

The Outlawed Clone or Alice in Wondercloneland

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Desperately lonely, on you will understand why, Alice was leaving for France.

At Waterloo station she got on the Eurostar railway; while entering the tunnel she became somehow nervous since she remembered the pursuit of the white rabbit in the depth of earth. This rabbit had become for her a kind of obsession. Very soon she dozed off and began dreaming.

Was it a dream or a nightmare? It looked like she had arrived at Gare du Nord and took the first taxi available. She was surprised by the look of the drivers : they were two instead of one. «Well», she thought, «the French have found an original way to solve unemployment». Yet, she could make another strange observation directly linked to her obsessivel dream: the two taxi drivers looked like white rabbits, with big ears covered by the cap, long foreteeth, and red eyes. And they were very similar, not really identical but similar. Indeed both were born at the INRA station in Jouy en Josas, where Charles Thibault's experiments led to the first IVF rabbit, a long time ago. They were produced by a successful nuclear transfer after splitting several zygotic blastomeres into enucleated oocytes, four in fact. The four neo-zygotes were implanted in different surrogate uteri, but all were more or less affected by the large offspring syndrome and their pregnancies were overdue. The fetuses were extracted but two of them died soon and the remaining two became those nightmare taxi drivers. They were larger than normal, and apparently similar. However, when carefully examined, small differences were obvious from the physical point of view, and their common friends and relatives could tell you they were still much more different from the psychological point of view. Nobody knows precisely if these differences were due to the mitochondrial DNA heredity, or to the epigenetic gestational influence, but their behaviour as well as their way of thinking were really opposite:

—One was very optimistic, always smiling, ready to offer help and to take in charge responsibilities; he was trusting the good aspects of research and discoveries, maybe a little too much overenthusiastic, and anyway very grateful to modern science, to Charles Thibault, Bob Edwards and Ian Wilmut for his present existence. His name was Charybdis.

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—The other one was always angry, pessimistic, announcing disasters and taking pleasure in pointing them out. He sometimes wrote anonymously papers in the newspaper *Le Monde*, where all the new steps of reproductive experimentation and medicine were taken as examples of the devilish way taken by humanity. His name was Scylla.

Alice asked the drivers to go as fast as possible and both hurried up, saying «we are late, we are late !» The taxi went rapidly from Gare du Nord to the UNESCO headquarters Place Fontenoy (as you know, the French like giving names of military victories to streets and squares, and thus are not very pleased to take the train at Waterloo station...)

Alice entered the building with both drivers and watched a very large poster with all the official declarations about human cloning from UNESCO, EU, WHO, Council of Europe, as well as those of Presidents Clinton and Chirac.

She suddenly looked at a full-length mirror and saw her own image. She observed that the movements of this image were not symmetrical to her own, but independent: in front of her, it was not Alice any more, but her double, Alicia, who crossed the mirror, jumped at her and kissed her with great pleasure and satisfaction. The two drivers, more informed about cloning, were less surprised.

1) Alice and Alicia, Both of the Same Age

In fact, Alice's mother, who was sterile, and went through IVF in order to conceive, had only had one fertilized zygote and asked for those two blastomeres to be split. Thus, this artificial twin suddenly appeared in Alice's life, and she and Alicia heard the comments made by Charybdis and Scylla.

Charybdis: Is it not marvellous? Alice has now a sister of the same age; they will be able to play together, dream together. The dreams might not be similar, since, although quite similar, they bear some very clear differences, as we do. In their case, I can even say that they are more similar than we are: they are like monozygotic «mirror image» spontaneous twins; one embryological step further, they could have been a «double monster». With our different mitochondrial-cytoplasmic and surrogate mothers, we are also more different. But despite this monozygosity, they are still not identical: the mysteries of epigenesis!

Tell me, Scylla, I have a sudden doubt: don't you think that our dignity has been threatened, due to the loss of our identity and singularity, which is linked to our surgical and biological origin, and that our dignity has been more offended than the dignity of monozygotic spontaneous twins ?

Scylla sniggered sarcastically: my poor Charybdis!; we have kept our dignity because we are rabbits. Should we be humans, it would have been a quite different story, and this dignity would have been lost, since it is obvious that it pertains to the way people are conceived.

Charybdis: What do you mean by «way»? Do you really think that there is more human dignity

in the unconscious conception of a child, in a natural way after a drunken party, than by a voluntary act, with the help of a medical technique, but in an environment of love and tenderness?

Scylla: Don't confuse the use of a medical technique in order to overcome infertility and its use for the sole purpose of fulfilling the phantasmagoric dream of creating twins. And this at the very time when all involved in IVF and ovarian stimulation try to reduce the risk of multiple pregnancies. Do you forget the adverse consequences of multiple pregnancies, including «simple» twinning, prematurity, fetal growth retardation, neurological defects, etc.?

At that time, Alice suddenly saw behind her a second mirror with the reflection of Alicia—or was it her own, she didn't know—, and the same in the front mirror, and again the same in the rear mirror, so that hundreds of Alice-Alicias were appearing, smiling, then less and less, then astonished, now anxious, now afraid.

Scylla: Do you see, my dear Charybdis, where this is leading us? To have twins voluntarily might be acceptable, although relatively expensive. But now, there could be ten, a hundred, a thousand identical copies. There is no limit to the delirious fantasies of humanity. Aldous was right, and despotic powers could make numerous domesticated and identical slaves, underhumans ready for any evil purpose.

Charybdis: With the risk of revolution of these slaves... Be serious, Scylla.

And he broke the rear mirror, leaving Alice and Alicia alone together, reassured and happier...

2) 20-year-old Alice, 10-year-old Alicia

Alice was a lonely girl. She had dreamed for years of a sister. But Alice's mother was sterile, as we know. In the mirror at the UNESCO building Alice discovered another Alice, 10 years younger, looking as she had 10 years earlier, with only some slight differences (always the epigenesis...) She was very pleased, but also felt apprehensive. At the age of 20 one does think about one's own identity. This young girl in the mirror, was it herself 10 years ago, or somebody else, but similar, belonging to the present?

She did not know that when she was 9 years old she developed leukaemia. Treatments were already efficient at that time, and amongst the various possibilities, Gluckman's publications about the use of cord blood had stimulated a very large interest. It was well known that some couples had requested to use such cord blood from an ongoing pregnancy in order to help cure their ill child. It is difficult to determine with a high degree of accuracy if this ongoing pregnancy was fortuitously used for that purpose or deliberately conceived with this aim.

Scylla: Look, this is a typical instrumentalization of a human being, particularly if the child was conceived with this idea in mind.

Charybdis: But who can pretend to know the obscure procreative desires occurring in the heart of humans ? And if the use of the cord blood was the main, or the only, purpose for procreation, is it to be condemned? Is it wrong ? And has the child who was thus conceived lost her dignity?

Scylla: But think, this is a dangerous slippery slope. I agree that Alicia may have been conceived for several reasons, for her own sake, as well as a cure for Alice. I agree, from a consequentialist or utilitarian point of view, that the results of this conception are good : Alicia's cord blood has been efficiently used, Alice is in good condition, Alicia is a marvellous child, and her parents are very happy. However you cannot ignore the fact that the conception and the body of Alicia, more specifically the blood of her own cord, have been used, for the purpose of somebody else, without her consent. It is a typical case of instrumentalization, of reification of the human body. It falls foul of the Kantian imperative.

Charybdis: It is exactly the same situation when you use the heart or the kidneys from somebody in a vegetative state after a car crash, or, in a perinatal context, from an anencephalic fetus, whose pregnancy has been more or less artificially prolonged to term instead of interrupting it at 5 months.

Scylla: No, it is not the same, since the car crash or the anencephalic condition has not been deliberately provoked in order to get organs.

But I was talking about a slippery slope. Suppose Alice's mother became sterile after Alice's birth, due to tubal obstruction. She could request IVF, even if definitely linked to the desire of having the cord blood ready for Alice's treatment. Again it could be considered as ethically justified. Suppose now that the hyperstimulation leads to a large number of oocytes, with a good fertilization rate and that Alice's parents have now 20 zygotes cryopreserved in surplus of Alicia's zygote, who, once implanted, would grow beautifully. Alice's parents do not wish to have more than two children. What are they going to do with the 20 spare zygotes? In the U.K. they could donate them to another couple, ask for their destruction, or accept, under precise conditions, their use for research purpose. Don't you think it is also instrumentalization?

Charybdis: Yes, but with a legitimate purpose.

Scylla: According to French law, no purpose which affects the integrity of the zygote may be accepted. This is because, despite several divergent opinions, this zygote, even severely malformed (for example with chromosomal abnormalities), even near cellular death, even condemned to die, is still considered as an actual human person, protected by the law from any experimentation. Paradoxically, death can be accepted since death is the ultimate event of every human life, so that to stop cryopreservation may be admitted under precise conditions, but not experimentation. In other words, destruction can be performed in order to avoid any kind of instrumentalization, according to Kantian principles. Indeed research is instrumental, death is not.

Charybdis: But such an attitude prevents any further research, any further progress, in the field of artificial reproduction, as well as in the one of natural reproduction, like infertility, miscarriage, etc. Kant's principles are respected, but not the interests of humanity. If such an

attitude had been followed by Edwards and Steptoe, IVF would not have existed, and this would have been detrimental for many couples.

Scylla: Where lie the interests of humanity ? In the interests of quite a few people or in the protection of humanity as a whole ? You are in favour of this utilitarian attitude. I am in favour of respect for the transcendental principles of respect of identity and dignity of human beings.

Please, let us go back to the U.K. and the 20 frozen eggs. Suppose that Alice's parents agree to use them for research, and more specifically to extract the embryonic stem cells and obtain cultures of hematopoietic, skin, muscular, nervous cells for therapeutic use in other children, maybe Alice herself, or adults with several kinds of diseases, as is at present done in mouse embryos. Would you agree?

Charybdis: I hesitate.

Scylla: The French National Ethical Committee did not protest in 1994 when zygote experimentation for reproduction studies was banned. It now proposes to change the law, to allow the use of embryonic stem cells, once its safety and efficiency are demonstrated for humans. The reasons are the possible therapeutic benefit, but also economic reasons, in order not to have to buy such cells abroad. This is the slippery slope towards more instrumentalization of the human being, less respect for human dignity, providing you of course consider that the zygote is actually a human person, even with a soul.

And now, let us go further. Alice developed leukaemia and recovered well. But suppose now that Alice was affected a few years later by a kidney disease leading to removal of both organs. Don't you think her parents would be ready to consider the possibility of grafting a kidney from Alicia to Alice ? What if Alice and Alicia were natural twins? You certainly remember that the possibility of having a clone kept as an organ or cells donor in reserve was at one time presented as an argument in favour of human cloning. I don't really know if this was a serious proposal, or a kind of provocative humour. But it was taken as a vigorous counter-argument by those like myself opposed to human cloning.

Charybdis: Is it legally possible?

Scylla: Not in France where organ donation from a minor is strictly forbidden, except for bone marrow transplant.

Charybdis : You give me an argument in favour of cloning when this highly questionable use of clones as organ donors is relatively easy to forbid! On the other hand, a cloned adult would certainly be able to protect him/ herself and to defend his or her identity. After all, who is the person, and who is the clone ? Thus this argument of the slippery slope towards the clone reserve organs is not valid.

Scylla: But a point remains : if we have several clones issued from blastomeric splitting, cryopreserved and implanted in different recipient mothers, then a definite risk of transgenerational consanguinity exists. And this risk could modify our concepts concerning the meaning of generations, and the relationships between them.

Charybdis: Yes, but that means only that specific means of protection have to be implemented and not necessarily a ban on cloning, which in some situations may be useful.

Scylla : Which ones?

3) Transmission of Mitochondrial Disease

Charybdis: Let us suppose that Alice's mother was affected by a congenital disease due to transmission of defective mitochondrial DNA, and that all the preceding children died. The only way to protect a further child is to fertilize an oocyte, transfer the blastomeric nucleus into the healthy donor oocyte cytoplasm and implant the resulting zygote into the uterus of the original woman, or of a surrogate.

Scylla: Are you sure of the efficacy and of the safety of such procedure?

Charybdis: Not yet. To the best of my knowledge it has not been attempted but it could be, and for a legitimate purpose. Note that this will certainly be defined as reproductive cloning with nuclear transfer.

Scylla: No, it is nuclear transfer, without cloning.

Charybdis: Yes, if only one blastomere is used. But this would be unethical since the success of the first attempt is not assured. It follows that a good precaution would be to apply the same procedure to several oocytes at the same time, or to several blastomeres, i.e. clones.

Scylla: What about safety? We know of the large offspring syndrome, possibly due to nuclear transfer, of risks of telomeric changes, uncertainties about the process of ageing of such cells, risks of carcinogenesis, even in further generations. More generally the role of mitochondrial DNA in a lot of metabolic or evolutionary processes calls for serious precautions and research before using this technique in humans.

Charybdis: I quite agree. But those are precautions, not interdiction.

Scylla: And what about the psychological aspects? You have evoked the possibility of a surrogate mother. The child would then have 3 mothers: the nuclear DNA donor (i.e. the true «genetic» mother), the donor of the oocyte cytoplasm and of mitochondrial DNA (to be called «mitochondrial mother»?) and the surrogate (uterine) mother.

Charybdis: And maybe also, an «adopting» mother. I agree that this is a confusing situation.

4) Cloning and Germline Gene Therapy

Charybdis: You know about Polly. You will agree that the association of transgenesis to cloning is useful in animals.

Scylla: Without the slightest hesitation. But I'm reluctant to accept it in humans, for two reasons: one is that germline gene therapy is almost universally criticised, and because it would require the creation of embryos for research. Also, even if gene therapy is performed, there is no need for cloning.

Charybdis: May we consider your last remark? You will probably admit that success here again is not guaranteed. So that instead of doing several attempts, it could be better, and more ethical, to process simultaneously several zygotes, or in association with cloning.

Now you are reluctant for two main reasons, the need for zygote research and creation of zygotes for research and the objection to gene therapy itself. Let us consider the first reason. What are your arguments?

Scylla: First of all, note that you are considering both kinds of research at the same time. This is questionable. The French forbid both for the sake of the principle of the sanctity of the human person from the time of conception, even if the conception is abnormal, dying, or abandoned. This attitude stems from the direct influence of both religious beliefs (the notion of the immortal soul) and philosophical Kantian principles (refusal of instrumentalization of human person and principle of universality). The weakness of this position, although highly respectable, is that it does not prevent the destruction of this early human life, neither in law (on the contrary, to «stop cryoconservation» may be mandatory), nor in jurisprudence (remember the shocking decision of the Court of Appeal of Toulouse, concerning the obligation to destroy the two cryopreserved zygotes of Madame Pires, whose husband died in a car crash and who desperately wished for and was refused posthumous implantation). Thus, French law leads to this situation: death yes, since it is not a person, experimentation, no, since it is a person, although the Conseil Constitutionnel said it «understood» that the protection established by the law in favour of the human person from «its beginning» does not apply to zygotes «in vitro», and the decision of the Court of Toulouse indicated that these zygotes must be destroyed since they are neither persons, subject to rights, nor things, belonging to their «mother», and object of rights.

So what are that «human zygotes», persons, and not persons, but not things? It is clear that to say a «potential» for a person or a «potential human person» may be considered as an amusing or provoking semantic play on words, masking a difficult reality, but not helping to solve the dilemma. Some people propose a third entity, submitted to a particular kind of moral and legal protection evolving with time, linked to specific rights. But it is almost unthinkable to be brave enough to admit considering this third entity when we have lived for centuries with concepts inherited from Roman law, well before in vitro fertilisation had become a classical way of coping with infertility problems.

In this respect, the position of the Catholic church forbidding at the same time any kind of research and the destruction of human zygotes, and any kind of in vitro fertilization can be considered as dogmatic, brutal, far from charitable, but certainly logical and coherent. Its weakness lies in the difficulty to decide from a biological point of view when a new life begins. It must be added that the Vatican never decided that this life begins «at conception» nor that this new entity is an actual human person, but must be considered as a human person.

The British, on the contrary, acknowledge IVF legitimate, of course, research on embryos until the 14th day, and creating embryos for research purpose. This is again a quite logical and coherent attitude based on the utilitarian principle of efficiency, of benefit for many, without harm to others, implicitly recognising that these zygotes are not «others», i.e. «other human persons».

In between these two logical, coherent, philosophically grounded attitudes, we found the position of many official and non-official bodies, national and international, governmental and

non governmental, which try to reach the impossible consensus in saying that research could be admitted, but only on «spare» zygotes or embryos, which (or who?) for any reason could not or were not to be implanted. This was, for instance, the decision of the Council of Europe. Understandably that decision was criticised, particularly by the British, on two accounts: the first was raised at a meeting in Strasbourg on the status of the embryo. Mrs. Inéz de Beaufort pointed out that this restriction could be overcome by the stimulation of many oocytes in IVF cycles, leading automatically to the creation of many zygotes and embryos without any hope of implantation, and consequently ready for research.

The second and more important one is that such a rule would lead unavoidably to unethical attitudes. Suppose indeed a new scientific advance like for example oocyte cryopreservation, or germline gene therapy. Would it be ethically acceptable to implant the first human zygotes obtained following such a technique? Obviously not, not until careful examination (including for example laryotyping, etc.) were performed and the absence of any adverse effect could be ascertained. So that the first embryos would have been scientifically examined and **destroyed**, consequently made for «legitimate» research purpose. What I question is this legitimacy.

Charybdis: Here we differ. I am ready to admit it. This is a matter of philosophical opinion.

Scylla: Let us consider now the criticisms against germline gene therapy in itself. I refer to two arguments : the first one is that any change imposed on the human genome, either in its haploid, gametic, situation, or in its diploid, blastomeric state, whatever the purpose, bears the risk of positive eugenics.

Charybdis: Please don't use this kind of political or mediatic argument. You know, like myself, that the most unacceptable forms of eugenics, including its extreme representation, leading to genocide, had nothing to do with the advances in genetics and were linked to aberrant ways of thinking. I prefer this last term to the one of philosophy, since, in my opinion, the cult of superior men or races, as well as the description of «untermenschen» cannot be considered as a philosophical matter. What we have in mind here is to look for gene therapy which instead of trying to cure the pathology of an affected person (somatic gene therapy) will cancel out the deleterious effects of this abnormality, and at the same time protect the individual concerned and its progeny. This could be done by either a modification of the haploid genome of a male gamete, in the case of genetic spermatogenic dysfunction, or a change in the genome of a blastomere. I still do not understand the criticisms raised against the principles of such a goal. May I add that two moral and legal authorities, which cannot be considered as particularly audacious, agree on this principle: on the one hand the French law of 1994, which admits the principle of research for this purpose. On the other hand Catholic authorities, which through their representatives at the meeting on the embryo in Strasbourg admitted this research which aims to care very early for this «human person». Recently, the Assembly of French bishops were reluctant «at the present time» to underwrite it, implicitly admitting the lack of any dogmatic objection against it.

Scylla: But there is no need for such research, because as stressed by very prominent geneticist, another solution always exists, preimplantation genetic diagnosis (PGD). If there is a

risk of transmission of genetic diseases, since several fertilized zygotes are usually available, the goal is to select the ones phenotypically normal (either homozygous or heterozygous) by PGD. So that there is no need for a difficult and risky transgenesis.

Charybdis: I don't agree with this simplistic view of the situation for three main reasons. First they are genetic situations (abnormal phenotypes due to recessive homozygous disorders, of hearing or visual systems for example) where the affected people frequently live in specialised institutions and are prone to marry and to have affected children, where no phenotypically normal zygotes can be obtained.

Second, in the more frequent situations linked to dominant or recessive, heterozygous genotypes, there could be no normal zygote available ; in this case the decision to attempt IVF and PGD again, with its inconvenients and risks, or to proceed further, if scientifically possible, towards gene therapy would be the choice of the parents.

And third, from the beginning of the process, it could be also the parental choice to refuse for philosophical or religious reasons a kind of selection of normal zygotes and of discrimination against abnormal ones. Thus Vatican authorities preferred to undertake the earliest therapeutic approach, i.e. to correct the zygotic (or gametic) abnormality for the benefit of the child to be and of its progeny. Thus it cannot be said that there is no a priori indication for germline gene therapy.

Scylla: Your arguments can only be accepted if you agree on the premise of the legitimacy of manipulation, and finally instrumentalization of human embryos. You deny these embryos the status of actual human being. Here lies the huge gap between us : for you the end justifies the means, and your goal may be logical and for the benefit of other humans. Again this is a consequentialist approach. For me this goal does not justify the destruction of a human body, whether it has a soul or not, and the embryo is an actual human person. This is a transcendental approach.

Charybdis: If I have been unable to convince you in this matter, I suspect I will be still even less successful concerning Alice's family.

5) Cloning from Adult Cells (Dolly)

I wish now to apologise, since I notice that I haven't told you all the truth concerning Alice and her family.

I mentioned that Alice's mother was sterile, but I didn't tell you what happened when Alice reached 25 : her father was involved in a car crash, transferred in a vegetative state, and the decision to withdraw care was finally taken. Alice's mother was desperate. She was 45 years old. She had been very happy with her husband despite all the medical problems she had to cope with. Now she was about to lose her loved husband.

Scylla: I know what happened. She saw one of these crazy advertisements or read some crazy information in the newspapers and she asked this man in Chicago to do something for her. He accepted, took a cell from the husband before stopping the machine. Of course an

electroejaculation could have been done also with either artificial insemination or IVF. But remember she was 45 and the chances of success were very few. She could have obtained a donated oocyte, and/or a surrogate mother, but in all these situations she would obtain **only** another child, girl or boy. And this was not **what** she was expecting. I use voluntarily this word of «what» instead of «whom», in order to make clear, once again, she was wanting something, more than somebody. So that she requested a somatic cell from her husband ; the nucleus of this cell was implanted into the enucleated oocyte from a donor (since Alice's mother's ovaries were near failure), and a good zygote was obtained and cryopreserved in order to give her time to think more carefully about the future. Actually, she was facing a complex choice: she could seek a surrogate mother, who would give birth to a child with Alice's father's nuclear genome, the mitochondrial genome of the donor, the biological influences of the surrogate during pregnancy, and nothing finally related to herself.

Charybdis: It is exactly the same for both of us, except that we come from fertilized eggs. But we have also experienced the various effects of mitochondrial heredity and epigenesis. So in is this situation this child would be very similar to the father, of the same sex, but not really identical.

Scylla: Yes, and Alice's mother would look after and educate someone looking like her former husband, but without any family or social link with her. One may even wonder what could be her rights on this zygote and child. This is why she took the alternative choice, i.e. to have this «husband zygote» implanted in her own uterus. Here we observe what could be really called a «Charybdis to Scylla situation».

Charybdis: Don't joke about our names, please...

Scylla : Indeed, trying to establish stronger links with her dead husband's cell, she created a really unbearable situation : this boy, made with the nuclear genome of her husband, developed in her uterus, so that, in the end, she delivered a baby boy quite similar, if not identical to her dead husband. She could become at the same time the widow of her husband, his mother, and her own mother in law. As far as Alice was concerned this young boy could be considered to be simultaneously her younger brother, but also her younger father. When Alice's mother was nursing the baby she had feelings not completely devoid of some incestuous connotation, and when Alice or Alicia were taking care of their young brother they also both experienced difficulties in stating their precise individual and familial relationship.

Charybdis : What happened ?

Scylla : A tragic end, which was not at all unexpected : Alice's mother became seriously disturbed by this unbearable situation. And this situation became still worse when this baby, maybe damaged by the nuclear transfer, died of a sudden death syndrome at the age of 4 months. Alice's mother committed suicide a few weeks later, as did Alicia whose own psychological situation with respect to Alice was never clearly established.

You understand now why Alice is leaving her country and experiencing not dreams but nightmares when entering the tunnel.

Charybdis: I fully agree with you. Such situation is not acceptable. Particularly, as already

said, because of the complete disturbances in familial and social relationships due to the delay for «creating» such a new individual. I agree with you that all these manipulations must not be done, whatever the circumstances.

Scylla: But some people have considered the possibility of cloning for various reasons, death of husband as for Alice's family, death of a child, maybe the least unacceptable situation, desire to obtain a zygote from a Nobel Prize winner, wish for immortality (two particularly stupid ideas). This explains probably both the strong reactions of so many people and these many decisions to outlaw human cloning. It must be added that the new possibility of nuclear transfer in two steps, with an intermediary step in an oocyte which could be obtained from corpses, fetuses, or even animals (with the risk of virus infection) renders such attempts still more frightening and justifies interdiction or at least a moratorium.

Charybdis: I personally would prefer a moratorium. Since I am still not convinced of the legitimacy of such a rigid attitude claimed by so many national and political authorities, international agencies, non governmental organisations, media, etc...

Scylla: Wouldn't they be useful in stating officially that whilst animal cloning has numerous scientific and medical applications, human cloning is fundamentally opposed to the natural order of things, since the dignity, identity and variability of the human species must be protected — including by law— against all the fantasies of mad scientists?

Charybdis: Let me remind you of several points : first, up to now, the disasters which have jeopardised the present and the future of humanity have been caused more directly by people and governments under the influence of their philosophical and religious beliefs or of their racial prejudice, than by biologists.

Second, we are considering here scientific progress of two different types: blastomere splitting, and even nuclear transfer from embryonic or fetal cells have been known and performed now for years. Numerous animals of different kinds have been born that way. So that the potential dangers of human applications of such techniques could have been considered for a very long time. Why did politicians, philosophers, media professionals remain silent, then so excited after the birth of Dolly ? Because of the scientific achievement of the dedifferentiation-return to differentiation process ? Indeed a remarkable step forward, once demonstrated as reproducible, but obviously not adaptable to mankind, due to the high number of necessary attempts and the uncertainties about the precise nature of the original «Dolly» cell. Aren't you tempted to irrespectfully think that all these people have precipitously taken this opportunity to affirm their existence, to demonstrate their usefulness and to provoke within the public a gratifying anxiety concerning the progress of biology. Some may have enjoyed establishing international codes because of their philosophical or political tendency to impose strong rules of totalitarian nature, instead of trying to stimulate public opinion to think and decide on their own.

It is clear that the human applications of cloning are very limited: there are no real indications for blastomere splitting, those of nuclear transfer (like mitochondrial diseases) are exceptional, those associated with germline gene therapy are still problematic, and the achievement of a

human Dolly bears so many uncertainties —including the next generations— that it would be irresponsible behaviour to undertake it at present. There are indeed at present enough technical limits to such application to humans that it seems unnecessary to refer to fundamental principles which, like so many others, could prove sooner or later to have been ill understood. Let us be pragmatic and consequentialist. This is the reason why I am personally more in favor of a scientific moratorium than of a set of international and national prohibitions.

Scylla: Yet, this scientist from Chicago announces human applications for soon.

Charybdis: Too much noise has been made around this questionable announcement. You know, another American started selling land on the moon. And people bought some! Such attitudes are always observed, and have little to do with scientific and medical progress.

6) The Next Step : Artificial Meiosis

Scylla: Since we are talking about scientific evolution, let me provoke you a little: don't you think that the cellular manipulation which led to the birth of Dolly could lead us to a revolutionary change within the process of mammalian reproduction, i.e. artificial meiosis?

Charybdis: What do you mean?

Scylla: The main criticism against cloning from adult cells is the fact that the resulting individual would be very similar to the original adult (with the mitigation of mitochondrial and/or epigenetic influences). This similarity leads obviously to a loss of identity for individuals and of evolutionary change to the species. Suppose now that this diploid somatic cell could be manipulated in such a way that, during the course of its dedifferentiating process, it went back to a haploid state. This strange idea came already to the mind of G. David who was the founder of the CECOS in France. Such a haploid cell could be fused with another haploid cell, either a gamete or another transformed somatic cell, and possibly after nuclear transfer produce a diploid zygote.

Charybdis: I see immediately a possible application in the case of irremediable infertility. It would make all donation of gametes or embryos unnecessary. A scientific achievement solving ethical dilemmas ! At the same time this haploidization process would give the resulting individual an identity and restore the diversifying evolution of mankind.

Scylla: As usual you are overoptimistic. I personally see other consequences : of course Miss Josephine «Turner» could get married with Harold «Klinefelter» and have children on their own. That's perfect. Alice's mother could have an oocyte fertilized with a somatic haploid cell from her husband, and have a quite «normal» posthumous child. That's again fine. But look : Alicia, instead of committing suicide, could have requested to have her own somatic haploid cell fertilized with either one of her own oocytes, or if much older, with another of her own somatic haploid cells, realising a new type of parthenogenesis- a new type since the forthcoming child would be different from the mother.

Interesting from the scientific point of view because it would allow the careful study of mitochondrial heredity! But socially? This could be done also by her brother should he have

survived, with the help of a surrogate mother. And of course by homosexuals of both sexes, with implantation into the uterus of one of the two females for lesbians, in a surrogate for men. And they would be the **true** children of both members of the couple. Frightening, isn't it?

Charybdis: This is frightening. I see another consequence : if this happens, the male sex and the Y chromosome will become useless. There are already 3 times more X chromosomes than Y. That means that the male sex will unavoidably disappear..

Scylla: Now you understand my reservations.

Charybdis: However, once again, the important thing is not the technique but the purpose...

It is exactly at that time that, probably frightened by this horrifying vision, Alice woke up from her nightmare. Anyway the Eurostar just pulled into Gare du Nord. She jumped out on the platform and fell into the vigorous arms of her French boyfriend, Guillaume, whom, after so many adventures, she intends to marry and have many children with, if possible following the «traditional» method and conventional rules. But what is a tradition, what is a rule?*

* Nothing to do, of course, with William the Bastard...