HUMAN CLONING

ETHICAL ISSUES

UNESCO

UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION

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United Nations Educational, Scientific and Cultural Organization

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Illustrations: Jérôme Lo Monaco

Further information:

Secretariat of the Bioethics Section
Division of Ethics of Science and Technology
Social and Human Sciences Sector
United Nations Educational, Scientific and Cultural Organization (UNESCO)
1, rue Miollis, 75732 Paris Cedex 15, France
Tel. 33 (0)1 45 68 37 81
Fax. 33 (0)1 45 68 55 15
http://www.unesco.org/bioethics

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C O N T E N T S

PREFACE

In this new century, there has been no slackening of the pace of scientific research and discovery. Academic publications and the mass media inform us, virtually on a daily basis, of new and profound discoveries that seem to probe further than was ever believed possible, penetrating to the very core of the universe and unveiling the essence of what constitutes human beings.

Few discoveries exemplify these sweeping developments more than cloning – the laboratory-aided replication of a strand of DNA that is used to produce an identical being. Suddenly, concepts and practices that just a generation or two ago would have been relegated to the realms of science fiction are fast becoming reality.

However, with such rapid scientific progress come reflection and often concern about its proper use. The question constantly arises as to how far the practice of cloning should be allowed to proceed.

Some ethical guidelines have been successfully established by the international community through the Universal Declaration on the Human Genome and Human Rights, adopted by UNESCO's General Conference in 1997 and endorsed by the United Nations General Assembly the following year. This document delves into the heart of the matter when it asserts that human life has an intrinsic value. It further states that "practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted".

While each nation must determine for its society the proper limits to set on cloning, much can be gained from discussion and reflection at the international level. Understandably, it has been decision-makers, scientists and bioethicists who have assumed a leading role in the discussions relating to cloning and the profound ethical questions that it poses for humanity. However, other bodies of opinion, including the public at large, also have a major stake in a wider ethical debate and they often wish to know more.

It is up to UNESCO, custodian of an ethical mandate that remains unique within the United Nations system, to continue being vigilant on this matter, to monitor the direction in which research is going and to provide governments, policy-makers, the scientific community and the general public with the accurate, reliable information they require when making decisions about cloning. It is also the role of the Organization to work with all the relevant stakeholders and assist them in reconciling rapid developments in science with the ethical values we all cherish.

This is why I am pleased to present this explanatory brochure, which outlines the main phases of development of the cloning sciences and describes the efforts that have been made to make sense of what may be a vast new frontier for the biological sciences.

Koïchiro Matsuura
Director-General of UNESCO

A Brief History of Cloning

Cloning may seem to be a relatively recent laboratory phenomenon, but the word itself derives from antiquity: the Greek word *κλων* for "twig". Initial use of the term applied to early 20th century botany, designating plant grafts. "Clone" eventually came to be used for micro-organisms as well. Then, by the 1970s, the word came to designate a viable human or animal generated from a single parent. Over the last few years, cloning has come to mean any artificial, identical genetic copy of an existing life form. How is cloning different from natural reproduction? Many organisms including human beings result from sexual reproduction. That is, the female egg is fertilized by the male sperm, and an embryo forms (*fig.1*). The embryo's genetic structure, those pairs of chemicals, which determine human characteristics, is located in the chromosomes[1] found in the nucleus of every embryonic cell. The new organism obtains one half of its genes from the mother's egg and the other half from the father's sperm.

In cloning by nuclear transfer, on the other hand, the egg nucleus is removed through a microscopic laboratory procedure and replaced with a donor's nucleus, containing the unique genes of that individual.

[1] **chromosome** – A threadlike structure several to many of which are found in the nucleus of plant and animal (eukaryotic) cells. Chromosomes are composed of chromatin and carry the genes in a linear sequence; these determine the individual characteristics of an organism. *A Dictionary of Biology.* Oxford University Press, 2000. *Oxford Reference Online.* Oxford University Press. 10 October 2003 <http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t6.000855>

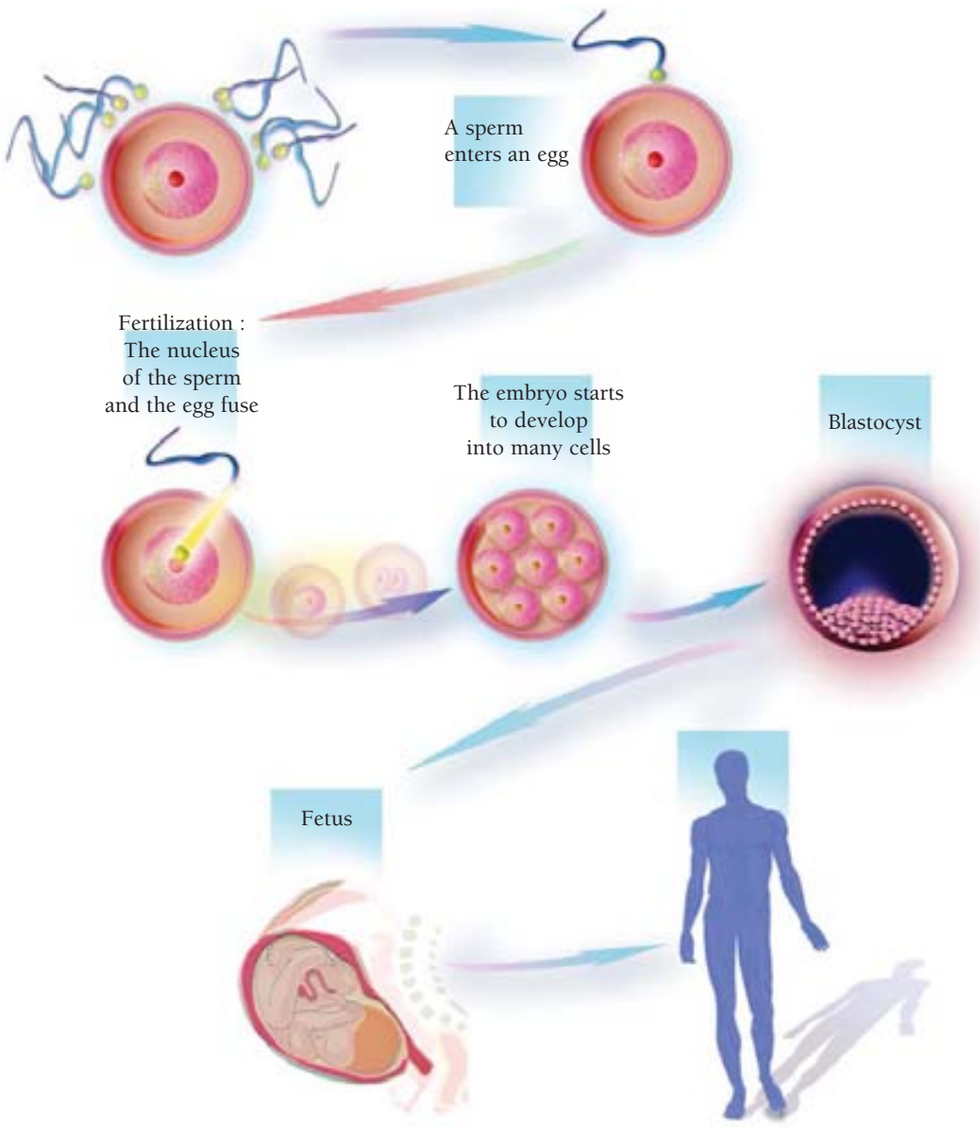

Fig.1 : Development of an Embryo

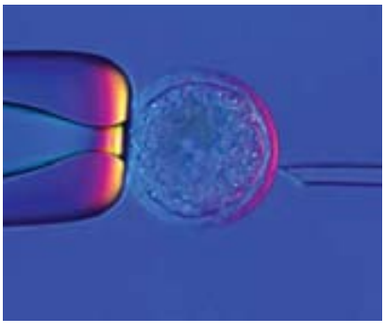

Photo 1. Image of Nuclear Transfer: The nucleus of the egg is removed through a microscopic laboratory procedure and replaced with the nucleus of a donor cell

The egg, which grows into an embryo, therefore contains only the donor's genes (*photo 1*). The cloned organism is a near genetic copy of its sole "parent", (0.05% to 0.1% of genes are carried by cytoplasmic[2] components such as mitochondria[3]) rather than a random genetic combination of two parents.

The pioneer era of cloning dates to 1952 with the work of biologists Robert Briggs and Thomas King in Philadelphia. Scientists already knew about natural cloning in some forms of invertebrates (organisms without a spinal structure). For example, an earthworm divided in two could regenerate into a complete individual. But cloning vertebrates through human intervention seemed far more complex. Briggs and King decided to experiment on the frog species. They approached their task by using "somatic cell nuclear transfer", a method first theorized in its rudiments in the 1930s by German embryologist Hans Spemann, who had done laboratory work on salamanders. This procedure involves removing the nucleus of a somatic cell[4] and inserting it into an "enucleated"[5] unfertilized egg cell (*fig. 2*).

[2] **cytoplasm** – the jelly-like substance that surrounds the nucleus of a cell. *Concise Medical Dictionary.* Oxford University Press, 2002. *Oxford Reference Online.* Oxford University Press. 10 October 2003 <http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t60.002431>

[3] **mitochondrion** – (chondriosome) n. (pl. mitochondria) a structure, occurring in varying numbers in the cytoplasm of every cell, that is the site of the cell's energy production. Mitochondria contain ATP and the enzymes involved in the cell's metabolic activities, and also their own DNA; mitochondrial genes (which in humans encode 13 proteins) are inherited through the female line. Each mitochondrion is bounded by a double membrane, the inner being folded inwards to form projections (cristae). *Concise Medical Dictionary.* Oxford University Press, 2002. *Oxford Reference Online.* Oxford University Press. 10 October 2003 <http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t60.006317>

[4] **somatic cell** – any cell of an organism other than the reproductive cells. *The Concise Oxford Dictionary.* Oxford University Press, 2001. *Oxford Reference Online.* Oxford University Press. 11 October 2003 <http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t23.053122>

[5] **enucleate** – remove the nucleus from (a cell). *The Concise Oxford Dictionary.* Oxford University Press, 2001. *Oxford Reference Online.* Oxford University Press. 10 October 2003 <http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t23.018458>

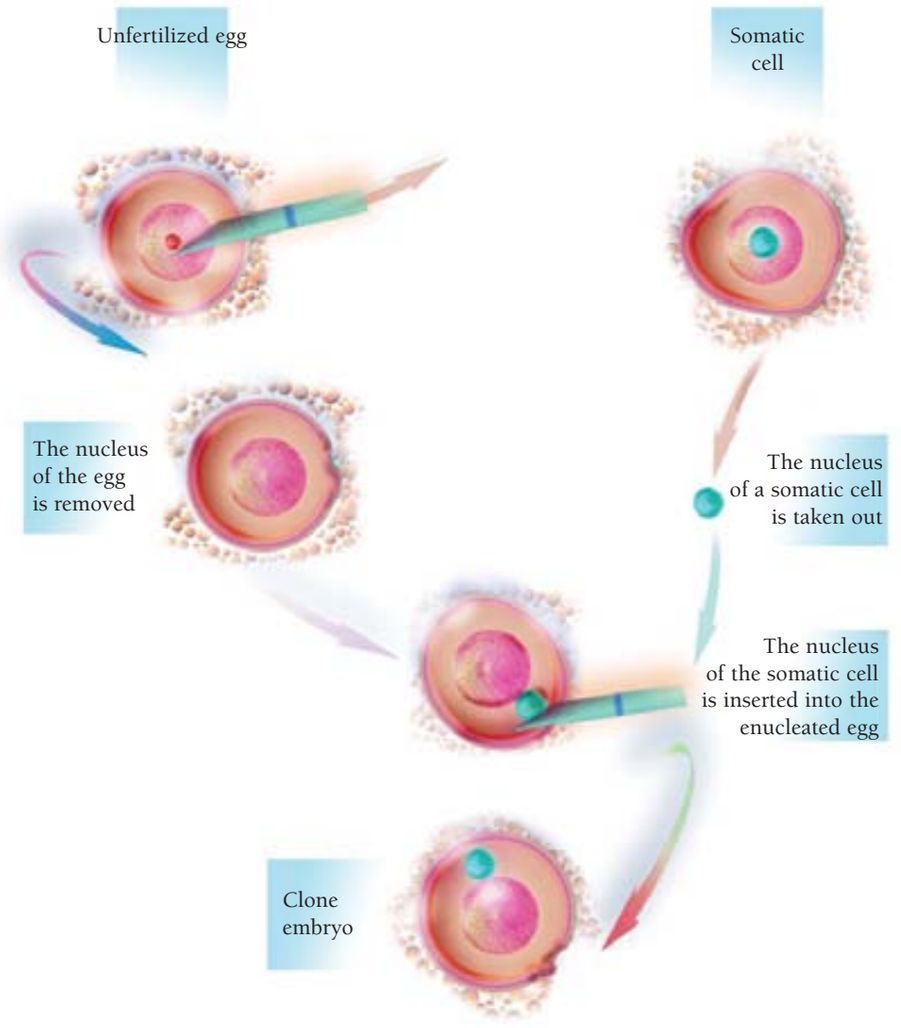

Fig.2 :Cloning by Somatic Cell Nuclear Transfer (SCNT)

The transplanted nucleus then begins to divide and multiply, as in a normal cell, while retaining its unique genetic identity. When Briggs and King first succeeded in cloning tadpoles, they transferred embryo cell nuclei into enucleated eggs. However, when they used nuclei derived from more advanced cells, the survival rate of the nuclear transplant embryos decreased. It suggested that as embryos develop to differentiated cells, an irreversible change would occur in genes and they could not be reactivated. If so, it would be impossible to create a clone, a genetic copy of an adult animal, using its somatic cell. It was in the 1970s that this theory was reversed when British biologist John Gurdon successfully cloned a tadpole from a somatic cell proving that a developed embryo or differentiated cells can be reactivated and can produce a new life.

Photo 2. The world's first cloned mammal; Dolly the sheep (left) and its surrogate mother (right)

To accomplish the same feat on mammals, however, appeared a quantum leap since cloning a mammal involves technically more complicated procedures than with amphibians. In particular, collecting mammalian eggs is harder than frog eggs since they are much fewer and require invasive procedures to remove. Cloned embryos must then be transplanted into a womb and result in a pregnancy in order to reproduce a mammal clone. Thus, for many years, cloning in more complex species, such as mammals, appeared a remote possibility and remained largely of interest only to the scientific community.

But that situation changed abruptly in early 1997 when a Scottish team announced the birth in the previous year of Dolly, a lamb cloned from an adult sheep (*photo 2*). This biological breakthrough earned

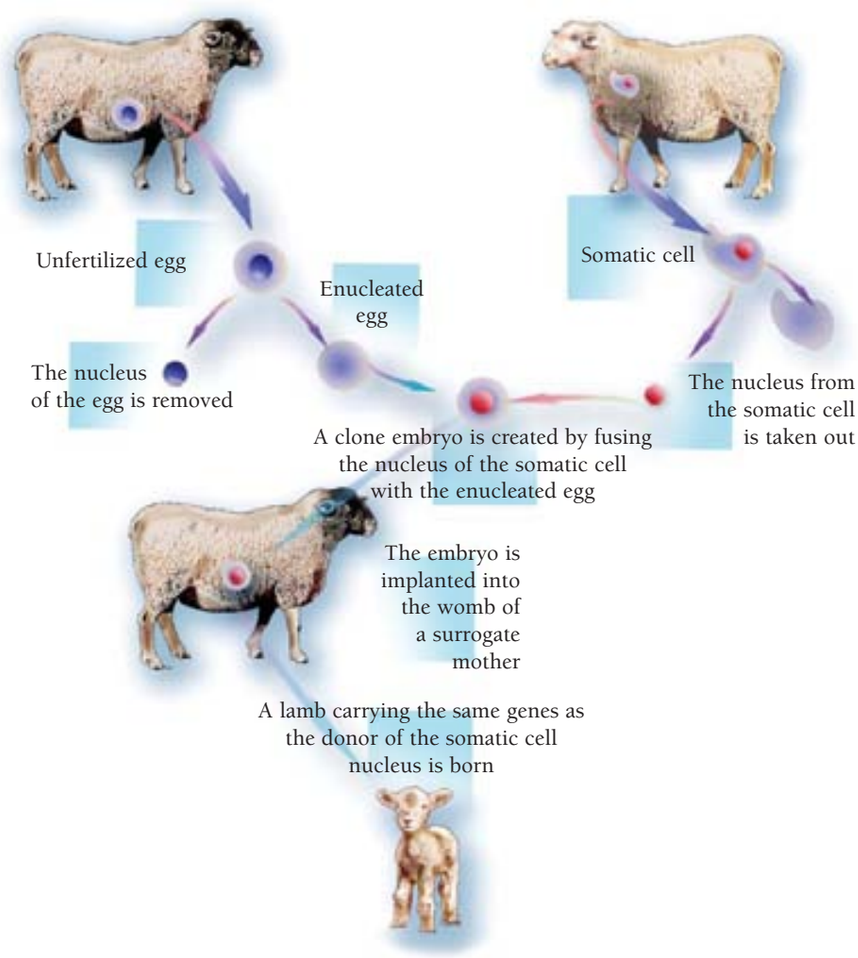

FIG.3 : REPRODUCTIVE CLONING OF SHEEP

front-page attention around the globe and seemed to open the perspective of a new biomedical world, fraught with consequences. Dolly's birth was engineered by veterinary researcher Dr Ian Wilmut and his colleagues at the Roslin Institute, and their achievement shattered the belief that adult mammal cells could not be used to re-create a genetic copy. Wilmut's group in Edinburgh employed an updated version of the Briggs-King technology, subsequently refined by British biologist John Gurdon.

To create Dolly, Wilmut's group used the nucleus of a "quiescent" mammary cell from a white Finn Dorset sheep, that is, a cell that had stopped dividing when it was previously deprived of nutrients. Next, the nucleus was implanted through the protective zona pellucida into an enucleated oocyte (unfertilized egg) from a Scottish Blackface ewe, and a minute electric charge helped it fuse with the oocyte's cytoplasm. After many failed attempts, the researchers managed to obtain an egg cell that began dividing normally, and this was implanted into the surrogate Scottish Blackface mother. After a normal gestation period of about five months, Dolly was born (*fig.3*). Genetic tests proved her to be a clone, and Dolly became an international icon.

Recent Development of Cloning Research on Animals

Since Dolly, the cloning of several mammal species has resulted in many live births. Pigs, sheep, cows, cats, rodents and, most recently, a mule have been successfully cloned (but not yet dogs or monkeys) (*photo 3*). The cloned mule gained some special attention since that species — a hybrid of a horse and a donkey — is normally sterile. Interestingly, cloning does not always result in a visual lookalike, as in the case of a common house cat cloned in 2001 with fur colour different from its gene donor. Several genes situated in the X chromosome are involved in cat fur colouring, and some of these genes are randomly inactivated during embryo development for female cats, since they have two X chromosomes. Therefore, even derived from a same donor, some cells will produce a black coat if the other colouring genes are suppressed, and others will result in an orange coat when inserted into an enucleated egg and developed to a kitten.

Photo 3 :
Cloned cat CC:
The first cloned cat CC has quite a different character and fur colouring from its gene donor

Cloned mule:
"Idaho Gem", first cloned animal in the horse family

Cloned pigs:
Some research focuses on pig clones as organ suppliers for human transplants

Three generations of mice created by cloning

Cloned calves:
Ten cloned calves of a single adult Jersey cow were born alive

Cloned rabbit:
Cloned rabbits and other cloned animals may be useful to investigate the causes of human diseases

The main purpose behind developing animal cloning techniques is to facilitate the genetic engineering of animals. Traditionally, new DNA for modifying animal genes can be inserted only into very young embryos, usually at the 1- or 2-cell stage. But whether these genes are incorporated into the embryos is determined purely by chance. Thus, the success rate is very low and the procedure time-consuming. With cloning techniques, the DNA is added to dish-cultured cells by the thousands or millions. It then becomes feasible to detect which cells have incorporated the inserted DNA. Then, technicians can transfer the nucleus of such cells to enucleated egg cells to produce embryos, which contain modified DNA.

Therefore, animal cloning would also interest some food and drug industries if it could result in consistently high-quality, marketable products such as milk or meat or, with genetic engineering, if it could generate therapeutic proteins from goat or cow milk or chicken egg whites (commonly called "pharming"), or even pig organs transplantable to humans without immune rejections. One biotech company, PPL Therapeutics, Inc., working with the Roslin Institute, cloned "Polly" in 1997, a sheep produced from an embryonic cell that had been genetically transformed. Polly secretes a human blood-clotting protein in her milk, useful for treating haemophilia. International standards for regulating such a technique have not been established, and various non-human cloning efforts have sprouted here and there.

News of successfully cloned animals has caught public attention, but scientists are far from perfectly controlling the results. Success rates for producing cloned embryos depend on the species and types of cells used, but they remain generally very low. Even with a successful birth, a wide range of abnormalities and defects are observed in cloned animals, among them, one known as Large Offspring Syndrome (LOS). Cloned animals are often too large for normal delivery, and the placenta has grown abnormally.

Such defects are not yet fully explained, but one possibility is that a nucleus removed from a somatic cell may not be properly reprogrammed to develop into a normal offspring. According to some, such cloning technique flaws will be resolved as research progresses. Others argue that cloning a perfectly healthy offspring is ultimately impossible and that even apparently healthy cloned animals may contain genetic defects.

What are the Ethical Issues regarding Human Cloning?

The possibility of human cloning has long fired the popular imagination, including in the world of popular entertainment. For example, a thriller novel, *The Boys from Brazil*, subsequently made into a 1978 Hollywood film, depicted a Nazi war criminal who raises a colony of young Hitler "clones". For many others, cloning implied overtones of human immortality or of assembly-line eugenics. Hoaxes, wild claims and media speculation have inevitably intruded into the cloning discussion, sometimes originating more in pure science fiction than actual scientific experiments. Dolly gave added impetus to talk — and concern — about human cloning.

The cloning debate involves scientists, legislators, religious leaders, philosophers and international organizations, but not always harmoniously. General agreement, if not absolute unanimity, evolved that human "reproductive" cloning — for the purposes of producing a human genetic-copy baby — is unethical. Wilmut himself explained to the United States Congress that cloning a mammal involved a high failure rate, since of his 277 "reconstructed" embryos, only 29 were implanted in ewes and only one developed successfully. "Similar experiments with humans would be totally unacceptable", Wilmut concluded.

Box 1: Ethical Issues regarding Human Reproductive Cloning

- Technical and medical safety
- Undermining the concept of reproduction and family
- Ambiguous relations of a cloned child with the progenitor
- Confusing personal identity and harming the psychological development of a clone
- Concerns about eugenics
- Contrary to Human Dignity
- Promoting trends towards designer babies and human enhancement

The high failure rates (more than 90 per cent) and high morbidity of animal cloning strongly suggests its inapplicability to humans. Furthermore, cloned animals seem to suffer high deformity and disability rates. Dolly herself was finally put down in 2003, at the age of just six and a half years, even though many sheep live more than 10 years. She had developed a progressive lung disease, which is usually found in older sheep, as well as premature arthritis. Some cloning experts have consequently hypothesized that cloned humans might need hip replacement surgery while still adolescents and might suffer from senility by the age of 20.

The ethical ramifications of cloning, especially with regard to humans, seem to defy easy limitation. Even if cloning technique problems are resolved with time, many questions remain. On what grounds could reproducing children by cloning be allowed or prohibited? Should cloning be used for sterile couples or for homosexual couples who want biological offspring? How would a child born by asexual reproduction experience life, as a unique individual or as a genetic "prisoner"? Is a cloned child simply a twin of its genetic donor, with a certain time lag? Should parents choose the traits of a future child, as is possible with cloning? Those and other such issues now preoccupy scientists and bioethicists who see in cloning procedures the potential to endanger human identity (Box 1).

The world community provided an answer when it declared human cloning contrary to human dignity, in Article 11 of the Universal Declaration on the Human Genome and Human Rights (1997), elaborated by UNESCO. In Section C of the Declaration, "Research on the Human Genome", it is stated *"Practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted…".*

After careful consideration, several countries have formulated opinions and regulations on human reproductive cloning. In France, the National Consultative Ethics Committee for Health and Life Sciences (CCNE – *Comité consultatif national d'éthique pour les sciences de la vie et de la santé)* addressed central dilemmas when in 1997 it rejected human reproductive cloning: "The notion that perfect genetic similarity would in itself lead to perfect psychic similarity is devoid of any scientific foundation", stated the Committee, adding that human reproductive cloning would cause "a fundamental upheaval of the relationship between genetic identity and personal identity in its biological and cultural dimensions". (Opinion Nº 54, "Reply to the President of the French Republic on the subject of reproductive cloning", April, 1997). Other nations concurred, citing the sheer risks involved in cloning ventures, notably to mothers and babies.

For Japan's Council for Science and Technology, human cloning had no usefulness to commend its practice. It added that medical applications using human cells obtained through cloning "may lead to breeding of human beings and violation of human rights" (Final Report Requesting Legal Regulations of Production of Humans by Clone Technology, November 1999). Furthermore, the Japanese expert committee concluded that asexual reproduction through cloning would destroy the family concept in their society.

In its "Human Cloning and Human Dignity" study in 2002, the President's Council on Bioethics in the United States observed that efforts to clone a human would be unethical "at this time" because of "safety concerns and the likelihood of harm to those involved". A wealth of other concerns could well preclude ever attempting human clones, the report said: "The notion of cloning raises issues about identity and individuality, the meaning of having children, the difference between procreation and manufacture, and the relationship between the generations". These conclusions seemed to promise a debate over the morality of biological sciences and cloning that would continue for many years to come.

In Tunisia, the National Medical Ethics Committee examined the issue of reproductive cloning at the request of the Minister of Health in 1997 and concluded that any technology of human cloning should be banned. It deemed the practice as undermining the concept of human reproduction and the dignity of human beings, and an open door to all forms of abuse.

Some 30 countries including Australia, Colombia, Costa Rica, Denmark, Georgia, Germany, Japan, Latvia, Norway, Peru, Spain and United Kingdom have so far enacted a variety of laws that prohibit reproductive cloning.

Is Research Cloning different from Reproductive Cloning?

Meanwhile, biomedical researchers have focused their attention since Dolly's birth on experimental, so-called "therapeutic" cloning, centering on the use of the cloning technique to obtain embryonic stem cells[6] for research and potential therapeutic purposes. Since the notion "therapeutic" suggests possible beneficial applications of cloning, which at the present time seem completely unjustified, it is more appropriate to change this positive connotation and use a more neutral wording, viz. research cloning. In the case of reproductive cloning, the aim of somatic cell nuclear transfer is to create an embryo carrying the same genetic information as the progenitor and to implant this embryo into a womb to generate a pregnancy, and from there to produce a

[6] **embryonic stem cell (ES-cell)** cultured embryonic cells that can proliferate indefinitely and differentiate into many different tissues. McLaren A. et. al., *"Ethical eye: Cloning"*, Council of Europe Publishing, Strasbourg, 2002

baby. The goal of research cloning, however, is to create an embryo in the same manner as for reproductive cloning, not to produce a child but in order to derive embryonic stem cells which contain the same genetic characteristics as the progenitor. The embryo is unavoidably destroyed during this process.

Human embryonic stem cells, first isolated in 1998, are sometimes described as essentially "blank" cells in humans, which could potentially be transformed into almost any type of body tissue (Box 2). Separating some inner cell mass from the embryo at the blastocyst stage, they can be cultured to produce pluripotent stem cells, capable of developing into blood, muscle or many other kinds of tissues and organs of the body (*fig. 4*). Many medical biologists consider this field vastly promising for future cures, since embryonic stem cells can be systematically "grown" in laboratory petri dishes. One could, for example, transform a stem cell through laboratory cloning procedures into a blood cell or into a cardiac muscle cell, for injection into the heart of a cardiac patient, in order to reverse a malfunction. In this manner, researchers hope eventually to use these versatile cells to overcome chronic or degenerative diseases, such as Parkinson's disease, Alzheimer's disease or diabetes, which afflict millions of people.

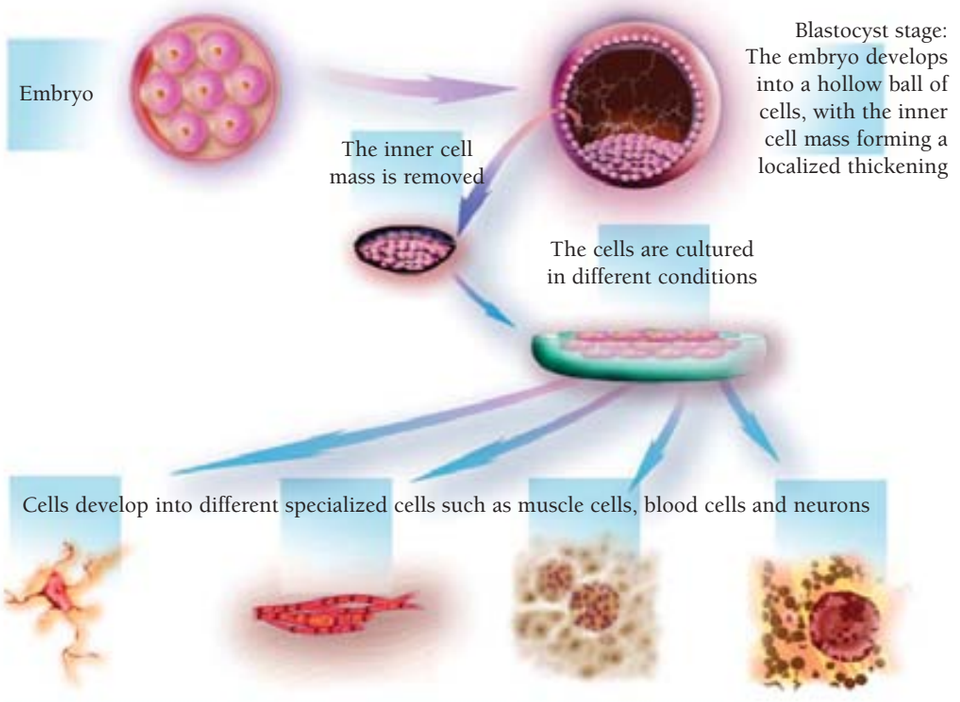

FIG.4 : EMBRYONIC STEM CELLS

One source of stem cells comes from embryos created by *in vitro* fertilization laboratories. Once couples with infertility problems have conceived their babies, "leftover" embryos can be preserved in liquid nitrogen and, in some countries they can be used for research with the couple's informed consent. Thousands of such frozen embryos exist in laboratories (some 400,000 in the United States alone, according to a study completed in May 2003). Also in the United States, where the most intense embryonic stem cell research occurs, current government policy requires biologists working in federally funded laboratories to use older stem cells, from embryos destroyed before 9 August 2001. Recently, many of them have noted this ruling limits their findings, since they cannot test new methods of deriving or culturing stem cells. For example, recent work indicates stem cells from 5-day-old embryos can transform more readily into a variety of other cells and prove useful in treating heart disease, spinal cord injuries and other disorders.

However, stem cells that are derived from surplus embryos may cause immune rejection when transplanted to a patient, much as in organ transplants received by a third person. If the cells or tissues to be transplanted to a patient originate from the same patient, such problems do not arise.

Therefore, some researchers believe that research cloning to create an embryo in order to derive genetically identical cells from a patient, to cultivate and develop them to targeting cells or tissues, then to transplant them to the patient, will help avoid immune rejection (*fig. 5*).

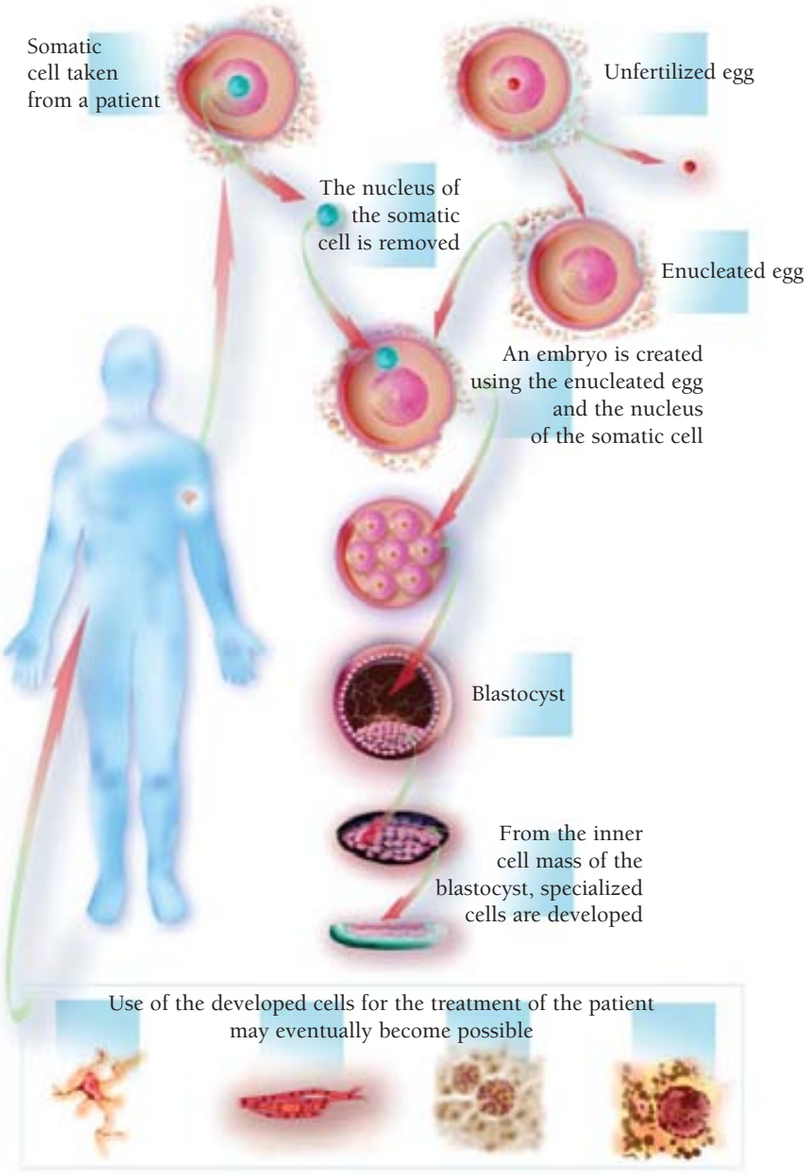

FIG. 5 : RESEARCH CLONING

A major ethical question in conducting research cloning and embryonic stem cell research hinges on the moral status of embryos. Their use has raised objections by those opposed to abortion on moral, religious and other grounds and by those who oppose any research that involves the destruction of a human embryo. The moral argument here is that embryos should be protected from the instant of conception onwards since this is the moment that a new human entity comes into existence that potentially, and in adequate circumstances, develops into a unique human being. Since human beings ought not to be sacrificed for any purpose, the destruction of embryos for research cannot be justified.

A different moral argument underlines that embryos do deserve protection and a certain respect, but not to the same extent as fully developed babies. From this viewpoint, the moral status of embryos gradually increases with their development and, once they are born, they are entitled to enjoy full rights and protection as human beings. The moral status of an embryo is not absolute but relative to other moral goods. Therefore when the status of an embryo at a certain stage of development is weighed against the moral principle to relieve suffering, destruction of embryos can be justified to provide a

treatment for patients. This argument provides justification for embryo research for therapeutic purposes, although the alleviation of suffering at the moment is only hypothetical.

A third type of moral argument points out that certain milestones exist in embryonic development that change the status of embryos. For example, an embryo at a very early stage of development has the potential to develop into either one individual or several, such as identical twins, because each cell of the embryo has the potential, if separated, to develop into an individual fetus. But after a certain period of time, an embryo can no longer develop into more than one individual because cells of an embryo start to differentiate into specific cell types and become inseparable and integrated parts of a whole. The earliest sign of such a point of "no return" can be observed at around 14 days after fertilization when the primitive streak,[7] the rudiments of the nervous system, appears. This is why this argument makes a critical distinction in time. Prior to 14 days of development, embryos may be used for research if the potential benefits contribute to relief of suffering of other human beings. After 14 days, the moral status of the embryo outweighs the (potential) interests of others.

These types of argument regarding the moral status of embryos together with various religious teachings and sociocultural values have influenced the development of different regulations concerning embryo protection and research with embryos at the national level.

In some countries, such as Costa Rica and Germany, it is prohibited to destroy embryos for research purposes. An argument against the use of surplus embryos obtained through *in vitro* fertilization is that they result from a previous selection by which only the "best" embryos (morphologically) are used for implantation in the uterus. However, other countries such as Belgium and the United Kingdom allow research on surplus embryos as well as the creation of embryos for research purposes within 14 days after fertilization before the primitive streak appears.

Distinct from the use of surplus embryos produced by *in vitro* fertilization, "therapeutic" cloning may involve the creation of embryos for the purposes of research. Some favour making a distinction between research using surplus embryos, that would otherwise be discarded, and the specific creation of embryos, either by fertilization or by cloning technique, for research purposes. In some countries such as Denmark, this argument allows for research on surplus embryos while prohibiting the creation of embryos solely for research purposes.

The creation of human embryos for research purposes, however, requires the harvesting of eggs. Thus there may emerge difficulties, ethical and otherwise, in obtaining eggs to produce clone embryos. If hundreds of unfertilized eggs prove necessary to produce one human clone embryo, as in animal cloning, how will those eggs be provided? Obtaining eggs from a woman's body is invasive, and some have expressed concern that it could lead to exploitation of women and commercialization of human eggs.

[7] **primitive streak** – The longitudinal groove that develops in the gastrula during the development of bird and mammal embryos. The cells in the primitive streak proliferate rapidly to form mesoderm cells, which migrate to the interior of the embryo. *A Dictionary of Biology.* Oxford University Press, 2000. *Oxford Reference Online.* Oxford University Press. 10 October 2003 http://www.oxfordreference.com/views/ENTRY.html?subview=Main&entry=t6.003588 It is the first indication that the nervous system is developing.

Can Adult Stem Cells replace Embryonic Stem Cells?

Preliminary research is proceeding on so-called "adult" or "somatic" stem cells, which derive not from embryos or fetuses but from sources such as bone marrow, the umbilical cord or even from tissues of a grown individual. In fact, stem cells have been detected in several body organs and tissues (Box 2). Adult stem cells in an organism exist in small numbers to maintain and repair tissue cells, and scientists have been studying them since the 1960s. If their transformation into specific cell types could be controlled in a laboratory setting, adult stem cells could be valuable in curing diseases.

The first advantage of adult stem cells is of a moral nature. Since they do not derive from an embryo, objections based on protection of potential human life do not arise. Another possible advantage in using such stem cells, if they originate from the patient himself, would be to avoid immunity system rejection problems, which might occur in using foreign-body stem cells. But it is not yet clear how

useful these adult stem cells could prove. Embryonic stem cells can be grown in large quantities in laboratory cultures, but adult stem cells are not numerous in mature tissues.

Views differ regarding the future potential of adult stem cells. Previously, it was thought adult stem cells occurred in very limited cell types and developed only into those cells, but recently many more types of adult stem cells have been found to exist in the body, with the flexibility to develop more variably. However, some researchers note that even in this case, some limitations persist. For example, deriving brain stem cells from a patient remains difficult, and not all types of stem cells are found in adult stem cells. Some researchers believe that as research progresses, greater potential will be found in adult stem cells, so they could replace embryonic stem cell research.

Box 2 : **Totipotent, Pluripotent and Multipotent Cells in Embryo Development**
The fertilized egg is "totipotent", meaning that any of its cells, if placed in a uterus, may develop into a fetus. After several days of fertilization, these totipotent cells begin to specialize, forming a hollow sphere of cells, called a blastocyst, an inner cell mass that will form virtually all the human body tissues. Although each cell itself can no longer become a fetus, it can produce many different cell types necessary for fetal development. Because they have the potential to differentiate into many different cells, they are "pluripotent" cells. Since these are found only in embryos, they are called embryonic stem cells. The pluripotent stem cells then undergo further specialization into stem cells that produce cells governing a particular function. Examples include blood stem cells which develop red blood cells, white blood cells and platelets; or skin stem cells that give rise to various skin cell types. These more specialized "multipotent" stem cells, found in somatic cells, are called adult stem cells.

The focus is primarily on fundamental research rather than on clinical applications. If fundamental research increases our insight into processes of differentiation and de-differentiation, all cells could be transformed into stem cells and again developed into more specialized tissues. The problem of using embryonic stem cells therefore may only be temporary in view of the advancement of fundamental research in the life sciences.

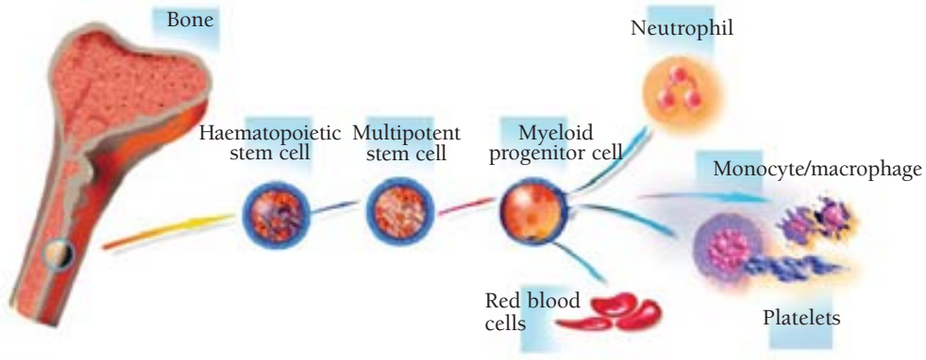

FIG. 6 : ADULT STEM CELLS (EX.HAEMATOPOIETIC STEM CELL)

Cloning and the International Community

While the cloning issue seemed to project endlessly into the future, the task of setting and implementing an international ethical and legal framework for human cloning was all the more pressing by the cascade of laboratory developments at the end of the 20th century. In addition, the scope of bioethical concerns was expanding dramatically, with cloning advances providing a new dimension also because of the public and political concerns about these developments.

At the international level, the issue of reproductive cloning was urgently addressed in several UN agencies following the announcement in 1997 of Dolly's birth. For example, the World Health Assembly of WHO affirmed in its resolution WHA50.37 (1997) and resolution WHO51.10 (1998) that "*cloning for the replication of human individuals is ethically unacceptable and contrary to human dignity and integrity*".

Six months after the announcement in 1997 of Dolly's birth, the 29th UNESCO General Conference adopted the Universal Declaration on the Human Genome and Human Rights, a landmark document that took its place in the growing discussion of cloning. The following year, in 1998, the United Nations General Assembly endorsed the Declaration.

Box 3: *"Practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted. States and competent international organizations are invited to co-operate in identifying such practices and in taking, at national or international level, the measures necessary to ensure that the principles set out in this Declaration are respected."* (Article 11, The Universal Declaration on the Human Genome and Human Rights, 1997)

In its 25 articles, the Declaration reaffirms the human genome as "the heritage of humanity" and recognized the "inherent dignity and diversity" of the human family. It was "imperative" the Declaration added, "not to reduce individuals to their genetic characteristics". And the Declaration expressly banned, as mentioned above, the reproductive cloning of human beings (Box 3).

At its session held in May 2001 in Paris, UNESCO's Intergovernmental Bioethics Committee (IGBC) encouraged the Organization's Member States "to take appropriate measures, including legislative and regulatory, in order to prohibit effectively human reproductive cloning". As for embryonic stem cell research, the IGBC encouraged Member States "to hold debates on the ethical issues raised…involving all actors concerned". It also called for national regulations or laws on the use of embryonic stem cells in therapeutic research, for example, on the question of the import and export of embryonic cells to or from countries where embryo research is prohibited.

A Round Table composed of 101 Member States' and Observer States' science ministers or their representatives, focused on bioethics during an October 2001 meeting at UNESCO Headquarters. The participants asserted "the imperative of freedom of research" for the world scientific community but also called on researchers "to anticipate the problems and take up the challenges posed by scientific and technological progress rather than attempt to deal with them after the fact". Reiterating its opposition to human reproductive cloning, the Round Table called for "informed, pluralistic public debate" in Member States that takes into account "the various schools of thought, value systems, historical and cultural backgrounds and philosophical and religious convictions that make up our various societies". "Bioethical standards", the ministers and their representatives added, "must be based on the practice of democracy". This position is in line with the earlier report of UNESCO's International Bioethics Committee (IBC) on "The Use of Embryonic Stem Cells in Therapeutic Research" (2001) (Box 4).

In another multilateral attempt to define a framework for scientific research and cloning practices, the Council of Europe in April 1997 enacted the "Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Oviedo Convention). The document forbids the creation of human embryos for research purposes.

Box 4: **The IBC report on "The Use of Embryonic Stem Cells in Therapeutic Research (2001)"**

55. A.) The IBC recognizes that human embryonic stem cell research is a subject on which it is desirable for a debate to occur at national level to identify which position on this issue to be adopted, including abstaining from this research…

B)…When authorization of donations of supernumerary pre-implantation embryos from IVF treatments for therapeutic embryonic stem cell research is under consideration, particular attention should be given to the dignity and rights of both parental donors of embryos…

And, where national legislation permits research on embryos *in vitro*, it calls for adequate protection of the embryo. On 12 January 1998, the Council opened for ratification its Additional Protocol to the Convention on Human Rights and Biomedicine on the Prohibition of Cloning Human Beings. This protocol, not yet ratified by most Member States of the Council, described cloning as a valuable and ethical biomedical technique, and it acknowledged differences of opinion about the cloning of undifferentiated cells of embryonic origin. Thus, while the Protocol did not take a specific stand on the cloning of cells for research purposes, it prohibited any deliberate cloning of human beings as a threat to human identity.

These deliberations and the gravity of the issue prompted the United Nations General Assembly to commence discussion in 2001 following a French-German initiative to draft a convention against the reproductive cloning of human beings, as the best and most reasonable way to regulate such phenomena. UNESCO, which supported the project, made substantial contributions to the scientific, technical, ethical, philosophical and legal fields, supporting the Ad Hoc Committee established to consider a draft. A number of UNESCO documents in the bioethics field were made available to Committee members. The positions of UN Member States pointed to a divide between two differing approaches: (1) a broad-scope ban on both reproductive and research cloning and (2) a restricted-scope ban on reproductive cloning while research cloning to be addressed separately. This opposition was not resolved by the Working Group held during the UN General Assembly in 2003 and it was decided to postpone the discussion of this issue until the UN General Assembly in 2004.

Unsubstantiated media claims by a sect in late 2002 to have cloned the first human being underscored the urgency of cloning guidelines. The Director-General of UNESCO, Mr Koïchiro Matsuura, promptly issued a reminder for the international community to act. "This news, whether or not it is confirmed, brings home to us the urgent need to do everything possible, at both the national and international levels, to prohibit experiments that are not only scientifically risky but also ethically unacceptable, constituting as they do an intolerable violation of human dignity", the Director-General stated. He added: "There can be no progress for humanity in a world where science and technology develop independently of all ethical imperatives". The Director-General called on political leaders in every nation to cooperate "in taking all appropriate measures…to respond as swiftly as possible to these challenges, which are a threat to the irreplaceable uniqueness of the human being".

In October 2004, the UN General Assembly re-opened the discussion on the elaboration of a convention on human cloning. After intensive discussion on the draft text of the convention, a proposal was made to elaborate a United Nations declaration on human cloning instead of a convention. In March 2005, a United Nations Declaration on Human Cloning proposed by the Sixth Committee was adopted by vote at the UN General Assembly, which calls upon the Member States to prohibit all forms of human cloning inasmuch as they are incompatible with human dignity and the protection of human life (Box 5).

Box 5: **United Nations Declaration on Human Cloning**

" *a) Member States are called upon to adopt all measures necessary to protect adequately human life in the application of life sciences;*

b) Member States are called upon to prohibit all forms of human cloning inasmuch as they are incompatible with human dignity and the protection of human life;

c) Member States are further called upon to adopt the measures necessary to prohibit the application of genetic engineering techniques that may be contrary to human dignity…"

Ongoing Discussion on Ethical Issues

Discussions of how to regulate cloning techniques must involve both experts from various fields and the lay public since the issues of reproduction and the moral status of embryos touch on the very meaning of "life" for humans. Concepts of life, values and rules concerning reproduction have developed in each society and are deeply embedded in culture, tradition and religious teachings. However, rapid developments in genetics and biotechnology easily transcend national borders and sometimes challenge such values. Thus, the urgent need emerges for international harmonization and regulation on human cloning issues. Understandably, to respect each society, differing national rules may govern the application of certain technologies. But the fundamental value of "human dignity" remains a touchstone to guide us all in the quest for answers.

Further Reading

Books

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Useful Website Links

United Nations
- Ad Hoc Committee on an international convention against the reproductive cloning of human beings
http://www.un.org/law/cloning/

United Nations Educational Scientific and Cultural Organization (UNESCO)
- Bioethics
http://www.unesco.org/bioethics

World Health Organization (WHO)
- Ethics and Health
http://www.who.int/ethics/topics/cloning/en/

European Commission
- European Group on Ethics in Science and New Technologies to the European Commission
http://europa.eu.int/comm/european_group_ethics/index_en.htm

Council of Europe
http://www.coe.int
- Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine
http://conventions.coe.int/Treaty/EN/CadreListeTraites.htm

Division of Ethics of Science and Technology

Since the 1970s, UNESCO has been addressing the ethical issues raised by the rapid development of science and technology, and playing a role as a lead agency in this field in the international community. The Universal Declaration on the Human Genome and Human Rights (1997) and the International Declaration on Human Genetic Data (2003) prepared with the assistance of the International Bioethics Committee of UNESCO (IBC) and adopted by the General Conference of UNESCO provide the Organization's Member States with the universal principles in the field of genetics to be implemented into national regulations. Among its principal activities, the Division organizes conferences and symposiums on bioethics, publishes a series of books and brochures, and promotes networking among bioethics institutions. Since 2002, the bioethics programme has become one of UNESCO's five priorities and the Division is committed to further promote its ethical mission.

Secretariat of the Bioethics Section
Division of Ethics of Science and Technology
Social and Human Sciences Sector
United Nations Educational, Scientific and Cultural Organization (UNESCO)
1, rue Miollis, 75732 Paris Cedex 15, France
Tel. 33 (0)1 45 68 37 81
Fax. 33 (0)1 45 68 55 15
http://www.unesco.org/bioethics