



Bioethical Issues

EDUCATIONAL FACT SHEETS

Everything
you need
to lead
a classroom
a debate

Publishing
Editions



General introduction

Train your pupils in a participatory approach, fundamental to education for citizenship, by organising an informed, multidisciplinary debate on bioethical issues.

“Moderator” fact sheets

1. Presentation of the teaching aid
2. Tips for leading the discussion

“Participant” fact sheets

Organ donation

Medically-assisted procreation

Genetic testing

Biomedical research on human beings

Cloning

Each theme is elaborated in 5 fact sheets:

1. Context
2. Scientific data
3. Key points
4. Concrete situations
5. Find out more

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Bioethical Issues

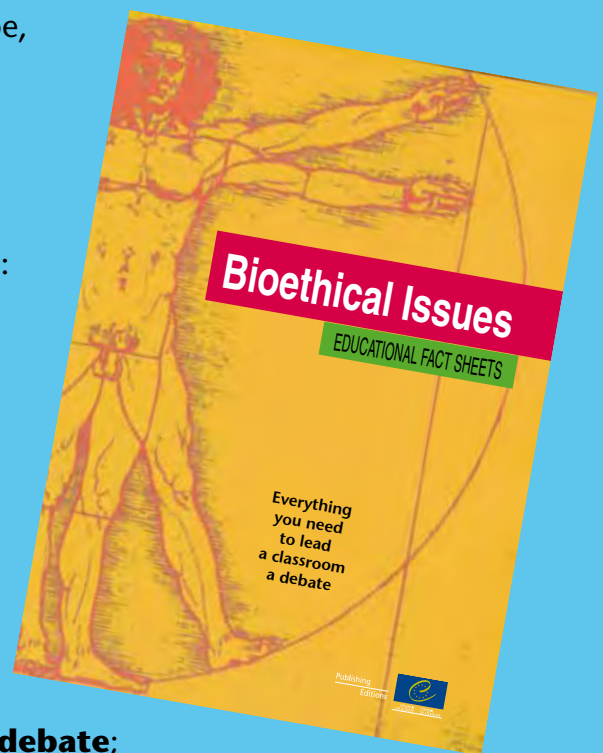
Educational Fact Sheets

Train your pupils in a participatory approach, fundamental to education for citizenship, by organising an informed, multidisciplinary debate on bioethical issues.

This teaching aid, developed by the Council of Europe, is designed in particular for fourth form to upper sixth form teachers of **biology, philosophy** and **civic education**.

It has been reviewed by teachers of different subjects and tested in the classroom, and is designed:

- To make young people aware of bioethical issues and encourage an open debate on the subject;
- To foster **independent thinking**;
- To promote a **participatory approach** to debates on social issues (**education for citizenship**) through the analysis of concrete cases;
- **To open up the European dimension of the debate**;
- To clarify key **scientific and medical concepts** by means of examples taken from everyday life.



Five initial themes are addressed in this publication:

- *organ donation*;
- *medically-assisted procreation*;
- *genetic testing*;
- *biomedical research on human beings*;
- *cloning*.

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"Discussion moderator" fact sheets

Designed for teachers, these facilitate the organisation of debates by setting out topical bioethical issues and providing practical tips for moderating a discussion.



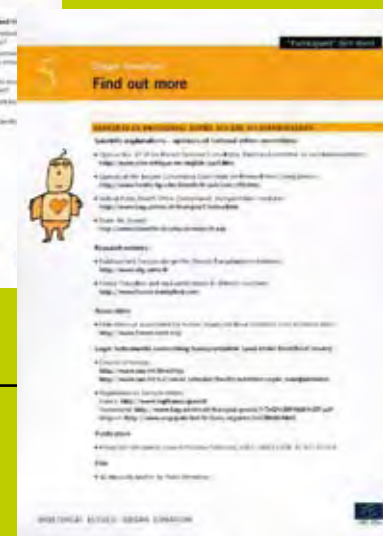
Scientific information is presented in simple terms that everyone can understand.



Some key points provide an introduction to the ethical and legal aspects of the issue.



Concrete situations, along with questions relating to the various ethical issues they raise, provide material for a genuine debate.



Further references (websites, publications, etc.) provide rapid access to information, for a more in-depth study of the subject.

"Participant" fact sheets

Each theme is elaborated on in five fact sheets printed on both sides.



A general introduction sets the issue in context, describes the historical background and provides some key figures.

These fact sheets set out key data that make it possible to find out about the various aspects of the issue in question and organise a constructive debate, regardless of the school subject in the context of which it is held. Discussion is facilitated through the presentation of specific examples, followed by questions to help launch and structure the debate.

The fact sheets take account of the often limited time available to teachers for organising such activities. They may be used both for a short debate, once the students have read the fact sheets individually, and for a longer activity after more detailed preparation with the help, in particular, of the references to books, websites and films on the last fact sheet.

1

Presentation of the teaching aid

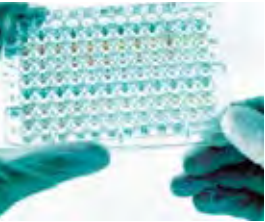
Making young people aware of bioethical issues through debate

TOPICAL ISSUES

While scientific and technical developments in biology and medicine have brought progress, they often raise numerous ethical issues.

Central to these issues is the protection of human beings and their fundamental rights and freedoms. It is necessary to be able to distinguish between what is technically feasible and what is morally acceptable, and there are many views on the subject.

Scientific and technical developments are going to influence the future, and the whole of society is concerned. So it is important that young people, as future citizens, should be aware of the ethical issues raised by these developments and be fully involved in discussions on the subject, which form part integral of democratic debate.



FOR WHOM IS THIS TEACHING AID DESIGNED ?

This teaching aid is principally intended for all Europe’s young people from the age of 15 upwards, regardless of their level of education and the subjects they are studying.

It can also be used in other contexts, in particular by the medical profession.

It is designed for anyone who wishes to raise bioethical issues with young people (teachers and moderators).



THE OBJECTIVES OF THIS TEACHING AID ARE

- > To **make young people aware** of bioethical issues:
 - to elicit their interest in such issues;
 - to prepare them to cope with situations that may directly concern them.
- > To **initiate an open debate** on these issues (taking account of the various viewpoints):
 - to foster independent thinking;
 - to promote active participation in debates on social issues (education for citizenship).
- > To open up the **European** (and even international) **dimension** of these issues.
- > To **explain** and **clarify** abstract **scientific and medical** concepts by means of examples taken from everyday life.



THE TEACHING AID

This project covers various topics that raise biomedical ethical issues (organ donation, cloning, etc).

Fact sheets for moderators and students

- > To familiarise them with the subject.
- > To provide key information about the issue, which can be updated by means of the Internet.
- > To provide examples and put questions.
- > To prepare the debate (in the case of the moderator).
- > To suggest visual support (film, video, cartoon).

WHO IS OFFERING THIS TEACHING AID?

The Council of Europe

Set up in 1949, the Council of Europe is an intergovernmental organisation with permanent headquarters in Strasbourg, France. It has 47 European democracies as member states.

Its aim is:

- > To protect human rights and the rule of law in the member states;
- > To seek solutions to such social issues as discrimination, intolerance, human cloning, drug trafficking, terrorism, corruption and organised crime;
- > To foster an awareness of European identity and diversity;
- > To help consolidate democratic stability in Europe by supporting political, legislative and constitutional reform;
- > To promote social cohesion and social rights.



THE COUNCIL OF EUROPE'S BIOETHICS DEPARTMENT

This department manages the Council of Europe's activities in the bioethics field.

Much of its work is devoted to the preparation of international legal instruments.

The Council of Europe drafted the 1997 Convention on Human Rights and Biomedicine, which serves as an international standard in the field of bioethics.

This convention seeks to protect human rights and human dignity with regard to the application of biology and medicine. It is supplemented by other legal instruments (additional protocols) concerning specific fields: the transplantation of organs and tissues of human origin, cloning and biomedical research. Other instruments (on genetic testing, for example) are being prepared.



2

Tips for leading the discussion

Making young people aware of bioethical issues through debate



“DEMOCRATIC” DEBATE IS BASED ON TWO PRINCIPLES

The principle of autonomy.

The principle of equality: everyone must have the same opportunity to take part.

SUGGESTIONS FOR THE PRACTICAL ORGANISATION OF THE DEBATE

> **Appropriate spatial arrangements**

(For example, chairs set out in a horseshoe) Good organisation facilitates dialogue and hence debate.

> **Establishment of a reassuring atmosphere**

The participants should feel free to react but not forced to talk about intimate, personal matters if they feel uncomfortable doing so.

> **Suitable group size**

A group of 15 to 30 people.

> **Vocabulary**

It is desirable to use vocabulary that is familiar to the whole group or to explain unfamiliar terms so that everyone can take part in the debate.

> **Running the debate**

As the objective is to prompt people to think about the issue and make up their own minds, it is important not to suggest “answers” or “solutions” to the problems raised.

> **Joint leadership**

A debate led in collaboration with a colleague or speaker is conducive to a lively discussion and makes it easier to sum up afterwards.



SUGGESTIONS FOR ORGANISING THE DEBATE

A one-off activity (one to two hours)

The participants may be asked to prepare briefly for the debate. They can do some research or work on the basis of the fact sheets proposed.

During the debate, the moderator may use the concrete situations set out in the fact sheets to make the participants aware of the issues and trigger a discussion.

At the close of the debate, the views and arguments put forward may be analysed in order to highlight key points and single out those on which people agree and those on which they differ.

In conclusion, the participants may be asked to express their views on the benefits of such a debate in the light of the pre-set objectives.

A longer activity

After a session of the kind described above, the discussion leader may continue with activities that require somewhat more preparation.



> *Role-playing*

The participants improvise a short psychodrama. The purpose of role-playing is to throw light on a type of situation that is unfamiliar to the participants.

When assigning roles, the moderator should pay special attention to the personal experience of the participants and the extent to which they can identify with their roles.

> *Simulation*

This is similar to role-playing but there is no improvisation: a short play is based on a script that has already been written. For example, a court hearing may be simulated.

> *The dilemma game*

After three or four controversial assertions have been made, the participants may be asked to take up a position in relation to a line on the floor. The further they are from the line, the more marked their position (they agree or disagree completely); the nearer they are to the line, the more they have mixed feelings about the issue.

The participants then explain the reasons for their choice.

This is a way of encouraging everyone to express his or her views and listen to the others. Positions may change as new arguments are put forward. The advantage of this technique is that the various positions can be visualised in relation to one another. It does, however, mean that specific questions must be raised at the start.

Taking things a stage further...

The analytical and summing-up stage can also, for instance, prompt the drafting of an article setting out the various positions.

The activity may be continued throughout the year on different subjects (science, philosophy, civic education, etc.) if questions addressing new bioethical issues are formulated.

1

Organ donation

Context

A REVOLUTIONARY PRACTICE

ORGAN TRANSPLANTATION

At present, organ transplantation is usually carried out to replace certain organs that no longer function properly. It is one of the major medical advances of the second half of the 20th century.

... AND THE ISSUE OF ORGAN DONATION

The growing success of transplants is leading to an ever-larger discrepancy between the number of organ donors and the steadily increasing number of potential recipients.

This growing demand is raising numerous ethical problems.

There are currently immense technical possibilities, but how far should one go?

Should one really use every means possible to prolong human life?

We are in a paradoxical situation: we want scientific and medical progress in order to cure illness and prolong human life and improve its quality, but at the same time we must learn to live with the reality of death.



BIOETHICS

Bioethics is concerned with the problems raised for human beings by advances in biology and medicine.

Essentially, bioethics is a multidisciplinary and pluralist reflection of the issues facing all citizens. It must also take account of the fact that science and technology are constantly progressing.



HISTORICAL REFERENCES

- > **1906:** transplant of a pig kidney (France).
- > **1933:** transplant of a human kidney (Ukraine).
- > **1950s:** introduction of the concept of “immunosuppression”, the aim being to ensure that transplants are better tolerated (and rejection avoided).
- > **1954:** kidney transplant between identical twins (United States).
- > **1967:** first heart transplant (South Africa).
- > **from the 1980s onwards,** considerable technical progress substantially improves the results of transplants.
- > **1981:** first combined heart-lung transplant (United States).
- > **1998:** first transplant of a hand by an international team of surgeons (France).

ORGAN DONATION: A FEW FIGURES

In Europe, **120 000** patients undergo regular dialysis and nearly **40 000** (over 5 000 in France) are awaiting a kidney transplant.

Because of the shortage of organs in Europe, **15 to 30%** of patients die while they are on a waiting list.

Number of patients requiring transplants every year in Europe

In France, for example, some **4 000** new patients every year need transplants (of organs, tissues or cells), but there is usually a long wait.

Comparison of the percentage of people in favour of organ donation and the actual decisions taken when a relative dies

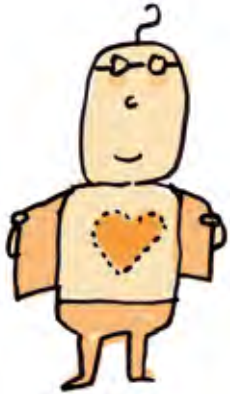
In France, for instance, although **89%** of people are in favour of organ donation, **30%** of families refuse to allow an organ to be removed from a brain-dead relative.

Trend towards a decline in the number of people refusing to donate organs

In Spain, for example, the rate of refusal to donate an organ fell from **27.6%** in 1992 to **23%** in 2002.

The survival rate after one year is higher for transplants from living donors than for those from deceased donors.

In practice, there are substantial differences between countries: the number of transplants from living donors in proportion to the total number of transplants is ten times smaller in France than in Scandinavia.



2

Organ donation Scientific data

A transplantation* is usually carried out in order to replace or "take over the job of" a vital organ* which is failing in its functions.

Transplantation* entails removing an organ or tissue from one person and grafting it to another person.

ORGANS AND TISSUES THAT MAY BE TRANSPLANTED

Living donors

Living people may donate bone marrow, a kidney or skin.

Deceased donors

Only organs and tissues that are still viable may be transplanted. Essential organs such as the heart and the lungs remain viable for a short period after death. If the person in question is considered brain-dead* (rare situation), however, certain bodily functions (for example, heart and lungs) may be artificially maintained and, after authorisation, organs and tissues may be removed.

THREE TYPES OF TRANSPLANT

Autografts

The donor and the recipient are the same person (as in the case of a skin graft).

Allografts

The donor and recipient are separate but belong to the same species.

Heterografts/xenografts

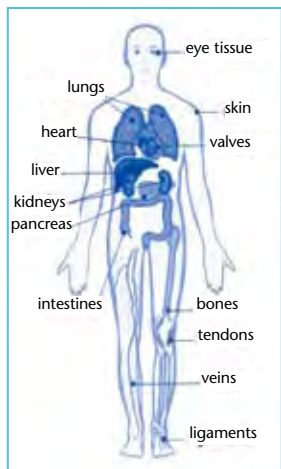
The donor and recipient are from different species.

A xenograft* entails, for instance, transplanting animal organs or tissues into a human being. It is mainly relevant to experimental research.

The term "heterograft" is also used when the transplanted organs are artificial.

COMPATIBILITY AND THE IMMUNE SYSTEM

Everyone is familiar with the A B O system blood groups, which determine whether a donor and a recipient are compatible and hence whether a blood transfusion will be successful. In the case of transplants, compatibility between the donor and the recipient is based on the HLA* (Human Leucocyte Antigen) system, also known as the MHC (Major Histocompatibility Complex) system, which can be considered to provide a tissue identity card. The molecules present on the surface of every cell in an individual, which are coded by this system, allow the immune system to differentiate between "self" and "non-self". In the case of a transplant (allograft or heterograft), the recipient's immune system will identify these molecules on the surface of the cells of the transplanted organ. If it identifies them as alien, a defence process designed to eliminate the transplanted organ is set in motion: this is known rejection*.



Organs:

heart, lungs, liver,
kidneys, pancreas

Tissues:

cornea, skin,
bones, heart valves,
blood vessels

THE VARIOUS STAGES OF TRANSPLANTATION



1. Ascertainment that the person in question is brain-dead



2. Consultation of the family of the deceased person and authorisation to remove organs



3. Removal of one or more organs and lymph nodes



4. Choice of a recipient



5. Transport of the organ or tissue to the recipient



6. Analysis of the characteristics of the donor on the basis of the lymph nodes removed



7. Preparation of the recipient



8. The graft: the surgeon replaces the diseased organ or tissue by the transplant from the donor



9. The recipient must rest after the operation and begin a new life as a transplant patient

WHAT MAKES A TRANSPLANT SUCCESSFUL?

Why does a transplant succeed?

For a transplantation* to be successful, it is necessary to choose a tissue or organ whose tissue characteristics are as similar as possible to those of the recipient.

The more distant the donor and the recipient are in genetic terms, the stronger the rejection* of the transplant. It is stronger still in the case of a transplant between different species.

Rejection is the main complication of organ transplants, but there are other risks, such as the transmission of diseases.

How can rejection of a transplant be avoided?

The main thing is to ensure that the donor and recipient are as compatible* as possible, immunologically speaking. This is true in the case of closely-related family members (parents, children).

The recipient must also receive appropriate treatment with powerful immunosuppressant* drugs to avoid the natural phenomenon of rejection of the transplant. Such treatment attenuates the body's response to the intrusion of foreign bodies.

3

Organ donation Key points

FUNDAMENTAL PRINCIPLES

- The dignity and identity of all human beings must be protected.
- Everyone must be assured of respect for his or her integrity, other rights and fundamental freedoms with regard to the application of biology and medicine.
- The transplantation of organs and tissues helps to save human lives or considerably improve their quality.
- The shortage of organs and tissues necessitates appropriate measures to encourage people to donate.
- The ethical, psychological and socio-cultural problems inherent in the transplantation of organs and tissues must be taken into consideration.
- Improper use of transplantation could threaten people’s lives and well-being and undermine human dignity.
- Transplantation shall take place under conditions that protect the rights and freedoms of organ donors, potential donors and recipients and ensure that human body parts are not sold.

Legal references

Convention on Human Rights and Biomedicine (known as the Oviedo Convention), Council of Europe, April 1997

Additional Protocol to the Oviedo Convention concerning Transplantation of Organs and Tissues of Human Origin, Council of Europe, January 2002

CONSENT

Organs* are removed primarily from deceased people. It is possible to envisage removing organs that are not vital and tissues such as skin from a living person.

- In any event, “an intervention in the health field may only be carried out after the person concerned has given free and informed consent* to it” (Article 5 of the Oviedo Convention).
- The potential donor must therefore be informed of the nature of the removal, the risks incurred and the consequences of the operation. The risks to the donor’s physical and mental health must be assessed and limited.
- It is necessary to obtain the donor’s consent (if he or she has registered during his or her lifetime on a list or register of donors) or the family’s agreement.
- In some countries, consent may be presumed: the person is considered to be consenting unless he or she registered a refusal during his or her lifetime.
- Special arrangements have been made for people considered not able to consent, such as minors and certain people with mental disabilities (Article 6 of the Oviedo Convention).

CONDITIONS PERTAINING TO THE REMOVAL

- An organ or tissue may not be removed from a deceased person unless the death has been duly ascertained in accordance with the law. Criteria for establishing death may vary from country to country.
- The doctors ascertaining the death must not be those directly involved in removing the organ or tissues or the subsequent stages of the transplant*.



ASSIGNMENT OF ORGANS

As there are not enough organs to fulfill the needs, it is essential to draw up **waiting lists**.

When an organ is available, what criteria are used to choose the recipient?

The **criteria** must be clearly defined in the light of medical factors. They must not be discriminatory (they must not, for instance, be based on age, sex, religion, social status or financial resources).

Other criteria have a role to play, for example immunological and clinical factors and urgency (in the light of the life prognosis). In the case of a kidney transplant, account is generally taken, when a kidney is assigned, of the waiting time and immunological compatibility criteria. In the case of a liver or heart transplant, however, the clinical urgency with which the recipient needs a transplant will be the determining factor, even though there is a risk of rejection* if the compatibility* criterion cannot be met.

PROHIBITION OF FINANCIAL GAIN FROM ORGAN TRAFFICKING

The human body and its parts must not, as such, give rise to financial **gain** (Article 21 of the Oviedo Convention) or similar advantages for the donor or a third party taking part in the transplantation process. Certain forms of compensation are, however, tolerated.

There is likewise a ban on **advertising** in connection with organ or tissue transplants for financial gain or in order to obtain a favour (by means of a personal advertisement on the Internet, for instance).

In most countries, transplantations involving payment of the donor are illegal.

If transplantations are **remunerated**, there is a risk of organ trafficking – of a poor donor providing a rich recipient with an organ.

Substantial trafficking of this kind has been found to exist and it is continuing to spread. International measures are being taken to combat such practices.

VARIOUS SCHOOLS OF THOUGHT AND THE POSITIONS OF DIFFERENT RELIGIONS

Generally speaking, the various religions are in favour of organ donation and encourage it.

Attitudes differ more with regard to xenografts, because animals are used.

GOOD MEDICAL PRACTICE

The existence of a “transplantation system” makes it possible to safeguard several principles:

- > The provision of **information** for the donor and recipient about the potential risks and benefits of the operation envisaged. All information must be treated **confidentially**.
- > Appropriate staff **training** in organ donation issues.
- > **Medical supervision** of both the donor and the recipient.
- > **The specificity** of consent

“When in the course of an intervention any part of a human body is removed, it may be stored and used for a purpose other than that for which it was removed, only if this is done in conformity with appropriate information and consent procedures.” (Article 22 of the Oviedo Convention)

PSYCHOLOGICAL PROBLEMS

The recipient may feel indebted to the donor, and this can give rise to a feeling of guilt.

In many countries, organ donation is anonymous in order to avoid any pressure

Firstly, the person in question has had part of himself or herself amputated and is vulnerable because of immunosuppressant treatment; secondly he or she has received an organ from someone else. The fact of having someone else inside oneself can cause one to ask oneself numerous questions about one’s identity and can cause great anguish

Depending on the culture, approaches to the body differ: is it merely an object of no interest after death or is it still a human being?

4

Organ donation Concrete situations



CASE No. 1

17-year-old Timothy is in hospital undergoing dialysis. He expresses his discontent with having to be there again. His doctor comes and sees him and explains once again why he needs dialysis, what purpose the kidney serves, what dialysis does, and so on.

When his parents arrive, the doctor informs them that their son needs a kidney transplant, but explains that Timothy and they are not immunologically compatible*. Timothy is put on the list of people awaiting a transplant and will need to wait until a compatible* kidney becomes available.

Timothy’s friends have got together in the school yard because they want to help him. His best friend, Frank, offers to donate one of his kidneys. Another of his friends takes the view that one cannot donate one of one’s organs just like that. He is afraid of falling ill at a later date and needing both his kidneys.

Timothy’s friends go to hospital to visit him. They ask him whether it is possible for a friend to donate one of his kidneys and want to know what formalities need to be completed. Timothy tells them there could be a compatibility problem. A discussion ensues with Timothy’s father. Who could donate an organ? Is it possible to obtain an organ elsewhere or to remove an organ from an animal?

QUESTIONS

Timothy’s position

- What are the advantages of a transplant for Timothy?
- Does he have reason to be afraid of a transplant?
- What about the possibility of transplanting an organ from a deceased person?
- Is it better to wait for an organ from a deceased person or to remove one from a relative or friend?
- If Timothy receives a transplant thanks to a donation, is it better that he should not know who the donor is?

The position of his family and friends

- What should be done if the medical team cannot find an available kidney?
- What should be done if no member of Timothy’s immediate family is immunologically compatible* with him?
- What about his friend’s offer to donate a kidney? Should this be allowed?
- What about people who go and buy organs in foreign countries?
- How far can one go to save Timothy’s life?





CASE No. 2

Two 3-year-old girls are twins. One of them suffers from a severe kidney disease. Given the urgency of the situation and the fact that no kidney from a deceased person is available, the parents would like a kidney to be transplanted from her disease-free sister.

QUESTIONS

Consent to a donation in the case of a minor

- Can one remove an organ from a minor who is not legally able to consent?
- Do the parents have the right to give their consent on behalf of the child? Does this situation not call into question the fundamental rights of the child from whom it is planned to remove an organ?
- Does this situation not call into question the conditions under which the donor can give his or her free and informed consent?

Choosing between different interests

- What attitude should be taken in this conflict between the right to live of the little girl who is sick and the right of her healthy sister to her physical integrity and future good health?

CASE No. 3

A 42-year-old man with two children (aged 12 and 7) is suffering from terminal cardiovascular failure as a result of a viral infection. With his consent, he has been on the list of patients entitled to a heart-lung transplant as a matter of extreme urgency. On the actual day of the transplant, when he is still conscious, he refuses to have the operation that is known to be capable of saving his life. His family – his wife and children – ask the medical team to go ahead with the operation regardless.

QUESTIONS

Consent and the right of refusal

- Should the patient's wishes be taken into account or not?
- Can the fact that the patient initially agreed to the transplant be taken into consideration when the medical team takes its decision? Can the wishes of the family be allowed to override those of the patient?
- Is it not contrary to respect for the patient to force him to undergo an operation he does not want?

Understanding the patient's refusal

- Does his refusal stem from a fully understandable but transient fear of the operation or from clearly thought out, properly reasoned objections?
- Some people consider that life has supreme value. Does someone have the right to forfeit life or kill himself or herself?

Excessive medical zeal

- There are those who consider that this twofold transplant is in the experimental stages. Could this situation be considered to lie at the boundary between respect for life and excessive medical zeal?

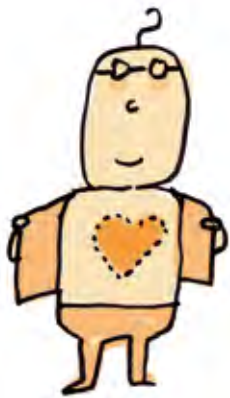


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Organ donation Find out more

INFORMATION ON ORGAN TRANSPLANTATION

- Organ Donation: The Gift of Life?, leaflet of the Irish Council for Bioethics
www.bioethics.ie/extras/Roadshow.html
- On-line patient education brochures
<http://www.a-s-t.org> "For patients" section



INFORMATION ON QUESTIONS RAISED BY ORGAN TRANSPLANTATION

- Convention on Human Rights and Biomedicine (Oviedo Convention), Council of Europe, 1997
<http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm>
- Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin, Council of Europe, 2002
<http://conventions.coe.int/Treaty/en/Treaties/Html/186.htm>
- Bioethics at the Council of Europe
www.coe.int/bioethics
- Ethics and xenotransplantation, opinion No. 61 of the French National Council on Ethics, 1999
www.ccne-ethique.fr
- Organ Donation, Informed or presumed consent?, report of the Danish Council of Ethics, 1999
www.etiskraad.dk
- Animal-to-Human Transplants: the Ethics of Xenotransplantation, report of the Nuffield Council on Bioethics, 1996
www.nuffieldbioethics.org
- Book: *Ethical eye: transplants*, Council of Europe Publishing, 2003, ISBN-13:978- 92-871-4779-0
- Film: *All About My Mother*, by Pedro Almodovar



GLOSSARY

Antigen: chemical substance, isolated or carried by a cell or a micro-organism which, when introduced into the body, can trigger a specific reaction of the immune system leading to its destruction or neutralisation.

Brain-death: irreversible loss of brain function, as ascertained by means of specific signs. Conditions for the ascertainment of brain death may vary from country to country.

Compatible: that match despite different origins. Compatibility may concern the blood group and the tissue identity.

Consent, free and informed: “free” because the person in question is not subject to any constraints or influence in taking his or her decision and “informed” because he or she is told about the risks attached to the operation and the implications of the intervention.

Presumed consent: when, in their lifetime, people have not specified that they do not want to donate their organs after their death, they are presumed to have consented and their organs may be removed for transplantation purposes.

HLA (Human Leucocyte Antigen) system, also known as the MHC (Major Histocompatibility Complex) system: a tissue identity card. The molecules present on the surface of every cell in an individual, which are coded by this system, enable the immune system to differentiate between “self” and “non-self”.

Immunosuppression: inhibition of the immune system mechanism in order to prevent rejection of the transplant (by drugs known as immunosuppressant).

Incompatibility: leads to agglutination of the donor’s red blood cells in the recipient’s blood and may lead to the latter’s death. This occurs when systems such as the HLA system of the donor and recipient are very different.

Organ: a structured mass of tissue which, if completely removed, cannot be regenerated by the body. Examples are the heart, the lungs, the liver and the kidneys.

Rejection of a transplant: the result of an immune system reaction that recognises the cells of the transplanted organ or tissue as alien.

Traceability: makes it possible to follow the path of all organs and tissues from the donor to the recipient, and vice versa. This is necessary because of the risk of diseases being transmitted from the donor to the recipient and of contamination of stored materials.

Transplant/graft: transfer of an organ, part of an organ or tissue into a body.

Transplantation: the entire procedure involving the removal of an organ or tissue from one person and the grafting of this organ or tissue on to another person. The transplantation system ensures that the information needed to ensure the traceability of organs and tissues is collected and registered.

Xenograft: transplant between two different species (for example, between a pig and a human being).

1

Medically-assisted procreation

Context

Bioethics

Bioethics is concerned with the problems raised for human beings by advances in biology and medicine. Essentially bioethics is a multidisciplinary and pluralist reflection of the problems facing all citizens. It must also take account of the fact that science and technology are constantly progressing.

TECHNIQUES FOR COMBATING INFERTILITY...

Over the last 30 years, new medical techniques have been developed to help couples who have problems in conceiving a child, whether the problems originate with the man, the woman or both. These techniques are grouped together under the term “medically assisted procreation” (MAP).

Many infertile* couples can considerably enhance their chances of having a child in this way.

... AND THE ISSUES THEY RAISE

Medically-assisted procreation techniques allow many infertile couples to have children, which would not have been possible just a quarter of a century ago.

These techniques have become particularly important because of the evolution of western society. Current lifestyles mean that the average age at which women first become pregnant is rising, whereas the period for which women remain fertile has stayed the same. Recourse to MAP can help to compensate for the decline in fertility, linked among other things to age.

MAP techniques do, however, entail treatment that may be more or less difficult for women and interfere with the process of the creation of life. They therefore raise numerous ethical issues.

OTHER USES OF MAP

MAP techniques are sometimes used for reasons other than infertility:

- > to avoid passing on a serious genetic abnormality to the unborn child (pre-implantation diagnosis*)
- > to avoid transmitting a viral disease such as AIDS to the partner or child
- > to enable single women or a homosexual couple to have a child.

All these uses raise other ethical and social issues.





HISTORICAL REFERENCES

- > **1790** first artificial insemination*: the sperm of a man is introduced into the vagina of his wife by means of a feather.
- > **1884**: first artificial insemination with the sperm of a donor (United States).
- > **1953** first birth after the use of sperm stored by freezing.
- > **1959**: birth of the first “test-tube animal”, a rabbit.
- > **1969** first fertilisation of a human egg* in a test tube by Robert Edwards, biologist (United Kingdom).
- > **1978** birth of Louise Brown, the first baby to be born after in vitro fertilisation (IVF)*, carried out by Robert Edwards, biologist, and Patrick Steptoe, gynaecologist (United Kingdom).
- > **1981** birth of Amandine, the first baby to be born in France after IVF, carried out by Jacques Testart, biologist, and René Frydman, gynaecologist.
- > **1992** development of ICSI* by André Van Steirteghem, biologist (Belgium), making it possible, among other things, to compensate for certain forms of male sterility.
- > **1995**: birth of a baby boy after fertilisation of an oocyte* by a spermatid* (immature spermatozoid*).

MAP, A TOPICAL ISSUE

Some figures [source: INSERM (French Health and Medical Research Institute)/INED (French Demographic Studies Institute)]

In 1991 the World Health Organisation (WHO) estimated that 50 to 80 million people in the world, in other words one person in ten, wanted a child but had difficulty in conceiving.

The level of infertility* is much lower in northern countries than in southern ones, where genital infections are much more common. It is estimated that one couple in three in sub-Saharan Africa suffers from infertility.

IVF is used far more in Europe than in other continents.

In 1999, 3% of children were born as a result of IVF in Denmark, 2.6% in Finland, 1.4% in France, 1.1% in the United Kingdom, less than 1% in Italy and just under 0.1% in Portugal.

The success rate of IVF is about 20% per oocyte* puncture; this figure is comparable to the likelihood of a fertile couple conceiving a baby in any particular cycle*.

One IVF pregnancy in four involves twins.

In France:

For every 100 couples wanting a child, 20 to 25 achieve a pregnancy the first month of trying, 65 to 70 in the first six months and 80 to 85 in the first year. 15 to 20 couples fail to achieve a pregnancy after trying for a year.

In 2003, fewer than 5% of French mothers underwent treatment for infertility*. In half the cases, treatment simply involved hormonal stimulation; in one-third IVF was carried out, and in a quarter, insemination.

Between 1982 and 2000, 85 000 children were born as a result of IVF in France.

Since 2000, one in vitro fertilisation in two has been carried out by intracytoplasmic sperm injection (ICSI)*.

In 2001, there were 105 000 frozen embryos, initially produced for reproductive purposes; 27 000 of them had been frozen for over five years.

2

Medically-assisted procreation Scientific data

NATURAL REPRODUCTION

The human embryo* is the result of the meeting and fusion of two reproductive cells: the woman’s oocyte and the man’s spermatozoid.

During sexual intercourse the man ejaculates millions of spermatozoids, which enter the woman’s uterus. It is estimated that about 150 000 of them reach the end of the Fallopian tube*, where the oocyte is to be found after ovulation*. Just one spermatozoid penetrates the oocyte. This constitutes fertilisation.

The fertilised oocyte divides to form two cells, then four, eight, and so on. At the same time, it migrates from the Fallopian tube to the uterus. About a week after fertilisation, the embryo implants in the lining of the uterus, where it develops. The limbs and organs gradually appear over the first two months. Fully formed, the embryo becomes a foetus in which the limbs and organs that have already formed will develop until birth.

Generally speaking, a fertile couple has about one chance in four of achieving a pregnancy during any particular cycle*.



MAP

The term “medically-assisted procreation” covers a range of biomedical techniques that make it possible to carry out or facilitate in a laboratory certain stages of procreation.

WHY RESORT TO MAP?

Medically-assisted procreation makes it possible to overcome certain obstacles to conceiving a child.

- The infertility* from which certain couples suffer, which concerns men and women roughly equally, may be due to:
 - > ovulation disorders, problems in the Fallopian tubes or the uterus which hinder, in particular, movement of the oocyte or its implantation after fertilisation, anomalies in the cervical mucus* or alterations in the sperm;
 - > the absence of gametes*, in which case a spermatozoid or oocyte donation or an embryo donation may be proposed;
 - > unknown causes (8 to 30% of cases).
- MAP may be used without there being an infertility problem if there is a risk of passing on:
 - > a genetic abnormality: to prevent its transmission, the donation of a gamete from a donor who does not carry the abnormality may be proposed, or a pre-implantation diagnosis (PGD)* may be carried out to identify embryos not affected by the abnormality;
 - > a viral disease (such as AIDS) that can be transmitted to the child or partner. Treatment of the sperm or recourse to gamete donation considerably reduces the risk.

TWO MAP TECHNIQUES AND VARIATIONS ON THEM

Artificial insemination entails placing the spermatozoid at the level of the cervix or directly into the womb by means of a thin, flexible tube. The sperm, which has been treated beforehand in a laboratory, may be fresh or thawed.

In vitro fertilisation* (IVF) entails bringing oocyte and spermatozoids together in a culture dish to make it easier for them to meet. After two or three days, one or more of the embryos that have been obtained are transferred to the mother’s uterus. In some cases, the embryo may be kept in vitro for up to three more days so that it can be transferred at a more advanced stage.

ICSI* is a recent variation on IVF that involves forcing the gametes to meet in vitro. The biologist injects a spermatozoid directly into an oocyte with the help of a microscope and microsyringe.

THE VARIOUS STAGES OF IVF

1. Information and consent

After being informed of the implications of medically assisted procreation, both members of the couple must give their consent to the entire treatment and the procedure envisaged.



2. Ovarian stimulation

For about 12 days, the woman receives treatment that stimulates her ovaries. Contrary to what occurs in the absence of such stimulation, she will produce several fertilisable oocytes; this increases the chances of obtaining embryos that can be transferred.



3. Removal of the oocytes

When the oocytes have reached maturity, the doctor removes



them directly from the ovary by means of a needle (oocyte puncture), usually collecting between five and ten oocytes.

On the same day,

the fresh or thawed sperm sample is treated to select those spermatozooids* which appear to be most fertile.

4. Fertilisation

The oocytes and spermatozooids are placed in a suitable culture medium and kept at 37°C. After 48 to 72 hours' incubation, the embryos obtained are ready to be transferred to the mother's uterus.



5. Transfer of the embryos

One to three embryos are removed by suction



using a thin, flexible tube. They are placed via the vagina into the uterus, where they are deposited. Any other embryos that have been formed may be stored (in liquid nitrogen) for a subsequent attempt.



6. Pregnancy?

It takes about 12 days for the embryo to implant in the uterus. An ultrasound scan two to three weeks after the transfer makes it possible to determine how many embryos, if any, have implanted.

RESULTS

The results vary greatly according to the fertility problems encountered, the woman's age and the quality of medical supervision provided. It is estimated that artificial insemination roughly doubles the chances of pregnancy for an infertile couple and multiplies them by five when it is combined with ovarian stimulation. On average, 20% of embryo transfers in the context of IVF lead to pregnancy. Three-quarters of these pregnancies lead to the birth of a child.

In France, about 23% of pregnancies obtained through MAP are multiple pregnancies: two or three fetuses may develop, depending on the number of embryos transferred. There is a higher risk of miscarriage* and premature birth* than in the case of a single pregnancy. Improvements in the techniques are, however, making it possible to reduce the number of embryos transferred, which limits the number of multiple pregnancies.

If the number of embryos created exceeds the number of embryos transferred, it is possible to freeze the surplus embryos for further attempts. They may be stored for several years in this way.

3

Medically-assisted procreation Key points

Legal references

Convention on Human Rights and Biomedicine (known as the Oviedo Convention), Council of Europe, April 1997

FUNDAMENTAL PRINCIPLES

The dignity and identity of human beings must be protected.

- Everyone must be assured of respect for his or her rights and fundamental freedoms with regard to the application of biology and medicine (Article 1 of the Oviedo Convention).
- The interests and welfare of human beings must prevail over the sole interest of society or science (Article 2 of the Convention).
- Recourse to MAP techniques raises important ethical, legal and social issues: the fact that humans are intervening in what is a fundamental natural process; the fate of the frozen embryos; the fact that some of the techniques used are too recent to be properly assessed, and so on.

THE FATE OF THE EMBRYO

- “The human body and its parts shall not, as such, give rise to financial gain.” (Article 21 of the Convention).
- The non-commercialisation of the human body implies that the embryo cannot, as such, be sold, and nor may sperm and oocytes.

INFORMED CONSENT

- “An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it.” (Article 5 of the Convention)
- The consent of both parents is needed where the creation and fate of an embryo are concerned.
- Both members of the couple – or the woman alone in countries that allow women who are not part of a heterosexual couple to benefit from MAP – receive comprehensive information about the procedure and a description of the forms of intervention envisaged and their implications, including the fate of embryos that are not transferred, before they give their consent.
- One or other member of the couple may, at any time, freely withdraw his or her consent, in the knowledge that this choice will also affect his or her partner.
- Some stages are, however, irreversible, for example the transfer of embryos to the uterus or the destruction of supernumerary* embryos. The couple must therefore clearly understand the implications of their choice and take time to think about them.



3 Key points

GOOD MEDICAL PRACTICE

The medical personnel must inform the person concerned of the potential risks and benefits of MAP in general and the selected technique in particular, including its chances of success, possible complications and the risks to the mother and foetus in the event of a multiple pregnancy.

They must also draw the couple's attention to the fate of supernumerary* embryos.

Healthcare personnel must also be trained in the issues involved in medically-assisted procreation, including its ethical aspects.



DIFFERENT APPROACHES IN EUROPE

Recourse to MAP is possible in all European countries, though there are restrictions to varying degrees depending on the country concerned.

While several countries (for example, Estonia, Belgium and Spain) allow women not living as a member of a heterosexual couple to benefit from these techniques, many others allow only heterosexual couples access to MAP (as in France).

Gamete donation is generally authorised in Europe, although countries authorising it do not always

allow embryo donation (examples being Sweden, Portugal and Slovenia).

Some countries, such as Germany and Italy, prohibit the production by in vitro fertilisation of a larger number of embryos than the maximum that it is desirable to transfer during a cycle, i.e. three embryos.

A number of countries expressly authorise surrogate* motherhood, but solely on a non-commercial basis.



4

Medically-assisted procreation Concrete situations

CASE No. 1

Veronica and Stephen are going to use in vitro fertilisation (IVF)*. They know that several oocytes will be removed from Veronica’s ovaries in order to increase the likelihood of success. IVF often produces more embryos than are transferred to the uterus. Veronica and Stephen have mixed feelings about the fate of these embryos. Veronica would like them all to be transferred, but a multiple pregnancy can have tragic consequences: a miscarriage*, often late in the pregnancy, or a premature birth, which can create serious health problems for the children. Stephen wants to store the embryos for a further attempt; Veronica does not want to have to take a decision about their fate. In fact, embryos can be stored for only a limited amount of time, and the couple will therefore have to decide whether to give them to another couple, authorise their use for research purposes or have them destroyed.

QUESTIONS

- Is it ethical to destroy a human embryo or carry out research on it that entails its destruction? Should an embryo that has not been transferred be protected differently from one that has been transferred to the uterus?
- Is it better to allow research that improves our knowledge of human reproduction and MAP techniques or only to allow the embryos to be destroyed?
- By giving the embryos to another couple, would Veronica and Stephen make it possible to accomplish what the embryos were conceived for?

CASE No. 2

Amanda and John have been trying for a baby for two years, without success. Medical tests have not revealed any problem with Amanda, but John’s spermogram* has shown that he has very few spermatozooids and that they are immobile. In the circumstances, the doctor suggests two medical solutions: artificial insemination* with sperm from an anonymous donor or ICSI*. In the case of ICSI, a spermatozoid* will be injected by means of a micropipette into each oocyte that has been punctured for in vitro fertilisation*. The doctor warns Amanda and John, however, that as this technique has not been around for very long, it is not possible to know what all the possible implications will be for the health of the future child.

QUESTIONS

- Is it possible to envisage using a technique when the consequences for the child are not fully known?
- Should the desire of the parents to have children that are biologically their own prevail?
- What are the implications for the parents of resorting to a donation of gametes? And for the future child?



CASE No. 3

After a highly active life, Suzette is satisfied with her career and now wants a child. Her husband is not very enthusiastic: is it reasonable to embark on such an adventure at the age of 57, even if MAP* techniques make it possible? Is Suzette, who is old enough to be a grandmother, not too old to be a mother?

QUESTIONS

- Should MAP techniques be used to push back the natural limits to reproduction so that people can choose when they want to become pregnant?
- Should MAP be used to satisfy the desire for a child regardless of other considerations?
- What consequences might this have for the child?
- Should MAP be used to satisfy the desire for a

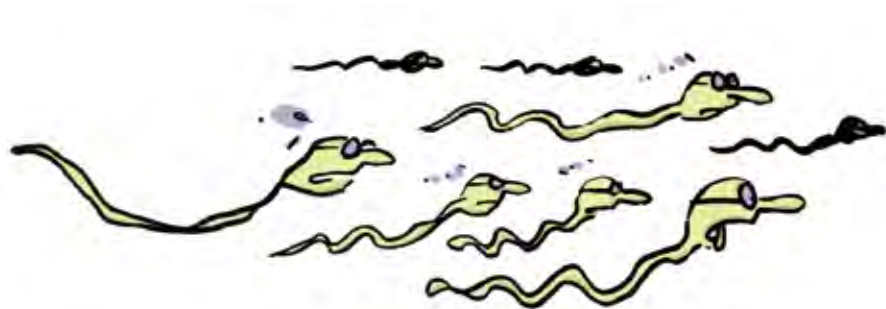


CASE No. 4

Claire had to receive radiotherapy for leukaemia at the age of 26, which left her sterile. Having been warned by her doctor before starting the treatment that this would happen, she decided with Tom, her partner, to conceive embryos by IVF, store them and transfer them once she was cured. She has now recovered, but has separated from Tom. Yet she wants to have children and would like to have the embryos they conceived together transferred. Tom, who has got married in the meantime, refuses to allow the embryos produced with his sperm to be transferred.

QUESTIONS

- Should Tom be refused the opportunity to withdraw his consent before the embryos are transferred?
- Should Claire be refused the opportunity to found a family with children that are biologically her own?
- Is it conceivable that the views of one of the two parents should be overridden?



5

Medically-assisted procreation Find out more

... ABOUT QUESTIONS RAISED BY MAP

- Convention on Human Rights and Biomedicine (Oviedo Convention), Council of Europe, 1997
<http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm>
- Bioethics at the Council of Europe
www.coe.int/bioethics
- Current Practices and Controversies in Assisted Reproduction, report of the World Health Organization, 2001
www.who.int/reproductive-health/infertility/report_content.htm
- Medically Assisted Procreation, opinion No. 44 of the Portuguese National Council of Ethics for the Life Sciences, 2004
www.cnecv.gov.pt/cnecv/en/opinions
- Opinions of the French National Council on Ethics on MAP (Nos. 40, 69)
www.ccne-ethique.fr

... SOME SCIENTIFIC AND TECHNICAL INFORMATION ON MAP

- The IVF processes, step by step, including illustrations and animations
www.abc.net.au/science/lcs/ivf.htm
- Data collections on European IVF-monitoring
www.eshre.com
- Information about fertility treatments
www.hfea.gov.uk/en/270.html



GLOSSARY

Artificial insemination: MAP technique which entails depositing spermatozoid at the level of the cervix or directly in the uterus.

Cervical mucus: sticky, opaque secretion protecting the entrance to the uterus, where spermatozooids ejaculated in the vagina are filtered. At the time of ovulation the mucus becomes clear and runny, facilitating the entry of the spermatozooids into the uterus.

Cycle (ovarian): set of periodical changes in the ovary, which take place on average over 28 days. Ovulation generally takes place in the middle of the cycle.

Embryo: first stage of development of a fertilised oocyte. It consists of several cells. One generally talks of embryos up to the third month of pregnancy and fetuses after that.

Fallopian tubes: very fine tubes that link the uterus to the ovaries and catch the oocytes during ovulation. It is in the tubes that natural fertilisation takes place. Contractions of the tubes carry the embryo to the uterus, where it implants.

Fertilisation: penetration of an oocyte by a spermatozooids. Fusion of nuclei of the two cells leads to the formation of an embryo.

Gamete: male or female reproductive cell.

ICSI (intracytoplasmic sperm injection): a technique derived from in vitro fertilisation, which entails injecting a spermatozoid directly into an oocyte by means of a micropipette.

Infertility: difficulty with procreation.

IVF (in vitro fertilisation): medically-assisted reproduction technique where the fertilisation process takes place in a laboratory.

MAP (medically-assisted procreation): set of techniques facilitating human procreation.

Miscarriage: spontaneous abortion.

Oocyte: woman's reproductive cell.

Ovulation: expulsion of the oocyte from the ovary.

Pre-implantation diagnosis (PID): technique making it possible, thanks to a genetic test, to select an embryo that does not carry a genetic abnormality, obtained by in vitro fertilisation, for transfer to the mother's uterus.

Premature birth: birth before the end of the normal duration of pregnancy. Depending on the stage of pregnancy at which it takes place, it may have very serious implications for the child's health.

Spermatid: immature male gamete destined to be transformed into a spermatozoid.

Spermatozoid (plural: spermatozoa): male reproductive cell. Spermatozoa are mobile cells that move by means of a tail.

Spermogram: analysis of the characteristics of the ejaculated sperm.

Supernumerary embryos: embryos which are no longer to be used for planned parenthood. They have been obtained by means of IVF, were not transferred and are stored in liquid nitrogen at -196°C .

Surrogate motherhood: a pregnancy carried to term by a woman for the benefit of a couple who cannot have children. The gametes that enabled the embryo to be created may have come from one or both members of the couple, or have been donated. The woman bearing the child is commonly known as a "surrogate mother".



1

Genetic testing

Context

Bioethics

Bioethics is concerned with the problems raised for human beings by advances in biology and medicine. Essentially bioethics is a multidisciplinary and pluralist reflection of the problems facing all citizens. It must also take account of the fact that science and technology are constantly progressing.

A REVOLUTIONARY DEVELOPMENT: THE ANALYSIS OF THE GENOME OF A PERSON...

Analysis of the genetic characteristics of an individual can make it possible to discover an abnormality responsible for a disease or disorder.

The abnormality is identified by means of a **genetic test**: the **diagnosis*** of a genetic disease in someone presenting symptoms* of that disease can be confirmed by the information obtained. It can also serve a **predictive*** purpose by providing information about the risk of developing a disease that has not yet appeared or of transmitting the abnormality to one’s children.

Depending on the case, the results of genetic testing may render it feasible to adapt treatment to the disease identified, limit the symptoms or prevent their onset. They may make it necessary to take preventive measures to stop the disease from developing or to take measures for closer medical supervisions to detect the first symptoms as early as possible. Lastly, they may make it possible to take steps to avoid passing on a genetic abnormality to future children.

... AND THE ISSUES IT RAISES

More and more tests are available for detecting genetic abnormalities but, at the same time, effective forms of treatment for slowing the development or preventing the onset of the diseases associated with these abnormalities are still very limited.

An examination of genetic characteristics, regardless of the result, can have serious repercussions on the life of the individual concerned. The “revelation” of the risks to his or her future health may change the person’s view of his or her existence and the way in which other people and society perceive him or her.

The situation is paradoxical: genetic testing makes it possible to know more about one’s future health, but this knowledge may have implications for the life of the person being tested that are difficult to foresee.



GENETIC INFORMATION: A SPECIAL KIND OF INFORMATION

The results of genetic testing are different from other forms of medical information because:

- > they may concern other family members;
- > they are often predictive;
- > the results very often indicate a likelihood and not a certainty.

HISTORICAL REFERENCES

- > **1866**: Gregor Mendel discovers the laws of heredity by means of experiments on pea plants.
- > **1900-1950**: discovery of the basis of genetics.
- > **1953**: James Watson, Francis Crick and Maurice Wilkins discover the structure of deoxyribonucleic acid (DNA*), which carries the body's genetic information.
- > **1961**: François Jacob, Jacques Monod and André Lwoff discover how genes* function.
- > **1966**: the genetic code* is "cracked": Marshall Nirenberg, Heinrich Mathaei and Severo Ochoa show that a sequence of three nucleotides* provides a code for each of the 20 amino acids*.
- > **1970**: discovery of the first gene involved in cancer.
- > **1980**: invention of a technique (PCR*) that makes it possible to replicate DNA sequences, which constitute an essential tool for working with genes.
- > **1983**: discovery of the mutation involved in Huntington's chorea (a neurological disease); this leads to the development of a genetic test.
- > **1990-2004**: genome* of the human species deciphered.



GENETIC TESTING: A TOPICAL ISSUE

A few figures

There are currently over **10 000** genetic disorders (genetic diseases in the strict sense of the term and chromosome diseases), of which roughly **1 700** are due to specific mutations of the genome.

Down's Syndrome (a disease caused by an extra copy of chromosome 21) affects **one child in 800**. There are currently **400 000** people with Down's Syndrome in Europe and **8 million** in the world.

50 million people in the world suffer from sickle-cell anaemia, a genetic disease that affects the red blood cells, restricting the supply of oxygen to the body's cells. It is present in certain parts of India, in the West Indies and in South America, among Afro-Americans, and particularly in inter-tropical Africa.

In France newborn babies are systematically tested for **five** genetic diseases, including sickle-cell anaemia and cystic fibrosis.

Haemophilia is a genetic disease that impairs coagulation of the blood. There is Haemophilia A, which affects one person in 10 000, and Haemophilia B, which affects one person in 150 000. It is estimated that there are **400 000** haemophiliacs in the world. Serious cases of haemophilia mainly affect men.

Some **5%** of cases of breast cancer are due to a genetic predisposition. Women with this predisposition are eight times more likely than other women to develop this type of cancer.



2

Genetic testing Scientific data



GENETIC HERITAGE, THE LEGACY OF OUR PARENTS

The human body has some 70 000 billion cells, each of which contains “instructions” for the whole body, in the form of the genome*, written on a long molecule known as DNA*.

In human beings, the DNA is organised into **46** chromosomes. A part of a chromosome known as a **gene** helps to produce a hereditary characteristic. We have between 20 000 and 25 000 genes.

23 chromosomes come from the father and **23** from the mother. There are two copies, in pairs, which carry the same genes* (except in the case of the sex chromosomes), but these may be expressed (by means of the production of RNA* or proteins) differently.

We all carry variations – DNA mutations – without their necessarily affecting our health in the course of our lives.

THE VARIOUS TYPES OF GENETIC DISEASES ...

Sometimes a simple change in the genome* may cause a disease:

- A change in the number of chromosomes or their structure. In this case one talks of a **chromosome** disease.
For example, Down’s Syndrome is an abnormality caused by the presence of a third copy of chromosome 21.
- The alteration of one or more genes (known as a mutation). In this case one talks of a **monogenic** or **multigenic** disease.
An example is sickle-cell anaemia, a disease of the blood due to a mutation of a gene on chromosome 11.

Most genetic diseases are caused by a combination of genetic and environmental factors, in which case one talks of **multifactorial diseases**.

For example, in insulin-dependent diabetes there are environmental causes that are still poorly understood, along with a genetic predisposition due to mutations of the genes on chromosome 6.

... THE DIFFERENT TYPES OF GENETIC TESTS

Genetic test

A genetic test involves analysing genetic material (generally a chromosome or DNA) to identify a possible genetic abnormality. This type of analysis requires only a small sample of biological material (blood, a few cells obtained by scraping the inside of the cheek, etc.).

- A **diagnostic test** makes it possible to confirm the genetic origin of an existing disease.
For example, a test showing a mutation of the DMD gene confirms the presence of Duchenne muscular dystrophy rather than another type of muscular dystrophy.
- A **pre-symptomatic test** makes it possible to establish the likelihood that the person tested will develop a hereditary disease from which members of his or her family suffer before the onset of the first symptoms.
For example, Huntington’s chorea does not normally set in before the age of 40. A genetic test makes it possible to know with certainty whether the person concerned carries the mutation that causes the disease.
- A **predisposition test** provides information about the genetic component of a multifactorial disorder. For example, if there is a mutation of one of the BRCA genes, the risk of developing breast cancer before the age of 50 is 20% (BRCA2) to 40% (BRCA1). Factors other than genetic ones also come into play.
- A **test identifying a healthy carrier** makes it possible to ascertain whether someone in good health carries a genetic abnormality linked to a disease that he or she will not suffer from (a recessive disease) but is likely to pass on to his or her children.
For example, beta-thalassaemia is a disease that can lead to fatal anaemia. It occurs in a child only if both (healthy) parents pass on the modified gene.

THE VARIOUS STAGES OF GENETIC TESTING



1. Information and genetic counselling

The patient is informed of the implications of the genetic test for him or herself and members of his or her family. They are often offered **genetic counselling** to help them, in particular, to understand all the implications clearly.



2. Consent

The patient can then consent to the genetic test.



3. Removal of a bodily sample

A genetic test is carried out on a few cells, which are usually taken from the blood but may be taken from the saliva, skin, etc.

4. Genetic analysis: study of the chromosomes or the DNA

*Chromosome study: preparation of the karyotype **

The division of a cell is stimulated and then blocked at the stage when the chromosomes are as condensed as possible. The cell is then made to burst and the artificially stained chromosomes are photographed with a microscope and then classified.



DNA study

Preparation of the DNA: the DNA is extracted from the cells and purified. The gene* that is to be examined is identified and copied a large number of times by PCR*. It is said to undergo "amplification".

Identification of mutations: mutations of a gene are identified by radioactive probes and by electrophoresis*, and the gene being analysed is compared with a reference gene. The differences observed indicate genetic abnormalities.



5. Interpretation of the results

The results of a genetic test are difficult to interpret: expertise in genetics is required.



6. Genetic counselling

Genetic counselling helps patients to understand the implications of the results for their lives and those of their family more clearly and to take decisions (treatment, prevention, informing the family, etc.).

DIFFICULTIES AND LIMITATIONS OF GENETIC TESTING

As in the case of any biological test, genetic tests must meet proper scientific criteria if they are to be reliable. While the technique is relatively simple to perform, it is more complicated to obtain reliable data from the raw results which are relevant to the person concerned.

For example, even if a mutation is identified, it is sometimes impossible to predict at what time and to what extent it will manifest itself. Some people suffering from a particular mutation will have benign symptoms, while others will suffer from serious disorders.

Moreover, it is necessary to have information about the genetic origin of the disease (gene or chromosome) in order to search for a mutation. The fact is that at present we do not always have enough genetic knowledge to know where to look on the genome. Conversely, the presence of a mutation responsible for a multifactorial disease is not always sufficient to trigger the disease. In that case, one can merely say that there is a likelihood of developing it. With the exception of a few diseases, a positive test result does not necessarily mean that the person will become ill.

3

Genetic testing Key points

FUNDAMENTAL PRINCIPLES

The dignity and identity of human beings must be protected

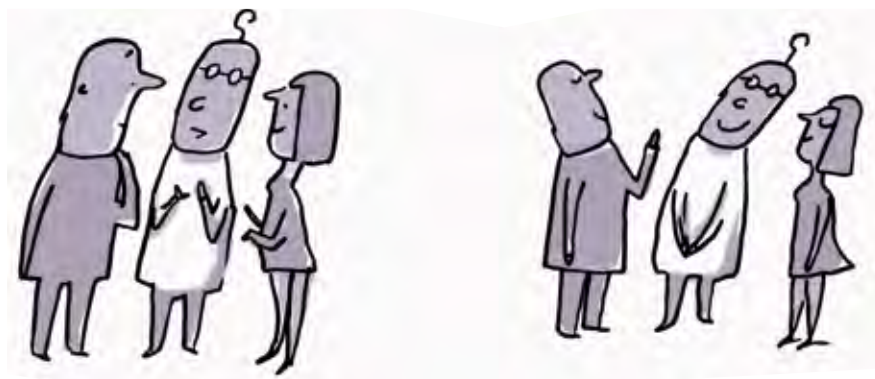
- Everyone must be assured of respect for his or her rights and freedoms with regard to the application of biology and medicine.
- The use of individual genetic information raises major ethical, legal and social issues.
- Improper use of the results of a genetic test could lead to **discrimination** in access to employment or insurance and be a source of **stigmatisation*** for the person concerned.
- “Tests which are predictive of genetic diseases or which serve either to identify the subject as a carrier of a gene responsible for a disease or to detect a genetic predisposition or susceptibility to a disease may be performed only for health purposes or for scientific research linked to health purposes, and subject to appropriate genetic counselling.” (Article 12 of the Convention)
- “Any form of discrimination against a person on grounds of his or her genetic heritage is prohibited.” (Article 11 of the Convention)

Legal references

Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine» (known as the Oviedo Convention; Council of Europe, April 1997)

INFORMED CONSENT

- “An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it.” (Article 5 of the Convention)
- The person concerned may freely withdraw his or her consent at any time.
- Genetic information makes it possible to know, to some extent at least, what the state of health of the person concerned will be in the future. The person undergoing genetic testing must therefore clearly understand the nature of the test, the significance of the results for himself or herself and, where applicable, for members of his or her biological family, whether there are any means of prevention or treatment and, if so, the constraints attached to them.
- Special attention must be paid to people considered legally not able to give free and informed consent, for example minors and certain people with mental disabilities (Article 6 of the Convention).



INFORMING THE PERSON CONCERNED AND THE FAMILY

Anyone undergoing genetic testing is entitled to know the information about his or her health obtained from the test.

Some people prefer not to know that they might develop a disease for which there is as yet no treatment available. In that case, the person's wishes must be respected.

Everyone is entitled to respect for his or her privacy and may refuse to inform others of the results of a genetic test. The results may, however, also concern the health of family members. The person concerned must therefore be made aware of this, though his or her wishes in this regard must be respected.

GOOD MEDICAL PRACTICE

The medical personnel must inform the person concerned of the potential risks and benefits of the genetic test. Especially when the implications may be substantial, as in the case of predictive tests, genetic counselling shall be offered.

All information must be treated confidentially. The

doctor must observe medical secrecy, which forms the basis of the patient's trust.

Healthcare personnel must be informed of the issues arising in connection with genetic testing, including the ethical aspects.

PSYCHOLOGICAL PROBLEMS IN RESPONSE TO THE RESULTS

The results of a genetic test may profoundly affect the life of the person concerned and his or her family.

Knowing that one carries a genetic disease may cause psychological problems. It may affect the decision to have children, and parents may feel guilty for passing on a genetic abnormality to their children.

Knowing that one does not carry a genetic disease may provide relief. Yet some people may feel guilty if other members of their family are affected by the genetic abnormality.



USE OF TEST BY EMPLOYERS AND INSURERS

All candidates for a job must be assured of equal opportunities.

Any test must clearly be carried out in the interests of the health of the person concerned. There can therefore be no question of carrying out predictive genetic tests on the occasion of a medical examination prior to employment if their purpose is not to benefit the health of the person concerned.

If, however, working conditions could have harmful effects on someone's health on account of his or her genetic characteristics, an appropriate genetic test may be offered, without this dispensing the employer from being obliged to provide a working environment that is adapted in such a way as to

protect the health of employees as effectively as possible.

In addition, the law may provide for exceptions in cases where the health of the person concerned may cause a risk, in an occupational context, to other people (as in the case of an airline pilot or bus driver, for instance).

If the aim of the test is not to benefit the health of the person concerned, an insurer is not entitled to ask for a predictive genetic test to be carried out as a prerequisite for the conclusion or amendment of an insurance contract. Such a request would constitute a disproportionate interference with the respect for private life.

4

Genetic testing Concrete situations

CASE No. 1

Detecting a predisposition

Anna, aged 18, is afraid of getting breast cancer as her mother and grandmother did. Might there not be a genetic factor responsible for the numerous cases of cancer in her family? In order to be clear in her own mind, Anna chooses to undergo the genetic test suggested by her doctor. If she carries a mutation of the BRCA1 gene, she has a 40% risk of developing breast cancer before the age of 50. If the result of the test is positive, Anna knows that, as a preventive measure, she can be regularly screened by X-ray so that any tumour is detected as early as possible. A friend has also told her about countries where surgical removal of the breasts is proposed, in which case the risk of cancer is reduced to 3%. Regardless of the result, she does not want to talk to her family about it so as not to cause panic, particularly in her 10-year-old sister.

QUESTIONS

- Would you have made the same choice as Anna? Would you want to know if you had a predisposition or not?
- If the test is positive, what solution would you choose? The radical solution of surgical removal of the breasts (mastectomy) considerably reduces the risk, but it entails permanent mutilation to prevent a disease that may never occur.
- If the result of the test is positive, should Anna not warn her little sister of the risk that she too faces, so that she can take preventive measures?
- Can the doctor warn Anna’s sister if he or she knows that Anna does not want to tell her?
- Does the doctor not risk losing Anna’s trust? Can medical secrecy be overridden in the interests of another person?

CASE No. 2

Testing a child

32-year-old Martha’s father has just died of Alzheimer’s disease. She wonders whether there might be a genetic predisposition in her family and plans to undergo the test and have her four-year-old son John tested. She is afraid that she may have passed on “bad genes” to her son. Her husband does not agree that John should undergo the test: the first symptoms of the disease appear at an advanced age and there is no preventive treatment. Why bother John with a result that will have no consequences for many years?

QUESTIONS

- Is Martha entitled to take this decision on behalf of her son? Should she not wait until he is old enough to understand the situation, or has reached the age of majority so that he can decide for himself?
- Is John not entitled to an “open future”? Should he not be allowed to decide for himself whether or not he wants to know if he has a predisposition to the disease?
- Would it not be preferable to have the agreement of both parents for such a decision? Could a meeting with a specialist in the context of genetic counselling not help them to make up their minds?



CASE NO. 3

Access to genetic tests

55-year-old Peter has found a website that offers a genetic test for determining the risk of cardiovascular disease. He decides to order the sample kit. It is simple to use: one need only scrape the inside of one's cheek with a spatula and return the sample to the address indicated. Three weeks later, the results arrive by e-mail: "Risk of cardiovascular disease: 42%".

QUESTIONS

- What do you think of the fact that it is possible to obtain access to this type of test without going through a doctor?
- Peter is entitled to find out about his health, but is it reasonable to do so without medical support? Has he received appropriate information about the implications of the test result? How should the result be interpreted?

CASE NO. 4

A test for a job

25-year-old Alison has just finished a work placement in the town planning department of a town hall. To obtain a permanent post, she has to undergo a medical examination, during which the works doctor discovers that her father suffers from an incurable genetic disease, Huntington's chorea. The symptoms of this fatal disease – unco-ordinated movements and mental disorders that can go so far as dementia – do not appear before the age of 40. Alison has one chance in two of developing the disease. The young woman refuses to undergo the genetic test that would remove the uncertainty. Although she currently fulfils the requirements for the job, the doctor advises against her being recruited, for if she carries the genetic abnormality she will not be able to work until retirement age. Instead of the job she expected, she is offered a three-year renewable contract.

QUESTIONS

- Can the doctor take account of Alison's family history when assessing her suitability for the job in question?
- Does the risk referred to by the doctor constitute sufficient grounds for turning Alison down for the job? Is the principle of equal opportunities with regard to access to work being respected?
- What is one to think of the use of genetic testing for job-recruitment purposes? Can Alison legitimately refuse to undergo the genetic test?



5

Genetic testing

Find out more

SOME SCIENTIFIC AND TECHNICAL INFORMATION ON GENETICS

- DNA from the beginning: animations, image gallery, video interviews, problems, biographies and links on the basics of DNA, genes and heredity
www.dnaftb.org
- Your Genes, Your Health: easy-to-understand information about a specific genetic disorder
www.ygyh.org
- Understanding Genetics: A Guide for Patients and Professionals, manual edited by Genetic Alliance
www.geneticalliance.org/understanding.genetics
- Informations on genetics, genetic disorders and genetic predisposition proposed by the Genetic Interest Group
www.gig.org.uk/education.htm
- Website providing information on rare diseases
www.orpha.net

... ABOUT QUESTIONS RAISED BY GENETIC TESTING

- Additional protocol to the Convention on Human Rights and Biomedicine concerning genetic testing for health purpose, Council of Europe, 2008
www.coe.int/bioethics
- Quality & Safety in Genetic Testing: An Emerging Concern: a complete file from the World Health Organization
www.who.int/genomics
- Genetic Investigation of Healthy Subjects, Report on Presymptomatic Gene Diagnosis, report of the Danish Council of Ethics, 2001
www.etiskraad.dk
- Who owns our genes? File about genetic information and the questions it raise from the legal perspectives of eight European countries
www.bionetonline.org

... ABOUT CONSENT AND INFORMATION TO FAMILY

- Opinions of the French National Council on Ethics (No. 70; 76)
www.ccne-ethique.fr

... ABOUT GENETIC TESTING AND THE EMPLOYMENT

- Genetics and employment: a file of the UK Human Genetics Commission, 2002
www.hgc.gov.uk «information» item
- Ethical aspects of genetic testing in the workplace, Opinion No. 18 of the European Group on Ethics in Science and New Technologies to the European Commission, 2003
http://ec.europa.eu/european_group_ethics/avis/index_en.htm
- Guidance of workers to risk-bearing occupations - Role of occupational physicians and reflections on the ambiguity of the concept of aptitude, opinion No. 80 of the French National Council on Ethics, 2003
www.ccne-ethique.fr
- Predictive health information in pre-employment medical examinations and Predictive health information in the conclusion of insurance contracts, opinions of the German National Ethics Council, 2005 and 2007
www.ethikrat.org
- Genetic susceptibility and health at work
www.genetic-testing-and-work.be



... ABOUT ACCESSIBILITY TO TESTING

- Private genetic testing services, file of the UK Human Genetics Commission, 2007
www.hgc.gov.uk «information» item
- Thinking of buying a health-related genetic test over the counter or from the Internet?, file of the UK Human Genetics Commission
www.hgc.gov.uk «information» item
- Free availability of genetic tests, opinion No. 32 of the Belgian Advisory Committee on Bioethics, 2004
https://portal.health.fgov.be/portal/page?_pageid=56,8546420&_dad=portal&_schema=PORTAL
- Problems connected to marketing self-test kits for HIV screening and diagnosis of genetic disease, opinion No. 86 of the French National Council on Ethics, 2004
www.ccne-ethique.fr

... ABOUT QUESTIONS RAISED BY GENETICS

- Convention on Human Rights and Biomedicine (Oviedo Convention), Council of Europe, 1997
<http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm>
- Bioethics at the Council of Europe
www.coe.int/bioethics
- Book: *Ethical eye: the human genome*, Council of Europe Publishing, 2001, ISBN 978-92-871-4568-0
- Film: *Gattaca*, by Andrew Niccol, 1997: a movie about a society where genetic perfection is the norm



GLOSSARY

Amino acids: the basic constituents of proteins. There are 20 amino acids: nine of them, known as “essential” amino acids, cannot be synthesised by the body and must therefore be provided through food. The human body is able to manufacture the other 11.

Chromosome: a long filament of DNA wound round proteins. It is visible as a rod-shaped structure only when the cell is dividing. The number of chromosomes varies from one species to another: in human beings, each cell contains 23 pairs of chromosomes (including one pair of sex chromosomes), one chromosome in each pair being inherited from the mother and the other from the father.

Diagnosis: identification of a disease from its symptoms.

Discrimination: the fact of treating someone differently without adequate justification, or disproportionately in relation to the intended purpose.

DNA (*abbreviation of deoxyribonucleic acid*): a long molecule containing all the genetic information of a living organism. It is found in the nucleus of virtually all cells, in the form of chromosomes, and takes the form of a twisted ladder (“double helix”) made up of nucleotides, in which the rungs are chemical bonds. The structure of DNA is the same in all species.

Electrophoresis: a technique for separating and identifying the components of a mixture (in this case, DNA fragments) by making them migrate under the effect of an electric field.

Gene: DNA segment that controls the development of a specific hereditary characteristic. Each gene occupies a specific location on a chromosome.

Genetic code: system for translating the genetic information carried by DNA into proteins. A particular sequence of three nucleotides corresponds to an amino acid.

Genome: all the DNA contained in a cell.

Hereditary characteristic: a characteristic that parents can pass on to their children.

Karyotype: a map of the chromosomes in the nucleus of a cell, arranged in pairs (homologous chromosomes) according to their size and shape and the location of their centre.

Nucleotide: a chemical “building block” of DNA or RNA.

PCR (*polymerase chain reaction*): a technique for obtaining large quantities of a specific DNA fragment from a small sample. The order of magnitude is one million copies in a few hours.

Predictive (test): which makes it possible, by studying genetic characteristics, to determine the likelihood of developing a disease or disorder.

Pre-symptomatic: which precedes the appearance of the symptoms.

Recessive disease: a disease that occurs only if the genetic abnormality is passed on by both parents, in contrast to a **dominant disease**, which occurs even if only one **parent** passes on the abnormality.

RNA (*abbreviation of ribonucleic acid*): a molecule produced by the transcription of DNA and consisting of a single chain of nucleotides. It is used by the cell to transport the genetic information carried by the DNA outside the nucleus, and then to synthesise proteins on the basis of this information. Several types of RNA can be distinguished in the cells, according to their function. The three main types are messenger RNA, transfer RNA and ribosomal RNA

Stigmatisation: an action or judgment on the part of a group or society that is negative or perceived as such, directed against an individual or group.

Symptom: a manifestation of a disease or disorder.

Syndrome: a set of symptoms characterising a pathological condition.

1

Biomedical research on human beings

Context

RESEARCH WHICH HAS REVOLUTIONISED TREATMENT OF, AND KNOWLEDGE ABOUT, THE HUMAN BEING...

Lifespan and health standards have greatly progressed since the Second World War thanks to socio-economic development and medical advances.

The achievements in biology and medical science, which have contributed to these improvements, are dependent on knowledge and discoveries which are themselves derived in particular from research conducted on human subjects.

... AND WHICH RAISES MANY QUESTIONS



Biomedical research* requires the participation of persons in good health as well as those who are ill, willing to submit to various interventions (administration of drugs, blood-sampling, etc.), which determines namely the validity of the scientific approach.

By definition, the effects of an intervention carried out in a research context are not wholly foreseeable. Biomedical research carries inherent risks that are to be determined. This is one of the reasons why research must be regulated so as to prevent undue risks for participants.

Furthermore, volunteers for a research project help to advance knowledge or to perfect medical applications which may work to the benefit of very many other people, though seldom directly to their own.

In particular, certain persons who may be taking part in a research project are especially vulnerable because of their condition, their age, their capacity to understand, or their financial or social circumstances, and they must receive close attention.

Research conducted in developing countries, often financed by Western countries, raises specific ethical issues in that regard.

BIOETHICS

Bioethics is concerned with the problems raised for human beings by advances in biology and medicine. In essence, bioethics is a multidisciplinary and pluralist reflection on the problems facing all citizens. It must also take account of the fact that science and technology are in constant progress.

In research, a complex balance has to be struck between the need to take knowledge and technology forward and the protection of research participants.

LANDMARKS IN HISTORY

Discoveries

- > **1747:** James Lind, a Scottish doctor, described the effect of lemon juice in preventing scurvy, administering six different treatments to 12 affected sailors.
- > **1885:** Louis Pasteur, a French biologist, performed the first rabies vaccination on a boy who had been bitten by a rabid dog, injecting dried contaminated bone marrow.
- > **1896:** Johannes Fibiger, a Danish physiologist, made a systematic comparison of diphtheria treatments with and without serum.
- > **1918:** Adolf Bingel, a German doctor, conducted the first randomised double-blind clinical trial* to test and demonstrate the effectiveness of anti-diphtheria serum.
- > **1948:** Austin Bradford Hill, a British medical statistician, experimentally proved the effect of streptomycin in the treatment of tuberculosis, and laid the foundations of the procedure to be applied for controlled clinical trials.
- > **1959:** Leonard Cobb, an American surgeon, carried out the first controlled blind clinical trial of the effectiveness of a surgical operation.

Adopted texts

- > **1945-46:** The first of the Nuremberg trials, "The Doctors' Trial", tried 20 doctors and three Nazi officials for their implication, during the Second World War, in human experimentation infringing fundamental ethical principles.
- > **1947:** Drafting of the Nuremberg Code which lays down the ethical principles to be observed in all research on human beings.
- > **1964:** The Helsinki Declaration, drawn up by the World Medical Assembly, defined the 12 ethical principles applying to biomedical research.
- > **1981:** The Manila Declaration, drawn up by the World Health Organization and the Council for International Organizations of Medical Sciences, issued guidelines on the conduct of clinical studies in developing countries.
- > **1997:** The Convention on Human Rights and Biomedicine (Oviedo Convention), drawn up by the Council of Europe, laid down the principles for the protection of human rights with regard to the application of biology and medicine.
- > **2001:** Directive 2001/20/EC, relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, was adopted (European Union).
- > **2005:** An additional protocol to the Oviedo Convention concerning biomedical research supplemented the provisions of the Convention, specifying the ethical principles which apply to research on human beings.



BIOMEDICAL RESEARCH, A TOPICAL ISSUE

Life expectancy

Worldwide, today people live for 65 years on average, compared to only 25 years a century or two ago.

The average lifespan ranges from 45 years in Southern Africa to 79 years in Western Europe.

Conception of a drug

The development of a new drug takes 10-12 years on average, and perfecting a new molecule represents an average investment of 500-800 million euros.

Economics of drugs

In 2003 world consumption of drugs was worth 492 billion dollars, 88% relating to North America, Europe and Japan.

1450 new drugs were marketed between 1972 and 1997, but only 13 were for tropical diseases.

Clinical trials

Clinical trials represent nearly a third of the cost of developing a drug.

An estimated 100 000 clinical trials are carried out annually around the world, 10% of them in developing countries. Clinical trials in Africa cost up to five times less than in the developed countries.

Wrongful practices

From 1932 to 1972, the US public health service carried out a study to observe the natural evolution of syphilis in 400 infected black men without their receiving any treatment.

An accident

In March 2006, the clinical trial of TGN 1412, a drug for treating rheumatoid polyarthritis, multiple sclerosis and leukemia among other complaints, ended dramatically when six of the eight participants, in good health at the start of the trial, were admitted to hospital in a serious condition; the other two had been given a placebo.

2

Biomedical research on human beings

Scientific data

THE HUMAN BEING - A COMPLEX RESEARCH SUBJECT

The human being are very complex as subjects of research. Their physiological* mechanisms are by no means all known and understood, and moreover often interact with environmental factors according to processes ill-defined as yet. Besides, physiological and psychological reactions can vary greatly between individuals.

Thus it is difficult to establish a model for studying the human being. For better knowledge of, say, a disease or the effect of a drug, trials have to be conducted on a significant number of persons allowing scientifically valid and representative conclusions to be drawn.

SCIENTIFIC METHODS OF INVESTIGATION

Biomedical research is based on rigorous scientific methods.

Accordingly, in clinical trials* two groups of volunteers are subjected, under identical conditions, to two different treatments, and the effects of these are monitored with the same measuring instruments. Three methodologies may be employed and combined:

- A controlled trial involves comparing the reaction of the group of subjects under the experimental treatment to that of the "control" group which receives a conventional treatment or a placebo*.
- A randomised trial involves allocating the subjects at random to the two groups.
- Blind trials keep the subjects uninformed as to whether they are receiving the experimental treatment or the control treatment. In a double blind situation, the staff conducting the trial are as ignorant as its subjects about who receives the control treatment and who is under the experimental treatment.

THE FOUR PHASES OF A CLINICAL DRUG TRIAL

A clinical trial determines the effects of a drug according to a four-phase protocol:

- Phase 1 studies the toxicity and pharmacological properties of the new drug. The trials are generally carried out with healthy participants.
- Phase 2 evaluates the effectiveness of the drug and its safety for patients.
- Phase 3 aims to demonstrate or confirm the benefit of the drug compared to existing treatments. Studies on large populations, at different stages of the disease or in association with another drug, complement the information on the proper use of the tested drug.
- Phase 4 is carried out once the drug has been approved. It makes it possible to refine its dosage, to examine its toxicity and its long-term efficacy, to test new interactions with other drugs, etc.



THE VARIOUS STEPS IN BIOMEDICAL RESEARCH INVOLVING INTERVENTION* ON A HUMAN BEING

1. Conception of a biomedical research project

Working from the hypotheses which they have laid down, the researchers define a precise protocol to verify them. The protocol specifies the general conditions under which the research is to proceed, its various stages, and the scientific methods chosen. These elements also determine the criteria for recruiting the participants, the funding requirements, etc.



ETHICS COMMITTEE



2. Submitting the project to an ethics committee

The research project is submitted to an ethics committee*. If the research is carried out in more than one country, this procedure must be followed in each. The committee satisfies itself as to the ethical acceptability of the research conditions. Permission to proceed with the research is granted by a competent authority which takes account of the ethics committee's opinion.

3. Recruiting the participants

Potential research participants receive information on the project. In particular, they are informed of its objective, sequence and planned interventions, and of its risks and expected benefits. The arrangements made to ensure just compensation in the event of damage are made clear. The origin of the funding for the research is announced. On the basis of this information, the persons concerned are expected to be able to decide in a free and informed manner whether or not to participate in the project. If they accept, they can subsequently withdraw their consent at any time.



4. Experimentation phase

The researchers apply the protocol establishing the sequence of the research. The persons taking part must be informed of any new elements emerging in the course of the project. Once the experimentation phase is completed, the results are analysed with a view to publication.

3

Biomedical research on human beings

Key points

FUNDAMENTAL PRINCIPLES

Primacy of the human being

"The interests and welfare of the human being participating in research shall prevail over the sole interest of society or science" (Article 3 of the Additional Protocol).

Research shall be carried out freely, subject to the respect of the dignity and identity of the human being. Respect for everyone's integrity and other fundamental rights and freedoms shall be guaranteed (Article 4 of the Additional Protocol).

Absence of alternatives

"Research on human beings may only be undertaken if there is no alternative of comparable effectiveness" (Article 5 of the Additional Protocol).

Risks and benefits

"Research shall not involve risks and burdens to the human being disproportionate to its potential benefits" (Article 6 of the Additional Protocol).

Ethical acceptability

"Every research project shall be submitted for independent examination of its ethical acceptability to an ethics committee. Such projects shall be submitted to independent examination in each state in which any research activity is to take place" (Article 9 of the Additional Protocol).

The purpose of this examination is to protect the dignity, rights, safety and well-being of potential research participants.

Scientific quality of the research

"Any research must be scientifically justified, meet generally accepted criteria of scientific quality and be carried out under the supervision of an appropriately qualified researcher" (Article 8 of the Additional Protocol).

Protection of private life and confidentiality

"Respect for the private life of research participants and confidentiality regarding the data collected concerning them must be guaranteed" (Article 25 of the Additional Protocol).

Legal references

Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Council of Europe (April 1997)

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, Council of Europe (January 2005)

INDEPENDENCE OF THE ETHICS COMMITTEE AND ITS MEMBERS

The ethics committee examining the research project shall not be subject to undue external influences. Its members shall declare any conflict of interest relating to the research project put to them. One example is a link, whether or not direct, with the laboratory submitting the research project. Here, the member concerned shall not participate in the examination of the project in question (Article 10 of the Additional Protocol).



FREE AND INFORMED CONSENT

Prior information

The person shall be given full information on the procedure, the description of the planned interventions and their implications, in comprehensible language, before giving or refusing consent (Article 13 of the Additional Protocol).

Consent is essential

No research on a person may be conducted without the informed, free, express, specific and documented consent of the person (Article 14 of the Additional Protocol).

Such consent may be freely withdrawn by the person at any phase of the research.

Absence of pressure

The compensation that the persons may be offered shall not be an incentive to participate in research (Article 12 of the Additional Protocol).

Where patients refuse to participate in research, they must not be penalised in their access to care (Article 14 of the Additional Protocol).



PROTECTION OF PERSONS WITHOUT THE CAPACITY TO CONSENT

Persons regarded by law as lacking the capacity to consent, such as minors or certain adults suffering from a mental disorder, benefit from additional protective measures.

Research cannot be conducted on these persons unless it is of direct benefit to their health. If not,

and in exceptional circumstances only, it may be permitted on the specific condition that it eventually benefits persons with the same disease or disorder and involves only slight risk and burden for the participants (Article 15 of the Additional Protocol).

PARTICIPANTS' SAFETY

Researchers take all necessary steps to ensure participants' safety and minimise the risk and burden

which they might undergo during the research (Article 21 of the Additional Protocol).



THE PLACEBO QUESTION

The fact of participating in research is not to delay, nor deprive patients of, treatments necessary for their health. The use of placebo* is permissible only where there is no treatment of proven effectiveness,

or where withdrawal (or withholding) of treatment does not entail an unacceptable risk or burden for the patients participating in research (Article 23 of the Additional Protocol).

THE SPECIFIC PROBLEMS LINKED WITH BIOMEDICAL RESEARCH IN DEVELOPING COUNTRIES

The fundamental rights of the persons participating in biomedical research must be secured irrespective of their socio-economic circumstances.

Research carried out in developing countries raises specific ethical issues in this respect.

Is such research, whose funding often originates from other countries, consistent with the health needs and priorities of the country where the trials are staged?

Are the same rules to be applied everywhere, without considering the local cultures and the systems, values and beliefs of the society in question?

How are the persons concerned to be informed, in a genuinely suitable manner, about the conduct of the research and its inherent risks, given the possible wide variations in knowledge, habits and cultural references?

In countries where the economic and health situation is often difficult, is there not a likelihood of any compensation to volunteers, or access to care during the research, acting as means of coercion for recruitment of participants?

Should the care given to participants not be continued once the research is completed? For how long? Should it be restricted to participants alone?

4

Biomedical research on human beings

Concrete situations

CASE No. 1

Julian is a history student. To supplement his income, he volunteers for a clinical trial* in phase 1. The girl living with him is anxious, having heard of a recent trial that turned out very badly: the subjects lapsed into a coma soon after the molecule being tested was administered to them. Julian is in perfect health, so why should he run such a risk? For him, the story told by his girlfriend is an isolated example. Clinical trials are strictly controlled; risks of accident are low.



QUESTIONS

- What might be Julian's motives for accepting the burdens and risks of a trial?
- The payment which he will receive is compensatory, and cannot be large enough to make him accept risks indiscriminately. Some people are admittedly more prone to financial pressure, so how are they to be protected?
- Which other types of pressure are to be feared? Which persons are the most vulnerable?

CASE No. 2

Mary has just learned that she is suffering from skin cancer at the age of eighteen. Treatments exist, but are of very limited effectiveness. Her doctor suggests that she take part in a clinical trial to test a new drug which has yielded very interesting results in the laboratory. The use of a placebo* is foreseen. Mary will have no way of knowing whether or not she receives the experimental treatment. She is outraged and does not understand why she is not immediately given the benefit of this treatment that might perhaps cure her.

QUESTIONS

- Can Mary run the risk of having treatment not all of whose effects are known? What does this risk amount to by comparison with the risk of her cancerous condition?
- Is it acceptable to resort to a placebo in the case of this research?

CASE No. 3

Scott, son of Laura and Simon, suffers from muscular dystrophy. This neuromuscular disease, incurable at the present time, causes degeneration of the muscles. At 8 years of age, Scott can no longer walk but gets about in a wheelchair. The doctor attending him asks his parents whether Scott can take part in a research project on muscular dystrophy. This is unlikely to benefit his health but will allow the processes of the disease to be better understood. Laura and Simon hesitate.

QUESTIONS

- Can Laura and Simon commit themselves on Scott's behalf? Can they decide to impose the burdens of research on their child and subject him to its risks?
- Can they agree to let Scott participate in a research project when its results will be of no direct benefit to him?

CASE No. 4

A treatment for meningitis is tried out in Nigeria during an epidemic. The scientists in charge of the study inform the inhabitants of the village concerned about the aim, the stages and the risks of the research. They want to obtain everyone's consent before embarking on the trials, but the villagers defer to the head of the community for their acceptance or refusal to participate. So, the latter has to give overall consent for all participants, and is also to receive the sum of the compensation granted for the burdens linked with the research. Before agreeing, he wants to know whether his village will be able to continue receiving drugs to combat meningitis once the trial is completed.

QUESTIONS

- Can scientists accept collective consent to participate in research, when the risks incurred are individual? Conversely, can this community's values and organisation be transgressed so as to obtain individual consent?
- Considering the compensation and the access to treatment for patients during the epidemic, is the headman really at liberty to refuse the scientists' offer?
- Can therapeutic trials be undertaken on a population which we know will not have the human, material and financial resources to secure the treatment thereafter?



5

Biomedical research on human beings Find out more

... ABOUT QUESTIONS RAISED BY BIOMEDICAL RESEARCH

- Convention on Human Rights and Biomedicine (Oviedo Convention), Council of Europe, 1997
<http://conventions.coe.int/Treaty/EN/Treaties/Html/164.htm>
- Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, Council of Europe, 2005
<http://conventions.coe.int/Treaty/EN/Treaties/Html/195.htm>
- Bioethics at the Council of Europe
www.coe.int/bioethics
- Opinions of the French National Council on Ethics (Nos. 2; 7; 11; 34; 38; 58; 73)
www.ccne-ethique.fr
- Book: *Ethical Eye - Biomedical Research*, Council of Europe Publishing, 2004



... ABOUT QUESTIONS RAISED BY BIOMEDICAL RESEARCH IN DEVELOPING COUNTRIES

- Ethical aspects of clinical research in developing countries, Opinion No. 17 of the European Group on Ethics in Science and New Technologies to the European Commission, 2003
http://ec.europa.eu/european_group_ethics/avis/index_en.htm
- The Ethics of Research Related to Healthcare in Developing Countries, report of the Nuffield Council on Bioethics, 2002
www.nuffieldbioethics.org

GLOSSARY

Biomedical research: all research activities in the sphere of human health, ranging from study of molecular and cellular mechanisms to diagnostic, therapeutic, preventive and epidemiological studies.

Clinical trial: experiment intended to determine the effect of a drug, surgical technique, diagnostic test, etc. with a view to being put on the market.

Dosage: indication of the quantity of a drug to administer to a patient.

Ethics committee (for biomedical research): independent multidisciplinary group responsible for examining the ethical acceptability of research projects involving interventions on human beings. It is composed of persons appointed for their competence and representativeness, belonging to the scientific and medical fields as well as other sectors (philosophers, theologians, lawyers, other members of civil society, etc.).

Intervention: any act, whether medical or related to health or well-being, performed for purposes of therapy or scientific research (drug treatment, diagnostic tests, surgical operations, preventive measures ...).

Pharmacological properties: properties of drugs

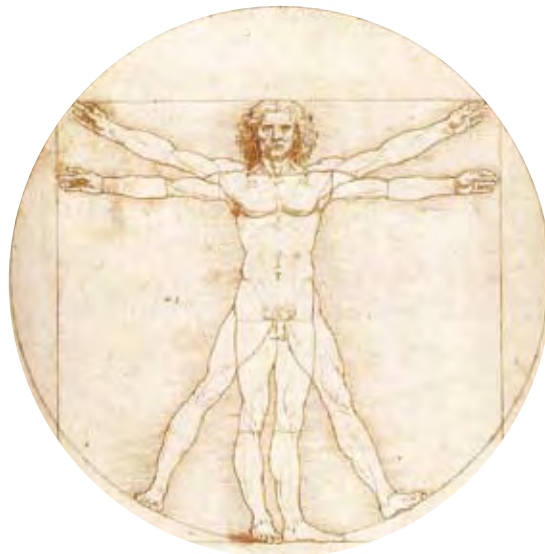
inside an organism (transformation in the organism, action on a healthy organism, activity, etc.).

Physiological: relating to the functions and properties of living organs and tissues.

Placebo: a product, pharmacologically inactive but with a presentation identical to an active product. In a research context, the substitution of a drug by a placebo is intended to identify only the effects of the experimental treatment by comparison.

Protocol: study plan specific to a given biomedical research project. It is meticulously prepared not only to guarantee the protection of the participants but also to provide answers to the questions raised by the research. The protocol states the aim of the research, the characteristics and number of those taking part in the trials, the intended interventions and procedures, whether or not a placebo will be used, the expected results and benefits, and the duration of the research.

Toxicity: measurement of the capacity of a substance to have adverse effects on the system, tissues or cells.



1

Cloning Context



A TECHNIQUE WHICH COULD, ONE DAY, BECOME REALITY...

In recent years, developments in biology have paved the way for cloning by nuclear transfer*.

For ten years now, it has been possible to clone certain mammals using this method and as a result cloned cows, sheep and horses have been born.

If it proved possible to create a cloned human embryo, two distinct applications could become feasible:

- “reproductive cloning”: the birth of a baby genetically identical to another human being;
- “scientific cloning”: whereby embryonic stem cells*, having predetermined genetic characteristics, could be obtained from the cloned embryo. The possibility of obtaining such cells with precise genetic characteristics could be of significant interest for research. In addition, in the much longer term, it is thought that these could be used for treatment purposes.

... BUT ONE WHICH RAISES MANY QUESTIONS

To date, it has not been possible to create human embryos by cloning. However, this technique could one day be perfected. Accordingly, we need to address now the ethical questions raised by human cloning.

The creation of a human being genetically identical to another human being would turn upside down the concept of human identity, which is based on the uniqueness of the genetic characteristics of each individual. This uniqueness is a result of the naturally occurring recombination of the genetic make-up passed on by the spermatozoon* and the oocyte*. This random process does not take place in cloning by nuclear transfer, and the human being that would be created from this process would have the same genetic characteristics as the being of which it was a clone. For many people, such genetic predetermination of a human being by a third party equates to an act of instrumentalisation and poses a threat to human dignity.

Bioethics

Bioethics looks at the problems for human beings raised by advances in biology and medicine.

By its very nature, it involves a multi-disciplinary and pluralistic approach to issues of relevance to all citizens. It must also take account of the evolving nature of science and technology.

AN INTERNATIONAL BAN

In view of these very serious implications, the Council of Europe and most countries in the world have outlawed human cloning: any intervention seeking to create a human being genetically identical to another human being, whether living or dead, is prohibited (Additional Protocol to the Convention on Human Rights and Biomedicine, on the Prohibition of Cloning Human Beings).

Reproductive cloning of a human being is not allowed, but scientific cloning to obtain genetically determined embryonic stem cells is possible in some countries (eg the United Kingdom and Belgium).

CLONING TIME-LINE

- > **In 1914** Hans Spemann, a German embryologist and winner of the Nobel prize in physiology, successfully carried out the first nuclear transfer on Triton cells. This technique is the basis for cloning, and led to the creation of Dolly the sheep eighty-two years later. Spemann subsequently raised the possibility of transplanting cell nuclei into oocytes*.
- > **In 1952** Robert Briggs and Thomas King, American biologists, carried out the first transfer of a nucleus from embryonic cells to an oocyte whose own nucleus had been removed.
- > **In 1962** John Gurdon, a British biologist, announced that he had cloned a toad by nuclear transfer using an adult intestine cell. A number of tadpoles developed.
- > **In 1996** Ian Wilmut, a British biologist, created the first cloned mammal by nuclear transfer: Dolly the sheep was cloned using the nucleus of an adult cell* (a cell taken from the mammary gland).
- > **In 1997**: – Ian Wilmut created Polly, a cloned transgenic sheep, whose milk contains a human protein* that can be used for treatment purposes.
– Don Wolf, an American biologist, created the first cloned primate by transferring the nucleus of an embryonic cell.
- > **In 1998**, for the first time, human stem cells* from non-cloned embryos were cultured.
- > **In 2001** the American company Advanced Cell Technology announced that it had obtained a human embryo by nuclear transfer. However, the embryo ceased developing at the stage of 6 cells.
- > **2005**: Woo-suk Hwang, a South-Korean biologist, announced the first successful cloning of human embryos, from which eleven stem cell lines had been extracted. These results proved to be faked.



Adopted texts:

- > **1998**: Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings.
- > **2005**: United Nations Declaration on Human Cloning.

CLONING, A TOPICAL ISSUE

A few figures

Cloning of animals

By 2007, 16 species of mammals had been cloned by nuclear transfer of adult cells (wolf, mountain sheep, cat, dog, lamb, mule, buffalo, mouse, goat, rabbit, horse, bison, cow, pig, rat, ferret).

By late 2005, some 1 500 cloned cattle had been recorded in the world, including 72 in France.

February 2005 saw the birth of Pieraz-Cryozootech-Stallion, the first clone of a competition horse, created to conserve the genetic material of the champion, Pieraz, castrated before being able to reproduce.

In 1997, 6 cloned and genetically modified sheep were created to produce milk containing a blood coagulation factor essential for people suffering from haemophilia. Since then, goats, sheep, cows and rabbits have been created to produce milk containing molecules of pharmaceutical interest.

Limited results

For animals bred in farms, less than 5% of cloned embryos culminate in a birth.

60% of cloned calves born alive reach adult age. For lambs, the figure is just 30-40%.

2

Cloning Scientific data

HUMAN REPRODUCTION

Human reproduction is the result of the fusion of two reproductive cells, the woman’s oocyte* and the man’s spermatozoon*. The fertilised oocyte divides to become two cells, then four, eight, etc which form the embryo.

Each of the two reproductive cells provides half of the genetic make-up of an embryo which has its own unique genetic identity.

TWO CLONING TECHNIQUES...

Cloning is the asexual reproduction*, from one cell or organism, of biological entities which are genetically identical to that cell or organism.

There are two techniques that can be used to obtain clones in mammals: the division of embryos or nuclear transfer*, the latter having been used only on certain mammals.

- The division of embryos involves separating into two equal sets the cells formed during the very first divisions of the fertilised oocyte. Each single set carries the same genetic information and can subsequently develop into an embryo.
- Nuclear transfer entails introducing the nucleus* of an adult cell* into an oocyte whose own nucleus has been removed. This cell will then have the nuclear genome* of the adult donor cell. It may subsequently develop into an embryo.

Cloning

Cloning means making an identical genetic reproduction. This can apply to cells or whole organisms. Sometimes, it occurs naturally (cell proliferation, twins, etc) but it can also be technically prompted by human intervention (division of embryos, nuclear transfer, etc).

... BUT WITH MIXED RESULTS

It has never yet been possible to form human embryos by nuclear transfer.

Researchers have managed to clone certain mammals, such as rabbits, cows, sheep, cats and horses. But even in species for which these techniques work, results are very mixed.

Success rates are very low since only 5% of cloned embryos result in the birth of an animal. Dolly was the only survivor from 277 attempts. In addition, only 60% of cloned calves reach adult age, and only 30-40% of lambs. Cloned animals often have immune system* or heart-related problems.

Lastly, it should be noted that the clone is not physically identical to the original. Even with identical genetic characteristics, the gene expression may vary from one individual to another (for example, the location of blemishes, birthmarks etc).

THE PRINCIPLE OF CLONING BY NUCLEAR TRANSFER

Nuclear transfer was the technique used to create Dolly the sheep. Two types of cells are required to carry out this technique: an adult somatic cell* and an oocyte.

1. Cell removal

Adult cell

A number of cells are removed from the sheep: in Dolly's case, these were cells from the mammary gland.



Oocyte

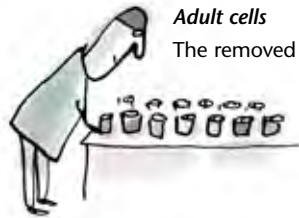
The oocyte is obtained from another sheep given hormonal treatment to stimulate its ovaries. Once the cell has matured, it is removed from the ovary.



2. Cell preparation

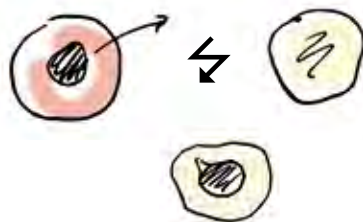
Adult cells

The removed cells are then cultured.



Oocyte

The oocyte is enucleated – in other words, its nucleus, containing the genetic information, is removed by aspiration.



3. Cell fusion

The enucleated oocyte and the adult cell are then placed in a fusion chamber and fused via electrical stimulation: the nucleus of the adult cell penetrates the enucleated oocyte. The resulting cell contains the same genetic information as the adult cell.

APPLICATIONS

The cell obtained following the nuclear transfer divides in two, then four, eight, etc. Five to seven days later, it has become a blastocyst* capable of implanting itself in the wall of the uterus. There are then, in theory, two conceivable applications: reproductive cloning and scientific cloning.

- Reproductive cloning entails the transfer of the blastocyst into the uterus. This has been successfully carried out in several species of mammals. International agreements prohibit its being carried out in humans.
- Scientific cloning involves removing cells from the blastocyst, culturing them and obtaining embryonic stem cell* lines which are genetically identical to the donor cells. The embryonic stem cells¹ are capable of developing into any type of cell (liver, heart, etc). For research purposes, embryonic stem cells obtained by cloning could make it possible to monitor the development of cells having specific genetic characteristics, and therefore give new insight into genetic diseases. In the medical field, it has been suggested that these stem cells could be used to produce healthy tissue which would not be rejected by the patient. It should then be possible to carry out transplants to treat degenerative and metabolic diseases and those involving cell necrosis, which are incurable at present.

1. Embryonic stem cells may also be obtained from non-cloned embryos, such as surplus embryos derived from medically assisted procreation. The genetic characteristics will be known in advance only in the case of stem cells obtained from a cloned embryo.



3

Cloning Key points

FUNDAMENTAL PRINCIPLES

The dignity and identity of human beings must be protected (Article 1 of the Convention).

Everyone, without discrimination, must be guaranteed respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine (Article 1 of the Convention).

“The interests and welfare of the human being shall prevail over the sole interest of society or science” (Article 2 of the Convention).

Legal references

“Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine”, Council of Europe (April 1997)

“Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings”, Council of Europe (January 1998), the only international legally binding text.

A BAN ON CLONING

“Any intervention seeking to create a human being genetically identical to another human being, whether living or dead, is prohibited” (Article 1 of the Additional Protocol).

What would be the identity of a clone, a genetic copy of another human being?

Many people believe that naturally occurring genetic recombination, which ensures the essentially random nature of genetic make-up, creates more freedom for the human being than a genetic make-up predetermined by another person.

Other ethical reasons for banning the cloning of human beings are based primarily on respect for human dignity. Deliberately creating genetically identical human beings would equate to an act of instrumentalisation posing a threat to human dignity.



COLLECTING OVOCYTES

While removing adult cells is a straightforward procedure, retrieval of oocytes is more restrictive and involves fairly intensive treatment for women who undergo it.

Cloning by nuclear transfer requires numerous oocytes given the poor success rate of the procedure. If human cloning were to become feasible, would it be possible to obtain the required number of oocytes under ethically acceptable conditions?

“The human body and its parts shall not, as such, give rise to financial gain” (Article 21 of the Convention).

THE FATE OF THE EMBRYO

Is it possible to create an embryo other than for purposes of procreation without this being regarded as an act of instrumentalisation?

“The creation of human embryos for research purposes is prohibited” (Article 18 of the Convention).

DEFINITION OF THE EMBRYO

There is no agreement at international level on the definition of an embryo. While there is consensus on considering that the result of the fusion of a spermatozoon and an oocyte is an embryo, the same cannot be said for what is obtained from nuclear transfer.

FUTURE PROSPECTS

Access to health care of appropriate quality must be equitable for all (Article 3 of the Convention).

It is conceivable that cloning techniques could ultimately offer an individualised solution to each patient in order to treat a disease or defective organ. Using embryonic stem cells obtained by cloning a patient's cells, it could be possible to develop tissues which would not be rejected by the patient. Would this individual approach (which would be very costly) be accessible to everyone?

DIFFERENT APPROACHES IN EUROPE

Human cloning, for whatever purpose, is forbidden by law in some countries such as Germany and Austria.

Other countries, such as the United Kingdom, Belgium and Sweden, authorise scientific cloning.



4

Clonage Concrete situations

CASE NO. 1

Peter and Mary have just lost John, their only child in a road accident. They cannot get over this tragedy and would like their son to be still alive. They ask a doctor if it would be possible to clone John. The doctor explains that human cloning is impossible and, moreover, forbidden. The doctor spells out the implications of such a step.

QUESTIONS

- If it were possible to clone John, would his clone really make the young man live again?
- What would be the child's identity? Would Peter and Mary consider him as being John or as an entirely different person?
- What psychological consequences could there be for this child conceived to replace a dead person?



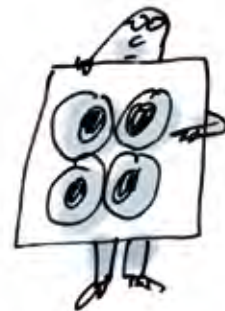
CASE No. 2

Stephanie and Sebastian would like to have a baby. Medical tests have shown that Sebastian is sterile. Although they know that they cannot undertake such a procedure, they imagine the potential outcome of transferring a nucleus from one of Sebastian's cells to one of Stephanie's oocytes whose own nucleus had been removed. This would result in a child containing all of his father's genes, a clone of Sebastian.

QUESTIONS

- How would Sebastian view this child? As his son or another, younger version of himself? How would Stephanie view the child? As her son, even though he did not carry any of her genes, or a double of her partner?
- How would the child view Sebastian? As his father or as a reflection of what he would become when he got older?
- What freedom would a child have if his genetic identity were known in advance without

the random dimension of naturally occurring genetic recombination?



CASE No. 3

Leo has a serious kidney problem. His kidneys do not function as they are supposed to. A friend tells him about embryonic stem cells and their unbelievable properties. He says that using these cells it is possible to create all types of body cells. Using nuclear transfer, it would be possible to obtain embryonic stem cells having Leo's genetic characteristics, which could produce kidney cells that his body would not reject. These kidney cells could be transplanted and Leo could be cured. Leo starts dreaming about cloning, even though he knows that it has never been successfully carried out on humans and that human cloning is banned. In theory, however, it is quite simple: in order to obtain embryonic stem cells, the nucleus of one of Leo's cells would need to be transferred to a woman's oocyte, from which its own nucleus had been removed.

QUESTIONS

- How could one obtain oocytes to perform this cloning?
- The cell formed by nuclear transfer is not the result of the fusion of an oocyte and a spermatozoon and yet, once it was transferred to a uterus, it could, in theory, develop into a foetus. Can one consider that the result of nuclear transfer is an embryo? Depending on the answer, what are the implications for the uses that could be made of this cell?
- What difference is there between this form of cloning (termed "scientific") and "reproductive" cloning?
- Is it acceptable to carry out cloning for scientific purposes?



5

Cloning

Further information

... ABOUT QUESTIONS RAISED BY HUMAN CLONING

- Convention on Human Rights and Biomedicine (Oviedo convention), Council of Europe, 1997
<http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm>
- Additional Protocol to the Convention on Human Rights and Biomedicine, on the Prohibition of Cloning Human Beings, Council of Europe, 1998
<http://conventions.coe.int/Treaty/en/Treaties/Html/168.htm>
- Bioethics at the Council of Europe
www.coe.int/bioethics
- United Nations Declaration on Human Cloning
<http://www.pre.ethics.gc.ca/english/pdf/UN%20Nations%20Resolution%202005.pdf>
- Human Cloning, Ethical Issues, United Nations Educational, Scientific and Cultural Organization, 2005
<http://unesdoc.unesco.org/images/0013/001359/135928e.pdf>
- Cloning for reproductive purposes and cloning for the purposes of biomedical research, opinion of the German National Ethics Council, 2004
www.ethikrat.org
- Human cloning and human dignity: an ethical inquiry, report of the American Council on bioethics, 2002
www.bioethics.gov "cloning" section
- Ethical aspects of cloning techniques, opinion No. 9 of the European Group on Ethics in Science and New Technologies to the European Commission, 1997
http://ec.europa.eu/european_group_ethics/avis/index_en.htm
- Reproductive human cloning, opinion No. 10 of the Belgian Advisory Committee on Bioethics, 1999
https://portal.health.fgov.be/portal/page?_pageid=56,8546420&_dad=portal&_schema=PORTAL
- Reply to the President of the French Republic on the subject of reproductive cloning, opinion No. 54 of the French National Council on Ethics, 1997
www.ccne-ethique.fr
- Cloning, statement from the Danish Council of Ethics
www.etiskraad.dk
- Ethical eye: cloning, book, Council of Europe Publishing, 2002
- Reproductive cloning, topic of the UK BioCenter
www.bioethics.ac.uk



IN LITERACY

- *Brave New World*, Aldous Huxley, 1932: a society in the future uses genetics and cloning to condition and control individuals.
- *The Boys from Brazil*, Ira Levin, 1976: a number of fanatical Nazis give birth to little Hitlers thanks to cells taken from the deceased dictator.

GLOSSARY

Adult or somatic cells: any cell, with the exception of the germline (sexual) cells (oocytes and spermatozoa), in humans after birth.

Asexual reproduction: reproduction without the involvement of the male and female reproductive cells.

Blastocyst: the development stage of the fertilised oocyte normally reached between the 5th and 7th day after fertilisation, and when the process of implantation in the uterus begins. This is the stage when embryonic stem cells are removed from an area of the blastocyst called the inner cell mass.

Cloning by nuclear transfer: cloning technique where the nucleus of a cell from the individual to be copied genetically is transferred into an oocyte whose own nucleus has been removed.

DNA (the abbreviation of Deoxyribonucleic acid): a long molecule containing all the genetic information of a living being and found in virtually all cells. It looks a little like a twisted rope-ladder ("double helix"), comprising just four different types of molecules, known as nucleotides (A, T, G, C). This double helix structure is the same in all species.

Embryonic stem cells: cells obtained from an embryo at the blastocyst stage (5 to 7 days). They are able to differentiate into a wide variety of tissues. However, they cannot themselves reconstitute an embryo.

Genome: a complete set of DNA contained in a cell. The largest part of the genome is situated in the nucleus of the cell (nuclear genome). A small part is to be found in the mitochondria, small elements of the cell outside the nucleus which produce energy (mitochondrial genome).

Immune system: the organism's defence system.

Nucleus: the heart of the living cell, containing most of the cell's DNA.

Oocyte: the female reproductive cell.

Spermatozoon: the male reproductive cell.

Stem cells: cells which have the unique capacity to renew themselves and differentiate into other types of specialised cell. For example, haematopoietic stem cells are those which give rise to blood cells. There are three main categories of stem cells: embryonic, foetal and adult. Each category is distinguished by its capacity for differentiating into different types of specialised cells: embryonic stem cells can produce virtually all tissue types (pluripotent); this capacity is reduced for foetal and adult stem cells, which can produce only a limited number (multipotent or unipotent).

Surplus embryos: embryos which are no longer part of any parental project; they have been created by in vitro fertilisation for procreation purposes, but have not been transferred and are conserved in liquid nitrogen at - 196°C.



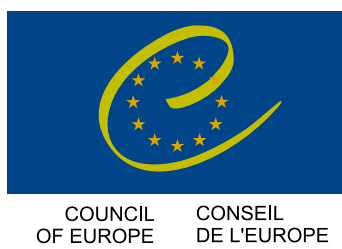
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