

confidential and above all a frank doctor-patient relationship at an early stage is instrumental in helping these couples to overcome or even avoid psychic side effects. Before the initiation of IVF a realistic explanation about possible complications, the psychic burden and the still small rate of success is of the greatest importance. Thus too strong a dependence on the doctor and an overlarge psychic burden may be avoided.

Finally it should be pointed out that in consequence of the IVF procedures a new dimension has entered medicine which it is hard to survey. For the first time it is possible to observe directly the genesis of a human being in the laboratory. Thereby, prospects are opened up which should stimulate all of us to pose some important questions, e.g.: 'Where are the limits of what is technically feasible?' 'Is misuse not already preprogrammed?' 'Should we not try to understand the over-valued desire of such couples for a child more often on the level of depth psychology?' 'Do we not conjure up the danger that our technical development will leave our spiritual development behind?'

At the University Women's Hospital of Berlin-Charlottenburg all the terms and conditions concerning IVF are summarized in the so-called *Berlin-Model*. With this

model we want to designate directly the sensitive points in order to make other groups working in this field aware of the problems involved.

The conditions are the following:

- 1) IVF: only within the family structure (no ova from a donor, no semen from a donor, no surrogate mother)
- 2) IVF: only without manipulation altering the embryo (no wasting experiments)
- 3) IVF: only with moderate stimulation (every embryo will be transferred to the mother; no cryoconservation of embryos)
- 4) IVF: only when it is clearly indicated, from the psychosomatic point of view as well.

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Human in vitro fertilization and embryo transfer: expectations and concerns

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Key words. Human IVF-ET; human sterility; bioethics; medical issues; legislation; research.

In vitro fertilization (IVF) is the fusion of an instrumentally removed human ovum with a spermatozoon in a culture dish. The transvaginal introduction of the developing embryo into the uterine cavity is called embryo transfer (ET) or embryo replacement. These new procedures in reproductive medicine give rise to a number of medical, ethical and legal questions. Some of these have been debated intensively in the scientific literature and also in the popular press. Owing to sensational reports in the media it has been difficult for the general public to form an objective opinion. The one-sidedness of the discussion about IVF and ET increases the general fear relating to scientific progress. The public is often left with the impression that progress in research, especially in the area of human reproduction, might lead only to Frankenstein-type experiments. In order to clear up this uncertainty and to ensure an acceptable application of the new technology it is necessary to establish certain norms. Many national organizations, and also the Council of Europe, have set up committees to deal with the bioethical and legal problems related to IVF and ET¹. In Switzerland the Academy of Medical Sciences has taken the initiative in examining and considering the existing problems^{8,9}.

Infertility as a disease

About 10 to 15% of the couples in European countries are unintentionally childless. Many problems resulting from this condition are not recognized by the public. They are also not spoken about, since the sex act and procreation are still considered taboo. So it is not surprising that the medical evaluation of each of the partners in a sterile couple is often carried out separately.

In a society in which the family is an important institution childlessness is invariably a source of strain. Our society treats childless couples, and particularly childless women, in an inept and often truly tactless manner which does not make it easier for the affected persons simply to accept their situation as is often advocated. With her personality and upbringing not every woman is capable of finding another aim than that of motherhood.

Blockage due to inflammation or malformation and absence of the fallopian tubes are obviously physical defects, which can only in a few cases be rectified by microsurgery. IFV and ET can be considered as another medical aid to couples who wish to have a child of their own^{2,4,6,7}. Also, under normal conditions, sexual intercourse is only a prerequisite for subsequent procreation.

IVF and ET can be seen as a supplement to or an extension of the normal process of reproduction with the goal of giving birth to a child. Even if this comparison cannot be accepted by everybody, the fact remains that in nature, even in vertebrates (including amphibians and reptiles) the gametes usually meet outside the bodies of the parents.

Medical considerations relating to IVF and ET

The health risk to the mother associated with repeated laparoscopy and even laparotomy under anesthesia is small. With regard to the health of the child it must be borne in mind that the natural incidence of human embryonic and fetal wastage is high. In no period of life does nature dispose of so many human beings as before birth. This great loss is due on the one hand to genetic factors (e.g. chromosomal abnormalities in the embryo) and on the other hand to often poorly-defined factors in the reproductive tract of the mother. The genetic quality of embryos produced in vivo as well as in vitro depends largely on the quality of the gametes which meet at conception. Since the normality of the gametes cannot yet be checked, it is inevitable that a proportion of genetically abnormal embryos will also be produced in vitro and transferred back into the mother.

Reliable genetic tests cannot yet be done on an embryo with confidence that it will not be damaged. However, on the basis of the small amount of existing experience and of experiments with animals, it must be said that the danger on an increased incidence of birth defects is not high, if it exists at all^{1,2}.

One must also consider the psychological situation and in particular the emotional distress of infertile couples seeking treatment, as well as the distress caused by the long drawn-out procedure. Not every couple is qualified to bring up children. A child should not be misused as a means of psychological therapy. It therefore seems important to include psychologists in the medical teams performing IVF and ET in order to make the technology accessible primarily to suitable couples.

Bioethical and legal considerations

Whereas IVF and ET can be regarded as aids to the normal endeavor to procreate in couples in whom normal reproduction is prevented by a simple defect, the problems that can occur as a consequence of this technology are more complex. The evaluation of these problems must take into account legislation and the religious and moral attitudes of the local population. However, when dealing with these problems, it is also necessary to consider the fact that the desire of some couples for children of their own may be stronger than the need for a responsible attitude towards the customs of the society they live in, so that they will do everything in their power to fulfil this desire.

It would be wrong if the medical profession and the universities of a country were to close themselves to new medical possibilities because they are a matter of public discussion and could be rejected by some people. The result of this would be that these methods would be employed by individuals who were not prepared to report

on their activities, successes and failures in accordance with scientific principles or that citizens of a country would seek the relevant aid abroad.

The transfer of embryos produced in vitro to a non-biological mother is a controversial procedure. There are obvious benefits from such a 'surrogacy' for a woman who is not capable of carrying a pregnancy to term because of poor health or because her uterus is malformed or absent. However, this procedure may have to be rejected. The situation is complicated by too many human and also legal problems, particularly if something goes wrong and a handicapped child is born. One needs only to consider all the problems which would have to be covered by an agreement laying down the responsibilities and rights of the biological parents and also those of the surrogate mother. In addition, surrogacy leads to the misuse of socially underprivileged women who utilize this opportunity to earn more money.

Further problems can result from the fact that gametes and the embryo are not protected by the bodies of the parents or rather by that of the mother and could be objects of manipulation. The number of ova that can be obtained per cycle cannot be precisely controlled and their fertilization capability cannot be determined in advance. Consequently IVF and ET programs inevitably produce embryos that cannot be transferred back to the mother. One of the most urgent tasks is certainly to take measures in order to prevent the misuse of spare embryos.

In the discussion on misuse, however, it must also be borne in mind that many of the indicated possibilities are not practicable and that on close examination they often represent a complete lack of any sense of proportion. One should consider the value the complex method would really have to a totalitarian state. It could achieve its aims utilizing much simpler ways.

Research with human gametes and embryos

Traditional medicine is applied research, since it is always a question of finding better ways of treatment and matching these to the individual manifestations of diseases. Thus the application of IVF and ET solely for the treatment of infertility cannot be free from research, particularly as in this field there is a need for research aimed at perfection of the method.

The research in relation to IVF and ET can be categorized into at least four groups:

- 1) Registration of all events relating to the procedure of obtaining and transferring embryos and their evaluation according to scientific standards.
- 2) Improvement of the methodology using germ cells and embryos without the aim of transferring them back to the mother.
- 3) Basic research on the process of fertilization and the early stages of embryonic development, using spare embryos.
- 4) Utilization of embryos for applied research such as mutagenicity testing or toxicology.

The first category of research is acceptable without any reservation. In contrast, categories 2-4 are subject to debate. There is a widespread view that the embryo itself should not be made the object of research. However, it is

often difficult to draw clear boundary lines¹⁰. Thus I personally consider it important that an embryo that has not been transferred on the assumption that it is not normal should be carefully studied by scientific methods. In this way it would be possible to gather knowledge which is essential for deciding the fate of future embryos. This kind of research is already unacceptable for many. For obvious reasons the embryo has until now not been covered by legislation. Its position must therefore be examined and considered from the beginning. Various endeavors have been made to define the beginning of human life, and different conclusions have been reached depending upon outlook and intention. It is certain that the zygote already contains all the genetic information that is needed for an individual with his or her own characteristics and abilities to develop. On the other hand it has to be seen that nature is not squeamish about deciding the fate of normal and abnormal embryos³.

No manipulation can be permitted which may affect the genome of gametes and embryos obtained for IVF and ET. We still know too little about the structure of our genetic material and have no way of making selective changes in the human genome. So long as this is the case there remains the possibility of transplanting genes to wrong segments so that these would no longer be subject to natural control. This could have fatal consequences in later life. Further, one cannot foresee the consequences of gene manipulation for future generations.

The status of the embryo is not clear. The ways of thinking in society with regard to abortion, birth control, prenatal diagnosis and IVF show that public opinion is only beginning to form. Therefore it is very important that the medical, ethical and other aspects of IVF and ET, and especially their consequences, should be discussed by the general public to promote a better understanding of the methods involved and to ensure that an appropriate discussion and dissemination of information can take place. Scientists and other experts should inform not only their colleagues but also the general public

about the value of their procedures and their implications. We must therefore provide each other with explanations of complex situations and each must listen patiently to the views of the other. Only in this way is it possible to find a practicable solution for our society.

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Full Papers

Fetal rat brain hemisphere tissue in nonadherent stationary organ culture

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Summary. A simple organ culture system for brain tissue is described. Fragments of fetal rat brain hemisphere tissue are explanted to multiwell dishes base-coated with semisolid agar. In this system nonadherent organ culture can be performed for at least 50 days. Cell migration, biochemical and morphological differentiation and the formation of a layered architecture seem to mimic some of the phenomena occurring in the developing rat brain in vivo. The fragments may therefore be a useful organ culture model for nervous tissue.

Key words. Rat brain fragments; stationary, nonadherent organ culture; cell differentiation and migration.