

Opinion no. 3 of 17 November 1997 on sex selection

Request for an opinion of 29 March 1996 from the Flemish Minister of Finance, the Budget and Health Policy

“Given Article 8 of the Cooperation Agreement of 15 January 1993 establishing a Bioethics Advisory Committee, I would like, as the Minister responsible for health policy in the Flemish Community, to submit the following questions for the opinion of the Committee:

There are about ten clinics throughout the world that practice sex selection. Most of them are in the United States, Asia or the Middle East. The first European "Gender Clinic" opened in London in January 1993. The Netherlands have since followed this example. In November 1995 the media announced that the founders of the Dutch clinic intended to set up an establishment of this kind in Flanders.

Given the current state of medical knowledge, what are the medical techniques used for sex selection? How reliable are they?

What are the medical indications for which these techniques can be applied?

Can indications other than strictly medical conditions be envisaged?

What are the risks involved in this technique for the embryo, for the individual, for groups in society and for society as a whole?

Are these risks such that uncontrolled application of these techniques is not justified?

Does the law as it stands at present offer possibilities for preventing or combating unwanted applications of these techniques? If not, does the Committee see any reason to undertake any legislative action in this area or promote in some another way the adoption of rules designed to prevent the unwanted applications referred to above (e.g. codes of conduct; medical code of ethics, etc.)?

Does the policy adopted in Great Britain and the Netherlands where these techniques already exist provide relevant reference elements?”

Foreword

The Committee examined the questions asked by Ms Wivina Demeester-De Meyer and put forward an opinion.

The Committee notes that sex selection for non-medical reasons poses particularly complex ethical problems. Three visions may be discerned within the Committee as regards sex selection for non-medical reasons. Some members radically reject any form of sex selection for non-medical reasons, others are in favour of this, while others still only accept it under certain conditions. It is therefore essential to take time to thoroughly analyse and discuss in detail the ethics of this technique, as well as its psychological and social implications.

However, this does not prevent the Committee from expressing an opinion on the various methods of sex selection for medical reasons (a “State of the Art”) and opinion on the use of these methods for medical reasons. At the same time, the Committee proposes to expand its Select Committee to engage in an in-depth discussion of the ethical and interdisciplinary aspects of the issue of using sex selection techniques for non-medical reasons.

Opinion

1. Given the current state of medical knowledge, what are the techniques used for sex selection? What are the medical indications for which these techniques can be applied? How reliable are they?

There are currently two main methods used for the purpose of sex selection: pre- and post-conceptual methods. So-called natural methods (e.g. special diet) are also practised, but these are not entirely reliable.

1.1 Pre-conceptual methods: sperm selection

Sperm is selected in order to separate spermatozoids carrying a Y chromosome (which would produce a boy) from those carrying an X chromosome X (which would produce a girl). The various techniques developed so far are based on three properties:

1. the difference in weight between the two groups of spermatozoids (Y spermatozoids are 3% lighter in weight than X spermatozoids);
2. the difference in the speed at which the two groups of spermatozoids migrate through a layer of albumin (see the Ericsson method described below).
3. fluorescent colouring of spermatozoids.;

Insemination can then be carried out using spermatozoids enriched with Y chromosomes if a boy is wanted and with X chromosomes if a girl is wanted.

The existence of an adequate and totally reliable method of separating the X and Y spermatozoids in the ejaculate would facilitate the prevention of sex-related hereditary diseases. Most of these diseases are due to mutations of genes found in the X chromosome. Girls have two X chromosomes. If one of these two chromosomes is carrying the mutated gene, in most cases the girl will not be affected by a genetic anomaly. However, she could pass the disease on to her sons. In couples who have a high risk of a severe disorder related to the X chromosome, it would be possible to inseminate the woman with X-enriched spermatozoids or – if necessary – these spermatozoids could be used for medical assisted procreation such as in vitro fertilisation. Various enrichment methods have been tested over the past few decades, including Sephadex filtration or the use of an albumin gradient. None of these methods can be used to prevent sex-related disorders as they are not sufficiently reliable, although they do enable a certain level of enrichment of X or Y spermatozoids. A more recent method involves colouring X and Y spermatozoids with specific fluorescent probes, after which the two groups are sorted using flow cytometry. The sorted fractions contain 82% X spermatozoids or 75 % Y spermatozoids. The level of enrichment is therefore too low for the purpose of insemination to prevent sex-related hereditary diseases. This method could possibly be used to obtain more feminine embryos after in vitro fertilisation – embryos the sex of which then has to be determined subsequently. Some researchers have also expressed reservations about this method, which involves the use of potentially mutagenic substances (fluorochrome and laser beams).

The method used in most of the “gender clinics” is the Ericsson method, which is based on the difference in the speed at which X and Y spermatozoids migrate through a layer of albumin (cf. Ericsson, R.J., Langevin, C.N. and Nishino, M., Isolation of fractions rich in human Y sperm, in Nature, 1973, 246, 421-424). No harmful effect for the embryo or the child has been observed further to the use of this technique. This method has an 80 to 85 % success rate for the selection of a boy. This rate is lower for the selection of a girl (It should be remembered that the chance of having a child of one sex or the other naturally is approximately 50 %).

Assessment. These techniques are not applied in Belgium. They are not expensive. However, they are not very reliable. Sex selection on the basis of the sperm does not therefore offer sufficient guarantee at the moment to be medically justified.

1.2. Post-conceptual methods

We will look in succession at prenatal diagnosis and recent developments in the field of in-vitro embryo examination, that is preimplantation genetic diagnosis (PGD).

1.2.1. Prenatal diagnosis

Conventional prenatal diagnosis can be used to determine the sex of the child after a karyotype on the foetus cells. The result is known during the first quarter of the pregnancy after an examination of the chorionic villus or during the second quarter of the pregnancy after an examination of the amniotic cells obtained after an amniocentesis. The application of these techniques requires close cooperation between obstetrics centres and genetic centres.

What are the indications to determine the sex by means of prenatal diagnosis? Various genetic disorders are related to sex, such as Duchenne muscular dystrophy and fragile X syndrome. Generally speaking, males are more frequently affected as most of these diseases are due to gene mutations carried by the X chromosome. As women have two X chromosomes, the healthy gene compensates and the disease will not usually develop. The lack of the gene or an abnormal gene from the maternal X chromosome can therefore have serious consequences for the health of the boy. For a few years now it has been possible to determine by analysing the DNA whether or not the foetus is affected. However, a precise diagnosis is not possible in a number of cases. Serious genetic disorders related to the X chromosome for which there is no treatment constitute an indication for a prenatal diagnosis to determine the sex of the baby. If it is a boy, parents who do not object can opt to have an abortion. As it is not possible to tell whether or not the boy is affected, it may be that a boy that is not affected is aborted.

Assessment: The prevention of serious sex-related diseases by means of prenatal diagnosis is reliable. The risks of error are very slight. The analyses carried out for this purpose are done in specialised genetic centres, by specialised staff. However, this remains a costly procedure to implement.

1.2.2. Preimplantation genetic diagnosis (PGD)

Preimplantation genetic diagnosis or PGD to determine the sex of a baby involves three stages: in vitro fertilisation; determination the sex of the embryo and the transfer of the embryo into the woman's uterus. PGD can therefore be used to determine the sex of the child before the embryo is transferred to the uterus. However, PGD remains an experimental technique which is only applied in a limited number of centres around the world. The major difference compared with prenatal

diagnosis is that PGD can be used for the purpose of genetic examination before the pregnancy itself occurs.

After in-vitro fertilisation, one or two blastomeres are taken using micromanipulation techniques on embryos up to the stage of eight cells. The sex of the embryo can be determined using these isolated blastomeres by means of two techniques: a chain polymerisation reaction (CPR) or, as is more usually the case these days, *in situ* hybridisation using fluorescent probes (FISH).

CPR has to be carried out using specific X and Y probes and requires specific precautions to prevent contamination of the DNA.

At the moment, sex is determined mainly using the FISH technique. This technique consists of identifying a particular chromosome segment on a preparation of cellular chromosomes (X or Y if the sex of the embryo is to be determined) using a specific molecular probe marked with a fluorochrome. The presence of two X chromosomes in the blastomeres indicates a female embryo; the presence of one X chromosome and one Y chromosome points to a male embryo. This technique takes just a few hours and can therefore be used for a preimplantation diagnosis. It is less liable to error than the CPR and can also be used to detect numerical chromosome anomalies and mosaicisms with a high degree of reliability.

Ten to twenty centres in the world use these two techniques (FISH or CPR) for the preimplantation determination of sex. Around a hundred children have already been born using this method. Given that these techniques are still very recent, a prenatal diagnosis is offered if a pregnancy occurs in order to check the results. Moreover, to ensure that the preimplantation diagnosis is not harmful, children born further to the application of this diagnosis have to be followed up. .

Assessment: so far this test appears to be very reliable. However, the cost of this method is extremely high. Preimplantation diagnosis is indicated solely in the event of serious hereditary diseases. Determining the sex by means of preimplantation diagnosis is only considered if the hereditary disease cannot be diagnosed precisely. The method is very demanding owing to the need to use in vitro fertilisation.

To the extent that both post-conceptual methods involve manipulation of the human embryo and sometimes lead to its destruction, some members of the Committee reiterated their objection on ethical grounds to these methods, which they consider to be prompted by a eugenic will and for which – in their view – there is no justification.

2. Opinion on the current position of sex selection techniques and the advisability of sex selection clinics.

Given the current position as regards science and medical techniques, the establishment of a gender clinic cannot be accepted. In fact, pre-conceptual methods are not reliable and do not offer any guarantee of a good result.

Moreover, the Committee advises limiting the application of post-conceptual sex selection methods to the prevention of serious sex-related hereditary diseases, and only when it proves impossible to obtain a precise diagnosis of the hereditary disease.

The Committee believes that these post-conceptual methods of sex selection can only be applied in establishments that include a centre for medically assisted procreation and a centre for human heredity, which work closely together. The Committee believes that the competent authority should only approve establishments staffed by sufficiently qualified personnel.

The opinion was prepared by select commission 96/2, consisting of:

Joint chairmen	Joint reporters	Members	Member of the Bureau
Chr. Hennau-Hublet	N. Becker	J.-P. Cobbaut	E. Vermeersch
P. Devroey	P. Schotsmans	G. Evers-Kiebooms	
		M. Roelandt	
		R. Winkler	

Experts consulted

- M. Abramovicz, J.-J. Cassiman, L. Roegiers, G.-A. Rose, E. Van Mos, A. Van Steirteghem

The working documents of select commission 96/2 - request for opinion, personal contributions of the members, minutes of meetings, documents consulted - are stored as Annexes 96/2 at the Committee's documentation centre, where they may be consulted and copied.
