Activities with gametes and embryos

Research in the overlapping fields of reproductive genetics and reproductive medicine focuses on two areas: improving the possibilities to help couples with higher genetic risks to have healthy children, and improving or extending existing forms of reproductive assistance for couples with fertility problems. This monitoring report looks at four techniques in various phases of development, each of which raises specific ethical questions.

1. Pre-implantation genetic diagnostics (PGD) have been in use in our country for ten years now, albeit only in one centre and in the form of scientific research. New ethical questions relate, for example to the acceptability of the possible application of the technique for reasons other than the possibility of a disorder in the child to be conceived. A current issue of particular interest is whether the recent ban on PGD for HLA typing is not too strict. Here, the aim is to make it possible for parents to conceive a child that may be a suitable 'donor' of stem cells for the treatment of a brother or sister with a serious illness.
2. Pre-implantation genetic screening for aneuploidy (PGS-A) involves the routine chromosome testing of IVF embryos, mainly to increase the possibility of pregnancy and reduce the number of multiple births. This technology was introduced to our country very recently in the form of clinical research into its added value. If the screening also covers chromosomal abnormalities that, although they reduce the risk of a successful pregnancy, are compatible with life (such as trisomy 21: Down syndrome), PGS-A will also prevent pregnancies that may result in the birth of a handicapped child.
3. Ooplasm transfer is intended to be a new auxiliary technique for the treatment of female subfertility. It involves the injection of a small amount of ooplasm obtained from a young egg donor into the ovum of a woman with a history of unsuccessful IVF attempts. The possible target groups include women in whom reduced fertility is linked to advanced age. Without prior safety studies, the technique has already been used abroad.
4. A range of possibilities are being examined for reproductive assistance for men with severely impaired spermatogenesis. One of these is the transplantation of sperm-forming stem cells from the infertile male into animal testicles (interspecies transplantation of spermatogonia). In the second environment, the stem cells could develop into mature sperm that can be used in medically-assisted reproduction. This technique is in the preclinical research stage with laboratory animals. Introduction would amount to a form of xenotransplantation.

The possible risks of medically-assisted reproduction require constant attention. The introduction of new techniques must only be considered on the basis of adequate prior research in animals, or in human embryos, and it should be linked to sound follow-up research - covering the long and short terms - into possible consequences for the health of children conceived in this way. Follow-up research of this kind also remains necessary for the existing forms of biomedically-assisted reproduction, including IVF. A major problem is that it sometimes fails to get started - or to be carried out properly - because of a lack of funding.

The dynamic nature of the developments in reproductive medicine and reproductive genetics requires a constant review of the basic principles and purposes of research, and of the assistance to

be provided in this field. It is the duty of the government to encourage the public debate about this issue; health professionals can make a major contribution here by clearly formulating the concrete questions and dilemmas they face in practice. It is also important for them to draw up guidelines for the sound implementation of techniques that have been introduced (PGD), or will be introduced, into the clinical environment.

Screening of neonates for congenital metabolic disease

In the Netherlands, neonatal screening using heel-stick blood was introduced in 1974. The aim is to detect certain severe congenital diseases in neonates, including the metabolic disorder phenylketonuria (PKU). A new analysis technique (tandem mass spectrometry) makes it possible to test the heel-stick blood taken from neonates for dozens of rare metabolic diseases at the same time. These are usually severe, life-threatening disorders, and often, if they are detected early, damage to health can be prevented with dietary measures or medication. However, not all of these disorders are equally well understood; some of them occur in both severe and mild forms and levels of treatability vary.

Particularly in the United States, there is a strong lobby of patient associations and parent organisations. They advocate using this new screening test as much as possible, arguing that the fastest possible diagnosis is always the best thing, if not directly for the child, then certainly for the parents and the family. The benefit for parents of the early detection of untreatable disorders is that they may obtain timely information about the risk of recurrence. In the Netherlands, the new method is still only being tried out at present on a single disorder (which is severe and amenable to treatment). Depending on the results of that study, the question will arise of whether more widespread use is justified. If this is the case, which of the disorders that can be detected with the new test should be included in screening?

It is important to avoid a situation in which decisions in this respect are determined solely by the enormous diagnostic potential of the new technology. More widespread use should be based on scientific research that demonstrates - for each separate disorder to be screened - that the benefits for the participants clearly outweigh the drawbacks. For the time being, only ‘PKU-like’ (severe, well-defined and treatable) diseases qualify. Before considering screening neonates for metabolic diseases that are not (or less) amenable to treatment, a public discussion is required in this respect about the basic principles and acceptability of such screening. Further psychosocial research is also required, for example into the dynamics of the decision process and the feasibility of informed consent.

Medicines for children

Adults who are prescribed medicines can be sure that there has been extensive testing of safety and efficacy in adults. This is a precondition of admission to the market (registration). The same cannot be said of children. Most medicines they are given are tested in adults only, but not in children. Often, medicines for children are not available in appropriate forms and doses. The limited knowledge about medicines for children is an international phenomenon with which paediatricians have been struggling for decades. It is time to take steps to improve this situation. A recent report from the Health Care Insurance Council (CVZ) made important recommendations in this respect.

An important issue, in addition to the aspects to which the Health Care Insurance Council has drawn attention, is the actual participation of children in pharmaceutical trials. However convincing the advantages of well-designed scientific research may be, there are difficulties in actual implementation, if only because the researchers must inform parents about the uncertainties associated with prescribing medicines to children. Doctors do not always find it easy to talk about this uncertainty. And parents have the – understandable – tendency to refuse to allow the participation of their children in scientific research involving risks, however minor those risks may be. Clinical pharmaceutical research in children can only be brought up to scratch successfully if proper attention is paid to training doctors' communicative skills and to the quality of information provision and counselling.

Engineering people

Under the influence of scientific and technological developments, the theme of 'engineering people' is receiving increasing attention. The health care system also, to an increasing degree, has to deal with the possibilities provided by the biomedical sciences for perfecting healthy people in accordance with their own preferences. In medical ethics, this theme is known as 'enhancement': the use of genetic, biomedical or pharmacological knowledge to make improvements in human characteristics. This enhancement can involve people's appearance, performance or personality. At present, the best-known forms of enhancement are found in cosmetic surgery and, more covertly, in the use of anabolic steroids in sports. However, there is an impression that conventional medicines (for example Prozac, Ritalin and Viagra) are also being used more and more often for non-medical purposes. Furthermore, during the next decade, new substances and methods for engineering healthy people will probably emerge in a rapid tempo. They vary from cosmetic gene therapy and a new generation of anxiety inhibitors and mood modulators, to psychotropic medication that boosts cognitive abilities (concentration, memory) and a drug that would allow women to optimise their sexual functioning. Billions are being invested in development.

In our society, all adult and competent individuals are themselves responsible for the use of enhancers, at least in so far as they cause no harm to others. In principle, the government should adopt a neutral position towards ideas about personal well being which are at the root of this use of enhancers. It does, however, have a major responsibility to ensure that adequate information is provided, to protect minors and legally incompetent individuals, to safeguard quality, to protect public goods in so far as the use of enhancers constitutes a threat to them, to monitor access to enhancement and to encourage a public discussion. This should cover the conditions for the inclusion of enhancement in the responsibilities assigned to doctors. In any case, it is clear that this question will not be answered on conceptual grounds (for example on the basis of a concept of disease). The question is normative in nature and moral considerations will be decisive when answering it.