Medical-ethical guidelines for the transplantation of human foetal tissue

Preamble

Doctors and researchers expect the transplantation of human foetal tissue[1] to provide a more effective treatment of certain serious diseases. The advantages of foetal cells are considered to be on the one hand their high growth potential and on the other their low antigenicity and the consequently reduced risk of immunological rejection. These guidelines apply exclusively to the transplantation of foetal tissues within the framework of defined research projects.

The therapeutic trials carried out until now have concerned Parkinson's disease (transplantation of foetal dopaminergic neurones), hereditary metabolic disorders (transplantation of medullary or hepatic embryonic cells), juvenile diabetes mellitus (transplantation of pancreatic islet cells) and retinitis pigmentosa (transplantation of foetal retinal cells). In accordance with the provisions of Art. 24^{novies} of the Federal Constitution, the use of foetal germinal cells cannot be considered in Switzerland.

Termination of pregnancy is generally undertaken in the first trimester; therefore ample foetal tissue would be available from this stage of pregnancy, provided the transplantation is carried out within the framework of a therapeutic trial. Should the need arise for the routine use of such tissue in the future, these guidelines would have to be revised.

The foetal tissue used for the purpose of transplantation is obtained in the course of induced termination of pregnancy. This fact has given rise to serious discussion of the ethical and political aspects: among other things, it is feared that a therapeutic need for foetal tissue would lead to additional interventions or that it would give the termination of pregnancy a social acceptance that it does not enjoy today. A woman's decision to have an abortion should therefore be influenced as little as possible by her knowledge regarding the possible subsequent use of the foetal tissue. In view of this particular concern, the woman's consent to the later use of such tissue should be obtained only after the decision to terminate the pregnancy has been made.

---

[1] Applies to tissue during the embryonic and foetal stages. See also Chapter 3, "Commentary", first paragraph.

Transparency concerning the procedure is essential, i.e. all the necessary relations and contacts between the medical teams involved in the removal and transplantation of the foetal tissue must follow a clearly defined procedure. A Coordinating Office will be set up, which will create the contacts between the medical teams involved and will keep an appropriate protocol. This Coordinating Office will be under the supervision of the Central Ethical Committee of the SAMS.

In view of the ethical pluralism that exists in our society, the new therapeutic possibility must be made available, while at the same time the opinions of those who reject it for reasons of conscience must be respected.

1. ETHICAL STANDARDS

1.1 Respect for the foetus; exclusion of any commercial use

Because of its human entity, the foetus is entitled to appropriate respect. The foetus, its organs and its cells, as such, must not be the subject of any kind of commercial transaction. In particular, any reward to the woman for the donation of tissue must be strictly refused and any agreement on direct or indirect advantages in this connection between the medical teams that remove and transplant foetal tissue is forbidden.

1.2 Indications

A transplantation of foetal tissue may be carried out only if it is medically and scientifically indicated.

1.3 Declaration of consent by the woman

When a woman decides on termination of a pregnancy, this does not mean that she ipso facto loses the possibility of deciding on the subsequent fate of the foetus. Tissues and cells from the foetus may therefore not be used with-out her written consent. However, the question of the possible scientific or therapeutic use of foetal tissue must be put to a woman only if her decision to undergo termination of a pregnancy is already clearly established. Her consent to both the termination of the pregnancy and to the planned use of the foetal tissue must be obtained in writing after appropriate personal discussion. The woman must also give her consent to diagnostic investigations carried out not in the interest of her own health, but for the protection of the health of the recipient of the transplant (e.g. detection of possible infectious pathogens).

1.4 Prohibition of the planned donation of foetal tissue

The termination of a pregnancy performed for the purpose of providing a third party with transplantable foetal tissue is not permitted. A doctor who knowingly takes part in such an arrangement would be committing a serious violation of the medical-ethical standards. The woman cannot nominate a specific recipient for the tissue obtained from her foetus and does not have the right to information concerning the identity of the recipient.

1.5 Decision on the timing and the procedure for the termination of the pregnancy

The choice of the timing of the termination of a pregnancy must not be influenced by consideration of the subsequent use of the foetal tissue. In the choice of the timing and the method used for termination of the pregnancy, minor adjustments in view of the purpose for which the foetal tissue is to be used are permitted, provided they do not prejudice the interests of the woman.

1.6 Declaration of Consent and obligations of the recipient

The recipient of the foetal tissue must be informed, in an appropriate manner, of the origin of the tissue that is to be transplanted. He[2] must give written consent. The recipient may not be given the possibility to contact the woman concerned in his particular case and may not offer any financial reward by way of inducement or as a form of pressure.

1.7 Approval by an ethical committee

Any transplantation of foetal tissue must take place within the framework of a research project that has been checked and approved by the responsible Ethical Committee.

1.8 Reservation concerning a decision of conscience for medical persons

The medical personnel involved in transplantations must be informed concerning the nature of the tissue and the research project. Each person has the right to refuse to participate, without this being to his disadvantage in any way.

1.9 Respect of privacy

From the ethical point of view, respect of privacy, both of the woman taking part in the research project with foetal tissue and of the recipient, is very important. Medical personnel who are involved in such transplantations must respect, absolutely, the anonymity of both the donor and the recipient.

2. REALISATION IN PRACTICE

2.1 Coordinating Office

In principle, the doctors involved (gynaecologists and transplant surgeons) work independently of one another. A strict separation between the two medical teams is, however, impracticable, because the transplantation of fresh tissue requires direct contact for logistic reasons. In view of the small number of transplantations of foetal tissue that are to be expected in the near future, the best solution in the meantime would seem to be a simple Coordinating Office under the direction of a medical coordinator.

2.2 Tasks of the Coordinator

The coordinator

- registers the names of medical teams that are able to obtain foetal tissue and keeps a record of the timetables of the planned interventions;

---

[2] For the sake of simplicity, the masculine form is used for both genders.

- registers the names of medical teams that plan transplantations and notes their needs;
- authorises the hand-over of the foetal tissue by the doctor who has removed it to the surgeon who is to perform the transplantation, after checking the written documentation and finding that it conforms to items 1.1 to 1.7 of these guidelines;
- is responsible for the archiving and anonymisation of all the documents; the list of the persons involved must be kept separate from the other data;
- is responsible for the safekeeping of the data.

The coordinator is provided with the necessary means to fulfil these tasks.

2.3 Supervisory authority

The Central Ethical Committee (CEC) of the SAMS monitors the activity of the coordinator and decides in the event of conflicts or points that are unclear.
The CEC assesses and authorises attempts to make a scientific evaluation of the data stored by the coordinator, which can be accessed only in anonymised form.

2.4 Agreement at the international level

The international exchange of foetal tissue is possible within the framework of cooperative research projects with teams working abroad. In this case, the ethical guidelines in force in our country are applicable, or the requirements in force in the other country if they are more restrictive. The cooperation must be restricted to countries and researchers whose standards are equivalent to those in Switzerland. The CEC and the coordinator must be in agreement with the international exchange of foetal tissue.

3. COMMENTARY

Nomenclature: In embryology, the differentiation is usually made between the embryonic phase (2nd to 10th week of pregnancy) and the foetal phase (from the start of the 11th week of pregnancy). In the literature concerning tissue transplantation that is available today, however, the term "foetal tissue" is always used. This internationally established term is, therefore, also used in these guidelines.

The transplantation of foetal tissue raises the same general questions as organ transplantation. Additional ethical questions arise, however, due to the connection with the subject of termination of pregnancy. From the medical-ethical viewpoint there is no contradiction between the rejection of termination of pregnancy for reasons of conscience and the authorisation of the use, for medical purposes, of foetal tissue that is anyway available.

Re 1.1: Tissues and cells removed from human foetuses must be treated with appropriate respect. This applies even when such tissues or cells are not intended for further use.

According to the SAMS guidelines on Organ Transplantation, any trading in human tissues and organs, and thus also any trading in foetal tissues, is forbidden.

Re 1.2: Transplantations of foetal tissue are at present performed only within the context of experimental therapeutic studies. A transplantation plan must be scientifically documented, and an accurate follow-up control and subsequent retrospective evaluation of the results must be included in the plan.
The coordinator has the task of constantly updating the list of recognised indications for the transplantation of foetal tissues and of submitting this list to the Central Ethical Committee at regular intervals. In this, he works together with medical teams competent in this field.

Re 1.3: The requirement that the woman concerned should give her consent to this procedure in full knowledge of the planned use of the foetal tissue is today self-evident ("informed consent"). This requirement of course does not exclude the doctors and nurses freely answering any questions that the woman may put to them. An under-age woman capable of giving informed consent may herself decide on the possible donation of foetal tissue. Such donations are not permitted in cases of women who are not competent to judge.
The decision to have a pregnancy terminated must be clearly separated from the subsequent use of the foetal tissue. Non-observance of this separation involves two possible dangers, whereby inducement could be made or pressure exerted: on the one hand the woman could be offered material advantages, and on the other subtle pressure of a psychological or social nature are conceivable. For example, in the sense of a utilitarian cost-benefit calculation it could be argued that the "good" (the therapeutic benefit of a transplantation) would outweigh the "bad" (the termination of the pregnancy). Considerations of this nature could confront a woman with the difficult decision of whether she should have her pregnancy terminated or whether she should continue to full term, or they could for the first time confront doctors with the moral problem of termination of pregnancy. The guidelines, however, try to avoid emotional involvement of this type as far as possible, by laying down a clear sequence for the timing of these two essential decisions.
A further burden for a woman who is prepared to take part in a research project are the requirements for protection of the recipient: in order to protect him from the possible transmission of infections, additional diagnostic tests have to be carried out on the donor which would not be necessary for the maintenance or improvement of her health. The findings of these tests could reveal the presence of unwanted conditions that would only be disturbing for the woman. Examples are certain viral infections (CMV, HCV, HIV, etc.) where, because of the limited therapeutic possibilities at present available, an early diagnosis would bring no advantages and "not knowing" would ensure years free from this worry. In order to protect the interests of both parties - the pregnant woman and the

recipient of the foetal tissue - the woman's consent for the necessary tests to be carried out must be obtained, after the interest of the recipient and the possible consequences for herself have been explained to her. The similarity to the situation of the blood donor is obvious.
This situation could change in the future, if new techniques are developed by which the microorganisms mentioned above can be reliably detected in the tissue sample itself.
It must once again be expressly emphasised that the doctor should thoroughly discuss the necessary decisions (concerning the termination of the pregnancy, the use of the foetal tissue and the additional tests) with the woman in terms which she understands and should record her decision in writing.

Re 1.4: Individual cases have been reported in which a woman became pregnant with the intention of having the pregnancy terminated in the 3rd month in order to make the foetal tissue available to her father who was suffering from Parkinson's disease. Such procedures are not permitted according to the terms of these guidelines.

Re 1.5: The medical team that undertakes the termination of the pregnancy could be induced to considerably alter the timing of the operation and the procedure, in order to improve the amount or the quality of the transplantable foetal tissue obtained. According to the conditions of these guidelines only minor adjustments are permitted, provided they are not detrimental to the woman's health.

Re 1.6: According to the conditions of the SAMS "Guidelines on Research Investigations in Humans", the recipient must confirm his consent in writing, after the aims and the risks of the project have been explained to him orally and presented in writing, in terms he can understand.
The recipient could perhaps blame a later, unfavourable development of his disease on certain properties of the transplanted material and on this account could make claims against the woman taking part in the research project. In order to exclude all conceivable legal claims in this respect, from the outset, the woman concerned must be relieved of any responsibility of this nature.
In connection with the use of foetal nerve tissue, one is sometimes confronted with the concept of a "transplantation of the personality". This idea is unrealistic, because only fragments of brain tissue or isolated cells can be transplanted, but not the character-forming properties of important connecting links between nerve cells and nerve centres.

Re 1.7: A local Ethical Committee must review each individual research project on the basis of the following documents:
- Indications (see item 3, re 1.2);
- Declaration of Consent by the woman after she has been fully informed regarding the planned use of the tissue and the additional diagnostic tests (see item 3, re 1.3);

- Description of the procedures to be followed by the two medical teams (see item 3, re 1.5);
- Informed consent of the recipient (see item 3, re 1.6);
- Instructions in the study protocol, that the project conforms to the standards applicable for experiments in humans, and in particular to the guidelines of the SAMS on this subject.

The local Ethical Committee draws up a written appraisal for the Coordinator.

Re 1.8: Similar to the refusal to assist in the termination of pregnancy for reasons of conscience, all medical persons have the right to refuse to assist in experimental therapy with foetal tissue.

Re 1.9: If the woman who is participating in the research project and the recipient are treated in the same hospital, it would be relatively easy to know their identities. All the persons involved are therefore to be reminded of their obligation to maintain professional secrecy. Especially in the case of new medical procedures, particularly strict maintenance of secrecy as far as the public domain is concerned is essential.

Re 2.1: The Coordinating Office must ensure that foetal tissue is made available only in accordance with these guidelines. It is possible that the two medical teams, the one that removes the foetal tissue and the other that carries out the transplantation, are already in contact before the planning of a transplantation, for example when they both belong to the same institution. Even in this case they must inform the Coordinator each time foetal tissue is handed over or is used for transplantation, and must submit the above mentioned documents to him so that he can check, approve and archive them.

Re 2.2: Among the various tasks of the Coordinator, particular emphasis has to be placed on the archiving of the documentation.
The long-term storage of the documentation on every transplantation of foetal tissue has three main objectives:

- The transplantation of foetal tissue must be carried out in a clear, transparent manner by doctors who are fully responsible for this procedure.
- The statistical evaluation of the results must facilitate the long-term assessment and lead to improvement in the determination of the possible indications.
- It must be possible, in well-founded cases, to trace back from the recipient of a transplant to the woman participating in the research project who provided the foetal tissue, for example if the medical team responsible for the transplantation come across new scientific facts and information that could be of importance for the health of the woman.

Approved by the Senate of the SAMS on 3.6.1998.

Prof. W. H. Hitzig, Zurich
Chairman of the Central Ethical Committee

4. LITERATURE REFERENCES

4.1 Guidelines and official texts

1. Ethical guidelines for the use of human embryonic or foetal tissue for experimental and clinical neurotransplantation and research, GJ Boer (on behalf of the Network of European CNS Transplantation and Restoration (NECTAR)) J. Neurol. *242*, 1-13, 1994.

2. Report of the Human Foetal Tissue Transplantation Research Panel. Consultants to the Advisory Committee to the Director, Bethesda, Md: National Institutes of Health; 1988: 1 & 2.

3. Review of the Guidance on the Research Use of Foetuses and Foetal Material ("Polkinghorne Report"). Her Majesty's Stationery Office (HMSO), London, 1989, Cm 762.

4. United States Congress, House of Representatives: H.R. 2507 A Bill to amend the Public Health Service Act to revise and extend the programs of the National Institutes of Health, and for other purposes (introduced by Mr. Waxman, June 3, 1991).

5. Comité consultatif national d'éthique (National consultative committee of ethics) (France): Avis sur les greffes de cellules nerveuses dans le traitement de la maladie de Parkinson (Report on neurone transplants in the treatment of Parkinson's disease). 16 October 1989.

6. Avis concernant des greffes intracérébrales de tissus mésencéphaliques d'embryons humains chez cinq malades parkinsoniens dans un but d'expérimentation thérapeutique (Report concerning intracerebral transplants of mesencephalic tissue from human embryos in five parkinsonian patients, for the purpose of therapeutic research). 13 December 1990.

4.2 Analysis and Commentaries

7. Vawter Dorothy E. et al. (eds.): The Use of Human Foetal Tissue: Scientific, Ethical and Policy Concerns. vii + 271p. + Appendices. Center for Biomedical Ethics, University of Minnesota, January 1990.

8. Childress James F.: Ethics, Public Policy and Human Fetal Tissue Transplantation Research. Kennedy Institute of Ethics Journal *1*: 93-121 (1991).

9. Gareth Jones D.: Fetal neural transplantation: placing the ethical debate within the context of society's use of human material, Bioethics *5*: 23-43 (1991).

10. Fassbender Pantaleon: Die Verwendung foetalen Gewebes in der Neurochirurgie - ein ethisches Problem? (The use of foetal tissue in neurosurgery - an ethical problem?) Ethik Med. *3*: 114-120 (1991).

11. Hoffer Barry J. and Olson Lars: Ethical issues in brain-cell transplantation. TINS 14: 384-388 (1991).

12. Strong Carson: Foetal tissue transplantation: can it be morally insulated from abortion? J. Med. Ethics *17*: 70-76 (1991).

13. Garry Daniel J. et al.: Are there really alternatives to the use of fetal tissue from elective abortions in transplantation research? N Engl J. Med *327*: 1592-1595 (1992) - see other articles in this edition.

14. Peschanski Marc: Transplantations de neurones foetaux; nouveaux succès mais risque de dérapage (Transplantations of foetal neurones; new successes but risk of rejection), Médecine/sciences *9*: 76-78 (1993).

15. Anderson Fionn et al.: Attitudes of women to fetal tissue research. J. Med. Ethics 20: 36-40 (1994).

Members of the Sub-committee responsible for the formulation of these guidelines:

Prof. W. Hitzig, Chairman, Zurich; PD Dr. K. Bürki, Basle; Dr. G. de Candolle, Geneva; Prof. B. Courvoisier, Geneva; Prof. O. Guillod, Neuchâtel; Prof. H.P. Ludin, St. Gallen; Dr. Marina Mandofia-Berney, Geneva; Prof. A. Mauron, Geneva; Prof. Hj. Müller, Basle; Silvia Rauch, Zurich; Prof. H. Ruh, Zurich; Dr. Gertrud Siegenthaler, Zurich †; Prof. P. Sprumont, Freiburg i.Ü.