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NATIONAL BIOETHICS COMMITTEE

CLONING

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(21st of March 1997) **8**

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INTRODUCTION

In the Opinion on assisted procreation techniques of the 17th of June 1994, it is already possible to witness the National Bioethics Committee's strong position with regards to cloning. In paragraph 2.1, after highlighting the different viewpoints expressed by its members about important bioethical issues linked to assisted procreation, the NBC unanimously recommended the prohibition of early embryonic fission, cloning and exogenesis for procreation purposes. In the document of the 22nd of June 1996, titled Identity and Status of the Human Embryo, the NBC expresses an identical assessment. I will report some important lines from that document, taken from paragraph 10:

The Committee unanimously recognises the moral duty to treat the human embryo, from the moment of fertilisation, with the same criteria of respect and protection that must be adopted towards human beings, to which we commonly attribute the characteristic of being persons, and this, regardless of whether we recognise to the embryo, from the beginning and with certainty, the characteristic of being person in its technically philosophical sense, or whether such characteristic can be attributed only with a high level of plausibility, or whether we prefer not to use the technical concept of person and only refer to embryos as belonging to the human species, which cannot be contested to them from their first instants and it does not undergo any alterations during their further development.

From this, the Committee unanimously deduced a series of instructions with regards to morally illicit treatments towards human embryos, at any stage of their development:

- *production of embryos for experimentation, commercial or industrial purposes;*
- *multiple creation of genetically identical human beings through twin fission or cloning.*

When it was reported, in February 1997, that the Roslin Institute in Edinburgh had managed to clone an adult sheep, the NBC seriously considered the possibility of reopening – after having expressed such explicit points of views as the ones mentioned above – the debate on this issue or whether instead to stress the statements already made, without being swept by the theatrical sensationalism that the case of Dolly the sheep was inevitably destined to arise. The first of the two options prevailed, also because of an explicit invitation, by the Health Minister, to elaborate an ad hoc opinion. The NBC responded to the Minister's request on the 21st of March 1997, therefore in a very short time and in a necessarily synthetic form: it is a text that, unanimously approved, continues to represent the NBC's bioethical evaluation of this issue (this

can be read at the beginning of this publication and it has the function of giving the reader a quick and broad, but not lacking, point of reference on this topic. In addition, the NBC's intellectual effort to draw up this short text was considerable and fuelled, in the Committee's members, new argumentative needs and new problematic issues. From this the decision, also unanimously taken, to reflect upon cloning again and to draw up a much more detailed document that, without naturally presuming to be exhaustive, would offer the reader an adequate picture of the topic, in that interdisciplinary spirit that characterises bioethics in general and, in particular, the one presented by the National Bioethics Committee. On the 18th of April 1997, a specially appointed working group met for the first time, presided by Prof. Luigi De Carli, and including Prof. Gaddini, Prof. Coghi, Prof. Zanella, Prof. Stammati, Prof. Nordio, Prof. Agazzi, Prof. Tarro, Prof. Romanini, Prof. Piazza, Prof. Cosmi, Prof. Fiori, Prof. Danesino, Prof. Chieffi, Prof. Bompiani, Prof. Loreti Beghe', Prof. Cattorini, Prof. Sgreccia, Prof. Leocata. Also thanks to the contribution of experts, including Prof. Clara Frontali, to whom the NBC owes a great debt of gratitude for her generous commitment, the working group, in October 1997, elaborated the final draft of the document, which was presented to the Committee in a plenary meeting and that, after discussions which often led to the drawing up of appropriate amendments to the text, on the 17th of October 1997 was in the end unanimously approved. The document published here must therefore be attributed to the whole of the Committee; this, notwithstanding the fact that we must remember how the individual paragraphs were drafted in their final form by the working group, using the specific competences of some of the Committee members. Therefore, the scientific-biological parts of the document were drawn up because of Prof. Chieffi, Prof. Cella, Prof. De Carli and Prof. Piazza's efforts; paragraph 3 originated from a text presented by Prof. Agazzi and then integrated with Prof. Cattorini, Prof. Piazza and Prof. Sgraccia's observations; the paragraph on international legislation and international documents benefited from Prof. Adrianna Loreti Beghe's competence and from Prof. Adriano Bompiani and Prof. Amgelo Fior's experience; the psychological observations were stimulated by Prof. Renata Gaddini's reflections; paragraph 5.2 (one of the most innovative in the document) was elaborated by Prof. Sergio Nordio. The Glossary was edited by Prof. Frontali and Prof. De Carli.

It is well known that, on a strictly scientific-factual level, the exact interpretation of the Edinburgh experiment and more in general of the question of the clonability of human beings, is still widely discussed. This continues to make some bioethicists think, still today, that it is preferable not to enter the debate on this issue, to avoid discussing something that,

although it can be abstractly believed to be possible (but in abstract anything is possible!), could in the end reveal itself to be factually impracticable. The NBC has evidently made a different choice, and it has made it consciously, believing that it is its duty to intervene on an hypothesis that, even though certainly not current with regards to human beings, in any case has raised debates, emotions, international viewpoints deserving of attention and respect. In offering – as it is its duty – these reflections to our County's Institutions, the NBC offers them also to the evaluation not only of the scholars involved, but especially to civil society, not in the illusion of having contributed conclusively to the topic, but in the certainty that everybody can appreciate the seriousness and the rigour of the work that has been carried out.

Francesco D'Agostino
President of the National Bioethics Committee

OPINION OF THE NATIONAL BIOETHICS COMMITTEE
"Cloning as Bioethical Problem" (21st of March 1997)

1. The NBC has already expressed, in previous documents and in particular in that of the 17th of June 1994 titles *NBC's Opinion on Assisted Procreation Techniques. Synthesis and Conclusions* (paragraph 2.1), and in that of the 22nd of June 1996 dedicated to the *Identity and Status of the Human Embryo* (paragraph 8.1.2), its unanimous opinion of absolute aversion to the cloning of human beings. This opinion, in addition, referred to cloning as a mere biological possibility, as the results of recent experiments in this area, which have caused in the last few weeks so many discussions and anxieties in the scientific community and in the public opinion of the whole world, were not yet known when the Committee was expressing it.

2. In the plenary meeting of the 21st of March 1997, urged by a specific request of the Health Ministry for another opinion on this topic, the NBC again examined the entire issue, after having adequately studied the new scientific data available and having further reflected on the ethical problems linked to it. Following an intense working session, the NBC unanimously confirmed the opinion already expressed previously with regards to the non-ethicality of the cloning of human beings. The NBC's conclusions are expressed as follows, after some scientific and ethical premises, which we felt we had to formulate.

3. We define as clone a molecular unit of DNA, cells or entire organisms, deriving from successive duplications of a sole progenitor, of which they are basically identical copies.

There are essentially two clone producing methods in pluricellular organisms and they are asexual reproduction processes:

a) separation of single cells or subdivision of groups of cells in the first phases of embryonic development, when the cells are totipotent, capable, that is, of generating an entire organism;

b) transplant of a nucleus obtained from cells at various stages of development in fertilised or non-fertilised oocyte cells, after having physically eliminated or deactivated the resident nucleus or nuclei.

Recent experiments made known by Wilmut and others, on the 27th of February 1997, consisted in fact of the fusion of the nucleus of a cell belonging to a sheep's mammary gland with another sheep's denucleated oocyte, and in the transferral of the embryo formed in this way, in the

uterus of yet another sheep, in order to obtain the development and then (although in only one case, starting with 277 fusions) the birth of a lamb.

4. The bioethical evaluation of the process described above requires a fundamental premise, also in order to avoid unacceptable, but very widespread, misunderstandings, and in order to contribute to the reassurance of that part of public opinion that, troubled by the vertiginous progress of biology, sometimes doubts the value of knowledge and scientific progress. The NBC believes that it is indispensable to remember that the freedom of science rightly has, in our law, a constitutional foundation (art.33). The NBC is convinced that it is not only good in itself, but that one of the roots of human dignity is the passionate desire – typical of scientists – to know, with regards to nature as well as man, the intrinsic order of things or, as some would prefer to say with a more philosophical expression, the truth: in other words, ignorance cannot have more ethical value than knowledge.

From what stated above, follows that it is not the desire to know or knowledge itself that are ethically questionable, but:

a) the eventual methods adopted by research, in particular scientific research, as well as the applications that can derive from it;

b) the specific objectives towards which it is directed;

c) the eventual alteration of the social or virtual world or in any case of the natural order, to which it can lead if it involves a serious or unfair prejudice towards human beings.

5. The NBC consequently believes that the cloning of human beings cannot be ethically condemned as a violation, from science and scientists, of the limits that human knowledge is not permitted to overcome. The Committee thinks that such limits do not exist and those who state their existence have an ethically unacceptable attitude towards science.

The cloning of human being is instead to be condemned:

a) for the purposes for which it is carried out, that is:

a') as it represents a danger to the biological uniqueness of the human subject, generated through cloning. This uniqueness, in fact, although it does not exhaust personal individuality (individuality that is both a genetic and environmental expression) is at the basis of that dignity and of those rights of the individual, the protection of which even the European Parliament has recognised as being an "absolute priority in contrast to any social or other interest";

a'') as it concerns every human being's right to dignity, due to the fact that the right to self-determination could be affected. This crisis

can be generated by the fear of the man, generated through cloning, to be biologically or culturally conditioned by the genetic constitution of the adult individual from whose cell the cloning has been carried out;

b) for the ways in which it can manifest itself, when the methods involve a manipulation and/or commercialisation of the human body or of some of its parts, or a mixture of genes from different species in order to generate chimeras, and in particular when this happens for a financial gain.

And finally cloning can be condemned for the risk that this practice could affect any balance founded on biological diversity, provoking in the medium and long term consequences that are not international, but are extremely dangerous for future generations. Even though at the moment there is no rigorous proof that these risks are real and cannot be confronted otherwise, their plausibility, together with their danger, should impose on researcher the moral duty to be extremely cautious and on those who are in government, the relative duty to control cloning practices.

6. Not included in the ethical condemnation expressed above are:

a) interventions on the human genome for therapeutic purposes (according to NBC guidelines in the document *Genetic Therapy* of the 15th of February 1991);

b) biological techniques which aim not at the cloning of a human being, but of tissue or single organs, and that have an explicit and coherent therapeutic purpose;

c) animal and vegetal cloning practices on condition that:

c') they have an explicit objective that is in line with the promotion of an adequate human and environmental good, in particular therapeutic and in any case not exclusively linked to a financial gain;

c'') they do not imply, for the animals experimented on, unjustified suffering that is not proportional to the good it can achieve (a topic, this, on which the NBC has already partially commented in previous documents – in particular *Drugs Experimentations* of the 17th of November 1992 and *Report on the Patentability of Living Organisms* of the 19th of November 1993 – and on which is about to intervene in a particularly in depth manner in a new document, which will be titled *Experimentation on Animals and the Health of Living Creatures*);

c''') they do not imply any attacks or risks to biodiversity.

7. According to the NBC, the ethical evaluations summarised above deserve to be strengthened by adequate legal authorisations and prohibitions, which can obviously only be issued by the Parliament. In additions, the NBC, accepting that some aspects of the research on

cloning generates some anxiety, hopes that any research on this topic will be carried out following rigorous protocols, scientifically and ethically assessed and that it will undergo adequate controls. In particular, with regards to the possibility of creating human beings through cloning, the NBC highlights how its position is in full agreement with the evaluation of illegitimacy expressed by the European Parliament with the very recent resolution of the 12th of March 1997.

PREMISE: CLONING, CONCEPTS AND LIMITS

The news of the cloning of a sheep obtained with an apparently simple technique from a group of researchers in Edinburgh, provoked curiosity and interest about a recurring topic in the collective imagination: the transferral of this type of reproduction to man, with the possibility of rendering the genetic make-up of an individual, perennial. This has been the central theme of the debate encouraged by the mass media, which moved the attention from technical-scientific and economic, to scientific-social and ethical-philosophical aspects. Although we don't reject the opportunity to discuss the ethical implications of a hypothetic and, at the moment, improbable as well as unlikely project of cloning man, we believe that the problem must be seen in its real dimension and brought back within technical-scientific limits, dictated by the current experimentation on animals. We will then be able to demonstrate that Wilmut's experiments, rather than leading to the cloning of man, open extraordinary research possibilities in the field of the biology and genetics of development and offer the means to make the creation of genetically modified animals more efficient, quicker and more economic.

As well as an excessive emphasis on aspects that can catch the imagination and provoke emotions, we have also witnessed some confusion with regards to the terminology defining the process of cloning. This is partly due to the evolution of the concept of clone, originally introduced in vegetal biology to indicate the cutting capable of growing into a duplicate of the same plant. The concept was then borrowed by biologists studying microorganisms, and cellular biologists, to describe the type of growth of a certain cellular population based on direct division, in the absence of any mechanisms for the exchange of genetic material through sexual reproduction.

In the 1970s the concept of clone entered molecular biology following the creation of procedures for isolating and transferring DNA fragments, reproduced in an elevate number of identical copies, in guest cells. In these systems, cloning is an open process, as the production of identical cells molecules is practically unlimited. The same characteristic can be observed in somatic cells populations of superior organisms, both *in vivo*, for some tissues like bone marrow, as well as for a wide variety of cellular types in cultures *in vitro*.

For pluricellular organisms, the concept of clone is less easily defined and linked to unicellular models. Every single individual can be considered a clone, as a group of cells derived by the zygote through successive mitotic divisions. But at the level of an *in toto* organism, a clone must be formed by at least two genetically identical individuals,

that is, derived from the same zygote, like mono-oocyte twins. A further element of complication is determined by the fact that, as we will see in the methodological part, there are two procedures for the production of clones in superior organisms: cloning by fission and cloning by nuclear transplant or cellular fusion. Wilmut's experiments have been carried out with this second method.

The criteria adopted in this document for the definition of clone, will be clarified at the beginning of the technical-scientific part. This will be articulated in the various aspects that mirror the state of the art in this field: aims, methods, experiments successfully carried out on animals, possibility of transferral to man as *in toto* organism or to human cellular lines, assessment of the biological risk and of the benefits for animals and humans. Contributions dedicated to moral, psychological, legal and epistemological reflections and to the examination of the law and of international documents on cloning, will follow.

1. THE BIOLOGICAL PROBLEM OF CLONING

The reproduction modalities of living organisms

Asexual and sexual reproduction. The simplest way to reproduce consists in the division of a cell into two offspring cells. The entirety of the descendants from a single starting cell is called *clone* (from the Greek *clon* = bud). This reproductive way, called *agamic* or *asexual*, is typical of prokaryotes (bacteria) and of many eukaryotes, both unicellular and pluricellular (plants and animals). In bacteria, the duplication of chromosomes makes the genetic inheritance identical in the two offspring cells; in eukaryotes the division process of the genetic material happens in more complex ways, which need various phases, all necessary to correctly ensure the complete communication of the genetic information that can be found in the chromosomes; this process takes the name of *mitosis.* In unicellular eukaryotes, mitosis coincides with reproduction, whilst in pluricellular eukaryotes it causes the organism to grow or the substitution of the cells lost due to wear or traumas.

In the majority of vegetal and animal eukaryotic organisms, as in some unicellular eukaryotes, reproduction is *sexual*, also called *gamic* or *amphigonic*, because it is entrusted to special cells *(gametes)* produced by two individuals of the opposite sex. Following the fertilisation process, that is, the penetration of the male gamete into the female gamete and the consequent fusion of their two genetic inheritances (*kariogamy*), a new individual is formed, similar to the parents but at the same time different from each of them.

In plants. Asexual reproduction in plants is called *vegetative propagation* and in some cases (potatoes, sugar cane and strawberry) is their principal form of reproduction. The propagation happens thanks to vegetative organs containing sleeping gems that can be, according to the different species, bulbs, rhizomes, tubers: the plants so originated are genetically identical to the “mother” plants, except for those variations due to mutations that have happened in one or more peripheral meristems. This type of reproduction is substantially different from sexual reproduction through cross pollination, where the encounter of gametes from different individuals produces genetic variability. An important peculiarity of vegetables is their totipotency, that is, the ability to regenerate fertile plants starting with differentiated somatic cells. In these, we can observe the restart of cellular division both *in vivo*, after an injury, and in culture, provided that the vegetable cuttings are exposed to the action of appropriate substances regulating growth, called

phitoregulators (in particular auxin and cytokine). Even though it has been demonstrated that this ability is not indistinctly possessed by all the cells of an organism (strong variations in regenerative abilities can be observed between species and, within the same species, in cultivated varieties). It remains one of the most important premises for its applicative aspects linked to vegetal cellular biotechnologies.

The availability of techniques for *in vitro* cultures, today makes the culture of vegetable tissue and cells on synthetic sub-strata an in organ axenic conditions, possible. In this way from a single merismatic peak, we can obtain tens of buds, that is, a *clone* of genetically identical plants; starting with one plant it is possible to obtain thousands of individuals within a few months. The technique called *micro-propagation or clonal propagation* has been used with hundreds of species; it is widely used in the plant growing industry for the vegetative propagation of species that are commercially interesting like, for example, strawberries, olive trees, orchids.

Starting with vegetable cells cultivated in vitro at the undifferentiated stage, it is possible to regenerate whole plants. The regeneration can happen through two different processes: organogenesis and somatic embryogenesis. In the first case, the regeneration of a plant happens in successive and distinct stages in response to the action of external phitoregulators; the exposition to growth regulators, like cytokine, supports the formation of areal organs (stem and leaves), whilst the exposition to auxin boosts the formation of roots. In the case of somatic embryogenesis, the most representative example of which is the carrot, the cells in culture are induced to differentiate organised structures similar to those formed in sexual reproduction through the division of the zygote. The induction is subordinated to the reduction of cellular concentration and to the removal of phitoregulators from the culture. In this way we can obtain a practically unlimited number of somatic embryos, starting with embryogenic cellular cultures; in this case as well, we are faced with a *clonal propagation* of great proportions.

It has however been observed that whilst maintaining the vegetable cells at the differentiated state, both genetic mutations and genomic alterations can take place (the nature of which has not yet been fully understood), which in the subsequent regenerative phase, very frequently give raise to variant phenotypes. The phenomenon that takes the name of *somaclonal variation* is certainly undesired in the process of clonal propagation but it can be used as a source of genetic variability.

In plants, sexual reproduction is characterised by an alternation of haploid sexual generations and diploid asexual generations. This is particularly evident in ferns where the diploid individual produces, through mitosis, haploid spores that create an haploid individual; it is this

individual that produces gametes which, after the fertilisation, again generates a diploid organism. On the contrary, in superior plants, the two generations are not so clearly separate and the haploid individual is extremely reduced.

Whilst in animals we can observe a clear distinction between somatic cells and germinal line cells (which form and separate in the first stages of embryonic development), in plants growing from the seed in germination, cellular divisions are limited to two areas, apical and radical, called meristems; following the differentiation of the offspring cells, they contribute to the organogenesis and to the formation of the soma. In response to environmental and/or endogen stimuli, areal meristems differentiate the floral reproductive tissues and stop contributing to the formation of the soma. This means that if a mutation should occur in a meristematic (somatic) cell in the early stages of vegetative growth, it can be transferred to the germinal line and therefore be sexually transmitted.

In animals. In animals asexual reproduction is very common in protozoan. In pluricellular animals (metazoans) agamic reproduction occurs mostly through a simple fragmentation of the body. Examples of this reproductive method are frequent between coelenterates, plathelminthes (flat worms), annelids, etc.

Amphigonic sexual reproduction, which requires the participation of two individuals of a different sex, is much more frequent. In this case the offspring will be similar but not identical to the parents. However, even organisms reproducing sexually can create clones. This happens in *parthenogenic* and *hermaphrodite* species. In the first case the development of the individual starts with only one of the two gametes (in natural conditions, the female gamete). Even in this case we call it sexual reproduction, because the individual gamete is a differentiated cell with the characteristics of a sexual cell (an oocyte). Parthenogenesis can be linked to amphigonic reproduction through a series of intermediate levels, so that it can be considered to be deriving from it. In hermaphrodites, the egg cell is fertilised by a spermatozoon produced by the same individual. As both gametes have the same genetic make-up, the offspring will be identical to the parent.

Although the asexual and parthenogenetic methods of reproduction are more “economical” in comparison to sexual reproduction (amphigonic), this last one has prevailed because it allows *genetic variability.* Asexual organisms are generally haploids and despite they successfully reproduce, they manifest two limitations: 1) being *haploids* (that is, they have only one series of chromosomes); 2) being genetically homogeneous. These organisms in fact have only one mechanism to ensure a certain degree of genetic variability: *mutation*, that is, sudden

and hereditary changes of the genetic material. Mutated individuals enter in competition with the non-mutated ones for their survival in a certain environment.

Although many protozoans of any class still only and successfully reproduce asexually, there are also species that use sexual reproduction making a considerable evolutionary step. And this for two reasons: 1) because sexual reproduction potentially starts a *diploid* (double series of chromosomes), which, if not essential, is highly helpful to the organism; 2) because brings the organism to *meiosis* (a particular type of cellular division, which in animals is exclusive to germ cells as it leads to the halving of the number of chromosomes). This is an important event from an evolutionary point of view, as it gives the organism the advantage of *crossing over*. This process, exchanging genetic material between paternal and maternal chromosomes, creates new genetic combinations and it so amplifies the genetic variability of the species. Therefore, it makes the selection of the best adaptation to the environment, possible. These innovations (meiosis and sexual reproduction), which happened first in protozoans, can be found in animals and plants and it is very probable that were passed on to them after having been acquired by protozoans.

The more easily and quickly a species can adapt to new needs, due to a change in the environmental conditions, the more likely it is to survive. Let’s consider the case of a *species* reproducing exclusively asexually and made up by a variety of clones that cannot be mixed. Should they have to face adverse environmental conditions and should some particular characters be necessary to overcome them, if these characters are distributed between the clones, obviously, as not one individual possesses all of the characters together, they would succumb. However, with sexual reproduction, the probability that particular characters, present in different individuals, would come together in other individuals, is not negligible. These individuals are therefore able to face the new environmental conditions, and their species can in this way overcome the biological barrier.

Genetic variability in any case is also ensured in species that reproduce asexually, through parthenogenesis, or are hermaphrodites, due a general phenomenon common to all organisms, that is, *mutation*, which we have already mentioned. To this variability factor, we must add the *sexual* phenomena, that is, an exchange of genetic material between individuals who are part of the same population. Therefore the concept of sexuality does not coincide with the type of reproduction, as it can happen in species that reproduce agamically, like bacteria, through different mechanisms (*transformation, conjugation, transduction*), in protozoans (*conjugation*) and even in viruses. Consequently, even in

species that reproduce asexually, the individuals generated from a clone are not all genetically identical, due to mutations or even eventual sexual phenomena.

In the case of parthenogenesis, often this reproductive method alternates with amphigonic reproduction (*heterogeneity*). Even asexual reproduction can alternate amphigonic sexual reproduction (*metagenesis*).

In order to favour genetic variability, hermaphroditism is mostly made "insufficient", that is, anatomic causes intervene (significant distance between the masculine and feminine genital openings) or temporal causes (different maturing times of the masculine and feminine gametes, so that the encounter between the gametes belonging to the same individual is impossible, and only the encounter between gametes belonging to different individuals are possible).

In the species that reproduce only asexually and amphigonically, clonal reproduction does not exist in natural conditions. At most we can obtain populations that are genetically quite uniform, due to successive pairings of blood related individuals. After at least twenty generations (crossing brothers and sisters after each generation), the lineage can be considered relatively uniform and is called *biotype.* In these species cloning is possible only experimentally, that is, transplanting the somatic cells nucleus of an adult individual in denucleated egg cells. In this way, we obtain numerous copies of the same individual. Once those new individuals have developed from the eggs, from those we could obtain other individuals, genetically identical to the previous one, with the same technique, and so forth. Taking into account that there is also and extra-nuclear DNA (mostly mitochondrial and of maternal origin), "true" experimental cloning is therefore obtained by the nuclear transplant of a feminine somatic cell in the denucleated egg cell of the same individual. But even in this case the material of the transplanted nucleus might not be identical to the donor's original one, due to mutations that happen to somatic cells during the course of a life.

The first cloning experiments started in the 1940s with the purpose of studying one of the most fascinating biological problems in depth: *the problem of the embryonic differentiation*, that is, investigate the mechanisms that lead to a structural and functional diversification of embryonic cells, despite the fact that they all maintain the same genetic inheritance.

Cellular lines and clones in "in vitro" cultures. The *in vitro* culture offers the possibility of maintaining and in many cases propagate, in an artificial environment, made with the right supports and nutritional liquids, organs, tissue and cells isolated by the organism isolated by the organism in different phases of development. The type of culture we are

interested in for donation purposes, is that starting from single cells. The initial material can be constituted from tissue fragments or from cells already divided *in vivo*, like peripheral blood lymphocytes. After a more or less long period of mass culture, single cells can be isolated and from them we can derive colonies, representing real gifts, according to the definition given at the beginning of this chapter. Multiplying, the cells of the colonies can create organised structures or simply cellular line stumps, depending on their development potential. Organised structures include organs, tissues or entire organisms. Cellular stumps generally have a limited life span, whilst cellular lines are permanent and undergo a process that is often defined as immortalisation, which has some characteristics in common with tumoral transformation. The ability to evolve in organised structures is particular of embryonic cells, defined as totipotent when they are capable of generating an entire organism, and multipotent when they form tissues or organs. After being implanted into the uterus, embryos lose their totipotency and gradually even the multipotency. Some cells however, still have a regenerative capacity even in the adult individual, together with the ability of producing specialised cells. These elements, called stem, are the progenitors of cellular populations with slow or rapid renewal, like bone marrow. All the cells of the organism that do not belong to this category and that are not part of the germinal line from which gametes are originates, form the population of differentiated cells in the adult's variety of tissues. Prolonging the *in vitro* culture, generally leads to the disappearance of the functions linked with their development and differentiation, and they can be maintained or recuperated, in some cases, with the transferral *in vivo.* The production of cellular lines of clonal origin, whether deriving from embryonic tissue or adult tissue, is in any case based on the fission method, that is, on cellular division, which does not involve phenomena of cellular fusion of nuclear transplantation. In all of these cases, therefore, it is a cellular donation restricted to the somatic area, particularly interesting to research and with applications limited to the transplant of cells or tissue. The only exception is that of embryonic cells in the totipotent phase; from them we can derive ES (Embryonic Staminal) cellular lines able to contribute to the formation of a complete organ.

The cellular transplant or fusion method, experimented by Wilmut in the sheep, offers an alternative way to produce cellular lines of clonal origin. But, with the currently used technique, which requires a complete reprogramming of the somatic cell subjected to cloning, the formation of an embryo in the first stages of development is compulsory. The problem of the donation of cellular lines with these methodologies, takes us back to the problem of experimenting on embryos.

1.2 Cloning experiments and practices on animals

Definition and methods of cloning. We call clone a group of individuals (DNA molecules, cells or entire organisms) deriving from a single progenitor, of which they are identical copies (see glossary) through successive duplications.

The methods for the creation of clones in pluricellular organisms are essentially two and they are part of the processes of asexual reproduction:

a) multiplication through the disaggregation of single cells or through the subdivision of groups of cells (through *fission* or *splitting*) in the first phases of embryonic development, when the cells are totipotent or pluripotent, that is, able to generate, alone or in association, an entire organism;

b) transplant of nucleuses obtained from cells at various stages of development in non-fertilised or fertilised egg cells, after having physically eliminated or deactivated the resident nucleus or nuclei. In place of the nucleus, the denucleated egg cell can be transplanted or, better, fused, with an entire somatic cell.

Cloning purposes. Cloning has so far been practiced on lab animals and in domestic animals for two principal reasons: the first interests basic research and aims at clarifying the mechanisms of the development process and of normal and pathological differentiation; the second, which has an applicative character, has its in objective the creation of genetically identical animals useful: a) to experimentation (for example to study the effect different dosages of drugs); b) for their economically advantageous characteristics (for example meat quality and quantity); c) for the production, in great quantities, of substances useful to man (for example molecules that are pharmaceutically interesting because of their therapeutic function).

The fundamental question in the study of the differentiation processes is whether the changes in the activity of genes that happen during those processes correspond to irreversible modifications in the structure and organisation of the genetic material or are the result of more or less stable functional modulations. Cloning experiments of nucleus transplantation in animals, can give important contributions not only to the understanding of the processes that determine cellular specialisation, including the defects that can bring developmental anomalies or neoplastic degeneration, but also to the possibility of controlling these processes.

The most directly applicative experiments, like those that investigate the susceptibility to environmental variations determined by the exposition to chemical or physical agents or to pharmacological treatments, find in cloning an extremely efficient instrument, as their effects can be analysed without taking into account inter-individual variability. Finally, we must not overlook the fact that one of the objectives of animal cloning involves both theoretical studies on evolution and intervention instruments aimed at maintaining the biological balance: in fact, cloning can be the only way to save animal species facing extinction.

Experimental precedents in amphibians and mammals. Cloning experiments, using the method of transplanting the nucleus, have been successfully carried out for the first time in amphibians, in the 1960s. Donor cells were removed from organisms that had not yet achieved adulthood. Cloning with cells removed from not completely developed organisms, was achieved in 1975 by Gurdon, using amphibians. Then it was demonstrated that transplanting nuclei from the skin cells of a frog into egg cells with a nucleus deactivated by ultraviolet radiations, it was possible to obtain the formation of tadpoles but not of adult frogs. It is this line of research that constituted the basis of the experiments carried out by the Edinburgh group using sheep mammary cells.

The experimental model had already been proposed by the same group a year ago, when the data of a nuclear transplant, successfully carried out using, as nuclei donors, embryonic cells cultivated *in vitro*, were published (Campbell et al., 1996). Using the same experimental conditions, the investigation was extended to animal adult cells with which it was possible to generate, through the fusion with a denucleated egg cell, an apparently normal sheep having genetic characteristics that were identical to those of the animal donating the nucleus.

Cloning techniques by fission had a parallel evolution. In zoo-technology the creation of identical individuals with this technique is a consolidated practice.

Experiments carried out by the Edinburgh Group: the last outcome. The technique used (Wilmut et al., 1997) consists of fusing, through an electric discharge, a cell removed from a short term culture of mammary gland tissue from a pregnant donor sheep, with another sheep's denucleated egg cell, and in transferring in the uterus of a third sheep the product of the fusion after a short stay in a sheep's tied oviduct or, in a few cases, of *in vitro* incubation. The conclusion of the Authors of the experiment is that an adult organism's differentiated somatic cell does not undergo irreversible modifications in the structure of the genome, such that they can hinder a reprogramming of its activities towards the

development of a new, complete organism. Totipotency, which so far has been recognised only in embryonic cells in their fist stages of development, in this way can be extended to adult tissues, in particular those that have differentiating and proliferating characteristics comparable to those of the mammary gland. This "continuity" of the human genome through the different stages of its expression, once confirmed by other experiments, would be an extremely important novelty for the study of cellular differentiation and genic expression.

The factors considered essential for the success of the experiment were:

- the regenerative state of the tissue from which the cell was removed;
- the *in vitro* culture of the cells donating the nucleus and the induction of a quiescent state;
- the coordination between the phase of the cellular cycle of the cell donating the nucleus (Go) and that of the denucleated egg cell (metaphase II).

The problems that could limit the applicative pitfalls of the experiment, probably are:

- the fact, explicitly admitted by the authors, of "not being able to exclude the possibility that next to a huge quantity of mammary gland epithelial cells, in the cellular culture there was also a minimal fraction of relatively undifferentiated stem cells, capable of contributing to the regeneration of the mammary gland";
- the very high number of fusions (277) necessary in order to obtain a positive result;
- the lack of a genetic documentation and of data (in reality impossible to collect at the moment) on the longevity and fertility of the cloned sheep.

1.3 Expected risks and benefits

The biological risk linked to cloning techniques: the effects in the individual and on the population. Why, as we have said, does the cloning method described by Wilmut display a low efficiency (a positive result on 277 trials carried out)? There are a variety of causes for the lack of development of the cloning product and they are due to the absence of fusion between the donor cell and the egg cell, to an arrest in the early

stages of the formation of the embryo, to a failure to implant into the uterus, to the loss of foetuses, to prenatal death. Foetal loss reaches 62% and must be compared to the data we can observe (in sheep) in their reproduction based on the normal sexual mechanisms. A high fraction of anomalies is possibly due to chromosomal alterations of number and structure, which lead to aneuploidy and to chromosomal mutations. The probable cause of these alterations is the fusion process itself and the *in vitro* culture, which notoriously destabilises the chromosomal order. We need to take into account all of these errors not only in order to determine the induced biological damage, which represents the first level for the formulation of an ethical assessment. This is even more important when we consider the possibility of a transferral to man of the nuclear transplant technique, even if just limited to the production of differentiated cellular lines.

Cloning techniques, both by fission and by transplant, aimed at producing animals, also pose a populationistic and environmental problem. Their widespread use would certainly have the effect of reducing genetic variability, which represents a biological reserve of primary importance for the balanced management of environmental resources.

This kind of problems have already been presented because of interventions both through the typical techniques of genetic crossing and the new biotechnologies applied in the vegetable (agronomic) and animal (zoo-technical) field. Controlling all of these applications (including animal cloning) would be desirable in any case. But, if it is true that cloning, as a technique for reproduction, can bring new undesired effects, introducing an element of decrease in genetic variability, we cannot deny that it can be an extremely efficient instrument in safeguarding species facing extinction, contributing to animal repopulation where necessary or desirable and therefore to the reconstitution of any compromised ecological balance.

Benefits of animal cloning trials for the progress of knowledge on development biology and for biomedical research. One of the positive ethical implications of the animal cloning experiments is first of all their effect of the progress of basic biological knowledge. The nuclear transplant method has been revealed to be a very efficient instrument, probably the only one, to study gene inactivation and activation during the genetic development and variations happening during the course of the differentiation and senescence. More specifically, two problems of fundamental biological-medical interest could be studied through cloning trials on an adult mammal like the one described: a) the mechanisms that guarantee the stability of the states of differentiation with the obvious

applicative perspective of controlling tumoral proliferation; b) the existence or not of the species barrier: for example, would it be possible to transplant a sheep's nucleus in a mouse's denucleated egg cell? What properties would the sheep born in this way have?

The animal models are very helpful in understanding analogous processes in man and in perfecting both diagnostic and therapeutic instruments for hereditary and congenital pathologies determined by development anomalies. Every new approach allowing us to study in more depth and accelerate the research in this direction, can be enhanced and encouraged in view of the potential benefits it brings for the production of goods useful to man, and for healthcare. The same group of researchers guided by Wilmut and funded by the industry, propose to produce large quantities of a substance (-1-antitripsin) in sheep's milk, which inhibits elastase, an enzyme the presence of which damages lungs and the pancreas in cystic fibrosis, a frequent hereditary illness that is still lethal today. Other groups of researchers plan to use sheep's or other mammals' milk to secrete into in large quantities of useful substances also in zootechnics or in agriculture: in this sense the use of animal cloning becomes analogous to that of the generation *of transgenic or genetically modified animals,* in which certain genes are substituted and/or transformed in order to produce substances useful to man through genetic engineering technologies that are currently universally widespread and standardised.

Legitimacy of animal trials. Cloning trials on animals, from the bioethical point of view, does not present any problems that are substantially different from those posed for the creation of genetically modified animals through the transferral of non-human genes. The modifications regarding the expression of the genes can cause, in the cloned animal, various types of anomalies with consequent suffering, the assessment and regulation of which must be carefully followed by appropriate technical-scientific organisations. If, from the individual level, we move to the consideration of the population, we must highlight on the one hand the danger, certain but not new, of interventions that can have negative consequences for the maintaining of genetic variability; on the other hand, if properly regulated, the positive potentialities of those interventions for the conservation of animal species facing extinction.

2. POSSIBILITY OF TRANSFERRING CLONING METHODS TO MAN

2.1 Attempts of cloning by fission: Hall and Stillman's experiments

In man, the first cloning trial by embryonic fission was carried out in 1993 by Hall and Stillman, from the George Washington University School of Medicine, using the products of in vitro fertilisation considered unsuitable for the transferral into the uterus because they presented chromosomal anomalies. The results of this trial (presented at the annual Chromosomes of the American Fertility Society, but which were considered unsuitable for publication in extensor because of the clamour raised and the inquest immediately indicted by the University) demonstrated that it was possible to obtain distinct embryos, able to develop up to the stage of 8-16 cells, from cells isolated from embryos at the stage of 2-8 cells. Declared aim of this research was to contribute to the improvement of in vitro fertilisation techniques, to study the development of the embryos in their first phases and to guarantee a better efficiency of preimplantation diagnosis.

2.2 Prospects of clinical applications of the nuclear transplant method in enucleated oocytes

The chances of a transferral of cloning to man as in toto organism, the assessment of the biological risk and of the benefits deriving from it from man, are obviously the issues under discussion which have the bigger impact on public opinion and on the institutional organisations that are entrusted with regulating this matter. If today there is unanimity on the fact that the cloning of man cannot be recommended, it is important to stress the eventual benefits that the cloning of man in toto could offer in the future.

We must start by saying that the discussion contained in this section is only technical-scientific: it is, in fact, a series of suppositions on which we cannot express an ethical judgement, which will be the topic of the following chapter.

Wilmut's trials, whilst giving us the proof that variations in the structure of the genome following cellular differentiation and specialisation can be reversible, does not demonstrate however that the results highlighted in sheep can be extrapolated to other mammals, including man. Mice, for example, have been so far unresponsive to cloning using the method described, even when embryonic cells are used

as donors. This leads us to think that the response to this type of experiments could be different from organism to organism.

The results on cloning presented here, as well as requiring a confirmation in the same species, wait to be verified in other lab or domestic animal species, before being considered for an eventual transferral to man. We must also highlight, always from this perspective, that the transplant of a nucleus into a denucleated egg cell does not lead necessarily and exclusively to the cloning of the entire organism but can offer the means to clone single cells and generate cellular lines capable of carrying out specific functions, like liver, pancreas or thyroid cells. The maintenance of these functions only through *in vitro* cultures, so far has not given encouraging results. Cellular lines obtained by fusion with egg cells could be created and become a valid proposition when the nuclear transplant in egg cells is confirmed in different animal species and it is proven that the production of differentiated cellular lines does not necessarily require the development of an embryo. We must also stress that the contribution of the denucleated host egg cell to the development of the cloned mammal is considerable, actually, it is essential: the cytoplasm of the host egg cell, that is, in that part that excludes the nucleus, also includes mitochondria, a little organ containing DNA (mitochondrial DNA) and the formation of which is fundamental to the supply of energy to the cell.

Once the abovementioned doubts on reproducibility have been overcome, we must ask ourselves what could be the scientific and medical "justifications" for applying cloning to man. The scientific debate preceding the publication of Wilmut's experiments on sheep already identified the potential use of this technology of asexual reproduction in the preparation of differentiated cellular lines – for example hematopoietic ones – suitable for transplantation. The availability of a reserve of autologous therapeutic cells (in addition they can be corrected *ex vivo* in the case of genetic illnesses) would increase the possibility of curing various pathologies like cancer, degenerative illnesses, viral or inflammatory diseases.

The so called "incomplete cloning", aimed at obtaining cells useful to patients suffering certain illnesses, could become a very interesting technology for the production of transplant tissue: in reality, the ethical problem is in this case independent from the fact that the transplant tissue was obtained through cloning, but it rather refers to the fact that transplanting, for example, foetal nervous tissue in culture (for Parkinson disease) parts of the biological substratum of superior intellectual functions is implanted.

With regards to the perspectives for the clinical applications of complete cloning, we can consider three exemplar cases: 1) healthy

parents carriers of the same pathological gene of recessive hereditary transmission: to avoid having affected children, the father could donate a nucleus to be inserted in the mother's denucleated egg cell. The individual generated would not be an exact copy of the father: he would have nuclear genes identical to those of his father, but the mitochondrial genes would be of paternal and maternal origin; 2) a woman suffering from an illness linked to her mitochondrial DNA: she could generate children without that illness by transplanting the embryo's nucleus in an egg cell of a donor with normal mitochondrial DNA and then grow the donated egg cell modified in this way; 3) the cloning of a sterile person.

The whole of the available data leads us to believe that there are no valid general reasons to trial adult cloning in man, even if it could be carried out with the outmost efficiency. The cases listed above, although exceptional, deserve however careful and balanced consideration and it is for this reason that Dulbecco believes that it would be wise to have a moratorium of human cloning at least until the studies on animals have clarified in detail the biological mechanisms of cloning on the various species, but leaving open the possibility of revoking it and substituting it with appropriate and severe regulations upheld by control instruments.

2.3 Possibility of clinical trials

In the current state of knowledge, human cloning seems impossible both from a biological point of view and for the effects that it could have on our evolution. Even if the technique object of the experimentation, still inadequate for animals, was transferrable to man, there would be problems that at the moment seem difficult to overcome. First of all, the biological risk for the individual would be difficult to assess without adequate experimentation, and the experimentation, which traditionally would move to animals increasingly close to man from an evolutionary point of view to arrive eventually to man, would be extremely complex and, at least at the beginning, certainly not very efficient and extremely risky; secondly, the effects of a large scale spreading of this practices would be damaging for the genetic structure of human populations, as they would reduce their genetic variability, an inheritance necessary also from a cultural point of view. Even if these problems were in the future clinically solvable, the first by plausible biotechnology, without risks and efficient, the second by sporadic and controlled applications aimed exclusively at therapy, remains the consideration of a fundamentally ethical nature of a biotechnology that to progress needs, realistically, trials on the human embryo. On this point, it is common knowledge that opinions, even within the Committee, are divided, but it is still difficult to

identify, at least today, therapeutic instruments that, with the exception maybe of the already identified very particular cases of mitochondrial illnesses and sterility, necessarily and exclusively find in the cloning of a human organism the only possibility of realisation. A completely different point, as already said, could regard the production of human cellular lines.

Conclusions

1. At the moment, the data on sheep cloning gives us limited information because it can hardly be reproduced with regards to the ability of cells derived by mammals' differentiated tissue, of developing complete individuals following a fusion with denucleated egg cells. In particular, we still don't have the genetic data of the cloned individual, as it is obvious, neither on its longevity nor its fertility.

2. The technique finalised and the results obtained, especially when it will be possible to exclude the presence of an under-population of undifferentiated stem cells, in the population of differentiated epithelial cells (of the adult sheep mammary gland) cultivated *in vitro,* constitute a progress of great importance for the advancement of knowledge in the biology of development, with potentially very useful consequences for the application in biomedicine and zootechnology, from a technological point of view.

3. Currently the conditions for the transferral of this methodology on man are not defined.

3. MORAL ASPECTS OF THE CLONING PROBLEM

We take for granted, in these reflections, the scientific definition of the concept of cloning in its diverse variants, as well as the descriptions of the possible techniques adopted or adoptable, in order to obtained it. Therefore, the moral problems linked to those techniques will not be the object of consideration, even though some of them could be significant. Our attention will therefore be focused exclusively on that particular significance of cloning that can be represented in the creation of a living individual *genetically identical* to another individual, in the sense that it is clarified in the part of the document illustrating the biological aspects of cloning; first of all, we will look at the moral legitimacy of pursuing this immediate end. This can, in many cases, be an intermediate aim in comparison to other purposes, which will be taken into consideration at another time.

3.1 The cloning of non-human living creatures

The most important moral problem with regards to cloning (intended in the abovementioned sense), as we will shortly see, seems to be the fact that it violates in some way the living being's *individual identity*. This problem could lead us to pose moral objections against cloning in itself, if the right of the inviolability of our individual identity should be recognised to all living beings. Moral conscience in contemporary culture has taken many steps in the direction of the recognition of the duty of respect towards living creatures, and in particular of animals. However we must also recognise that the common moral conscience accepts that we can sacrifice animals (given certain conditions and with certain modalities), when this serves man's needs, and that this attitude even admits that (with adequate reasons) we could disrespect their individuality, especially as (in the absence of a true self-consciousness) it is doubtful whether we can talk about individual identity in animals, in its full sense.

In reality, since unmemorable time, man has tried to mould or change vegetable or animal species for his own purposes, through procedures of selection, hybridising and crossing: genetic engineering techniques have given a great boost to this process, without essentially altering the moral sense of the problems linked to it. According to these considerations, it seems reasonable, when we have a living being (animal or vegetable) that has certain "useful" phenotypical characteristics, to try and ensure the existence of other beings that are as much as possible

"identical" and, instead of entrusting this to natural or artificial reproductive techniques, "copy" it with that particular reproductive technique that is cloning. Especially if there are good reasons to believe that those phenotypical characteristics are determined (completely or mostly) by its genotype, and also if we can believe (as it happens in the case of cloning) that even genetic characteristics expressed in the somatic line can be "reprogrammed" in the germinal line.

At this point, to reinforce the thesis of the legitimacy of cloning non-human living creatures, we must take into consideration the ulterior motives why cloning is practiced and planned: agro-alimentary purposes are well known, and to those we can add today the medical use of substances, tissues, organs, as well as the possibility it offers to experimental investigations in the medical field, stressed in a variety of ways in the current debate on cloning. In other words, we don't see why, whilst we accept without scruples that millions of animals are slaughtered to provide us with meat (not to speak of their fur), it is not just as licit to breed cloned animals to sacrifice them or as common lab animals, or to remove from them organs or tissues to use in human medicine. The choice of practicing animal cloning is, in any case, to be subordinated to the real need for this experimentation, taking into account the suffering that it can cause to the animals as well as the danger of altering the balance of the ecosystem.

3.2 The cloning of human beings

The case of man is different: his *individual identity* must be the object of the utmost respect. This is an idea referred to not only by many historical religions (according to which each human being is individually wanted by God), but that finds its roots in the "secular" conscience of our times, which has expressed it in the notion of the fundamental *autonomy and self-determination* of each single human individual. To protect this individual identity, it is not just relevant to have a profound awareness that "there is no other being in the world like me", as even a monozygotic twin (although possessing practically the same genetic make-up) would not have had the same "environmental influences" (as often said), but also and above all because what I am derives from the way in which I have lived these environmental experiences and, even more, from the choices that I have freely made along my personal history (a factor that is almost always ignored). If all this was sufficient to respect individual identity, cloning (as it could at most give me a genetic make-up identical to that of another human being), would only touch a part of my individual identity and, therefore, it would not be ethically abhorrent. In reality

there's much more: the respect of individual identity implies that no-one has the right to decide what I must be. For this reason modern times, and even more contemporary times, have stated a series of "human rights" that, in essence, indicate a variety of *non-interferences* in each individual's free choice of being and behaving, as well as a series of conditions to allow us to concretely realise this autonomous growth. Therefore, the genetic make-up clearly does not exhaust all human individuality, as highlighted in this document in the part dedicated to the psychological aspects of human cloning, but it is certainly its basis, and it is damaging to human dignity that somebody could completely decide someone else's genetic make-up. It is not frequent that an individual is unhappy with his height, the colour of his skin, the predisposition to a pathology, his own temperament (all aspects also linked, with more or less intensity, to our genetic make-up), but in general we can only resign to it, try and adapt our lives to those situations created by genetic chance. The situation would be very different if we could blame somebody for predetermining conditions we do not accept. In other words, until today we have (justly) tried to guarantee to individuals their autonomy of judgement, of political and ideological choice, of religious opinion, of moral decision. Today we need to worry about protecting also their genetic autonomy, as cloning techniques can seriously threaten it, and this, independently from the perspective (intrinsically not very plausible even though journalistically presented to us as a bogeyman) of preparing ourselves to a humanity of copied individuals.

More in general, an individual that is born into the world as an intentionally created "copy" of another human being, would be burdened with very peculiar expectations, not linked to the expression of his single and unique personality, but to the copied representation of the qualities that belong to another individual (even if he was a deceased relative). In this way there would be, effectively, a weakening of the value of individual identity, as a human individual would be considered not for what he is in himself, but in comparison to how it approximates an original and archetypal that would assume, even in the clone's mind, a value of reference. The importance of this character of uniqueness and exceptionality has been at times called "right to ignorance", to be intended as the right of every man to live his experiences for the first time and originally, and to become himself in the encounter with his life, that does not have a known paradigm. In particular, the argument put forward by the philosopher Jonas, for whom the cloning of a person would deny to the cloned person the right of ignoring his genes and therefore it would condition his existence with an unacceptable psychological burden, it's much more subtle and acceptable. Reality is however even more subtle and shaded: it is in conflict situations that it is difficult to apply ethical

principles of absolutely universal value. If for example we believe that for a woman the act of bearing a child can be as important as being his true biological mother and if we also consider that the mother would contribute to the newborn with her cytoplasm and her mitochondria, a significant contribution, the consideration of having to bring up a "twin" of the biological father, which today is foreign to our knowledge and culture, could tomorrow be, for some, culturally acceptable: firstly, because a younger monozygotic twin of the husband father would certainly be a different and autonomous person (genes are not all, it is the environment in which he will be raised that will differentiate him); secondly, it could not be clear why a son obtained through heterological insemination can be ethically and responsibly accepted, whilst a son similar but not identical to the father, responsibly accepted and carried by the mother, should be refused in any case. For others, this hypothetical solution cannot be proposed.

In general, the unavailability of the human being, in the sense that it cannot be "made available" to anybody, is a shared moral principle, a principle usually expressed in the imperative that no human being can be treated exclusively as a means to an end. Therefore, it would suffice to ask why some think that they are able to justify the cloning of human beings, to realise that in effect they think they can use these individuals essentially as means to an end. Some clues were already evident before the explosion of the debate on cloning. A specific example is the case, rare but real, of couples who have generated a child with the aim of making the transplant of immunocompatible bone marrow possible, in favour of another child born previously, affected by a tumour that cannot be treated otherwise, obviously without any prejudice for the health of the first: cloning practices could be inspired to similar purposes.

Apparently, it appears that we could say: in the end, we remove a few cells from the patient (e.g. from his skin), we separate the nucleus, we transfer it in an "emptied" human oocyte and we grow a copy of the patient: it is still him that continues in his cloned descendant and therefore we could use organs and tissues to cure his illness. In reality, it is not so: the descendant will be a complete human individual, and it is not legitimate to bring him into the world for the primary purpose of donating organs. Therefore, even wanting to hypothesise the cloning of human individuals for therapeutic purposes, this does not commonly seem to be morally acceptable. In general, it does not appear licit to invoke the possible progress of medicine as a sufficient reason to justify cloning; however, some Committee members believe that there could be situations of conflict between different ethical values, towards which there are no absolute judgements of moral disapproval, but an assessment

must be made case by case, taking into consideration the specific importance of the values in conflict.

Cloning seems even less justifiable if we think of using it for more futile or pathetic reasons, like those, often mentioned, of parents who want a child with blue eyes, or a "copy" of a famous person or of a loved one. Besides the scientifical impossibility of being able to obtain such "copies" (for the already mentioned fact that the genetic make-up does not exhaust the totality of the factors constituting the individual personality), the moral illegitimacy of wanting to generate a human individual on request and according to some else's wishes, would be even more evident.

From a moral point of view there are other, more serious risks, for example "eugenic" ones. It is not about cultivating the sci-fi dream of having legions of men "all equal", but about "selecting race", planning, even though only on a genetic level, future generations, so that they will match an arbitrary "model", not only in the sense of "bizarre", but also in the sense of being moulded "ad arbitrio" by someone (individual or ruling class), who assumes the right to dispose of the personality of others, not only relatively to those characteristics they "must" have, but also with regards to an infinity of very positive characteristics they risk not having, because they are not included in the genetic make-up of the prototype or prototypes from which they have been "copied". This issue also has genetic implications, on which we don't intend to dwell (in essence, it is about the biological value, and not only biological, of "genetic variability"), but its moral relevance is more important than its biological relevance.

Finally, there is one last type of moral argument that is sustained by those sectors of the current bioethical reflection that see a very important connection between procreation and sexuality. This is linked to the fact that in cloning, the creation of a human being would be completely entrusted to a technical intervention, in a totally asexual form, taking to the extreme that schism between sexuality and reproduction, which is already present in many practices of assisted reproduction (and that, in the eyes of some, is a reason for the moral condemnation of these practices). In the case of cloning, this schism could even lead in a form of explicit refusal of sexual procreation.

In conclusion, the NBC believes that the moral unacceptability of the cloning of human beings, on which there is today unanimous consensus, has been sufficiently clarified by the previous considerations. It also stresses that it is not about a simple problem of private morality, because the attack to the integrity of human individuality that it involves, is a very important issue of public ethics, also with regards to the social consequences that the establishment of this practice would inevitably

entail. Therefore, the NBC believe that, in the current state of affairs, laws, rigorously and knowledgeably regulating all the aspects of this complex issue, are urgent, in accordance with the general trend of opposition to cloning present in our legislation and in international documents on this topic, and recently expressed in a formal prohibition to the cloning of human beings, which can be found in the additional protocol to the “Convention for the protection of human rights and the dignity of the human being with regards to Biology and Medicine applications”.

For an in depth examination of these documents, we refer you to the following chapter.

4. CLONING IN INTERNATIONAL LAW AND DOCUMENTS

The fear of an improper use of scientific research and of their applications to man, has pushed the international Community to have a vigilant attitude towards practices that can damage the respect for human beings, their integrity, their singularity, all the essential elements of the human condition and of the dignity of the individual.

The condemnation of human cloning – seen as the replication of one or more individuals identical to the donor – has been, as a consequence of this attitude, the object of a specific law by the international Community, both at a global level (WHO, UNESCO, U.N. Commission of human rights) and at a European level, by the Council of Europe and the European Community, through the elaboration of various "statements" in documents that will be examined as follows.

In the meeting of the 16-17th of June 1997, the State and Government leaders gathered in Amsterdam, issued a Council of Europe Declaration prohibiting human cloning, inviting on the one hand European Community organisations and, on the other hand, the member States, to take any necessary measures, within their own national regulations, to unequivocally prevent, forbid and condemn, in Europe, human cloning, accepting the Opinion on the ethical aspects of cloning techniques expressed by the Group of Councillors for ethics in biotechnology at the European Commission on the 29th of May 1997.

Considering the universality of the principles relative to the protection of human dignity, already stated in numerous international documents, a commitment both of States and international Organisations has been deemed indispensible, in order to prevent situations irreversible in practice and to efficiently and explicitly, worldwide, prohibit the reproduction of a "conform copy" of man (even if it has been stated that, currently, cloning is only an hypothesis).

Italy, as a member State of all international, universal and regional Organisations abovementioned, participated to the elaboration of the regulations and of the opinions expressed to safeguard human dignity and fundamental human rights. An examination of recent international initiatives will help in assessing if our current legislation protects human beings against the actions threatening the natural rights of the individual.

We distinguish:

European Community

a) European Parliament Resolution (DOC. A 2.327/88); DOC. B-1519/93; DOC. B 4-0209-242/97 of the 12th of March 1997.

b) AVIS "Ethical aspects of cloning techniques" of the Group of Councillors for Ethics in Biotechnology at the European Commission.

c) Amsterdam Declaration (16-17th of June 1997) of the Heads of State and Government (Council of Europe).

d) Directive Proposal of the Commission for the protection of biotechnological inventions (1/9/1997).

Council of Europe

a) Recommendations of the Council of Europe Parliamentary Assembly number 1046 (1986).

b) AVIS of the Comite' Directeur pour la biothique (CDBI) and the Projet de protocole additional a la Convention pour la protection des droits de l'homme at la dignite' de l'être humain à l'égard des applications de la biologie at de la medicine, portent sur l'interdiction du clônage d'etres humains (DOC. C M (97) 111).

World organisation documents

a) Resolution of the World Health Organisation (WHO) on cloning in human reproduction (DOC.WHA 50.37 of the 14th of March 1997).

b) Project of Universal Declaration on the human genome and human rights (UNESCO, Doc.1310/97; CONF.201/6 of the 25th of July 1997).

We will conclude this brief review with the United States "CLONING PROHIBITION ACT", adopted following the "Opinion" of the National Bioethics Advisory Committee (NBAC) in 1997, as an example of national law.

4.1 European Community

European Parliament

1. The European Parliament, in the Resolution on the ethical and legal problems of genetic manipulation (Doc.A 2.327/88) (in G.U. European Community 16th of March 1989), expressed the following point with regards to cloning: "*it believes that a legal prohibition is the only possible reply to the possibility of creating human beings by means of clones, as well as to all experiments aiming at cloning human beings*".

2. The European Parliament, in the Resolution on the cloning of human embryos (Doc. B 3-1519/93 of the 20th of October 1993, in G:U: Eur. of the 22-11-93) in response to the first "published" of

the cloning of human embryos (J. HALL, of the George Washington University Medicenter communicated at the meeting of the American Fertility Society in Montreal), condemned the "*cloning of human beings notwithstanding the reasons for, including research, as it represents a violation of the fundamental human rights and does not respect people. Furthermore it is not unacceptable from an ethical point of view*".

3. Following the news of Dolly the sheep's birth by "cloning", the European Parliamentary Assembly Committee for sciences and technology, in the meeting of the 11th of March 1997 – recalling the fact that *implicitly* article 13 of the Convention on human rights and biomedicine would prohibit the cloning of human beings, including the use of somatic (non-reproductive) cells – invited the President of the Assembly to present this position to the Ministers Committee, so that it would be passed on to the Committee of experts entrusted with drawing up the protocol on the protection of human embryos and foetuses.

4. The European Parliament stresses the condemnation of human cloning in the Resolution of the 12th of March 1997, stating that the "*cloning of human beings – whether experimentally, in the context of fertility treatment, preimplantation diagnosis, tissue transplantation or for any other purposes whatsoever, cannot under any circumstance be justified or tolerated by any society, because it is a serious violation of the human rights, and contrary to the principle of equality of human beings (as it permits a eugenic and racist selection of the human race) it offends against human dignity, and it requires experimentation on humans*". (point B of the Preamble).

Consequently, taking into account that the "*Convention on human rights and biomedicine"* of the Council of Europe (see later) does not clearly forbid the cloning of human beings and – in addition – the Convention is not yet in force, stressed[1]:

a) the right of all individuals to their genetic identity;

b) the need to prohibit human cloning, through an explicit worldwide interdiction;

[1] To improve the understanding of the list of documents, we highlight that the Council of Europe elaborated – through the activity of the Directive Committee for Bioethics (DCB) – a complex "*Convention on the protection of human rights and the dignity of the human being with regards to biology and medicine applications: Convention on human rights and biomedicine"* between 1992-1996, concluding their work on the 19th of November 1996. Article 15-18 of the text makes provisions for regulations on scientific research. Article 18 – dedicated to the research on in vitro embryos – states:

"When research on in vitro embryos is accepted by law, it ensures an adequate protection of the embryo.

The creation of human embryos for research purposes is forbidden."

In this article, as in the others, there's no explicit mention of the problems of cloning.

c) the request to member States to forbid the cloning of human beings at the different stages of their formation and development, without distinction with regards to the method used, and to provide penal sanctions to repress the violation of this law;

d) the request of a spontaneous moratorium for biological and medical researchers waiting for a legal definition of the problems of cloning;

e) the usefulness of biotechnological research in fabricating proteins, drugs and vaccines useful to man, in order to combat some illnesses, the need for the scientific Community and Governments to give to the population correct information about the current state of genetic research;

f) the usefulness for the Commission to draft a European law on the cloning of animals, on the scientific novelties deriving from it, within a rigid control to guarantee human health, the continuity of the species and of animal breeds and to safeguard biological diversity[2].

It requested the spreading of the Resolution to the Commission, to the Council, to the Governments of member States[3], to the General Secretary and the Parliamentary Assembly of the Council of Europe, as well as the General Secretary of the United Nations.

Group of councillors for the ethics of biotechnologies at the European commission

This Organisation, reacting to the request formulated by the European Commission on the 28th of February 1997, discussed and approved an interesting document (Avis) on the 28th of May 1997, prepared by the embryologist A. Mcaren, on the "*Ethical aspects of cloning techniques*".

In the first part, we offer definitions and technical-scientific information.

[2] The Resolution of the 12th of March 1997 contains also other requests, and in particular:

a) a report on eventual research on this issue;
b) verifying of the existence of research programs on the cloning of human beings funded by the European Community and – if there are – stopping their funding;
c) elaborating ethical regulations founded on the respect of human dignity for biologists and biotechnologist-medical researchers;
d) creating an Ethical Committee for the European Union, entrusted with following the ethical aspects of genetic technologies and put together in the outmost transparency and democratic principles.

[3] Even though the Parliament's Resolutions are not binding, the member States have adapted to the European Community regulations, asking national Opinions on cloning from competent organisations (Italy, see NBC's Opinion of the 21st of March 1997; in France Avis of the Ethics National Advisory Committee of the 22nd of April 1997).

1.1 Cloning[4] consists in producing genetically identical organisms, both by embryo splitting so that the nuclear and mitochondrial genes in small number are "identical" between the two resulting embryos, and by nuclear *transfer*, in which case only the nuclear genes are identical. However, as much as genes can undergo mutations or disappear in the course of their development, the initial genetic make-up of the two individuals can become different.

1.2 Sexual reproduction processes generate individuals that are different from a genetic point of view, whilst asexual reproduction (*clonage*) creates identical individuals. This is useful in botany, in agriculture, in veterinary.

Remembering the various experiments carried out so far by nuclear *transfer* in vertebrates (frogs 1952; 1960 etc.), those obtained by embryonic *splitting* in ovines and bovines and then the 1996 experiments by the Edinburgh Group, the Document of the Councillors for ethics in biotechnologies discusses potential applications of animal cloning.

It recognises their usefulness:

a) in the field of medicine and medical research (for the knowledge on acquirable fundamental processes);

b) in the field of transgenic animal breeding (even with the reserve on the uncertainty of the processes relative to the changing of this products).

It identifies a potential risk in the decrease of genetic variability that it produces in breading farms, if extensive.

Finally, it expresses the following opinions on cloning for its implications regarding man:

a) convenience in clearly distinguishing reproductive cloning aimed at obtaining identical individuals (which has never been done so far in man) from non-reproductive cloning, which concerns only the in vitro phase of the embryonic development;

b) convenience in distinguishing the technique of embryonic *splitting* (or fission, or blastomeres fractioning, etc.) from the technique of the *transfer* of a somatic nucleus into a denucleated oocyte: the convenience is in the fact that with this procedure we can prevent the hereditary transmission of mitochondrial illnesses.

The Councillors'Avis believes that this method – for these precise purposes – should be considered within the prohibition of creating

[4] The terms *clonage* (French) and *cloning* (English) of the two official international languages correspond, in fact, to the expression "clonazione", the terms could however be translated also with "clonaggio", intending the practices (modalities) leading to cloning, as the objective of the process.

genetically identical individuals, but as a procedure in itself (although it also presents specific ethical problems).

c) The need to recognise that – at the moment – there is no evidence that embryonic *splitting* offers better results in assisted procreation practices (FIVET). We also have no evidence that this technique was used for human reproduction (from birth).

d) The need to recognise that even monozygotic twins are different and to admit that even cloned individuals would be different from their nuclear donor, because of the different mitochondrial make-up, of the different age, of the different environmental influences, etc.

e) The existence of genetically identical individuals does not raise technical objections in itself (discriminations, etc.); however, there would be objections for the use of embryonic human cells (or nuclei) as donors for the creation of genetically identical individuals.

f) The research on nuclear *transfer* can have important positive therapeutic consequences (the creation of cultures of stem cells for repairing human organs, etc.).

g) The consequences on the eventual use of adult cells as nucleus donors are largely unknown, and this raises questions about the researchers' responsibility towards the "exploitation" of the human being so created.

As a consequence of these evaluations, whilst we express a favourable opinion towards animal cloning (on condition of avoiding or minimising the suffering caused to animals, limiting experiences to cases in which there is no better alternative and operating in favour of maintaining of genetic diversity), with regards to human cloning we offer the following proposals to the European Commission:

a) Avoiding egotistical suggestions, which exploit man and present great uncertainties. Therefore, every attempt of creating a genetically identical human being by nuclear *transfer*, starting with a human cell – adult or from a child – (so called "*reproductive clonage"*) must be prohibited.

b) The abovementioned ethical objections are applicable also to the attempt of obtaining identical embryos in medically assisted fertilisation techniques, both by embryonic *splitting* and by nuclear transfer.

c) Before the event, any attempt at producing many identical individuals by reproductive *clonage* must be considered unacceptable.

d) We must invigilate those Countries in which embryonic research is authorised, so that nuclear *transfer* techniques carried out to clarify the causes of human illnesses or to contribute to the research

aimed at alleviating human suffering, would exclude the re-implantation into the uterus of these modified embryos.

e) The European Community should strongly condemn human reproductive cloning, including it in appropriate texts and regulations as they are being drafted (as for example the decision regarding the adoption of the V framework of research and technological development (1998-2002), and as for example the proposition of directives about legal protection for biotechnological inventions).

The Avis ends recommending the European Commission to promote information and public discussion; as well as highlighting the growing human responsibility in the sectors of biotechnological research and innovation. This stresses the need to boost programs of ethical research in Europe.

The Council of Europe, in the abovementioned Amsterdam Declaration of the 16-17th of June, invited the Commission and the Council to issue a binding law, appealing to the reported Avis, unequivocally condemning reproductive cloning in Europe.

In a recent proposition for a Directive by the Commission for the protection of biotechnological inventions (1/9/1997 in Europe number 7048) it was reaffirmed the non-patentability of human reproductive cloning, of the modification of the germinal genetic identity and of the methods of use of human embryos.

4.2 Council of Europe

Today composed by 40 European States, it has, since the start of its activity, fixed a series of specific guarantees for the protection of individual rights (European Convention on the protection of human rights, 1950).

Being aware of the benefits, but also of the risks, inherent to an unlimited application of the new biomedical sciences, which have radically developed in the last 20 years, and recognising the need for a higher level of protection for the individual, the Council of Europe elaborated a new Convention for the Protection of Human Rights and the Dignity of the Human Being with Regards to Applications of Biology and Medicine (19/11/1996).

This Convention does not expressly sanction the prohibition of human cloning, even though the Parliamentary Assembly had already considered the problem. Recent facts in the news have induced the Committee of Ministers to integrate international laws with regulations ad hoc.

On occasion of the second Summit of the Council of Europe that took place on the 10-11th of October 1997, the Heads of State and Government members of the Council of Europe, in the final Declaration reaffirmed the prohibition of cloning human beings, committing themselves to forbidding any use of cloning techniques finalised to the creation of a human being genetically identical to another, and instructed the Ministers Committee to adopt as soon as possible, for this purpose, an additional Protocol to the Oviedo Convention on Human Rights and Biomedicine.

It is appropriate to recall the activities of the Council of Europe on this issue.

1. The Council of Europe's parliamentary Assembly, in the 1986 Recommendation 1046, regarding the use of human embryos and foetuses for diagnostic, therapeutic, scientific, industrial and commercial purposes, asked the Governments members of the Council of Europe to "*forbid … the creation of identical human beings by cloning or by any other method, whether for race selection purposes or not*" (point 14,4).

2. The ad hoc Committee of experts (CAHBI), entrusted with drawing up a report on artificial procreation techniques, in article 20 of its document (1989) stated that "*the use of artificial procreation techniques for the purpose of creating identical human beings by cloning or any other method, should be forbidden*".

3. The "mandate" of the Council of Europe's Ministers Committee.

The Council of Europe's Committee of Ministers, with mandate number CM/663 of the 14.5.1997, delegated the Bioethics Directive Committee (BIDC) to prepare – in a very short time (30th of June 1997) – an AVIS on the issue of human cloning.

The mandate, as well as indicating the definition of the best methods to create a legal instrument to bind the States, included also a precise, evident direction: to offer an AVIS containing useful elements for an eventual universal declaration binding the States in the direction to prohibiting human cloning, in view of its possible adoption during the Heads of State and Government's second Summit.

4. The AVIS' editing by the B.I.D.C.

The BIDC's Secretariat and Presidency entrusted the editing task to the working Group instituted for the drafting of the protocol on the protection of the human embryo and foetus (BIDC-CO-GT3) according to the *Convention on Human Rights and Biomedicine*, recently approved (19th of November 1996) and open to signing by the European States on the 4th of April 1997.

This method has allowed us, in effect, to draw up, in a short time, a text to present to the BIDC's plenary Meeting, anticipated for the 17-19th of June.

The text proposed three methods to proceed to a Declaration on human cloning:

a) as an additional and specific protocol to the abovementioned Convention

b) as an amendment to the Convention, an additional article

c) as an article to include in an appropriate additional protocol (e.g. the protocol on the embryo) to the Convention.

In view of the fact that variants a) and b) seemed to be the easiest way to adopt, in a short amount of time, the directives to forbid human cloning – requested by the Ministers Committee – whilst variant c) would have required the completion of a protocol regarding an already complex topic, variant a) was opted for, which required that the States that are already signatories of the Convention (21 at the moment) should reconsider the general problem, but only adhere (with the modalities anticipated) to the specific Protocol.

The text prepared by the Secretariat – after having recalled the exploitation of people that would occur with the deliberate creation of genetically identical individuals (even admitting the existence of the natural phenomenon of monozygotic twins), and recognising that such practices are against human dignity, representing also an improper use of biology and medicine – reaffirmed that the object of the Convention on human rights and biomedicine, anticipated the protection of the abovementioned dignity in force of the following text: *"Any intervention aimed a creating genetically identical persons, in the sense of individuals having the same nuclear genes in common, is forbidden"*.

Therefore the proposition was characterised by *prohibiting the objective*, not the means; in *restricting the objective to the person* (which – let's not forget – due to a long tradition in international law, is intended since the moment of birth) and finally (accepting A. McLaren's suggestion), in *limiting the "genetic identity" to the nuclear one.*

The "cover" towards the possible (minimal) variations between the two genetic arrangements that can occur during the embryonic development (as well as later, after birth) was referred to with the expression "group of nuclear genes".

The following articles included in the "Proposition", prohibited the possibility of expressing dispensations or reservations to this article in the Protocol, which was considered as additional to the text of the Convention and towards which all the directives anticipated by the Convention itself, would be applied (except – as specified – dispensations

and reservations). Therefore, even the "most favourable" hypothesis (in this case of stricter restrictions) that the national law could have in place with regards to the use of cloning methods (in any case not destined at creating cloned "children"). During the – very logical – debate that followed the Secretariat's proposition, the text was first reformulated in this way: *"Any direct intervention to create a human being identical to another person, living or dead, in the sense of persons having the same group of nuclear genes, is forbidden"*.

Afterwards, the Italian delegation – followed by the German one, the Austrian one and then others, suggested substituting the expression "person" with "human being". This expression can be found in article 1 of the Convention, within the European Parliament Resolution, and it generally has a wider meaning then "person".

The Secretary, accepting an indicative favourable vote, promoted the following text: *In human reproduction, any intervention having as its purpose the creation of a human being genetically identical to another human being, living or dead, is forbidden.*

In this article, the expression "genetically identical human beings" means "human beings having the same group of nuclear genes".

During the rest of the debate, it was decided (with a majority of 23 votes in favour, 6 against and 3 abstained) to eliminate the parenthesis: "In human reproduction" and to leave to each single State the decision of what meaning to attribute to the concept of "human being".

The final text, unanimously approved, is the following: "*Any intervention having as its objective the creation of a human being genetically identical to another human being, living or dead.*

In this article, the expression genetically identical "human being" means human beings who have the same group of nuclear genes".

A brief comment:

According to the majority, the meaning to be given to the expression "human being" will be decided by the individual national laws, and this certainly represents an incognita for the future.

The "ethical advantages" gained are that – in any case – the concept of human being is the widest that can be identified according to the Convention (therefore it can include in the prohibition a wider number of manipulation possibilities); it does not imply a discussion on the limits to attribute to the concept of *embryo* (including the issue of the "pre-embryo") and finally it is an "intuitive" concept from the point of view of public opinion, very sensitive to the fear that we will arrive at human cloning.

In concrete, introducing the term "human being" should limit the production of human embryos in cloning attempts which – although they were in some way forbidden by the text of the Convention in article 18

(because this article prohibits the creation of embryos for experimental purposes) – would maybe be possible on supernumerary oocytes (that is, destined to constituting embryos for reproductive purposes in assisted procreation techniques), misunderstanding (in a certainly illicit manner) the directive in article 18, attributing such use not "to research purposes" but "to therapeutic purposes" (although different from procreation, which is what the Convention forbids).

In any case, they also rejected the hypothesis (also presented by all delegations) of creating, by cloning, embryos destined to be only *organ banks* for transplant purposes, hypothesising for example the possibility of growing foetuses for a certain amount of time (e.g. up to the IV month) and then "abort" them at a time when they are certainly non-viable (unable to survive outside the uterus) but used for medical purposes, in this way, by-passing the legal concept of person (applied to those born once they are viable).

It remains open – in any case – the possibility (still hypothetical today) of the *nuclear transfer* coming from one of the first blastomeres (obtained by in vitro fertilisation with the gametes of a couple having, for example, already had a child affected by a mitochondrial illness) in a denucleated oocyte for the prevention of mitochondrial illnesses in the infant: a "therapeutic" purpose that was theoretically impossible to prevent, but that in any case involves the "donation" of an oocyte from another woman.

In addition, it is still possible to clone human "cellular" or "tissue lines", for research or therapeutic purposes.

Anyway, in accordance with what already stated in the document by A. McLaren, cloning for modified cellular culture purposes should not lead to the formation of an embryo.

Other suggestions on these issues, anyway, will be given in the Protocol relative to the embryo.

The document elaborated by the National Bioethics Committee last June was successively examined by the Parliamentary Assembly on the 23rd of September 1997, and the Assembly issued Directive number 534, relative to the research and cloning of human embryos, inviting the scientific Community to prevent any type of human cloning and to adhere to the regulations sanctioned by the Convention on Human Rights and Biomedicine and by the additional Protocol being drafted.

The Science and Technology Commission, on its Opinion (document number 7895 of the 23rd of September 1997) and the Legal and Human Rights Commission (document number 7906 of the 23rd of September 1997) both elaborated specific documents stating that human cloning is contrary to the dignity of the human being, as it reduces the individual from subject to object.

4.3 **Documents by world organisations**

Resolution of the World Health Organisation (WHO) on cloning in human reproduction.

The WHO, in the 50th World Assembly on the 14th of May 1997, expressed the following Resolution:

a) It stated that the use of cloning in the reproduction of human beings is not acceptable from an ethical point of view and contrary to the integrity of the human being and of moral.

b) It invited the Director General to take the initiative and clarify and assess the ethical, scientific and social consequences of cloning in human health, consulting (if necessary) other international organisations, governments and professional and scientific associations, and examining the connected legal aspects with the help of competent international Organisations; it also invited the Director General to keep Member States informed in order to support a public debate on these issues and to draft a detailed report on the topic.

Following this invitation, Dr. Hiroshi Nakajima – Director General of the WHO – has prepared and distributed a Rapport on *Cloning, Biomedical Technologies and the Legislative Role of the WHO.*

After a preamble, the Rapport focuses on recent events that have caused apprehension in public opinion.

The Director General appeals to wisdom, I order to avoid acritically and indistinctly condemning those forms of cloning human cellular lines that are usefully employed in the production of monoclonal antibodies for diagnostic and research purposes in illnesses like for example cancer. Equally, it invites us to consider that animal cloning opens the possibility of developing the research on the etiology, diagnosis and therapy of human illnesses. The study of the nuclear *transfer* can lead to a better understanding of the aging process and of the interaction between genetic information in the nucleus and the mitochondria. Having identical genetic organisms allows us to highlight the interactions between genetic and non-genetic factors in the evolution of individuals.

Finally, favourable applications (potentially or partially in force) of animal cloning reside in the use of transgenic animals (in which human genes have been introduced) to obtain tissues, therapeutic substances and, in perspective, even large numbers of transplant organs at a lower cost. This seems positive for human health.

The WHO will work, within its competences, along this “optimistic” line in the near future, despite maintaining the condemnation and the interdiction of human cloning for reproductive purposes.

UNESCO, in the course of drafting the Project of Universal Declaration on the Human Genome and Human Rights during the Meeting of the 22-25th of July 1997 in Paris, inserted, in the text of the international document, an interdiction of human cloning for reproductive purposes.

Article 11 of the project states: *"practices that are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted. States and competent international organisations are invited to cooperate 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"*.

The *Report explicatif* stresses the respect for human rights and states that practices contrary to human dignity must be banned. In addition, it recalls the responsibility of the States and international Organisations with regards to this, as the obligation to cooperate to ensure that the rights and dignity of the human being are respected, had already been accepted by the States in the U.N. Declaration of the World Conference on Human Rights on the 26th of June 1993.

The 1997 Cloning Prohibition Act by the United States of America and the opinion of the National Bioethics Advisory Commission (NBAC).

President Clinton requested an Opinion on the issue of Human Cloning to the National Bioethics Advisory Commission (NBAC), presided by H. Shapiro.

The advisory organ, formed recently, unanimously expressed the opinion *"that it is morally unacceptable for anyone to attempt to create a child with the technology used to create Dolly the sheep"*.

It especially insists on the fact that the use of the technique of *transferring* the somatic nucleus poses great risks for the future child, as well as raising ethical problems of other nature, which are deserving of further discussion.

Therefore, it recommends a moratorium on this issue[5].

However, the National Bioethics Advisory Commission (NBAC) highlights that the new cloning technologies can have great agricultural

[5] In the letter to President Clinton, passing on the requested Report, Prof. H.T. Shapiro highlights how many of these problems can be at least temporarily resolved by a wider public discussion and education on this topic.

In pluralistic and democratic societies, like the American one, this is supported by the following reasons: there is not a universally accepted ethical theory, on these issues, Americans follow various moral and religious perspectives; there are conflicting values; different traditions of thought; tolerance (agreeing to disagree) governs vast areas of national life; and in the context of a consolidated historical tradition, we propend to leave to individual conscience the responsibility of actions that do not damage others and on which there is no moral consensus.

and medical benefits, including the development of therapies for diseases such as cancer, cystic fibrosis, diabetes and the possibility of repairing human tissues. The NBAC concluded that the cloning of DNA, cells, tissues and non-human animals, using somatic cell nuclear transfer and other cloning techniques, is not ethically problematic when conducted in compliance with existing regulations and "guidelines".

Following this opinion, President Clinton proposed a law prohibiting for 5 years the use of somatic cell nuclear *transfer* for the creation of human beings, inviting the NBAC to present a report and an indication of whether such prohibition must be maintained or can be removed after 4 years and 6 months of observation. The proposal ensures that there will be no interferences with the positive activities of cloning in the vegetable and biomedical fields.

President Clinton, agreeing with the NBAC's proposal, in addition:

- reaffirmed the prohibition of assigning federal funds to researchers working on cloning
- invited researchers and doctors who work with private funds to adhere to the moratorium, whilst waiting for a law to come into force
- invited the creation of international laws prohibiting cloning. Great Britain, Denmark, Germany, Australia and Spain have already produced laws prohibiting human cloning, and Italy has produced a three months moratorium by Ministerial Decree, awaiting the conclusions of an especially formed work Committee.

Conclusions

From all of the Documents examined it seems evident:

1) That every cloning episode reported by the press, creates alarmism and a response by international Organisations, which seem increasingly aware of the fact that, with the passing of time and the progress of research, it will be increasingly difficult to prevent human cloning.

The European Parliament's response to the "embryonic fission" (or separation of embryonic blastomeres) cloning experiments carried out by Hill and Coll. (1993) – although practiced on embryos unable to continue in their development, which raised alarm as it highlighted current experiments – was followed by a wider and "organic" response not only by the European Parliament, but by various European States, by the European Commission Committee of experts, by the Council of Europe and by the USA, when the "Dolly case" became known.

2) That the breadth of the “prohibition” is intended in different ways. Whilst all the documents examined forbid the creation of embryos destined to develop until birth (cloning for reproductive purposes), the various proposals elaborated so far tend to leave a margin of freedom – more or less wide – to cloning for the production of therapeutic materials (cells, tissue culture, etc.). This is achieved in the Documents produced so far, despite some considerable ambiguity in the terminology adopted.

DOCUMENTS

Comunità Europee

a) Resolution du Parlement Europeen sur le clonage (B4 0209,0213,0214) (adopté le 12 mars 1997).

b) Dichiarazione del Consiglio europeo sul divieto di clonazione (Allegato IV-Conclusioni Presidenza, Amsterdam 16 giugno 1997).

c) Avis du Groupe de Conseillers pour l'Ethique de la biotechnologie auprès de la Commission Européenne.

Consiglio d'Europa

a) II° Summit: du Conseil de l'Europe — Strasbourg 11 ottobre 1997. Declaration Finale.

b) Comite directeur pour la bioethique (CDBI) — Avis sur le clonage humain du 19 juin 1997.

c) Projet de Protocole additionel à la Convention pour la protection des droits de l'homme et de la dignité de l'être humain à l'égard des applications de la biologie et de la médecine, portant interdiction du clonage d' êtres humains (1-4 juillet 1997).

d) Assemblée parlementaire 23 settembre 1997, Avis n. 202 (1997).

e) Rapport sur l'interdition du clonage d'être humains doc. n. 7895 de la Commission de la science et de la tecnologie.

f) AVIS sur le projet de Protocol additional 12 settembre 1997 doc. n. 7906 della Commission des questions juridiques et des droits de l'homme.

g) Directive n. 534 (1997) relative à la recherche et au clonage d'êtres humains (23 septembre 1997).

OMS

h) Resolution de la Cinquantieme Assemblee Mondiale de la Santé «Le clonage dan la reproduction humaine» (14 mai 1997).

Council of Europe
Conseil de l'Europe

Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings

Protocole additionnel à la Convention pour la protection des Droits de l'Homme et de le dignité de l'être humain à l'égard des applications de la biologie et de la médecine, portant interdiction du clonage d'êtres humains

Provisional edition/Edition provisoire

The member States of the Council of Europe, the other States and the European Community Signatories to this Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine.

Noting scientific developments in the field of mammal cloning, particularly through embryo splitting and nuclear transfer;

Mindful of the progress that some cloning techniques themselves may bring to scientific knowledge and its medical application;

Considering that the cloning of human beings may become a technical possibility;

Having noted that embryo splitting may occur naturally and sometimes result in the birth of genetically identical twins;

Considering however that the instrumentalisation of human beings through the deliberate creation of genetically identical human beings is contrary to human dignity and thus constitutes a misuse of biology and medicine;

Considering also the serious difficulties of a medical, psychological and social nature that such a deliberate biomedical practice might imply for all the individuals involved;

Considering the purpose of the Convention on Human Rights and Biomedicine, in particular the principle mentioned in Article 1 aiming to protect the dignity and identity of all human beings,

Have agreed as follows:

Article 1

1. Any intervention seeking to create a human being genetically identical to another human being, whether living or dead, is prohibited.

2. For the purpose of this article, the term human being «genetically identical» to another human being means a human being means sharing with another the same nuclear gene set.

Article 2

No derogation from the provisions of this Protocol shall be made under Article 26, paragraph 1, of the Convention.

Article 3

As between the Parties, the provisions of Articles 1 and 2 of this Protocol shall be regarded as additional articles to the Convention and all the provisions of the Convention shall apply accordingly.

Article 4

This Protocol shall be open for signature by Signatories to the Convention. It is subject to ratification, acceptance or approval. A Signatory may not ratify, accept or approve this Protocol unless it has previously or simultaneously ratified, accepted or approved the Convention. Instruments of ratification, acceptance or approval shall be deposited with the Secretary General of the Council of Europe.

Article 5

1. This Protocol shall enter into force on the first day of the month following the expiration of a period of three months after the date on which five States, including at least four member States of the Council of Europe, have expressed their consent to be bound by the Protocol in accordance with the provisions of Article 4.

2. In respect of any Signatory which subsequently expresses its consent to be bound by it, the Protocol shall enter into force on the first day of the month following the expiration of a period of three months after the date of the deposit of the instrument of ratification, acceptance or approval.

Article 6

1. After the entry into force of this Protocol, any State which has acceded to the Convention may also accede to this Protocol.

2. Accession shall be effected by the deposit with the Secretary General of the Council of Europe of an instrument of accession which shall take effect on the first day of the month following the expiration of a period of three months after the date of its deposit.

Article 7

1. Any Party may at any time denounce this Protocol by means of a notification addressed to the Secretary General of the Council of Europe.

2. Such denunciation shall become effective on the first day of the month following the expiration of a period of three months after the date of receipt of such notification by the Secretary General.

Article 8

The Secretary General of the Council of Europe shall notify the member States of the Council of Europe, the European Community, any Signatory, any Party and any other State which has been invited to accede to the Convention of:

a) any signature;

b) the deposit of any instrument of ratification, acceptance, approval or accession;

c) any date of entry into force of this Protocol in accordance with Articles 5 and 6;

d) any other act, notification or communication relating to this Protocol.

2. In respect of any Signatory which subsequently expresses its consent to be bound by it, the Protocol shall enter into force on the first day of the month following the expiration of a period of three months after the date of the deposit of the instrument of ratification, acceptance or approval.

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b) the deposit of any instrument of ratification, acceptance, approval or accession;

c) any date of entry into force of this Protocol in accordance with Articles 5 and 6;

d) any other act, notification or communication relating to this Protocol.

In witness whereof the undersigned, being authorised thereto, have signed this Protocol.

Done at Paris, this 12, day of January 1998, in English and French, both texts being equally authentic, in a single copy which shall be deposited in the archives of the Council of Europe. The Secretary General of the Council of Europe, shall transmit certified copies to each member State of the Council of Europe, to the non-member States which have participated in the elaboration of this Protocol, to any State invited to accede to the Convention and to the European Community.

5. HYPOTHESIS OF HUMAN CLONING

5.1 Trends and psychological considerations

We could say that recent developments in the field of genetic research on cloning, have brought to the fore again the old controversy between nature and environment in determining individual identity, a controversy that was somehow waning in favour of a continuous interaction individual-environment since the reproduction of the first asexual cell.

This relational point of view was strengthening within biological circles and, less so, clinical circles, when Dolly the sheep was revealed (Wilmut and Campbell, 1997) and, with it, the information that, in the last few years, animal research has been carried out with the purpose of obtaining genetically modified cellular lines to use in splicing and transplants.

The success of the Edinburgh cloning experiments conducted on the differentiated cells of an adult sheep, which quickly reached public opinion, raised the most diverse reactions. Facing the technical possibility of a practically unlimited reproduction of "equal" individuals starting with non-germ cells from adult subjects, the European Parliament, as reported elsewhere in this document, stressed its "firm conviction" that "the cloning of human beings cannot be absolutely justified or tolerated by society". Even religious institutions have expressed the preoccupation that every discovery that touches human procreation does not only involve the body but also the spirit, as man is one and mortal, and his uniqueness is at the basis of human dignity.

Public opinion's response, amply informed, has been of a very varied nature and information has not impeded, in many cases, an identity crisis. In fact, the problem in many people's mind is whether there can be in the world a being like another, in the sense of a conform copy. This issue raised a first question with regards to the positivity or not of this new situation, and another question regarding, instead, the issue of the specificity of a person's development, of the freedom of autonomous determination, and of the possibility of free will.

The psychological consideration, in these circumstances, is if and how a person is influenced by knowing that they are not an individual in themselves, but that they are instead in some way another person's duplicate, in the sense of a conform copy. In other words, the possible

psychological state of a cloned individual. Could it not be better? A sort of empathy could develop between the cloned individual and his alter ego, or instead he could develop a strong defence of his own uniqueness, of the loved ones with whom the individual grew up, a protection of himself as a person generated and loved from birth as himself, an entity that cannot be confused with any other in the world, and therefore not prepared to live in another's shadow.

As we have said, the idea of cloning can lead to an identity crisis. The idea of violating human rights and the possibility of accomplishing our own development autonomously, as its our individual right, so that we can look at the world from our personal point of view and we can live in it as such, is felt as a challenge, and is the source of serious worries. In this perspective we defend the uniqueness of the human being and his individuality, and we don't accept the existence of duplicates, because of the risk of losing man's right to his own dignity. An example of this point of view can be represented by a mother who would never want a cloned son because she knows that he will not be the same one she lost, and she wants to reserve her unique and unrepeatable love for the child who died, and there could be instead another mother who lost a child and asks to be able to have a conform copy who will be able to fill, in her words, her sense of loss.

We recall here the great theme of genetics and of identity, which we take into consideration through the development and the progressive processes of identification.

In what measure is the individual the son of the parents who have generated him, and in what measure is he the son of the environment and culture in which he lives? Even assuming that he was able to internalise his parents as models, it is not sure whether the process of identification with his parents would always be positive, having to take into account the "psychic-affective metabolism" and the experiences relative to the environment which are personal to the individual, and his defence mechanisms. Therefore, how much individual identity depends on the parents and how much on the environment, as said, is today more than ever under discussion.

It is now clear that the mind's development seems to be influenced by the first environment in life, especially in the first year, much more than by the genetic make-up.

Amongst the research in this field, there is a study carried out conjunctly by Kansas University and Alaska University (Herald Tribune, 18th of April 1997) from which we learn that the number of words we tell a child in his first infancy during the day, by persons who are emotionally connected to him (therefore not Radio or TV), is the most important

indicator of what will be his future intelligence, his academic success and his social competence.

In addition, it has been known for more than 50 years (Bakwin, 1942, Spitz 1945, Bowlby 1950) that there is a strong relationship between care and mental development, and in particular it is well known the influence that language has on the development of a child's mind when used to address him during his first infancy.

The problem of the relationship between genetic and environment, between gene and meme, is complex, and continually evolving. With regards to Bioethics, which also includes clinical ethics, it is evident that it will have to be considered at all times, it will have to be an integral part of science at critical times like now, and it will have to act in complete transparency and with continuous exchanges of points of view. Science moves fast, along a path that can seem promising and that therefore can easily seduce, particularly when one can be reborn or, at least, be reborn through their offspring, even if cloned. An example of this are those who, after having faced numerous reproductive incidents (prolonged sterility, abortions, still born, children affected by malformations or metabolic genetic errors) animated by narcissistic fantasies, would like a child to use as organ donor for his relatives, or "just a made-to-measure son" or those who think of selecting individuals for eugenic purposes. Genetic experiments on animals – the only ones legally allowed at the moment – are rapidly advancing. Knowing that cardio-circulatory problems, which today are the most frequent cause of death for adult individuals, could be reduced in their atheromatous component, introducing genes that attenuate the hardening of arteries through the use of specifically implanted ad hoc viruses, cannot but influence the imagination of those individuals who are at risk and, in the long term, affect culture and public opinion.

In addition, culture has been changing for a while, and in many of our patients the desire of protecting their uniqueness has been substituted by the tendency to assume an imitative identity (Gaddini E. 1984). This becomes evident in psychoanalysis, where an imitative *transfer* has taken the place of known defence mechanisms which are, usually, part of the *transfer* in the analytical process, which we were used to in the past[6]. The imitation of the individual who is looking for his form during the analysis is now being extended to culture.

Particularly serious events, which can pass unnoticed, can today reveal the spreading of a new pathology that can rarely be the object of

[6] The patient now tends to be the analyst and to oppose any movement in the direction of the object (which means environment and therefore growth) still raising in the analyst, thanks to the particular characteristics of imitative learning, the feeling that there have been qualitatively objective transformations in the analytical relationship.

attention. With a more in depth study, we then discover that this new form of psychopathology is very different from the past, and identifying it and, most of all, treating it, requires a high level of diagnostic refinement. The change regards not only patients, but also analysts, who are now in the position of having to be able to focus on the very first stages of life, and on the establishment of the very first objective relationships. The always present terror of madness as the end of the world, often found in imitators, in fact comes from the time in which thought has not yet matured and a lack – any lack – is seen as a catastrophe or even death.

Even in ancient times, observations were made about the tendency to be completely self-contained and to avoid the external world, of which Ovid's poetic work is a famous example. (Year 8 D.C.) In his "Metamorphosis" Ovid described the "baby Narcissus" who, because of the "unusual love" for his own image reflected in the clear water of Rhamnusia "… Flat on the ground, he contemplates two stars, his eyes, and his hair, … he gazes at that false image with unsated eyes, and loses himself in his own vision".

Narcissus, according to the myth, avoided the environment because of his love for himself "… he does not have eyes for any other but for himself, who he madly loves" Ovid says.

More recently many people have noticed the tendency of avoiding the external world and of hiding within an imitative identity as early defence. With this evasion however, we lose the possibility of building our own autonomous identity through processes of internalisation and introjection, and to reach in this way a mature identity. Imitation, which almost "by magic" takes the place of a long and complex process of identification is, in this perspective, seen as an early defence against anxiety and fear, and leads to the assumption of an imitative identity.

On its own it does not allow internalising, because it does not allow us to conceive an external object: imitating, we magically "become" what, otherwise, should be recognised as an external object. As it does not allow internalising, imitation is not a structural defence.

Originally in fact, it is an elementary defence protecting the self. Introjection instead implies the ability to recognise the object as external, the self separated from the object, and therefore the primitive dynamic of eating or being eaten. We introject instead of incorporating in order to make what is outside of us, a part of us. Even introjection is therefore a magical and primitive defence, but its omnipotence is limited by the anxiety of forever losing the object, after having incorporated it, and of not being able to survive without the object (which is the first to appear in the sense of a real dependence). Therefore we should distinguish between two types of omnipotence: with the first, total, we escape the instinctual anxiety by magically becoming the object; with the second, pulsional and

magically more limited, we are obliged to recognise the object and to face the anxiety of a real dependence for their survival". (Gaddini E. 1984, point 4 p. 648).

We can understand how, in a culture where what reigns is the fear of not fulfilling televised myths (and not only) and the anxiety of losing oneself, cloning, with which we can achieve maximum imitation, can find a place as a defensive solution.

On the other hand, any discovery involving the formation of a (human) person does not only affect our body but also our psyche, and it represents a risk to our authenticity and uniqueness.

Many highlight that the entire individual identity, deriving only partially from genetic identity, must be protected, safeguarding its characteristics of uniqueness, which must be intended as the right each of us has to live our experiences for the first time and originally, and to become ourselves in the encounter with our life, of which there is not an already known paradigm. There is however a difference if we talk about genetic identity or entire individual identity. In the first case the term "moral legitimacy", used with regards to cloning, (see the text by Agazzi, Sgreccia and Cattorini, 10-12th September '97) is admissible. It is not the same if we talk about individual identity in the wider sense where, next to genetic factors, the process of development and maturity comes into play, regulated not only by conscious thought but also, in great part, by unconscious fantasies, for which reason and rules don't matter, especially when we deal with the identification and the construction of our individual identity. Even the development of the (sense of) Self, which is the centre of the person and, therefore, the localisation of this Self, in the child can happen much later of what we tend to believe if we think about identity in purely genetic terms[7].

We can also often notice that whilst a conscious element of the person hopes to achieve an individual identity and to defend its uniqueness, at the same time another element can hope for the opposite, as differentiation, detachment and autonomy have a high price, like the renunciation to a symbiosis with the mother, of whom, at least at the beginning, we want to be clones.

It is a series of subliminal recordings which, without reaching the consciousness of the individual, become more or less part of him, on the basis of the genetic make-up but also of the infinite number of events that his encounter with the environment promotes in terms of early

[7] It is well known the case of a patient (Winnicot 1945) who only in analysis realised that for all of her first year of life and even later, had been convinced that her twin, who slept on the other side of the crib, was herself. Therefore, she was surprised when her twin was picked up and she (herself) remained where she was. Her sense of herself, and of other-from-self, in the first infancy was not, in this child, developed in any way.

occurrences and experiences, which we know are decisive in the creation of an individual and personal identity.

If we take into account the infinite multifactoriality concurring to typify individual identity, and the many shades of correlation between genetic and nurtured from which derive the conditions that come together to defend or compromise its uniqueness, it seems appropriate that, in discussing these difficult issues, we maintain a flexibility of thought, admitting the possibility of moving in the world of hypothesis and of trying, in some way, to foresee the future.

In closing, we can briefly mention a clinical case as example of a specific method of clinical psychology applied to bioethics and as an illustration of what we have been saying. The patient read something on cloning and talks about it. “I have always wanted to have a twin, and I am convinced that if I had had an identical twin, a clone to support me, I would not have had to face so many fears, and I would have moved in the world much better. I could have studied a subject, and then presented myself twice to the exam, once for me and once for my sister. She could have done the same for another exam, so that the subjects would have been halved. Having a person like me reassures me. Also, I have heard talk of an understanding, a secret language between twins.

Growing alone is an unsustainable enterprise, I have always asked my mother to give me at least a sister. “It does not come” she answered. “Then buy her” I said. Why I have always felt guilty being an only child, is not clear. Maybe because when you say that you are an only child they look at you strangely, and I can’t bear it. When I go out with someone, the first thing I ask is whether there are twins in his family. I think about Bonny and Clyde and about how strong they were. Complicity helps. How I wanted, as I child, someone who would support me even in my naughty enterprises, who would be my accomplice even in my troubles! G. (current partner) supports me in front of others. Even if I say something wrong, he is always on my side. I have finally found my “clone”.

5.2 A legal point of view

Human cloning as voluntary activity characterised by a typical purpose

Human cloning, which from now on will be always intended in the specific sense of the cloning of a human being (*total direct cloning* and then paragraphs 6-5, *total indirect cloning*) and not as the cloning of particular components of his physical or genetic constitution (*partial indirect cloning*), does not interest the law in itself, that is, as a

phenomenon characterised by the genetic identity of two or more living organisms coming from the same progenitor or by the genetic identity of the generated and of the generating living organism. This phenomenon also does not interest the law as the outcome of a process occurring spontaneously (assuming that, relatively to man, it can be objectively verified). Instead, legally significant cloning is the consequence of a human intervention specifically aimed at achieving the particular reproductive result that characterises it. Therefore, this interests the law, not as a fact, but as activity carried out to achieve that fact.

However we must add, in apparent contradiction with what just stated, that the activity of cloning does not interest the law for the technical specificity distinguishing one or the other of its two forms, but it interests the law as it can be identified as a typical activity that, independently from its particular, intrinsic technical characteristics, despite, that is, being an activity aimed at achieving a process of embryonic fission or an intervention of nuclear transplant, it appears in both cases, as an activity aimed at creating beings mutually linked by their identity, both horizontally and vertically, producing what biologists properly call a "clone". In short, cloning is considered by the law only because of it typical purpose, inherent to all its various forms and not for the peculiarity of the specific forms of each of these methods.

Being aware of the difference between the two cloning techniques is naturally relevant for the jurist, however not on principle, but as fact. It can be in some way relevant knowing, for example, that one (embryonic fission), for its rudimentary character, is less useful than the other for the purpose of producing a large number of living organisms with identical characteristics to another, pre-existing or co-existing, living being; or even knowing that one (embryonic fission) can happen spontaneously as well as non-spontaneously, whilst the other (cloning by nuclear transplant) can only happen following a determining human intervention aimed at producing living beings with the abovementioned characteristics. But this knowledge does not affect the essential aspects of that particular reproductive activity called cloning: that it is *voluntary* and has a specific *purpose*, which the law uses to identify the structural aspects of cloning.

Human cloning as reproductive activity considered illicit by the generalities of the law

Once we have identified the more abstract aspects making human cloning legally relevant, we must, in order to completely define it and

assess it, expose it to the light of conceptual and positive categories more concrete than the ones used so far.

In this second perspective, human cloning can be legally relevant for being a particular activity that, together with others of a different form, is aimed at reproductive purposes.

Seen in this perspective, cloning has a subjective meaning. Within this, in fact, cloning stands out as an activity that can be attributed to an individual, alone or, eventually, in agreement with another subject, based on the interest of that only subject (or the two subjects) to reproduce with one of the cloning methods, and with the effects that are characteristics of its proper nature. Therefore, from this point of view we have the problem of legally qualifying the nature of the interest that a physical person x can eventually show towards reproduction, his own or another's, as that interest intends to be satisfied by recurring to cloning techniques.

Consequently, the question that first arises from the need to assess the eventual existence and consistence of an imaginary right to give birth to a human clone (to be cloned, to obtain that somebody is cloned), does not seem different from that which is typical of any form of human reproductive activity. Towards each of this forms, more and more fluid and numerous because of the progress of reproductive technologies, we ask in fact if, as the existence of an inviolable right of man to reproduce is generally accepted, such a right is so comprehensive that includes any form of human reproduction and, therefore, also the form of reproduction n+1, unknown and impracticable until recently.

So, keeping ourselves to simply considering facts, we must accept that, even if the question raised by the possibility of a hypothetic activity of human cloning is not different from the question that could arise with regards to any other form of assisted procreation, the answer given to such a question by a variety of positive legal pronouncements shows the characteristics that make it profoundly different from the answer generally given to others. If, in fact, we explore the normative formulae chosen to qualify acts of assisted procreation, we face a situation of this type. Of some acts, those that can be called of *general assisted procreation* (homologous and heterologous assisted procreation), the various legal ordinances offer a largely common positive assessment; others, those that can be called of *special assisted procreation* (assisted procreation of a single woman, of a woman of non-fertile age, procreation for others), they offer, instead, largely different assessments where such acts are sometimes generally rejected, sometimes partially accepted and partially rejected, sometimes, finally, are almost completely accepted. So that we can say that acts of special assisted procreation are not generally accepted in legal pronouncements, but we cannot say that they are the

object of negative assessments at the same time general and convergent in such pronouncements.

With regards to human cloning, which can also be considered as an additional special form of the assisted reproduction, we can observe, instead, that legal pronouncements, when discussing it, have consistently presented a negative assessment and they have consequently declared, in a generalised manner, its legal illegitimacy and its punishability, almost as if such an activity has characteristics preventing them from finding, in addition to the positive aspects and to the non-negative aspects already mentioned, also a negative aspect, never or almost never reached in the topic under discussion.

This is, we were saying, a common negative attitude which needs, first of all, to be simply contested. In a wider problematic perspective it certainly cannot be pointed out as the cause of the negative convergence between legal pronouncements; on the contrary, the fact that legal pronouncements have felt them to be so persuasive that they accepted them, is certainly the effect of one or more causes. Therefore, in a wider perspective, this attitude leads to an unequivocal solicitation to find and analyse the roots of its causes. So that we need to focus our attention, although concisely, on identifying these causes.

Interests of the subject requesting cloning, interests of the cloned, interests of the law: an abstract schematisation of their relationship

First of all, it is a fact, as we were saying, that human reproduction by cloning is not generally considered licit by law.

To this we can add another point, the significance of which certainly exceeds mere factuality, the point according to which the negative legal qualification of the future use of human cloning is also pretty much shared by the bioethical regulations on the issue of technically assisted procreation; where we find a bioethically positive assessment of the negative legal assessment found in the law. Even those most inclined to widen the applicative horizon of the primary right of man to reproduce. In fact, they avoid stating that it also includes the right to create a “clone” (to clone oneself or, eventually, to clone “some” others) and agree, not less than others, with national directives and the points of view sometimes adopted by supranational authorities of various nature, which consider illicit, according to the penal law, the activity of human cloning.

Therefore, both the commonly expressed negative assessment of human cloning by law, and the general agreement to it in bioethics, as well as, finally, the penalistic forms through which such an assessment is

manifested in the legal sphere, seem to come from a special significance. All these elements, in fact, shed light on the entire internal structure of the activity of human cloning, which makes it possible to try and identify individual and collective interests measuring against each other should someone, hypothetically, expect to create a clone, to try and grasp the legal consistency, absolute and relative, of each of them (the interest of the cloning or of the individual requesting a human cloning, the interest of the cloned) and, finally, to try and verify if cloning also involves essential values of constitutional law that cannot be linked to any of the interests belonging to the first two.

With regards to this we can observe, proposing for the moment a still abstract reflection, that relatively to the expectation of reproducing by cloning that can be eventually put forward by a physical person, and even more, relatively to the expectation by the same person that others, close to him, are reproduced by cloning, the law, in forbidding and sanctioning by penal law the actualisation of such an expectation, implicitly illustrate at least three main mutually linked evaluations.

The first and central evaluation refers to the interests of the hypothetical clone. This, despite his typical identity (son of the requesting individual, son of the son of the requesting individual, or other), would come to life as a subject already devoid of some inviolable rights, that is, as a subject who, for the intrinsic necessity of the activity of cloning, would be born without essential constitutional rights which, by law, no man can be deprived of. Therefore the cloned, would embody the irreconcilable contradiction between the legal statute he represents and the statute that, according to the constitution (and according to concurring pronouncements by now numerous in international documents on the issue of human cloning in the last decade), must identify every man: human cloning would exemplify the hypothesis, devoid of constitutional citizenship, of a legal pronouncement that could happen only at the cost of violating rights that have been proclaimed constitutionally inviolable. In a typical situation like the one presented, it is, therefore, understandable that established legal pronouncements defend, with the instruments offered by penal law, the interest of the hypothetical cloned subject, not only to protect him, but also to protect the interest of the law itself. Protecting the interests of the cloned subject, in effect, legal pronouncements also protect some of their own interests.

The second evaluation implicitly illustrated by the legal pronouncements regards the interests of the subject requesting the cloning. These can be evaluated in themselves, or in relation to the interests of the cloned subject. From the first point of view, the interests

under consideration can be evaluated in a variety of ways, and could even be considered banal by law and, as such indifferent, or insignificant or even, in some ways, considerable. From the second point of view they reveal, instead, those interests that can be realised only by a necessary violation of contrasting interests like, as we have just demonstrated, those that are a part of every person and of the constitutional pronouncement intended as a whole.

Further considerations on the first and second type of reflection allows, therefore, to observe: that the interests of the first are taken into account by the legal pronouncements as important in themselves, essential for the law overall, and prevalent towards the counter-interests of the subject requesting the cloning; that the interest of the second type are considered, by those same legal pronouncements, as not very significant in themselves, indifferent for the law and, most of all, not comparable to the very high value of the interests that they should necessarily sacrify.

There is, then, the third evaluation carried out by legal pronouncements, which can also be deduced only indirectly, but not for this less clearly, from them. It concerns the obvious violation, which would occur because of the cloning of human beings, of the fundamental values expressed by the law. The law, that is, appears involved in that activity, not only because it incorporates some of the irrefutable rights of the cloned individual, and identifies with them, as we have already observed, but also because it contravenes some of the principles that more profoundly characterise its structure, which do not coincide with the fundamental rights of the cloned individual, but are no less called negatively into question in connection with the violation of those subjective rights.

The interests that are engaged in making up the internal structure of the laws on cloning, are, therefore, mutually interconnected by law according to a rigidly hierarchical criterion, neatly subordinating the interests of the individual requesting the creation of a “clone” to those of the hypothetical “cloned” individual and of the law itself.

It is then the particular configuration of the relationship between those interests that, according to the law, characterises the structure of cloning, and differentiates it from other methods of special assisted human procreation. In those methods, in fact, although the subjective interest to reproduce is not so strong that it always prevails, according to more balanced positions, because of the conflicting interests of an individual or collective nature, at the same time it is not so feeble in comparison to them, that uniformly leads the law towards decreeing the prohibition of its realisation.

It is legitimate, therefore, at this point, to state that any activity carried out for the purpose of creating human "clones", for all the reasons we have discussed, has an internal equilibrium involving absolutely particular axiological peculiarities, which cannot be found in any other method of technological assisted procreation.

Particular analysis of the interests, subjective and objective, involved in an eventual activity of human cloning

The previous considerations have been carried our following a still abstract comparison between the various interests within the structure of the procreation by cloning. A further approach to the theme under consideration, that wants to be the concrete and almost necessary development of the somewhat abstract previous considerations, is pushed by the need to identify in concrete and to denominate the various interests that characterise in a rigidly hierarchical and dialectical sense the structure of the activity of cloning. It is possible to consider these mutually connected interests according to a relationship of reciprocal exclusion, both in the sense that the realisation of some is not compatible with the protection of the others, because of the impossibility of bringing together the first and the second within the logic of a mutual equilibrium, and in the more specific sense that the realisation of those interests that are axiologically more feeble and historically stronger, that is, the interests of the subject requesting the start of a cloning process (who are responsible for its beginning), would imply the de-realisation of the interests that are axiologically stronger and, hypothetically, historically more feeble, contrasting the first.

In quick succession, therefore, we intend to present the three categories of interests involved in the activity of human cloning, starting with those that would push for it to begin. These are the interests of the subject requesting the cloning (the cloning individual or other subject) and of the legal values corresponding to this, less frequently explored and therefore less known than others; of the interests attributed to the hypothetical cloned subject, linked to the inviolable rights taken into account, which should however be institutionally sacrificed because of cloning; and, finally, of the constitutional values which would also be institutionally weakened because of carrying out reproductive processes using cloning techniques.

A) Values attributed to the interest of those requesting the cloning

- In this category we seem to have to identify some main subcategories, to be built on the basis of two main coordinates: those of the nature of the subject requesting the cloning, depending on whether it is a physical person or a public authority; that distinguishing the activity of cloning, depending on whether it is suggested for oneself or for others. The construction of different subcategories can facilitate the identification of the reasons (of the interests) at the basis of the cloning request.

It is widely believed that there is a minimal common denominator connecting all species of interest, individual and public, to the creation of "clones", which is to immortalise someone, oneself or another. However, this not only assumes characteristics and meanings that are very different in each of the typical cloning requests here hypothesised, according to whether they can be considered an "egotistical" or an "altruistic" cloning, but it does not succeed, in any of these two perspectives, to overcome the intrinsic fragility of the interest to create a human "clone".

A1) Physical persons requesting the cloning for themselves, (right to impotence)

In this typical subcategory, possibly the most unrealistic, the interest to cloning is closer, more than in all the other hypothesis, to the interest that, in its pure state, supports cloning requests: the desire to survive ourselves, to become eternal, which we think of satisfying, instead than in other ways, by opening up to a sort of delirium of omnipotence, of personal megalomania. It is also the hypothesis in which the interest of the cloning individual obscures the interest of the cloned most, who, in the intention of the first, should re-enact with his existence the value and the actions of his "creator".

A2) Physical persons requesting the cloning of others (right to cloning)

The subcategory proposed in the title corresponds, instead, to an hypothesis less unrealistic than the first, which is more easily evoked in discussions about cloning: the desire of not losing a loved one definitively, whoever that might be, of having him/her live again in another, who will be at the same time, the same and different from the first. In this hypothesis, the desire to remember prompts the wish to recreate the remembered person is the nucleus of the interest of the individual requesting the cloning. This individual, therefore, is completely separate from the will of the cloning subject, as well as,

naturally, of the cloned subject; it is the link between two people and their lives, assuming, in this way, a superior role to that of each of them, almost as regulator of their destinies.

A3) Institutions requesting the cloning of a person (right to glorification)

In this hypothesis, cloning is a need of perpetuating symbolic characters, who have dominated, because of their intelligence, their beauty, their moral or political authority. In this hypothesis, the interest behind the request or the direct realisation of the cloning is directly in the social or political interest of the requesting institution, which tries to use it in favour of its power, also in this case in contrast with the will of the subjects having a cloning relationship. In addition, this interest assumes, more than in the other hypothesis, eugenic, idolatric, and potentially racist connotations, which must be added to the intrinsically discriminatory value (cloning reserved for great men) which constitutes its most evident distinctive trait.

None of these interests and of the three hypothetical rights which could be imaginatively linked to them, seems to deserve legal protection; all of them, instead, are irreconcilably in contrast with other interests, individual and social, not only non-disposable, but also non-renounceable, both by the individual and by society as a whole.

However, some situations in which the interest of the individual requesting the cloning is not presented in its pure state, that is, as the expression of a desire of becoming eternal that is expressed in direct forms, living and not symbolic, are left out of the picture presented, and without a doubt deserve particular and more problematic considerations. In fact, such an interest is eclipsed in those situations, overcome by different interests of a more significant constitutional value, which completely qualify the request of reproducing by cloning.

These situations and the more evident balance between the contrasting interests of those requesting the cloning and those enduring it, which represents its most distinguishing trait, will be discussed later. Their existence however allows us to observe how the interests overcome by the eventual requests of human cloning cannot be appreciated by the law for what they mean in themselves, but, hypothetically, only when their level of appreciation undergoes a growth due to their imbrication with constitutionally stronger interests, through which it becomes possible to see cloning not as an end, but as a mean that can be eventually used to protect them.

B) Interests of the hypothetical clones and the constitutional rights protecting them

The interests of the clone are much more known than the interests of the cloning individual and, in contrast to those of the subject requesting the cloning, have value in themselves, as constituting his identity, and not because of the effect of their occasional amalgamation with interests of other, superior, nature.

Here, we want to analyse both in absolute, considering them in themselves, and in relation to the interests of the subject requesting the start of a process of human cloning in some of the perspectives that have been briefly presented.

We often talk, commonly, in moral science and, naturally, in the various conventions, resolutions and recommendations on bioethics adopted by various international bodies, of every man's right to genetic identity, especially in its important meaning of his right to genetic diversity, of his right to respect for his moral dignity and in particular to respect for his right of ignorance of his own future, of every individual right to not be genetically discriminated against, to not be subjected to genetic selection practices, etc.

Here we need to see how the assertion of such solemn rights can be corroborated by statements that can be deduced by the Italian constitutional charter, considering that in it, those rights are not explicitly enunciated, but that, despite this, it must be considered as the only positive source of all of man's inviolable rights. The hypothesis of work taken as guide for this reading was that the issue of human cloning raises problems which are all centred on the identity of the cloned. First of all, naturally, the physical identity-diversity, as the activity of cloning has as its object and purpose that of intervening on itself; but, then, also his other identities, symbolic personal identity, collective (associative) and general (that is, political) identities, in which personal identity is destined to flow. It seems difficult to deny that symbolic identities are joined to the first through the same line of identities, although any expectation to suggest statements relative to the way in which the different aspects of this line are mutually linked, is far from the spirit of this reflection.

The rights of the hypothetical cloned in the absolute perspective.

B1) The right to physical identity-diversity and, therefore, to genetic identity-diversity and its derivation from various constitutional directives (articles 2, 3, 24)

It is known that the right to identity, although not explicitly enunciated in the constitution can, however, be derived from more than

one of its directives. However, what we are most interested in here is not our right to a symbolic identity (moral, scientific, political, etc.), of which legal literature, public and private, as well as jurisprudence, constitutional and ordinary, are increasingly more interested in with the passing of time, ascribing it to the growingly crowded category of personal rights. In fact, the issue of human cloning involves primarily physical identity, and in particular every man's genetic identity, which cannot be tackled with the same dogmatic systems with which we tackle the issue of the symbolic identity of the same man and we try and respond to his problems.

Therefore, here we will essentially look at the first issue, the physical identity-diversity, which until today seemed unproblematic. Instead, we will deal with the other issue, the symbolic identity, only indirectly, that is, relatively to the less contestable aspects that the negation of the first seems to have on the second.

The protection of each person's singularity, even physical (and therefore also genetic), must be necessarily assumed, for example, by the protection of the inviolable rights of man which, according to article 2, has its roots in it. The famous directive of principle in the cited article is built, in fact, on the tension of two opposites, that of every person's singularity-diversity and that of the generalisation of all the rights of all the single-different persons, without which the constitutional concept of man cannot even be identified, that is, "inviolable rights". The person protected by the constitution is, therefore, one to which all inviolable rights are attributed, as to all others. If, therefore, the right to genetic identity is an inviolable right, then the hypothetical clone would be denied it, in violation with the abovementioned principle. But is it an inviolable right? Until now it has not been taken into consideration, even implicitly, in the various catalogues of rights of that nature which have been elaborated (the so-called new rights). In effect, it seems that we must consider this to be a result of the circumstances according to which the genetic identity-diversity has been until today considered as undisputable on the one hand, a simple premise of the exercise of inviolable rights, not as an inviolable right in itself. Today, however, a change in the legal qualification of genetic diversity, from premise to inviolable right, seems compelling, in parallel with the fact that the data of genetic diversity, as the one identifying each physical person, ceases to be undisputable and pacifically contested, and it appears to be a character, a physical quality, which could be denied to someone. Therefore, genetic diversity, as it cannot be automatically referred to the subject in which it was immersed so far anymore, and being distinctly identifiable, potentially disassociated from the physical structure of that subject, becomes the objective of a radical legal overhaul, that is, of an inviolable

right, the respect of which is requested by an individual in order to defend his own genetic identity-diversity.

However, as this right of the hypothetical clone could not be put forward by him if not after its violation, it seems that we must conclude that the situation described, of the transformation of genetic diversity from a premise for the exercise of inviolable rights, has a purely meiotic value. In fact, it only serves to show all the importance of the decisive legal values (and, among them, also inviolable rights) which hide in that apparently unremarkable premise, the importance of which would paradoxically be fully shown precisely when those values would be concretely affected by the constitutional transgression that cannot be overcome, and is inherent to the activity of human cloning.

B2) The hypothetical clone's right to genetic integrity, that is, his right to receive a doubly derived genetic make-up and to be protected from interventions aimed at otherwise manipulating his genetic make-up.

B2.1) The right to the integrity of the genetic make-up in relation to the physical integrity-difference and the symbolic identity.

The legal situation of the person hypothetically born following practices of human cloning can be considered by law also from the point of view of a necessary violation of the clone's right to integrally receive a genetic make-up, that is, his right to receive a genetic make-up transmitted to him by his natural parents, even hypothetically, different from his social or legal parents. Clearly, the perspective would not change if his birth is due to a cloning process carried out on a person who is not in a relationship; in this last hypothesis, if anything, the violation of the clone's right to have a genetic make-up deriving from two adults of the opposite sex, would also be an argument against the admissibility of cloning practices carried out on people who are not in a relationship.

To begin with, the clone's right to the integrity of his genetic make-up develops in at least two main directions:

a) *First of all, it is the right to a double derivation of the genetic make-up,* which seems to be the most intimate essence of his inviolable right to physical identity-diversity. In fact, if it is true that only from this last one and its corresponding inviolable right, it is possible to reach the concept of a right to a double derivation of the genetic make-up, the reciprocal perspective is not less true. In reality, only if we recognise the existence of this second (and in a certain sense, more radical and final) inviolable right, it is possible to give concrete substance to everyone's right to physical identity-diversity, which would be empty, and, then, denied to some, when it is not substantiated by the double

composition of his genetic make-up. In the end, according to different points of view, the right to the double derivation of a genetic make-up seems either as an addition, or as the authentic matrix of the right to physical identity-diversity. In fact, this cannot be regarded as satisfied only because the clone is outwardly distinguishable from any other person, including the cloned individual; instead, to satisfy it, it is necessary that the clone's individuality-diversity comes from a more profound level, the level of the double structure of the genetic make-up, because, if it does not reach that level, the clone's individuality-diversity is forced to manifest itself in a different and weaker form then the expression of the individuality-diversity of all other physical persons. But if strong individuality-diversity is the basis for identifying every person, or, as we have already stated, is everyone's "inviolable right", then constitutional law does not admit delays to its universal ratification. However the weak individuality-diversity ascribed to the clone represents and exception that cannot be justified if not in the presence of particular and very strong reasons, in contrast with the attribution of a strong individuality-diversity to everyone else.

From this point of view, therefore, we can say that the two rights, the physical identity-diversity and the double derivation of the genetic make-up, appear distinguishable only if we look at them from the necessarily fractioned perspectives of analytical investigation. Instead, from that point of view, they seem in concrete as the two different denominations of a right that seems effectively unitary, which, to be realised, must not go through (as mostly happens for the right of symbolic identity) a series of gradual and progressive acts of recognition, but must present itself (as happens for other aspects of the right to symbolic identity: name, legal capacity, citizenship), all at once and from the beginning.

b) *secondly, it is the natural premise of the right to everyone's symbolic identity-diversity.* In fact, it seems legally contradictory to interpret the constitution as an act protecting symbolic identity-diversity to the highest degree, both in its expressions, formal, immediate and attributed from the outside (like those identified in article 22), and in its expressions constructed autonomously and progressively by each of us, and as an act that, at the same time, is not employed with the same force in the projection of the material substratum of symbolic identity, as it is that constituted by physical identity-diversity. In fact, one thing is to state the existence of a relationship of rigid conditionality between the two forms of identity, another is to allow that one of them (genetic identity) receives a not equally strong protection than that owed to the other (symbolic identity). Therefore, the question to ask is another: can a

constitutional ordinance that is not prepared to recognise as its constitutive element everyone's right to the integrity (double derivation) of their genetic make-up, credibly stating to want to offer stronger guarantees of everyone's right to each of the various identities, symbolic, personal, collective political? If, as it appears, a relationship between the various identities, from the most elementary and immediate, to those that are more rarefied and mediated by personal work, cannot be denied, unless we want to deprive the symbols of any specific material root, then, it is legitimate to state that the constitutional protection given to the symbolic, personal, collective and general identities, poses the presence, in the constitution, of a strong authentication of the physical identity-diversity, in which all the others, according to a non-deterministic logic, necessarily find their initial anchoring point.

B2.2) The "inviolable right" to be protected by interventions negating the right to the integrity of the genetic make-up, that is, its double derivation.

There is, in any case, a second and different direction of analysis, beyond the positive one adopted so far, from which the right to genetic identity, in the specification offered of a right to the double derivation of the genetic make-up, can be considered. In particular we can look at it in the negative perspective of everyone's expectation to be protected from interventions on their body, according to material modalities of the most varied nature, similar in the fact that they are realised either against the will of the interested individual, or completely outside his will.

From this point of view, it is clear that no-one can authorise our parents to determine our birth, but it is just as clear that the argument cannot be used with regards to their expectation to give birth to a son institutionally generated by only one of them and, therefore, deprived of his "inviolable right" to receive the genetic make-up of both. So that, if we cannot completely recognise the right not to be born because of the deprivations to which the event of his birth seems to expose him, the same cannot be said with regards to everyone's right to receive a maimed genetic make-up in the sense clarified as follows, that is, not derived by one or the other of his parents. Therefore, we can hypothesise that legal protection against this type of interventions could be claimed by the son born by cloning, basing it, first of all, on article 13. Read in the sense that it forbids any type of intervention directed to negatively affect someone's body. On the other hand, because even from the perspective we have just adopted, as also in the one already considered, the contestation of the maiming choice could not propose to repair the damage by now irrevocably caused, and to eliminate the effects of the intervention, the

birth of a person by cloning could not be in any case considered other than the effect of the violation of his “inviolable right” not to undergo the transmission of a genetic make-up derived by only one of his parents, instead than by both.

B3) The right to equal moral dignity, in its aspects, negative (right to not be deprived of essential rights) and positive (right to full self-determination)

The discussion about the moral dignity, as the one about social dignity, which is notoriously enunciated in the 1st subsection of the third article of the Constitution, leads us, like the other one, fully into the topics relative to the various symbolic identities that are part, in different ways, of every man. Here, however, as we have said from the beginning, we want to consider the moral dignity of a very limited perspective, in which it appears to function from a point of view of balance between each person’s physical identity-diversity and symbolic identities.

B3.1) The violation of personal dignity from a negative point of view: two aspects

With regards to the clone’s right to equal moral dignity, we can repeat the observation already mentioned with regards to his right to a different physical identity.

In itself, peoples’ moral dignity represents a constitutional value, a principle involving a series of particular rights and freedoms, which can only happen if they feed on it. And however, with regards to the clone, that value, which works as a premise, as a general feeder of rights, becomes, as happens for the right to the physical identity-diversity, an “inviolable right” to dignity when we state that someone’s dignity, before any other particular determination, has been directly violated because it has had to suffer an offense that has hindered its full formation. If, in fact, we have denied the clone an “inviolable right” even before he, unlike any other person, becomes a person, then, rather than talking about the damage to his constitutional right, we can talk about the damage to moral dignity which is constitutionally ensured to everyone, and which is expressed, first of all, in the absolute equality that must exist amongst all men with regards to “inviolable rights”.

In the hypothesis of cloning as an activity finalised to genetically structure the clone following a method that is not only exceptional, but also maiming (in the sense clarified as follows) in comparison to any other, can be considered as damaging an inviolable right to human dignity, still under a negative profile, also from another point of view.

In fact, it presumes that the destiny of aspects so essential to each human being can depend on decisions that, except in the case of very particular circumstances, are uniquely focused on the particular interests, certainly not constitutional, of the subject requesting the cloning, which can happen only by neglecting, and in fact completely sacrificing, the more vital interests of the clone. It is in relation to this profile, which we could call *a moral maiming of the clone*, that we can identify a very clearly perceptible damage to the clone's dignity, which becomes a constitutionally guaranteed right because of the very particular circumstances in which it is called into question, and the radical and unalterable way in which it is neutralised.

The legal suggestion of an equal moral dignity for the clone, as the one proposed, also has a solid constitutional basis: again in article 2, individuals are considered not only as the centre of inviolable rights, but as value in themselves and, therefore, they cannot be freely conformed to needs that cannot be so strong as to lead to a constitutional guarantee of the activity of cloning, which would inevitably be in contrast with the protection given to the individual.

B3.2) The violation of personal dignity under the positive profile.

However, when we move on to consider, after the negative one, the positive legal aspect of every person's right to equal dignity, we can easily identify its protection in other articles of the Constitution; for example articles 13, 19 and 21, considered, each in its own way, the starting point for every individual's internal freedom and on this basis, of the freedom to make choices guided by a conscience capable of self-determination, in a way that is as much as possible free. In effect, if it is true that the activity of human cloning is founded on the imperative and characterised point of view of someone who is not prepared to limit himself when facing the elimination of his own son's genetic uniqueness, it cannot be excluded, even without indulging in a vision of individual human life inspired to genetic determinism, that this parental decision, if put at the centre of the clone's psychological life, could exercise a psychological influence that could be as strong as the decision from which it springs, and therefore destined to unpredictably affect the dynamic of his psychological processes and his most fundamental choices, even internal. With regards to this, we have talked about a "right to ignorance" about the developments of our own future life, which could be considered as an internal component of "the equal right to moral dignity", which should be guaranteed to the clone in the same way in which it is guaranteed to any other person. In fact, there is no doubt that he is owed, according to the constitution, the same possibility to exercise

his fundamental rights of positive self-determination that the abovementioned constitutional directives ensure to everyone else.

The rights of the hypothetical clone in the relative perspective

It is really difficult, as we have said, to deny that the clone's interests correspond to a series of every person's inviolable rights, the characteristic of which is to be considered equally essential, both in the possibility of a free personal life, and in the possibility of social cohabitation, unnerved by liberal-democratic institutions.

To the extraordinary importance of these rights and of the exhortative and normative enunciation about them, can benefit, more than by replicating – often too standardised – the formulas to protect such original and originating rights – also, and maybe especially, the contrast between them and the weakness of the reasons sustaining the interests of the subjects (physical persons or institutions) hypothetically requesting the reproduction of themselves or others through cloning procedures. From this point of view, there is no doubt that even those who seem reluctant to follow a path that is often perceived as excessively full of apodictic statements, should not encounter any difficulties in recognising the disproportion between those that have been imaginatively defined, like the rights to omnipotence, to consolation and to glorification, and the right to genetic identity, to not have a maimed genetic make-up, to equal moral dignity.

The very strong disproportion between them, suggests that we should limit ourselves here, to simply enunciating the method of comparison, neglecting to discuss its various arguments. In this way we can talk about a comparison, between two series of rights, carried out from a static point of view and from a dynamic point of view. The first perspective, in which mere faculties and rights of the highest constitutional level are contrasted, as well as choices aimed at satisfying particular interests and universal rights, is also such that it reveals the gap between one and the other. The second perspective, then, is such that it emphasizes even more the abovementioned gap, because of the fact, already recalled, that as these are not categories of mutually stable situations, or, according to a legal expression, mutually balanced, the activity of human cloning should be necessarily forced (and in this we must see its intrinsic illegitimacy) to scarify stronger rights in favour of weaker rights, which, to make the discussion easier, we have also tried to identify and denominate.

The schemes of analysis and evaluation proposed seem correctly applicable to the generality of the activities of cloning. What will be

problematically examined in the conclusive part of this reflection, is whether from these we can remove the cloning activity sustained by the need to remedy a couple's serious genetic deficiencies, or of one of the individuals in the couple, so that we can state that it would happen to protect the members of the couple (or one of them) and especially to protect their child's health, who could not be born healthy but by cloning.

C) Constitutional values applied to cloning: equality and autonomy in the development of moral conscience. Minimal starting points for reflection.

In all the typical situations considered, emerges the problem of respecting the *equality principle* between all men, which the activity of human cloning seems to be able to threaten. But it appears to be able to highlight new and up to now still under-examined aspects of this principle. If, in fact, this, in its strong nucleus, which in the Italian Constitution occupies the introductory part of its first subsection, declares its duty to consider as irrelevant the differences between men with regards to sex, race, language, religion, political opinions, personal and social conditions, that declaration has been constantly doubly intended; on the one hand, with regards to the physical differences between people, it had the purpose of forbidding discriminatory legal treatments on the basis of these differences; on the other, with regards to ideological and sociological differences, it did not only have the purpose of manifesting a constitutional favour towards those differences and their vital plurality. Physical differences were considered as a fact not to be penalised; differences of other nature, and in particular ideological ones, were seen as a reality, not only not to be penalised, but also to preserve, or to encourage. Accordingly, the activity of human cloning seems to support a way of reading the equality principle which takes away the need not only to respect the physical differences as they exist in nature, but also the ulterior, and so far unconsidered, need of seeing them as positive realities, which is absolutely indispensable to preserve directly opposing activities, even if on a quantitatively negligible scale, to attenuate the variety of those differences. In fact, genetic diversity seems, in the light of the equality principle, as a diversity to necessarily preserve in any man, and from this point of view the principle presents itself in a form that could be said very strong, which, unlike or even in contrast to other attitudes of the same principle towards those differences (which must, depending on the case, be neutralised, made flexible or eliminated from the law) needs the generalisation of this specific difference in every man's universe.

In its significance as a future institution which utterly strains constitutional values and which represents a privileged opportunity to

discover “new values”, the cloning institution can also confirm the validity of those constitutional trends, highlighted by jurisprudence in recent years, according to which the important point of the protection of autonomy in personal evaluations and choices, is progressively moving from the moment in which the evaluation and the choice take place, to the one preceding it, in which resides the possibility to consciously prevent those determinations. The formal non-interference of public authority in the private choices of each of us, in fact, does not represent a sufficient guarantee of freedom anymore, when facing the innumerable forms of invasion of the sphere of personal self-determination exercised by the most varied expressions of economic-technological power. And it is this insufficiency, these multiplied invasions, to determine the discovery of “new values” within those already known, of “new rights” that are the source of those already known, without which we realise, after a time, that they could not have been protected or even conceived. It is this tendency to regression and anticipation of the legal protection of these rights that the hypothesis of the possible cloning of human beings, with its invasive physical and moral characteristics, sets in motion some constitutional directives. And the obstacles that they oppose to its realisation are therefore deduced not so much directly by the principle of freedom of conscience, but by the principle of dignity (also as equality that cannot be reduced to single principles), that is, by a principle that precedes and supports the other, and that would be a safeguarding clause of the substance that should increase its content.

Human reproduction by cloning in some exceptional circumstances. Hypothesis on total indirect cloning: problematic considerations.

A) Introduction to the issue

More than once, during our reflection so far, we have observed that, beyond the fences against the practicability of human cloning erected as a conclusion to the arguments developed according to a logic of principle, we can imagine certain exceptional circumstances for which it seems that we can adopt a more problematic consideration of the issue of human cloning for the future,. As we have anticipated, the particular character of the situations that we want to briefly outline resides in the fact that, with regards to them, the activity of cloning, instead of being the aim of the person requesting the cloning, is an exceptional mean to achieve purposes that, in a certain way, transcend it.

In relation to this, biologists (see, for example, the document by De Carli-Piazza) outline various typical situations in which the activity of

cloning human beings, according to different viewpoints, could be seen in perspective beneficial, or in which it should in any case be the object of a more problematic rejection of that generally pronounced in its regard.

Beyond their empirical plurality, which can also be definitely determined with difficulty, such situations, if we order them in a conceptual way, can be brought back to *two typical occurrences*: a couple in which both partners are affected by the inability of producing gametes (sterility); a couple which, although not sterile, is already affected by (or carrier of) serious illnesses of various nature (mitochondrial illnesses of the mother; high risk of generating children affected by genetic illnesses where other practices of assisted procreation cannot be carried out; mosaic genetic constitution of the embryo) which, ineluctably, or with a very high degree of probability, would be transmitted to the product of the conception.

B) Cloning as a remedy to a couple's sterility

Ba) Negative perspective

The first hypothesis rests on the eventuality of the donation of an oocyte in which the nucleus is substituted with that of a somatic cell of one of the partners, presumably (but not necessarily) the male; the woman, evidently, would have the task of developing the product of the cloning operation that has been described. In this situation, the interests at play would be displaced as follows: on the one hand there would be the couple's right to reproduce and the right, instrumental to the first, to use all the necessary means to overcome (as it cannot be cured) the condition of sterility; on the other, there would be the rights of the clone, to be identified and analysed. In this typical situation, human cloning would be, therefore, a mean to overcome the natural impossibility to reproduce of an adult heterosexual couple (*cloning-mean or non-self-sufficient cloning*).

We try and offer a legal evaluation of this situation, considered in the components in which it is articulated, we need to choose whether we want to put ourselves within or outside of the frame of principles previously presented.

If we put ourselves within that frame (as it appears inevitable, in this case, in order to be coherent), the hypothesis of considering as legitimate the activity of cloning for the purpose of remedying the couple's sterility, does not seem acceptable for a variety of reasons.

The first is that the intrinsic complexity of the situation under examination cannot be resolved by ordering the rights battling each other within it, but only, as abovementioned, sacrificing some rights (those of

the clone) for the opposing rights (those of the person requesting the cloning). The relationship between the two sets of rights is one of mutual exclusion or, as it is also said, of null outcome.

The second is in the fact that, whilst the couple's right to reproduce, even if we ascribe it to the category of inviolable right, is still a renounceable right, the opposing rights to physical identity-diversity, to the double derivation of the genetic make-up, to the respect of the conditions constituting our moral dignity, are, at the same time, inviolable and non-renounceable.

In addition, we can observe that, considering human cloning as a possible remedy for a couple's sterility, not only would lead to totally homologate it to other practices of assisted procreation, so that it would lose its exceptional character, but it would also realistically lead to giving it a preferential position in comparison to them, and in particular, in comparison to heterologous assisted procreation. In fact, it cannot be denied that in cloning the incidence of the intervention of a subject external to the couple in the reproductive activity, although not necessary with regards to the possibility of reproducing, it is not so at all (for what we know) with regards to the genetic make-up of the product of cloning; and this seems to be a realistically decisive reason for preferring procreation by cloning to other forms of assisted procreation in which the intervention of a third person has a larger and more significant part. Because of this preference, therefore, the phenomenon constituted by what could be called "vertical twin births" would be completely normalised.

This last argument, clearly, can be opposed only to the facultative use of cloning as a direct instrument to overcome the condition of sterility; instead, it is irrelevant in the hypothesis in which cloning is the only instrument (if we don't consider the extreme instrument of embryo donation) that can be used to overcome that condition, which happens when the inability to produce gametes affects both partners in a couple.

Instead, with regards to this last hypothesis, are the two observations preceding it, relevant?

The issue rides on a subtle equilibrium, as it is held by a weave of values that can be disentangled in a variety of ways, according to how we look at the interests involved. In the logic of the reflection carried out so far, which essentially is based on the decisive value attributed to the right of double derivation of the genetic make-up, however, we must give a positive answer to the question asked here. In fact, both the argument that points out to the fact that there is no balance between the expectations of the subject requesting the cloning and those of the subject enduring it; as well as that focusing on the fact that the rights of the first of the subjects abovementioned can be renounced and the rights of the second of the

subjects (the “clone”) is non-renounceable, can also be used to oppose the use of cloning as a necessary, direct instrument in overcoming the obstacles of the condition of sterility, which, in the language used here, is defined by the only circumstance that the very particular reproductive technique we are talking about would be used to overcome: those situations of sterility where cloning would be aimed at resolving a condition of sterility shared by both partners within the couple.

Therefore, it does not seem strictly necessary to discuss such typical situation, which is more restricted than that in which sterility can be by-passed with the use of other reproductive techniques, involving arguments different from those already considered.

Bb) Some objections to the negative perspective

It has been said that we can look at the cloning issue as a remedy for the sterility of the couple, choosing to tackle it from a different point of view from that presented here.

It would be the task of this eventual, different viewpoint, to illustrate the arguments that can be put forward to support such a perspective. However, here it is possible, and in fact it seems necessary, to present a couple of the most important objections that, as experience suggests, could be made towards the principles recommended in their essential aspects.

We can imagine that such objections can be posed against the principles expressed earlier, aiming at attenuating the significance of both of the elements at their basis: that attributed to physical identity-diversity and that attributed to the need of not disturbing the relationship between physical identity-diversity and the various symbolic identities, first of all personal identity, which affects every person. These objections, therefore, regard the premises on which we have so far based our discussion on the issue of cloning as eventual, future remedy to sterility, not, instead, directly this last issue. It is therefore clear that, should they successfully affect those premises, as a consequence, they would also affect the negative response here hypothetically offered to the eventuality that the law could in the future legitimise the use of cloning as a remedy against sterility. Therefore we cannot deny that, even though in the following pages this last issue will not be discussed, it will still be the motivating element of the dialectic reflection that follows.

i) Objections to the relevance of physical identity-diversity: the twin birth argument.

An argument aimed at exalting the similarities between the situation of monozygotic twins who share the same genetic make-up, and the situation of a son generated by cloning, who shares the genetic make-up of one of his parents, is usually used against the importance attributed to physical identity-diversity. With regards to this, we stress that we have a completely different attitude towards the first (not at all worried) and towards the second and no objections are raised, no arguments to contrast the possibility of legally legitimise, in the future, the practice of human cloning.

An objection like this seems to be supported by an argument mirroring the other, aimed at adding value to the aspect of substantial diversity existing between the two situations, those of the horizontal and vertical twin births. In fact, in the first, the fact that twins share the same genetic make-up goes together with the fact that such make-up has been transmitted to them by both parents; instead, in the second situation, that of vertical twin births, sharing the genetic make-up is achieved by excluding one or the other of the parents from the reproductive process. Therefore, the two types of twin birth are radically different in form, that is, in the way in which the genetic make-up of the twin, son or brother, is formed. Also different, in the same formal aspect, is their relationship with other reproductive methods: in fact, horizontal twin births are no different from any other type of procreation, assisted or not assisted by medical interventions; instead, vertical twin births, having the purpose of achieving a twin birth, is radically different, for that same reason, from any other form of procreation.

In addition, even when compared to each other from the point of view of their substance, the two situations are more different than what may at first appear. It is in fact true that although we can find the genetic identity of two people in the two forms or twin births, however, such a phenomenon cannot be fully evaluated without analysing the structure of the relationship in which such identity is introduced. In fact, in horizontal twin births, the genetic structure of one twin, although identical to that of the other twin, is, however, completely independent from it; in fact, they both are created by the particular and unpredictable way in which the dynamic of the first part of the development process happened. In vertical twin births however, the son’s genetic structure is not only identical to that of the cloned parent, but it is directly dependant on it.

In one (horizontal twin birth) there is a direct relationship (with both parents) of identity-diversity; and there is an indirect relationship (with the twin-brother) of identity-equality. Therefore, in the first, there are two relationships, and the one of identity-diversity is more important than that of identity-equality; in the second however, as there isn’t a relationship of identity-diversity between the subjects involved in the

reproductive process, the identity-equality between the subjects of that process dominates without contrasts.

Overall, the abovementioned considerations leads us to believe that the physical (and psychological) difference between twin births assimilating the twin to the father (or the mother) and that assimilating him to his brother (or sister) is extremely important, and such a difference is even greater when we take into account that in vertical twin births the infraction to the constitutional principle of the absolute uniqueness of each individual is an *avoidable infraction*, whilst, in horizontal twin births, that *infraction* is *inevitable.* Therefore, it follows that horizontal twin births, for being such, cannot even be evaluated from a legal point of view (legally it is not an infraction), and consequently they can lend themselves, for their own nature, to evaluations destined to presents themselves only as facts. In conclusion, it also follows that the impact of horizontal twin births on the formation of the twin's identity cannot be compared legally or from other points of view, to that exercised on them in vertical twin births. Therefore, with regards to vertical twin births, the arguments of principle stated above seem to maintain their critical force, and, with them, the more particular arguments brought forward as a criticism to the hypothesis of using the cloning technique to fight against the sterility of an adult heterosexual couple.

ii) Objections to the special relevance of the relationship between physical identity and symbolic identities in the process of human cloning.

Another objection generally made towards the ethical and theoretical constructions ex ante against the practice of human cloning, is that contesting the special influence it exercises on the relationship between our individual physical identity-diversity and the symbolic identities of any subject. In fact, any reproductive activity, both natural and technologically assisted, is every individual's determinant material identity, and therefore, although according to methods that are difficult to determine, it affects our process of self-constructing our symbolic identities; so, from this point of view, cloning would not exercise an effect substantially different from that of any other reproductive activity on the relationship between physical identity-diversity and the various symbolic identities, personal or collective, linked to it.

The objection seems to deserve an answer with regards to the part where it tends to assimilate the effect exercised on the relationship between the identities we are talking about, from the common to the less common reproductive practices and from cloning, which is, at the moment, only imagined. In fact, it is evident that the basic difference between the influence of the various practices of human reproduction and

that of cloning, on the material basis of the symbolic identities that afterwards take root in them, from this, we can say that only cloning is representative of an activity aimed at achieving, not only the reproductive process (like other reproductive practices), but also the particular material outcome, the precise make-up of the genetic structure, which that reproductive process aims at. Therefore, it has symbolic values that are stronger than those inherent to any other reproductive process and, evaluated on its outcomes, much stronger then those intrinsic to horizontal twin births. These, involuntarily, are the potential outcomes of many practices, through which a weak symbology is transmitted, more solidaristic than antagonistic, linked to the brother; the other, vertical twin births, absolutely voluntary, comes from one practice, through which we explicitly transmit a strong symbology, a combination of rebellion and submission, linked to the father or the mother.

If we then reflect on the fact that the activity of cloning, when evaluated in itself, not only affects a wider object, but it identifies with such an object so profoundly that it becomes its purpose, then it is possible to assess, in their full extent, the expectations connected to the practice of cloning; in fact, it seems clear that these cannot be contained within the limits of the immediate purpose of that practice, but inevitably expand to ulterior purposes proposed by the subject requesting the cloning, not of a material character, but of a symbolic character.

Naturally, the answer should be reformulated in light of the circumstances, which are here particularly discussed, that in certain cases we can assign a purpose to cloning that coincides with the simple realisation of its subject, as it happens when the reproduction of a genetic identical subject to the generating one is wanted to realise an interest deserving of protection like overcoming a condition of sterility. But, as we have already discussed the issue here presented in a previous stage of development of this work, we can certainly refer to it.

C) Cloning as a remedy for the couple’s transmissible illnesses

The eventuality of using cloning as a reproductive technique is also discussed in relation to one or both of the partners within a couple having an illness or a genetic alteration, if those illnesses are destined to be transmitted to the product of conception, or have already been transmitted, as can be ascertained through diagnostic assessments carried out in the early stages of gestation. In this outline of the problem, the suggestion to discuss the relationship between cloning and these situations of illness is implicit, as the reflection moves around the criterion that they are ascertained before conception, and therefore have

not yet been transmitted to the conceived, or have already been ascertained in the early stages of embryonic development, if they have already been transmitted.

Ca) Cloning as a reproductive technique aimed at preventing the transmission of illnesses or genetic alterations to the product of conception. Synthetic presentation of the hypothesis.

This is a hypothesis that can easily be understood immediately and that, unlike those preceding and following it in this reflection, needs to be carefully set up technically, in order to offer the necessary objective background to any legal evaluations. In this way, as we will see, we become aware of the intrinsic tendency of this hypothesis to break up into autonomous parts which, because of their characteristics, seem to conceptually slide towards each of the other two exceptional hypotheses illustrated in this work (that of sterility and that of embryonic cloning). Therefore, because of the abovementioned tendency, within the hypothesis under consideration, we find a limited amount of situations, which are in any case less varied than what we would have imagined before this analysis. So, it is logical that, even in the extreme assumption that such a hypothesis would reveal itself to be devoid of content, nevertheless it would have shown, from a methodological point of view, its usefulness, also by demonstrating how and why it disappears into one or the other of the two previously described hypotheses.

i) Features of the hypothesis under consideration.

In concrete there is the possibility, generically presented at the moment, that, if there is a high risk that the couple's offspring is going to be affected by a genetic illnesses and if the couple excludes the recourse to heterologous procreation, the nucleus of one of the male's or of the female's somatic cells could be transplanted in the female's denucleated oocyte. The oocyte obtained with this cloning technique would then be implanted in the female's uterus, so that a normal pregnancy can follow.

The hypothesis must be discussed from an objective and from a subjective point of view.

The first aspect must be examined, because only after having unravelled its intrinsic complexity, it is possible to establish in which precise situations the law, wanting in the future to legitimise the recourse to cloning practices, could invoke, in support of its choice, the reason that it would be the only one to protect the offspring's health, if the couple is determined to reproduce naturally despite the fact that their state of

illness or genetic alteration advices against reproduction for reasons linked to the health of the product of conception and ethics.

With regards to the subjective aspect, its relevance comes from the fact that the couple under consideration in the hypothesis we want to analyse is not, in principle, physically hindered in the autonomous realisation of its reproductive wishes and, therefore, with regards to the law and the directives within it, it seems to find itself in a position of dependency which is much less pronounced than that of the sterile couple. Consequently, we must evaluate if the law can be justified in the choice of authorising reproduction by cloning for a couple that is ill or carries genetic anomalies, when it can list in its support one or more of the following reasons: dissuading the couple from recurring to sexual reproduction; giving it the possibility of choosing, within the various methods of assisted procreation, the most effective one to avoid transmitting the illness or the genetic alteration; making it face its determination of not recurring to a method of procreation that, although effective, would be, however, much more complex than cloning by transplanting the nucleus of an adult cell belonging to one of the partners.

The two aspects must be examined individually, but, immediately after, linked. In fact, the hypothesis presented, until now still generically, is generally characterised because of the presence, within it, of objective and subjective aspects and, on their part, the particular hypotheses that can be identified within it can be identified by how differently those aspects are distributed and mutually connected. The analysis therefore must bring to light these different links, for the fact that each of them seems to be able to differently and decisively influence the legal evaluations which, in order not to be misleading, must be carried out on the basis of facts ascertained with rigorous methods.

ii) Conceptual breakdown of the hypothesis under consideration.

In order to assess how much the wish of a couple affected by genetic illnesses or carrier of such illnesses, asking to access a cloning technique as an alternative to sexual reproduction, can be considered by the law so relevant that it influences its evaluation of how to tackle the issue of human cloning, it is necessary, as we have originally stated, to proceed to the objective breakdown of the hypothesis presented in C) where we introduce the issue, which has been so far taken into consideration as a whole.

1. Along this direction of thought, the first sub-hypothesis to consider is that of a couple in which both partners are affected by a genetic illness.

In a situation like this, there are various possibilities.

In some cases, the couple affected could be able to reproduce naturally.

In these cases: if the couple reproduced naturally, their offspring would be with certainty affected by his parents' genetic illness, if the illness gene is recessive; it would be so with a possibility of 75%, if the illness gene is dominant (assuming the condition of heterozygosis, realistic for both parents). If the couple decided to recur to heterologous procreation, in the case of an illness with a recessive altered gene, a child carrier of the genetic alteration would be born with certainty; in the case of an illness with a dominant altered gene, their child would have a 50% chance of being affected and a 50% chance of being completely healthy.

In other cases, the couple described in the hypothesis could be absolutely incapable of producing gametes and therefore be completely sterile. In these cases, consequently, it would find itself, on the one hand, in a situation that can be fully assimilated to that of a couple afflicted by absolute sterility; on the other hand, instead, it would find itself in a situation worse than that of such a couple, as the specificity of the cause of this type of sterility (genetic illness) would objectively preclude the possibility of recurring not only to other types of assisted procreation (we hypothesise that in the condition described the partners could only donate their cytoplasm to their offspring), but also to cloning.

Finally this last one, within the various situation of the sub-hypothesis under examination, would certainly transfer to the cloned child the genetic illness of the parent chosen to be "cloned", so it would not only reveal itself to be unsuitable in achieving beneficial results for the clone's health, but, on the contrary, it would act as an instrument suitable in transmitting to him those ills we want to protect him from. Therefore, for the negative reasons discussed, which are not balanced by positive reasons of an at least equal efficacy, there are no reasons why the law, instead of forbidding it, should accept cloning.

2. The second sub-hypothesis to consider is that in which only one of the partners in the couple is affected by a genetic illness, whilst the other could be either the healthy carrier of a genetic illness, or tout court healthy.

In the first alternative of the sub-hypothesis taken into consideration (partner affected by a genetic illness + carrier partner), if the partners created a child through sexual reproduction, in the case of an illness with a recessive altered gene, he/she would be affected by genetic illnesses in the 50% of cases; and in the other 50% of cases he/she would be a healthy carrier of the genetic illness.

If, instead, the gametes of the partner who is the healthy carrier would be used to activate a process of heterologous in vitro procreation, the product of conception would be a healthy carrier of a genetic alteration in the 50% of cases; in the other 50% of cases, he/she would be completely healthy. Instead, if we hypothesise the cloning of the nucleus of an adult cell of the partner carrier of the genetic anomaly, the offspring would be a healthy carrier of the genetic anomaly in a 100% of cases. In such a case, therefore, cloning seems to be able to produce, for the product of conception, a less favourable outcome than what could be obtained recurring to heterologous procreation.

In addition, it seems rational to hypothesise, from a subjective point of view, that the partners in the double situation described would not choose to procreate a child by a natural reproductive process, preferring the assisted one we have illustrated, if the law denies them the opportunity of recurring to reproduction by cloning. Therefore, even in this hypothesis, the legalisation of cloning seems objectively unjustified and, in this context, it does not seem that the eventually different, objectively irrational, choice of the partners could lead the law to adopt non-negative solutions towards cloning.

In the second alternative of the sub-hypothesis under consideration, where the partner is affected by an illness with a dominant or recessive gene and the other partner is healthy, if the partners chose to reproduce naturally, they would have a child affected by the illness in the 50% of cases, in the other 50% of cases they would have a completely healthy child, if the illness gene was dominant; if, however, the gene was recessive, the child would be certainly a carrier; but, if the gametes of the healthy partner were used to activate a process of heterologous in vitro procreation, the product of conception would be, obviously, definitely healthy. In the same case, even the cloning of the adult cell of a healthy parent, transplanted in a denucleated oocyte, would create an embryo absolutely devoid of any genetic alterations. Even in a case like this, cloning, from a strictly genetic point of view, would not be objectively justified, as the health of the offspring would be protected as much as in a different procreative process which, from an ethical and legal point of view, would not raise the serious problems we have with regards to cloning. It seems, therefore, rationally founded, from a strictly genetic point of view, the hypothesis that the partners, in the alternative under consideration, cannot choose to create a child by natural procreation if access to cloning if denied, as it would not guarantee a better result than that achieved by heterologous procreation.

3. The third sub-hypothesis to consider is that in which both partners in a couple are the healthy carriers of a genetic anomaly.

In the condition described, if the partners wanted to reproduce sexually, as the altered gene is not necessarily recessive, there would be a 25% probability of creating a child affected by the alteration, a 50% probability of procreating a healthy carrier, a 25% probability of procreating a completely healthy child. If one of them gave his/her gametes to activate a process of heterologous procreation, there would be a 50% probability of creating a child carrier of the illness, if they had the possibility of accessing assisted reproduction by cloning, there would be the certainty that the child would have his/her parent's genetic anomaly. Therefore, in this last case, there would be a less favourable result than that, already illustrated, achievable by any of the other two avenues.

As a consequence of this, even in the described sub-hypothesis, it is completely improbable, if we keep to an exclusively rational point of view, that the partners would expect the law to legitimise cloning as a means to resolve the procreative problems linked to their condition of genetic anomaly and, as an effect of this, there seems to be no reason why the law could decide to legitimise cloning.

4. The fourth sub-hypothesis to consider is that in which only one of the parents is the carrier of a genetic anomaly and the other is completely healthy.

This eventuality is, evidently, the least serious of the ones so far examined. In this condition, if the partners wanted to reproduce naturally, there would be a 50% probability of having a child carrier of the genetic alteration, as it would be necessarily recessive; instead, if the healthy parent offers his/her gametes to activate a process of heterologous procreation, the child would be completely healthy; if then the nucleus of a cell of the genetically healthy parent was cloned, we would have the same result. Consequently, with regards to the protection of the offspring's health, cloning would produce the same effects than heterologous procreation.

Even in this sub-hypothesis, therefore, from a strictly genetic point of view, there are no reasons why, in order to reproduce, the couple should prefer cloning to a different reproductive technique, as cloning is also full of problems, although they are generally considered to be less acute than those raised by the first. The law, consequently, from that same point of view, could not find rational reasons to legitimise cloning.

iii) Reflections on the possible further relevance of the couple's subjective attitude in the eventuality that the nucleus of an adult cell of one of the partners is reproduced by cloning.

So far, the overall assessment of the subjective aspects of cloning, in the hypothesis considered, has been carried out rigidly including those aspects within strictly genetic considerations.

On the basis of the method we have followed, we have discovered two typical situations, in which the eventual carrying out of cloning practices using the healthy partner's adult cell's nucleus has worse effects than that obtainable by recurring to heterologous assisted procreation; and those in which the activation of that hypothetical reproductive technique produces the same effects than heterologous procreation.

In addition, it is time to explain that the analysis carried out so far fully rests on the premise that the couple affected by genetic anomalies, in the different hypotheses, wants to actively explore all the possibilities to prevent the transmission of these anomalies to the offspring and therefore refuses, for this and other reasons, to accept that he/she is conceived in the certainty or high probability that he/she will be exposed to illnesses or genetic alterations, even if compensated by the opportunity of intervening afterwards with embryonic cloning, in the conception's pre-implantation phase, and, in this way, offering to the cloned embryo the chance of developing in conditions of genetic safety. In fact, if the couple opened to this last eventuality, the complex hypothesis examined so far would be highly impoverished of situations and meanings, and we would have to consider it largely absorbed within the hypothesis of using embryonic cloning for the purpose of freeing them of illnesses or genetic alterations that have been transmitted to them.

It is therefore the very special importance of the couple's attitude we have highlighted, which leads us to still discuss it in order to verify if, together with the genetic data we have previously acquired, we can attribute to it a greater relevance than that we have given it when we have examined it in a context of close dependence from those data.

However, it does not seem that considering the personal attitude of the couple affected by genetic anomalies in a variety of ways, towards the procreative techniques accessible to them, could lead to believe that an eventual preference to procreating by cloning is justified, even when there is objective evidence that recurring to cloning would be counterproductive to the offspring's health or would produce, in any case, less favourable results than those obtainable by recurring to different reproductive techniques. In fact, the discussion so far rests essentially on the hypothesis (not shared by some bioethicists) that reproduction by cloning can be taken problematically into account only if it is the only way, or the most efficient way, to guarantee the offspring's inviolable right to health, that is, his/her right to be born by the least dangerous methods; and to this hypothesis organically belongs the idea that the right of the genetically maimed parents to reproduce by cloning could acquire

legal importance, as it is supported by the purpose of protecting the offspring's health in the best way possible.

The consequence of what we have said is that the autonomous relevance of the couple's personal attitude to assisted procreation techniques and, in particular, to cloning, could be considered, or in situations (which by the way have not been discussed here) in which its realisation certainly involves benefits for the offspring's health, or in those situations we have previously examined, in which it produces effects that are equivalent to those that can be achieved with other reproductive techniques.

If we reason on the basis of this second eventuality (the only one that, previously, we have been able to formulate theoretically), the situation facing us lends itself to the following reflections.

First of all, we have to ask ourselves if, when the impact of the different reproductive practices is equivalent (heterologous procreation and cloning) to the offspring's health, then the special importance we have to recognise to the parental will with regards to ideas that can be formulated only on a purely genetic basis, can, in some circumstances, be enough to make us favour cloning, in case they prefer this reproductive technique. In the system of the considerations carried out so far, however, the answer has to be negative. In fact, if the effects produced by the two procreative forms are equivalent from a strictly genetic point of view, they are not so from a legal point of view. Actually, measured in this way, whilst heterologous procreation, which is still ethically controversial and can be accepted by the law only by correcting and integrating the current rules about procreating, is not generally considered as conflicting, in principle, with constitutional directives, the contrary, as we have demonstrated, can be said with regards to procreation by cloning. Without returning to the arguments already discussed, we cannot but state, on this basis, that parental will, within the situation under consideration, could not be supported by constitutional law, should it pronounce itself to be in favour of a procreative form of cloning, which, necessarily, would involve a violation of the offspring's very important constitutional, both human and citizenship, rights.

Therefore, the conclusions presented seem to end on a negative note the reflections carried out so far to organise the complexity of the problems raised by analysing the material collected within the hypothesis that encloses them in their entirety. However, some NBC members do not agree with these conclusions, when considering the manipulative and selective quality of the abovementioned reflections. They deserve a further and final check, before our discussion turns to other aspects of the issue of "the cloning of human beings". In fact, we can ask ourselves if the statement that the attitude of the couple hypothetically favourable to

conceiving a child by cloning could not prevail on the constitutional reasons opposing it, can be fully confirmed also when such an attitude is not supported by a simple subjective preference but, instead, is based on the need of protecting, as well as the offspring's health, also that of the couple. In fact, they seem to be, within the hypothesis under consideration, persons who are ill by definition or, in the most favourable case, carriers of genetic alterations, so that it does not appear unlikely that their physical-psychological health could be negatively affected by the possibility that, when requesting cloning in order to produce offspring, this is denied to them by law, despite their condition of illness or genetic anomaly. In conclusion, in the hypothesis discussed, cloning, whilst having effects equivalent to heterologous procreation with regards to the offspring, would instead have more positive effects with regards to the health of the future parents.

Therefore, from this point of view, the reasons presently expressed would act in favour of cloning, based on their right to health; the reasons connected to the offspring's health would be neutral; and the legal reasons of principle already discussed would act against it.

What should we think of the ideas just expressed? In abstract, it is realistic to imagine that they will be, in a future we cannot yet fix in time, a topic of debate between those in favour and those against hypothetical human cloning practices. In fact, the right to health is very important when we put it on one end of an imaginary scale destined to measure the merits of the respective reasons. However, in concrete, if we look at the particular hypothesis in which procreation by cloning produces effects that are equivalent to those of heterologous procreation, we can see that they are those in which the frailty of the couple's health conditions is less relevant. In fact, on the one hand, this equivalence of effects occurs in the fourth sub-hypothesis already identified, where both partners are healthy, although one of them is the carrier of a genetic anomaly; on the other hand, this same equivalence occurs in the second alternative to the second sub-hypothesis already identified, characterised by the presence of a partner who is affected by a genetic illness and a partner who is completely healthy. So, in the first of the situations mentioned here, it appears that the presence of two healthy parents considerably weakens any reference to the right to individual health, as we can rather identify problems linked to collective health and to the uniformity of the genetic pool. In the second situation, the problems relative to the couple's health can be hypothetically foreseen as being without a doubt more significant than those that appear in the previous case, but it is difficult to conjecture whether they will affect more probably the partner who would remain materially uninvolved in the reproductive process, due to being affected by a genetic illness, or the healthy partner, due to being effectively

involved. Therefore, it is unlikely that the law, in the situation hypothesised, can previously identify the cases in which the couple's suffering could turn, as the situation under examination would require, into a worsening of the condition of illness in the partner affected by the genetic illness. In any case, that identification, however difficult, seems to be no less necessary. If, in fact, because of the almost insurmountable difficulties on the way to it, the law would reject the early identification of those cases, it would overlook the need to prepare the necessary basis to discuss the possible legitimisation of the cloning of human beings and could not, for this reason, accept it. In fact, carrying on in this way would only legalise the right of couples affected by genetic anomalies to freely chose the procreative method they consider the most convenient, without any consideration for the variety of legal consequences that each of them could lead to and that, in some cases, like that of cloning, would inflict serious damage to the offspring's constitutional status.

Cb) Cloning as a reproductive technique aimed at avoiding the transmission of an illness or a genetic alteration to the product of conception.

i) General hypothesis.

The hypothesis presented in the title is considerably different from that already examined, as it is characterised by two aspects: the fact that in it the process of cloning does not intervene on an individual adult's (man or female) somatic cell but, instead, on an embryonic cell; and, obviously, the fact, connected to the first, that such a process is linked to a different procreative process, consistent, in most cases, with an in vitro heterologous procreation.

With regards to the theoretical frame of the legal issues concerning hypothetical situation, it presents, as well as a certain similarity with that mentioned above, also very important and, in the end, decisive differences, which come, as we will see, from a mutual displacement that is completely particular of the interests of the subjects, and which gives to cloning, when seen in the typical context we are about to examine, aspects that it does not possess in all other contexts, general and particular, we have discussed so far.

ii) Concrete expressions of the general hypothesis.

In the general hypothesis that, within the abovementioned limits, we are about to examine, biologists identify two particular situations

linked by the fact that in both there are embryos, who carry genetic alterations transmitted by their parents.

In the first, embryos are affected by mitochondrial illnesses transmitted by the mother; in this situation we hypothesise the possibility of intervening on the product of conception in the first stages of development, when cells are still totipotent, removing the healthy nucleus of a cell with genetically altered cytoplasm and then transplanting it in the oocyte of a donor with normal mitochondrial DNA. The oocyte, so modified, is destined to be implanted in the uterus of the woman affected by a genetic illness.

In the second, we hypothesise an intervention on the embryo when the preimplantation diagnosis reveals that it has a "mosaic" genetic constitution, in which, that is, there is a mixture of normal cells and genetically altered cells. In this context there is the possibility that, in order to avoid the suppression of the entire embryo, we can transplant the nucleus of one of his/her normal cells in the oocyte of a donor, with the aim of then transplanting the modified oocyte in the uterus of the woman in whom the "mosaic-like conception" occurred.

Therefore, in both hypotheses we carry out a process we could call "indirect cloning" or "mediated cloning", which, as we have mentioned at the beginning, is in a relationship of necessary dependence from a different reproductive practice.

iii) Reasons for recurring to embryonic cloning, or indirect cloning. The paradox of human cloning.

What are the reasons leading us to starting such a complex process? Why, if we want to recur to reproduction by cloning, we don't directly clone a somatic cell belonging to the genetically healthy parent? These are questions that leap to the mind of non-biologists and to which, aiming at including the situations described in an exhaustive legal reflection, we cannot not try and answer.

The first reason for the complex path described, presumably resides in the hope of the parents and health workers, that it is possible to avoid the experiment of cloning. In fact, when there is a high risk, but not the certainty, of transmitting the parents' illness or genetic alteration to the product of conception, then it is not illogical to try and reproduce through less impervious avenues than those represented by such an experiment. This, therefore, would be the probable but not necessary follow-up to the process of sexual reproduction and we should recur to it only in the case it created a genetically altered embryo. However, the reason adduced is inconsequential in the case that, instead of there being a risk, there is a certainty that the genetic illness of one or both of the

parents will be transmitted to the offspring through any reproductive technique. In this case, where there is no hope of creating a healthy embryo, why involve him/her in a form of cloning, rather than directly clone the healthy parent's adult cell?

The answer to this question leads directly to the decisive reason why, in both situations described, we choose to attach the asexual reproductive practice of cloning to a previous sexual reproductive practice. It resides in the fact that, cloning the non-genetically altered cell of an embryo whose other cellular components are, instead, altered, we act in a way that is coherent with the possibility of creating a human individual whose genetic make-up derives not just from one parent, but from both. In fact, attached to the wider procreative process already described, cloning receives from the embryo the character of being bi-parental, which is given to it by sexual reproduction, creating, when there are situations of illness like those examined, an individual who is genetically structured in two ways, instead that in the simple way that characterises individuals procreated by uniparental cloning, that is, by the cloning of the healthy parent's adult cells. In this way, what comes to life is what we could be called "the cloning paradox": if carried out on healthy individuals, for its necessary uniparental character, it unavoidably encounters all the objections of principle we have previously examined at length; if carried out on individuals affected by partial genetic alterations, on which a process of sexual procreation has been attempted, it presents, instead, characteristics that seem to bring it in line with those same constitutional principles that hinder the legitimisation of the other.

iiii) Legal observations as conclusions.

Therefore, taken into consideration in its possible use in relation to the last two situations presented, the technique of human cloning seems to touch its highest level of acceptability. In fact, on the one hand it satisfies the parents' right to have a child free from their condition of illness or genetic alteration; on the other hand, it can be carried out guaranteeing the clone that his/her "inviolable" rights will be respected: the right to physical identity-diversity, in the specific form of the right to the double derivation of his/her genetic make-up, and the right to health, in the specific form of the right to be created in a way that without a doubt guarantees his/her physical-psychological health, instead than in a way that, just as certainly, compromises it. Therefore, we can without a doubt state that in no other of the situations under examination it is possible to find such a clear balance between the opposed situations of those who demand cloning and those who suffer it, like that occurring within the

two particular situations comprising the general hypothesis that we have tried to analyse here.

A statement like this seems to be difficult to refute. However, it does not mean to overlook, or exclude, that ethical observations against the use of cloning, even in the situations highlighted, could be put forward. In fact, it is not difficult to imagine that they could affect one or the other of the phases of the procreative process in these situations.

The first of these phases occurring, as we have said, realistically in the form of heterologous assisted procreation, will be exposed to the criticisms advanced towards this procreative form, as we know, by large sectors of the bioethical reflection.

The second phase, in which the cloning practice occurs, is exposed to the criticism that it can only be realised, in both cases under examination, only through a process by some believed to be of embryonic selection, as some cells, in their totipotent state, which could develop in one or more human individuals, are suppressed. In fact, in the case of both the mother's mitochondrial illness, and the child who has inherited from her a "mosaic" genetic constitution, the transplant of the embryo's genetically healthy nucleus in the donor's oocyte, necessarily implies the suppression of the genetically altered cytoplasm in one case, and the suppression of the mosaic's altered cells (realistically together with some of the healthy cells), in the other.

It is clear that the hypothesised objections cannot be discussed within a legal reflection, even if full of ethical implications, and, amongst them, it is especially the second one to connect with the topic under examination. With regards to this, we can observe that, where the mixture of healthy cells with genetically altered ones is destined to become a human being with a certainly maimed genetic make-up, then, when embryonic selection happens in the pre-implantation phase, we can say that the impact of the ethical contraindication abovementioned is neutralised, if not completely, at least in part.

In addition, the process described, rather than as embryonic selection, can be interpreted as a microsurgical intervention or micromanipulation, finalised not at suppressing diseased embryos in order to allow healthy embryos to survive, but at curing a single, seriously ill embryo, with a brave and cutting-edge technique, which should be considered, from a bioethical point of view, because of its therapeutic purpose, not just merely legitimate but charged with positive value. However, some NBC members do not agree with such conclusions, when taking into account the manipulative and selective quality of the abovementioned interventions.

From a more generic point of view, simply stating the obvious, we can also observe that, in light of our experience of the development of

western law, we know that it tends to consider the answers, both positive and negative, to the abovementioned objections, as equally compatible with the structure of the liberal-democratic principles that are at its basis.

Finally, a concluding note. The reflection carried out, although it is maybe the first, or one of the first, to legally elaborate the topic of human cloning, comes, for this reason, "not in its time", like those reflections that, on the contrary, are too late for their time. In fact, human cloning, at the moment in which we are discussing it, is a practice that, from a technical point of view, is not yet operative, and maybe far from being so; from a general point of view, it is unable to present reasons to justify it; from a legal point of view, it is in conflict with the constitutional rights and principles we have mentioned.

Despite this, it would maybe be too much to apologise for having discussed it. In fact, the occasion not only has allowed us to start exploring its non-demonic face, but it has stimulated the beginning of a rational preparation for the advent of a phenomenon that, until yesterday, seemed to belong to science fiction and that, one day in the current year (1997), we have believed to be able to find on our doorstep, already understood by super-technicians and ready to be used.

Work's synthesis.

In the first part (paragraphs 1-3) we state that cloning regards the law as it is the result of an activity directly aimed at achieving it (paragraph 1); we observe how positive legal directives, and the position of various international and suprainternational bodies, even if they are very different from each other, share a common negative evaluation of the possibility of adding it to other reproductive techniques (paragraph 2); we analyse and discuss the reasons for this shared negative evaluation (paragraph 3).

In the central part (paragraph 4) we identify the subjective legal status affecting those requesting the cloning and, more in general, the legal status that should be guaranteed to the clone. In general, it does not seem that we can attribute to the first any constitutional value; instead, we have to attribute to the second the quality of an inviolable right that, if cloning was effectively carried out, would be necessarily violated. We also demonstrate, in the conclusive part, that cloning, as "law's future institution" could be in contrast with two of its founding principles, that of equality and that of freedom, seen more and more from the point of view of human dignity, which appears to be its true foundation.

In the conclusive part, finally, (paragraph 5) we discuss the possibility that the cloning technique, devoid of justifications in the general thesis, could find them if we use it in particular situations in

which it is the means of achieving aims variably linked to the protection of health (in these cases, we talk of indirect cloning), that is: to fight against sterility, in particular the absolute sterility of an adult heterosexual couple; to prevent the transmission of illnesses and genetic alterations to the product of conception; to remedy the transmission of illnesses or genetic alterations.

5.3 Reflections on human cloning in the context of artificial procreation.

The hypothesis of cloning a human being, which comes from the Edinburgh experiment, is difficult to accept within our normal way of thinking, as it does not follow the conceptual distinction founded on the functional discrimination of somatic cells and germ cells, it creates an outlook that alarms scientists themselves, because of the unpredictable developments of the research and of its possible applications. For a rational perspective on the issue, in this document we have chosen scientifically relevant arguments, and to those we have attached a glossary, in order to rationally frame the problem and to avoid equivocal interpretations of the language, to make it as rigorous and precise as possible. It can be useful to add some general epistemological reflections, in line with bioethical thought.

Bioethics links the achievements of science on man to the ethics of behaviour for their applications and to bio-legal law to establish shared norms of behaviour: this link has epistemological reflections as its unquestionable basis. This must not be considered only the responsibility of scientists, but also, at different levels of cultural elaboration, of the so-called common people. Even common people, who look at science for the care of their health, have the need to think about the meaning and the applications of scientific achievements and techniques, in which they feel more or less involved. It is a bioethical duty to understand and help satisfy this.

The hypothesis of cloning is the extreme expression of the idea, now widespread in popular culture, of having elements of artificiality in the procreative phases of man’s vital cycle, of concretely creating a moment of medical artificiality in the process that leads to the birth of a child. It is one of the most complex problems raised by the greatest medical developments, that the multiplicity of its aspects offers a complicated mixture of thoughts for reflection. These are thoughts about artificial procreation in general, about how people live and about how experts practice in vitro cultivation, about what can lead to conceiving and the very first undifferentiated phases of development with an artificial method, about conceiving by fusing a somatic cell with a sexual cell, about the wisdom of presenting future possibilities, about how to involve people in medical progress, about the increasingly more persistent risks of introducing needs.

This reflection, in line with the debate on the complexity and the objectivity of scientific knowledge, can be carried out here on the variety of observers and approaches to the problem, on the levels of description of the different scientific disciplines, on how effective is the

communication between them, and the effort to integrate them. The intention is therefore to oppose the temptation of reducing scientific descriptions to linear unidirectional relationships, running the risk of oversimplifying. The reflection is also carried out on the relationship between growing knowledge and the experiences we have on a day to day basis. This is an essential point for the comparison between different cultures, not only scientific, and for the spreading of scientific knowledge in general culture. Human science operates in the complexity of the system of human relations. It is also important to reflect on language, on how this must and can be rigorous and precise when it describes human phenomena and events, natural or produced by man. Language must certainly link rigorous thought to precise words and words to the description of facts, but it cannot ignore the shades, the ambiguities that surround human facts, the limitations of their scientific describability, as expressions of common people's culture, of popular "cultural psychology".

Shades and ambiguities are part of people's lives, they are lived, existential problems, questions about living between science and nature, uncertainties and possible sufferings, that only individual and complex languages can express.

We cannot argue the relevance epistemology assumes from this conceptual point of view, as the critical thought on nature and on the limitations of scientific knowledge and, with regards to the issue of artificial procreation in particular, genetic epistemology concerning the knowledge of man. The idea of genetic epistemology derives from the study of the cognitive development of the child from the moment of birth, but it has left a trace in epistemological thought in general. Looking in more depth at the relationship between biology and knowledge, it presents the problem of knowledge at the centre of the problem of life.

Amongst the material domain and the conceptual domain of the investigation on man, we must distinguish between internal epistemology, concerning the scientific world, and derived epistemology, which takes into consideration the contribution that conjectures, hypothesis, theories and programmes of scientific research directly add to epistemological and gnoseological problems, therefore even the effects produced in people's cultures.

We cannot ignore this epistemology when we are convinced that the effect of science on man cannot be detached from the system of human relations and it reflects on what could make a difference to the prevailing conditions in which the procreative phase of man's vital cycle starts.

The epistemology of those who practice artificial fertilisation and tomorrow could practice cloning, is not like the one of the pure biologist,

who only describes biological data. Biological data are a subject's "source": described in a human zygote that is formed and starts its development in an artificial way, it signals the start of a complex process of cellular differentiation, of organs and functions and cognitive development. With in vitro fertilisation and the transferral of the embryo in uterus and hypothetically with cloning techniques, the human being that is or could be created and of whom we describe the initial biological events, is potentially a subject of knowledge. There can be many questions on his/her future. It seems that we can exclude direct influences of the in vitro fertilisation practice, however we must highlight that the checks on the condition of the child who is born and of his/her post-natal development, are not sufficiently extensive and prolonged in time, therefore internationally we recommend an accurate collection of data also through adequate follow-ups. With regards to the hypothesis of cloning, the questions cannot be answered today. What we know today is that the child would have the nuclear DNA of the somatic cell used in the fusion. The incognita would be the complex web of relationships and exchanges of signals between nuclear DNA and cytoplasmic components and of the working of epigenetic factors during the early phases of development, as well as with regards to maternal or paternal imprinting cancelled by reprogramming the nucleus. Certainly we can make a variety of philosophical, ethical, psychological, legal and scientific considerations, projections on the future and imaginative literature about making a baby who is the copy of another person, of the father, of a brother who is condemned to die and they want to reproduce, of who knows what other person, but for now the reality is a biological upheaval with at the very least unpredictable effects.

Different are the ways of thinking about the hypothesis of cloning within artificial procreation. These are those of scientists who rightly worry that a limitation of research will hinder scientific progress, who can see the benefits they could bring to man, to an improvement in diagnostics and of the therapy of congenital defects and of certain illnesses and of transplant practice; of who disseminates scientific news; of the couples that trustingly rely on medicine to help procreate and that tomorrow could accept the solution of cloning as well, and it is the doctors who are in situations of choosing and deciding the application of artificiality and could find themselves in other situations, increasingly complex and full of problems. The medical objective is also that of caring for our health, and not only people's physical health, of choosing and deciding between different possibilities with regards to human beings.

Reflection naturally extends to generativity that, as we recalled in a previous document by this Committee, is a significant indicator of how the individual faces and elaborates the different stages of evolution of the

epigenetic hierarchy of development. Birth is a biological and relational phenomenon, and biological conception is preceded if programmed, and accompanied if accidental but not refused, by imagining the child that will be born. Birth is also mental, the child is born also from his/her parents' mental state, he/she is an intersubjective reality, a form of life the parents express through their personal linguistic games. During pregnancy the woman has a view of herself as a mother and at the intraphysical level she starts the process of identifying with the being she has conceived and of feeling an attachment to him/her, a process that is favoured by the father's involvement. The involved mother and father elaborate fantasies about the child who they are waiting to see for real. We still do not have sufficient elements to answer the question about how mental birth can combine with artificial procreation, (staring with the process of in vitro fertilisation, which in cloning corresponds to the fusion of a somatic cell with a sexual cell), about how can be the reality of bringing into the world a child conceived in this way, about how this reality can influence the relationships that, once having been born, starts to happen with him/her during his/her development. Even with regards to the relational aspects of bringing the child up, as well as for the child's physical conditions, controls over time are in any case to be recommended. The question is not in line with the human capabilities of adapting to our parents' artificiality, to artificial procreation, of families who find themselves in a relational situation that could be created by this artificiality. It could be inconsistent, but it cannot be ignored, and if not ignored then removed, also because it shapes the way in which those who practice artificiality are and think, to the way of starting relationships with people who trust in them to procreate. At the moment, reflecting on the capabilities of human adaptation to the idea of cloning an entire individual is only a fantasy, adaptation which cannot be compared to that happening with regards to other forms of artificial procreation, about how mental birth can occur for a baby generated with the idea of creating a genetic identity, of limiting his/her right to ignorance of his/her future.

Maybe, faced with this extraordinary scientific progress, we can raise a basic question on the limitations of the research on man, a biological subject, and of knowledge and relational being, of research that at the differentiated organismic level moves towards the undifferentiated source of an individual life, a source that contains the potentiality of his/her development, with regards to what, because of the push of research, can be removed, what has been called epistemological humility and of evaluation.

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