infertility has had more eggs fertilized with her partner's sperm than are needed for treatment, she can donate the remaining fertilized eggs for research into stem cell development. In the USA, research is currently going on into stem cells formed from such surplus "IVF eggs". Of course, it is also possible to imagine fertilized eggs being produced *in vitro* with an exclusive view to using them for research. However, the latter option would be in contravention of article 18, para. 2 of the European Bioethics Convention, which Denmark has endorsed.

Embryonic Germ Cells

A slightly different type of non-cloned stem cell, is those taken from the human genital tissue of aborted fetuses. These cells are also pluripotent. So far, they have not been successfully cultured in the laboratory for more than 21 days.

Stem Cells from Adults

Scientists have isolated stem cells from some types of tissue in adults,

for example from blood and bone marrow. It was once assumed that these stem cells could only become certain types of cell in the body, as they are not toti or pluripotent, like embryonic stem cells. They are more specialized (so-called multipotent, see fact box 3). More recent research, however, indicates that these stem cells also have the potential to become far more-maybe even all-of the body's cells, that in other words they may prove to have the same potential as embryonic stem cells.

Stem Cells from Cord Blood

The umbilical cord blood of neonates contains a large quantity of stem cells, corresponding to the stem cells found in the bone marrow. It is not yet known what potential stem cells from cord blood have. If the stem cells prove capable of forming many types of tissue, and if the cord blood is collected from the patient herself at the time of the birth —as is being done on a trial basis in countries including Denmark— it may be possible to use the stem cells from the blood to cultivate tissue and organs genetically identical with the actual patient.

Somatic Cells Reprogrammed without the Use of Cell Nuclear Transfer

In the longer term one of the considered goals is to be capable of reprogramming cells from the adult body without the use of cell nuclear transfer, *i. e.* without first creating an embryo. For the time being, however, insufficient is known about the cellular development process and cell reprogramming to be able to accomplish this.

Compatibility with the Patient's Tissue

Some stem cells are more genitically compatible with the patient's own tissue than others. The most compatible ones originate from the actual patient and therefore have his or her genetic make-up. These are:

1. Stem cells from the patient's own tissue (*e. g.* the bone marrow).
2. Stem cells that have come about as a result of resetting the patient's own somatic cell (either by cell nuclear transfer or (—with time, perhaps—) by reprogramming in the lab).
3. Stem cells originating from the patient's cord blood.

Tissues or organs cultivated from the patient's own cells will presumably be more readily assimilated by the patient's organism without the problems of rejection that accompany the transplanting of tissues and organs from others. However, there are research results to indicate that embryonic stem cells not originating from the actual patient can be transplanted without any major rejection problems.

The Council of Ethics' Views on Reproductive Cloning

There is a consensus of opinion on the Danish Council of Ethics that human cloning must never take place. This view is in keeping with the Council's previous statement on reproductive cloning, sent out in spring 1997, just after Dolly was "publicized", which says that "*The Danish Council of Ethics is against human cloning. It is the Council's view that it is not necessary to argue in favour of the self-evident unacceptability of pro-*

ducing a human being that is a copy of a person already in existence".

The intuitive rejection of reproductive cloning is still shared by the Council's members, and a survey of the international debate shows that the vast majority dissociate themselves from it. In this regard it can be mentioned that many will fear the possibility of controls on cloning —or other manipulations of hereditary attributes— slipping through human fingers, of people being unable to take in the broader consequences or, in other words, not being wise enough to intervene in their own evolution in this crucial way. Developing the somatic cell nuclear transfer technique sufficiently for it to be used on human beings without a risk of either short or long-term injury to the children concerned is beyond our ken. Nor do we have any knowledge of the long-term effects of allowing these techniques to be used to create children, including whether serious mutations will occur for the clones, their children and subsequent generations.

So far, it may have appeared unnecessary to argue in favour of rejecting reproductive cloning in more detail. The fact that, as human beings, we are brought into existence by sexual reproduction has been such a matter of course that it has occurred to no one to ponder it. We are the fruit of a fusion of genetic material from two parents, one of either sex, and at birth are thus unique individuals with a unique genetic profile. That has been one of the pillars of life and has therefore not been open to discussion. However, the emergence of the somatic cell nuclear transfer technique, in particular, means that we cannot *but* discuss and evaluate arguments for and against reproductive cloning.

The initial motion, then, is that it must be up to those who subscribe to permitting reproductive human cloning to argue in favour of its desirability. Such advocates have now made themselves known in the debate, and some of the arguments they have advanced will be reproduced below. Against this, the Council's members will assert that, for a number of reasons, allowing reproductive human cloning would constitute an ethical slide.

Arguments in Favour of Reproductive Cloning

1. *Help for a Childless Couple*. Despite the many techniques that have now been developed for assisted reproduction, there will still be a small group of childless couples left who have been forced to abandon the idea of having genetically related children. For many people, having genetically related children rather than adopting, is an intense need, and there will therefore be a group —presumably limited in number— who wish to be allowed to use cell nuclear transfer to clone one of the partners so that they can have a child that is genetically related, at least to that partner.

It is possible, for instance, to envisage the couple having opted to insert a cell nucleus from the man into the enucleated egg cell of the woman. If this egg cell is then implanted in the woman's womb, the couple could have a son that was a clone of the father, genetically, while still having the 2%

or so of the mother's gene stock contained in the mitochondria. In genetic terms, then, the child will not stem quintessentially from the mother, but will nevertheless be her child in that she carries and nurtures it throughout the pregnancy in order to finally give birth to and nurse it. What is more, the egg cell (minus the nucleus) originates from her, contrary to the case with egg donation.

Some people claim that the human right, as indeed it is, to found a family must be respected, even though the offspring involved may have been cloned. They maintain that cloning must be reckoned among assisted reproduction methods and that this technique defers to the right to reproduce.

2. *Method of Avoiding Hereditary Disease*. Cloning can also enter the picture in cases where one of the parties in a relationship suffers from or is a carrier of a severe, genetic disease which the couple do not wish to pass on to the child-to-be. With the aid of cloning, they will be able to deselect the genetic material of one of the parties.

As in the example above, the couple might wish to insert a cell nucleus from the healthy party into an enucleated egg cell from the mother. This would create a clone of the healthy party. In this instance, however, the couple may have the alternative of being able to choose to use pre-implantation diagnosis, *i. e.* to fertilize several of the woman's eggs with the man's sperm *in vitro*. The fertilized eggs can then be examined to establish whether they carry the genetic disease, and only healthy eggs subsequently placed in the woman's womb.[2] For some couples, cloning may be preferable, as it will save them having to choose between fertilized eggs.[3]

3. *Surrogate for a Child that has been Lost*. Parents may wish to clone a dead or dying child and thereby have a replacement for the child they have lost or are in the process of losing. Here again, in technical terms, a somatic cell is taken from the child and the nucleus placed inside the enucleated oocyte (egg cell) from the mother, who will then be able to bring a virtually genetically identical child into the world.

4. *Help for a Child with a Fatal Disorder*. Recent years have seen reports of instances where the parents of a dying child needing a compatible bone marrow donor have conceived a new child in the hope of that child being able to be used as a donor for the dying child.

[2] See also the Council of Ethics' report Genetic Examination of Healthy Subjects (currently only in Danish) from 2000.

[3] It is worth mentioning here that there are also genetic diseases which are due to defective mitochondria in the egg, *i. e.* genetic material outside the cell nucleus. There are more than 50 inherited diseases known be caused by defects in the mitochondria. Here, too, cell nuclear replacement might be an option, inserting the nucleus from the woman's egg into another woman's egg with healthy mitochondria, having removed the nucleus beforehand, then fertilizing the egg with the man's sperm. In this case, however, the child will not be a clone of either parent, but strictly speaking a child with three genetic parents, since approx. 2% of the gene stock (the mitochondria) comes from the woman who donated the enucleated egg (see *Chief Medical Officer's Expert Advisory Group on Therapeutic Cloning*, june 2000, p. 27).

Among other things, then, the new child is created as a means of saving the dying child's life. The parents of the children mentioned did not take this view, however. They expressed the view that they would appreciate the new child regardless of whether or not it could be used as a donor. If bone marrow cells can be harvested from the new child's umbilical cord, for example, that child will be none the worse for the experience.

With normal fertilization there is the "risk" of the new child's genetic make-up not matching that of the sick child. In order to solve that problem, parents have been described as using assisted reproduction with the *in vitro* technique to allow them to select and insert into the womb an embryo genetically compatible with the sick child's tissue. Similarly, the couple could be envisaged as choosing, instead, to have a clone of the sick child in order to be sure that this new cloned child could act as a donor. Some people will feel that it would be right to help the sick child and its parents in this way not only to have a new child but at the same time to have the opportunity to cure their sick child of a fatal disease.

In the same way, taking things in a wider perspective, it will be possible to produce a new child that could act as a donor by giving one of its organs to a severely sick or dying child–*e. g.* a child could be cloned in order to harvest one of its kidneys for a sick brother or sister. Perhaps even vital organs could be harvested, but that would render the new child itself unable to continue living.

Rejection of Reproductive Cloning

As regards the rationale for rejecting the technique of cloning to produce genetic copies of human beings as a remedy for childlessness or as a way of securing genetically healthy offspring, or for the purpose of providing "surrogate children" and "spare-parts children", the Council's members refer to the fact that, cloning will be a violation of human dignity,[4] knowing that he or she has come into being as a clone will have adverse consequences for a person (right to an open future) and permitting reproductive cloning will reflect a disregard for the respect due to the moral status of embryos.

Notwithstanding that not all Council members endorse each and every one of these arguments–which are amplified below–or regard them as cogent, the arguments nevertheless all point in the same direction; and together, in the view of the Council, they constitute a sound basis for rejecting reproductive cloning on the grounds that it is ethically unacceptable.

Violation of Human Dignity

Basically, the Council's members consider that the aversion to reproductive cloning can be summarized in as much as this method of producing human beings will violate the dignity of mankind. This consideration is based not only on an evaluation of "what harm can that do?", but on questions like "what will happen in the long term with ourselves as people if we set out along this path?".

[4] Where mention is made here and subsequently of human dignity, it means the innate dignity of both humankind and the individual.

No one is very likely to be able to answer this in a way completely satisfactory to everybody, one reason perhaps being that the reply contains elements that elude formulation in logical linguistic usage. Maybe the answer is to be found within the wisdom that can best be expressed in art, legends, fairytales and so on. Some may articulate their intuitive dissociation from cloning by saying, for example: "Our self-knowledge as human beings forbids us from doing this. If we go ahead and do it anyway, we will have to change our self-knowledge, and to what?".

The concept of human dignity rests on the recognition that human beings are something special-partly in relation to all other life, partly by virtue of the fact that as humans we are not identical but different and unique. An increasing understanding of people's right to be different, to make different choices and to express their 'differentness' can therefore be seen as a manifestation of respect for human dignity too.

In rendering an account of its discussions, therefore, the Danish Council of Ethics' previous statement on cloning, referred to above, also stated that "*reproduction by cloning will be a violation of the fact that conceiving a child requires the presence of both sperm and egg, i. e. material from two different individuals.*" The statement is an expression of the basic human circumstance that new human life is formed by the union of a sperm cell and an egg cell from two different people of different sexes, thereby having both a biological father and a biological mother and simultaneously coming into existence as a unique individual that is not a replica of another person who has already lived. Precisely because each of us thus comes into the world as something new and something special —*i. e.* as oneself, not as someone else— cloning, which produces nothing new or nothing special, but a copy, a replication, must be regarded as an infringement of human dignity.

However, it must be stressed that reproductive cloning cannot be forbidden with reference to the fact that the clone's particular parentage infringes his or her dignity and integrity. Indeed, the clone can no more be held in contempt for its origins than it should be considered degrading for a child to have been born "clandestinely" or "illegitimately". Clones —were they to come about— are also entitled to have us respect their special human value and integrity. For with time, they too would take on an independent life with a special story, and thus be entitled to care and respect. Just as *Dolly* was a sheep, so too a human being formed by cloning would be a person.

Yet the need to forbid the possibility of reproduction through cloning exists because the actual notion of cloning also revolves around our attitude to that which is radically different, to the other person, to the Other, and to nature as the Other. The desire for cloning cannot be divorced from the desire to invalidate the different, the other, the alien that which is at variance with us, differs and never slots neatly into our all-purpose pigeonholes.

It is a universal trait that we are so easily tempted to oversimplify, to homologize and to subjugate this Other, and now also the Other person too.

But we may end up subjugating so much that our existence becomes vacuous. After all, without the Other we would not be able to enter into character as Ourselves.

So it is not merely our dignity or integrity as such that is violated by reproductive cloning, but on the contrary the actual vital instrumentality of our existence as social beings.

Man's dignity is also tied up with a principle that a person must never be treated merely as a means, but always concurrently as an end in itself. This principle rests on an assumption that every single individual belonging to the human race is equally entitled to be respected as an entity to be heeded on the basis of ethical considerations. This should be taken to mean that no one must be purely and simply "commodified" or seen as a resource for others, as everyone is part of the ethical community. This is precisely why all human individuals have a claim to respect. It stands to reason that producing a cloned child in order for it —as described above— to serve as a supplier of tissues and vital organs for another human being is pure objectification, possibly even in its ultimate form.

Similarly, it is worth pointing out that if permitting cloning changes the basic situation that conceiving a child requires the presence of both sperm and egg, parents will have the possibility of reproducing not merely to have a child, but to have *a specific child*, whose genes they can choose by having the child become a genetic copy of a person who is already alive or was once alive. Even today, of course, parents have the chance to influence their children's life choices etcetera. But to opt out of the genetic variation represented by sexual reproduction would be to create a tool for perfecting parents' attempts to control their child and its future. We would thus be approaching a situation in which parents of clones might view their offspring not as an end in their own right —as an independent individual with a will of its own— but as a means of fulfilling the parents' dreams and ambitions. Doing away with the genetically determined variation that is sexual reproduction would therefore constitute an objectification of the cloned individual as well, and a violation of that individual's dignity.

In Summary, Therefore, it Can Be Said that Reproductive Cloning:

1. Will be at odds with human dignity, because such cloning produces an identical copy, whereas human dignity requires precisely the creation of something new, unique and different.

2. Will deprive mankind of the fundamental given of having both a biological mother and a biological father.

3. Will affront our potential for growing and developing as social beings; 'commodifies' human life by turning it into a tool instead of respecting it as an end in its own right.

Not all people —nor all members of the Danish Council of Ethics— necessarily have the same basic outlook, although they unanimously regard reproductive cloning as being at odds with human dignity. Whereas for some members that dignity depends ultimately on regarding the individual person as having been created by God and in His image, for others on the

Council the concept of human dignity does not have a corresponding religious grounding but is rooted in a humanistically founded recognition of man's peculiar status in relation to other forms of life.

Right to an Open Future

All members consider that not only respect for certain fundamental ethical values but also the likely consequences of a human clone's self-understanding and viability militate decisively against allowing reproductive cloning.

Everyone has a right to an open future. Although the future is apparently mapped out in a comparatively fixed framework for many people, *e. g.* because of social conditions, and although genes are not the only determinant of a person's career, every human being has the right not to know the effect their genome can have on their future. One of the implications is that people are entitled not to enter the world as a genetic copy of a person who already exists in the world or who has existed. In part, that right is necessary to ensure that, wherever possible, people can live their lives in a spontaneous, free and authentic way.

The view can be put forward that monozygotic twins are also clones, as they have the same genome, and that being a clone is therefore no worse than being a twin. Identical twins, however, are born and grow up contemporaneously as two original individuals. Unlike a cloned child, they have no knowledge of what their "original predecessor" was like or how this person lived his or her life. There is thus a crucial difference between being a "simultaneous" or a "belated" twin. To put it another way: with identical twins it will not be possible to establish who is the original and who is the copy. Conversely, anyone born, so to speak, as a "belated" identical twin will know, or think they know, too much about themselves and their future destiny. The experience of *feeling* that the future is open is important, as is the feeling of being free to make one's own choices in life.

When the Council therefore takes the view that people should be entitled not to start out as copies of pre-existing (or previously existing) persons, it is not merely because they will then grow up as copies of that pre-existing person; it is also because they will probably *not* turn out like "the original", but on the contrary will end up living an obscure existence under pressure from themselves or the outside world to become like their prototype. This may be because they themselves or the world around them feel that, being a genetic copy of a pre-existing person, they must also become the way that person was socially and psychologically. Thus the clone can have a life-long experience of not being at liberty to live his or her own life and to make his or her own choices regardless of whether or not the outside world actually requires the person concerned to mirror his or her "original".

In this context it is worth mentioning that it may be negative for children to be born or adopted either as surrogate children for dead siblings or to come into the world under parents who, for other reasons, have an overt desire to shape their personality in the image of another. The negative experiences to which even non-cloned

offspring are subject dictate that we must not permit cloning, which can potentially result in an increase in the number of such fates, as expectations can potentially become even more precise and the disappointment all the greater if they are shattered.

Moreover, it is possible to conceive of stresses specific to a cloned person, such as "the original" developing a disease at a time of life after "the copy" has been formed. "The copy" will then have to live in the sure knowledge, or possibly just fear, that it too will be smitten by the disease.

Conversely, it can be argued that we have no way of sensing or knowing that all clones will feel that their future is fettered by another person with almost identical genes having lived previously. Nor, then, can this argument be used to reject cloning in every instance, but it must be seen in the context of the other arguments against cloning.

Respect for the Moral Status of an Embryo

For some of the Council's members (Lene Gammelgaard, Lisbet Due Madsen, Erling Tiedemann and Peter Ohrstrom) reproductive cloning is out of the question, in that it presupposes that human embryos are brought into the world in order to be involved in experiments on them–experiments which the members in question consider ethically unacceptable and incompatible with the moral status of the embryo. The standpoint on the moral status of embryos is expounded in a later section on the Council's stance on therapeutic cloning.

The Council of Ethics' Stance on Reproductive Cloning

Based on the above arguments, a unified Council of Ethics rejects human cloning ever being permissible for the purpose of creating a genetic copy of a human being. Although some of the Council's members acknowledge that the intuitive resistance to reproductive cloning cannot be substantiated in a single argument, the members nonetheless unanimously reject permitting reproductive human cloning on the basis of the comprehensive nature of the arguments set out above.

The Council of Ethics' Views on Therapeutic Cloning

A united council finds that no major ethical problems appear to be linked with research and possible treatment involving human stem cells that do *not* originate from embryos but are found in cord blood, in the adult body or possibly even, with time, are potentially capable of being produced from specialized cells.

Expectations are increasingly being voiced that the therapeutic advances for which embryonic stem cell research may foreseeably pave the way might otherwise be obtained using stem cells that can be found and cultured without requiring the use of human embryos.

As shown in the following, the Council of Ethics' members consider that what presents ethical problems is the application of *embryonic* stem cells for research and possibly therapeutic purposes. An account of these ethical problems is given below.

Use of Embryonic Stem Cells for Research and Therapeutic Purposes

The term *therapeutic cloning* in the heading to this chapter is commonly used, though not apt, since cloning is only one of a number or ways in which stem cells can be produced, as illustrated by the section "What is cloning?". It is the stem cells which form the basis for the promising treatment of severe disorders, not the fact that they are formed by cloning. *Embryonic stem cells* have aroused particular interest and expectations because, unlike stem cells from the adult organism, they:

— Are pluripotent and therefore capable of becoming all other tissues.

— Need no "reprogramming".

— Are relatively easy to procure and can be propagated in virtually unlimited numbers, whereas stem cells in the adult organism are rare.

— Are newly formed and therefore do not have an increased risk of mutation brought on by age.

— There are three essential, albeit not essentially different sources of embryonic stem cells:

— Embryos created by *in vitro* fertilisation but no longer needed for treating childlessness (sometimes called "spare embryos").

— Embryos formed by the *in vitro* technique *with a view* to gaining access to stem cells.

— Embryos formed as a result of somatic cell nuclear transfer (the "Dolly method").

All these instances involve cells that have been taken from an embryo, a fetus in the making, which —given the right conditions— would be capable of developing into an offspring.

The objectives of therapeutic and reproductive cloning are, of course, different. In one case the aim is to produce embryonic stem cells for researching and treating severe diseases that cannot be treated in any other way; in the other instance the purpose is to produce a child. But both techniques require research to be done on embryos in order to develop the techniques, thereby calling for a position to be taken on the moral status the early embryo possesses. The members of the Council assess the moral status of the embryo differently, and thus hold divergent views on the degree to which it is permissible to use it for human stem cell research.

An Embryo Must be Protected like Any Other Human Life

Faced with having to give an answer to what status a fertilized egg cell (zygote) or an embryo can be deemed to have, some of the Council's members (Lene Gammelgaard, Lisbet Due Madsen, Ragnhild Riis, Erling Tiedemann and Peter Ohrstrom) consider that any human being can spontaneously wonder: "When did I come into existence?" and for most people the obvious workaday answer to the question will presumably be "I did so when I was conceived". However, a biologically more specific approach must also lead to the recognition that human life comes about at fertilization, when egg and sperm fuse into something altogether new, which constitutes a developmental continuum from that point on. It was therefore perfectly natural as well as biologically sound for Danish parliament,

when passing the Act on the Council of Ethics, to work into Section 1 "The Council shall carry out its work on the assumption that human life begins at the moment of fertilization".

Needless to say, the development of a fetus is gradual. An embryo is not a ready-made human being, but at no point in time is there any question of the embryo having to be supplied with new information in order to continue developing. There is thus seen to be no biological basis for regarding a fetus as having different ethical status during pregnancy. Approximately 30 hours after fertilization the egg cell will have divided into two cells; and after five to six days, when it consists of several hundred cells, the embryo will make its way into the uterine mucous membrane. It is then a unique human organism with a special chromosome constitution that exerts chemical control over the maternal hormonal and immune system. To describe this life merely as *tissue* or *a cell culture* would be misleading.

The fact that this embryo can still spontaneously divide and turn into identical twins for another week does not challenge its moral status and the respect that needs to be shown for the human life evolving. The notion of allowing experiments on an embryo in connection with therapeutic cloning until the point when it normally becomes embedded in the uterine membrane (*i. e.* after a 5 to 6-day cycle) or until the formation of the neural groove (*i. e.* after a 10 to 14-day cycle) thus appears to be completely arbitrary. Based on previous experience, therefore, such an arbitrary limit must be expected to go by the board the moment scientists in contrast to the case at present spot a research interest or some other potential in prolonging experiments beyond these time limits.

An Early Embryo Need not be Protected to the Same Degree as Human Life

Other of the Council's members (Frederik Christensen, Asger Dirksen, Mette Hartlev, Ole Hartling, Nikolaj Henningsen, John Steen Johansen, Naser Khader, Pelse Helms Kaae, Karen Schousboe, Sven Asger Sorensen and Ellen Thuesen) do not feel that just because the embryo could be brought on to form an offspring, given the right conditions, that means it *is* an offspring, *i. e.* a human individual. So there is no question of objectifying *a human being* by using embryonic stem cells in this way; or in other words: it does not become a violation of a *person*.

It can be hard to indicate precisely when an embryo switches to having full human status. However, it does seem reasonable to claim that it is *after* the point at which the stem cells are taken from the embryo. This happens during the earliest phase of its development, *i. e.* after just six days or so of cell division. By this time the cells have not yet begun to specialize in forming the various tissues and organs of the body. One cannot yet speak of a fetus proper, therefore, but of cells that certainly have the potential ability to develop into a human being at a later juncture and under the right circumstances. As yet, however, *which* human being has not been established.

It might be expressed thus: the embryo does not become a human being

until it assumes a "face", an identity and is therefore not someone else. At this early juncture, for example, it has not yet been determined whether the embryo will result in one child, twins or triplets.

The view can be taken that conception occurs when the sperm cell penetrates the egg cell. But it can be asserted with equally great weight that conception, which originally means reception, occurs when the embryo is received by the womb. Only then does the embryo have a chance of continuing towards life out in the world. Conception thus takes the form of a process extending over time, including the time it takes the sperm cell to penetrate the egg cell, for example. In the case of somatic cell nucleus transfer it does not even involve conception, and here again no specific and precise moment of genesis will be ascertainable.

By way of summary, these members of the Council feel that the same moral status should not be ascribed to a fertilized egg, an embryo and an almost fully developed child. That means that at this earliest of embryonic phases there is no point speaking of an individual or of individuality. It is an early embryo, and just that; not a fetus.

Human Embryos Must Not Be Used for Research and Therapeutic Purposes

Some of the Council's members (Lene Gammelgaard, Lisbet Due Madsen, Erling Tiedemann and Peter Ohrstrom) feel that therapeutic cloning) —and the use of embryonic stem cells altogether— violates the moral status of the embryo in such a crucial way that these techniques ought to be banned. The notion that the moral status of a human embryo might be dependent on the intended purpose with which it is brought into existence must be rejected. Just as a child —irrespective of the intention with which a parenting couple have brought it into the world— is nonetheless a child, and its moral status and claim to protection are not a function of the parents' intentions, nor is the moral status of a human embryo dependent on the intention with which it has been generated, or the words used to describe it.

Against this background it cannot be considered ethically acceptable to use human embryos as experimental objects with a view to extracting stem cells. On the contrary, using an embryo for some purpose not beneficial to the embryo itself must be considered a radical objectification of human life and hence incompatible with respect for human dignity. In this connection there is considered to be no difference between so-called "spare embryos", brought into existence as a result of IVF treatment, and embryos brought directly into existence with a view to being made the object of research or stem cell recovery. The moral status must be regarded as the same in both cases. Ethically speaking, however, bringing human life into existence purely with an eye to destroying it by experimentation or by using it to produce stem cells is perceived as an exacerbation of that. It is presumably reflective of a similar view when the European Bioethics Convention, endorsed by Denmark, includes a ban on creating human embryos with a view to research (article 18, para. 2).

Correspondingly, these members dismiss the argument adduced by researchers that using human embryos to manufacture stem cells could be acceptable because it would only be a transitional stage in the development of research that would be abandoned again as quickly as possible. Such an argument is symptomatic of a philosophy of "the means justifying the end", which is ethically indefensible.

The position taken on the moral status of an embryo that has not (yet) been planted in a womb is significant not only for the question in hand cloning and the use of stem cells but will also assume importance for other problematic issues arising in the future. In reality, saying 'yes' to the intended application of embryos can very easily lead to a more or less automatic 'yes' to other, as yet unknown technologies in which the moral status of the embryo is the corresponding salient point. The form of argument frequently used, which seeks to deproblematize new and previously untried technologies ethically with reference to the fact that known technologies have already received the go-ahead, illustrates this point.[5] Neither the legislation nor practice in a field to date can be vested with the status of an ethical norm, however.

In this regard, therefore, it is also necessary to face the fact that some development towards reproductive cloning is only to be expected in the wake of research aimed at therapeutic cloning despite many people (albeit not everyone) currently taking issue with it. In the USA, there is strong advocacy in favour of permitting reproductive cloning. Assuming that such a form of cloning eventually becomes feasible and reasonably reliable without any appreciable malformations, it is only to be expected that people will come forward wishing for help with treatment, *e. g.* for childlessness, where all other options have been exhausted. If, in that situation, society has long since accepted the use of cloning for therapeutic purposes, with the disregard for the moral status of the embryo it entails, surely in the light of experience from similar situations it will prove difficult to turn down the medical researchers and patient groups subsequently wanting permission to carry out reproductive cloning and the experimentation preceding it. The prospect of being able to permit therapeutic cloning and stand firm in rejecting reproductive cloning in the longer term must be deemed unlikely.

The kind of cloning that was developed in conjunction with Dolly the sheep coming into existence immediately raises the question of whether the embryo involved was comparable with an embryo that has come about by natural or assisted reproduction of an egg cell. The mere existence of Dolly contains the answer to that question, however. Similarly, it must be recognized that a human embryo that needed to be brought about using similar technology and placed in a woman's uterus would become a child, were the implantation to succeed and the pregnancy continue to term. In this regard it can be pointed out that

[5] See for example *Chief Medical Officer's Expert Advisory Group on Therapeutic Cloning,* june 2000, pt. 4.12.

any statutory provision that cloning by somatic cell nuclear transfer *must* not be used for reproductive cloning will, per se, be tantamount to acknowledging that the embryo produced *does have* the same potential to become a complete human being, like the embryo resulting from assisted reproduction in a petri dish. There is considered to be no basis, therefore, for viewing such an embryo as having different moral status to any normal human embryo.

Consequently, whether the embryo is created by somatic cell nuclear transfer or by assisted natural fertilization, these members do not consider it ethically acceptable to use human embryos for medical experiments or as the basis for extracting stem cells for further production. As mentioned, anything of that kind would take the form of far-reaching objectification of human life, which is crucially at odds with human dignity.

When forming a Danish politic in this area these members have the view that there is a need to realize that the use of embryos as the subjects of therapeutic cloning experiments cannot be regarded as an isolated area of scientific research. Foreseeably, it is bound to become interlinked with other fields such as IVF techniques, pre-implantation diagnosis, gene therapy and genetic manipulation of germlines, which will increasingly be capable of shaking human self-understanding and draining the concept of human dignity of any substance.

Moreover, it is only to be expected that powerful economic forces associated with interested researchers will continue down the road of commodification by *patenting* stem cells and cells that have developed from them. The lower the moral status an embryo is considered to have and the more it is referred to as merely *a cell culture* or *tissue*, the more the way will be open for such developments, with their particularly far-reaching ramifications in ethical terms.

In principle, Embryonic Stem Cells May Be Used for Research and Therapeutic Purposes

Other of the Council's members (Frederik Christensen, Asger Dirksen, Mette Hartlev, Ole Hartling, Nikolaj Henningsen, John Steen Johansen, Naser Khader, Pelse Helms Kaae, Karen Schousboe, Sven Asger Sorensen and Ellen Thuesen) consider that although the early embryo *is* an embryo, it does not have the status of a fetus or a child. For these members conception, understood as "motherhood", is crucial to the consummation of the embryo towards life. Only assimilation in the womb provides possibilities for life, and only then does the fetus have its full moral status, therefore. The embryos under review here, which are in the early phase (up to six days), must be treated with respect, but that does not mean that the embryo must be respected, *qua* person. Nor, on the other hand, does it allow one to do absolutely anything with the embryo, *e. g.* use it to manufacture cosmetics. To do so would not be to treat it with respect. That respect for the embryo may consist of ensuring that it is not used arbitrarily or gratuitously, but only for research that will safeguard substantive values, such as alleviating human suffering. It might

even be alleged, moreover, that genuinely working to help and cure patients in distress is a display of respect for *those* people.

Against this backdrop these members feel that some research into embryonic stem cells should be permitted, where the objective is to develop treatments for severe disorders that cannot be treated in any other way.

It is an ethical rule that *a person* must be regarded as an end in his/her own right and never just as a means to another end. The purpose of such research and possible treatment is to help hitherto incurable patients, but for the above-mentioned reasons there is no question of turning *a person* into a means to other people's ends, nor of handling human tissue with disrespect.

It may be an essential rule of ethics *that the end must not justify the means*, but that rule is not relevant in this context. By attempting to apply it here, the implication is that the means has been "desecrated", and is therefore in need of "consecration" and that is not the case.

There is considered to be no reason to fear that permission for therapeutic cloning will lead us onto a slippery slope, making it impossible with time to retain the ban on performing reproductive cloning. This has to do with the fact that there is no difficulty in distinguishing between the two forms of cloning. There is a consensus on opposing reproductive cloning, also internationally, and that consensus, which became apparent in the years leading up to and after Dolly's birth, continues to assert itself pretty much unmoved by the discussion about therapeutic cloning.

Initially, Research Should Be Done on "Spare Embryos"

Some of the members (Frederik Christensen, Asger Dirksen, Mette Hartlev, Ole Hartling, Nikolaj Henningsen, John Steen Johansen, Naser Khader, Pelse Helms Kaae and Ellen Thuesen) who in principle endorse allowing research into embryonic stem cells for research-related and therapeutic purposes, simultaneously acknowledge that even though it is one option in an ethical dilemma it is one that is not yet regarded as urgent.

The purpose of a human embryo is to become a child. The purpose is the same, whether the embryo is formed by natural or assisted reproduction. Creating embryos using the IVF technique or somatic cell nuclear transfer with a view to researching and treating disease may signal a slide in values akin to that described above under the Council's stance on reproductive cloning. The dilemma arises because, conversely, not helping severely ill people to obtain treatment without having sufficiently weighty reason to deny them that help may also be wrong.

The potential for treating severe disorders promised by the use of stem cells is considered so important that, in accordance with this view, using embryos to some extent for research into such treatments can be approved. However, an embryo should not be produced solely with research purposes in mind unless there are imperative grounds for doing so. An alternative therefore emerges in the use of leftover embryos from IVF infertility therapy, that is to say embryos that have already been formed but are destined for destruction.

Adherents of this view thus feel that leftover embryos can be made the subject of research directed at treating disease and not merely, as now, at enhancing the IVF technique. Not many embryos are left over from IVF treatment, as performed in Denmark, and at any rate the parents' consent is required for the embryos to be used in research. But according to what the Council has been told, unlimited-and, in principle, immortal-stem cell lines can be formed from a single embryo. That can only mean that a restrictive approach-as set out here-into embryonic stem cell research need not pose a major obstacle to research.

Despite one of the Danish Council of Ethics' goals being to clarify the ethical position well before any ethical quandary turns into an acute dilemma and becomes a difficult forum in which to make choices, there would seem to be a case here for adopting a wait-and-see pose. This is because treating severe disease with stem cells is still only a theoretical eventuality for bioassays. Moreover, there may be grounds for caution. When it comes to producing embryonic stem cells from cloning with somatic cell nuclear transfer considerable technical problems remain to be solved even in animal cloning. For example, we are anything but familiar with the interaction between mitochondrial DNA and cell nucleus DNA; in reproductive cloning, the "reproduction" has only succeeded in a few cases, a number of cells have chromosomal anomalies, pregnancy is difficult, and any offspring produced are infirm, with infections and anaemia, for unknown reasons, and prone to contracting disease in a number of organ systems. Cloning with a view to forming stem cells, where embryonic development has to be halted again after having been set in motion, only to then be changed to form a specific tissue type, is scarcely any easier, and any risks there might be in transferring undesirable genetic material to the stem cells has not been clarified.

There is every reason to take small strides when advancing into unknown territory. Were there to prove to be vital breakthroughs in stem cell research and hence perhaps genuine scope for treatment with stem cells, so that in other words the possibility of alleviating suffering were no longer just theoretical, there might be reason to reconsider the issue of using other sources of embryonic stem cells. So there appears to be no reason to adopt a position on the dilemma until it actually occurs. There is no way of knowing whether it will even become an issue at a later juncture since, as mentioned in the introduction to this chapter, it is not unlikely that stem cells can be found and cultured without relying on the use of human embryos.

Controlled Research on Embryonic Stem Cells May Take Place

Some of the members (Karen Schousboe and Sven Asger Sørensen) consider that the use of therapeutic cloning with a view to research is ethically acceptable, provided a limit is set on the time such experiments are allowed to run for. In Denmark, where certain experiments with embryos are permitted, for instance, it is prohi-

bited to develop embryos beyond a fortnight (see appendix on the statutory basis). It is the view of these members that, at about that time, an embryo which has been formed as a clone cannot be regarded as a person, despite being theoretically capable of developing as a person.

These Council members do not feel that granting permission for therapeutic cloning under the conditions set out will entail an increased risk of reproductive cloning being introduced. The point of the two methods is so essentially different that there is no obvious correlation, virtually ruling out any likelihood of an emergent desire or need to extend therapeutic cloning to reproductive cloning just as the potential for gene therapy on somatic cells has not unleashed any demand or wish for gene therapy on germ lines.

Embryonic stem cells that have come about as a result of transplanting the nucleus from a somatic cell from the recipient's own body into a vacant egg cell, thus resetting the nucleus to embryonic stem cells identical in reality to the cells from which the actual person was originally created, should be regarded as an extension of that person's own body. They can therefore be used without ethical problems to treat the person concerned for severe disorders. If the patient is a woman, moreover, and she herself supplies the egg cell to be used in resetting the somatic cell, not even the 2-3% of the gene stock held in the enucleated egg cell is foreign tissue.

In the case of IVF treatment several embryos are usually developed (8-10 are aimed for), of which a maximum of two are implanted in the woman under current Danish regulations with a view to achieving a pregnancy, while the remainder of the embryos, which have the potential to become a child, are destroyed. That means that a number of embryos are made, in other words, while fully aware that the majority of them will have to be destroyed. By using the surplus eggs for research aimed at enabling severe disease to be treated, the production of surplus eggs is rendered meaningful, rather than pointlessly manufacturing them with an eye to destruction.

Comprehensive research is being conducted into the use of fetal cells to treat severe disorders. For instance, fetal cells are being transplanted to the brain of patients with Parkinson's disease and Huntington's chorea for the purpose of having the fetal cells develop into brain cells and replace those in the patient's brain that have died as a result of the disorder. Research of this kind is taking place in Denmark, as well as other countries, where it has been approved by the Scientific Ethical Committee System. The fetal cells used are from terminations, *i. e.* from fetuses that have been implanted in a womb and, unlike embryos, have a human attribute to them. It must be regarded as desirable and ethically more acceptable for research of this kind to be carried out on embryos to a greater degree.

Supporters of using embryos for research believe that there is no point in waiting till methods employing non-embryonic cells have been developed before using embryonic stem cells. This will not prevent the use of fetal cells-which already goes on, as mentioned and will mean appreciable delays to research that can potentially result in treatment for severe disorders.

The Council of Ethics' Stance on Therapeutic Cloning

The members of the Danish Council of Ethics have different views on which sort of moral status the early, fertilized egg possesses. As a result, its members also have different views on the ethical defensibility of undertaking research into early embryos and, in the fullness of time perhaps, developing therapies for serious disorders, treatment of which is based on embryonic stem cells.

Some members (Lene Gammelgaard, Lisbet Due Madsen, Ragnhild Riis, Erling Tiedemann and Peter Øhrstrøm) consider the moral status of the human embryo such that embryonic stem cells must not be used; others (Frederik Christensen, Asger Dirksen, Mette Hartlev, Ole Hartling, Nikolaj Henningsen, John Steen Johansen, Naser Khader, Pelse Helms Kaae, Karen Schousboe, Sven Asger Sorensen and Ellen Thuesen) find that, in principle, embryonic stem cells can be used as long as substantive benefits are available for treating disease.

Of those members able to approve the use of embryonic stem cells in principle, however, most (Frederik Christensen, Asger Dirksen, Mette Hartlev, Ole Hartling, Nikolaj Henningsen, John Steen Johansen, Naser Khader, Pelse Helms Kaae and Ellen Thuesen) find that there is no pressing need at the present to allow embryonic stem cells to be produced for research or possible treatment of disease, either by cloning or by the *in vitro* technique, as known from IVF therapy. This is because treating severe disease with stem cells is still only a theoretical possibility, and manufacturing embryos for any purpose other than having the embryo become a child may constitute a slide in values. Initially, therefore, these members recommend that research into embryonic stem cells be confined to embryos left over from IVF treatment.

Finally, two members (Karen Schousboe and Sven Asger Sorensen) feel that the use of therapeutic cloning with a view to research into the treatment of severe disorders is ethically acceptable, providing such research is carried out on very early embryos only-compare current legislation. Research involving the use of embryonic stem cells is, in the opinion of these members, also preferable to the fetal cell research currently taking place in Denmark, for example.

If it *is* decided to permit some research into cloned stem cells as a matter of policy, safeguards should be put in place to prevent such cells later becoming such commodities that the way is opened for making them patentable on a par with the previous patenting of other, similar cell cultures, *inter alia* in the USA. This is not deemed ethically acceptable, because the individual cloned cell line belongs, in a unique sense, together with and hence to the individual from whom the cell nucleus was taken, just like his/her organs and other tissues, which pursuant to Section 20, subs. 3 of the Danish Act on the Inspection of Corpses, Autopsy and Transplantation etc. must not be purchased or sold, but may be donated. The Bioethics Convention (article 21) also prohibits financial gain as such from interventions on the human body.

Finally, none of the Council's members see any ethical problems in research and treatment using stem cells that are not embryonic, but on the contrary think that research capable of clarifying the potential of this type of stem cell should be fostered.

Lars-Henrik Schmidt was unfortunately unable to take part in the Council's discussions on reproductive and therapeutic cloning. This member wished to have his views go on record as a matter of principle, and the Council has accepted. Lars-Henrik Schmidt indicates that the purpose of mankind issues from having diversified progenitors-as regards both gender and generation. That view excludes reproductive cloning.

Cloning autologous stem cells for therapeutic purposes must be regarded as extended regeneration. Thus therapeutic cloning does not provoke the cultural-historical renunciation of incest here in the sense of generational provocation.

Fact Boxes

Cloning by Embryo Splitting

Spontaneously occurring monozygotic twins and triplets, for instance, are the result of embryo splitting. It can also occur by intervention to the embryo. After a fertilized egg has divided several times and become 4-16 cells, it can be split; each individual part, if placed in a uterus, can become a normal individual. These individuals are artificially produced monozygotic twins and are genetically identical. Using embryo splitting, a maximum of 4-8 identical individuals can be produced.

For many years this technique has been used to clone animals, but has proved totally incapable of replacing ordinary breeding methods to produce offspring with valuable characteristics.

Cloning by Somatic Cell Nuclear Transfer

The body consists of billions of specialized cells (skin cells, bone cells, blood cells, brain cells etcetera). Normally, with cell division, a specialized cell can only become the same kind of cell, *i. e.* a skin cell keeps dividing into skin cells. But if the cell nucleus is moved from one cell to another cell that has had its own nucleus removed, the relocated cell nucleus will assume control of that cell.

With cloning by somatic cell nuclear transfer, a specialized cell is taken from an individual, cultured in the laboratory, enucleated and the nucleus transferred to an egg cell from which the nucleus has been removed. The egg cell "reprogrammes" the cell nucleus so that it "forgets" it was in a specialized cell (*e. g.* a skin cell) and now starts acting as if it were the nucleus in a fertilized egg. It starts to divide and develop an embryo which, if placed in a uterus, can become an individual more or less exactly like the individual that donated the cell nucleus. The offspring thus cloned has approximately 99% of the same genetic material as the individual from which the cell nucleus originally came. For some years now it has been possible to carry out embryonic cloning, but Dolly the sheep was the first somatic cloning of a mammal.

Stem Cells

Stem cells are non-specialized cells that can divide and become more specialized cells. There are different types of stem cells.

Stem cells are found partly in the early phases of the fertilized egg, *i. e.* in the embryo. These stem cells are therefore called *embryonic stem cells*. In an embryo that is up to about six days old, all the cells can differentiate into any of the cells which will constitute the fetus, including fetal membranes, placenta etcetera. and are therefore known as *totipotent*. At around six days, the germinal disc forms, going on to become the actual fetus. The cells from this are also stem cells and can become all types of tissue in the actual fetus, but not the tissue around the fetus, *i. e.* fetal membranes etc. These stem cells are called *pluripotent*.

By taking the preliminary steps of somatic cloning, which "regenerates" a cell from the soma by replacing its nucleus in the mature egg cell, it is possible to produce stem cells that are genetically identical to the individual from which the cloned cell nucleus comes. These stem cells are also called embryonic, because they come from an embryo. There is currently no other way of producing pluripotent stem cells, but there seems to be excellent scope for developing such stem cells from any cell whatsoever in the body.

Stem cells capable of becoming several cell lines, *e. g.* blood cells, can be found in cord blood and in smaller numbers in the individual's various organs, *e. g.* the bone marrow. They are called *multipotent*.

Appendix 1: Legal Basis for Reproductive and Therapeutic Cloning

The purpose of this memorandum is to provide an exposition of the rules of law governing reproductive and therapeutic cloning.

I. *Reproductive Cloning*

I.1. *Using Embryo Splitting and Embryonic Stem Cells Produced by Somatic Cell Nuclear Transfer*. Reproductive cloning can result from the division of a naturally fertilized egg (embryo splitting) or by a fertilized egg being formed from the nucleus of a somatic cell replaced in an egg cell (somatic cell nuclear transfer). The regulations concerning the use of fertilized and unfertilized eggs will be found primarily in the Danish Act on Assisted Procreation.[6]

In the field of health it is common practice not to delineate a legal framework for the therapeutic methods open to the doctor in charge of treating the patient. In one specific area, *i. e.* assisted reproduction, an overall legal framework for treatment of the patient by a doctor has been demarcated in the Act on Assisted Procreation. This framework-together with the rules in the Danish Practice of Medicine Act, to the effect that the doctor must exercise care and conscientiousness in his or her dealings-applies to a doctor's treatment

[6] Danish Act num. 460 of 10 june 1997 on Assisted Procreation in connection with Medical Treatment, Diagnosis and Research etcetera (Act on Assisted Procreation).

of women with assisted reproduction unless a special exception has been made in law.[7]

The Act on Assisted Procreation regulates the conditions under which a physicianmay use human eggs to treat a woman with a view to establishing a pregnancy in any way other than intercourse between a man and a woman. Similarly, the Act regulates the conditions under which a scientist may conduct biomedical research and experiments involving reproductive cells from human beings, fertilized eggs and pre-embryos.[8]

For Therapeutic Purposes:

In its basic form, reproductive cloning can be considered to be covered by the Act on Assisted Procreation, as treatment is administered with the purpose of bringing about pregnancy artificially, *i. e.* in some way other than intercourse between a man and a woman.

The Act on Assisted Procreation States:

"It shall be prohibited simultaneously or subsequently to implant identical unfertilized or fertilized ova into one or several women for the purpose of procreation".[9]

The provision covers not only cases in which an egg is divided (embryo splitting), but also cases in which it is attempted to induce cells from an individual already alive to resume production of tissue in a fertilized egg with a view to giving birth to an individual that is genetically (almost) identical with an individual already alive (somatic cell nuclear transfer).[10]

The Act, then, forbids a doctor from treating a woman with reproductive cloning. Furthermore, Section 2 of the Act must also be presumed to include a ban on reproductive cloning by somatic cell nuclear transfer.[11] The Danish Ministry of Health points out, with reference to Section 2 of the Act, that removing the nucleus of an egg cell and subsequently using it to treat involuntary childlessness thus presupposing the insertion of new genetic material as a substitute for the material removed will be banned, since such an application would entail genetic change (to an egg cell).[12]

7 A special exception has been made for *e. g.* single women and women over 45, *cfr*. Act on Assisted Procreation, Sections 3 and 4.

8 Act on Assisted Procreation, Section 1.

9 Act on Assisted Procreation, Section 4

10 See comments on the Danish Act on Assisted Procreation, Section 4 (Section 3 of the draft bill).

11 Section 2 of the Act on Assisted Procreation is worded as follows: Assisted Procreation may not take place unless it does so with a view to combining a genetically unchanged (unmodified) egg cell with a genetically unchanged (unmodified) sperm cell.

12 Letter to the Danish Women's Society from the Ministry of Health, 1st Division, ref. l.kt.jr.nr. 2000-7719-35, of 20 october 2000. The letter is excerpted in a written presentation entitled "Without Eggs, No Therapeutic Cloning", by Bente Holm Nielsen, MD, and associate professor Lone Nørgaard, MA, published in the conference folder for the Danish Board of Technology's hearing "Kloning til Behandling" [Therapeutic Cloning] on 20 november 2000.

There are two provisions in the law, therefore, forbidding reproductive cloning by somatic cell nuclear transfer.

In Research:

Research into embryo splitting and somatic cell nuclear transfer with a view to producing genetically identical individuals can basically be considered covered by the Danish Act on Assisted Procreation, as the Act regulates biomedical research and experiments incorporating reproductive cells from humans, fertilized ova and pre-embryos.

The Act states

"The following experiments shall not be made:

1) Experiments intended to enable production of genetically identical human individuals".[13]

From the explanatory notes, it is clear that the provision includes both embryo splitting and instances in which it is attempted to replace a somatic cell from an individual already alive to an emptied egg cell thus resuming production of tissue.[14]

The Act thus forbids conducting research into reproductive cloning.

I.2. *Using eggs from aborted female fetuses*. Reproductive cloning using eggs from aborted female fetuses will be prohibited just because the use of immature oocytes and ovaries or parts of the same from aborted female fetuses is forbidden in respect of treating childlessness.[15]

In the context of research, it must be assumed that eggs from aborted female fetuses cannot be used for experiments involving reproductive cloning, as egg extraction may only be performed with a view to researching into improvements in assisted reproduction techniques and pre-implantation diagnostics.[16]

Therapeutic Cloning

II.1. *Using Embryonic Stem Cells Produced by Somatic Cell Nuclear Transfer and Removed from Naturally Fertilized Eggs*. The point of therapeutic cloning using somatic cell nuclear transfer is to produce embryonic stem cells intended to result in the formation of specialized cells for engineering tissues and organs with which to treat sick people. Such embryonic stem cells can also be removed from a naturally fertilized egg. Cloning for therapeutic purposes is only performed on an experimental basis today, but a future scenario involving therapeutic cloning for treatment purposes may well arise.

The regulations governing the use of fertilized and unfertilized human eggs are found primarily in the Danish Act on Assisted Procreation.

13 Act on Assisted Procreation, Section 28.

14 Explanatory notes to the Act on Assisted Procreation, Section 28.

15 Act on Assisted Procreation, Section 10

16 Act on Assisted Procreation, Section 25, subs. 2. See also discussion below on the scope of the provision under pt. II.1.

For Therapeutic Purposes:

No direct mention is made of therapeutic cloning in the Danish Act on Assisted Procreation, and taking the wording of the Act as a basis, the conclusion arrived at is that the use of human eggs for any treatment other than that involving assisted reproduction falls outside the purview of the law. This means that medical treatment with therapeutic cloning will not be covered by the rules of law. If a method of treating disease using embryonic stem cells is devised in the future, the attending physician will have to respect the accountability provisions of the Practice of Medicine Act as well as the Ministry of Health's guidelines on accountability, including guidance on the introduction of new methods of treatment in the health services.

This construction of the regulatory basis governing treatment with therapeutic cloning pivots on an interpretation of the wording of the Act. As pointed out by Mette Hartlev,[17] the law and its lines of demarcation cannot be taken to mean that Danish Parliament has consciously omitted to put limits in place on the use of human eggs for this purpose, since unlike the "Dolly technique" this technology was not common knowledge at the time the law was enacted. Based on the antecedents to the Act, then, it cannot be inferred that Parliament wished to refrain from regulating therapeutic cloning when enacting the law. It is possible, on the basis of the preparatory works to the Act, to argue in favour of applying the rules of the law to therapeutic cloning by analogy, but given that a doctor violating the rules of the Act can attract a penalty in the form of a fine or imprisonment, this will not be a tenable solution.[18]

As the legal position is now, a doctor will be able to offer treatment with therapeutic cloning while honouring the rules of the Practice of Medicine Act, etcetera.

In Research:

The Act's application clause envisages the Act applying to biomedical research and experiments that incorporate reproductive cells from human beings, fertilized ova and pre-embryos, whatever the purpose of such experiments.[19] As pointed out by Mette Hartlev,[20] this may give rise to doubt whether the Act is intended to apply to any form of research on fertilized ova and reproductive cells. Looking at the research provisions of the Act, the provision appears to deal with "biomedical experiments on fertilized ova and reproductive cells inten-

17 "Den danske lovgivning om kloning" [Danish Legislation on Cloning], assistant professor Mette Hartlev, PhD. University of Copenhagen, written presentation, p. 4, published in the conference folder for the Danish Board of Technology's hearing "Kloning til Behandling" on 20 november 2000.

18 *Idem*.

19 Act on Assisted Procreation, Section 1.

20 "Den danske lovgivning om kloning", assistant professor Mette Hartlev, PhD, University of Copenhagen, written presentation, p. 2, published in the conference folder for the Danish Board of Technology's hearing "Kloning til Behandling" on 20 november 2000.

ded for use in fertilization".[21] The wording indicates that experiments on fertilized ova and reproductive cells (unfertilized eggs and sperm cells) not intended for use in fertilization are not covered by the legislative controls. Irrespective of these doubts, however, the Act does establish in very general terms[22] that it is forbidden to remove and fertilize human eggs with a view to conducting experiments other than those allowed by law. One can only conclude, then, that experiments on human eggs with a view to producing and extracting embryonic stem cells for treating disease are covered by the law.

The Act permits experiments to be carried out on human fertilized ova and reproductive cells intended for use in fertilization only when they serve to improve assisted reproduction techniques or pre-implantation diagnostics.[23] From this, it follows that any other form of research on human eggs is prohibited, including experiments on human eggs for the purpose of producing and extracting embryonic stem cells for treating disease.

II.2. *Using Eggs from Aborted Female Fetuses*. Therapeutic cloning using eggs from aborted female fetuses for therapeutic purposes will not be covered by the rules in the Danish Act on Assisted Procreation, since the utilization of human eggs for any treatment other than that involving assisted reproduction falls outside the purview of the Act.[24] As the legal position stands now, a doctor will be able to offer treatment involving therapeutic cloning using embryonic stem cells from aborted female fetuses, while still respecting the rules of the Danish Practice of Medicine Act etcetera.

In a research context it must be assumed that eggs from aborted female fetuses cannot be used for experiments with therapeutic cloning, as egg extraction for research purposes can only be done for the purpose of trying to improve assisted reproduction techniques and pre-implantation diagnostics.[25]

Thus it is not permitted to research into therapeutic cloning using embryonic stem cells from aborted female fetuses.

II.3. *Non-embryonic Stem Cells*. There are also attempts to use non-embryonic stem cells therapeutically. Use of these stem cells is not regulated by the Act on Assisted Procreation, but their use is subject to the rules otherwise applicable to the collection, donation and utilization of human tissue.[26]

The stem cells that are the subject of such interest are stem cells from umbilical cord blood, stem cells from

22 Act on Assisted Procreation, Section 25.

22 Act on Assisted Procreation, Section 25, subs. 2.

23 Act on Assisted Procreation, Section 25, subs. 1.

24 Act on Assisted Procreation, Sections 1 and 10.

25 Act on Assisted Procreation, Section 25. *Cfr*. discussion above on the scope of the provision, pt. II.1.

26 See "Den danske lovgivning om kloning", assistant professor Mette Hartlev, PhD, University of Copenhagen, written presentation, p. 5, published in the conference folder for the Danish Board of Technology's hearing "Kloning til Behandling" on 20 november 2000. The paragraph is based on this presentation generally.

adults and somatic cells from the adult body reprogrammed without the use of somatic cell nuclear transfer.

For Therapeutic Purposes

A distinction needs to be drawn between treatment involving the person from whom the tissue material originates and treatment of a different person (donation for transplantation).

Using stem cells to treat the person from whom the cells originate is permissible subject to compliance with the rules of the Practice of Medicine Act, etcetera.

Apart from the Practice of Medicine Act etcetera, donation of tissue for use in treating a different person is also covered by the rules in the Danish Act on the Inspection of Corpses, Autopsy and Transplantation etcetera,[27] which covers the donation of tissues from persons both alive and dead. This Act does not apply to "minor interventions" such as extracting blood and removing small sections of skin, *cfr*. Section 17, subs. 2.

Written consent is required for donating tissue from living persons. It is also a requirement that the tissue can be donated without any blatant risk to the donor. There are special restrictions on tissue donation from minors. This can only be done on an exceptional basis, and only where it involves regenerable tissue.

Tissues from dead people can be donated with the informed consent in writing of the deceased or next of kin. In conjunction with an autopsy, it is also allowed to extract tissues with a view to treating other people. However, the next of kin who have given their consent for the autopsy must be informed in advance and furnish their consent.

In Research

If cells from a living or deceased person are needed for use in an experiment involving cloning of stem cells, according to the Danish Act on the Central Scientific Ethical Committee System (the CVK Act) both the permission of the committee system and the informed consent of the person the tissue derives from must be obtained.

III. *Summary*

In Danish law there is a ban on a doctor treating a woman with reproductive cloning for therapeutic purposes, and there is a ban on conducting experiments with reproductive cloning.

There is no ban on administering treatment with therapeutic cloning. Treatment with therapeutic cloning is not covered by the rules of the Act on Assisted Procreation, but it is regulated by the Practice of Medicine Act. A doctor will thus be able to provide treatment with therapeutic cloning providing that he or she respects the accountability rules of the Practice of Medicine Act.

Conversely, Danish law must be construed to mean that experiments

[27] Danish Act num. 420 of 13 june 1990 on the Inspection of Corpses, Autopsy and Transplantation etc, as amended by Act num. 259 of 12 april 2000.

with therapeutic cloning are covered by the rules of the Act on Assisted Procreation, and that this Act contains a ban on conducting experiments with therapeutic cloning.

Consequently, some discussion needs to be devoted to the diverse legal position of therapeutic cloning for therapeutic purposes and experimentation.

No rules exist that directly address controls on the use of non-embryonic stem cells for treatment purposes, and no ban exists on such use.

Experiments involving therapeutic use of non-embryonic stem cells are not prohibited either, but can be conducted if permitted by the Scientific Ethical Committee System.

There might therefore be a need to conduct some discussion on the diverse legal status of therapeutic cloning in experimentation relating to the use of embryonic and non-embryonic stem cells.

Fact Box:

International Law. Examples

The Council of Europe's convention of 4 april 1997 on the protection of human rights and human dignity in connection with the use of biology and medical science (the Convention of Human Rights and Biomedicine), signed by Denmark and subsequently ratified in 1999, sets out that creating human fetuses solely for the purpose of research is not permissible.

In 1998 the Convention had a supplementary protocol added on banning human cloning. Article 1 of the protocol provides that any initiative aiming to create a human being genetically identical to another human being, alive or dead, is prohibited. Although the majority of the EU's member states signed the supplementary protocol, it has been ratified by only two EU countries, to wit Greece and Spain.[28]

In the UK, research into and treatment using human embryos is regulated by "The Human Fertilisation and Embryology Act" of 1990. Research centres and clinics handling human embryos must apply to the Human Fertilisation and Embryology Authority for permission. Until december 2000, research permission could be granted for the following specific objectives 1) increasing knowledge about miscarriages, 2) increasing knowledge about congenital disease, 3) promoting advances in the treatment of infertility, 4) developing more effective contraception and 5) genetic diagnosis. So there is no direct ban in existence on using research techniques like somatic cell nuclear transfer, providing that the purpose is one of those mentioned above.[29]

28 "Betydningen af national regulering af stamcelleforskning og kloning" [The Significance of National Regulation of Stem Cell Research and Cloning], Dr Karin Elisabeth Rosén, MD, PhD, University of Lund, written presentation, p. 2, published in the conference folder for the Danish Board of Technology's hearing "Kloning til Behandling" on 20 november 2000.

29 "Betydningen af national regulering af stamcelleforskning og kloning", Dr Karin Elisabeth Rosén, MD, PhD, University of Lund, written presentation, p. 3, published in the conference folder for the Danish Board of Technology's hearing "Kloning til Behandling" on 20 november 2000.

In december 2000, the British Parliament passed a draft bill[30] broadening access to human embryo research for two additional purposes, *i. e.* 6) therapies for mitochondrial diseases and 7) therapies for diseased or damaged tissues and organs. The Act was finally passed by the House of Lords on 23 january 2001 and will come into force on 31 January 2001. The House of Lords further decided to set up a special committee of the House of Lords to keep the implications of the Act under review, including monitoring the issue of licences.

The USA has no federal legislation prohibiting therapeutic cloning or research into embryonic stem cells. Every year since 1995 the American Congress has adopted a provision in the Budget prohibiting public financing of research with human embryos. This means that the National Institute of Health cannot conduct/initiate research on human embryos, but such research can be done freely in the private sector with no controls.

The Clinton administration has proposed that research to "derive" and "study" human embryonic stem cells should be permitted under certain conditions. In august 2000 the National Institute of Health published new guidelines according to which research on human embryonic stem cells can be financed by public funding, if two conditions are met:

1. Embryonic stem cells must be taken from frozen embryos superfluous to fertility treatment and the embryos must already be designated for discarding.

2. Public (federal) financing cannot be used to destroy embryos in order to obtain embryonic stem cells, which means that privately funded researchers must give embryonic stem cells to those researchers who are publicly (federally) funded.[31]

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30 The draft bill was formulated in accordance with a recommendation of the British Ministry of Health's Chief Medical Officer's Expert Group on Stem Cell Research: Medical Progress with Responsibility, june 2000.

31 "Betydningen af national regulering af stamcelleforskning og kloning", Dr Karin Elisabeth Rosén, MD, PhD, University of Lund, written presentation, p. 3, published in the conference folder for the Danish Board of Technology's hearing "Kloning til Behandling" on 20 november 2000.

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