Re-examination of the law on bioethics

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Introduction

Article 21 of law n° 94-654, dated July 29th 1994, provides for re-examination by Parliament no later than 5 years after the law's entry into force. This clause is justifiably inspired by the fact that the law's scientific foundation is, by its very nature, in a permanent state of evolution so that it is advisable to consider possible consequences of this fluctuation on the state of law. In view of the above deadline, Monsieur Bernard Kouchner, Secretary of State for Health, asked the National Consultative Ethics Committee (CCNE) to comment on those portions of the text which would in its view require addition or revision.

The Committee confined its comments to articles of the law which it felt deserved examination. Because subject matters were closely connected, the Committee felt it should also express opinions on some aspects of law n° 94-653 of July 29th, 1994, and of law n° 88-1138 of December 20th 1988.

It should be added that ever since it was established, the Committee has taken a keen interest in the possibility of legislation emerging from some of its Opinions. A number of them had no such follow up for reasons which the Committee has no brief to evaluate. However, it thought that a useful purpose would be served by seeking out and collecting together these Opinions to submit them to Parliament which could then, when it undertakes its programme of work, keep them in mind as a source of complementary reflection on subjects germane to those which it is directly tasked to deal with.

PROPOSALS IN VIEW OF REVISION OF THE LAWS ON BIOETHICS

Reference : Law n° 94-654, dated July 29th 1994, governing the donation and use of elements and products of the human body, medically assisted reproduction, and prenatal diagnosis.

CCNE PROPOSALS

Reference : Law n° 94-654, dated July 29th 1994, governing the donation and use of elements and products of the human body, medically assisted reproduction, and prenatal diagnosis.

Preliminary Proposal

Article 21. The present law shall be the object, after evaluation of its implementation by the Parliamentary Bureau for the evaluation of scientific and technological decisions, of re-examination by Parliament no later than 5 years after the law's entry into force.

Considering continuing progress achieved by research and changes in society regarding subjects governed by the law submitted for re-evaluation in 1999, CCNE recommends that Parliament considers re-examination every five years.

I. SAMPLING

- EMBRYO/FOETUS, DECEASED, AFTER ELECTIVE ABORTION, FOR THERAPEUTIC OR RESEARCH PURPOSES.

Reference : no legislation

Reminder for information : CCNE :

Opinion n° 1 on sampling of dead human embryonic and foetal tissue for therapeutic, diagnostic, and scientific purposes. (1984)

Opinion n° 52 on the creation of human embryonic organ and tissue collections and their use for scientific purposes (1997)

Opinion n° 53 on the establishment of collections of human embryo cells and their use for therapeutic or scientific purposes (1997)

CCNE proposal :

CCNE recommends that sampling and utilising normal embryonic tissue or organs should remain an exception, and only be considered when well defined protocols and research projects are submitted for approval to the National Commission of Medicine and Biology in the field of Reproduction and Prenatal Diagnosis.

- SAMPLING OF DEAD FOETUS FOR FOETOPATHOLOGICAL OR RESEARCH PURPOSES

Reference : Decree of May 28th, 1997 (follow up of law 94-954 of July 29th 1994)

- Art. R. 162 - 19 : includes a foetopathologist in the prenatal diagnosis team

- Art. R. 162-30 provides for foetopathological analysis in cases of abortion for therapeutic reasons

CCNE proposal :

Foetopathology, i.e. diagnosis after abortion for medical reasons, or foetal death in utero, is a developing medical discipline which has medical and social consequences deserving consideration by Parliament.

Moreover, there is no recognition of any particular status for the mother when foetal death occurs before the sixth month of gestation.

CCNE recommends that Parliament considers the consequences of gaps in legislation as regards :

1. autopsy and research on the foetus ;

2. for the mother, social, medical, psychological, and economic issues.

- SAMPLING ORGANS OF DECEASED PERSONS FOR THERAPEUTIC OR SCIENTIFIC PURPOSES

Reference : Art. L. 671-7 to 11.

Art. L. 671-7. - Sampling of organs of a deceased person may only be performed for therapeutic or scientific purposes and after death has been established in conformity with conditions defined by the decree of the *Conseil d'Etat* .

Sampling is permitted, providing the persons concerned did not make known their refusal of the procedure prior to decease.

Refusal may be made known by registration of that decision on an automated national register provided for that purpose. It may be rescinded at any time. Management and operating modalities of the register are governed by a decree of the *Conseil d'Etat* .

When a physician has no direct knowledge of the deceased person's wishes, the family must be consulted if possible to provide testimony.

Art. L. 671-8. If the deceased was a minor or a legally protected adult, sampling with a view to later donation is only permitted on the condition that each of the holders of parental authority or the legal representative give written and explicit consent.

Art. L. 671-9. No sampling for scientific purposes other than identifying the cause of death is permitted without either the consent of the deceased, expressed in person, or through the family's testimony.

However, when the deceased is a minor, consent may be expressed by one of the holders of parental authority.

Families are informed of sampling in view of identifying the cause of death.

Art. L. 671-10. Physicians establishing the death certificate, on the one hand, and those proceeding with sampling or organ transplant, on the other hand, must belong to separate units or departments.

The French organ graft establishment (Etablissement francais des greffes) is to be informed of any sampling referred to in article L. 673-8.

Art. L. 671-11. Physicians who have performed sampling on a deceased person are under obligation to ensure that the body is restored to a presentable condition.

CCNE proposals :

1. CCNE notes a contradiction in the law between two ways of dealing with the deceased person's consent regarding sampling for scientific purposes. Article L.671-7 refers to presumed consent, whereas Article L. 671-9 mentions a demand for explicit consent.

2. The three purposes of sampling should be clearly identified in the law :

a) therapeutic purpose, to donate an organ which can save a life in jeopardy, which is a true priority for public health;

b) medical purpose, for autopsy, the final medical act which can serve to identify the cause of death;

c) scientific purpose, which is related not only to harvesting organs, but also tissues, cells, and products of the human body.

3. Presumed consent must be retained in sampling for therapeutic and medical purposes, and extended to sampling for medical research.

This extension is proposed by a broad majority of the members of the CCNE. However, three members oppose the proposal.

4. The refusals register should be designed to record the wishes of the person concerned as regards the three possible purposes of sampling.

The public must be informed of the existence and mode of operation of the register.

5. The establishment of a refusals register to record opposition to sampling as regards each of its purposes, may appear to be in contradiction with retaining the family's testimony as a possibility, and all the more so because such testimony is sometimes taken to signify consent. However, in the interim period before the register is actually established, keeping the present system seems advisable. If that course is pursued, in any event, the role played by those tasked with contacting families must be spelled out so that it is clearly understood that they must steer a course between advocating solidarity as implied by sampling for the purpose of organ transplant, and respecting the autonomy of the deceased person's will. As a result, there is a clear need for training those who are in contact with families in such delicate circumstances, and this could be written into legislation. They need in particular to spare the feelings of the bereaved, observing the spirit of article L. 671-11 of the Code of Public Health.

- LIVE DONOR ORGAN SAMPLING

Reference : articles L.671-3 to 6.

Art. L. 671-3. Live donor organ sampling may only be performed to serve direct therapeutic interests of a recipient. The recipient must be the father, mother, son, daughter, brother or sister of the donor, except in the case of bone marrow sampling for transplant.

In an emergency, a spouse may be the donor.

The donor, having been previously informed of risks incurred and possible consequences of organ sampling, must express consent to the Superior Court Judge *(Président du Tribunal de grande instance*), or a magistrate designated by the Judge. In an emergency, consent is ascertained, by any means available, by the District Attorney (*Procureur de la République*). Such consent may be rescinded at any time, and in any manner.

Art. L. 671-4. No organ sampling for the purposes of donation may be performed on a living minor or on a living adult under legal protection.

Art. L. 671-5. By derogation to article L. 671-4, sampling of bone marrow may be performed on a minor for the benefit of a sibling.

Such a sample may only be taken if each of the holders of parental authority or the legal representative of a minor give consent. Consent is expressed to the Superior Court Judge, or a magistrate designated by the Judge. In an emergency, consent is ascertained, by any means available, by the District Attorney.

Authorisation to perform sampling is given by a committee of experts which verifies that the minor has been informed of the proposed sampling procedure, so that his/her wishes can be make known, if the minor is competent to do so.

If the minor refuses, sampling is prohibited.

Art. L. 671-6. The committee of experts referred to in article L. 671-5 is composed of three members designated for a three-year term of office by decree of the minister in charge of health. Two of its members are physicians, one of which is a paediatrician, and the third member is not a medical practitioner.

The committee takes a decision with due regard to the general principles and rules outlined in chapter I above. It appraises the medical necessity of the procedure, the risks entailed, and also predictable physical and psychological consequences.

Decisions by the committee of experts to refuse authorisation are not explained

CCNE proposal :

CCNE wrote a report on this subject dated March 27th, 1998. In this report, two proposals are made. The first bears on a controlled extension of categories of donors within the family framework and between non-related persons. The second proposal covers the mode of operation of the regional committee of experts, in particular in so far as it should be requested to explain reasons for refusal to authorise a transplantation. (cf. annexed text).

- DONATION OF BODY TO SCIENCE

Reference : no legislation

CCNE proposal :

CCNE recommends that legislation should be formulated to improve relations with families and how they should be approached and assisted at a time which commands respect for their feelings.

II. MEDICALLY ASSISTED REPRODUCTION

Reference : Article L. 152-1 to 10.

- Definition of medically assisted reproduction
- **Reference : Art. L. 152-1 :**

Medically assisted reproduction refers to clinical and biological procedures which enable conception in vitro, embryo transfer, and artificial insemination, as well as any technique of equivalent effect leading to reproduction by non natural processes.

CCNE proposal :

Taking into account CCNE's comments on the subject of inducing ovulation by ovarian stimulation in two of its Opinions, i.e. Opinion n° 24 *on embryonic and foetal reduction* (1991), and Opinion n° 42 *on the evolution of practices concerning medically assisted reproduction* (1994), CCNE proposes that legislation should broaden the definition of medically assisted reproduction by suppressing the words *in vitro* from article L. 152-1. In fact, therapeutic induction of ovulation is a form of medically assisted reproduction.

Including therapeutic induction of ovulation into medically assisted reproduction as defined by law would have the following immediate consequences (these consequences are already included in the provisions of the law) :

- mandatory written consent by the couple
- the possibility of evaluating and tracking ovulation induction procedures
- submitting such procedures to the rules of safe health care
- identification of practitioners and recognition of their competence by health care authorities

For more detailed information, a recent INSERM report on Immature Infants should be consulted, and also a summary of the issue in the annexed document *Example of an evaluation of medical practices, Ovulation inducers for the treatment of infertility.*

- Access to medically assisted reproduction

Reference : Art. L. 152-2 :

The purpose of medically assisted reproduction is to respond to a couple's wish to become parents.

It aims to surmount medically diagnosed pathological infertility. It may also serve to avoid transmitting a particularly severe malady to offspring.

The man and woman who form the couple must be living, of reproductive age, married or able to prove that they have lived together for at least two years and have given prior consent to embryo transfer or insemination.

CCNE proposal :

Conditions of access to medically assisted reproduction are based on a choice made by society to the effect that the interests of the unborn child are best served by being born and growing up in a family made up of a heterosexual couple. Changes in moral attitudes in the last five years do not seem to justify any modification of these conditions. At this point, therefore, CCNE is not proposing any modification.

- Role of the medical team in medically assisted reproduction

Reference : Art L. 152-10

Medically assisted reproduction must be preceded by private conference between the requesting couple and members of the pluridisciplinary medical team of the Centre, who may call upon the contribution, if required, of the social services as provided by heading VI of the Code for the Family and Social Assistance.

CCNE proposal :

So that the medical team can rely on the social services to which they could apply for counsel, CCNE proposes that in the text of the law, after "social services", should be added the following wording : *who will provide reasoned advice*.

CCNE adds that heading VI of the Code for the Family and Social Assistance is in fact no longer included in these texts.

- The embryo's future

When a couple decides not to go ahead with projected parenthood, or when a two-parent family is no longer an option (death of a spouse), there are three possible futures for the preserved embryo :

1. another infertile couple may receive it

2. it may be destroyed by terminating conservation

3. it may be used for study or research

CCNE proposal :

- on giving the embryo to another sterile couple :

Will the future child have the same rights as an adopted child, in particular as regards the right of being told the truth about his/her origins ? This is an important issue and deserves separate discussion.

- on terminating conservation

Reference : Art. 9 :

At the time the present law is promulgated, existing embryos, once it has been verified that they are no longer the object of parental projects, that there has been no opposition to their being given to another couple, and that they comply with health care safety rules in force at the time they are transferred, may be given to another couple who satisfy the conditions set out in article L. 152-5.

If they cannot be given away and if they have been stored for at least 5 years, storage is terminated.

CCNE considers that parents should be allowed to decide on the destruction of their embryos or use of them for research purposes after a two-year period for reflection.

- on prohibiting embryo transfer after the death of a spouse at a time when the couple has already launched medically assisted reproduction procedures :

CCNE has already observed in Opinion n° 40 of December 17th, 1993, on the transfer of embryos after the decease of the husband or partner :

"... In that case, the man's decease indeed does not deprive the woman of the rights that she may consider she possesses to these embryos, jointly created by herself and her deceased partner... the man having deceased, one cannot see who or what authority could, in the last instance, claim rights to these embryos equal to or stronger than those of the woman, or object to her explicitly stated project, about which she has been duly informed, to assume a pregnancy after the transfer of the frozen embryos...

... It is, however, appropriate to question the very different conditions which determine a woman's decision to request the transfer of embryos after her husband's death. It is to be feared that on account of her distress during the days and weeks following this death, she is in no condition to make such a decision. As long as the woman does not, when considering her future and that of her child, take into account the permanent absence of the co-author of the initial project, her request for a transfer might not express a clearly conceived wish. In addition, she may be subject to pressure from those around her, prompted not only by affection, but also by social and legal considerations which do not necessarily correspond to the preservation of her interests and do not ensure the independent nature of her decision. It would therefore be desirable to provide for a period of reflection of at least three months but no more than one year before any such decision is made."

As a consequence, CCNE proposes : An embryo frozen in the context of medically assisted reproduction already launched by the couple, may be transferred after decease of her spouse at the request of the woman, providing circumstances permit her taking a decision which is fully independent of psychological or social pressures.

- research on the in vitro embryo

Reference : Art. L. 152-8 :

Experiments of any kind on the embryo are banned... Exceptionally, the man and woman forming the couple may accept a study of their embryos... Such studies must be for medical purposes and may not harm the embryo.

Reminder for information : CCNE, Opinion n° 53 on the establishment of collections of human embryo cells and their use for therapeutic or scientific purposes (1997)

" Article L. 152-8 of the Code of Public Health at present bans any embryo research ; because of this, the creation of ES cell lines from human blastocysts obtained by *in vitro* fertilisation and cultivated *ex vivo* is not possible.

However, taking into account important prospects in the field of therapeutic research, new articles might well be drafted when the law is up for revision at the end of 1999 which should make it possible to modify the ban.

With that in mind, only frozen embryos donated by couples who have given written consent, forsaken their parental project and decided to put an end to conservation, could be used for research.

However, any creation *de novo* of human embryos for any purpose other than a parental project, is still not permitted."

CCNE proposals :

The word *research* could usefully replace the word *experiments* in the text of the law.

1) All research projects on fertilisation and/or the embryo must be examined on a case by case basis by the National Committee for Medicine and Biology of Reproduction and Antenatal Diagnosis (*Commission nationale de médecine et de biologie de la reproduction et du diagnostic prénatal - CNMBRDP*).

2) In this field, CCNE requests that the law should distinguish between research on the embryo for the purpose of intra-uterine transfer, and research which does aim to do so. In Opinion n° 53, CCNE accepted research which did not aim to achieve transfer and pregnancy.

3) Subject to a favourable opinion from CNMBRDP and respect of the rule of parental consent, research which does not aim to achieve intra-uterine transfer is allowable.

CCNE has already opposed the deliberate creation of embryos for research purposes.

- Cloning

Reminder for information : CCNE, Opinion n° 54, Reply to the President of the French Republic on the subject of reproductive cloning (1997).

CCNE proposal :

CCNE stated its position on this subject in Opinion n° 54, Reply to the President of the French Republic.

In this report, it censures "the dismal confusion between identity in the physical sense of sameness (idem) and in the moral sense of selfness (ipse)." "the notion that perfect genetic similarity would in itself lead to perfect psychic similarity is devoid of any scientific foundation."

CCNE sums up its arguments in the conclusion of the Opinion from which the following paragraphs are extracted :

"... If reproduction of human beings by cloning became a technical possibility, it is to be feared that its use would be demanded by those who claim it responds to so-called clinical indications, to the fantasy of immortality, or the desire for genetic perpetuation at any cost by those who cannot procreate.

An attempt at identical reproduction of human beings whose genome would no longer be the result of the " lottery of heredity" and instead depend on another's will, would seriously endanger essential original indetermination as well as other fundamental traits of a person. Furthermore, a person so created would become means in the service of an alien end. Such an undertaking must be proscribed once for all.

CCNE reaffirms the fundamental distinction which must be drawn between non reproductive cloning of human cells which cannot themselves engender human beings - a customary and long established practice for the purpose of research and biomedical analysis - and reproductive cloning to bring about the birth of a child.

CCNE wishes reproductive cloning of a human being to be prohibited more explicitly in the text of the law.

- Calling on a third party donor in medically assisted reproduction

Reference : Articles L. 665-12 ; 152-6 ; 673-1 to 7.

Art. L. 665-12. - Advertising to promote donation of components or products of the human body for the benefit of a given person or of a given establishment or organisation, is prohibited. The prohibition does not restrict informing the public to promote donation of components and products of the human body.

Information of this nature is provided under the responsibility of the Minister in charge of Public Health.

Art. L. 152-6. - Medically assisted reproduction with the help of a third party donor may only be used as a last resort if medically assisted reproduction by the couple themselves is an impossibility.

Art. L. 673-1. - Gamete donation is the contribution by a third party of sperm or oocytes for the purpose of medically assisted reproduction.

Art. L. 673-2. - The donor must be a member of a couple who have already procreated. Consent by the donor and by the other member of the couple must be given in writing. Written consent is also required from the two members of the recipient couple, and may be revoked, before any action is taken, by either of them.

Art. L. 673-3. - Artificial insemination with fresh sperm which was donated is prohibited, as is artificial insemination with a mixture of sperm.

Art. L. 673-4. - Using gametes from a single donor must not deliberately lead to the birth of more than five children.

...Art. L. 673-7. - Benefit of a gamete donation may in no way be subordinated to the designation by the recipient couple of a person who voluntarily accepted to make a donation in favour of an anonymous third party couple.

1. Donor recruitment

Some articles of legislation have had the effect of increasing the scarcity of donors, in particular as regards oocyte donation.

CCNE proposals :

1. Prohibition of a double gamete donation to conceive embryos for donation is a principle which should be reaffirmed.

2. Management of gamete donation and disposal must be the responsibility of multidisciplinary teams whose management activities would not give rise to any fee-for-service, regardless of whether such teams work in the public or the private sector.

2. Conditions for consent and withdrawal of consent

Reference : Law N° 94-653 dated July 29th 1994, Art. 311-20, 1st paragraph.

Spouses or concubinaries who resort to medically assisted reproduction involving the help of a third party donor, in order to procreate, must give prior consent to a judge or a notary in conditions which guarantee confidentiality, and the judge or notary must inform them of the consequences of their action as regards filiation.

CCNE proposal :

Consent expressed to a judge (to medically assisted reproduction involving the help of a third party donor) should be retained to ensure a sufficient degree of solemnity to the procedure.

Since consent given to a notary does not seem to have the same effect, this possibility could be eliminated.

3. Anonymity

Reference : Art. L. 665-14.

The recipient's identity may not be revealed to the donor, nor may the donor's identity be revealed to the recipient. Revealing information which can identify both a person who has donated a component or a product of his/her body, and the person who has received it, is prohibited.

The principle of anonymity must remain inviolate except in a case of therapeutic necessity.

CCNE proposal :

This principle can be d with the demands of the International Convention on the Rights of Children which has been ratified by France.

Two issues remain pertinent :

1. Does anonymity raise the same ethical problems for both gamete donation and acceptance of the embryo ?

2. Does the law not give better protection to the donor couple than to the future child to whom would be refused any knowledge regarding :

* biological parentage in the case of embryo reception,

* the gamete donor (sperm or oocytes) in the other case ?

There does not seem to be any new fact which argues in favour of removing the veil of anonymity for the gamete donor. However, in view of diverging positions adopted in other countries, a societal debate could be conducted on this point, inter alia within CCNE.

III. PRE-IMPLANTATION DIAGNOSIS

Reference : Art. L. 162-17, paragraph 5

Biological diagnosis using cells taken from an in-vitro embryo is only authorised in exceptional circumstances as follows :

A physician practising in a pluridisciplinary Antenatal Diagnosis Centre as defined by article L. 162-16 must certify that, because of the couple's family circumstances, there is a strong probability that the unborn child will be affected by a particularly severe disorder, known to be incurable at the time of diagnosis.

Diagnosis may not be performed before prior and precise identification has been

made, in one or other parent, of the anomaly or anomalies which are the cause of such a disorder...

Diagnosis may have no other object besides seeking out this disorder and how to prevent and treat it.

Reminder for information : CCNE : Opinion n° 19 (1990) on Embryo research aiming to achieve pre-transfer genetic diagnosis for which a moratorium was declared in 1986 (Opinion n° 8).

CCNE proposal :

CCNE recognises the exceptional nature of this diagnosis which concerns incurable diseases of particular severity which have been identified in one parent.

It notes the apparent contradiction in the text of the law between reference to the incurable nature of a disorder and the possibility of treating it.

IV. PRENATAL DIAGNOSIS

Reference : Art. L. 162-16, paragraph 1

Prenatal diagnosis refers to medical practices with the aim of detecting *in utero* in an embryo or foetus a particularly severe disorder. There must be a prior medical genetic counselling session.

CCNE proposals :

It should be mentioned that the obligation to conduct a prior medical counselling session, as stipulated in the text of the law, only refers to the biological diagnosis.

It is suggested that the word *specialised* replace the word *genetic* since other doctors besides geneticists may be called upon to conduct the session.

V. NATIONAL COMMITTEE FOR REPRODUCTIVE MEDICINE AND BIOLOGY

Reference : Art. L. 184-3.-

The National Committee for Reproductive Medicine and Biology and Antenatal Diagnosis is tasked with giving an opinion on requests for authorisation to practise medically assisted reproductive activities and prenatal diagnoses, following requests for acceptance from pluridisciplinary prenatal diagnosis centres, and also on decisions to withdraw authorisation. It participates in follow up and evaluation of the performance of authorised establishments and laboratories.

Reminder for information : CCNE : Opinion n° 53 on the creation of human embryonic organ and tissue collections and their use for therapeutic or scientific purposes (1997);

Opinion n° 56 on ethical questions raised when a couple, in which the man is HIV- positive and the woman is HIV-negative, wish to bear a child.

CCNE proposals :

As previously mentioned, the Commission's purview should be extended to include research projects on fertilisation, the embryo, the foetus, and research in foetal medicine. Such an extension requires of necessity a reinforcement of its resources and a broadening of its composition.

VI. GENETIC CHARACTERISTICS AND GENETIC IDENTIFICATION OF A PERSON (alive or deceased)

Reference : law n° 94-653 dated July 29th 1994, in particular articles 16-10 and 16-11 introduced into the *Code Civil* by this law.

Article 16-10 : The genetic study of a person's characteristics may only be undertaken for medical or scientific research purposes. Before such a study is undertaken, the person's consent must be secured.

Article 16-11 : Identification of a person using genetic prints is only permitted when the process is part of a judicial enquiry or of instructions implementing a judicial procedure, or for medical or scientific research.

In civil legal procedures, identification may only be sought in order to implement a judge's instructions in cases involving filiation claims or counterclaims, or obtaining or suppressing financial support. Prior and express consent must be secured from the person concerned.

When identification is for medical or scientific research, prior consent must be secured from the person concerned.

- Examination of the genetic characteristics of a person for medical, scientific, and judicial reasons .

CCNE proposals :

In the view of CCNE, the text of the law gives rise to some difficulties in its interpretation. Since there are no decrees of implementation, clarification is all the more necessary.

1. Genetic characteristics and identification of a person :

The expression identification of a person by genetic characteristics, DNA analysis in particular , should be reserved for cases of enforcement of judicial procedure, and excluded from use in a medical or research context,

and the expression examination of the genetic characteristics of a person kept solely for medical and scientific research.

2. Respect of consent (or refusal) expressed while alive, after a person's death :

Article 16-11 subordinates in civil law cases the identification of a person through genetic prints to a judicial decision and that person's prior consent. Recent events have led to controversy on the text of this law. Can it apply to the corpse of a person who had objected to such a procedure when alive ?

This issue deserves a debate by society of anonymity, individual rights, and the rights of children.

- Other purposes (insurance and employment)

Reminder for information : CCNE, Opinion n° 46, Genetics and Medicine : from prediction to prevention. Opinion. Reports. (1995).

In Opinion n° 46, CCNE stated its position on this issue. Pertinent passages of the opinion are quoted below :

"...Use of the results of a study of genetic traits for purposes other than medical or scientific, for instance for an insurance contract or for employment, is prohibited even though the tests may have been requested by the persons concerned or with their consent...

The use of genetic testing in occupational medicine must therefore be exceptional and rigorously restricted to cases on a limited list for which the risk for the individual is sufficiently established and cannot be removed by changes to the work environment...

Genetic tests give information on the identity of persons and emphasise their diversity which contributes to the rich nature of humankind. To use such information for the purpose of selection or of discrimination in social or economic terms, be that in the realm of public health policies, employment, or insurance systems, would be crossing a boundary of the most extreme gravity and would question those principles of equality of rights, dignity and solidarity for all human beings upon which society as we know it is based. CCNE insists on the necessity of observing those fundamental principles whatever aims may be pursued by genetic testing. Human Rights are at stake."

As things stand, CCNE's position is unchanged.

- DNA collections

I. For medical and scientific research

Reminder for information : CCNE, Opinion n° 4, on medical registries for epidemiological and preventive studies (1985).

Opinion n° 9, on problems arising because of the development of methods using human cells and their derivates (1987).

Opinion n° 25, regarding the application of genetic testing to individual studies, family studies and population studies. (Problems related to DNA "banks", cell "banks" and computerisation) (1991).

Opinion n° 46, Genetics and Medicine : from prediction to prevention. (1995).

CCNE proposals :

CCNE's position is summed up in the attached document adopted by the CCNE Technical Section on May, 13th, 1994 : "Ethical problems raised by the constitution and utilisation of biological sample collections in human genetics". The principal ethical demands are quoted hereunder :

* free, express, and informed consent given by persons from whom biological samples are taken for the purpose of genetic study.

* instigators of a research procedure using biological samples must inform the persons concerned of what happens to those samples once research has ceased.

* if a different scientific purpose from the one for which consent was given using samples taken and associated identifying and nominal data, renewed consent must be secured.

* in cases where instigators of research abandon the project as far as they themselves are concerned, they must inform the persons concerned of any modifications in the conduct of research procedures as a consequence of their decision to abandon.

* researchers working on samples from collections must make sure that the best interests of persons contributing samples are protected, in particular as regards preserving samples which could become necessary at a later date for diagnostic testing on themselves or their families.

* individual samples and collections of samples may not be bought, sold, or patented.

* collections could be managed by national or international organisations according to the principle of authorised collections or WHO reference centres, on the basis of rigorous respect of ethical principles.

* in any event, instigators of such collections must receive approval from appropriate authorities, in particular from CCPPRBs (comité de protection des personnes se prêtant à la recherche biomédicale) created by the law dated December 20th, 1988.

2. For judicial purposes

Possible destruction of DNA collections put together for the purpose of judicial inquest raises thorny problems deserving of discussion.

VII. SCIENTIFIC RESEARCH

- Reference : laws of July 24, 1994 and law - amended - dated December 20, 1988.

The Universal Declaration on the Human Genome and Human Rights, adopted in November 1997 by the General Conference of UNESCO, aims essentially at research on the human genome, but defines in articles 10 and 12 the ethical framework to which any scientific research must refer.

Article 10 : No research, or research on its applications concerning the human genome, in particular in the fields of biology, genetics and medicine, should prevail over respect for the human rights, fundamental freedoms and human dignity of individuals or, where applicable, of groups of people.

Article 12 a) Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard to the dignity and human rights of each individual.

Article 12 b) Freedom of research, which is necessary for the progress of knowledge, is part of freedom of thought. The applications of research, including applications in biology, genetics and medicine, concerning the human genome, shall seek to offer relief from suffering and improve the health of individuals and humankind as a whole.

CCNE proposals :

CCNE considers that the regulation of scientific research deserves a specific report.

However, as of now, and the following list is not exhaustive, it wishes to draw the attention of lawmakers to a number of difficulties which are connected to:

- legislative articles raising fundamental issues,

- legislative articles of a more "practical" nature ("research management" in the hands of a physician),

- decrees of implementation of laws,

- implementation by government departments,

- identical procedures for kinds of research in which individuals participating run widely divergent risks,

- multiplicity and complexity of administrative procedures.

- Research using components of the human body

Reference : law dated December 20, 1988, amended; law n° 94-654, Art. L. 665-11 to 15, recalling general principles and practical arrangements to be complied with.

Article L. 665-11. - Sampling components of the human body and collecting its products cannot be practised without prior consent from the donor. Consent can be revoked at any time.

Article L. 665-12. - Advertising to promote donation of components or products of the human body for the benefit of a given person or of a given establishment or organisation, is prohibited. However, informing the public to promote donation of components and products of the human body is not restricted....

Article L. 665-13. - No payment, in whatever shape or form, may be made to persons consenting to body component sampling or collection of body products...

Article L. 665-14. - The recipient's identity may not be revealed to the donor, nor may the donor's identity be revealed to the recipient...

Article L. 665-15. - Sampling of components of the human body or collection of its products for therapeutic purposes are subject to health safety rules as decreed by the *Conseil d'Etat* ...

CCNE points out that blood sampling for scientific research gives rise to difficulties.

It suggests that ethical requirements (information to and consent from donors, confidentiality) be respected but with a simplification of administrative procedures when they are not needed to ensure respect for consenting persons.

- Law dated December 20, 1998, amended

Reminder for information : CCNE : Opinion n° 38 on the Ethics of research in the sciences of human behaviour (1993).

As CCNE pointed out in this Opinion, including behavioural sciences, in particular psychology, within the scope of the law has intensified difficulties already noted by researchers in other fields, in particular :

- difficulty of interpreting the scope of the law

- obligation for investigators to be physicians and proposes :

- dissociation between scientific management and medical supervision of research;

- that the law should include general rules and also specific rules depending on the type of research. For example, a trial on a new antimitotic agent on one hand, and collecting a few extra mls of blood when blood is sampled for the purpose of making a diagnosis on the other hand, should be dealt with differently.

In particular, CCPPRBs should be asked to rule on the necessity or otherwise of certain procedures and on their implementation, e.g. : medical examination, approval of premises, recording names of subjects in national registers.

VIII. EXTRACTS FROM CCNE OPINIONS ON MATTERS NOT COVERED BY THE 1994 LAW BUT WHICH COULD BE CONSIDERED BY LAWMAKERS.

N° 35 : Ethics and sport : compensation of hormonal deficiencies in highly trained athletes. 1993

The Opinion refers to the law dated June 28, 1989 (which it approves) concerning the prevention and repression of the use of stimulants in sports contests which "bans the use of substances designed to improve performance during intensive training, whether or not they exist in the organism in the basal state. The limits are narrow between what is considered endocrine stimulation and endocrine compensation, one of whose aims may indeed be to maintain athletic performances, as they run the risk of declining if an endocrine deficiency is allowed to persist. Such a policy would lead to a situation in which athletes would no longer be doped, but only undergo compensation for endocrine deficits".

In the Report, CCNE recalls that " **That all doping** - that is, the use of substances which may or may not exist in the organism in the basal state - particularly all endocrine doping, to accompany intensive training designed to improve performance **is, from the medical point of view, ethically inadmissible and condemnable** for its effects on health."

Similarly, the Report rejects what it considers to be an unproved argument in favour of " endocrine compensation, one of whose aims may indeed be to maintain athletic performances, as they run the risk of declining if an endocrine deficiency is allowed to persist".

In conclusion, the Report considers that "priority should be given to systematic studies of the long-term follow up of athletes, and that such study and research must follow the rules of ethics, medical deontology, and the Huriet Law.

"... Nevertheless, **reflection is necessary regarding the specific problems involved in the application of the Huriet Law to the field of sport**."

Three Opinions suggesting the creation of ethical evaluation committees :

N°s 36, 38, 41.

N° 36 : Opinion on the use of somatic gene therapy procedures. 1993.

Somatic gene therapy can be defined as using genes as medication for treating hereditary or acquired disease, without modifying the patient's heredity. At the present time, **therapeutic trials** are involved which must conform to the rules defined by the Huriet Law, and "Moreover, whenever the use of genetic engineering methods is involved, the trial protocols must also conform with the provisions of the law, dated July 13th 1992, on the use of genetically modified organisms..."

The Opinion points out a gap in the Huriet law which does not provide for "careful monitoring of the results of trials" although this is essential because future applications may have a broad scope". It notes that this task is not within the competence of CCPPRBs set up by the law.

The Opinion considers such monitoring to be "essential" and recommends sharing the burden between a " **competent evaluation commission**" and CCNE which could pursue "general reflection on practical developments in the field".

It is not absolutely clear whether the authors of the Opinion felt that modification of the Huriet Law and of the CCPPRB's mission would fill the gap, or whether they were considering another kind of evaluation commission.

N° 38 : Opinion on the ethics of research in the sciences of human behaviour, 1993

This Opinion was published before the Huriet Law was revised in 1994. It pointed out some **gaps and problem areas in the 1988 version of the law** (not taking into account the special nature of problems arising for the protection of persons consenting to behavioural research, prohibition of the sharing of medical and/or psychological information concerning these persons, CCPPRB's inability to judge research protocols in human sciences other than medical).

The Opinion was followed in 1997 by a "Draft reply to Senator Huriet's question regarding "implementation of the law of December 20, 1988 on research undertaken in laboratories engaged in psychophysiology and experimental psychology" submitted to CCNE's Plenary Committee on October 1, 1997. It would appear that the Draft was not sent to Senator Huriet, and that it was set aside to be added to material for consideration by the working group on the revision of the law on bioethics of 1994.

Contained in the draft reply were :

- a proposal to re-discuss the **creation of CCPPRCs** (Consultative Committees for the Protection of Persons consenting to Behavioural Research) which was not adopted in the 1994 revision;

- a proposal that **CCPPs could exonerate researchers** from "certain obligations judged by

them to be unacceptable (medical examination of subjects, approval of premises, recording names of subjects in national registers, insurance, medical supervision)

- a request that account be taken of the **specific problem** of research in the neurosciences (and more generally research on human behaviour) "if the 94 version of the law on the protection of persons consenting to biomedical research is also to be revised".

Authors of the draft reply suggest that the law be modified to allow researchers concerned to be viewed as "responsible investigators", i.e. not subject to medical supervision.

On the subject of the scope of the law, they recommend, with supportive argument, "extension of the scope of the law to all scientific research on human beings".

N° 41 : Co-operation in the field of biomedical research between French teams and teams from economically developing countries, 1993

Considering that "Biomedical research projects involving French teams and teams from economically developing countries require special precautions, in order to guarantee the dignity and the safety of persons consenting to participate in research of general interest", CCNE states : "All such projects should be submitted, before they are undertaken, to a specialised committee to be created (French consultative committee for the protection of persons consenting to biomedical research in developing countries, or CCPPVD).

This specialised committee should include *inter alia* experts from the World Health Organization, with experience in the implementation or monitoring of such projects, and could be constituted under the aegis of ministerial departments responsible for Health, Research and Co-operation. This committee would be able to seek the advice of the French National Consultative Ethics Committee.

N° 39 : Opinion on the prescription of anti-androgenic substances to prison inmates sentenced for offences of a sexual nature, 1993

The Opinion simply points out a **problem of coherence** between article D380 of the Code of Criminal Procedure which prohibits trials involving prison inmates (text of the article not available), and article L209-5 of the Code of Public Health, following on from the Huriet Law, which authorises such trials under certain conditions "(Persons in detention by judicial or administrative decision may not be asked to participate in biomedical research unless direct and major benefit to their own health is expected therefrom.")

The Opinion does not make any recommendation on the subject.

N° 40 : Opinion on the transfer of embryos after the decease of a husband or partner, 1993 .

In this Opinion, CCNE drew the attention of lawmakers to **the necessity of modifying article 315 of the *Code Civil*** because of the use of in vitro fertilisation techniques. ("Presumption of paternity is not applicable to a child born more than three hundred days after marriage has been dissolved, nor, when the husband has been declared absent, to a

child born more than three hundred days after the husband's disappearance.")

N° 43 Reports on drug addiction, 1994

In the Conclusions, CCNE underlines deficiencies in the approach adopted by the law of 1970 "concerning prophylactic measures to combat drug addiction, repress drug trafficking and the illicit use of poisonous substances". It goes on to define the following objective for a new public health policy in this field. "The objective is that the population as a whole should be protected against the risk of developing drug addiction, by legislation which on the one hand makes it possible to control products and access to them, in the best interests of public health, and on the other hand sanctions proportionately abuse and wrong done to others, while fully respecting individual liberty and dignity".

With this aim, CCNE makes a series of recommendations :

1) " **regulating the use** of substances affecting the central nervous system... This should no longer be based on the present distinction between licit and illicit products. It should take into account, for each product, its toxicity, therapeutic utility, risks of dependence due to consumption, danger of de-socialisation it gives rise to, and risks that use may bring about harm to third parties. **Harm done to oneself calls for medical rather than penal response.** Harm done to others, using certain products in public, incitement to consume (including advertising) calls for sanction. A ranking of sentences should be established according to the severity of offences and/or harm done... This kind of modification to legislation (including penal) can probably only happen progressively. It should be reviewed periodically to evaluate results and take into account new data contributed by research ..."

2) " **Access to substitution products** must become possible within the legal framework. **This latter must be modified** so that present medical practices cease to contravene the law as they do when drugs are prescribed by attendant physicians for indications other than those specified by the AMM (marketing authorisation)".

N° 44 : Opinion on cochlear implants in prelingual deaf children, 1994

This Opinion does not require action by Parliament.

However, it adopts a position which goes against the wishes of those who applied to CCNE to "submit proposed cochlear implantation cases in prelingual deaf children to the CCPPRB". "Under present conditions, the CCNE does not consider it appropriate to submit the prospective implantation of prelingual deaf children to the CCPPRB for prior approval..."

N° 45 : Ethical questions arising from the transmission of scientific information concerning research in biology and medicine. Reports, 1995.

CCNE makes no recommendation to Parliament, but draws attention to "deviations" in the transmission of information and, quoting Paul Valadier :"This is a real problem ; journalists would be well advised for professional and ethical reasons to tackle it, because otherwise lawmakers or political authorities might well impose solutions which would not necessarily be optimal. At least this question should be addressed : how could the situation be regulated ?"

N° 49 : Contraception for the mentally handicapped, 1996.

CCNE draws attention to article 16-3 inserted into the *Code Civil* by law n° 94-653 dated July 29, 1994, which states : "The integrity of the human body cannot be impaired except if

there is therapeutic necessity. Prior consent of the person concerned must be obtained except if his/her condition makes it necessary to practise a therapeutic intervention to which he/she is not able to consent" and to Article 222-9 of the new *Code Pénal*, which sanctions the offence described as "violence resulting in mutilation or permanent disablement".

CCNE underlines that qualification of therapeutic necessity and consent from a handicapped person raise difficulties. It proposes decision-making modalities but does not request modification of the law.

N° 50 : Sterilisation considered as a means of permanent contraception 1996.

CCNE draws attention to French legislation on this subject.

It considers that " **A response to problems raised by requests for Opinions can only be given, if needs be, by legislators,** after a debate.

CCNE considers the possibility of a modification of the legal and regulatory framework : " If after debating these issues, it were decided to modify the legal and regulatory frameworks so as to grant legality to **sterilisation for other reasons than 'very serious medical reasons'**"... it discusses three possible methods "to avoid over hasty or abusive sterilisation".

It notes a paradoxical situation : on the one hand, some willing individuals are denied access to contraceptive sterilisation whereas others, who are vulnerable, are sterilised without their consent. " **lack of clarity about existing law** has as its counterpart divergent notions about what is acceptable in the case of sterilisation. CCNE concludes that this state of affairs calls for a societal debate about circumstances in which it can be considered that suppression of procreative capacity is morally acceptable".

CCNE offers three distinctive positions of principle : limiting solely to therapeutic necessity; adding flexibility to existing law; and accepting contraceptive sterilisation. The second and third of these courses have practical implications as regards modification of existing law. However, CCNE does not privilege one of them over the others. "CCNE considers it to be outside its purview to opt in favour of one or the other of these positions. In a democracy, the choice is up to society and the Legislator must have the final say.

Although no specific proposal is made regarding a modification of existing legislation, CCNE does take the following position : " CCNE considers that the cornerstone of any legal settlement of issues raised by sterilisation must remain the creation of a system in which precise information is given about procedures and their consequences, and in which consent or free and informed decision can be given by the person concerned."

N° 51 Recommendations on a draft bill "reinforcing prevention and repression of sexual offences against minors", 1996.

CCNE was consulted by Messrs. Barrot and Gaymard about a draft bill. After commenting on the draft from an ethical point of view (lack of consent to treatment, modification of the physician-offender relationship, exception to the rules of confidentiality) CCNE makes the following recommendation to lawmakers: " With due regard to the complexity and magnitude of issues raised, CCNE considers that provision should be made in an article of the text for an evaluation of the proposed system as a whole so that modifications can be made if necessary. The evaluation should take place in about 2 years time."

N° 54 Reply to the President of the French Republic on the subject of reproductive cloning, 1997.

After analysing existing legislation, CCNE considers that : "as far as is known at present, there is no need to modify the relevant articles of the *Code Civil* (Civil Code *)* to ensure conformity with the CCNE's proposals in the name of ethics."

The law, as it stands now, and supported by its examination by the *Conseil Constitutionnel,* condemns reproductive cloning of a human being. There is no need **for new legislation except for purposes of clarification.** For instance by declaring that regulations concerning medically assisted procreation do not concern reproductive cloning; and elucidating the ban by adding a sentence to the end of article 16-4 of the Civil Code as follows : " Are and remain prohibited, in particular, practices aiming to reproduce human beings by cloning".

However, CCNE points out that its members are not all agreed that such a complement is appropriate. There is on the one hand its educational and exemplary value, but on the other hand, there is a risk of weakening principles by attaching to them explicit and specific prohibitions.

CCNE hopes that France could take the initiative of an appeal to global conscience through a resolution by the General Assembly of the United Nations to proscribe reproduction of human beings by cloning.

Letter from M. le ProfesseurJean-Pierre Changeux, President of the French National Consultative Ethics Committee, dated March 27, 1998, to M. le Professeur Joël Ménard, Director General for Health.

Sir,

In response to your request, the National Consultative Ethics Committee offers hereafter its opinion on the re-examination of Chapter 1, sections 1 and 2 of the law n° 94-654, dated July 29, 1994, on the subject of living donor organ sampling. Further consideration will be forthcoming when on-going work concerning issues raised by the revision of the above law has been completed.

There is need for a reminder of the reasons why sampling and grafting on living persons are accepted on a restrictive basis and generally confined to members of the same family. The aim is to protect health and freedom of action, and the quality of mutual relationships which are deeply implicated in such a process. There is also a requirement to protect as completely as possible from any deviation - in particular financial, or even commercial - which could be detrimental to the ethical quality of a decision based on solidarity and generosity.

The restrictive nature of applicable legislation by virtue of the 1994 law contrasts with the law dated December 22, 1976 which did not seek to limit those who could donate their organs. However, medical practices in fact led to similar results. The reason was that at the time, immunosuppressive agents, for instance, to control rejection reactions had not yet been developed, so that in fact immunological compatibility was why the law covered only related donors.

While keeping in mind the risks of commercial transactions, it is important that action be taken to extend in a controlled way the list of donor categories so as to benefit potential recipients and reduce waiting lists. A further consideration is that live donor organs stand a statistically better chance of successful transplant than cadaveric donor organs.

However, as a preamble to proposals, it must not be forgotten that the technique itself is in derogation of two principles enshrined in the law ;

- injury to the human body only allowable in cases of therapeutic necessity,

- anonymity.

As we review articles of the Code of Public Health (*Code de la Santé Publique*) which, in the Committee's opinion, require revision, we will consider separately the case of adults and minors.

Some of these considerations were inspired by preparatory work accomplished before the law was drafted.

1. Organ donation between related persons (father, mother, son, daughter, brother, sister, ref. : Article L 671-3, para. 1° of the Code of Public Health)

On this point, the scope of the 1994 law should be extended within the family.

Adult brothers and sisters of the recipient should include those generally described as half-brothers and half-sisters, since by their common ancestry of one parent, they might be able to offer a compatible organ. This is not the case with adoption. However in cases of full adoption when the child is totally part of the host family, it could be prejudicial psychologically to exclude the child from possible donation.

2. Donation between non-related persons

2 - 1. According to the 1994 law, donation between spouses stands out as an exception since urgency is a condition : "in an emergency, the donor may be the spouse" (Article L 671-3, para. 2 of the Code of Public Health).

In these circumstances, the previously accepted family link is no longer sufficient.

The signatories are not convinced that para. 2, which requires urgency to lift the restriction, is justified.

2 - 2. This text therefore states that only a spouse may donate. It thereby excludes an unmarried partner. It follows that a newly-wed spouse may donate whereas a partner of several years may not do so. Such a limitation should also be reviewed. There should be a consideration of the possibility to extend the capacity to donate, without restricting to certain categories, to other persons on the condition that a loving relationship be invoked and established. The authenticity and sincerity of the wish to donate, the absence of any commercial element, and the absence of any abusive pressure on the donor, would all need to be verified. Such an evaluation could be undertaken by an ad hoc Committee, whose composition could be inspired by existing texts in the July 29, 1994 law, and in its decree of implementation 96-375 of April 29, 1996. These texts define the composition and tasks of Expert Committees for the evaluation of the situation of minors proposed for bone-marrow donation, subject to some comments concerning them as formulated below. The Committee's task would also include : making sure that the donor has received necessary information on inherent risks involved; receiving informed consent; and giving reasoned opinions for each case. Its essential task would be to protect donors against any form of pressure. With this in mind, it could be desirable to task such Committees to give hearings to all proposed donors, related or otherwise.

It would be useful to provide such a Committee for each region, as approved by the Ministry of Health on the recommendation of the French Transplant Establishment (*Etablissement Français des Greffes*).

3 - For minors (Articles 671-5 and 6 of the Code of Public Health)

The only acceptable course is to continue limiting organ sampling to bone-marrow for donation to a brother or sister. However, as previously mentioned, the question of half-siblings should be raised.

Some questions arise as regards Expert Committees.

First of all, one wonders, in the case of an emergency as defined in article L 671-5, para. 3, how an Expert Committee can make a valid decision for lack of time. In order to limit abusive proliferation, should there not be at least an exhaustive list of such emergencies to be defined jointly by organ transplant medical departments and the French Transplant Establishment. Furthermore, it would be entirely unacceptable that urgency be defined by the sole fact that donor preparation has begun before the would-be donor and family have been heard by the Expert Committee.

Finally, it must be mentioned that the Committee can authorise organ sampling or forbid it : it "evaluates the medical justification of the procedure". This is equivalent to stating that it may oppose the view of prescribing physicians and refuse authorisation to harvest bone-marrow if it considers that the minor is not sufficiently protected. ("it evaluates foreseeable physical and psychological risks and consequences").

If authorisation is refused, transplantation will have to be delayed. This however is only acceptable if *motives* for refusal are given. The last paragraph of article 671-6 should be modified accordingly.

However, responsibility for evaluating medical justification for the bone-marrow transplant indications should not be left to the Committee. Organ transplant medical departments should retain sole responsibility.

When transplant indication is related to extremely rare diseases, there could be some justification for thinking that proposed treatment involving the use of bone-marrow transplantation is within the definition of a therapeutic trial, and that the proposed protocol must therefore be referred to a CCPPRB.

Finally, the composition and prerogatives of these Committees will be given further in-depth consideration as part of the work of the CCNE on a re-examination of the 1994 law.

Articles L 671-4 and 5 did not give rise to any comment from CCNE.

Yours sincerely,
Jean-Pierre CHANGEUX
President of the French
National Consultative Ethics Committee.

Evaluation of medical practices

Ovulation induction in the treatment of infertility

A recent INSERM (*Institut National de la Santé et de la Recherche Médicale* (National Institute of Health and Medical Research). report on severe prematurity was requested to analyse an adverse trend. After a notable reduction of premature deliveries between 1971 and 1980 as a result of the perinatal campaign, figures stagnated between 1980 and 1989, and then began to rise again in 1990.

The report analyses various possible causes of this trend and emphasises that multiple births play a major role in increasing the risk. In the last ten years, taking the total number of births, there has been an increase in the frequency of twin births (25%), and particularly triplets (400%). Most of these increased figures are due to increased use of ovulation induction in the treatment of infertility. Thus, there is a close relationship between national consumption levels of gonad stimulating medications and the number of triplets. Consumption of HMG (human menopausal gonadotropin) was 500,000 vials per annum between 1980 and 1985, but grew to 3,500,000 in 1995. This corresponds to treatment for at least 60,000 women per annum. More than 75% of triplet births are the result of such treatment. Similar worrying situations exist in other industrialised countries.

When analysing this data, a distinction must be made between :

on the one hand treatment given in medically assisted reproduction centres -AMP (*Assistance Médicale à la Procréation*) - in which case such activities are regulated by a decree dated May 6th 1995 to implement the "bioethic" laws of July 29th, 1994;

on the other hand, treatment which is not regulated, prescribed by practitioners outside that framework.

1. In recent years, IVF (in vitro fertilisation) clinical and biological centres have initiated an evaluation of practices through an association called FIVNAT, with the help of INSERM. This ten year evaluation period will also serve to analyse the consequences of this data on modifications of medical practices during ensuing years.

Following IVF or ICSI (intracytoplasmic sperm injection), in 1995-6, there were about 5000 at term pregnancies each year, of which 24% were twins and 3% triplets (in the general population figures are about 1% twins and 1 in 10000 triplets). Such multiple pregnancies require special treatment for mothers. Embryonic reduction needs to be performed for approximately 3% of pregnancies (see CCNE Opinion N° 24). There is a great increase in the number of stays in hospital during pregnancy (63% in triple pregnancies), and of the number of caesarean sections (93% in triple pregnancies). At birth, severe prematurity (weight less than 1500 g) occurs for 6% of twins and 26% of triplets. Out of the 6500 children born of these 5000 pregnancies, a quarter spent some time in ICUs or neonatal care wards after their birth. There is a sharp increase in perinatal mortality and irreversible sequelae.

For IVF, the frequency of multiple gestation is directly connected to the number of embryos transferred. From 1990 onwards, the AMP centres began to reduce the number of transfers but the reduction is meagre as seen in 1995-1996 figures. The number of triplet gestations, before foetal reduction, was 8% in 1989 and dropped to 4.7% in 1994, and the figures for reductions were respectively 3.4% and 2.6%. There is still a long way to go. Some medical centres transfer no more than two embryos and so bring down their rate of triplets to less than 1%.

In Opinion n° 42, CCNE wrote :

"In this domain, there is a very real debate, and an ethical choice, between the success rate for IVF and the attempts to reach a record level on the one hand, and the serious consequences of multiple births with a record-breaking frequency that it would be better to avoid, on the other."

Perhaps it would be preferable to reduce the number of embryo transfers with a slight attendant drop of the success rate, and therefore also an increased number of attempts. However, there would be a drop in the frequency of multiple gestation and the cost of caring for mothers and children which, as things stand, is probably greater or equal to the cost of IVF for a single pregnancy.

2. Only an indirect evaluation can be made of the use of ovulation induction outside AMP centres. Based on figures of vials sold, multiple gestations, and very immature births, it can be estimated that much greater use is made of this procedure than in AMP centres, probably twice as much !

A 1996 CNMBRDP progress report explains the above as follows : "any doctor may prescribe ovarian stimulation

- there is public demand for such prescriptions as soon as a couple has any doubt about their fertility

- there is a convergence of resolve between the doctor (who gives assistance) and the patient (who feels supported) and yet there is neither ill health nor therapeutic necessity".

In the circumstances, use is made of a costly treatment, the efficacy of which remains to be evaluated but which is known indirectly to have adverse consequences, i.e. multiple gestation, which raises serious ethical issues :

- in many cases it serves no useful purpose and there is no evaluation of indications.

- consequences may be disastrous and are not evaluated :

- since this is "natural" fertilisation, the number of embryos conceived cannot be forecast, frequently because there is no ultrasonic monitoring of ovulation.

- embryo reduction is not a good solution and may lead to a termination of pregnancy (15% according to FIVNAT) (CCNE's opinion n° 24).

- female health, either immediately due to ovulation induction, or in the longer term (cancer of the ovary)

- children's health at birth and later

- stress for mothers and couples coping with multiple birth families.

As regards reproduction, ethical issues raised by new medically assisted reproduction techniques have been viewed with concern by legislators so that such practices are carefully controlled by law (the 1994 bioethics laws and their decrees).

An evaluation of such techniques is the subject of annual reports so that the situation can be examined.

A code of good clinical and biological practices as regards medically assisted reproduction is being drafted by members of the profession in a CNMBRDP commission, and should be printed in statutory documents in the near future. It includes recommendations concerning the avoidance of multiple pregnancy.

CNMBRDP in its annual report "wishes to extend its quality control of AMP procedures to the prevention of iatrogenic multiple gestations brought about by non-AMP ovulation induction protocols".

The aims of this procedure are of course very laudable, but the method of dissemination (publication via official channels) may seem a little too administrative for professionals to feel concerned.

There is a great need for widespread dissemination of information to both physicians and public so that there may be a better understanding of natural fertility. This should help guide public demand and medical response.

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Ethical problems raised by the creation and use of collections of biological samples in human genetics

- Discovering genes which specify particular characteristics, in particular susceptibility to human diseases, frequently requires the use of collections of DNA or of cells sampled from families in which the characteristic being studied is expressed. These collections of biological samples are the subject of files which may be computerised and which necessarily contain nominative data through which the persons concerned and their families can be identified. The National Consultative Ethics Committee was approached by an association of patients regarding the status of such collections. At the same time, the Ministry for Higher Education and Research created a working group on March 25, 1994, on the subject of "intellectual protection of results of research on the human genome and DNA data banks". CCNE wishes to contribute to thought which is presently being given to these issues by emphasising certain ethical principles which must govern the way in which this kind of research is undertaken.

Existing law and CCNE opinions have already dealt with conditions in which biological sample collections can be created and used, in particular for genetic research :

- Law dated January 6, 1978 on Data Processing and Liberties (informatique et libertés) ,

- Law dated December 20, 1988, amended on January 23, 1990, on the protection of persons accepting to participate in biomedical research.

- CCNE Opinions :

- Opinion n° 4 on medical registries for epidemiological and preventive studies - May 6, 1985

- Opinion n° 9 on problems arising because of the development of methods using human cells and their derivates - February 23, 1987 -

- Opinion n° 25 regarding the application of genetic testing to individual studies, family studies and population studies (Problems related to DNA banks, cell banks, and computerisation) - June 24, 1991 -

- Opinion n° 27 on not using the human genome for commercial purposes - December 2, 1991

It must be stated immediately that genetic research, unlike research which uses only personal medical data processing, does not concern solely individuals and their personal future, but also their collaterals and their descendants, existing or to come.

Furthermore, genetic studies of DNA or cell samples can extend far beyond the initial programme which motivated sampling for which consent was given.

Therefore, it is particularly important to be very respectful of the essential ethical principles which CCNE outlined in some previous Opinions and which also inspired the laws dated January 6, 1978 et December 20, 1988 :

- respecting the autonomy of decision of each person asked to supply biological samples for biomedical research,

- the right for those accepting to participate in such biomedical research to be informed of the aims of the research, to have access to all information which concerns them, and the right to benefit from possible diagnostic and therapeutic progress which the research might lead to.

- the right to withdraw from a research programme for which consent was given initially.

- the right to have information on individuals or their families kept confidential and to respect of privacy.

Information and consent

*Persons who have contributed biological samples for the purpose of genetic studies must have given free, express, and informed consent. Information which is essential for consent to be given, which is to be supplied by the instigators of the research programme, must include :

- A description of the purpose of the research and of the status of scientific

knowledge at the beginning of research.

- A description of the environment in which research will take place, i.e. involvement of medical or non-medical personnel; whether industry personnel will be active.

- A description of possible consequences of research, in particular as regards diagnosis, prevention and therapy, with reference to possible consequences for those participating in the study.

- Use to be made of data collected : publication, patents, likely research and development agreements.

- Destination of samples once the research project is terminated by its initial instigators.

*If research for a different scientific purpose from the one for which consent was given is considered using the samples already collected and the associated identifying and nominative data, fresh consent will need to be obtained, respecting the same constraints. If the individuals concerned are deceased, consent would be requested from close relatives.

*The right for persons to be informed of the nature of the research and of any information concerning them, is indefeasible.

*Samples, regardless of their characteristics, do not convey any rights of patrimony whatsoever to persons from which they were collected.

Rules of conduct for research using collections of human biological samples

- The motivation of individuals participating in a research programme in human genetics is frequently a desire to hasten progress in acquiring knowledge about a disease they or members of their family suffer from, or about its diagnosis, prevention and treatment. They might well justifiably ask that everything possible be done to achieve the aims pursued with the help of their DNA or cell samples. In the circumstances, if the collections are confiscated for a very long time by researchers who are not making optimal progress, this would probably not be very acceptable for those who contributed the samples and might even be said to violate an implicit commitment to them to do everything possible to achieve results which they can benefit from directly.

- Instigators of research for which a collection was created and for which consent was duly given, have a duty to carry out the research with all means available and according to procedures set out initially; they may also claim priority rights to use the collection for their own research.

- If instigators of research cease to pursue it themselves, they should inform those concerned of modifications in research procedures which occur as a result.

- It would therefore be necessary to set out reasonable time limits beyond which access to collections would be open to other research workers than those who instigated the research in the first place, so that work could be done on the programme for which consent was given, irrespective of whether the initial team has already achieved substantial results leading to publication or filing patents, or on the contrary, has failed to make progress.

- Researchers working on collection samples must make sure that the interests of persons from which samples were taken are safeguarded, in particular by preserving samples which might later be needed to carry out diagnostic tests on those persons themselves or their families.

Status of collections of biological samples in human genetics.

- Individual samples or collections of them cannot be bought, sold, or patented.

- Instigators of research who have given justification for a collection of samples to be made, may not alienate them, even on a temporary basis, by limiting their use by contract to a laboratory or a particular industrial entity, unless this had been specifically included in the information supplied, before consent was given, to persons consenting to sampling.

- Collections could be managed by national or international organisations on the basis of approved collections or WHO reference centres, with full respect of ethical principles outlined above. Handing over responsibility to such organisations could take place in the following circumstances :

- after instigators of research have relinquished interest,

- after a time interval, to facilitate free access to collections by other research teams working on the programme to which consent was given,

- immediately, provided the priority rights of the instigators of the programme to perform the research for which they made the collections, are safeguarded.

- In any event, instigators of the creation of such collections should be granted approval by appropriate bodies, in particular CCPPRBs as created by the law of December 20, 1988.

Such approval would take into account procedures implemented to harvest, store, and use the collections with a view to protect all persons concerned from any abuse of their samples and personal data. Using computerised and nominative data also implies registering with the National Data Processing and Liberties Commission (*Commission Nationale de l'Informatique et des Libertés*).

- Conditions of access to collections, whilst respecting ethical principles and personal consent, could be worked out to take into account the cost of harvesting, storing, and making available the collections. Compensation for such expenditure would be particularly justified if the collections were used for the development of an industrial project.